1. Reduction of Tertiary Benzamides to Benzaldehydes by an *in situ*–Generated Schwartz Reagent ($Cp_2Zr(H)Cl$); Formal Synthesis of Lysergic Acid

2. Ru-Catalyzed Amide-Directed Aryl C-H, C-N and C-O Bond Functionalizations: C-B Formation, C-C Suzuki Cross Coupling and Hydrodemethoxylation

by

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A thesis submitted to the Department of Chemistry

In conformity with the requirements for

the degree of Doctor of Philosophy

Queen's University

Kingston, Ontario, Canada

December, 2010

ABSTRACT

Chapter 2 of the thesis describes a highly efficient *in situ* method for the reduction of amides to aldehydes and aryl *O*-carbamates to phenols and other transformations involving hydrozirconations. The method, as a three-component-type reaction, involves *in situ* generation of the Schwartz reagent ($Cp_2Zr(H)Cl$) from Cp_2ZrCl_2 and the reductant, $LiAlH(O\text{-}t\text{-}Bu)_3$, and immediate reaction with a substrate. Substrates include aliphatic and aromatic tertiary amides which are reduced to aldehydes, aryl *O*-carbamates which are reduced to phenols, and alkynes which undergo other transformations via hydrozirconation. Compared to prior methods, this method has advantage in that reagents are inexpensive and stable, reaction times are short, and reaction temperatures are generally conveniently at room temperature. The use of the *in situ* method described herein instead of the requirement for the synthesis of the commercially available Schwartz reagent is estimated to provide more than 50% reduction in cost.

Chapter 3 of the thesis describes the discovery and development of efficient and regioselective Ru-catalyzed amide-directed C-H, C-N, C-O activation/C-C bond forming reactions, ester-directed C-O activation/C-C bond forming reaction, and amide-directed C-O activation/hydrodemethoxylation reactions under a simple $RuH_2(CO)(PPh_3)_3$/toluene catalytic system. Of these, the amide-directed C-H activation/cross coupling reaction proceeds well but uniquely on furan 3-amide substrates while the ester-directed C-O activation is effective on the 2-MeO-1-naphthoic acid methyl ester. On the other hand, the amide-directed C-N and C-O activation/coupling reactions are broadly applicable on benzamides and naphthamides. All of these achievements of directed C-H, C-N, C-O activation/coupling reactions complement and may supercede the DoM (directed *ortho* metalation)-cross coupling strategy, and establish the catalytic base-free DoM-cross coupling process at non-cryogenic temperature as a convenient,

economical and green alternative. The new catalytic amide-directed *ortho*-hydrodemethoxylation reaction has potential value in links to aromatic electrophilic substitution and DoM chemistries. Furthermore, a new borylation reaction via Ru-catalyzed amide-directed C-H activation/C-B bond forming process is also reported herein.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank Professor Victor Snieckus for providing me the opportunity to be a part of the incredible and unique group where, learning and practising chemistry under his constant guidance and encouragement, I have been achieving my dream to be a good synthetic chemist. His kindness, enthusiasm and patience are not only limited to research, but they are also much beneficial to my life.

Many thanks to Prof. Whitney and Prof. Jessop, committee members of my graduate research, for reviewing my progresses during these years. Special appreciations to Dr. Sauriol and Dr. Jiaxi Wang for the helpful discussions on NMR and MS analysis.

Many thanks also to Krista Voigt and Annette Keyes for their helps on my graduate study management.

Next, I would like to thank everyone who I work with over these years in my dear Snieckus group. We share friendship each other and leave many good memories with us. Graduate students: Xiongwei, Kevin, Chris, Justin, Sunny, Eric, Todd, Manlio, Tom, Katie, Zhongdong, Wei; Postdocs: Thomas, Till, Robert, Marc, Heiko, Barbel, Oleg, Toni, Jianxin, John, Tim, Jignesh, Emilie, Cedric, Matt; Visiting professors and scholars: Simon, Wole, Alcides, Haji, Xueling.

Finally, I thank my wife, Haixia, for her endless encouragement and understanding, and my son and daughter, Ryan and Eva, for their bright smiles. I owe everything to them for making this all possible.

STATEMENT OF ORIGINALITY

I (Yigang Zhao) hereby certify that all of the work described within this thesis is the original work of the author under the supervision of Prof. V. Snieckus. Any published (or unpublished) ideas and/or techniques from the work of others are fully acknowledged in accordance with the standard referencing practices.

Yigang Zhao

December, 2010

To Haixia, Ryan and Eva

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ABBREVIATIONS

Ac	acetyl
Boc	*tert*-butyloxycarbonyl
BPin	boropinacolate
BQ	benzoquinone
calcd	calculated
CIPE	Complex-Induced Proximity Effect
Cbz	benzyloxycarbonyl
Cp	cyclopentadienyl
Cy	cyclohexyl
dba	dibenzylideneacetone
DG	directing group
DIBAL-H	diisobutylaluminium hydride
DMAP	N,N-4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	N,N-4-dimethylformamide
DMG	directed metalation group
D*o*M	directed *ortho* metalation
D*re*M	directed *remote* metalation
E^+	electrophile
EDG	electron-donating group
EWG	electron-withdrawing group

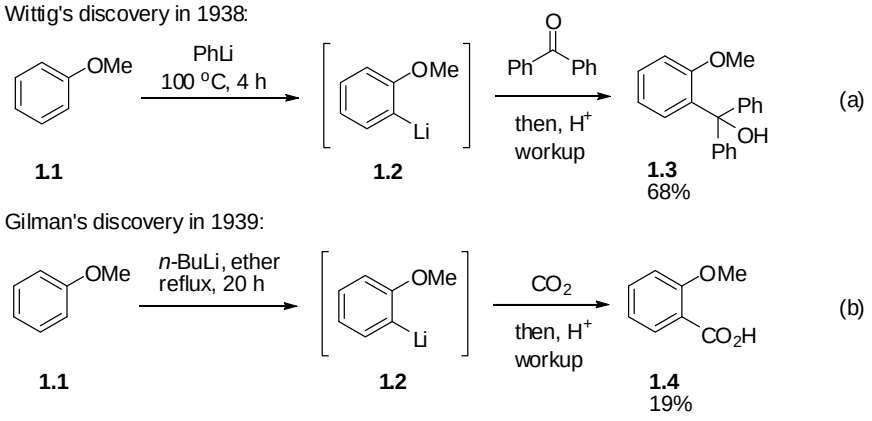
HRMS	high resolution mass spectrum
LAH	lithium aluminum hydride
LDA	lithium diisopropylamide
LDEA	lithium diethylamide
LG	leaving group
LiTMP	lithium 2,2,6,6-tetramethylpiperidide
LRMS	low resolution mass spectrum
Mes	mesityl
MOM	methoxymethyl
NBS	N-bromosuccinimide
n.d.	not detected
Piv	pivaloyl
rt	room temperature
S-Phos	2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl
TBAF	tetra-*n*-butylammonium fluoride
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMDS	1,1,3,3-tetramethyldisiloxane
TMEDA	N,N,N',N'-tetramethylethylenediamine
TMS	trimethylsilyl

Chapter 1

Introduction to the Directed *ortho* Metalation (D*o*M)

1.1 History

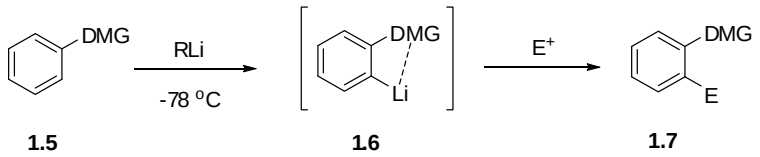
The directed *ortho* metalation (D*o*M) chemistry is an important fundamental methodology for the functionalization of aromatic compounds.[1-4] The origin of the directed *ortho* metalation (D*o*M) can be traced to more than 70 years ago. In the late 1930s, Wittig[5] and Gilman[6] independently reported a MeO-directed *ortho* metalation of anisole to afford *ortho*-substituted anisoles as demonstrated by electrophile quench experiments (ketone and CO_2 quench) (Scheme 1.1). Notably, no other regioisomeric products were observed. Although no other electrophiles were reported, the excellent regioselectivity indicated the discovery of the DoM reaction.



Scheme 1.1

In the subsequent 30 years, DoM research moved forward very slowly until the 1960s when Hauser contributed a series of systematic studies.[7-9] Then, with the commercial availability

of alkyllithiums in the 1970s as a result of the discovery of anionic polymerization, the study of DoM chemistry began to develop pace. Not only have a variety of directed *ortho* metalation groups (DMGs) been discovered, but systematic studies of DoM chemistry, including optimization of conditions, exploration of mechanism, its expansion and application, have become well-developed areas. To date, a large number of reviews have been published for this valuable strategy.[1,2,10,3,11,12,4,13-16] A general process is presented below, in which the formation of the intermediate **1.6** is suggested for the observation of the high *ortho*-regioselectivity (Scheme 1.2). Gradually, DoM chemistry has become a powerful synthetic protocol to functionalize aromatic and heteroaromatic compounds and has been widely applied in academic and industrial fields.[1-4] As a result of the continuous significant contributions from the Snieckus laboratories over thirty years in this area, the reaction is often named the *Snieckus directed ortho metalation (DoM)* reaction.[17]



Scheme 1.2

1.2 Directed *ortho* Metalation Groups (DMGs)

Subsequent to the discovery of the OMe as a directed *ortho* metalation group (DMG) by Wittig and Gilman, a significant number of DMGs have been developed.[18,3,19-21,4,22-27,7-9,28,6,5,29] Some common DMGs are listed in Table 1.1, classified as carbon-based, oxygen-based and other heteroatom-based DMGs. Of these, the $CONEt_2$ (tertiary amide) and $OCONEt_2$ (*O*-carbamate) discovered by Beak[25] and Snieckus[22] have become popular DMGs. An operative DMG should have two basic features: i) it must contain at least one heteroatom for generating coordination

with metal atom to form intermediate **1.6** (Scheme 1.2); ii) it must be inert or resistant to nucleophilic attack by organolithium bases. For example, a working DMG must be sufficiently encumbered to resist attack by an alkyllithium reagent. This requirement will by its very nature increase the difficulty of subsequent manipulations of DMGs. On the other hand, when a carbonyl moiety of a DMG such as CONHR is deactivated by formation of an *in situ* anionic species ($CON^{-}R$), attack is prevented by the created negative charge and the requirement of steric hindrance can be avoided.

Table 1.1 Common Directed Metalation Groups (DMGs)

C-based DMGs		O-based DMGs		N-, P- & S-based DMGs	
CONHR	*(Hauser, 1964)*[9]	**OMe**	*(Wittig, 1938 & Gilman, 1939)*[6,5]	**SO_2R**	*(Truce, 1951)*[28]
Oxazoline[a]	*(Gschwend, 1975)*[27]	**OMOM**	*(Christensen, 1975)*[26]	**SO_2NHR**	*(Hauser, 1968)*[8]
$CONEt_2$	*(Beak, 1977)*[25]	**$OCONEt_2$**	*(Snieckus, 1983)*[22]	**SO_2NR_2**	*(Hauser, 1969)*[7]
COOH	*(Mortier, 1994)*[21]	**OSO_2NR_2**	*(Snieckus, 2005)*[18]	**NHBoc**	*(Gschwend, 1979)*[24]
CONR(cumyl)[b]	*(Snieckus, 1999)*[19]	**$OP(O)(NR_2)_2$**	*(Snieckus)*[29]	**NHPiv**[c]	*(Muchowski, 1980)*[23]
				$P(O)t\text{-}Bu_2$	*(Snieckus, 1998)*[20]

[a] oxazoline = 

[b] cumyl = 

[c] Piv = C(O)*t*-Bu

The relative strength of DMGs has been studied by intra- and intermolecular competition experiments.[18,4,29] The power of DMGs is governed by a fine balance between inductive strength and coordination ability of DMGs, in which $OP(O)(NR_2)_2$ and $OCONR_2$ hold the highest strength among DMGs (Fig. 1. 1). The thus established hierarchy of DMGs is a useful guide for designing regioselective synthesis of multisubstituted arenes.

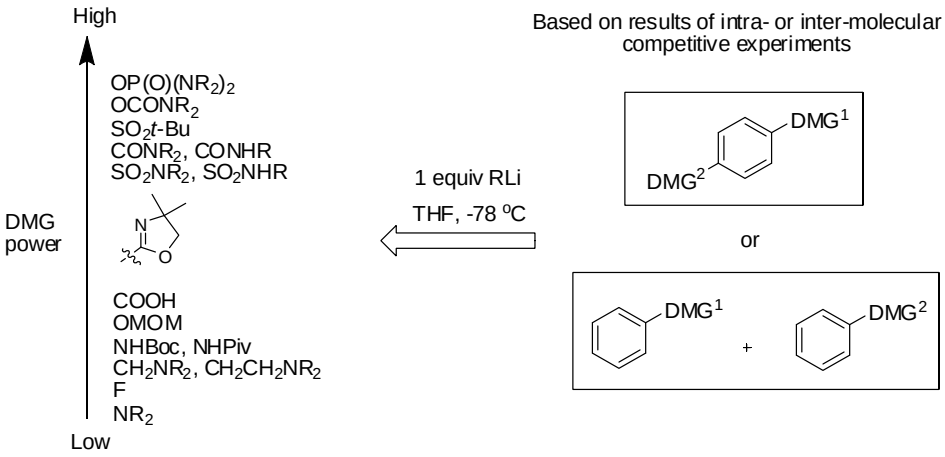


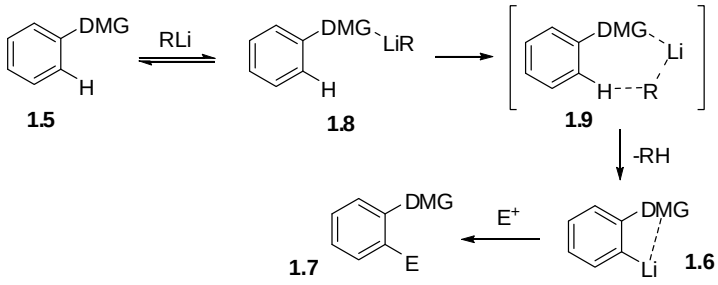
Fig. 1.1 DMG Hierarchy

1.3 Mechanism of DoM

Many mechanistic studies by qualitative NMR experiments,[30,31] kinetic isotope effects,[32,33] FT-IR measurements,[34,35] X-ray structural analysis[36-38] and theory calculations[39-42] as well as recent Collum's work on IR and NMR assisted kinetic and structural studies[43,44] have been carried out on the DoM reaction. However, due to too many factors involved in the DoM process such as variation of DMGs, bases and additives, no single mechanism to rationalize the DoM reaction has resulted. Two major mechanisms, named the complex-induced proximity effect (CIPE) and the kinetically enhanced metalation (KEM), have been suggested.

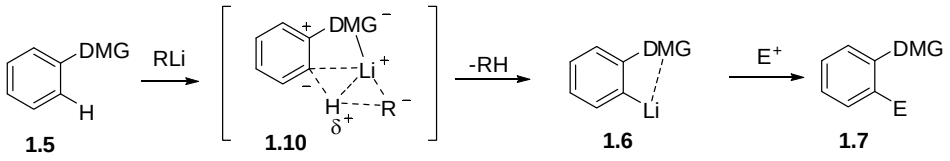
In the CIPE mechanism (Scheme 1.3), introduced by Beak and Meyers,[13,45] a two-step sequence for achieving an *ortho*-lithiation was proposed which starts from coordination of a DMG substrate **1.5** with an organolithium reagent to provide a pre-metalation complex **1.8** which brings the lithiating base in close proximity to the *ortho* hydrogen, followed by *ortho*-deprotonation to form the key *ortho*-lithiated species **1.6** (Scheme 1.3). Finally, quench of the lithiated species **1.6** by an electrophile affords the *ortho*-substituted aromatic product **1.7**. A fast

reversible complexation followed by slow deprotonation was observed by Beak on studies of intra- and intermolecular isotope effects.[32] The CIPE mechanism is suitable for powerful DMGs such as $CONEt_2$, in which strong coordination of DMGs with organolithium reagents will occur in equilibrium.



Scheme 1.3

Based on the results from *ab initio* calculations by the Schleyer group,[40-42] a one-step kinetically enhanced metalation (KEM) mechanism was proposed via a concerted-like formation of lithiated intermediate **1.10** (Scheme 1.4), that is, the simultaneous coordination of organolithium with the DMG and deprotonation for the DoM process is suggested. The favorable alternation of positive and negative charges is proposed to stabilize the transition state (**1.10**). The KEM mechanism is suitable for low power DMGs such as OMe, NMe_2, and F, in which strong inductive effects are apparent.

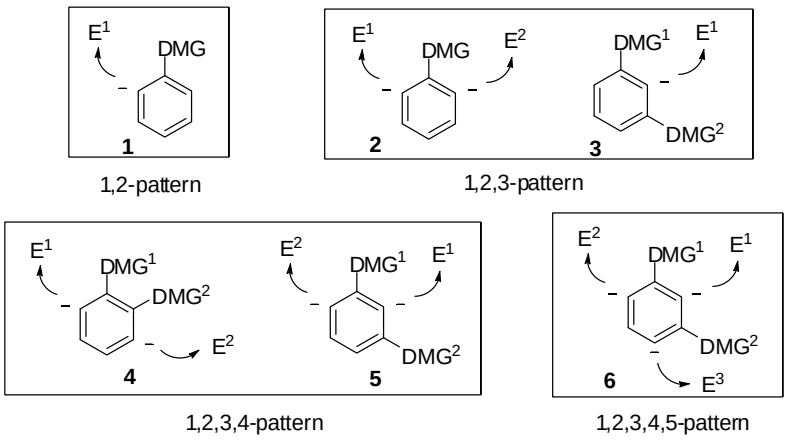


Scheme 1.4

1.4 Utility of DoM Chemistry

1.4.1 Utility of the D*o*M Reaction

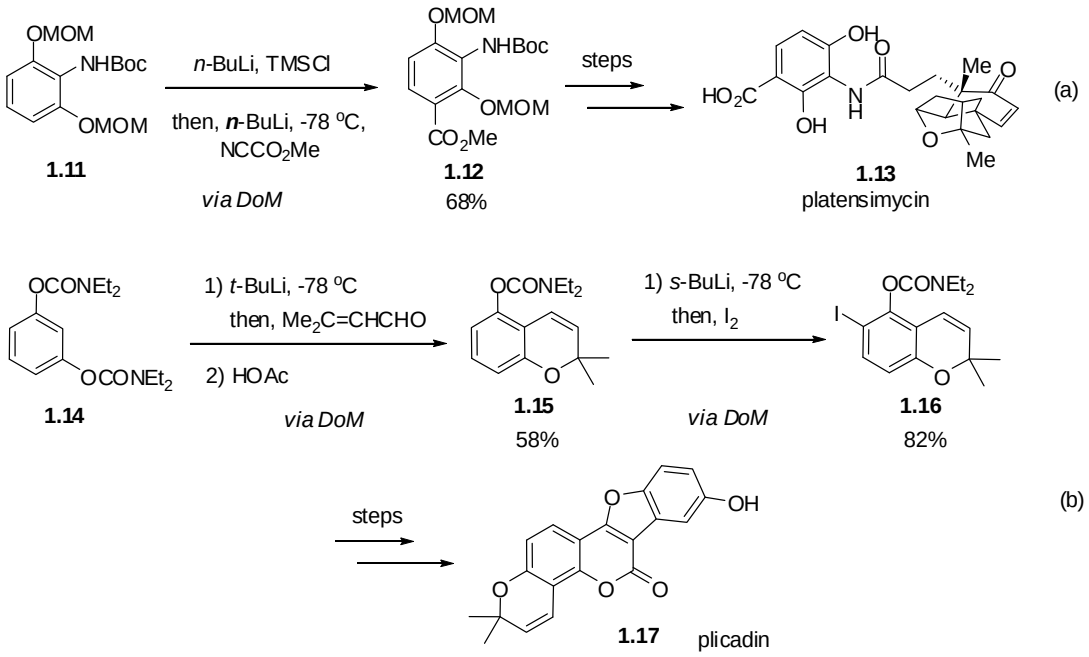
The developments over the last three decades have led to the DoM reaction becoming a robust method for the construction of multisubstituted arenes. While the classical electrophilic aromatic substitution reaction commonly suffers from low regioselectivity, the DoM chemistry is dependably *ortho*-regioselective. It provides a rapid and efficient method for the construction of a variety of polysubstituted arenes which are usually difficult to obtain by other classical substitution routes. Some typical substitution patterns via DoM are shown below, including the use of two DMGs with different DoM powers ($DMG^1 > DMG^2$ is assumed) (Scheme 1.5).[1,3,4] In a successive DoM process, the substituent such as E^1 formed by a previous DoM reaction has to be stable to strong bases or protected before a later DoM reaction proceeds.



Scheme 1.5

Two examples are given below which demonstrate the efficiency of DoM chemistry (Scheme 1.6). In the first, the DoM reaction was employed as the key step to synthesize a

polysubstituted aromatic moiety of a natural product, platensimycin **1.13** (Scheme 1.6 (a)).[46,47] In the second example, a 1,2,3,4-tetrasubstituted benzene **1.16**, obtained by successive DoM reactions, served as an intermediate in a total synthesis of plicadin **1.17** (Scheme 1.6 (b)).[48]

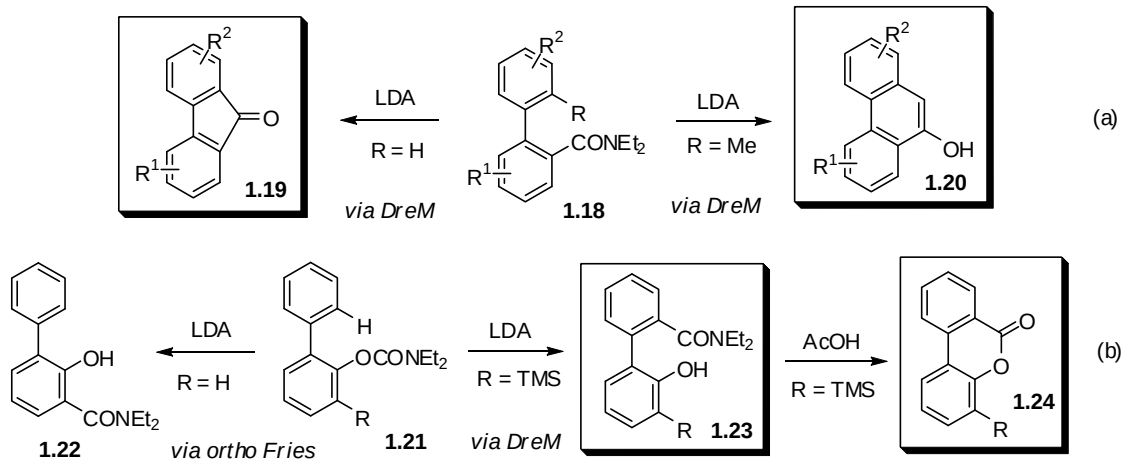


Scheme 1.6

1.4.2 Utility of the Directed *remote* Metalation (D*re*M) Reaction

As an extension of DoM chemistry, the directed remote metalation (D*re*M) reaction, discovered by the Snieckus group in early 1990s,[49,50] has received considerable attention.[1,3] This process involves the 2'-deprotonation of 2-DMG substituted biaryls **1.18** by treatment with a strong base (usually LDA but other bases may be used such as LiTMP and LDEA), followed by cyclization or migration in cases of DMG = $CONEt_2$ and DMG = $OCONEt_2$ respectively. When 2-$CONEt_2$ biaryl **1.18** (R = H) is employed, a fluorenone skeleton **1.19** is formed. However, with

1.18 (R = Me), the D*re*M reaction occurs at 2'-methyl position which is the more favorable deprotonation position, to afford a phenanthrol **1.20** (Scheme 1.7(a)). Employing 2-$OCONEt_2$ biaryl **1.21** for D*re*M, an additional protection, R = TMS is required to avoid the occurrence of an anionic *ortho* Fries rearrangement to give 2-hydroxy-3-$CONEt_2$ biaryl **1.22**.[22,43,44] With such protection, a remote anionic Fries rearrangement occurs to give the 2-hydroxy-2'-amidobiaryl **1.23** which may be easily converted into 6*H*-benzo[*c*]chromen-6-one **1.24** under acid-catalysis conditions (Scheme 1.7(b)). The D*re*M reaction is also suitable for condensed heteroaromatics.[3,51] The D*re*M chemistry has been widely applied for the construction of a variety of fused rings.[1,3]



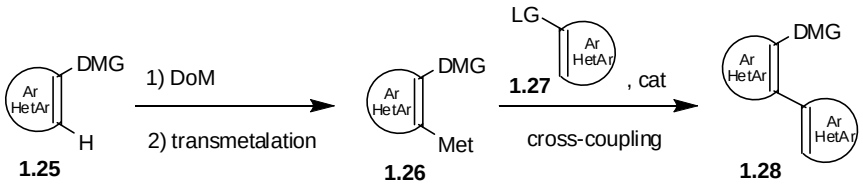
Scheme 1.7

1.4.3 The Combined D*o*M–Transition Metal-catalyzed Cross Coupling Reaction

The transition metal-catalyzed aryl-aryl cross coupling reaction is a powerful tool for the formation of biaryl compounds.[52-54] The Suzuki,[55] Kumada,[56,57] Negishi[58] and Stille[59] cross coupling reactions have gained wide recognition and application. The combination of DoM and transition metal catalyzed cross coupling, which may be carried out in a one-pot process, has

achieved considerable utility (Table 1.2).[51,60,61] This process starts by DoM of substrate **1.25**, followed by Li-metal exchange to form the species **1.26** which undergoes coupling reaction with partner **1.27** to afford a biaryl product **1.28**. The regioselectivity of DoM allows the construction of substituted biaryls which by virtue of the incorporated DMGs allows consideration of further D*o*M, D*re*M, and other cyclization processes. This strategy is suitable for construction of not only aryl-aryl but also heteroaryl-heteroaryl and their mixed systems. We have used this strategy as a key step in a study of the total synthesis of lysergic acid (Chapter 2, Section 2.7).

Table 1.2 Common DoM–Cross Coupling Combination Reactions



Met	LG	Cat.	Cross Coupling
$B(OR)_2$	I > Br > OTf	Pd	*Suzuki*
MgX	Hal, OTf	Ni	*Kumada*
ZnX	Hal, OTf	Ni	*Negishi*
SnR_3	Hal, OTf	Pd	*Stille*

1.5 Limitations

Low temperature and strong bases are always required in DoM reaction. At elevated temperatures and longer reaction times, side reactions increase greatly such as self-condensation and other nucleophilic attacks to DMGs (e.g. $CONEt_2$). In addition, the DoM process is not compatible with reactive functional groups such as nitro, ketone, aldehyde, ester, I and Br which

do not survive under organolithium base conditions. The necessity for these conditions (low temperature and strong bases) is a drawback of the DoM reaction.

DMG manipulation and conversion to other functionalities is an important post-DoM consideration for synthetic applications. Although weak DMGs such as NHBoc and OMOM are easily hydrolyzed under mild acidic conditions leading to anilines and phenols respectively,[62] the transformation of strong DMGs such as $OCONEt_2$ and electron-withdrawing DMGs such as $CONEt_2$ has been troublesome to synthetic chemists due to harsh conditions which are usually required for their manipulation. For example, the $ArOCONEt_2$ is cleaved to ArOH commonly by $LiAlH_4$ (LAH), KOH/MeOH/reflux or MeLi.[4,22] A Ni-catalyzed C-O bond cleavage of $ArOCONEt_2$ to form biaryls has been developed recently,[63,64] but continuing development of such mild and efficient procedures for the manipulation of these strong DMGs is highly desired for the application of DoM chemistry.

In this thesis, a new method for Schwartz reduction of amides to aldehydes is presented, which may solve problems in the manipulation of benzamide DoM chemistry in a convenient manner (Chapter 2); a new catalytic DoM-coupling reaction involving Ru-catalyzed C-H, C-N, C-O activations is described, which may achieve DoM-Suzuki cross coupling in a single step at non-cryogenic temperature and base-free conditions (Chapter 3). This new coupling reaction, together with the Schwartz reduction, promises to enhance the methodology for polysubstituted biaryl synthesis.

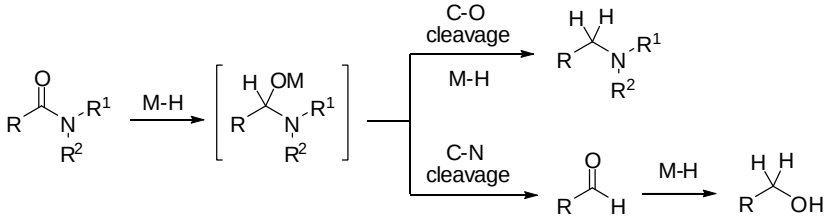
Chapter 2

Reduction of Tertiary Benzamides to Benzaldehydes by an *in situ*–Generated Schwartz Reagent ($Cp_2Zr(H)Cl$); Formal Synthesis of Lysergic Acid

2.1 Introduction

2.1.1 Reduction of Tertiary Amides

Reduction of the amide functionality constitutes an important manipulation in organic synthesis. A large number of methods have been developed for its transformations to amine, alcohol, and aldehyde functional groups.[65,66] This process involves the addition of a metal hydride to the C=O of a tertiary amide to form a tetrahedral intermediate, followed by cleavage of the C-O bond to lead to a tertiary amine or by cleavage of the C-N bond to form an aldehyde which may be easily over-reduced to a primary alcohol (Scheme 2.1). The selectivity of amide transformations depends on the reduction conditions.[66]



Scheme 2.1

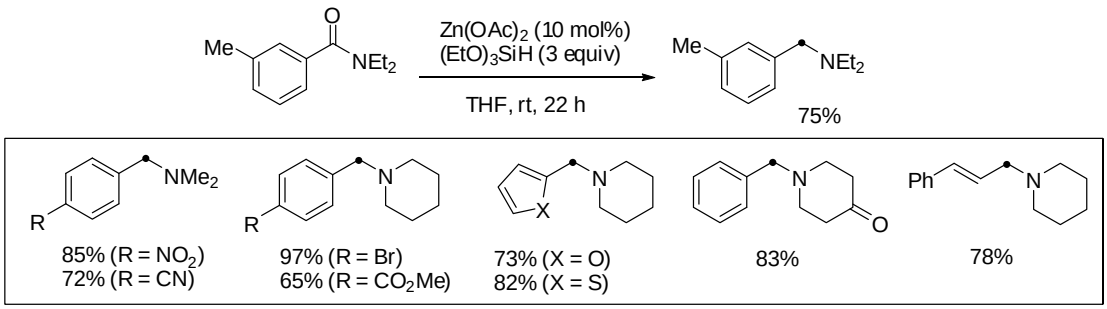
Of these amide transformations, the reduction of tertiary amides to amines is well-established and has been efficiently applied in organic synthesis, in which highly reactive

reagents such as traditional aluminum and boron hydrides are most commonly employed.[67] However, these methods have low functional group compatibility due to the powerful reducing properties of these reagents. For example, although $LiAlH_4$ (LAH) is a good reductant for reduction of amides to amines, many other functional groups such as halo, aldehyde, ketone, ester and nitrile groups are more rapidly or concurrently reduced in view of the difficulty of amide reduction.[68] The ease of reduction of functional groups with LAH is shown in Table 2.1. Thus, when highly functionalized molecules and most aluminum hydrides are employed, the chemoselectivity is often poor in spite of the fact that the amide reduction may occur in high yields. Boranes such as 9-borabicyclo[3.3.1]nonane (9-BBN)[69] are milder agents for this reduction but maintain the same drawback.[68]

Table 2.1 The Ease of Reduction of Functional Groups with LAH in Ether[68]

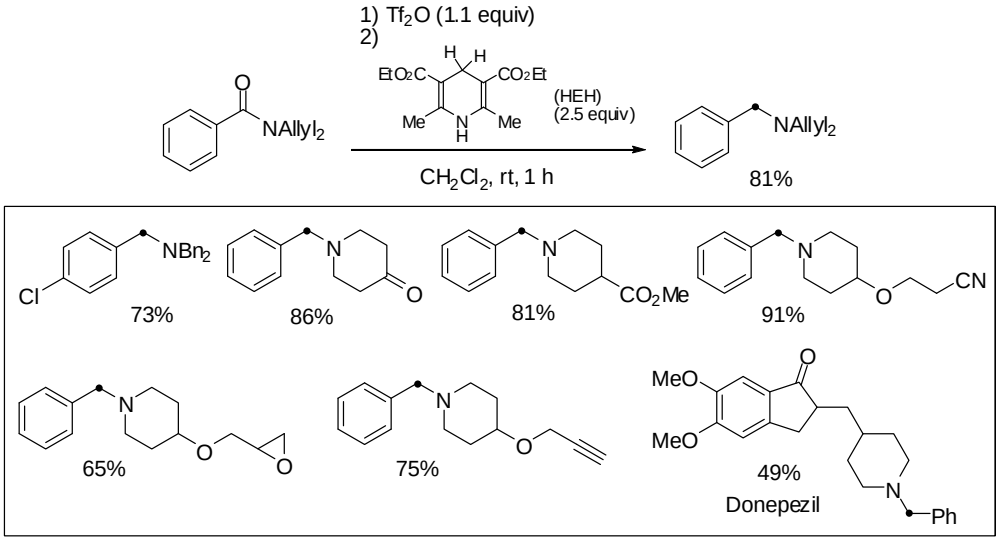
Substrate	Product	Ease of Reduction
RCHO	RCH_2OH	easiest
RC(O)R'	RCH(OH)R'	
RC(O)Cl	RCH_2OH	
epoxide	$RCH_2CH(OH)R'$	
RCOOR'	RCH_2OH	
RCOOH	RCH_2OH	
$RCONR'_2$	**$RCH_2NR'_2$**	
RCN	RCH_2NH_2	
RNO_2	RNH_2	most difficult
RCH=CHR'		inert

In order to improve the chemoselectivity of the amide reduction, metal-catalyzed hydrosilations of amides have been investigated widely during the last decade. Many metal catalysts involving Rh,[70] Ru,[71-73] Pt,[74,75] Mo,[76] In,[77] Fe[78,79] and Zn[80,81] have proven to be effective for the reduction of tertiary amides. Some of these, especially the newly developed methods, perform well under mild reduction conditions with high chemoselectivity in the presence of halo, ketone, epoxide, ester, nitrile and alkynyl groups. In 2009, a Fe-catalyzed reduction of tertiary amides to amines was concurrently developed by the Beller[79] and Nagashima[78] groups. Using $Fe_3(CO)_{12}$ as catalyst, a variety of tertiary amides were shown to undergo reduction using polymethylhydrosiloxane (PMHS) or 1,1,3,3-tetramethyldisiloxane (TMDS) to afford tertiary amines with good chemoselectivity. Notably, iron was shown for the first time, to be effective for amide reduction. Later, the Beller group reported a Zn-catalyzed reduction of tertiary amides to amines, in which $Zn(OAc)_2$ as catalyst and $(EtO)_3SiH$ as reductant were employed.[80] $Zn(OAc)_2$ plays the role of activating the silane reductant for the reduction process. The reaction proceeded well with high chemoselectivity and ketone, ester, nitro, nitrile and bromo groups are tolerated under the amide reduction conditions (Scheme 2.2). Another significant feature is that the reduction is performed at room temperature or 40 ^{o}C.



Scheme 2.2

Recently, a mild and highly chemoselective metal-free reduction of tertiary amides has been reported by the Charette group which employs the Hantzsch ester (HEH) as hydride donor under triflic anhydride (Tf_2O) mediation to form amines in moderate to good yields.[82] In this process, Tf_2O is suggested as an activating agent of the amide group to generate a highly electrophilic iminium salt which is easily reduced by HEH. Of the reduction results, more impressive is the high selectivity for tertiary amides reduction over a wide range of functionalities, e.g., halo, ketone, ester, nitrile, epoxide, alkene and alkyne groups (Scheme 2.3). A chemoselective synthesis of Donepezil, a drug for the management of Alzheimer's disease, was successfully tested as an application (Scheme 2.3). A drawback is that a stoichiometric amount of the expensive HEH reagent (US$ 54/g) is required for the reduction.

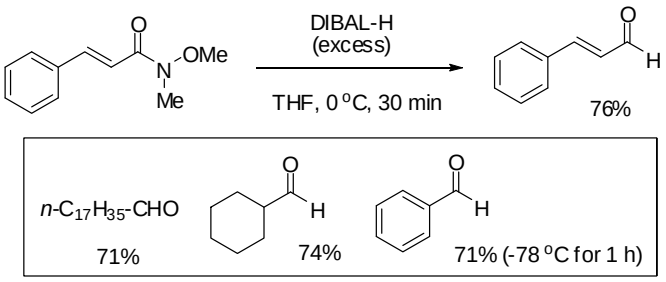


Scheme 2.3

Other than the reduction of amides to amines, the reduction of tertiary amides to alcohols is quite rarely reported and the formation of amines as a side reaction often plagues such

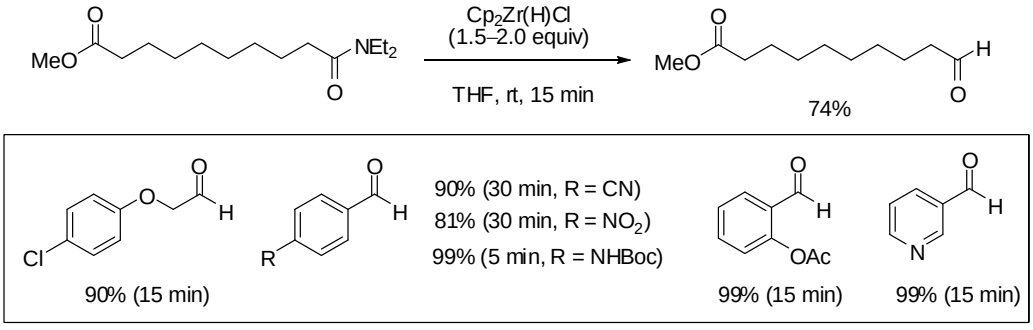
methodologies. To date, some less-hindered lithium aminoborohydrides such as LiH_3BNH_2[83] and lithium pyrrolidinoborohydride[84,85] have been found to be successful for the high yield reduction of a variety of amides to alcohols although sterically hindered lithium aminoborohydrides such as LiH_3BN*i*-Pr_2 still lead to reduction of amides to amines.[84,85] However, low functional group tolerance remains due to the powerful reduction properties of lithium aminoborohydrides. Therefore, finding a highly chemoselective reduction method for amides to alcohols is still a challenge to synthetic chemists.

Partial reduction of tertiary amides to aldehydes is generally difficult to achieve due to a more favorable over-reduction of the generated highly reactive aldehydes to alcohols. To date, only few methods are available for this challenging transformation. Using aluminum hydrides such as LAH and keeping amides in excess at 0 ^oC or lower temperatures, the reduction of tertiary amides always provides aldehydes in poor to moderate yields together with the corresponding alcohols and amines as byproducts.[66] Sia_2BH (diisoamylborane), which is not commercially available, has been reported as a good reductant for this transformation,[69] but the scope and the limitation of substrates was not well investigated. The problem concerning the functional group compatibility still remains in both of the above methods. Although some mild conditions, DIBAL-H[86] and Ph_2SiH_2/Ti(O*i*-Pr)$_4$,[87] were found for reductions of Weinreb amides (N-methyl-N-methoxy amides) and substituted acetamides to the corresponding aldehydes respectively in reliable yields with no or little over-reduction, these approaches are limited by specificity of substrates (Scheme 2.4).



Scheme 2.4

In 2000, Georg and co-workers reported an efficient, mild, and general method for the reduction of amides to aldehydes using the Schwartz reagent, $Cp_2Zr(H)Cl$ (bis(cyclopentadienyl)zirconium(IV) chloride hydride) (Scheme 2.5).[88] Reaction at room temperature, short reaction time, good functional group tolerance, and elimination of side reductions are key features of this important reaction. Combined with later studies,[89-91] the Schwartz reagent is becoming a general and powerful reductant for amide to aldehyde conversion (See section 2.1.2).



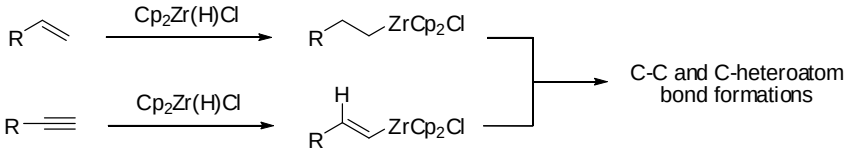
Scheme 2.5

Most recently, the Lemaire group reported another mild reduction of amides to aldehydes in which 1,1,3,3-tetramethyldisiloxane (TMDS) and $Ti(O\textit{i}\text{-}Pr)_4$ in stoichiometric amounts are

employed.[92] Like the Schwartz reagent, TMDS/Ti(O*i*-Pr)$_4$ effects reduction of both aliphatic and aromatic amides to aldehydes. However, over-reduction as a side reaction is always observed. Moreover, the substrate scope and functional group tolerance were not well investigated.

2.1.2 Schwartz Reagent and Georg's Discovery

Since the first preparation of $Cp_2Zr(H)Cl$ (bis(cyclopentadienyl)zirconium(IV) chloride hydride) by Wailes and Weigold in 1970,[93] organozirconium chemistry has been widely studied and applied in organic synthesis.[94-96] This reagent was developed by Jeffrey Schwartz in the mid-1970s and hence bears his name.[97-100] The hydrozirconation reaction, in which the addition of Schwartz reagent to alkenes and alkynes leads to organozirconocenes, can be considered as the first synthetically useful application of the zirconocene complexes in organic chemistry (Scheme 2.6).[94-96] Systematic investigations in the late 1970s and 1980s by Negishi further expanded the synthetic scope of these complexes.[101] Since then, the interest in organozirconium chemistry has been significantly increased due to the unique ability of the Schwartz reagent and related organozirconocenes to promote uncommon transformations. Meanwhile, many new reactions of the Schwartz reagent such as reductions have been uncovered and developed gradually.

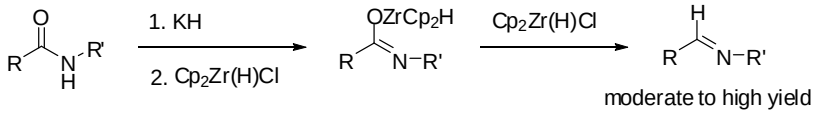


Scheme 2.6

Other than hydrozirconation applications leading to C-C and C-heteroatom bond formation, the Schwartz reagent has been found to be a powerful and selective reducing agent for

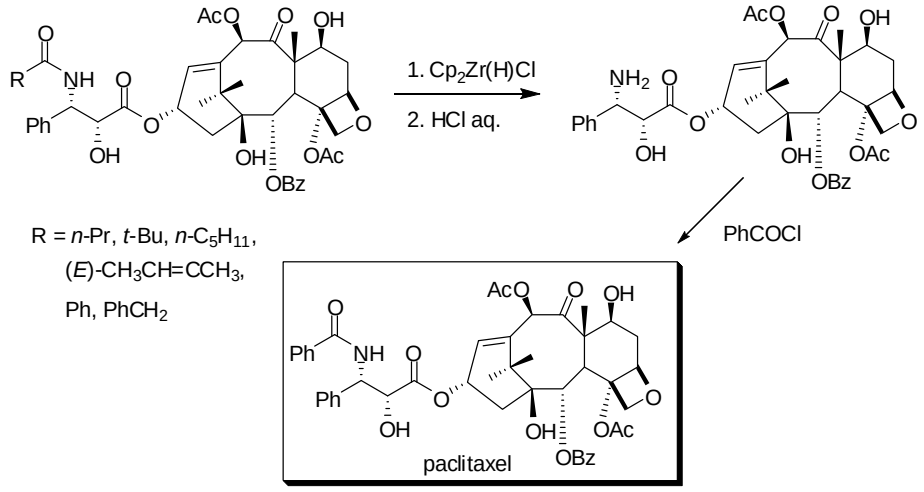
carbonyl group and other functional groups, especially amides. In the late 1980s, Wang and co-workers reported a series of results on reductions of aldehydes, ketones, epoxides and esters to alcohols as well as hydrozirconations of imines and nitriles using the Schwartz reagent in benzene in the 30-60 ^{o}C temperature range.[102-106] In 1997, Zablocka and co-workers found that Schwartz reagent effects reduction of a variety of phosphine oxides and sulfides to phosphines under mild conditions.[107] Reduction of phosphine oxides or sulfides can be achieved using several reagents, but most of the reducing reagents used, such as LAH, are not very selective.[107]

In 1990s, the Ganem group found[108] and developed[109] a new methodology for the reduction of secondary amides to N-substituted imines using the Schwartz reagent (Scheme 2.7). This is an important functional group interconversion because imines are usually reduced more rapidly than amides by most metal hydride reagents and thus the reduction of amides to imines is difficult to control. The Ganem method achieves this transformation.



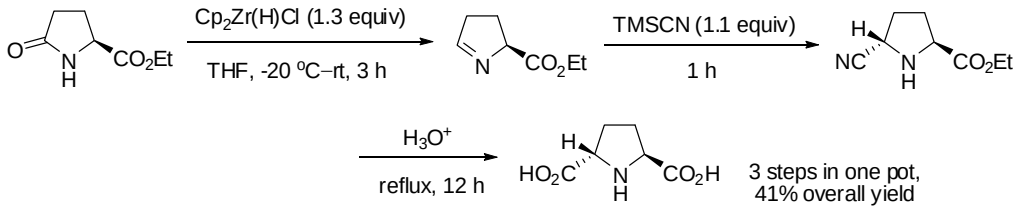
Scheme 2.7

The value of the Ganem protocol has been dramatically demonstrated in the large-scale synthesis of a taxol derivative in which the Schwartz reagent is used to reductively cleave the secondary amide in the side chain from a mixture of derivatives extracted from the yew tree, followed by benzoylation to synthesize paclitaxel, an anticancer drug (at least US$ 1 billion in sales per year) (Scheme 2.8).[110]



Scheme 2.8

Another recent application which shows the potential of the Schwartz reagent is the selective reduction of a lactam to an imine and its subsequent transformations (Scheme 2.9).[111]

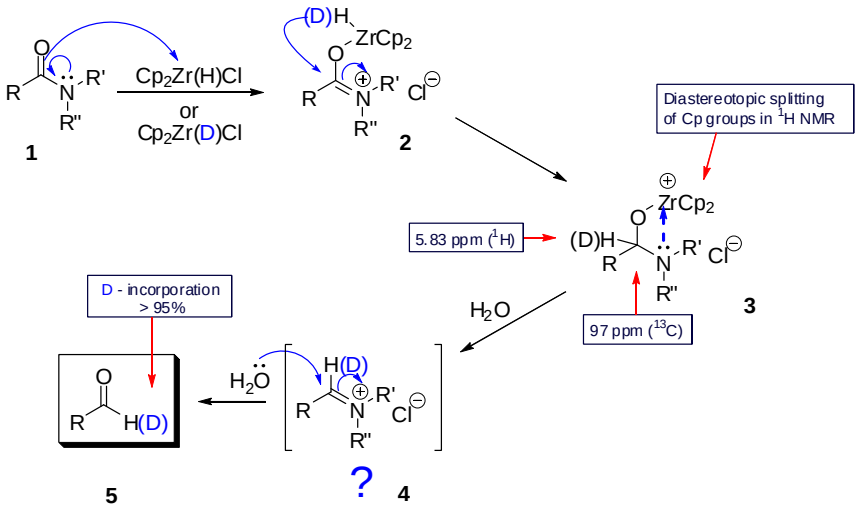


Scheme 2.9

As delineated in Section 2.1.1, tertiary amides are generally difficult to reduce selectively. A convenient procedure for the reduction of tertiary amides to aldehydes by $Cp_2Zr(H)Cl$ (Schwartz reagent) under very mild conditions was discovered by the Georg group in 2000 (Scheme 2.5).[88] Combined with later studies,[89-91] these results demonstrate the use of the Schwartz reagent as an effective method to reduce a variety of tertiary amides, including dialkyl,

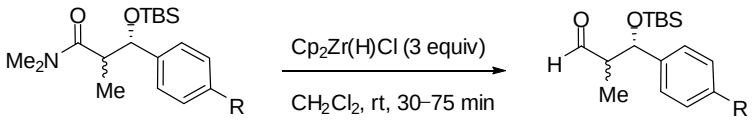
methoxymethyl (Weinreb amides) and even Evans N-acyloxazolidinone, directly to the corresponding aldehydes in high yields in very short reaction times (<30 min) at room temperature. Significantly, this method has excellent functional group tolerance and high selectivity with no or little over-reduction. It is noteworthy that ester, NHBoc, nitrile, halo and nitro groups survive the reduction conditions. Although not yet fully determined, the amide reduction overrides that of most other functional groups. However, ketone and aldehyde groups are reduced to the corresponding alcohols under the conditions which effect amide reduction at room temperature.

Why is the reduction of tertiary amides by Schwartz reagent highly controlled to form aldehydes without over-reduction even when an excess amount of Schwartz reagent is employed? A mechanism has been proposed for this process by Georg and co-workers (Scheme 2.10)[89] which begins with the addition of the Schwartz reagent to an amide **1**, followed by an intramolecular hydride transfer of **2** to form a zirconated tetrahedral intermediate **3** which leads, after quench with water, to the aldehyde product **5**. In this process, as a key feature, a coordination between Zr and N in the tetrahedral intermediate **3** is suggested which strongly stabilizes the intermediate delaying to collapse until hydrolysis. This feature has been supported by mechanistic studies using NMR assistance and the results are displayed in Scheme 2.10. This result can explain the reduction control from amides to aldehydes. Reduction by the deuterio Schwartz reagent confirms the origin of the hydride transfer reaction.[89] Density functional theory (DFT) calculations are consistent with the mechanism proposed by Georg.[112] However, direct observation for the existence of iminium salt intermediate **4** failed when Georg tried to monitor it by IR.[89]



Scheme 2.10

Most recently, this methodology has been successfully applied to the reduction of chiral amides with little or no erosion of diastereomeric excess (Scheme 2.11).[113]



R	syn : anti
H	35 : 1
Cl	24 : 1
OMe	> 50 : 1

R	syn : anti	Yield (%)
H	30 : 1	88
Cl	24 : 1	84
OMe	> 50 : 1	85

Scheme 2.11

The efficiency and chemoselectivity prompted the use of the Schwartz reagent in an approach to the synthesis of lysergic acid (Section 2.7) and, with success in this application,

motivated to undertake a study of benzamide to benzaldehyde reduction in the context of DoM substrates in order to provide a general route to polysubstituted benzaldehydes of synthetic value.

2.2 Research Goals

2.2.1 The Schwartz Reagent and D*o*M-Derived Benzamides

With the exception of Weinreb amides, tertiary amides were difficult to efficiently reduce to aldehydes before the discovery of Georg.[88] This direct amide to aldehyde reduction by Schwartz reagent is an important organic transformation which overcomes multi-step processes involving non-chemoselective harsh conditions and requirement for sequential processes, e.g. hydrolysis-esterification-reduction and reduction–oxidation (Scheme 2.12). Herein, we describe the extension of the Georg method for DoM–derived benzamides with attention to steric effects and chemoselectivity.

Aromatic amides, especially N,N-diethylbenzamides, are key substances for the directed *ortho* metalation reaction (D*o*M), a widely used method in organic synthesis.[1,51,60,3,4] Today, the DoM strategy is being especially applied in the pharmaceutical industry on multi-kg and multi-metric ton scale for the synthesis of commercial drugs in areas of antitumor and anti-inflammatory indications, among others.[3,4] Benzamide D*o*M chemistry provides access to a variety of polysubstituted aromatic and heteroaromatic compounds, in particular 1,2- and 1,2,3-substitution patterns which are difficult to achieve or cannot be achieved by classical routes (e.g. electrophilic substitution, nucleophilic substitution, Friedel-Crafts reaction). The aldehydes produced via reduction of amides are important intermediates for organic synthesis which undergo a multitude of transformations, e.g. classical Knoevenagel,[17] Reformatsky,[17] Wittig[17] reactions and aldol condensations.[114]

One purpose of the present research is to connect the Georg discovery of amide to aldehyde reduction with tertiary benzamide DoM chemistry in order to provide new synthetic processes of value for the construction of functionalized polysubstituted aromatic and heteroaromatic compounds.

2.2.2 Amide Reduction by the *in situ*–Generated Schwartz Reagent

The Schwartz reagent is widely used in synthetic organic chemistry in hydrozirconation and a number of reactions emanating therefrom.[94-96] Although the Schwartz reagent is commercially available, it is expensive (US$ 28/g) and is problematic for long-term storage due to its sensitivity to air, light and moisture.[94] To develop procedures for *in situ* generation of the Schwartz reagent from Cp_2ZrCl_2 was therefore considered a worthy undertaking. To date, *in situ* generation procedures using different hydride sources such as *t*-BuMgCl,[115] $LiEt_3BH$,[116] and DIBAL-H[117] for the hydrozirconation reaction have been reported, but all of these are based on the initial preparation of the Schwartz reagent for use in subsequent reactions (Fig. 2.1(a)). In the first reduction step, the Schwartz reagent formed is typically contaminated with Cp_2ZrH_2 and other salts.[94] In such a one-pot two-step process, if the reductant used to generate the Schwartz reagent were to remain, byproducts would contaminate the end product since the reductant would react with the substrate and intermediates. Thus, the disadvantages of pre-preparation of the Schwartz reagent remain in the procedures. As discussed above, these disadvantages include over-reduction, poor solubility, and contaminants that may affect efficient reduction. Therefore, a method is required that promotes generation of the Schwartz reagent by an *in situ* method in a manner that allows its rapid reaction once generated.

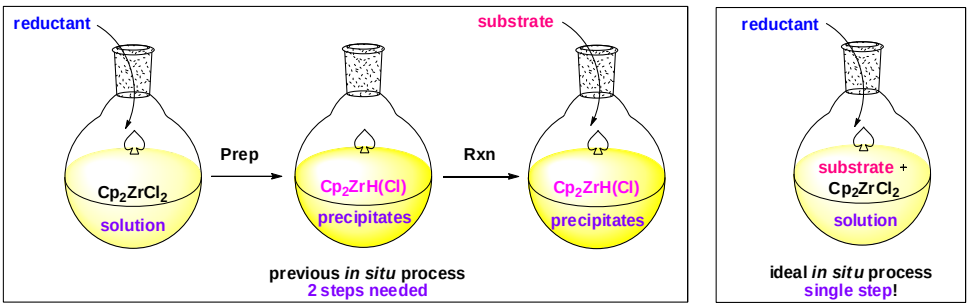


Fig. 2.1 *in situ* Processes

The ideal *in situ* procedure for the use of the Schwartz reagent in organic synthesis should have the following features: its preparation and reaction should be feasible in a real one-pot procedure in order that the *in situ* prepared reagent is in a pure and really fresh state for immediate reaction with a substrate (Fig. 2.1(b)). Thus, the *in situ* method should perform as a three-component reaction. The advantage of this procedure would be the avoidance of the step for separate preparation of the Schwartz reagent and its over-reduction to Cp_2ZrH_2 which constitute deficiencies in the previous preparations of the reagent.[94,118,119]

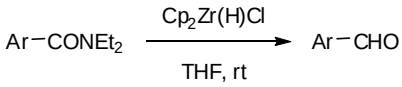
2.3 Results and Discussion

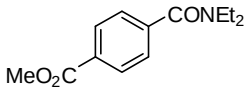
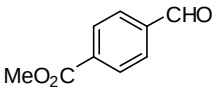
2.3.1 Reduction of DoM–Derived Benzamides by the Schwartz Reagent

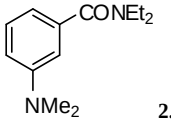
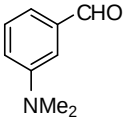
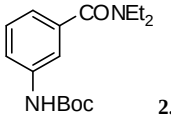
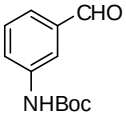
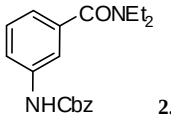
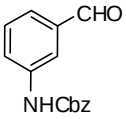
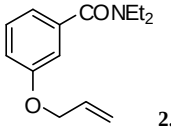
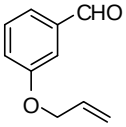
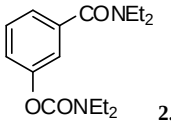
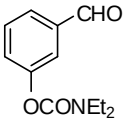
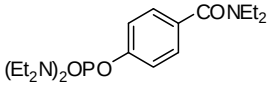
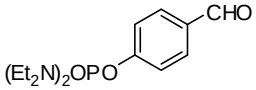
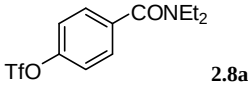
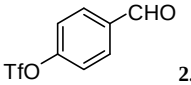
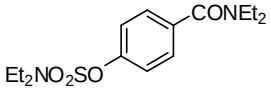
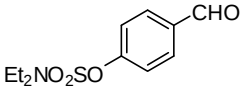
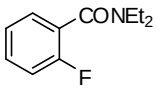
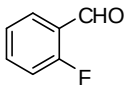
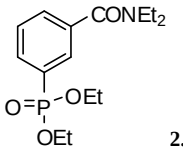
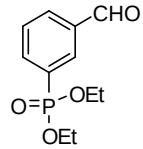
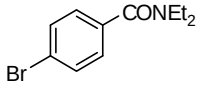
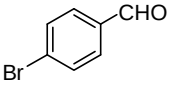
In initial studies, we applied the Georg conditions to the reduction of benzamides incorporating a variety of functional groups which were not examined previously.[89-91,88] The results are displayed in Table 2.2. All reactions proceeded in good yields. It was found that NHCbz, F, Br, OTf, CO_2Me, $OCONEt_2$, $OP(O)(NEt_2)_2$, OSO_2NEt_2 and $P(O)(OEt)_2$ groups were tolerated in the amide to aldehyde reduction. Of these functional groups, the powerful DMGs such as $OCONEt_2$, $OP(O)(NEt_2)_2$[29] and OSO_2NEt_2[18] are stable to the $CONEt_2$ reduction

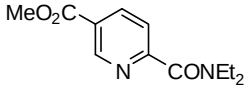
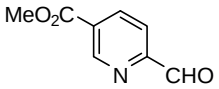
conditions. This selective transformation of amide rather than other DMGs is useful for designing syntheses based on DoM chemistry. Over-reduction was observed in a single case, that of the NHCbz benzamide **2.4a** which gave a 76% yield of the corresponding benzaldehyde product **2.4b** accompanied by 24% of the over-reduction benzyl alcohol byproduct **2.4c** (Table 2.2, entry 4). Interestingly, no analogous over-reduction product was found in the NHBoc benzamide case (entry 3). A minor competitive reaction occurred in the case of an amide-alkene co-existence situation (entry 5) which, aside from the benzaldehyde product **2.5b** (72% yield), led to the formation of the hydrozirconation product **2.5c** in 7% yield. It was also observed that the major benzaldehyde alkene **2.5b** underwent further hydrozirconation under prolonged reaction times in the presence of excess Schwartz reagent. Thus, in order to limit the occurrence of hydrozirconation, the amide reduction should be controlled to shorter reaction times for such derivatives. As known, ester,[106] $OCONEt_2$ (Scheme 2.17)[120] and $P(O)(OEt)_2$[107] groups may be reduced by using excess of Schwartz reagent under longer reaction times (hours) but are found to be stable under the amide reduction conditions (entries 1, 6, 11 and 13). Thus, the amide reduction is a fast reaction which suppresses other functional group reductions under short reaction time conditions.

Table 2.2 Functional Group Compatibility in the Schwarz Reduction of Substituted Benzamides



Entry	Amide	Schwartz Reagent (equiv)	Time (min)	Product	Yield (%)[a]
1	 **2.1a**	1.5	25	 **2.1b**	92

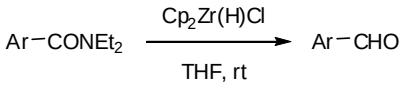
2	 **2.2a**	1.5	30	 **2.2b**	76
3	 **2.3a**	2.0	30	 **2.3b**	82
4	 **2.4a**	2.0	25	 **2.4b**	76[b]
5	 **2.5a**	1.5	20	 **2.5b**	72[c]
6	 **2.6a**	1.5	15	 **2.6b**	83
7	 **2.7a**	1.5	11	 **2.7b**	84
8	 **2.8a**	1.5	30	 **2.8b**	82
9	 **2.9a**	1.5	9	 **2.9b**	94
10	 **2.10a**	1.5	30	 **2.10b**	89
11	 **2.11a**	1.5	10	 **2.11b**	85
12	 **2.12a**	1.5	10	 **2.12b**	73

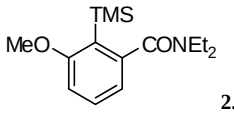
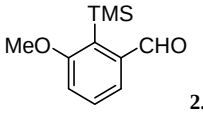
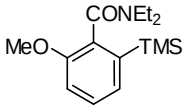
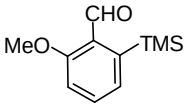
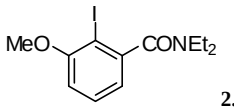
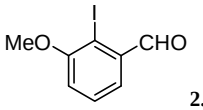
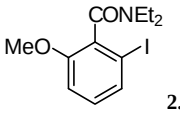
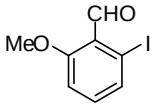
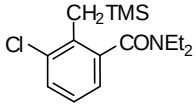
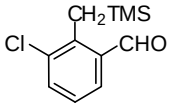
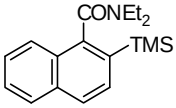
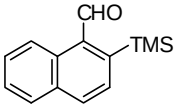
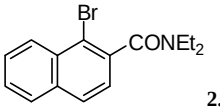
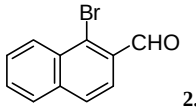
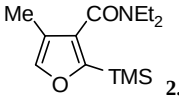
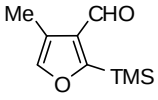
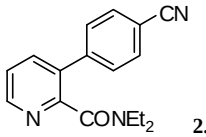
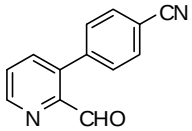
13	 **2.13a**	1.5	25	 **2.13b**	72

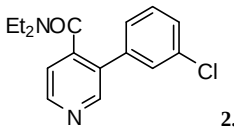
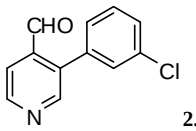
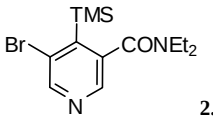
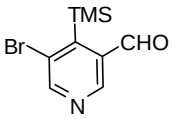
[a] Yields of isolated and purified products.
[b] Accompanied by the corresponding 3-(benzyloxycarbonyl)aminobenzyl alcohol **2.4c** (24%).
[c] Accompanied by the corresponding 3-*n*-PrObenzaldehyde **2.5c** (7%).

In order to connect the Schwartz benzamide to benzaldehyde reduction with tertiary benzamide DoM chemistry, a variety of amide substrates **2.14a-2.24a** obtained via DoM reaction was investigated. The results are tabulated in Table 2.3. Heterocyclic furan ring, iodo and TMS substituents were examined for the first time and were found to be tolerated under the reduction conditions. When amide substrates with mono-*ortho* substituents were employed, the reduction proceeded in good yields (Table 2.3, entries 1, 3, 5, 7 and 9-11). However, when di-*ortho* substituted amides **2.15a** and **2.17a** were tested, the yields of reduced products **2.15b** and **2.17b** decreased greatly (entries 2 and 4). The *peri*-hydrogen effect[121,122] was also observed to disturb the reduction of N,N-diethyl 2-TMS-1-naphthamide **2.19a** which proceeded in 41% yield even when treated with excess Schwartz reagent under prolonged reaction times (entry 6). As an exception, a di-*ortho* substituted furanamide **2.21a** was reduced to the corresponding aldehyde **2.21b** in good yield (entry 8). A possible rationalization is that the amide group in between two substituents on the furan ring is less-hindered than the corresponding situation on a phenyl ring due to bond angle differences of respective substituents.[123] Pyridine amides **2.22a-2.24a** (entries 9-11), including two derived from DoM-Suzuki cross coupling reactions (entries 9 and 10), also undergo efficient reduction to afford potentially useful aldehyde products **2.22b-2.24b**. We conclude that the Schwartz reagent is especially suitable for the efficient reduction of mono-*ortho* substituted benzamides and may also be used for the reduction of some di-*ortho* substituted benzamides albeit in moderate yields.

Table 2.3 Schwartz Reduction of DoM-Derived Benzamides and Naphthamides **2.14a-2.24a**

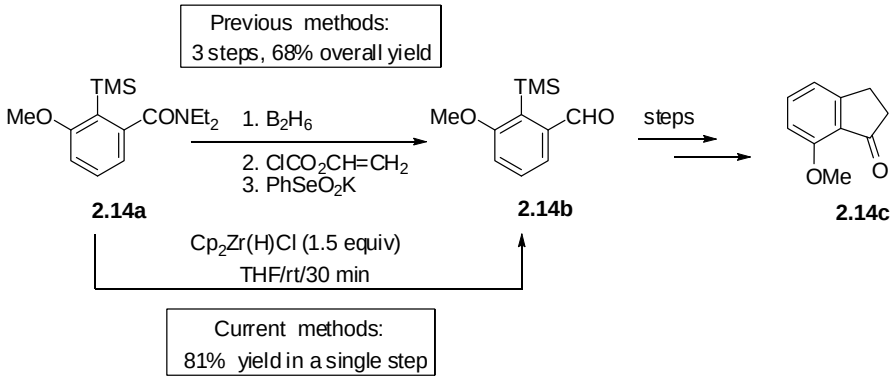


Entry	Amide	Schwartz Reagent (equiv)	Time	Product	Yield (%)[a]
1	 **2.14a**	1.5	30 min	 **2.14b**	81
2	 **2.15a**	2.0	25 min	 **2.15b**	37
3	 **2.16a**	1.5	10 min	 **2.16b**	72
4	 **2.17a**	2.0	1 h	 **2.17b**	26
5	 **2.18a**	1.5	20 min	 **2.18b**	83
6	 **2.19a**	3.0	2 h	 **2.19b**	41[b]
7	 **2.20a**	1.5	30 min	 **2.20b**	70
8	 **2.21a**	1.5	25 min	 **2.21b**	84
9	 **2.22a**	1.5	30 min	 **2.22b**	74

10	 **2.23a**	1.5	20 min	 **2.23b**	88
11	 **2.24a**	1.5 3.0	1 h 1 h	 **2.24b**	25[c] 66

[a] Yields of isolated and purified products. [b] Starting amide recovery (46%). [c] Starting amide recovery (62%).

The value of the amide to aldehyde Schwartz reduction protocol is demonstrated by reference to a previous synthesis of 7-methoxy-1-indanone **2.14c** (Scheme 2.12) in which the intermediate **2.14b** required a three-step preparation from the substituted benzamide **2.14a**.[124] Application of the Schwartz reagent allowed the synthesis of benzaldehyde **2.14b** in a single, higher yield operation.

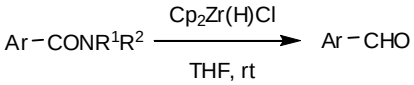


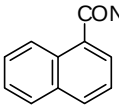
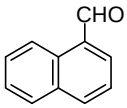
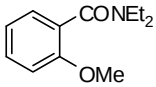
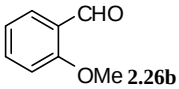
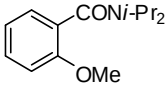
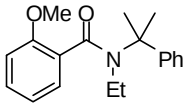
Scheme 2.12

Amide steric effects on the relative rate of the reduction were briefly investigated (Table 2.4). Less-hindered benzamides such as N,N-dimethyl- and N,N-diethyl derivatives **2.25a** and **2.26a** underwent reduction using Schwartz reagent in short reaction times and high yields (entries 1 and 2) whereas the bulky N,N-diisopropyl- and N-ethyl-N-cumyl benzamide (**2.27a** and **2.28a**)

reductions proceeded more slowly and led to the corresponding aldehyde products in modest yields even using an excess amount of Schwartz reagent and prolonged reaction time (entries 3 and 4). Thus, combining with steric effect on the reduction of di-*ortho* substituted amides **2.15a** and **2.17a** (Table 2.3), steric bulk around amide group of benzamides decreases the reduction efficiency.

Table 2.4 Amide Substituent Effects on the Facility of Benzamide Reduction by the Schwartz Reagent



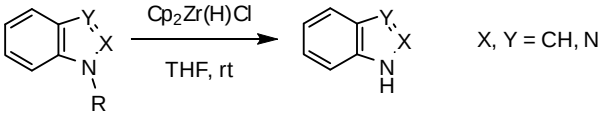
Entry	Amide	Schwartz Reagent (equiv)	Time	Product	Yield (%)[a]
1	 **2.25a**	1.5	10 min	 **2.25b**	80
2	 **2.26a**	1.5	10 min	 **2.26b**	94
3	 **2.27a**	2.0	1.5 h	**2.26b**	59
4	 **2.28a**	2.2	2 h	**2.26b**	55

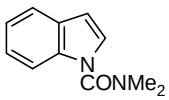
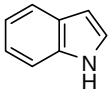
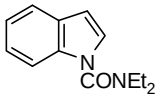
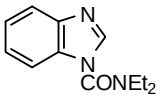
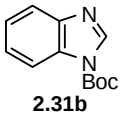
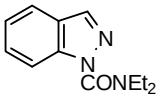
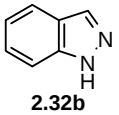
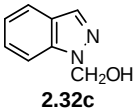
[a] Yields of isolated and purified products.

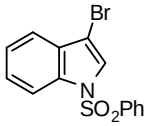
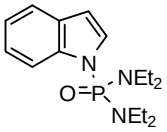
As a further brief extension, reductive cleavage of heterocyclic N-amides by the Schwartz reagent was tested. Thus, treatment of the indole- and benzimidazole-N-amides **2.29a-2.31a** with 2 equivalents of Schwartz reagent led successfully to carbamoyl reductive cleavage in good yields (Table 2.5, entries 1-3). In the indazole case, a 56% yield of the expected product

2.32b was obtained with a 43% yield of the side reduction product **2.32c** which may be fully converted into the expected product **2.32b** under basic conditions (entry 4).[125,126] However, the corresponding N-SO_2Ph and N-P(O)(NEt_2)$_2$ substrates **2.33a and 2.34a** did not undergo reduction even with an excess Schwartz reagent and under prolonged reaction times (entries 5 and 6). As known, the N-$CONEt_2$ of indole is a good DMG for preparation of 2- and/or 7-substituted indoles.[127] The current reductive cleavage method may be used on such indoles for DMG removal after DoM reaction.

Table 2.5 Reductive Cleavage of Indole and Benzimidazole N-Amides **2.29a-2.34a** Using the Schwartz Reagent



Entry	Substrate	Schwartz Reagent (equiv)	Time	Product	Yield (%)[a]
1	 **2.29a**	2.0	40 min	 **2.29b**	88
2	 **2.30a**	2.0	1 h	**2.29b**	94
3	 **2.31a**	2.0	15 min	 **2.31b**	82[b]
4	 **2.32a**	3.0	30 min	 **2.32b**	56
				 **2.32c**	43

5	 **2.33a**	1.5	30 min	n.d.	--[c]
6	 **2.34a**	3.0	24 h	**2.29b**	Trace[d]

[a] Yields of isolated and purified products. [b] Boc protection was used for ease of product isolation.
[c] Recovery of starting material (99%). [d] Recovery of starting material (96%).

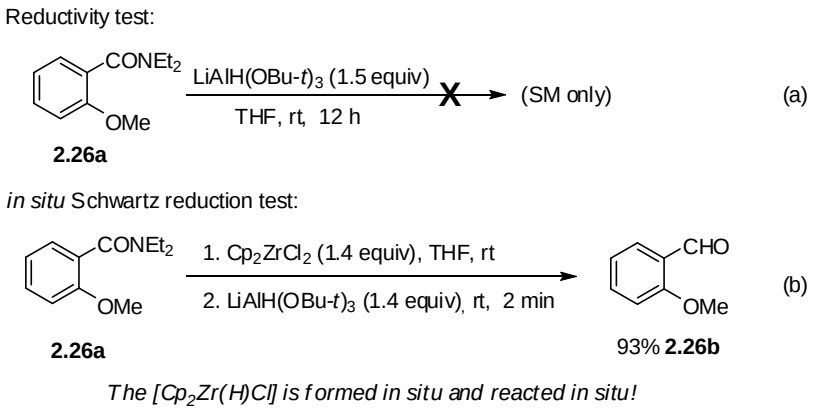
2.3.2 *In situ*–Generation of Schwartz Reagent and Use

2.3.2.1 Amide Reduction by the *in situ*–Generated Schwartz Reagent

To achieve the ideal *in situ* amide reduction as a three-component reaction of Schwarz reagent precursor, additional reductant and substrate, the most important requirement is that the reductant effects the reduction of Cp_2ZrCl_2 to the Schwartz reagent selectively and does not undergo reaction with substrates and intermediates generated from the reduction of the substrates by the Schwartz reagent. Hence, finding a proper reductant is the key of success.

The preparation of the Schwartz reagent by reaction of lithium tri-*tert*-butoxyaluminum hydride ($LiAlH(OBu\text{-}t)_3$) with Cp_2ZrCl_2 was first reported by Wailes and Weigold in 1970.[93] To the best of our knowledge, $LiAlH(OBu\text{-}t)_3$ has never been applied for the *in situ* generation of the Schwartz reagent. Due to its inertness to most of functional groups, $LiAlH(OBu\text{-}t)_3$ was initially chosen as a reductant to test our idea. As a first test experiment, $LiAlH(OBu\text{-}t)_3$ was examined for the reduction of the benzamide **2.26a** and led to the recovery of starting material even after 12 h reduction time (Scheme 2.13(a)). With great excitement, this reductant was applied in the ideal three-component reaction with Cp_2ZrCl_2 and substrate **2.26a** in stoichiometric amounts and was found to proceed in 2 min (TLC analysis) to furnish *ortho*-anisaldehyde **2.26b** in excellent yield (Scheme 2.13(b)). It is noteworthy that no Schwartz reagent precipitate was observed to form

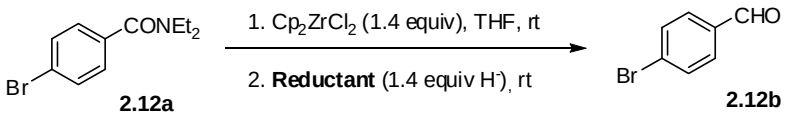
during the reaction as is the case for the reaction under Georg conditions.[88] This suggests that the Schwartz reagent [$Cp_2Zr(H)Cl$] is formed *in situ* and thereby is available for faster and more complete reaction with the amide substrate.



Scheme 2.13

Inspired by the above result, we further screened more reductants for the *in situ* method using 4-bromobenzamide **2.12a** as substrate. Besides $LiAlH(OBu\text{-}t)_3$ (Table 2.6, entry 1), $LiBH(s\text{-}Bu)_3$ was also found to be an efficient reductant (entry 2). When LAH was employed, the yield of the reduction product **2.12b** decreased. In this case, alcohol and amine products were observed in spite of short reaction times (2 min quench) (entry 3). When DIBAL-H was tested, a 50% yield of 4-bromobenzaldehyde **2.12b** was obtained together with 38% recovery of starting benzamide **2.12a** after a 30 min reduction time (entry 4). Hence, in the case of LAH and DIBAL-H, over reduction and incomplete reduction occur respectively, indicating that these reagents are unsuitable for the *in situ* method. Therefore, as the best choice, $LiAlH(OBu\text{-}t)_3$ was used for the further investigation.

Table 2.6 Screening Reductants for the *in situ* Schwartz Reduction of 4-bromobenzamide **2.12a**



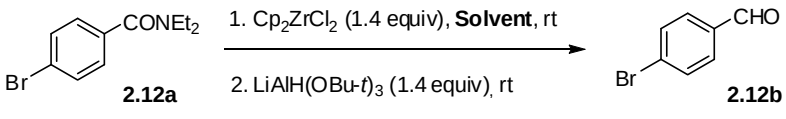
2.12a **2.12b**

Entry	Reductant	Equiv. of Reductant	Time (min)	Isolated Yield of **2.12b** (%)
1	$LiAlH(OBu\text{-}t)_3$	1.4	2	96
2	$LiBH(s\text{-}Bu)_3$	1.4	2	91
3	$LiAlH_4$	0.35	2	66[a]
4	DIBAL-H	1.4	30	50[b]

[a] Byproducts (benzyl alcohol and benzylamine) were also detected by GC-MS in a ratio of 8:1:1 of aldehyde:alcohol:amine).
[b] Starting material was also isolated (38%).

A variety of solvents was screened for the *in situ* method and the results are tabulated in Table 2.7. Besides THF, DME, dioxane and CH_2Cl_2 were found to be suitable solvents for the reduction process (Table 2.7, entries 1-3 and 6). As expected, due to the low solubility of Cp_2ZrCl_2 in Et_2O and toluene, these solvents are not suitable for the *in situ* method although, irrespectively, a high yield of reduction product was obtained in toluene (entries 5 and 8). Moreover, when 2-Me THF and $CHCl_3$ were tested, the amide to aldehyde reductions did not proceed well, probably owing to the presence of trace amount of water in the solvents (entry 4 and 7). Therefore, the readily available anhydrous THF was chosen in further studies.

Table 2.7 Comparison of Solvents for the *in situ* Schwartz Reduction of 4-Bromobenzamide **2.12a**



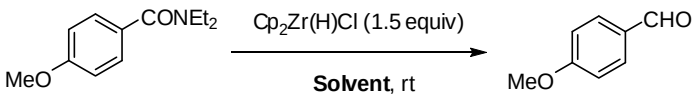
2.12a **2.12b**

Entry	Solvent	Time (min)	Isolated Yield (%)
1	THF	2	96
2	DME	2	97
3	Dioxane	8	96
4	2-MeTHF	10	84[a]
5	Et_2O[b] (low solubility)	8	75[a]
6	CH_2Cl_2	2	92
7	$CHCl_3$	8	80[a]
8	Toluene[c] (low solubility)	2	94

* Unless stated differently, solution concentrations were 0.1 - 0.3 M in substrate.
[a] Respectively with 8%, 18% and 19% starting material recovery (entries 4, 5 and 7).
[b] Carried out at 0.03 M of Cp_2ZrCl_2 concentration. The solution was not completely homogeneous.
[c] Carried out at 0.03 M of Cp_2ZrCl_2 concentration .

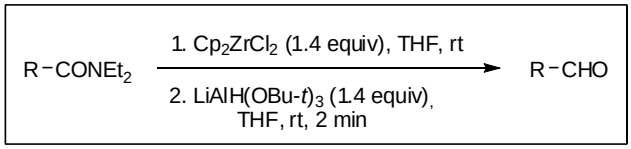
In spite of substrate differences, the above solvent effects are dramatically different in certain cases when compared to those observed by Georg[89] (Table 2.8). For examples, low or immeasurable yields were obtained by Georg when dioxane, chloroform and toluene were employed as solvents (Table 2.8, entries 3, 5 and 6), all of which were found to be successful solvents for the *in situ* method. Although the reasons are not clear, we suggest that the poor solubility of the solid Schwartz reagent in these solvents may affect the reduction efficiency greatly. Therefore, the *in situ* method for generating the Schwartz reagent appears to have an advantage over the Georg method.

Table 2.8 Comparison of Solvents in the Direct Reduction Reported by Georg[89]



Entry	Solvent	Time (min)	Isolated Yield (%)
1	THF	30	99
2	Oxetane	30	95
3	Dioxane	30	15
4	Pyridine	30	15
5	$CHCl_3$	30	0
6	Toluene	30	15

Based on the results of screening of reductants and solvents above, a standard set of conditions for the *in situ* Schwartz reduction of amides to aldehydes was established (Scheme 2.14) which was then employed for the studies concerning scope and limitations of the reaction.

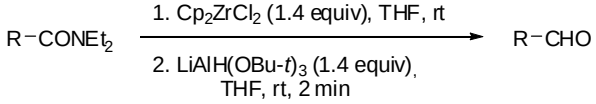


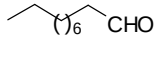
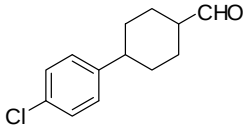
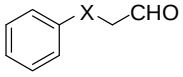
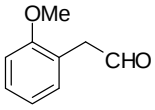
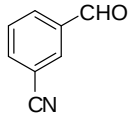
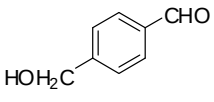
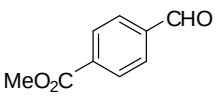
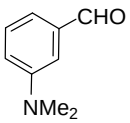
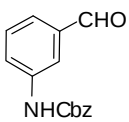
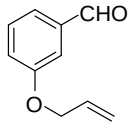
Scheme 2.14 Optimized Conditions for the *in situ* Schwartz Reduction of Amides to Aldehydes

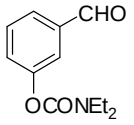
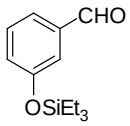
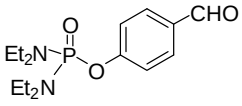
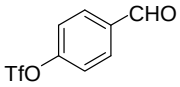
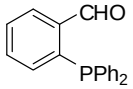
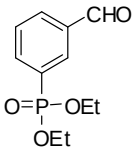
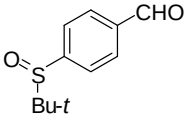
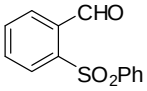
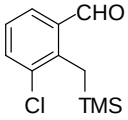
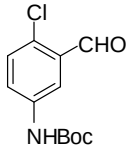
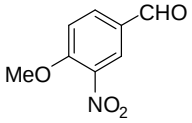
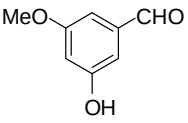
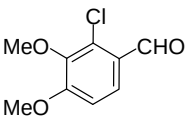
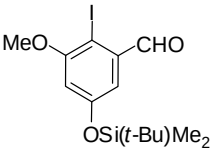
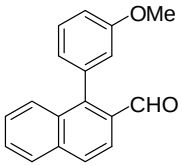
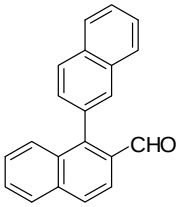
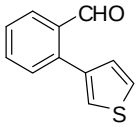
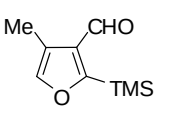
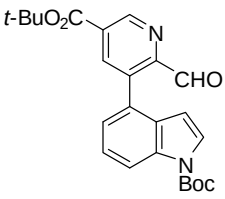
The initial studies showed that the *in situ* Schwartz reduction of benzamides was an efficient and robust process. The optimized conditions (Scheme 2.14) were then applied in the examination of the reduction of a variety of amides and the results are shown in Table 2.9. As expected, aliphatic amides **2.35-2.39** underwent the *in situ* Schwartz reduction in good yields (Table 2.9). Of these, linear amides **2.35** and **2.37-2.39** were reduced in 2 min, but a prolonged time and more reductant were required for reduction of branched amides **2.36** presumably due to steric hindrance. Excellent functional group tolerance was found in reduction of aromatic amides.

Thus, alkene, halogen, nitrile, nitro, ester, amino, NHCbz, NHBoc, OTf, $OCONEt_2$, $OP(O)(NEt_2)_2$, S(O)Bu-*t*, SO_2Ph, $P(O)(OEt)_2$ and TMS, were found to be stable to the reduction conditions. For substrates **2.41** and **2.48** bearing unprotected OH groups, a reverse addition procedure was required, that is, a solution of Cp_2ZrCl_2 (1.4 equiv) was added to a solution containing the substrate and $LiAlH(OBu\text{-}t)_3$ (2.4 equiv), in which an additional equivalent of the reductant was present to account for the reaction with the OH group. Heterocycles such as furan, thiophene, pyridine and indole survived under the *in situ* reduction conditions (**2.53, 2.21b** and **2.54**). *Ortho*-substituted benzamides prepared by DoM chemistry performed well under the reduction conditions to give corresponding benzaldehydes in good yields (**2.43, 2.18b, 2.49, 2.50, 2.21b** and **2.54**). These results establish a synthetically useful connection between benzamide *in situ* Schwartz reduction and DoM chemistry. Moreover, high yields were obtained in reduction of several substrates linked to the Ru-catalyzed amide-directed C-O activation/coupling reaction (**2.51-2.53**), new chemistry which we have developed (see Chapter 3).

Table 2.9 Reduction of N,N-Diethyl Amides via the *in situ* Schwartz Method



				
2.35 87%*	**2.36** 83%[a]	**2.37**, 86% (X = CH_2) **2.38**, 91% (X = O)	**2.39** 87%	**2.40** 94%[b]
				
2.41 93%[c]	**2.1b** 90%[d]	**2.2b** 81%	**2.4b** 99%[d]	**2.5b** 91%

				
2.6b 93%	**2.42** 91%[b]	**2.7b** 91%	**2.8b** 95%	**2.43** 93%[d]
				
2.11b 97%	**2.44** 95%	**2.45** 92%	**2.18b** 87%	**2.46** 77%[a]
				
2.47 83%[b]	**2.48** 80%[c]	**2.49** 97%[a]	**2.50** 97%[a]	**2.51** 90%
				
2.52 89%	**2.53** 88%	**2.21b** 77%[b]	**2.54** 67%[a]	

* Yields of isolated and purified products.

[a] Different conditions (equiv/min) were used as a function of substrate: 2.0/30 (**2.36** and **2.46**); 1.5/20 (**2.49**); 1.8/20 (**2.50**); 1.8/30 (**2.54**).

[b] Different reaction times were used as a function of substrate: 10 min (**2.40** and **2.42**); 20 min (**2.47** and **2.21b**).

[c] The reaction was carried out via reverse addition: a solution of Cp_2ZrCl_2 (1.4 equiv) was added to a solution of substrate and $LiAlH(OBu\text{-}t)_3$ (2.4 equiv).

[d] Different equivalents of the *in situ* Schwartz reagent were used as a function of substrate: 1.6 equiv (**2.1b**); 2.0 equiv (**2.4b**); 1.8 equiv (**2.43**).

The above results show that, compared with the Georg method, the *in situ* protocol is a more efficient process for the amide to aldehyde reduction. Besides advantages of high yields and very short reaction times, the *in situ* method highly suppresses side reactions. For examples, over-reduction or hydrozirconation which complicate the reduction of 3-NHCbz benzamide **2.4a** and

3-allyloxy benzamide **2.5a** by using the Georg method (Fig. 2.2), are not observed respectively under the *in situ* reduction conditions, smoothly affording products **2.4b** and **2.5b** in excellent yields (Fig. 2.2).

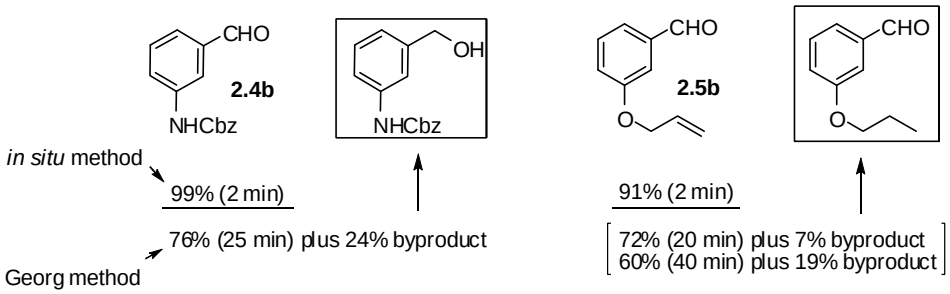
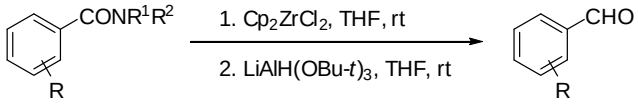


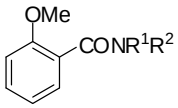
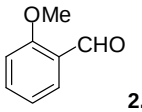
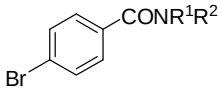
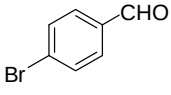
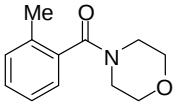
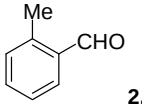
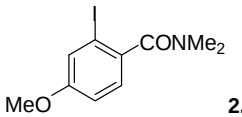
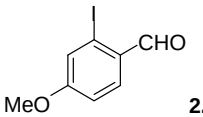
Fig. 2.2 Comparison of the Georg and *in situ* Schwartz Reduction Methods

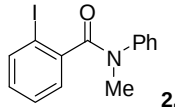
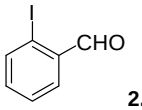
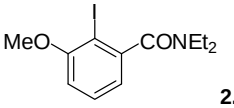
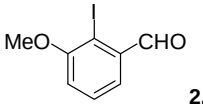
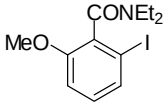
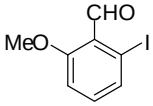
To broaden the scope of the *in situ* reduction method, differentially N,N-disubstituted benzamides were investigated and the results are presented in Table 2.10. Steric hindrance was shown to affect the reduction greatly. Thus, a N,N-diethyl amide **2.12a** underwent the reduction in high yield, but the corresponding N,N-diisopropyl amide **2.56a** required a prolonged reaction time and excess reductant to obtain a good yield of the aldehyde product **2.12b** (Table 2.10, entries 5 and 6). Less-hindered amides **2.55a**, **2.26a**, **2.57a-2.59a** with mono *ortho*-substituents were reduced in high yields (entries 1, 2 and 7-9). However, corresponding mono *ortho*-substituted bulky amides such as N,N-diisopropyl- and N-ethyl-N-cumyl amides **2.27a**, **2.28a** were resistant to reduction (entries 3 and 4). In comparison, these cases underwent reduction in moderate yields under the Georg conditions (Table 2.4, entries 3 and 4). A 2,3-disubstituted benzamide **2.16a** was reduced in moderate yield under the standard conditions (entry 10), but use of excess amount of reductant (1.8 equiv) pushed the reduction to completion to furnish aldehyde product **2.50** (Table 2.9) in 97% isolated yield. In the case of a di-*ortho* substituted benzamide substrate **2.17a**, no reaction occurred even when using 2 equivalents of reductant for a 2 h

reaction period (entry 11). Previously, a 26% yield of **2.17b** was obtained under the Georg conditions (Table 2.3, entry 4). On the basis of these comparative results, it appears that steric effects play a more significant role in the *in situ* method compared to the Georg method, which is presumably due to the mediation of $Cp_2Zr(H)Cl$-$Al(OBu\text{-}t)_3$ complexes generated in the *in situ* method.

Table 2.10 Reduction of Differentially N,N-Disubstituted Tertiary Amides via *in situ* Schwartz Method

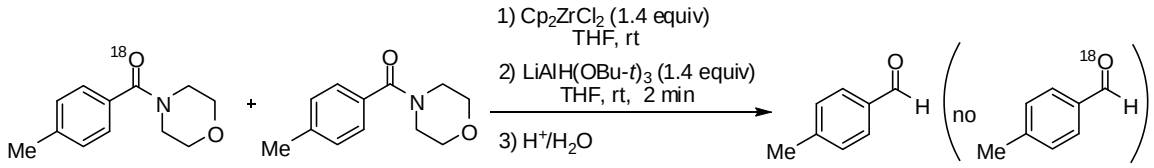


Entry	Amide	*In situ* Schwartz Reagent (equiv)	Time (min)	Product	Yield (%)[a]
				 **2.26b**	
1	R^1,R^2 = Me, Me (**2.55a**)	1.4	2		94
2	= Et, Et (**2.26a**)	1.4	2		93
3	= Et, cumyl (**2.28a**)	2.2	60		trace
4	= *i*-Pr, *i*-Pr (**2.27a**)	2.2	60		trace
				 **2.12b**	
5	R^1,R^2 = Et, Et (**2.12a**)	1.4	2		96
6	= *i*-Pr, *i*-Pr (**2.56a**)	2.2	25		88
7	 **2.57a**	1.4	2	 **2.57b**	95
8	 **2.58a**	1.4	8	 **2.58b**	89

9	 **2.59a**	1.4	7	 **2.59b**	90
10	 **2.16a**	1.4	25	 **2.16b**	46[b]
11	 **2.17a**	2	120	 **2.17b**	n.d.[c]

[a] Yields of isolated and purified products.
[b] Starting material (53%) was recovered.
[c] Starting material (95%) was recovered.

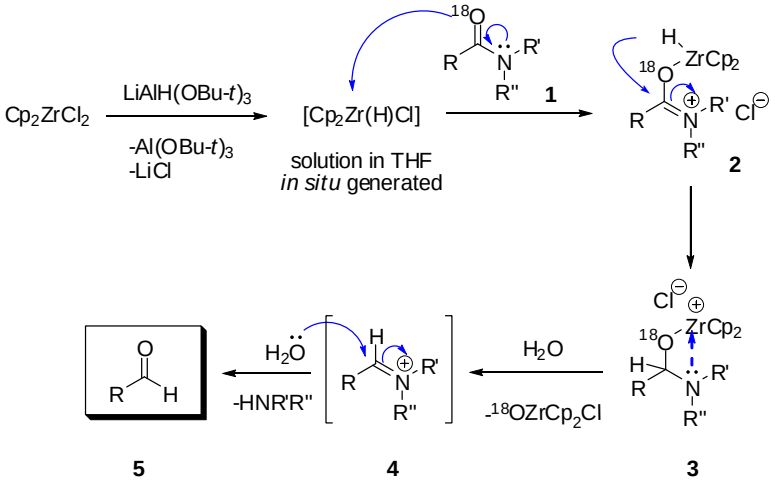
In order to determine the source of the oxygen of CHO in the *in situ* reduction product, an ^{18}O-labeled mixture of 4-methyl benzamides **2.60a, 2.61a** (O^{18}/O^{16} = 1 : 1) was chosen. Treatment of the ^{18}O-labeled mixture (**2.60a** and **2.61a**) with the *in situ* reductant for 2 min, followed by quench with normal isotopic H_2O^{16} water, and workup and purification, gave 4-methyl benzaldehyde **2.61b** was obtained in 97% isolated yield with complete loss of O^{18} (O^{18}/O^{16} < 1/100) as confirmed by HRMS (Scheme 2.15). This observation indicates that the oxygen of CHO in the *in situ* reduction product is derived from the H_2O^{16} water used for the quench of the reaction and is consistent with the results reported by Georg which involved addition of ^{18}O-labeled water (O^{18}/O^{16} = 1 : 1) to a Schwartz reduction of 4-methoxy-N,N-diethylbenzamide to finally form the ^{18}O-labeled aldehyde product with the ratio of O^{18}/O^{16} = 1 : 1).[89]



2.60a + **2.61a** (0.2 mmol ($^{18}O/O$ = 1/1)) → **2.61b** (97%) + **2.60b**

Scheme 2.15

Based on the above result and mechanistic studies by Georg,[89] we propose the following mechanism for the *in situ* Schwartz reagent reduction of amides (Scheme 2.16). The first step in the 3-component process is *in situ* generation of the [$Cp_2Zr(H)Cl$] which, once formed, immediately undergoes reaction with amide **1** to give intermediate **2**. After a hydride transfer as depicted in **2**, a zirconated tetrahedral intermediate **3** is formed which, by virtue of Zr-N coordination, is stabilized until water quench. Upon hydrolysis, the tetrahedral intermediate **3** collapses by C-O bond cleavage to give the iminium salt **4** which finally affords the aldehyde product **5** by hydrolysis. The isotopic ^{18}O experiment (Scheme 2.15) together with other results from Georg's laboratories including evidence from ^{1}H and ^{13}C NMR studies (Scheme 2.10) supports this mechanism. However, direct observation for the existence of iminium salt intermediate **4** is still not available due to inability to detect the iminium species **4** by React-IR, in which ν_{max} ~1680 cm^{-1} (iminium salt stretching vibrations) did not show up during reduction of N,N-diethyl *ortho*-anisamide by the Schwartz reagent.[128] This is consistant with the results from IR studies by Georg.[89]



Scheme 2.16

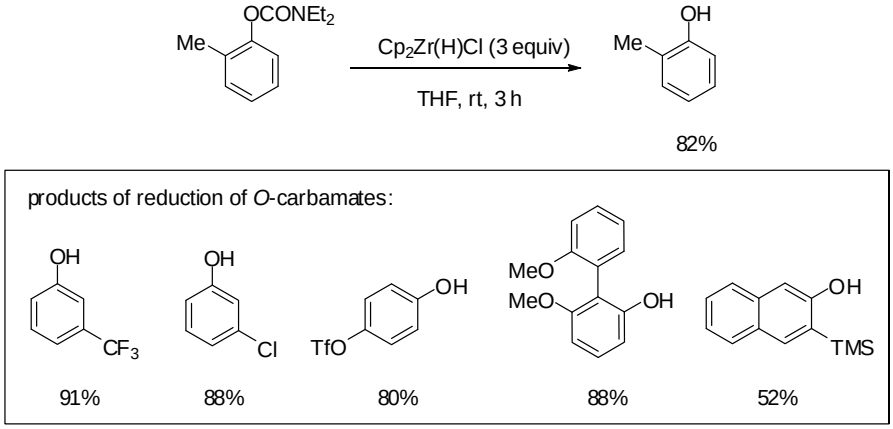
$LiAlH(OBu\text{-}t)_3$ has been found as an excellent reductant for the *in situ* Schwartz reduction of aliphatic, aromatic and heteroaromatic tertiary amides to the corresponding aldehydes. In this one pot procedure, $LiAlH(OBu\text{-}t)_3$ is directly added to a solution containing a substrate and Cp_2ZrCl_2 at room temperature. It may be postulated that these conditions avoid the generation of the THF-insoluble Schwartz reagent and provide a more reactive reagent in solution thereby effecting efficient and rapid (minutes) reduction of amides. A further major advantage of the *in situ* method is the inexpensive reagents ($LiAlH(OBu\text{-}t)_3$ 1M solution in THF–US$ 580/mol and Cp_2ZrCl_2–US$ 700/mol, in comparison with $Cp_2Zr(H)Cl$–US$ 3,020/mol)[129] which are stable at room temperature for long term storage. Moreover, as shown in Table 2.6, $LiBH(s\text{-}Bu)_3$ is also a good reductant for the *in situ* amide reduction.

Moreover, after our investigation, it is noteworthy that $Cp_2TiCl_2/LiAlH(OBu\text{-}t)_3$ cannot make such good reduction of tertiary amides to aldehydes as $Cp_2ZrCl_2/LiAlH(OBu\text{-}t)_3$.

The demonstration of the high efficiency of the *in situ* Schwartz reagent method ($Cp_2ZrCl_2/LiAlH(OBu\text{-}t)_3$) for amide reduction encouraged its expansion to other chemistry.

2.3.2.2 Reductive Cleavage of Aromatic *O*-Carbamates to Phenols by the *in situ*–Generated Schwartz Reagent

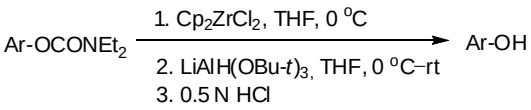
During the course of the amide reduction research as described above, my colleague, Justin Morin tested the Schwartz reagent for the reductive cleavage of aromatic *O*-carbamates.[120] In the event, the desired reaction proceeded in good yields but required longer reaction times (hours) and 3 equivalents of Schwartz reagent (Scheme 2.17).

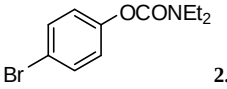
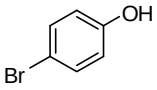
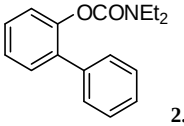
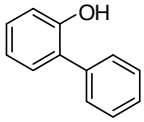
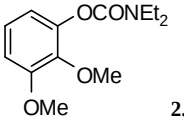
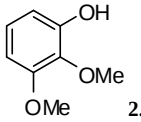
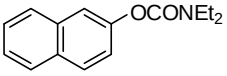
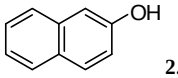
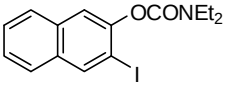
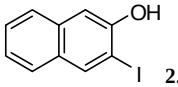
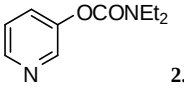
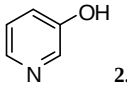


Scheme 2.17[120]

The above achievement by Morin[120] and success of the amide to aldehyde reduction by *in situ* Schwartz reagent method motivated the application of the *in situ* method to the reductive cleavage of aromatic *O*-carbamates. As shown in Table 2.11, the *in situ* method was demonstrated to be a very effective method for the reductive cleavage of aryl *O*-carbamates to phenols. Other than the Schwartz reagent in the *in situ* amide reduction (no precipitate formed), in terms of visual observation, the *O*-carbamate cleavage reaction showed the appearance of major precipitation which is assumed to be Schwartz reagent, presumably due to slow formation of the tetrahedral intermediate referred to in Scheme 2.16. However, after several hours, the reductive cleavage was completed (TLC analysis) and led to good yields of isolated products **2.62b-2.67b** (Table 2.11). Thus, overall, in comparison with the direct Schwartz reagent reduction, the *in situ* method is a more efficient and less expensive process for the reductive cleavage of aromatic *O*-carbamates to phenols which, by these preliminary studies appears to tolerate all functional groups previously established for the Georg method.[89,88]

Table 2.11 Reductive Cleavage of Aryl *O*-carbamates to Phenols via the *in situ* Schwartz Method

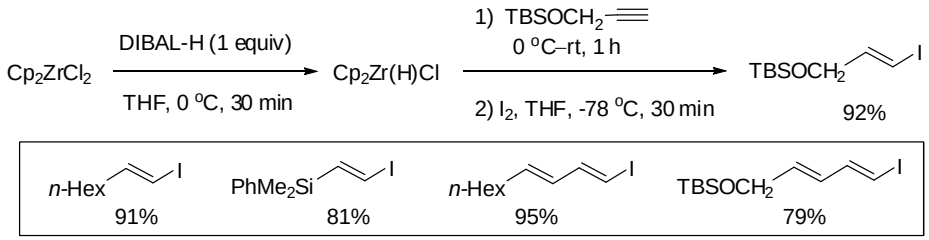


Entry	Substrate	Equiv. of *In situ* Schwartz Reagent	Time	Product	Yield (%)[a,b]
1	 **2.62a**	3.0	3 h	 **2.62b**	96 (88)
2	 **2.63a**	3.0	3 h	 **2.63b**	89 (88)
3	 **2.64a**	3.0	3 h	 **2.64b**	90 (78)
4	 **2.65a**	3.0	3 h	 **2.65b**	95 (81)
5	 **2.66a**	3.0	5 h	 **2.66b**	81
6	 **2.67a**	3.0	3 h	 **2.67b**	90 (87)

[a] Yields of isolated and purified products.
[b] Yields in parentheses represent those obtained by the Georg method (direct use of the Schwartz reagent).

2.3.2.3 Other Application of the *in situ*–Generated Schwartz Reagent

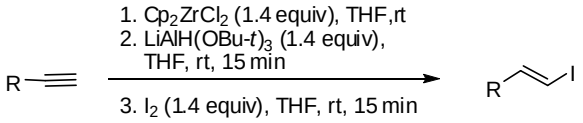
A three-step, one-pot process for conversion of alkynes to *E*-iodoalkenes using Cp_2ZrCl_2/DIBAL-H was reported by Negishi in 2006.[117] Good yields of products were obtained in this regio- and stereo-selective conversion (Scheme 2.18).

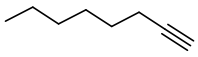
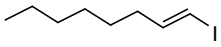
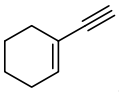
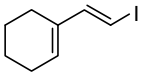
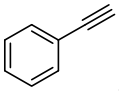
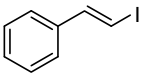


Scheme 2.18

With the aim of establishing the *in situ* method for the enhancement and abbreviation of the above Negishi chemistry, we briefly examined the conversion of several alkynes to the corresponding *E*-iodoalkenes via the *in situ* reduction method. The results, summarized in Table 2.12, demonstrate that aliphatic and aromatic alkynes **2.68a-2.70a** undergo conversion to the expected *E*-iodoalkenes **2.68b-2.70b** in high yields under simple reaction conditions (Table 2.12, entries 1-3). Notably, in contrast to the low reaction temperatures (0 °C and -78 °C) required for the Negishi method (Scheme 2.18), the new one-pot procedure involving the *in situ* method may be conducted at room temperature with high efficiency and simplicity, for example, 91% yield of **2.68b** by the *in situ* method was the same as that by the Negishi method (Scheme 2.18). Therefore, it may be anticipated that the *in situ* protocol may replace the Negishi method as a mild, efficient, and regio- and stereo-selective conversion of alkynes to *E*-iodoalkenes. The resulting *E*-olefins are useful for the important Negishi cross coupling procedures.

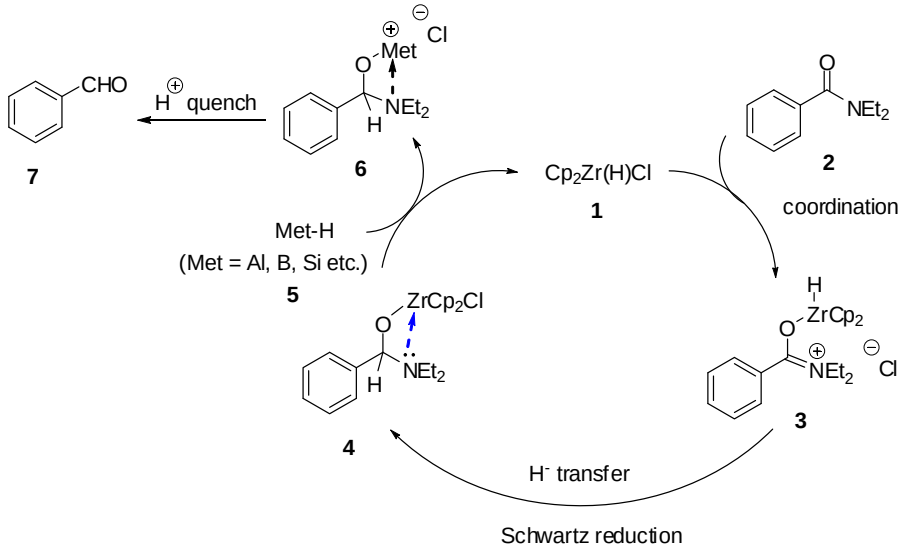
Table 2.12 Regio-and Stereo-selective Conversion of Alkynes to *E*-Iodoalkenes via *in situ* Schwartz Reagent Method



Entry	Substrate	Product	Isolated Yield (%)
1	 **2.68a**	 **2.68b**	91
2	 **2.69a**	 **2.69b**	91
3	 **2.70a**	 **2.70b**	94

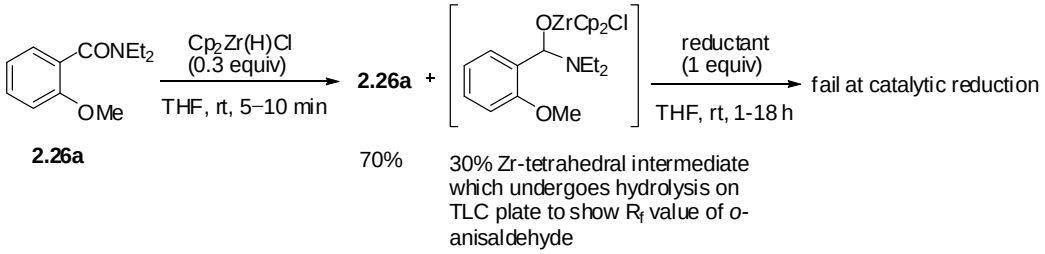
2.3.3 Attempts on Catalytic Reduction of Tertiary Amides to Aldehydes by the Schwartz Reagent

Due to the high cost of the Schwartz reagent (US$ 28/g), we aimed, based on the discovery of the *in situ* method, to discover a reduction process by catalytic amounts of the Schwartz reagent instead of the currently used stoichiometric amounts. The expected catalytic Schwartz reduction must have the following features in a catalytic cycle (Scheme 2.19): i) a reductant **5** employed in stoichiometric amounts can reduce -$ZrCp_2Cl$ to regenerate the Schwartz reagent **1** from Zr-intermediate **4** which is initially formed by catalytic amounts of Schwartz reagent **1**; ii) the amide substrate **2** must be inert to the reductant **5**; iii) the Met-intermediate **6** must be stable during the catalytic process until quench.



Scheme 2.19

A variety of reductants such as LiAlH(OBu-*t*)$_3$, DIBAL-H, TMSCl/ DIBAL-H, BH_3, $NaBH_4$, $NaBH_3CN$, MeI/$NaBH_3CN$, $NaBH(OAc)_3$, Cl_3SiH and Et_3SiH were employed for testing a catalytic reduction initiated by catalytic amounts of Schwartz reagent. Unfortunately, to date, all attempts to achieve a catalytic reduction process have failed (Scheme 2.20). We surmise that the regeneration of the Zr-H species (Schwartz reagent) did not occur.



Scheme 2.20

2.4 Conclusions

An *in situ* Schwartz reagent methodology for the general, highly efficient and practical reduction of amides to aldehydes and *O*-carbamates to phenols has been established. Furthermore, the use of *in situ* protocol for the hydrozirconation of alkynes to *E*-iodoalkenes has been demonstrated.

The *in situ* Schwartz method has the following features: i) avoidance of the step for the separate preparation of the Schwartz reagent and its over-reduction to Cp_2ZrH_2 which existed in the previous direct use of the reagent;[94,118,119] ii) generation of a Schwartz reagent which provides a more reactive reagent compared to that prepared in direct fashion; iii) high efficiency in amide to aldehyde reduction with excellent functional group tolerance (e.g. alkene, halogen, nitrile, nitro, ester, amino, NHCbz, NHBoc, OTf, $OCONEt_2$, $OP(O)(NEt_2)_2$, S(O)Bu-*t*, SO_2Ph, $P(O)(OEt)_2$ and TMS); iv) lower cost: above 50% cost reduction compared to direct use of the Schwartz reagent ($LiAlH(OBu\text{-}t)_3$ 1M solution in THF–US$ 580/mol and Cp_2ZrCl_2–US$ 700/mol, in comparison with $Cp_2Zr(H)Cl$–US$ 3,020/mol)[129]; v) less sensitivity in handling, and advantage of long-time storage of both reagents, $LiAlH(OBu\text{-}t)_3$ (1M solution in THF) and Cp_2ZrCl_2 compared to the Schwartz reagent which is sensitive to air, light and moisture.[94]

A patent for the *in situ* Schwartz reagent reduction has been granted.[130]

2.5 Utility of the *in situ*–Generated Schwartz Reagent Methodology

The broad utility and application of the *in situ* Schwartz reagent methodology may be anticipated. It is a convenient and practical method to replace any reaction which has been achieved by the use of the Schwartz reagent. Our work has demonstrated its use in the efficient reduction of amides to aldehydes and aryl *O*-carbamates to phenols, and in some

hydrozirconation reactions. Notably, the *in situ* Schwartz reduction, when connected to DoM chemistry of benzamides and aryl *O*-carbamates provides new routes to polysubstituted aromatic and heteroaromatic aldehydes and phenols which are not available or difficult to prepare by conventional aromatic chemistry. Thus, the *in situ* method may provide access to new commodity molecules that, aside from having intrinsic value, may be useful for conversion to substances that can benefit human health and material resources. The synthesis of paclitaxel, an anticancer drug employing the secondary amide to imine reduction as the key step, demonstrates the value of the Schwartz reagent (Scheme 2.8).[110]

2.6 Future Work

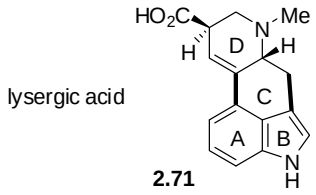
Only tertiary amide reductions to aldehydes, reductive cleavages of aryl *O*-carbamates to phenols, and limited hydrozirconation reactions have been investigated in our research. The expansion of the *in situ* method to other reactions such as secondary amide reduction and hydrozirconation-type reactions may be beneficially considered in the future.

NMR studies on determining the mechanistic process of the *in situ* method are needed, which may indicate the formation of intermediates and help demonstrate this 3-component reaction in detail.

The development of a catalytic method for the reduction of amides to aldehydes using the Schwartz reagent is still an interesting and challenging future research project.

2.7 Formal Synthesis of Lysergic Acid: Application of the D*o*M Strategy and Amide to Aldehyde Reduction by the Schwartz Reagent

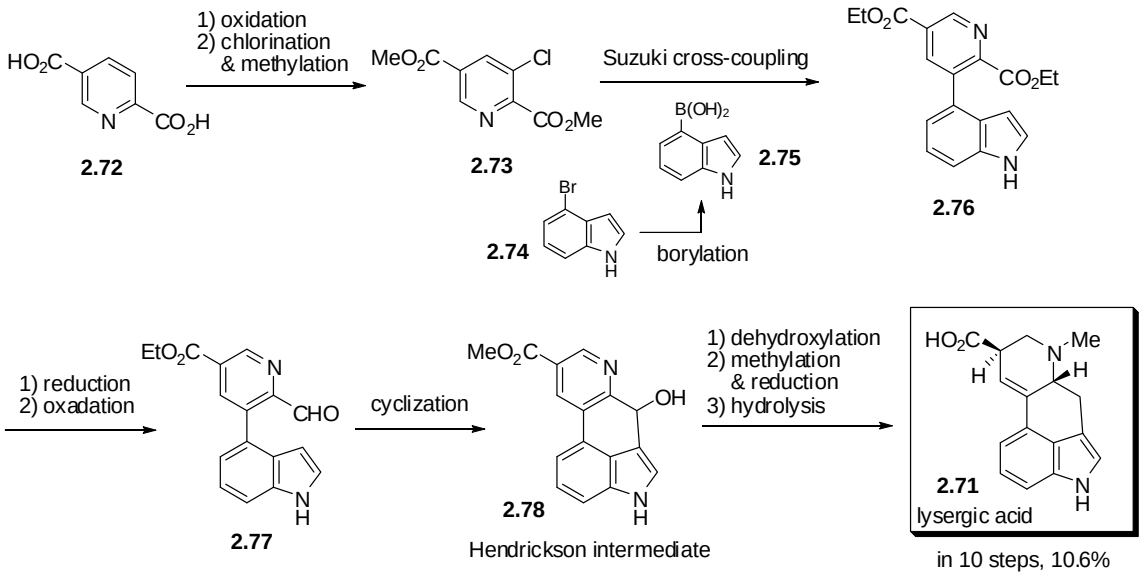
Lysergic acid (Fig. 2.3) is a representative of the Ergot alkaloids which possess the widest biological activity found in any family of natural products.[131,132] Since the first total synthesis of racemic lysergic acid by Woodward and co-workers in 1956,[133] this unique structure, exhibiting the tetracyclic ergoline skeleton which contains a tetrahydropyridine and a C3-C4 fused indole, has attracted the interest of synthetic chemists. To date, eleven syntheses of lysergic acid have been reported.[134-143,133]



2.71

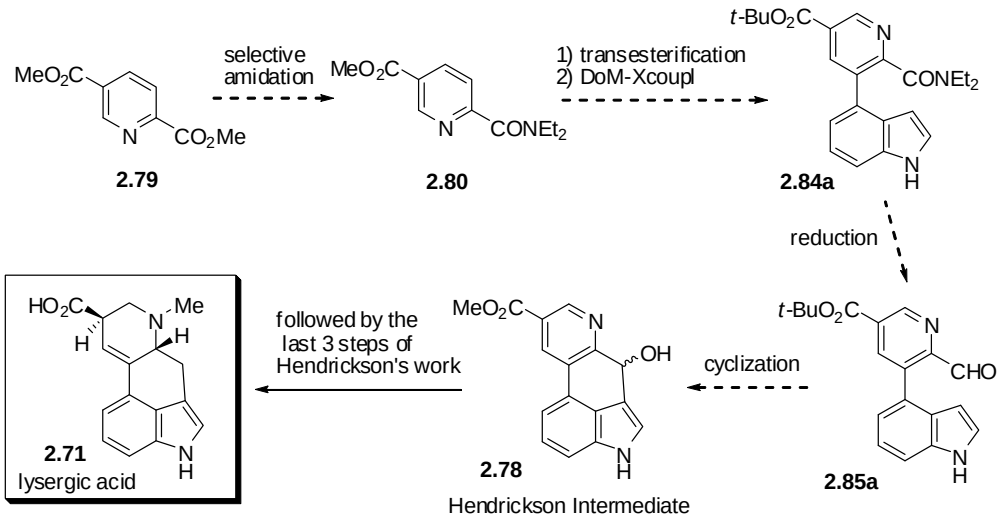
Fig. 2.3 Lysergic Acid

Of these, Hendrickson's total synthesis is a short and practical route which proceeds in 10 steps with 10.6% overall yield starting from simple commercially available materials (**2.72** and **2.74**) (Scheme 2.21).[136] Notably, while most reported syntheses use cyclization strategies for the construction of B and/or D rings, the Hendrickson route employs, for the first time, a cross coupling reaction between pyridine and indole moieties (**2.73** and **2.75**) which provides brevity in the overall synthesis by simple closure of ring C.



Scheme 2.21 Hendrickson's Total Synthesis of Lysergic Acid

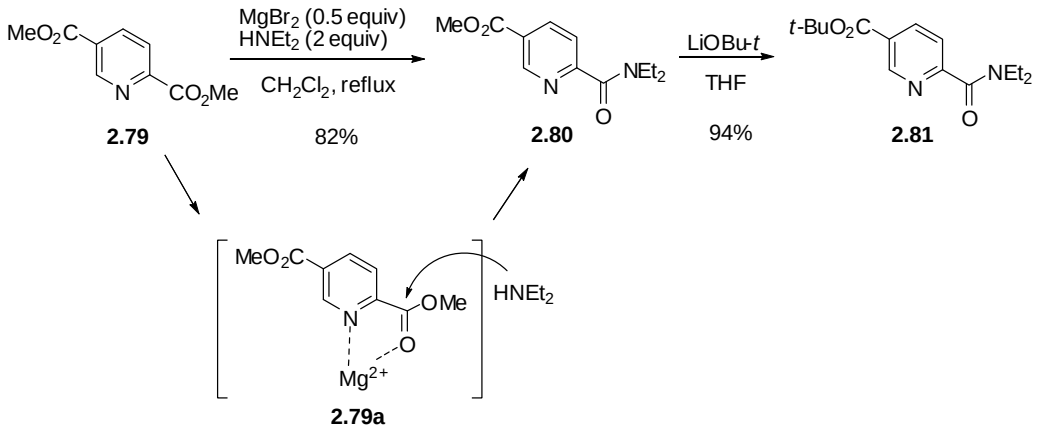
Inspired by success of Hendrickson's total synthesis and our *in situ* Schwartz reagent amide reduction results, we designed a new route towards the synthesis of lysergic acid **2.71** (Scheme 2.22) using a Directed *ortho* Metalation (D*o*M)-Suzuki cross coupling strategy which intercepts the Hendrickson cyclization-intermediate[136] **2.78** (Scheme 2.21) in a potentially more concise and efficient manner. The key steps are selective amidation, D*o*M-Suzuki cross coupling reaction and chemoselective amide to aldehyde reduction using the newly developed *in situ* Schwartz reagent method.



Scheme 2.22 Our Designed Route to the Synthesis of Lysergic Acid

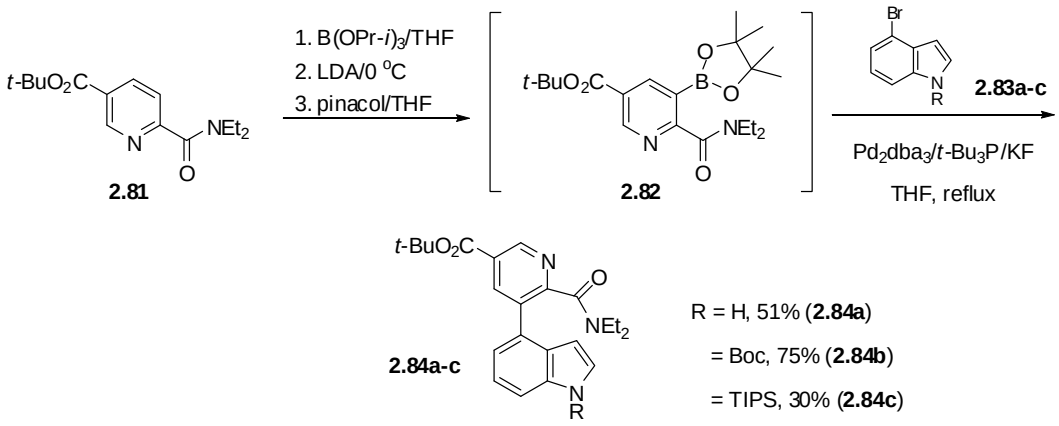
2.7.1 Results and Discussion

Starting from commercially available pyridine-2,5-dicarboxylic acid dimethyl ester **2.79**, the selective amidation to the picolinamide **2.80** was effected in 82% according to the excellent procedure[144] developed by Guo and co-workers. During this reaction, it is reasonable to assume that a substoichiometric amount of $MgBr_2$ plays a role in generating the selectivity by Mg^{2+} coordination with N of pyridine and O of 2-CO_2Me **(2.79a)** to provide higher reactivity of 2-CO_2Me to attack by amine compared to that of the 5-CO_2Me ester (Scheme 2.23). Even when an excess of the amine was employed, the 5-CO_2Me ester was still inert to amidation. Then, the use of the picolinamide **2.80** for LDA-mediated DoM is precluded owing to side reactions which were discovered by Andrew Larkin in previous approach to the total synthesis of lysergic acid:[145] i) amidation of the C5 ester by LDA attack; ii) intermolecular self-condensation of the DoM-formed C3-pyridine anion with the 5-CO_2Me of **2.80**. To avoid these difficulties, methyl to *t*-butyl ester transesterification[146] was conducted to afford compound **2.81** (Scheme 2.23).



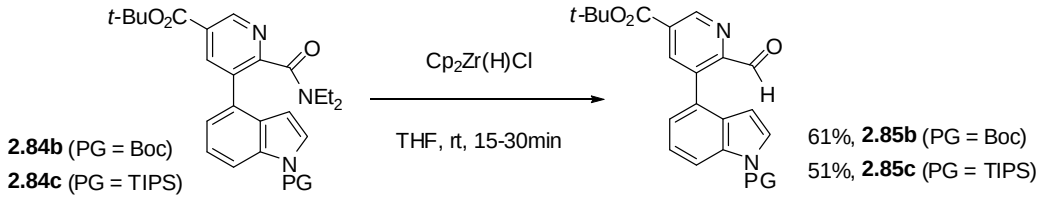
Scheme 2.23 Selective Amidation and Transesterification

Based on the one-pot DoM-Suzuki cross coupling method[147] reported by Alessi, Larkin and co-workers in our group, the one-pot process, **2.81** → **2.84**, was developed with moderate to good yields involving Pd_2dba_3/*t*-Bu_3P/KF/THF coupling conditions. In this process, a DoM-borylation of the amide **2.81** was conducted first to give boropinacolate intermediate **2.82** which was not isolated due to instability and directly subjected to Suzuki cross coupling with 4-bromoindoles **2.83** to afford the expected product **2.84** (Scheme 2.24). When the 4-bromoindole **2.83a** was employed, compound **2.84a** was obtained in 51% yield. However, using the N-Boc protected 4-bromoindole **2.83b** as a coupling partner, the one-pot reactions proceeded more efficiently to give **2.84b** in 75% yield. The use of TIPS-protected indole **2.83c** afforded **2.84c** in low yield (30%) presumably due to flouride-mediated desilylation. In order to improve the yield of the key intermediate **2.84**, other Suzuki cross coupling conditions, such as $Pd(PPh_3)_4/Cs_2CO_3$ and $Pd(OAc)_2$/S-Phos/K_3PO_4, were examined for the one-pot process but without success. Under these conditions, byproducts of desilylation, deborylation and debromination increased greatly resulting in low yields of cross coupling product **2.84.**



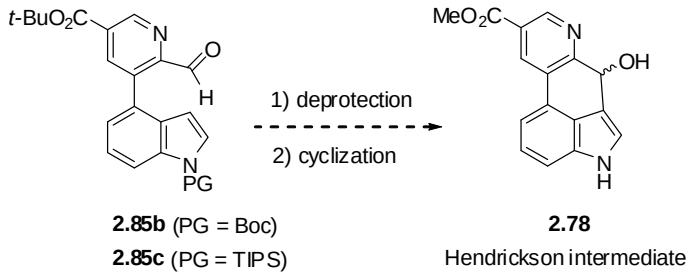
Scheme 2.24 D*o*M-Suzuki Cross Coupling Reaction

The decision to attempt the Schwartz reagent ($Cp_2Zr(H)Cl$) reduction of amide to aldehyde, **2.84 → 2.85**, according to the procedure of Georg[88] was a major event in our laboratories and initiated the generalization of the reaction and discovery and development of the *in situ* protocol described above. When N-H unsubstituted indole **2.84a** was treated with freshly prepared $Cp_2Zr(H)Cl$, total decomposition of starting material was observed without any isolable product. However, fortunately, when the N-protected indoles **2.84b** and **2.84c** were tested for the reduction, the expected products **2.85b** and **2.85c** respectively were isolated in moderate yields (Scheme 2.25). Moreover, **2.84b** was also examined in the reduction via *in situ* Schwartz reagent method and afforded **2.85b** in 67% yield.



Scheme 2.25 Chemoselective Amide to Aldehyde Reduction

With **2.85b** and **2.85c** in hand, only two steps (deprotection and cyclization) remain to reach the Hendrickson intermediate[136] **2.78** (Scheme 2.26).



Scheme 2.26 Proposed Conversion of Aldehydes **2.85b-c** to the Hendrickson Intermediate **2.78**

2.7.2 Conclusion and Future Work

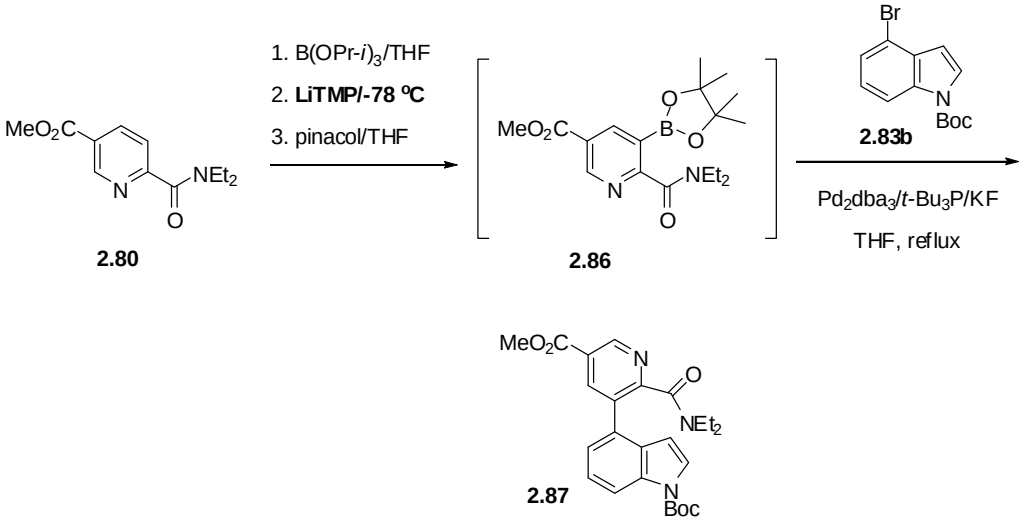
A short formal synthesis of lysergic acid has been developed which features selective amidation, a combined D*o*M-Suzuki cross coupling reaction and selective Schwartz reagent amide to aldehyde reduction. The remaining steps (TBAF/THF/5 min; NaOMe/MeOH/3 h) from aldehyde **2.85c** to intercept the Hendrickson intermediate **2.78**, were carried out once but on a small scale (NMR tube) which not allow full structural assignment of the product. Although the presently employed protection and deprotection steps will add two steps, an overall total synthesis (10 steps), the total synthesis will not be longer than that reported by Hendrickson.[136]

For the conclusion of the formal total synthesis of lysergic acid, the following modifications are proposed for experimentation:

i) as known, the CO_2Et function is tolerated under LiTMP/-78 ^oC conditions.[148] Therefore, application of these conditions to the DoM chemistry of **2.80** may avoid the necessity of the transesterification step and therefore save one synthetic step (Scheme 2.27).

ii) achievement of the modification i) will allow attempts to effect the de-Boc step on the methyl ester **2.87** which, in contrast to the CO_2Bu-*t* group, tolerates acidic conditions.

If these modification steps are successful, the synthesis of the Hendrickson intermediate **2.78** will be completed in 6 steps which compares favorably to the Hendrickson route of **2.78** in 7 steps.



Scheme 2.27

2.8 Experimental Section

General Methods

Melting points were obtained on a Fisher Scientific Melting Point Apparatus and are uncorrected. IR spectra were recorded on a BOMEM FT-IR or Varian 1000 FT-IR spectrometers. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance-400 or 500 MHz spectrometers. The chemical shifts of ^1H and ^{13}C NMR signals are quoted relative to internal C*H*Cl_3 (δ = 7.26) and *C*DCl_3 (δ =77.0) or tetramethylsilane (δ = 0.0). ^1H NMR data are reported as follows: chemical

shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, etc.), coupling constant (Hz) and relative intensity. ^{13}C NMR data are reported as follows: chemical shift in ppm (δ). The GC-MS analyses were performed on an Agilent 6890 GC coupled with an agilent 5973 inert MS under EI conditions. High resolution mass spectra were obtained on a GCT Mass Spectrometer (Waters, Micromass) and a QSTAR XL hybrid mass Spectrometer (Applied Biosystems/MDS Sciex). The React-IR study was carried out with a Mettler Toledo ReactIR™ 4000 equipped with a SiComp sensor.

The Schwartz reagent was prepared according to the Buchwald procedure[118] and was stored in a desiccator. Partial decomposition (color change from pale to light yellow) was noted under prolonged storage. Amide substrates were obtained from Snieckus group inventory or prepared from commercially available starting materials. All reduction experiments were carried out under an argon atmosphere in oven-dried glassware, using syringe-septum cap techniques. All Pd-catalyzed Suzuki cross coupling reactions were carried out under nitrogen in sealed vials (not dried). All reactions involving alkyllithiums were carried out under argon in flame-dried glassware, using syringe-septum cap techniques. Alkyllithiums were purchased from Sigma-Aldrich Chemicals Co. and titrated biweekly against N-benzylbenzamide.[149] LDA was freshly prepared before reactions by stirring a 1:1 mixture of dry diisopropylamine and *n*-BuLi at 0 ^{o}C in THF (0.5-1.0 M) for 30 min. Anhydrous THF was obtained by treatment under the Pure-Solv SPS-4-4 solvent purification system (Innovative Technology, Inc.). $Pd(PPh_3)_4$ and $Pd_2(dba)_3$ were obtained from Strem Chemicals, Inc., USA. All purchased chemicals were used without further purification. Flash column chromatography was carried out using Silicycle Silia-P silica gel (particle size: 40-60 μm, 60A).

General Procedures

A. Reduction of Amides to Aldehydes Using the Schwartz Reagent (Georg Method)

To a suspension of $Cp_2Zr(H)Cl$ (1.5-3.0 equiv) in THF at rt was added a solution of an amide in THF. The resulting mixture was stirred at rt for 9 min to 2 h and the reaction was monitored by TLC analysis. The reaction mixture was quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc. The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

B. Reductive Cleavage of Heterocyclic N-amides Using the Schwartz Reagent

To a suspension of $Cp_2Zr(H)Cl$ (2-3 equiv) in THF at rt was added a solution of a N-amide in THF. The resulting mixture was stirred at rt for 15-60 min and the reaction was monitored by TLC analysis. The reaction mixture was quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc. The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

C. Reduction of Amides to Aldehydes by the *in situ*-Generated Schwartz Reagent (*in situ* Method)

To a solution of an amide and Cp_2ZrCl_2 (1.4-2.2 equiv) in THF at rt was rapidly added a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (1.4-2.2 equiv). The resulting solution was stirred at rt for 2-30 min and the reaction was monitored by TLC analysis. The reaction mixture was immediately

quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc or ether. The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

D. Reductive Cleavage of Aryl *O*-carbamates to Phenols by the *in situ*-Generated Schwartz Reagent (*in situ* Method)

To a solution of an aryl *O*-carbamate and Cp_2ZrCl_2 (3 equiv) in THF at 0 ^oC was added a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (3 equiv). The resulting mixture was warmed to rt and stirred for 3-5 h and the reaction was monitored by TLC analysis. The reaction mixture was quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc. The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

E. Reductive Cleavage of Heterocyclic N-amides by the *in situ*-Generated Schwartz Reagent (*in situ* Method)

To a solution of a heterocyclic N-amide and Cp_2ZrCl_2 (3 equiv) in THF at 0 ^oC was added a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (3 equiv). The resulting mixture was warmed to rt and stirred for 10 min and the reaction was monitored by TLC analysis. The reaction mixture was quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc. The combined organic extract was washed with brine, dried ($MgSO_4$) and

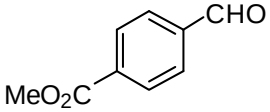
concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

F. Regio- and Stereo-selective Conversion of Alkynes to Iodoalkenes by the *in situ*-Generated Schwartz Reagent (*in situ* Method)

To a solution of an alkyne and Cp_2ZrCl_2 (1.4 equiv) in THF at rt was rapidly added a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (1.4 equiv). The resulting solution was stirred at rt for 15 min. Then, a solution of iodine (1.4 equiv) in THF was added. After additional stirring at rt for 15 min, the reaction mixture was quenched with a solution of 1 N HCl and extracted with ether. The combined organic extract was washed successively with saturated Na_2SO_3 and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

Experimental Procedures and Data

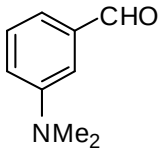
Methyl 4-formylbenzoate (**2.1b**, Table 2.2, entry 1)



According to General Procedure A and using the following materials and 25 min reaction time: methyl 4-(diethylcarbamoyl)benzoate (118 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (215 mg, ~90% purity, 0.75 mmol) and THF (3 mL), the title compound **2.1b** (75 mg, 92% yield) was obtained as a colorless solid. mp 61-62 ^oC (EtOAc/hexanes) (lit[150] mp 61-62 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.09 (s, 1H), 8.19 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H), 3.95 (s, 3H); ^{13}C NMR (101 MHz,

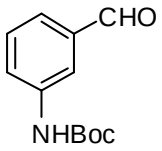
$CDCl_3$) δ ppm 191.55, 166.00, 139.12, 135.06, 130.15 (2C), 129.47 (2C), 52.53. The physical and spectral data were consistent with those previously reported.[150]

3-(Dimethylamino)benzaldehyde (**2.2b**, Table 2.2, entry 2)



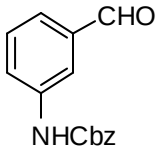
According to General Procedure A and using the following materials and 30 min reaction time: 3-(dimethylamino)-N,N-diethylbenzamide (154 mg, 0.70 mmol), $Cp_2Zr(H)Cl$ (291 mg, ~93% purity, 1.05 mmol) and THF (4 mL), the title compound **2.2b** (78 mg, 76% yield) was obtained as a yellow-green oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.22-7.13 (m, 2H), 6.97 (d, *J* = 7.3 Hz, 1H), 3.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 193.16, 150.74, 137.21, 129.55, 118.88, 118.25, 111.50, 40.37. The physical and spectral data were consistent with those previously reported.[151]

3-((*tert*-Butoxycarbonyl)amino)benzaldehyde (**2.3b**, Table 2.2, entry 3)



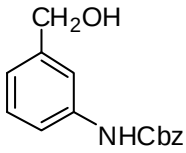
According to General Procedure A and using the following materials and 30 min reaction time: 3-((*tert*-butoxycarbonyl)amino)-N,N-diethylbenzamide (146 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (277 mg, ~93% purity, 1.0 mmol) and THF (2 mL), The title compound **2.3b** (91 mg, 82% yield) was obtained as a yellow solid. mp 90-91^{o}C (EtOAc/hexanes) (lit[152] mp 93 ^{o}C); IR (KBr) ν_{max} 3335, 1730, 1699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1H), 7.92 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 6.70 (brs, 1H), 1.53 (s, 9H);[152] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.14, 152.61, 139.37, 137.05, 129.56, 124.15, 124.00, 119.28, 81.01, 28.23 (3C). The physical and spectral data were consistent with those previously reported.[152]

3-((Benzyloxycarbonyl)amino)benzaldehyde (**2.4b**, Table 2.2, entry 4)



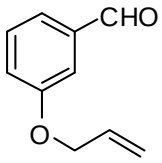
According to General Procedure A and using the following materials and 25 min reaction time: 3-((benzyloxycarbonyl)amino)-N,N-diethylbenzamide (163 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (277 mg, ~93% purity, 1.0 mmol) and THF (3 mL), the title compound **2.4b** (96 mg, 75% yield) was obtained as colorless solid. mp 105-106 ^oC (EtOAc/hexanes) (lit[153] mp 100-104 ^oC) IR (KBr) ν_{max} 3266, 1732, 1682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1H), 7.91 (s, 1H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.56 (d, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.43-7.32 (m, 5H), 7.14 (brs, 1H), 5.21 (s, 2H);[153] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.04, 153.26, 138.80, 137.07, 135.70, 129.70, 128.59, 128.41, 128.27, 124.62, 124.32, 119.29, 67.23. The physical and spectral data were consistent with those previously reported.[153] Compound **2.4b** was accompanied by the following byproduct **2.4c**.

3-((Benzyloxycarbonyl)amino)benzyl alcohol (**2.4c**, Table 2.2, entry 4)



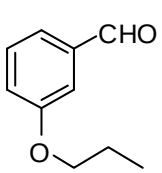
As a byproduct in the above reaction from column chromatography (eluent: EtOAc/hexanes), the title compound **2.4c** (32 mg, 25% yield) was obtained as a colorless solid. mp 75-76 ^oC (EtOAc/hexanes) (lit[154] mp 70-73 ^oC); IR (KBr) ν_{max} 3391, 3311, 1704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.50-7.33 (m, 6H), 7.32-7.22 (m, 2H), 7.01 (d, *J* = 6.1 Hz, 2H), 5.16 (s, 2H), 4.58 (s, 2H), 2.51 (bs, 1H);[154] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 153.47, 141.95, 137.92, 135.94, 129.10, 128.53, 128.28, 128.20, 121.90, 117.84, 117.19, 66.95, 64.78; MS EI *m/z* (rel. int.) 257 (M^+, 28), 213 (36), 149 (84), 120 (48), 108 (67), 107 (78), 91 (100), 79 (81), 77 (80); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{15}NO_3$ 257.1052, found 257.1048.

3-Allyloxybenzaldehyde (**2.5b**, Table 2.2, entry 5)



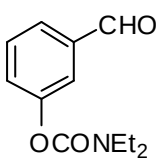
According to General Procedure A and using the following materials and 20 min reaction time: 3-allyloxy-N,N-diethylbenzamide (70 mg, 0.30 mmol), $Cp_2Zr(H)Cl$ (129 mg, ~90% purity, 0.45 mmol) and THF (3 mL), the title compound **2.5b** (35 mg, 72% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.96 (s, 1H), 7.49-7.36 (m, 3H), 7.24-7.15 (m, 1H), 6.05 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 5.43 (ddd, *J* = 17.2, 3.1, 1.5 Hz, 1H), 5.31 (ddd, *J* = 10.5, 2.7, 1.3 Hz, 1H), 4.59 (dt, *J* = 5.2, 1.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.99, 159.08, 137.74, 132.59, 130.00, 123.51, 122.03, 118.01, 113.08, 68.91. The physical and spectral data were consistent with those previously reported.[155] Compound **2.5b** was accompanied by the following byproduct **2.5c**.

3-(*n*-Propoxy)benzaldehyde (**2.5c**, Table 2.2, entry 5)



As a byproduct in the above reaction, the title compound **2.5c** (3 mg, 7% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 1700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1H), 7.47-7.41 (m, 2H), 7.38 (d, *J* = 2.2 Hz, 1H), 7.20-7.14 (m, 1H), 3.98 (t, *J* = 6.6 Hz, 2H), 1.83 (m, 2H), 1.05 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.16, 159.69, 137.76, 129.96, 123.25, 121.92, 112.79, 69.77, 22.45, 10.45; MS EI *m/z* (rel. int.) 164 (M^+, 24), 138(100), 122(45), 121(68); HRMS *m/z* (EI, M^+) calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0836.

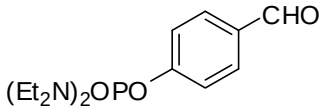
3-Formylphenyl-N,N-diethylcarbamate (**2.6b**, Table 2.2, entry 6)



According to General Procedure A and using the following materials and 15 min reaction time: 3-(diethylcarbamoyl)phenyl diethylcarbamate (146 mg, 0.50

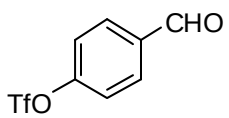
mmol), $Cp_2Zr(H)Cl$ (210 mg, ~93% purity, 0.75 mmol) and THF (3 mL), the title compound **2.6b** (78 mg, 83% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 1718, 1701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.99 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.64 (s, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 3.51-3.32 (m, 4H), 1.32-1.14 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.35, 153.65, 152.12, 137.57, 129.81, 127.98, 126.44, 122.48, 42.37, 41.96, 14.21, 13.29; MS EI *m/z* (rel. int.) 221 (M^+, 4), 121 (6), 100 (100), 72 (51); HRMS *m/z* (CI, $[M+1]^+$) calcd for $C_{12}H_{16}NO_3$, 222.1130, found 222.1139.

4-Formylphenyl N,N,N,N-tetraethylphosphordiamidate (**2.7b**, Table 2.2, entry 7)



According to General Procedure A and using the following materials and 11 min reaction time: 4-(diethylcarbamoyl)phenyl N,N,N,N-tetraethylphosphordiamidate (77 mg, 0.2 mmol), $Cp_2Zr(H)Cl$ (86 mg, ~90% purity, 0.3 mmol) and THF (2 mL), the title compound **2.7b** (52 mg, 83% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 1700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.93 (s, 1H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 3.22-3.04 (m, 8H), 1.09 (t, *J* = 7.1 Hz, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 190.91, 156.83 (d, J_{C-P} = 5.7 Hz), 132.22, 131.49 (2C), 120.58 (d, J_{C-P} = 5.4 Hz, 2C), 39.71, 39.66, 14.06, 14.03; MS EI *m/z* (rel. int.) 312(M^+, 16), 297(100), 240(48), 226(42), 207(62), 191(48), 76(52); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{25}N_2O_3P$ 312.1603, found 312.1595.

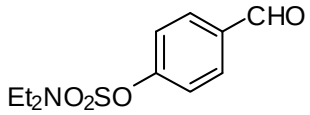
4-Trifluoromethanesulfonylbenzaldehyde (**2.8b**, Table 2.2, entry 8)



According to General Procedure A and using the following materials and 30 min reaction time: 4-trifluoromethanesulfonyl-N,N-diethylbenzamide (163

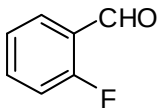
mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (215 mg, ~90% purity, 0.75 mmol) and THF (3 mL), the title compound **2.8b** (104 mg, 82% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.07 (s, 1H), 8.02 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 190.05, 153.19, 135.88, 131.73, 122.24, 118.67 (q, $J_{C\text{-}F}$ = 321 Hz). The spectral data were consistent with those previously reported.[156]

4-Formylphenyl N,N-diethylsulfamate (**2.9b**, Table 2.2, entry 9)



According to General Procedure A and using the following materials and 9 min reaction time: 4-(diethylcarbamoyl)phenyl diethylsulfamate (66 mg, 0.2 mmol), $Cp_2Zr(H)Cl$ (86 mg, ~90% purity, 0.3 mmol) and THF (2 mL), the title compound **2.9b** (48 mg, 94% yield) was obtained as a colorless solid. mp 46-47 °C (EtOAc/hexanes) (lit[157] mp 48-50 °C (ethanol)); IR (KBr) ν_{max} 1704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.00 (s, 1H), 7.92 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 3.42 (q, *J* = 7.2 Hz, 4H), 1.24 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 190.70, 154.94, 134.27, 131.42, 122.12, 43.45, 13.40; MS EI *m/z* (rel. int.) 257 (M^+, 35), 136 (100); HRMS *m/z* (EI, M^+) calcd for $C_{11}H_{15}NO_4S$ 257.0722, found 257.0724.

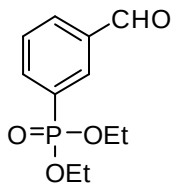
2-Fluorobenzaldehyde (**2.10b**, Table 2.2, entry 10)



According to General Procedure A and using the following materials and 30 min reaction time: N,N-diethyl-2-fluorobenzamide (146 mg, 0.75 mmol), $Cp_2Zr(H)Cl$ (310 mg, ~93% purity, 1.12 mmol) and THF (3 mL), the title compound **2.10b** (83 mg, 89% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.38 (d, 1H), 7.95-7.79 (m, 1H), 7.68-7.50 (m, 1H), 7.34-7.06 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 187.16

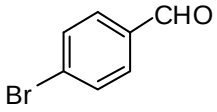
(d, $^{3}J_{C\text{-}F}$ = 7.5 Hz), 164.68 (d, $^{1}J_{C\text{-}F}$ = 255.2 Hz), 136.32 (d, $^{3}J_{C\text{-}F}$ = 9.2 Hz), 128.68, 124.62 (d, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 124.19 (d, $^{2}J_{C\text{-}F}$ = 7.4 Hz), 116.50 (d, $^{2}J_{C\text{-}F}$ = 20.6 Hz). The physical and spectral data were consistent with those previously reported.[158]

Diethyl 3-formylphenylphosphonate (**2.11b**, Table 2.2, entry 11)



According to General Procedure A and using the following materials and 10 min reaction time: 3-(diethylcarbamoyl)phenyl diethylphosphonate (63 mg, 0.2 mmol), $Cp_2Zr(H)Cl$ (85 mg, ~91% purity, 0.3 mmol) and THF (3 mL), the title compound **2.11b** (41 mg, 85% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.05 (s, 1H), 8.29 (d, $J_{P\text{-}H}$ = 13.4 Hz, 1H), 8.13-7.98 (m, 2H), 7.69-7.58 (m, 1H), 4.27-3.98 (m, 4H), 1.33 (t, J = 7.08 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.21, 137.23 (d, $J_{C\text{-}P}$ = 10.1 Hz), 136.25 (d, $J_{C\text{-}P}$ = 13.7 Hz), 133.38 (d, $J_{C\text{-}P}$ = 10.1 Hz), 132.55 (d, $J_{C\text{-}P}$ = 2.9 Hz), 131.08, 129.27 (d, $J_{C\text{-}P}$ = 14.6 Hz), 62.44 (d, $J_{C\text{-}P}$ = 5.6 Hz, 2C), 16.30 (d, $J_{C\text{-}P}$ = 6.3 Hz, 2C); ^{31}P NMR (162 MHz, $CDCl_3$) δ ppm 16.64 (s). The physical and spectral data were consistent with those previously reported.[159]

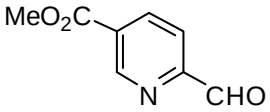
4-Bromobenzaldehyde (**2.12b**, Table 2.2, entry 12)



According to General Procedure A and using the following materials and 10 min reaction time: N,N-diethyl-4-bromobenzamide (128 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (210 mg, ~93% purity, 0.75 mmol) and THF (3 mL), the title compound **2.12b** (67 mg, 73% yield) was obtained as a colorless solid. mp 55-56^{o}C (hexanes) (lit[160] mp 54-56 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.98 (s, 1H), 7.75 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.02, 135.05, 132.42 (2C),

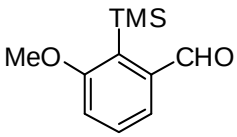
130.94 (2C), 129.76. The physical and spectral data were consistent with those previously reported.[160]

Methyl 6-formylnicotinate (**2.13b**, Table 2.2, entry 13)



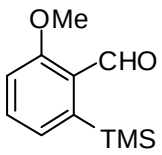
According to General Procedure A and using the following materials and 25 min reaction time: methyl 6-(diethylcarbamoyl)nicotinate (118 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (210 mg, ~93% purity, 0.75 mmol) and THF (4 mL), the title compound **2.13b** (59 mg, 72% yield) was obtained as a light yellow solid. mp 120-122 ^oC (EtOAc/hexanes) (lit[161] mp 115-117 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.12 (s, 1H), 9.34 (s, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.55, 164.75, 154.87, 151.15, 138.25, 129.16, 121.02, 52.80. The physical and spectral data were consistent with those previously reported.[161,162]

3-Methoxy-2-(trimethylsilyl)benzaldehyde (**2.14b**, Table 2.3, entry 1)



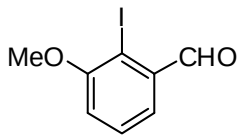
According to General Procedure A and using the following materials and 30 min reaction time: N,N-diethyl-3-methoxy-2-(trimethylsilyl)benzamide (140 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (210 mg, ~93% purity, 0.75 mmol) and THF (3 mL), the title compound **2.14b** (84 mg, 81% yield) was obtained as a light yellow solid. mp 82-84 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.34 (s, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.8, 1H), 7.05 (d, *J* = 8.1 Hz, 1H), 3.83 (s, 3H), 0.39 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 193.89, 164.98, 143.72, 131.23, 130.64, 121.04, 114.96, 55.43, 2.50; MS EI *m/z* (rel. int.) 193 ($[M-15]^+$, 100), 178 (4), 163 (22), 135 (9). HRMS *m/z* (EI, M^+) calcd for $C_{11}H_{16}O_2Si$, 208.0920, found 208.0928.

2-Methoxy-6-(trimethylsilyl)benzaldehyde (**2.15b**, Table 2.3, entry 2)



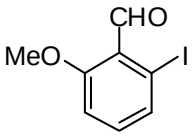
According to General Procedure A and using the following materials and 25 min reaction time: N,N-diethyl-2-methoxy-6-(trimethylsilyl)benzamide (140 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (277 mg, ~93% purity, 1.0 mmol) and THF (3 mL), the title compound **2.15b** (38 mg, 37% yield) was obtained as a yellow oil. IR (KBr) ν_{max} 1687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.59 (d, *J* = 0.6 Hz, 1H), 7.52 (dd, *J* = 8.3, 7.4 Hz, 1H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.03 (dd, *J* = 8.4, 0.6 Hz, 1H), 3.92 (s, 3H), 0.29 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.27, 163.01, 144.00, 134.47, 129.00, 127.76, 112.53, 55.65, 0.03; MS EI *m/z* (rel. int.) 193 ($[M-CH_3]^+$, 100), 178 (22), 163 (39), 145 (19), 135 (34); HRMS *m/z* (EI, $[M-CH_3]^+$) calcd for $[C_{11}H_{16}O_2Si-15]$ 193.0685, found 193.0686.

2-Iodo-3-methoxybenzaldehyde (**2.16b**, Table 2.3, entry 3)



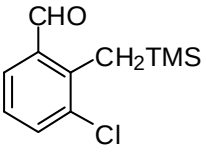
According to General Procedure A and using the following materials and 10 min reaction time: N,N-diethyl-2-iodo-3-methoxybenzamide (167 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (210 mg, ~93% purity, 0.75 mmol) and THF (3 mL), the title compound **2.16b** (94 mg, 72% yield) was obtained as a colorless solid. mp 83-84°C (EtOAc/hexanes) (lit[163] mp 84 °C (EtOAc/hexanes)); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.19 (s, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 196.46, 158.26, 136.72, 129.46, 122.28, 116.00, 93.88, 56.83.

2-Iodo-6-methoxybenzaldehyde (**2.17b**, Table 2.3, entry 4)



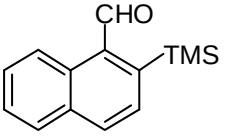
According to General Procedure A and using the following materials and 1 h reaction time: N,N-diethyl-6-iodo-3-methoxybenzamide (100 mg, 0.3 mmol), $Cp_2Zr(H)Cl$ (167 mg, ~93% purity, 0.6 mmol) and THF (3 mL), the title compound **2.17b** (20 mg, 26% yield) was obtained as a yellow solid. mp 55-56 ^oC (EtOAc/hexanes) (lit[164] mp 56-57 ^oC). ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.25 (s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 8.1 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 3.91 (s, 3H);[164] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.75, 161.82, 135.08, 133.77, 124.90, 111.92, 96.43, 56.00. The physical and spectral data were consistent with those previously reported.[164]

3-Chloro-2-((trimethylsilyl)methyl)benzaldehyde (**2.18b**,Table 2.3, entry 5)



According to General Procedure A and using the following materials and 20 min reaction time: N,N-diethyl-3- Chloro-2-((trimethylsilyl)methyl)benzamide (149 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (208 mg, ~93% purity, 0.75 mmol) and THF (3 mL), the title compound **2.18b** (94 mg, 83% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 1700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.15 (s, 1H), 7.68 (d, *J* = 6.3 Hz, 1H), 7.56 (d, *J* = 6.9 Hz, 1H), 7.19 (t, *J* = 6.2 Hz, 1H), 2.93 (s, 2H), 0.02 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.86, 142.60, 134.77, 134.46, 134.18, 131.42, 124.93, 20.00, -0.85 (3C); MS EI *m/z* (rel. int.) 226 (M^+, 29), 211 (54), 191 (25), 73 (100); HRMS *m/z* (EI, M^+) calcd for $C_{11}H_{15}OClSi$ 226.0581, found 226.0582.

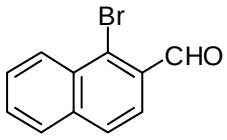
2-(Trimethylsilyl)-1-naphthaldehyde (**2.19b**, Table 2.3, entry 6)



According to General Procedure A and using the following materials and 2 h reaction time: N,N-diethyl-2-(trimethylsilyl)-1-naphthamide (75 mg, 0.25

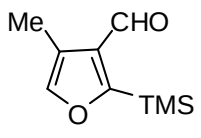
mmol), $Cp_2Zr(H)Cl$ (208 mg, ~93% purity, 0.75 mmol) and THF (3 mL), the title compound **2.19b** (23 mg, 41% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 1687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.95 (s, 1H), 9.03 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.4 Hz, 1H), 0.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 193.67, 146.55, 136.59, 134.04, 132.95, 131.62, 130.79, 128.57, 128.36, 126.86, 124.47, 1.07; MS EI *m/z* (rel. int.) 228 (M^+, 2), 213 (100), 198 (20), 183 (39), 167 (24), 155 (39), 139 (21); HRMS *m/z* (EI, M^+) calcd for $C_{14}H_{16}OSi$, 228.0970, found 228.0963.

1-Bromo-2-naphthaldehyde (**2.20b**, Table 2.3, entry 7)



According to General Procedure A and using the following materials and 30 min reaction time: N,N-diethyl-2-bromo-1-naphthamide (77 mg, 0.25 mmol), $Cp_2Zr(H)Cl$ (104 mg, ~93% purity, 0.38 mmol) and THF (3 mL), the title compound **2.20b** (41 mg, 70% yield) was obtained as a colorless solid. mp 117-119 °C (EtOAc/hexanes) (lit[165] mp 116-118 °C); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.66 (s, 1H), 8.56-8.43 (m, 1H), 7.99-7.75 (m, 3H), 7.74-7.61 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.76, 137.16, 132.03, 131.23, 131.14, 129.67, 128.42, 128.22, 128.16, 128.05, 124.03. The physical and spectral data were consistent with those previously reported.[165,166]

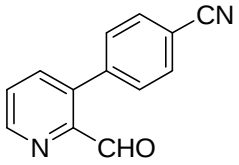
4-Methyl-2-(trimethylsilyl)furan-3-carbaldehyde (**2.21b**, Table 2.3, entry 8)



According to General Procedure A and using the following materials and 25 min reaction time: N,N-diethyl-4-methyl-2-(trimethylsilyl)furan-3-carboxamide (76 mg, 0.30 mmol), $Cp_2Zr(H)Cl$ (129 mg, ~90% purity, 0.45

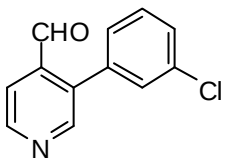
mmol) and THF (2 mL), the title compound **2.21b** (46 mg, 84% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.14 (s, 1H), 7.37 (s, 1H), 2.22 (s, 3H), 0.37 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 186.96, 172.87, 144.57, 135.88, 119.83, 8.84, -1.14 (3C); MS EI *m/z* (rel. int.) 182 (M^+, 29), 167 (100), 111 (31), 83 (35); HRMS *m/z* (EI, M^+) calcd for $C_9H_{14}O_2Si$ 182.0763, found 182.0762.

4-(2-Formylpyridin-3-yl)benzonitrile (**2.22b**, Table 2.3, entry 9)



According to General Procedure A and using the following materials and 30 min reaction time: 3-(4-cyanophenyl)-N,N-diethylpicolinamide (84 mg, 0.30 mmol), $Cp_2Zr(H)Cl$ (125 mg, ~93% purity, 0.45 mmol) and THF (3 mL), the title compound **2.22b** (46 mg, 74% yield) was obtained as a light yellow solid. mp 158-160 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2267, 1707 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.09 (s, 1H), 8.89 (dd, *J* = 4.5, 1.1 Hz, 1H), 7.78-7.69 (m, 3H), 7.60 (dd, *J* = 7.8, 4.6 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.18, 149.92, 148.96, 141.74, 139.05, 137.41, 132.10 (2C), 129.82 (2C), 126.73, 118.43, 112.33; MS EI *m/z* (rel. int.) 208 (M^+, 40), 180 (85), 179 (100), 152 (25); HRMS *m/z* (EI, M^+) calcd for $C_{13}H_8N_2O$ 208.0637, found 208.0639.

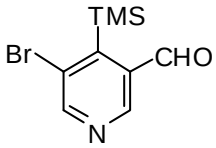
3-(3-Chlorophenyl)isonicotinaldehyde (**2.23b**, Table 2.3, entry 10)



According to General Procedure A and using the following materials and 20 min reaction time: 3-(3-chlorophenyl)-N,N-diethylisonicotinamide (87 mg, 0.30 mmol), $Cp_2Zr(H)Cl$ (125 mg, ~93% purity, 0.45 mmol) and THF (2 mL), the title compound **2.23b** (57 mg, 88% yield) was obtained as a light yellow solid. mp 49-51

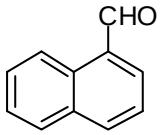
^{o}C (EtOAc/hexanes). IR (KBr) ν_{max} 1704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.04 (s, 1H), 8.83 (d, *J* = 5.0 Hz, 1H), 8.79 (s, 1H), 7.77 (d, *J* = 5.0 Hz, 1H), 7.50-7.38 (m, 3H), 7.30-7.24 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 190.93, 151.88, 150.02, 138.55, 136.91, 135.77, 134.99, 130.08, 129.90, 129.07, 128.40, 119.74; MS EI *m/z* (rel. int.) 217 (M^+, 71), 189 (53), 182 (100), 154 (73), 127 (47); HRMS *m/z* (EI, M^+) calcd for $C_{12}H_8NOCl$ 217.0294, found 217.0294.

5-Bromo-4-(trimethylsilyl)nicotinaldehyde (**2.24b**, Table 2.3, entry 11)



According to General Procedure A and using the following materials and 1 h reaction time: 5-bromo-N,N-diethyl-4-(trimethylsilyl)nicotinamide (99 mg, 0.3 mmol), $Cp_2Zr(H)Cl$ (250 mg, ~93% purity, 0.9 mmol) and THF (3 mL), the title compound **2.24b** (51 mg, 66% yield) was obtained as a light yellow solid. mp 69-71 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 1685 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.35 (s, 1H), 8.83 (s, 1H), 8.80 (s, 1H), 0.52 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.92, 155.58, 151.83, 148.08, 139.16, 129.43, 2.27 (3C); MS EI *m/z* (rel. int.) 244 ($[M-CH_3+2]^+$, 98), 242 ($[M-CH_3]^+$, 100); HRMS *m/z* (EI, $[M-CH_3]^+$) calcd for $[C_9H_{12}BrNOSi$ -15] 241.9637, found 241.9633.

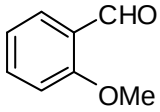
1-Naphthaldehyde (**2.25b**, Table 2.4, entry 1)



According to General Procedure A and using the following materials and 10 min reaction time: N,N-dimethyl-1-naphthamide (100 mg, 0.50 mmol), $Cp_2Zr(H)Cl$ (210 mg, ~91% purity, 0.75 mmol) and THF (3 mL), the title compound **2.25b** (62 mg, 80% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.41 (s, 1H), 9.26 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.2 Hz, 1H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.77-7.59 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 193.53, 136.66, 135.29,

133.72, 131.41, 130.53, 129.06, 128.45, 126.96, 124.87 (brs, 2C). The physical and spectral data were consistent with those previously reported.[160]

2-Methoxybenzaldehyde (**2.26b**, Table 2.4, entries 2-4)

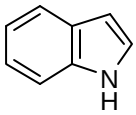


According to General Procedure A and using the following materials and 10 min reaction time: N,N-diethyl-2-methoxybenzamide (146 mg, 0.70 mmol), $Cp_2Zr(H)Cl$ (290 mg, ~93% purity, 1.05 mmol) and THF (3 mL), the title compound **2.26b** (89 mg, 94% yield) was obtained as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.47 (s, 1H), 7.82 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.58-7.49 (m, 1H), 7.06-6.93 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 189.79, 161.78, 135.90, 128.50, 124.78, 120.61, 111.57, 55.58. The spectral data were consistent with those previously reported.[167]

According to General Procedure A and using the following materials in a 1.5 h reaction time: N,N-diisopropyl-2-methoxybenzamide (118 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (277 mg, ~93% purity, 1.0 mmol) and THF (2 mL), the title compound **2.26b** (40 mg, 59% yield) was obtained as a light yellow oil. This compound was shown to be identical to that obtained above by comparison of spectral data.

According to General Procedure A and using the following materials in a 2 h reaction time: N-ethyl-N-cumyl-2-methoxybenzamide (149 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (310 mg, ~93% purity, 1.1 mmol) and THF (3 mL), the title compound **2.26b** (37 mg, 55% yield) was obtained as a light yellow oil. This compound was shown to be identical to that obtained above by comparison of spectral data.

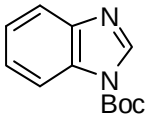
Indole (**2.29b**, Table 2.5, entries 1 and 2)



According to General Procedure B and using the following materials and 40 min reaction time: N,N-dimethyl-1*H*-indole-1-carboxamide (94 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (287 mg, ~90% purity, 1.0 mmol) and THF (3 mL), the title compound **2.29b** (51 mg, 88% yield) was obtained as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.13 (brs, 1H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.32-7.12 (m, 3H), 6.60 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 135.74, 127.82, 124.06, 121.96, 120.70, 119.79, 110.96, 102.63. The physical and spectral data were consistent with those previously reported.[168]

According to General Procedure B and using the following materials in a 1 h reaction time: N,N-diethyl-1*H*-indole-1-carboxamide (108 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (284 mg, ~91% purity, 1.0 mmol) and THF (2 mL), the title compound **2.29b** (55 mg, 94% yield) was obtained as a light yellow solid. This compound was shown to be identical to that obtained above by comparison of spectral data.

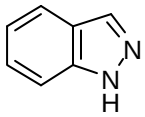
N-Boc-1*H*-benzo[d]imidazole (**2.31b**, Table 2.5, entry 3)



To a suspension of $Cp_2Zr(H)Cl$ (284 mg, ~91% purity, 1.0 mmol) in THF (3 mL) at rt was added a solution of N,N-diethyl-1*H*-benzo[d]imidazole-1-carboxamide (110 mg, 0.5 mmol) in THF (1 mL). The resulting mixture was stirred at rt for 15 min and the reaction was monitored by TLC analysis. The reaction mixture was subjected to filtration through a short silica gel column and the filtrate was concentrated *in vacuo*. Then, the residue was dissolved in THF (5 mL) and DMF (0.5 mL). Boc_2O (170 mg, 0.75 mmol) and a catalytic amount of DMAP was added. The solution was stirred at rt for 12 h (overnight), water

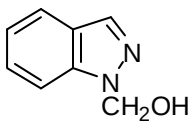
(10 mL) and EtOAc (10 mL) were added, the layers were separated, and the water layer was extracted with EtOAc. The combined organic extract was washed with 0.5 N HCl (3 mL), 0.5 N $NaHCO_3$ (3 mL) and brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.31b** (89 mg, 82% yield) was obtained as a colorless solid. mp 88-89 ^oC (hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.43 (s, 1H), 8.03-7.93 (m, 1H), 7.81-7.72 (m, 1H), 7.43-7.29 (m, 2H), 1.69 (s, 9H);[169] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 148.00, 144.00, 141.95, 131.31, 125.13, 124.18, 120.54, 114.30, 85.53, 28.02. The physical and spectral data were consistent with those previously reported.[169]

1*H*-Indazole (**2.32b**, Table 2.5, entry 4a)



According to General Procedure B and using the following materials and 30 min reaction time: N,N-diethyl-1*H*-indazole-1-carboxamide (110 mg, 0.5 mmol), $Cp_2Zr(H)Cl$ (420 mg, ~93% purity, 1.5 mmol) and THF (4 mL), the title compound **2.32b** (33 mg, 56% yield) was obtained as a colorless solid. mp 149-150 ^oC (EtOAc/hexanes) (lit[170] mp 147-149 ^oC). ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.70 (s, 1H), 8.14 (s, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 140.03, 134.82, 126.81, 123.17, 120.97, 120.87, 109.71. The physical and spectral data were consistent with those previously reported.[171] Compound **2.32b** was accompanied by the following byproduct **2.32c**.

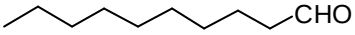
1-Hydroxymethyl-1*H*-indazole (**2.32c**, Table 2.5, entry 4b)



As a byproduct in the above reaction from column chromatography (eluent: EtOAc/hexanes), the title compound **2.32c** (26 mg, 43% yield) was obtained

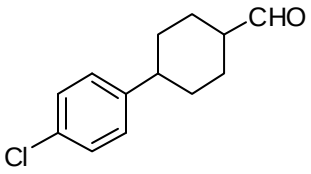
as a colorless solid. mp 110-112 °C (EtOAc/hexanes) (lit[172] mp 113-114 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.02 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 5.87 (s, 2H), 5.58 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 139.44, 134.55, 127.24, 124.38, 121.47, 121.20, 109.40, 71.09. The physical and spectral data were consistent with those previously reported.[172,173]

Decanal (**2.35**, Table 2.9)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyldecanamide (68 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (2 mL), the title compound **2.35** (41 g, 87% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.76 (t, *J* = 1.8 Hz, 1H), 2.41 (td, *J* = 7.4, 1.8 Hz, 2H), 1.68-1.56 (m, 2H), 1.37-1.19 (m, 12H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 202.86, 43.90, 31.83, 29.36, 29.33, 29.21, 29.15, 22.63, 22.08, 14.06. The physical and spectral data were consistent with those previously reported.[174]

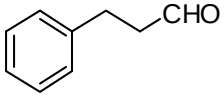
4-(4-Chlorophenyl)cyclohexanecarbaldehyde (**2.36**, Table 2.9)



According to General Procedure C and using the following materials and 30 min reaction time: 4-(4-chlorophenyl)-N,N-diethylcyclohexanecarboxamide (88 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.36** (55 g, 83% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2926, 2855, 2718, 1722, 1492, 1449, 1090, 1013, 925, 828, 670, 531

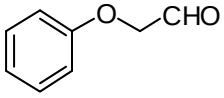
cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.67 (d, *J* = 1.0 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 2.45 (tt, *J* = 11.5, 3.2 Hz, 1H), 2.35-2.22 (m, 1H), 2.17-2.07 (m, 2H), 2.04-1.96 (m, 2H), 1.54-1.34 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 204.12, 145.01, 131.70, 128.46 (2C), 128.05 (2C), 49.78, 43.16, 32.86 (2C), 26.19 (2C). MS EI *m/z* (rel. int.) 222 (M^+, 79), 138 (100), 125 (75); HRMS *m/z* (EI, M^+) calcd for $C_{13}H_{15}ClO$, 222.0811, found 222.0815.

3-Phenylpropanal (**2.37**, Table 2.9)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-3-phenylpropanamide (62 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.37** (35 mg, 87% yield) was obtained as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.83 (d, *J* = 1.3 Hz, 1H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.25-7.15 (m, 3H), 2.97 (t, *J* = 7.5 Hz, 2H), 2.79 (td, *J* = 7.2, 0.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 201.45, 140.29, 128.55 (2C), 128.24 (2C), 126.25, 45.22, 28.09. The physical and spectral data were consistent with those previously reported.[175]

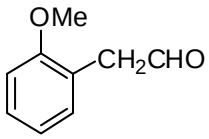
2-Phenoxyacetaldehyde (**2.38**, Table 2.9)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-2-phenoxyacetamide (62 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.38** (37 mg, 91% yield) was obtained as a colorless solid. mp 126-128 ^oC (EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.87 (t, *J* = 0.8 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 2H), 4.57 (d, *J* = 0.8 Hz, 2H);

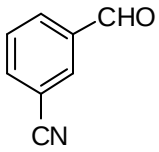
^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 199.37, 157.60, 129.72 (2C), 121.93, 114.54 (2C), 72.61. The spectral data were consistent with those previously reported.[176]

2-(2-Methoxyphenyl)acetaldehyde (**2.39**, Table 2.9)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-2-(2-methoxyphenyl)acetamide (62 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.39** (39 mg, 87% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.68 (t, *J* = 2.2 Hz, 1H), 7.30 (td, *J* = 8.0, 1.7 Hz, 1H), 7.15 (dd, *J* = 7.3, 1.5 Hz, 1H), 6.95 (td, *J* = 7.5, 1.0 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 3.83 (s, 3H), 3.65 (d, *J* = 2.1 Hz, 2H);[177] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 200.23, 157.58, 131.22, 128.93, 121.20, 120.77, 110.44, 55.33, 45.41. The physical and spectral data were consistent with those previously reported.[177]

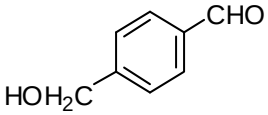
3-Formylbenzonitrile (**2.40**, Table 2.9)



According to General Procedure C and using the following materials and 10 min reaction time: 3-cyano-N,N-diethylbenzamide (61 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.40** (37 mg, 94% yield) was obtained as a light yellow solid. mp 76-77 ^{o}C (EtOAc/hexanes) (lit[178] mp 76-77 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.04 (s, 1H), 8.16 (dd, *J* = 1.6, 1.0 Hz, 1H), 8.12 (dt, *J* =7.8, 1.3 Hz, 1H), 7.91 (dt, *J* =7.7, 1.3 Hz, 1H), 7.69 (t, *J* =7.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 189.86, 137.15, 136.82,

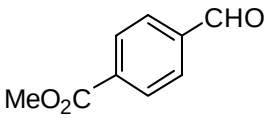
133.23, 133.08, 130.05, 117.49, 113.67. The physical and spectral data were consistent with those previously reported.[179]

4-(Hydroxymethyl)benzaldehyde (**2.41**, Table 2.9)



To a solution of N,N-diethyl-4-(hydroxymethyl)benzamide (42 mg, 0.20 mmol) in THF (1 mL) at rt was slowly added a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (0.48 mL, 0.48 mmol). The resulting solution was stirred at rt for 15 min. A solution of Cp_2ZrCl_2 (83 mg, 0.48 mmol) in THF (1.5 mL) was added rapidly. After stirring for 2 min, the reaction mixture was immediately quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc. The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.41** (26 mg, 93% yield) was obtained as a colorless viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 4.78 (s, 2H), 2.34 (brs, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.07, 147.83, 135.56, 129.97 (2C), 126.91 (2C), 64.46. The physical and spectral data were consistent with those previously reported.[180]

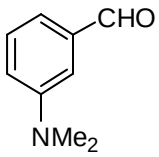
Methyl 4-formylbenzoate (**2.1b**, Table 2.9)



According to General Procedure C and using the following materials and 7 min reaction time: methyl 4-(diethylcarbamoyl)benzoate (76 mg, 0.30 mmol), Cp_2ZrCl_2 (147 mg, 0.48 mmol), a 1 M THF solution of

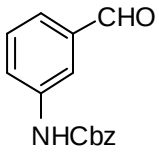
$LiAlH(O\textit{t}\text{-}Bu)_3$ (0.48 mL, 0.48 mmol) and THF (1.5 mL), the title compound **2.1b** (44 mg, 90% yield) was obtained as a light yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

3-(Dimethylamino)benzaldehyde (**2.2b**, Table 2.9, entry 9)



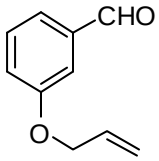
According to General Procedure C and using the following materials and 2 min reaction time: 3-(dimethylamino)-N,N-diethylbenzamide (110 mg, 0.5 mmol), Cp_2ZrCl_2 (207 mg, 0.7 mmol), a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (0.7 mL, 0.7 mmol) and THF (2 mL), the title compound **2.2b** (61 mg, 81%) was obtained as a yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

Benzyl 3-formylphenylcarbamate (**2.4b**, Table 2.9, entry 10)



According to General Procedure C and using the following materials and 2 min reaction time: 3-((benzyloxycarbonyl)amino)-N,N-diethylbenzamide (32 mg, 0.1 mmol), Cp_2ZrCl_2 (59 mg, 0.2 mmol), a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (0.2 mL, 0.2 mmol) and THF (1 mL), the title compound **2.4b** (25 mg, 99% yield) was obtained as a colorless solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

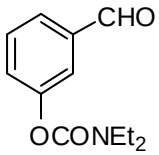
3-(Allyloxy)benzaldehyde (**2.5b**, Table 2.9, entry 11)



According to General Procedure C and using the following materials and 2 min reaction time: 3-allyloxy-N,N-diethylbenzamide (70 mg, 0.30 mmol), Cp_2ZrCl_2

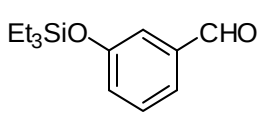
(124 mg, 0.42 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.5b** (44 mg, 91% yield) was obtained as a colorless oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

3-Formylphenyl N,N-diethylcarbamate (**2.6b**, Table 2.9, entry 12)



According to General Procedure C and using the following materials and 2 min reaction time: 3-(diethylcarbamoyl)phenyl diethylcarbamate (58 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1 mL), the title compound **2.6b** (41 mg, 93% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

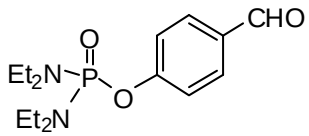
3-(Triethylsilyloxy)benzaldehyde (**2.42**, Table 2.9, entry 13)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-3-(triethylsilyloxy)benzamide (62 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1 mL), the title compound **2.42** (43 mg, 91% yield) was obtained as a light yellow solid. mp 98-100 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2958, 2878, 1703, 1597, 1583, 1482, 1446, 1278, 1258, 1003, 830, 747, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1H), 7.46 (dt, *J* = 7.5, 1.3 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.33 (dd, *J* = 2.2, 1.5 Hz, 1H), 7.12 (ddd, *J* = 8.0, 2.5, 1.1 Hz, 1H), 1.00 (t, *J* = 7.9 Hz, 9H), 0.77 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.04, 156.35, 137.92, 130.05, 126.34, 123.43, 119.64, 6.53 (3C), 4.95 (3C); MS

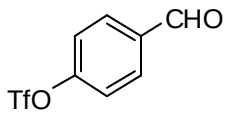
EI *m/z* (rel. int.) 236 (M^+, 23), 207 (100), 179 (61), 151 (31), 123 (26); HRMS *m/z* (EI, M^+) calcd for $C_{13}H_{20}O_2Si$ 236.1233, found 236.1231.

4-Formylphenyl N,N,N,N-tetraethylphosphordiamidate (**2.7b**, Table 2.9, entry 14)



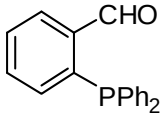
According to General Procedure C and using the following materials and 2 min reaction time: 4-(diethylcarbamoyl)phenyl N,N,N,N-tetraethylphosphordiamidate (38 mg, 0.10 mmol), Cp_2ZrCl_2 (41 mg, 0.14 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.14 mL, 0.14 mmol) and THF (1 mL), the title compound **2.7b** (29 mg, 91%) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

4-Trifluoromethanesulfonylbenzaldehyde (**2.8b**, Table 2.9, entry 15)



According to General Procedure C and using the following materials and 2 min reaction time: 4-trifluoromethanesulfonyl-N,N-diethylbenzamide (65 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1 mL), the title compound **2.8b** (48 mg, 95%) was obtained as a colorless oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

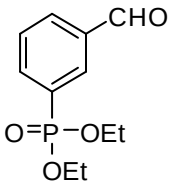
2-(Diphenylphosphino)benzaldehyde (**2.43**, Table 2.9, entry 16)



According to General Procedure C and using the following materials and 2 min reaction time: 2-(diphenylphosphino)-N,N-diethylbenzamide (36 mg, 0.10 mmol), Cp_2ZrCl_2 (53 mg, 0.18 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$

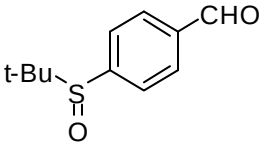
(0.18 mL, 0.18 mmol) and THF (1 mL), the title compound **2.43** (27 mg, 93% yield) was obtained as a light yellow solid. mp 113-115 °C (EtOAc/hexanes) (lit[181] mp 115-116 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.51 (d, J = 5.4 Hz, 1H), 8.01-7.93 (m, 1H), 7.54-7.42 (m, 2H), 7.41-7.22 (m, 10H), 7.01-6.93 (m, 1H);[181] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.66 (d, $^3J_{C\text{-}P}$ = 19.4 Hz), 141.14 (d, $^1J_{C\text{-}P}$ = 26.4 Hz, 2C), 138.44 (d, $^1J_{C\text{-}P}$ = 14.8 Hz), 136.09 (d, $^2J_{C\text{-}P}$ = 9.7 Hz), 134.03 (d, $^2J_{C\text{-}P}$ = 20.4 Hz, 4C), 133.84, 133.62, 130.60 (d, $^2J_{C\text{-}P}$ = 3.8 Hz), 129.09 (2C), 128.84, 128.70 (d, $^3J_{C\text{-}P}$ = 7.3 Hz, 4C); ^{31}P NMR (162 MHz, $CDCl_3$) δ ppm -11.52 (s). The physical and spectral data were consistent with those previously reported.[181]

Diethyl 3-formylphenylphosphonate (**2.11b**, Table 2.9, entry 17)



According to General Procedure C and using the following materials and 2 min reaction time: 3-(diethylcarbamoyl)phenyl diethylphosphonate (63 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1 mL), the title compound **2.11b** (47 mg, 97% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

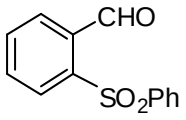
4-(*tert*-Butylsulfinyl)benzaldehyde (**2.44**, Table 2.9, entry 18)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-4-(*tert*-butylsulfinyl)benzamide (113 mg, 0.40 mmol), Cp_2ZrCl_2 (166 mg, 0.56 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.56 mL, 0.56 mmol), THF (2.5 mL) and CH_2Cl_2 (0.5 mL), the title compound **2.44** (80 mg, 95% yield) was obtained as a light yellow solid. mp 77-79 °C (EtOAc/hexanes); IR

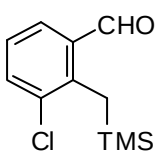
(KBr) ν_{max} 2976, 1704, 1593, 1383, 1365, 1201, 1169, 1076, 1044, 1012, 828, 688 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.06 (s, 1H), 7.98 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.1 Hz, 2H), 1.17 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.21, 147.04, 138.17, 129.25 (2C), 126.85 (2C), 56.69, 22.77; MS EI *m/z* (rel. int.) 210 (M^+, 1), 154 (90), 153 (25), 125 (21), 97 (18), 78 (20), 77 (20), 57 (100); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{11}H_{15}O_2S$, 211.0792, found 211.0796.

2-(Phenylsulfonyl)benzaldehyde (**2.45**, Table 2.9, entry 19)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-2-(phenylsulfonyl)benzamide (127 mg, 0.40 mmol), Cp_2ZrCl_2 (166 mg, 0.56 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.56 mL, 0.56 mmol) and THF (2.5 mL), the tile compound **2.45** (91 mg, 92% yield) was obtained as a light yellow solid. mp 91-93 °C (EtOAc/hexanes); IR (KBr) ν_{max} 1697, 1447, 1320, 1192, 1156, 1123, 1089, 762, 736, 687, 590, 566 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.85 (s, 1H), 8.19 (dd, *J* = 7.6, 1.1 Hz, 1H), 8.02 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.90 (d, *J* = 7.4 Hz, 2H), 7.81-7.69 (m, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 189.30, 142.25, 141.45, 133.94, 133.84, 133.75, 133.67, 129.61(2C), 129.54, 129.49, 127.42(2C). MS/MS ESI *m/z* (rel. int.) 247 ($[M+1]^+$, 4), 169(100), 105(15); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{13}H_{11}O_3S$ 247.0428, found 247.0425.

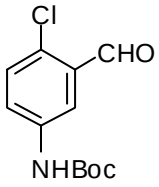
3-Chloro-2-((trimethylsilyl)methyl)benzaldehyde (**2.18b**, Table 2.9, entry 20)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-3-Chloro-2-((trimethylsilyl)methyl)benzamide (89 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}$

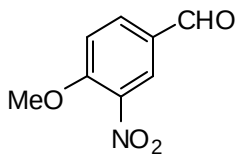
Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (1.5 mL), the title compound **2.18b** (59 mg, 87% yield) was obtained as a colorless oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

***t*-Butyl 4-chloro-3-formylphenylcarbamate** (**2.46**, Table 2.9, entry 21)



According to General Procedure C and using the following materials and 30 min reaction time: *t*-butyl 4-chloro-3-(diethylcarbamoyl)phenylcarbamate (65 mg, 0.2 mmol), Cp_2ZrCl_2 (118 mg, 0.4 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.4 mL, 0.4 mmol) and THF (1 mL), the title compound **2.46** (39 mg, 77% yield) was obtained as a light yellow solid. mp 108-110 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 3341, 2979, 1730, 1701, 1603, 1586, 1530, 1478, 1409, 1393, 1368, 1311, 1280, 1236, 1158, 1073, 1060 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.41 (s, 1H), 7.79 (d, *J* = 6.7 Hz, 1H), 7.72 (d, *J* = 2.8 Hz, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 6.71 (brs, 1H), 1.52 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 189.45, 152.37, 137.94, 132.49, 131.27, 131.10, 125.06, 118.40, 81.36, 28.24 (3C); MS EI *m/z* (rel. int.) 255 (27), 201 (24), 199 (76), 157 (23), 155 (79), 154 (27), 57 (100); HRMS *m/z* (EI, M^+) calcd for $C_{12}H_{14}ClNO_3$ 255.0662, found 255.0666.

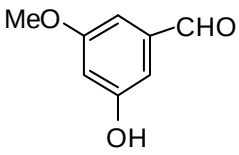
4-Methoxy-3-nitrobenzaldehyde (**2.47**, Table 2.9, entry 22)



According to General Procedure C and using the following materials and 20 min reaction time: N,N-diethyl-4-methoxy-3-nitrobenzamide (76 mg, 0.30 mmol), Cp_2ZrCl_2 (124 mg, 0.42 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.42 mL, 0.42 mmol) and THF (1 mL), the title compound **2.47** (45 mg, 83% yield) was obtained as a light yellow solid. mp 83-84 ^oC (EtOAc/hexanes) (lit[182] mp 82-84 ^oC); ^{1}H

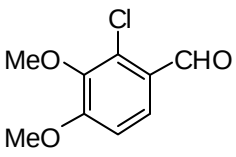
NMR (400 MHz, $CDCl_3$) δ ppm 9.95 (s, 1H), 8.36 (s, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 4.08 (s, 3H);[182] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 188.70, 157.09, 139.81, 134.70, 129.00, 127.33, 113.79, 57.04. The physical and spectral data were consistent with those previously reported.[182]

3-Hydroxy-5-methoxybenzaldehyde (**2.48**, Table 2.9, entry 23)



To a solution of N,N-diethyl-3-hydroxy-5-methoxybenzamide (22 mg, 0.10 mmol) in THF (0.5 mL) at rt was slowly added a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.24 mL, 0.24 mmol). The resulting solution was stirred at rt for 15 min. A solution of Cp_2ZrCl_2 (41 mg, 0.24 mmol) in THF (1 mL) was added rapidly. After stirring for 2 min, the reaction mixture was immediately quenched by H_2O. A solution of 0.5 N HCl was added to adjust the pH < 7 and the whole was extracted with EtOAc. The combined organic extract was washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.48** (12 mg, 80% yield) was obtained as a colorless solid. mp 126-127 ^{o}C (EtOAc/hexanes) (lit[183] mp 129-130 ^{o}C); ^{1}H NMR (400 MHz, CD_3CN) δ ppm 9.85 (s, 1H), 7.44 (brs, 1H), 6.95 (dd, *J* = 2.3, 1.2 Hz, 1H), 6.90 (dd, *J* = 2.2, 1.2 Hz, 1H), 6.66 (t, *J* = 2.3 Hz, 1H), 3.80 (s, 2H); ^{13}C NMR (101 MHz, CD_3CN) δ ppm 193.13, 162.39, 159.56, 139.77, 109.50, 108.33, 106.94, 56.20. The physical and spectral data were consistent with those previously reported.[183]

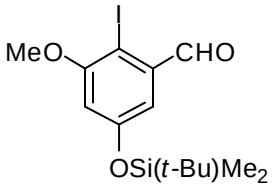
2-Chloro-3,4-dimethoxybenzaldehyde (**2.49**, Table 2.9, entry 24)



According to General Procedure C and using the following materials and 20 min reaction time: N,N-diethyl-2-chloro-3,4-dimethoxybenzamide

(3.86 g, 14.2 mmol), Cp_2ZrCl_2 (6.22 g, 21.3 mmol), a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (21.3 mL, 21.3 mmol) and THF (40 mL), the title compound **2.49** (2.76 g, 97% yield) was obtained as a colorless solid. mp 69-70 ^oC (EtOAc/hexanes) (lit[184] 69-70 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.33 (s, 1H), 7.72 (d, *J* = 8.7 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 3.95 (s, 3H), 3.89 (s, 3H);[184] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 188.81, 158.68, 145.38, 132.50, 126.36, 125.75, 110.28, 60.76, 56.27. The physical and spectral data were consistent with those previously reported.[184]

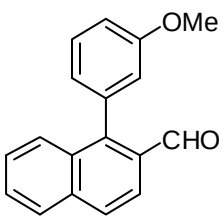
5-(*tert*-Butyldimethylsilyloxy)-2-iodo-3-methoxybenzaldehyde (**2.50**, Table 2.9, entry 25)



According to General Procedure C and using the following materials and 20 min reaction time: N,N-diethyl-5-(*tert*-butyldimethylsilyloxy)-2-iodo-3-methoxybenzamide (46 mg, 0.10 mmol), Cp_2ZrCl_2 (53 mg, 0.18 mmol), a 1 M THF solution of $LiAlH(O\textit{t}\text{-}Bu)_3$ (0.18 mL, 0.18 mmol) and THF (1 mL), the title compound **2.50** (38 mg, 97% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 1694 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ ppm 10.15 (s, 1H), 7.00 (d, *J* = 2.6 Hz, 1H), 6.59 (d, *J* = 2.6 Hz, 1H), 3.89 (s, 3H), 0.99 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 196.03, 159.13, 157.56, 136.59, 112.84, 109.18, 83.94, 56.72, 25.59, 18.19, -4.44; MS EI *m/z* (rel. int.) 392 (M^+, 42), 335 (100); HRMS *m/z* (EI, M^+) calcd for $C_{14}H_{21}IO_3Si$ 392.0305, found 392.0310.

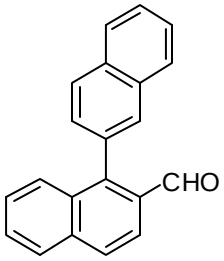
1-(3-Methoxyphenyl)-2-naphthaldehyde (**2.51**, Table 2.9, entry 26)

According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-1-(3-methoxyphenyl)-2-naphthamide (17 mg, 0.05 mmol), Cp_2ZrCl_2 (21 mg, 0.07



mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.07 mL, 0.07 mmol) and THF (0.5 mL), the title compound **2.51** (12 mg, 90% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2850, 1692, 1678, 1597, 1577, 1487, 1462, 1429, 1286, 1256, 1224, 1046, 821, 781, 764, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.92 (s, 1H), 8.06 (d, *J* = 8.6 Hz, 1H), 7.94 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.51-7.40 (m, 2H), 7.07 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.96 (s, 1H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.69, 159.36, 146.33, 136.55, 136.05, 132.34, 131.09, 129.30, 128.75, 128.33, 128.17, 127.70, 126.86, 123.54, 122.03, 116.59, 113.94, 55.33. MS EI *m/z* (rel. int.) 262 (M^+, 100), 261 (36), 233 (28), 231 (44), 203 (42), 202 (31), 201 (28), 189 (45), 149 (43); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{14}O_2$, 262.0994, found 262.0994.

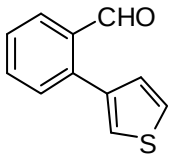
1-(Naphthalen-2-yl)-2-naphthaldehyde (**2.52**, Table 2.9, entry 27)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-1-(naphthalen-2-yl)-2-naphthamide (18 mg, 0.05 mmol), Cp_2ZrCl_2 (21 mg, 0.07 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.07 mL, 0.07 mmol) and THF (0.5 mL), the title compound **2.52** (13 mg, 89% yield) was obtained as a light yellow viscous oil. IR (KBr) ν_{max} 3058, 2849, 1689, 1678, 1228, 821, 765, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.92 (s, 1H), 8.11 (d, *J* = 8.6 Hz, 1H), 8.05-7.93 (m, 4H), 7.92-7.82 (m, 2H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.65-7.57 (m, 3H), 7.54 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.63, 146.41, 136.09, 132.92, 132.81, 132.65, 132.57, 131.48, 130.42, 128.77, 128.61, 128.45, 128.26, 128.06, 127.89 (2C), 127.79, 126.94, 126.91,

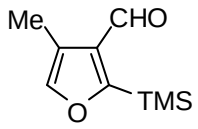
126.76, 122.18. MS EI *m/z* (rel. int.) 282 (M^+, 100), 281 (54), 253 (42), 252 (56), 149 (21), 126 (37); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{14}O$, 282.1045, found 282.1049.

2-(Thiophen-3-yl)benzaldehyde (**2.53**, Table 2.9, entry 28)



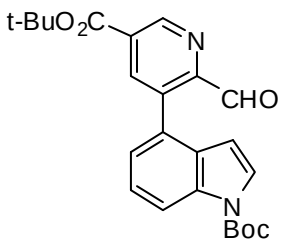
According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-2-(thiophen-3-yl)benzamide (26 mg, 0.10 mmol), Cp_2ZrCl_2 (41 mg, 0.14 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.14 mL, 0.14 mmol) and THF (0.5 mL), the title compound **2.53** (17 mg, 88% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2849, 1687, 1597, 1196, 793, 760, 654 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.11 (s, 1H), 8.00 (d, *J* = 7.3 Hz, 1H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.53-7.38 (m, 3H), 7.30 (d, *J* = 1.6 Hz, 1H), 7.20 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.38, 140.42, 138.30, 133.98, 133.64, 130.56, 129.30, 127.78, 127.57, 126.24, 125.01. The physical and spectral data were consistent with those previously reported.[185]

4-Methyl-2-(trimethylsilyl)furan-3-carbaldehyde (**2.21b**, Table 2.9, entry 29)



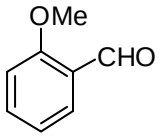
According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-4-methyl-2-(trimethylsilyl)furan-3-carboxamide (25 mg, 0.10 mmol), Cp_2ZrCl_2 (41 mg, 0.14 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.14 mL, 0.14 mmol) and THF (1 mL), the title compound **2.21b** (14 mg, 77% yield) was obtained as a light yellow oil. The compound was shown to be identical by comparison of spectral data with those of the material **2.21b** prepared above (**2.21b**, Table 2.2, entry 21).

***tert*-Butyl 4-(5-(*tert*-butoxycarbonyl)-2-formylpyridin-3-yl)-1*H*-indole-1-carboxylate** (**2.54**, Table 2.9, entry 30)



According to General Procedure C and using the following materials and 30 min reaction time: *tert*-butyl 4-(5-(*tert*-butoxycarbonyl)-2-(diethylcarbamoyl)pyridin-3-yl)-1*H*-indole-1-carboxylate **2.84b** (99 mg, 0.20 mmol), Cp_2ZrCl_2 (106 mg, 0.36 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.36 mL, 0.36 mmol) and THF (2 mL), the title compound **2.54** (56 mg, 67% yield) as a yellow solid. mp 61-63 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1735, 1722, 1415, 1370, 1348, 1316, 1284, 1259, 1160, 1137, 1116, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.98 (s, 1H), 9.36 (s, 1H), 8.40 (s, 1H), 8.31 (d, *J* = 8.1 Hz, 1H), 7.65 (d, *J* = 3.3 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 6.24 (d, *J* = 3.4 Hz, 1H), 1.69 (s, 9H), 1.63 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 190.59, 163.28, 151.34, 150.17, 149.43, 140.69, 138.41, 135.09, 129.93, 129.80, 127.72, 127.38, 124.38, 124.04, 116.00, 105.05, 84.28, 83.07, 28.15 (3C), 28.10 (3C); MS EI *m/z* (rel. int.) 422 (M^+, 6), 366 (15), 248 (100), 238 (94), 203 (87), 176 (81); HRMS *m/z* (EI, M^+) calcd for $C_{24}H_{26}N_2O_5$ 422.1842, found 422.1861.

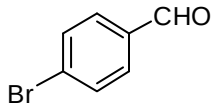
2-Methoxybenzaldehyde (**2.26b**, Table 2.10, entries 1 and 2)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-dimethyl-2-methoxybenzamide (36 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (2 mL), the title compound **2.26b** (26 mg, 94%) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-2-methoxybenzamide (42 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (2 mL), the title compound **2.26b** (25 mg, 94%) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

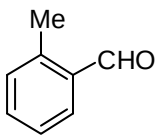
4-Bromobenzaldehyde (**2.12b**, Table 2.10, entries 5 and 6)



According to General Procedure C and using the following materials and 2 min reaction time: N,N-diethyl-4-bromobenzamide (128 mg, 0.5 mmol), Cp_2ZrCl_2 (207 mg, 0.7 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.7 mL, 0.7 mmol) and THF (3 mL), the title compound **2.12b** (89 mg, 96% yield) was obtained as a colorless solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

According to General Procedure C and using the following materials and 25 min reaction time: N,N-diisopropyl-4-bromobenzamide (29 mg, 0.10 mmol), Cp_2ZrCl_2 (65 mg, 0.22 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.22 mL, 0.22 mmol) and THF (1.5 mL), the title compound **2.12b** (16 mg, 88% yield) was obtained as a colorless solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

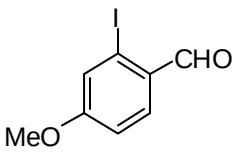
2-Methylbenzaldehyde (**2.57b**, Table 2.10, entry 7)



According to General Procedure C and using the following materials and 2 min reaction time: morpholino(*o*-tolyl)methanone (41 mg, 0.20 mmol), Cp_2ZrCl_2 (83

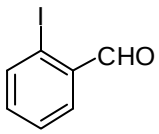
mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1 mL), the title compound **2.57b** (23 mg, 95% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.27 (s, 1H), 7.80 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.48 (dt, *J* = 7.5, 1.4 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 2.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.75, 140.57, 134.12, 133.60, 132.00, 131.73, 126.28, 19.55. The physical and spectral data were consistent with those previously reported.[186]

2-Iodo-4-methoxybenzaldehyde (**2.58b**, Table 2.10, entry 8)



According to General Procedure C and using the following materials and 8 min reaction time: N,N-dimethyl-2-iodo-4-methoxybenzamide (61 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (2 mL), the title compound **2.58b** (47 mg, 89%) was obtained as a colorless solid. mp 112-113 ^{o}C (hexanes) (lit[187] mp 113-114 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.92 (s, 1H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.43 (d, *J* = 2.1 Hz, 1H), 6.97 (dd, *J* = 8.6, 1.6 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 194.41, 164.29, 131.49, 128.55, 125.36, 114.77, 102.26, 55.84. The physical and spectral data were consistent with those previously reported.[187]

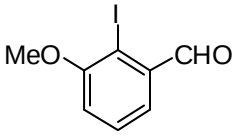
2-Iodobenzaldehyde (**2.59b**, Table 2.10, entry 9)



According to General Procedure C and using the following materials and 7 min reaction time: N-methyl-N-phenyl-2-iodobenzamide (68 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1.5 mL), the title compound **2.59b** (42 mg, 90%) was obtained as a yellow

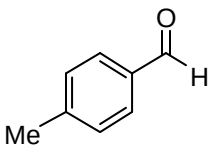
solid. mp 36-37 °C (hexanes) (lit[188] mp 37-38 °C (hexanes)); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.07 (s, 1H), 7.96 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.88 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.29 (td, *J* = 7.4, 1.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 195.75, 140.62, 135.44, 135.12, 130.24, 128.70, 100.66. The physical and spectral data were consistent with those previously reported.[188]

2-Iodo-3-methoxybenzaldehyde (**2.16b**, Table 2.10, entry 10)



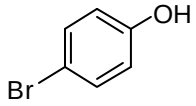
According to General Procedure C and using the following materials and 25 min reaction time: N,N-diethyl-2-iodo-3-methoxybenzamide (67 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1.5 mL), the title compound **2.16b** (24 mg, 46%) was obtained as a yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

4-Methylbenzaldehyde (**2.61b**, Scheme 2.15)



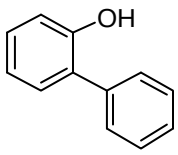
According to General Procedure C and using the following materials and 2 min reaction time: morpholino(*p*-tolyl)methanone (C=O^{18}/C=O^{16} = 1) (41 mg, 0.20 mmol), Cp_2ZrCl_2 (83 mg, 0.28 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.28 mL, 0.28 mmol) and THF (1 mL), the title (C=O^{16}) compound **2.61b** (23 mg, 97% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.96, 145.51, 134.17, 129.81 (2C), 129.67 (2C), 21.86. The physical and spectral data were consistent with those previously reported.[189]

4-Bromophenol (**2.62b**, Table 2.11, entry 1)



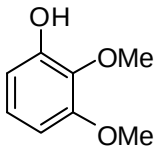
According to General Procedure D and using the following materials and 3 h reaction time: 4-bromophenyl diethylcarbamate (82 mg, 0.3 mmol), Cp_2ZrCl_2 (266 mg, 0.9 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.9 mL, 0.9 mmol) and THF (4 mL), the title compound **2.62b** (50 mg, 97% yield) was obtained as a colorless solid. mp 63-64 ^oC (EtOAc/hexanes) (lit[190] mp 63-64 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.33 (d, *J* = 8.9 Hz, 2H), 6.72 (d, *J* = 8.9 Hz, 2H), 5.04 (brs, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 154.59, 132.44 (2C), 117.17 (2C), 112.84. The physical and spectral data were consistent with those previously reported.[190,191]

Biphenyl-2-ol (**2.63b**, Table 2.11, entry 2)



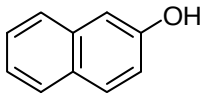
According to General Procedure D and using the following materials and 3 h reaction time: biphenyl-2-yl diethylcarbamate (40 mg, 0.15 mmol), Cp_2ZrCl_2 (133 mg, 0.45 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (0.45 mL, 0.45 mmol) and THF (2 mL), the title compound **2.63b** (23 mg, 89% yield) was obtained as a colorless solid. mp 51-52 ^oC (EtOAc/hexanes) (lit[192] mp 51-52 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.53-7.44 (m, 4H), 7.43-7.36 (m, 1H), 7.30-7.20 (m, 2H), 6.99 (t, *J* = 7.3 Hz, 2H), 5.20 (brs, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 152.38, 137.04, 130.20, 129.27, 129.14, 129.06, 128.09, 127.86, 120.81, 115.79. The physical and spectral data were consistent with those previously reported.[192,193]

2,3-Dimethoxyphenol (**2.64b**, Table 2.11, entry 3)



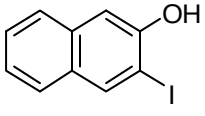
According to General Procedure D and using the following materials and 3 h reaction time: 2,3-dimethoxyphenyl diethylcarbamate (76 mg, 0.3 mmol), Cp_2ZrCl_2 (266 mg, 0.9 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.9 mL, 0.9 mmol) and THF (4 mL), the title compound **2.64b** (42 mg, 90% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.93 (t, *J* = 8.3 Hz, 1H), 6.60 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.48 (dd, *J* = 8.3, 1.3 Hz, 1H), 5.82 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H);[194] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 152.51, 149.45, 135.60, 124.03, 108.06, 104.10, 60.89, 55.80. The physical and spectral data were consistent with those previously reported.[194]

Naphthalen-2-ol (**2.65b**, Table 2.11, entry 4)



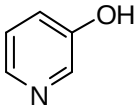
According to General Procedure D and using the following materials and 3 h reaction time: naphthalen-2-yl diethylcarbamate (73 mg, 0.3 mmol), Cp_2ZrCl_2 (266 mg, 0.9 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.9 mL, 0.9 mmol) and THF (4 mL), the title compound **2.65b** (41 mg, 94% yield) was obtained as a light yellow solid. mp 121-122 °C (EtOAc/hexanes) (lit[195] mp 121-123 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 2.3 Hz, 1H), 7.11 (dd, *J* = 8.8, 1.7 Hz, 1H), 5.13-4.88 (br, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 153.23, 134.54, 129.84, 128.93, 127.74, 126.52, 126.34, 123.62, 117.68, 109.48. The physical and spectral data were consistent with those reported.[195]

3-Iodonaphthalen-2-ol (**2.66b**, Table 2.11, entry 5)



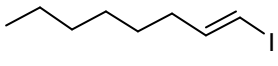
According to General Procedure D and using the following materials and 5 h reaction time: 3-iodonaphthalen-2-yl diethylcarbamate (111 mg, 0.3 mmol), Cp_2ZrCl_2 (266 mg, 0.9 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.9 mL, 0.9 mmol) and THF (4 mL), the title compound **2.66b** (66 mg, 81% yield) was obtained as a light yellow solid. mp 94-95 ^oC (EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.26 (s, 1H), 7.71-7.63 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.35 (s, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 5.48 (brs, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 151.36, 138.34, 134.71, 130.22, 127.06, 126.52, 126.48, 124.27, 109.48, 88.32. The spectral data were consistent with those previously reported.[196]

Pyridin-3-ol (**2.67b**, Table 2.11, entry 6)



According to General Procedure D and using the following materials and 3 h reaction time: pyridin-3-yl diethylcarbamate (58 mg, 0.3 mmol), Cp_2ZrCl_2 (266 mg, 0.9 mmol), a 1 M THF solution of $LiAlH(Ot\text{-}Bu)_3$ (0.9 mL, 0.9 mmol) and THF (4 mL), the title compound **2.67b** (26 mg, 91% yield) was obtained as a pale solid. mp 127-128 ^oC (EtOAc/hexanes) (lit[197] mp 127 ^oC); ^1H NMR (400 MHz, DMSO) δ ppm 9.86 (s, 1H), 8.12 (d, *J* = 2.5 Hz, 1H), 8.02 (dd, *J* = 4.4, 1.2 Hz, 1H), 7.19 (dd, *J* = 8.2, 4.5 Hz, 1H), 7.14 (ddd, *J* = 8.2, 2.7, 1.4 Hz, 1H);[197] ^{13}C NMR (101 MHz, DMSO) δ ppm 153.54, 140.14, 137.88, 123.99, 121.87. The physical and spectral data were consistent with those previously reported.[197]

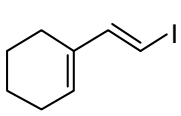
(*E*)-1-Iodooct-1-ene (**2.68b**, Table 2.12, entry 1)



According to General Procedure F and using the following materials: oct-1-yne (113 mg, 1.0 mmol), Cp_2ZrCl_2 (413 mg, 1.4 mmol), a 1 M

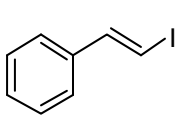
THF solution of LiAlH(O*t*-Bu)$_3$ (1.4 mL, 1.4 mmol) and THF (4 mL), a solution of iodine (355 mg, 1.4 mmol) in THF (2 mL), the title compound **2.68b** (217 mg, 91% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.51 (dt, *J* = 14.3, 7.1 Hz, 1H), 5.97 (d, *J* = 14.3 Hz, 1H), 2.05 (dt, *J* = 7.0, 6.7 Hz, 2H), 1.45-1.34 (m, 2H), 1.33-1.18 (m, 6H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 146.78, 74.21, 36.03, 31.56, 28.58, 28.32, 22.54, 14.04. The physical and spectral data were consistent with those previously reported.[198]

(*E*)-1-(2-Iodovinyl)cyclohex-1-ene (**2.69b**, Table 2.12, entry 2)



According to General Procedure F and using the following materials: 1-ethynylcyclohex-1-ene (107 mg, 1.0 mmol), Cp_2ZrCl_2 (413 mg, 1.4 mmol), a 1 M THF solution of LiAlH(O*t*-Bu)$_3$ (1.4 mL, 1.4 mmol) and THF (4 mL), a solution of iodine (355 mg, 1.4 mmol) in THF (2 mL), the title compound **2.69b** (212 mg, 91% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2928, 2858, 2832, 1447, 1434, 1180, 948, 744 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.01 (d, *J* = 14.6 Hz, 1H), 6.10 (d, *J* = 14.6 Hz, 1H), 5.79-5.66 (m, 1H), 2.18-1.97 (m, 4H), 1.70-1.62 (m, 2H), 1.62-1.54 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 148.43, 136.71, 131.10, 72.31, 25.69, 23.90, 22.20, 22.07. MS EI *m/z* (rel. int.) 234 (M^+, 44), 127 (21), 107 (40), 91 (52), 79 (100), 77 (47); HRMS *m/z* (EI, M^+) calcd for $C_8H_{11}I$, 233.9906, found 233.9902. Compound **2.69b** undergoes decomposition on standing at room temperature in hours.

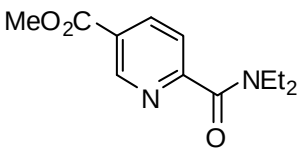
(*E*)-1-(2-Iodovinyl)benzene (**2.70b**, Table 2.12, entry 3)



According to General Procedure F and using the following materials: phenylacetylene (104 mg, 1.0 mmol), Cp_2ZrCl_2 (413 mg, 1.4 mmol), a 1 M THF

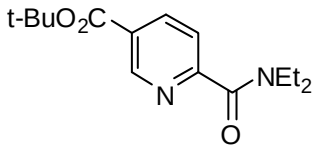
solution of LiAlH(O*t*-Bu)$_3$ (1.4 mL, 1.4 mmol) and THF (4 mL), a solution of iodine (355 mg, 1.4 mmol) in THF (2 mL), the title compound **2.70b** (216 mg, 94% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.43 (d, *J* = 14.9 Hz, 1H), 7.38-7.20 (m, 5H), 6.83 (d, *J* = 14.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 144.98, 137.68, 128.69 (2C), 128.34, 125.98 (2C), 76.62. The physical and spectral data were consistent with those previously reported.[199]

6-(Diethylcarbamoyl)nicotinic acid methyl ester (**2.80**, Scheme 2.23)



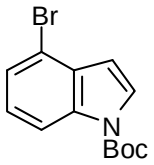
To a solution of pyridine-2,5-dicarboxylic acid dimethyl ester **2.79** (0.98 g, 5.0 mmol) in CH_2Cl_2 (15 mL) at rt was added $MgBr_2$ (0.47 g, 98% purity as labelled, 2.5 mmol). The resulting slurry was stirred at rt for 5 min, followed by the addition of $HNEt_2$ (1.04 mL, 10.0 mmol) in CH_2Cl_2 (5 mL) dropwise. The mixture was warmed to reflux and stirred at reflux overnight until the reaction was complete as monitored by TLC analysis. During that time, the slurry turned to a red solution. After cooling to rt, the reaction was quenched with 1 N HCl to neutral pH = 6-7 and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.80** (0.96 g, 82% yield) was obtained as a light yellow solid. mp 40-41 ^{o}C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.16 (d, *J* = 1.3 Hz, 1H), 8.37 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.64 (dd, *J* = 8.1, 0.5 Hz, 1H), 3.95 (s, 3H), 3.56 (q, *J* = 7.1 Hz, 2H), 3.32 (q, *J* = 7.0 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.43, 165.08, 158.26, 149.38, 138.12, 126.12, 122.69, 52.52, 43.15, 40.18, 14.19, 12.75. The physical and spectral data were consistent with those reported.[147]

6-(Diethylcarbamoyl)nicotinic acid *tert*-butyl ester (**2.81**, Scheme 2.23)



To a solution of *t*-butanol (0.7 mL, 7.2 mmol) in THF (10 mL) at -78 ^{o}C was added *n*-BuLi (2.38 M in hexanes, 3.0 mL, 7.2 mmol) dropwise. The resulting colorless solution was stirred at -78 ^{o}C for 5 min, followed by the addition of 6-(diethylcarbamoyl)nicotinic acid methyl ester **2.80** (1.42 g, 6.0 mmol) in THF (5 mL) dropwise. The orange solution was warmed to rt and stirred at rt overnight until the reaction was complete as monitored by TLC analysis. The reaction was diluted with EtOAc (20 mL) and then quenched with 1 N HCl to neutral pH = 6-7. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.81** (1.56 g, 94% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 9.10 (dd, *J* = 2.0, 0.7 Hz, 1H), 8.31 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.61 (dd, *J* = 8.1, 0.8 Hz, 1H), 3.55 (q, *J* = 7.1 Hz, 2H), 3.32 (q, *J* = 7.1 Hz, 2H), 1.59 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.47, 163.63, 157.70, 149.18, 138.04, 127.86, 122.59, 82.42, 43.13, 40.17, 28.08 (3C), 14.21, 12.76. The physical and spectral data were consistent with those reported.[147]

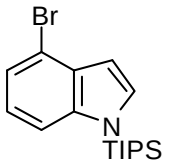
N-(*tert*-Butoxycarbonyl)-4-bromoindole (**2.83b**, Scheme 2.24)



To a solution of 4-bromoindole **2.83a** (0.51 g, 96% purity as labelled, 2.5 mmol) and DMAP (9 mg, 3 mol%) in CH_2Cl_2 (3 mL) at rt was added a solution of Boc_2O (0.59 g, 97% purity as labelled, 2.6 mmol) in CH_2Cl_2 (1 mL). The resulting solution was stirred at rt for 1 h until the reaction was complete as monitored by TLC analysis. The reaction was quenched with 1 N HCl (2 mL) and the aqueous layer was extracted with

CH_2Cl_2 (2 x 5 mL). The combined organic layers were washed with aq. $NaHCO_3$, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.83b** (0.75 g, 99% yield) was obtained as a light pink oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.11 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 3.7 Hz, 1H), 7.39 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.64 (dd, *J* = 3.7, 0.5 Hz, 1H), 1.68 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ ppm 149.43, 135.58, 131.13, 126.44, 125.53, 125.11, 114.66, 114.23, 107.07, 84.24, 28.15 (3C). The physical and spectral data were consistent with those previously reported.[200]

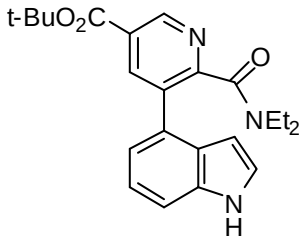
N-(Triisopropylsilyl)-4-bromoindole (**2.83c**, Scheme 2.24)



To a solution of 4-bromoindole **2.83a** (1.02 g, 96% purity as labelled, 5.0 mmol) in THF (20 mL) at -78 ^{o}C was added *n*-BuLi (2.33 M in hexanes, 2.2 mL, 5.2 mmol) dropwise. The resulting solution was stirred at -78 ^{o}C for 20 min. Then, a solution of TIPSCl (1.2 mL, 97% purity as labelled, 5.2 mmol) in THF (3 mL) was added dropwise at -78 ^{o}C. The resulting solution was warmed to rt over 2 h and stirred at rt for an additional 2 h until the reaction was complete as monitored by TLC analysis. The reaction was quenched with saturated aq. NH_4Cl (10 mL) and the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.83c** (1.76 g, 99% yield) was obtained as a colorless solid. mp 63-64 ^{o}C (hexanes) (lit[145] 64-65 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 3.3 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.01 (t, *J* = 7.9 Hz, 1H), 6.70 (d, *J* = 3.2 Hz, 1H), 1.78-1.62 (m, 3H), 1.15 (d, *J* = 7.5 Hz, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 141.02, 132.09, 131.68,

122.73, 122.18, 114.44, 112.95, 105.08, 18.05 (6C), 12.77 (3C). The physical and spectral data were consistent with those previously reported.[145]

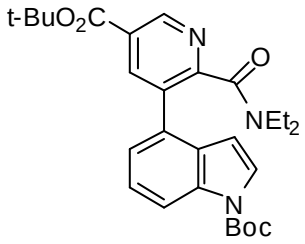
6-(Diethylcarbamoyl)-5-(4-indolyl)-nicotinic acid *tert*-butyl ester (**2.84a**, Scheme 2.24)



To a solution of 6-(diethylcarbamoyl)nicotinic acid *tert*-butyl ester **2.81** (0.14 g, 0.50 mmol) and B(O*i*Pr)$_3$ (0.24 mL, 98% purity as labelled, 1.00 mmol) in THF (2 mL) at -5 ^{o}C was added a freshly prepared solution of LDA (see General Information) (0.76 M in THF, 0.85 mL, 0.65 mmol) dropwise over 10 min. The resulting red solution was stirred for 15 min at 0 °C until the borylation was complete as monitored by TLC analysis. A solution of pinacol (0.15 g, 98% purity as labelled, 1.30 mmol) in THF (0.5 mL) was added and then the reaction mixture was allowed to warm to rt with stirring over 30 min. Following filtration through a short silica gel pad, the resulting solution was degassed and then 4-bromoindole **2.83a** (0.10 g, 96% purity as labelled, 0.50 mmol), Pd_2dba_3 (5 mg, 1 mol%), *t*-Bu_3P (10% wt in hexanes, 30 mg, 3 mol%) and KF (90 mg, 1.50 mmol) were added to the above solution. The mixture was warmed to reflux and stirred at reflux for 18 h. After cooling to rt, the reaction was quenched with 1 N HCl to neutral pH = 6-7 and the aqueous layer was extracted with EtOAc (3 x 3 mL). The combined organic layers were washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.84a** (0.10 g, 51% yield) was obtained as a pale solid. mp 220-221 ^{o}C (dec); IR (KBr) ν_{max} 3280, 1723, 1616, 1458, 1436, 1406, 1372, 1339, 1316, 1281, 1258, 1161, 1127, 762 cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ ppm 11.33 (brs, 1H), 9.03 (d, *J* = 1.9 Hz, 1H), 8.36 (d, *J* = 1.9 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.42 (t, *J* = 2.7 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.1 Hz, 1H), 6.29 (brs, 1H), 3.23 (q, *J* =

6.4 Hz, 2H), 2.88 (q, *J* = 6.9 Hz, 2H), 1.57 (s, 9H), 0.82-0.72 (m, 6H); ^{13}C NMR (101 MHz, DMSO) δ ppm 166.52, 163.32, 156.95, 147.66, 138.14, 135.96, 132.95, 127.03, 126.49, 126.31, 126.23, 120.54, 119.30, 111.92, 99.17, 81.87, 41.82, 37.63, 27.61 (3C), 13.18, 11.66. MS EI *m/z* (rel. int.) 393 (M^+, 20), 266 (62), 72 (58), 56 (100); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{27}N_3O_3$ 393.2052, found 393.2038.

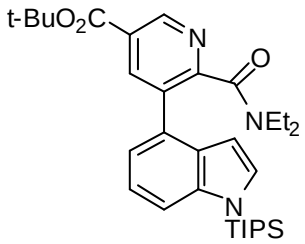
6-(Diethylcarbamoyl)-5-(N-*tert*-butoxycarbonyl-4-indolyl)-nicotinic acid *tert*-butyl ester (**2.84b**, Scheme 2.24)



To a solution of 6-(diethylcarbamoyl)nicotinic acid *tert*-butyl ester **2.81** (1.80 g, 6.4 mmol) and B(O*i*Pr)$_3$ (2.0 mL, 98% purity as labelled, 8.3 mmol) in THF (7 mL) at -5 ^{o}C was added a freshly prepared solution of LDA (see General Methods) (0.76 M in THF, 9.0 mmol) dropwise over 40 min. The resulting red solution was stirred for 1 h at 0 °C until the borylation was complete as monitored by TLC analysis. A solution of pinacol (1.54 g, 98% purity, 12.8 mmol) in THF (7 mL) was added and then the mixture was allowed to warm to room temperature with stirring over 1 h. Following filtration through a short celite pad, the resulting solution was degassed and then N-*tert*-butoxycarbonyl)-4-bromoindole **2.83b** (1.70 g, 5.8 mmol), Pd_2dba_3 (0.12 g, 2 mol%), *t*-Bu_3P (10% wt in hexanes, 0.52 g, 4 mol%) and KF (1.12 g, 17.4 mmol) were added to the above solution. The mixture was warmed to reflux and stirred at reflux for 16 h. After cooling to rt, the reaction mixture was passed through a short silica gel pad and concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.84b** (2.12 g, 75% yield) was obtained as a light yellow solid. mp 124-126 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 1736, 1721, 1642, 1142, 1370, 1347, 1314,

1284, 1259, 1160, 1137, 1126, 762, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.18 (d, *J* = 1.9 Hz, 1H), 8.38 (d, *J* = 1.9 Hz, 1H), 8.26-8.15 (m, 1H), 7.62 (d, *J* = 3.7 Hz, 1H), 7.37-7.30 (m, 2H), 6.44 (d, *J* = 3.7 Hz, 1H), 3.31 (q, *J* = 7.1 Hz, 2H), 2.83 (q, *J* = 7.1 Hz, 2H), 1.68 (s, 9H), 1.61 (s, 9H), 0.82 (t, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.91, 163.68, 156.92, 149.50, 148.89, 139.28, 135.26, 132.57, 129.34, 128.31, 127.31, 126.74, 124.12, 123.71, 115.58, 105.37, 84.06, 82.51, 42.46, 38.53, 28.14 (3C), 28.12 (3C), 13.48, 11.97; MS EI *m/z* (rel. int.) 493 (M^+, 9), 266 (39), 72 (100); HRMS *m/z* (EI, M^+) calcd for $C_{28}H_{35}N_3O_5$ 493.2577, found 493.2555.

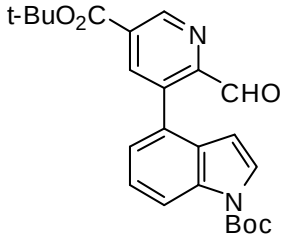
6-(Diethylcarbamoyl)-5-(N-triisopropylsilyl-4-indolyl)-nicotinic acid *tert*-butyl ester (**2.84c**, Scheme 2.24)



To a solution of 6-(diethylcarbamoyl)nicotinic acid *tert*-butyl ester **2.81** (0.89 g, 3.2 mmol) and $B(OiPr)_3$ (1.0 mL, 98% purity as labelled, 4.2 mmol) in THF (4 mL) at -5 °C was added a freshly prepared solution of LDA (see General Methods) (0.76 M in THF, 5.8 mmol) dropwise. The resulting red solution was stirred for 1 h at 0 °C until the borylation was complete as monitored by TLC analysis. A solution of pinacol (0.77 g, 98% purity, 6.4 mmol) in THF (4 mL) was added and then the mixture was allowed to warm to room temperature with stirring over 1 h. Following filtration through a short celite pad, the resulting solution was degassed and then N-(triisopropylsilyl)-4-bromoindole **2.83c** (1.01 g, 2.9 mmol), Pd_2dba_3 (0.06 g, 0.02 equiv), *t*-Bu_3P (10%wt in hexanes, 0.26 g, 0.04 equiv) and KF (0.56 g, 3.0 equiv) were added to the above solution. The mixture was warmed to reflux and stirred at reflux for 17 h. After cooling to rt, the reaction mixture was passed through a short silica gel pad and

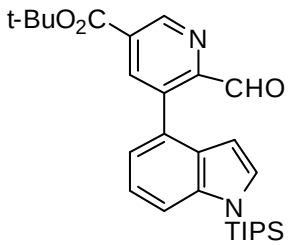
concentrated *in vacuo*. After purification via flash SiO_2 column chromatography, the title compound **2.84c** (0.53 g, 30% yield) was obtained as a yellow viscous oil. IR (KBr) ν_{max} 1720, 1645, 1313, 1282, 1266, 1164, 1136, 1124, 884, 753, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.18 (d, *J* = 1.9 Hz, 1H), 8.55 (d, *J* = 1.9 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.28 (d, *J* = 3.2 Hz, 1H), 7.24 (d, *J* = 6.8 Hz, 1H), 7.20-7.14 (m, 1H), 6.48 (d, *J* = 2.8 Hz, 1H), 3.38-3.19 (m, 2H), 2.75 (q, *J* = 7.0 Hz, 2H), 1.78-1.65 (m, 3H), 1.62 (s, 9H), 1.15 (d, *J* = 7.5 Hz, 18H), 0.71 (t, *J* = 7.1 Hz, 3H), 0.61 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.74, 163.74, 156.40, 148.19, 140.83, 139.69, 133.96, 132.10, 130.36, 127.49, 127.40, 121.24 (2C), 114.39, 103.09, 82.51, 42.37, 38.23, 28.17 (3C), 18.06 (6C), 13.14, 12.80 (3C), 11.80; MS EI *m/z* (rel. int.) 549 (M^+, 38), 422 (100), 379(19), 72 (40); HRMS *m/z* (EI, M^+) calcd for $C_{32}H_{47}N_3O_3Si$ 549.3387, found 549.3392.

6-(Formyl)-5-(N-*tert*-butoxycarbonyl-4-indolyl)-nicotinic acid *tert*-butyl ester (**2.85b**, Scheme 2.25)



To a suspension of $Cp_2Zr(H)Cl$ (200 mg, 95% purity as labelled, 0.74 mmol) in THF (1 mL) at rt was added a solution of 6-(diethylcarbamoyl)-5-(N-*tert*-butoxycarbonyl-4-indolyl)-nicotinic acid *tert*-butyl ester **2.84b** (200 mg, 0.41 mmol) in THF (1 mL). The resulting mixture was stirred at rt for 20 min during which time the reaction mixture turned to a clear orange solution. Following concentration *in vacuo* and purification via flash SiO_2 column chromatography, the title compound **2.85b** (103 mg, 61% yield) was obtained as a yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously (**2.54**, Table 2.9).

6-(Formyl)-5-(N-triisopropylsilyl-4-indolyl)-nicotinic acid *tert*-butyl ester (**2.85c**, Scheme 2.25)



To a suspension of $Cp_2Zr(H)Cl$ (0.43 g, 95% purity, 1.57 mmol) in THF (2 mL) at rt was added a solution of 6-(diethylcarbamoyl)-5-(N-triisopropylsilyl-4-indolyl)-nicotinic acid *tert*-butyl ester **2.84c** (0.48 g, 0.87 mmol) in THF (1 mL). The resulting mixture was stirred at rt for 30 min during which time the reaction mixture turned to a clear yellow solution. Following concentration *in vacuo* and purification via flash SiO_2 column chromatography, the title compound **2.85c** (0.22 g, 52% yield) was obtained as a yellow viscous oil. IR (KBr) ν_{max} 1720, 1718, 1317, 1282, 1259, 1164, 1135, 882, 836, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.97 (s, 1H), 9.34 (d, *J* = 1.8 Hz, 1H), 8.52 (d, *J* = 1.9 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 3.3 Hz, 1H), 7.28 (dd, *J* = 8.1, 7.3 Hz, 1H), 7.08 (d, *J* = 6.9 Hz, 1H), 6.34 (d, *J* = 2.6 Hz, 1H), 1.78-1.68 (m, 3H), 1.63 (s, 9H), 1.17 (d, *J* = 7.5 Hz, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 190.66, 163.53, 151.27, 149.92, 140.69, 140.53, 132.91, 131.13, 129.92, 126.76, 121.85, 121.47, 114.82, 102.94, 82.85, 28.13 (3C), 18.10 (6C), 12.82 (3C); MS EI *m/z* (rel. int.) 478 (M^+, 100), 351 (63), 249 (53), 131 (41), 103 (54), 75 (76); HRMS *m/z* (EI, M^+) calcd for $C_{28}H_{38}N_2O_3Si$ 478.2652, found 478.2672.

Chapter 3

Ru-Catalyzed Amide-Directed Aryl C-H, C-N and C-O Bond Functionalizations: C-B Formation, C-C Suzuki Cross Coupling and Hydrodemethoxylation

3.1 Introduction

Transition metal-catalyzed cross coupling reactions are arguably the most important C-C bond formation tools in organic synthesis in last 40 years.[52-54] Of these, aryl-alkene and aryl-aryl sp^2-sp^2 cross couplings, such as the Mizoroki-Heck, Suzuki-Miyaura, Negishi, Migita-Stille and Kumada-Corriu cross couplings discovered in the 1970s, have been well-explored and broadly used for constructing C-C bonds.[52-54] Most of these reactions involve cleavage of carbon-halogen and carbon-pseudohalogen bonds with transition metals (mostly Pd and Ni) and coupling with organometallic reagent species C-B, C-Zn, C-Sn and C-Mg in the Suzuki-Miyaura, Negishi, Migita-Stille and Kumada-Corriu cross couplings respectively. These couplings, in which both aryl halides and organometallic reagents are required and which we can call *traditional cross couplings*, generate stoichiometric amounts of halogen ions and metal species as undesired byproducts which, except for boron, are ecologically harmful. Since the seminal work of Murai,[201] chemists have turned to invent and develop cross coupling reactions which originate from the direct activation of unreactive bonds, especially C-H, C-O, C-N bonds which are among the most abundant bonds in organic molecules.

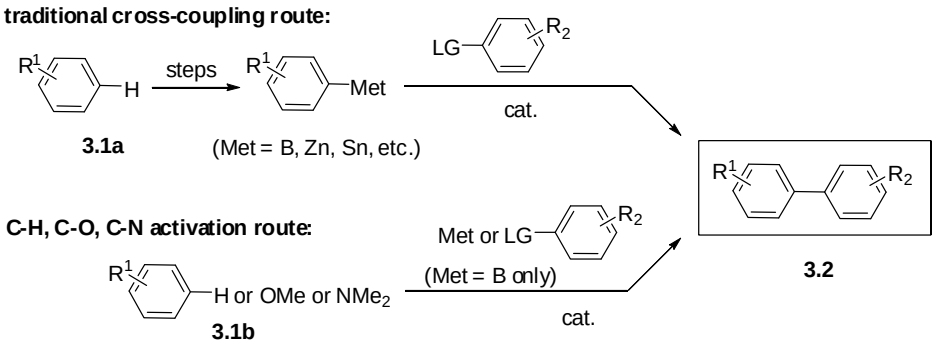
The direct use of relatively inert C-H, C-O, C-N bonds in transition metal catalyzed C-C bond forming reactions is a highly challenging research area. Data on bond enthalpies of

oxidative addition to transition metals are unavailable as a direct reference. Hence prediction of bond cleavage trends cannot be made with certainty. However, data of monofunctionalized phenyl compounds shown in Table 3.1 indicate that phenyl C-H, C-O, C-N bonds have higher dissociation energies than phenyl C-Cl, C-Br, C-I bonds,[202] that is, the cleavage of the bonds of the former group is more difficult. This incomplete and inadequate analysis has been used by synthetic chemists to rationalize experimentation for activation of inert bonds by transition metals for the discovery of new C-C bond construction methods.

Table 3.1 Bond Dissociation Enthalpies of Phenyl Compounds

Bond	Bond Enthalpies, DH_{298} (kcal/mol)
Ph—I	67
Ph—Br	84
Ph—Cl	97
Ph—OMe	101
Ph—NH_2	104
Ph—OH	112
Ph—H	113
Ph—F	127

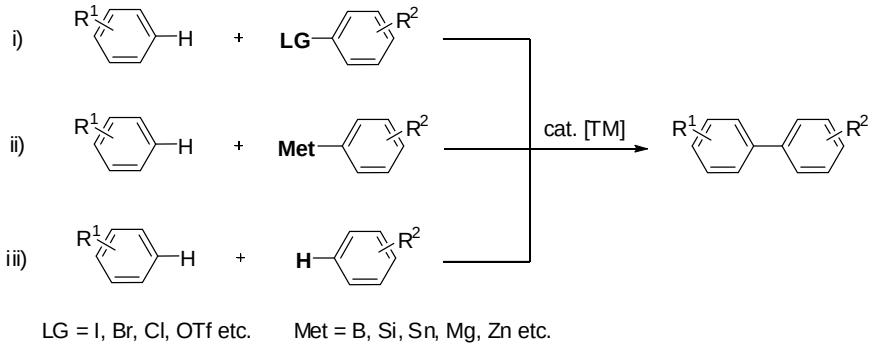
Catalytic activations of C-H, C-O and C-N bonds for C-C bond formation have been investigated intensively since the early 1990s, which will be introduced respectively in later sections. These conceptually new reactions, **3.1b → 3.2** are becoming powerful synthetic strategies for C-C bond formation and establishing convenient, economical and *green* alternatives to the traditional cross coupling processes **3.1a → 3.2** (Scheme 3.1).



Scheme 3.1

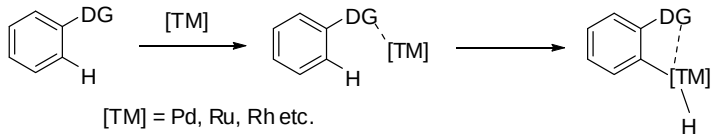
3.1.1 Directed *ortho* C-H Bond Activation and Aryl-Aryl Cross Coupling

Transition metal-catalyzed C-H bond activation/C-C bond formation, especially aryl C-H activation/cross coupling, has been extensively studied in order to develop efficient alternatives for traditional cross couplings between preactivated metal (Met) and leaving group (LG) arenes for the synthesis of biaryls. The C-H activation/arylation may be generally classified into three modes: i) arylation of an aryl C-H bond with aryl halides or aryl pseudohalides; ii) arylation of an aryl C-H bond with aryl organometallic reagents; iii) arylation of an aryl C-H bond directly with another aryl C-H material (Scheme 3.2).[203,204]



Scheme 3.2

In reactions of substituted, electronically unbiased arenes without directing-coordinating groups for C-H activation, a mixture of possible regioisomers and multiarylated products will be formed due to the presence of more than one C-H bond with similar reactivity in a substrate. Thus, uncontrollable selectivity is a major drawback for this type of coupling reaction. The introduction of a directing group (DG) may overcome this problem and generate high regioselectivity control. The main DGs studied to date are heteroatom containing groups directly substituted on the aryl ring in which the DGs effect coordination–*ortho* C-H activation. Three important features are involved in the reaction of a DG substrate: i) coordination of a heteroatom of a DG to a transition metal (TM) brings the metal in proximity to an *ortho* C-H bond; ii) stabilization of the C-[TM]-H species, formed by insertion into the *ortho* C-H bond, by DG–TM coordination; iii) achievement of high *ortho*-regioselectivity due to chelation assistance (Scheme 3.3). Overall, these features lead to a minimization of reaction steps and a reduction of byproduct formation.[203-207]

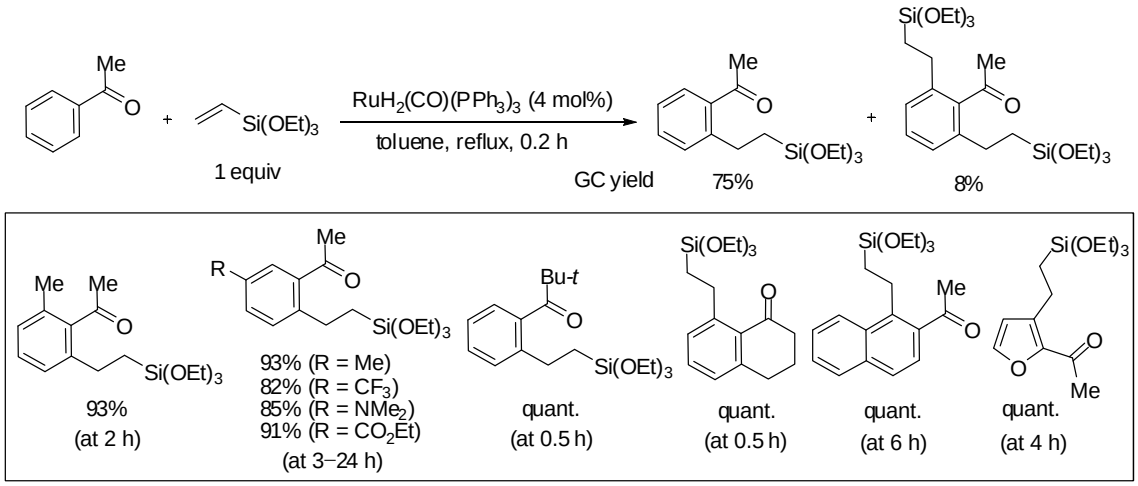


Scheme 3.3

Before systematically describing the various C-H activation/aryl-aryl coupling reactions, let us introduce the Murai reaction,[208-210] an aryl C-H activation/olefin coupling reaction.[211] Why? The reasons are as follows: i) it is the first highly efficient and selective catalytic C-H bond activation-functionalization to form a C-C bond; ii) the original Murai catalytic system has been expanded for activating arylations of C-H, C-O and C-N bonds; iii) it allows appreciation of the

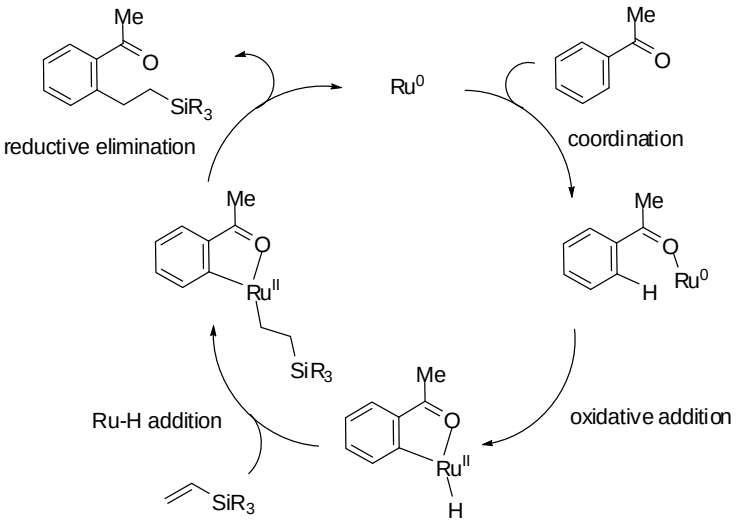
typical mechanism for the directed *ortho* aryl C-H activation/C-C bond formation via chelation assistance.

The Murai reaction, that is, the Ru-catalyzed ketone-directed aryl C-H activation/olefin coupling reaction, was reported by Murai, Kakiuchi and co-workers in 1993 in *Nature*.[211] The reaction involves the cleavage and addition of an *ortho* C-H bond of aryl ketone to an olefin. The catalytic alkylation proceeds efficiently with high regioselectivity under operationally simple conditions and is general (Scheme 3.4).[211-219] Without ketone chelation assistance, the reaction does not take place.



Scheme 3.4

Considerable investigation by the Murai group[218] has led to a mechanistic proposal which involves a $Ru^{0/II}$ catalytic cycle initiated by oxidative insertion of Ru metal into an *ortho* C-H bond via chelation assistance, addition of the resulting Ru-H to an olefin and reductive elimination to give the *ortho*-alkylated aryl ketone product (Scheme 3.5).[211,214]



Scheme 3.5

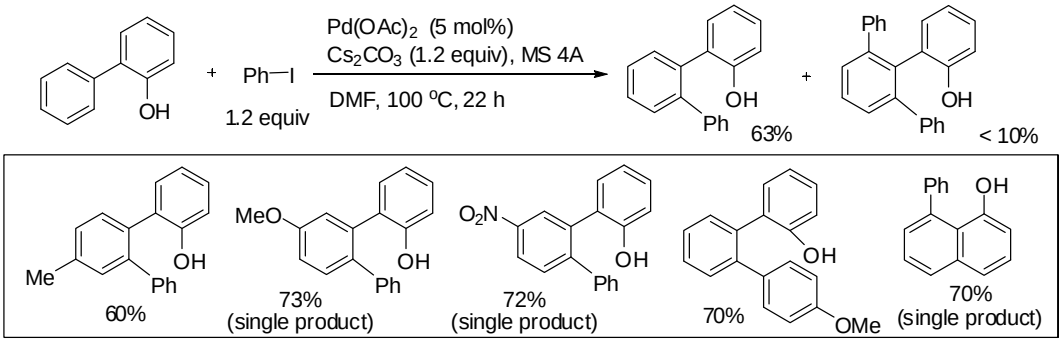
In subsequent studies, Murai and co-workers found that, besides ketones, other groups such as ester,[220,221] aldehyde,[222] imine,[223,224] hydrazone[225] and cyano[226] can also be used as DGs. Recently, the Ru catalytic system has been further expanded for activating directed arylations of C-H, C-O and C-N bonds, which will be described later.

The Murai reaction brought the directed *ortho* aryl C-H activation/C-C bond forming reaction into a new epoch. Since then, studies on directed catalytic arylation of a C-H bond via chelation assistance have been broadly pursued and, to date, a large number of selective reactions have been developed.[203-207,227-231] The following introduction of directed *ortho* aryl C-H activation/arylation reactions will focus on arylation with aryl halides and arylation with organometallic reagents. The directed aryl C-H activation/coupling with a C-H bond of another arene will not be discussed due to low selectivity involved in the second C-H activation step making this reaction less synthetically useful (Scheme 3.2 (iii)).

3.1.1.1 Arylation with Aryl Halides

Phenol as a directing group

In 1997, the phenol as a directing group for Pd-catalyzed arylation of a C-H bond with organohalides was discovered by the Miura group.[232,233] When $Pd(OAc)_2$ and Cs_2CO_3 were employed as the catalyst and base respectively, the monoarylated products were formed along with less than 10% diarylations products (Scheme 3.6). Meta-substitution effect led to monoarylation selectively even when 2 equivalents of organoiodides were used. Interestingly, under the catalytic conditions, 1-naphthol was selectively C-8 (*peri*) arylated to give 8-phenylnaphthol. A mechanism involving the key coordination between the phenolate oxygen of the substrates and the arylpalladium intermediate formed from oxidative addition to the aryl iodide was proposed without evidence.

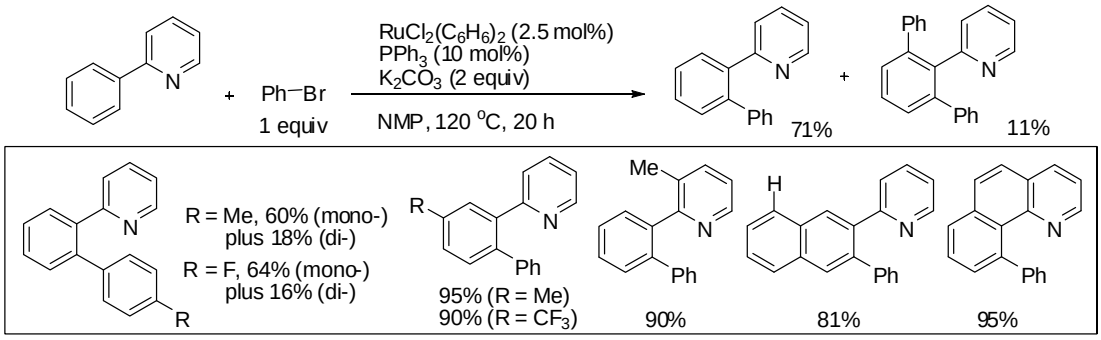


Scheme 3.6

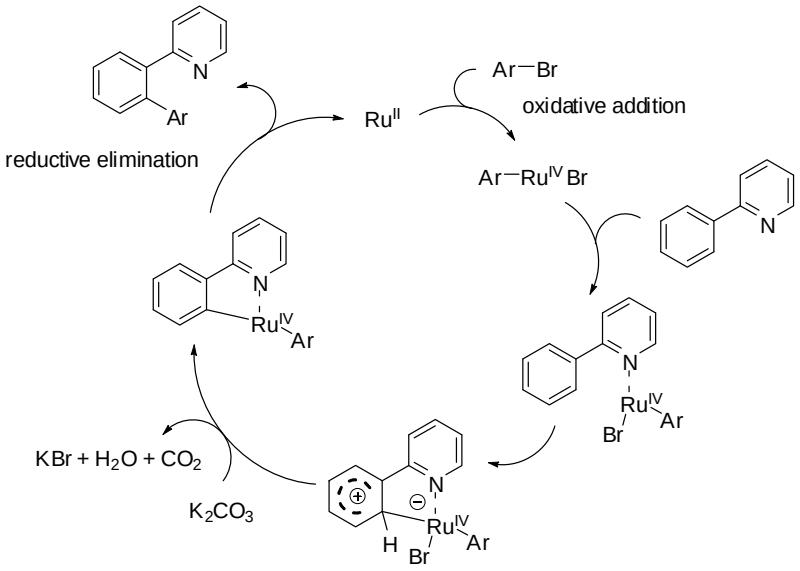
Heterocycles as directing groups (DGs)

In 2001, Oi, Inoue and co-workers reported a Ru-catalyzed pyridyl-N directed C-H activation/cross coupling with aryl bromides.[234] C-C bond formation occurred selectively at the position *ortho* to the pyridyl group. Although mixtures of monoarylation and diarylation products

were formed in some cases, the monoarylated products were predominated by steric effects, including *meta*-substitution eliminated the formation of diarylation products (Scheme 3.7). A mechanism[234] different from that given for the reaction of 2-hydroxybiaryl above was proposed involving a $Ru^{II/IV}$ process and initial chelation assistance by the pyridine-N, followed by formation of a cationic intermediate without evidence (Scheme 3.8).



Scheme 3.7



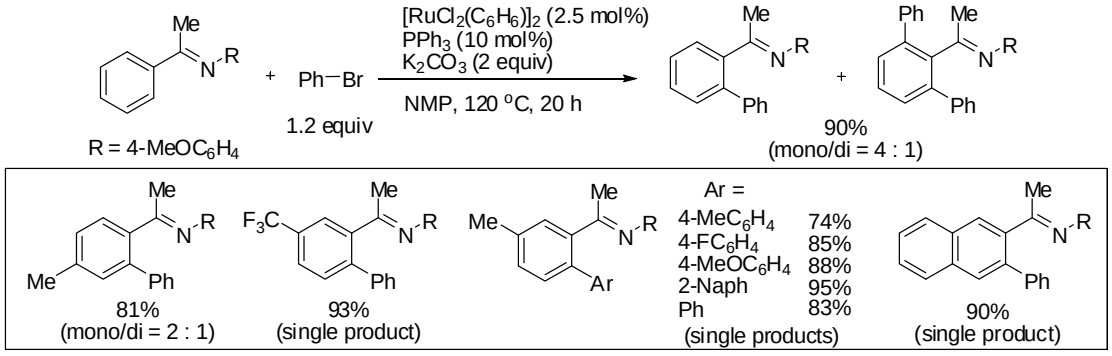
Scheme 3.8

Several years later, the Ackermann group reported additional examples of pyridyl-directed arylation with organohalides in which $[RuCl_2(p\text{-cymene})]_2$ catalyst and a phosphine oxide ligand were employed for the direct diarylation with less reactive aryl chlorides to give aza tetraaryl products in good yields.[235] Furthermore, a ligand-free catalytic C-H activation/arylation sequence with good functionality tolerance by $RuCl_3(H_2O)_n$ catalysis was demonstrated utilizing pyridyl as a directing group.[236,237]

More recently, Ru- or Pd-catalyzed C-H activation/arylation reactions were developed using other heterocycle DGs such as pyrazole,[237] triazole, [238,239] oxazolines[240,236-238], imidazolines[240] and benzoxazole[241] in reaction with aryl halides.

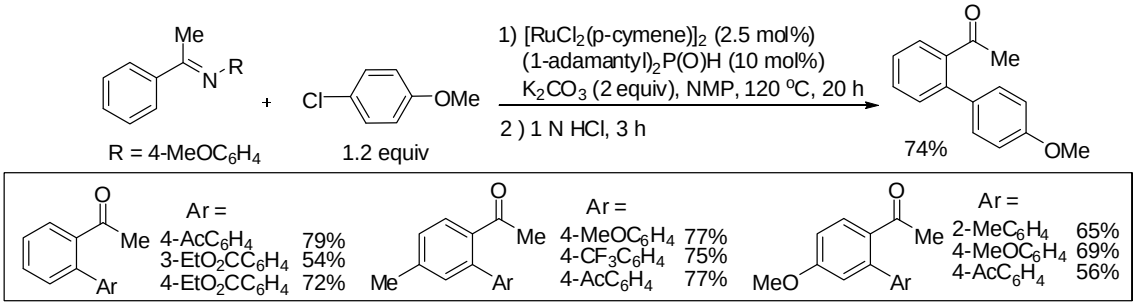
Imine as a directing group

In 2002, the imine DG was discovered by Oi and co-workers in a Ru-catalyzed C-H activation/arylation reaction with aryl bromides.[242] As in previous cases above, the formation of mixtures of monoarylation and diarylation products was observed in some cases with monoarylated products as major. Also as in previous cases (Scheme 3.6), *meta*-substituted substrates led to monoarylated products presumably owing to a steric effect (Scheme 3.9). A mechanism involving $Ru^{II/IV}$ process was provided without evidence.



Scheme 3.9

Subsequently, Ackermann reported another Ru-catalyzed imine-directed arylation with organochlorides as coupling partners.[235] Using a sterically hindered adamantyl phosphine oxide ligand, only monoarylated products were formed with good functional group tolerance. After hydrolysis, the corresponding ketones were isolated in good yields (Scheme 3.10). High monarylation selectivity and the use of less reactive aryl chlorides are two features of the reaction.

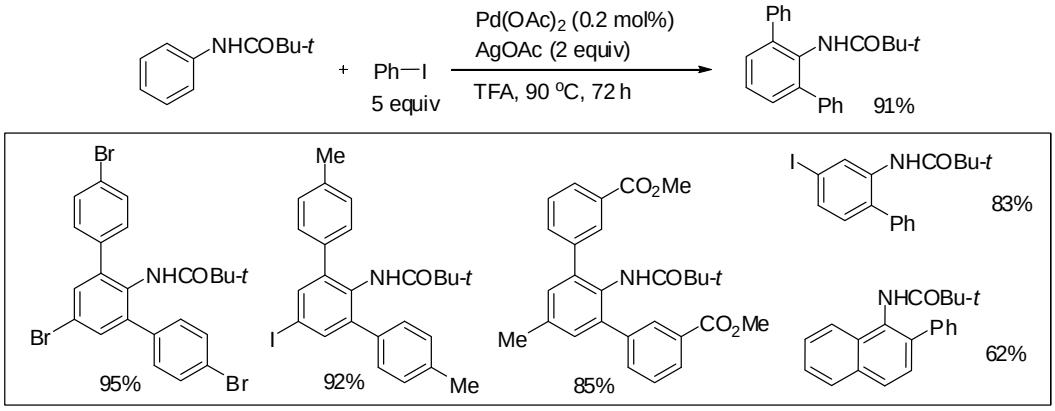


Scheme 3.10

Acylamino as a directing group

In 2005, Daugulis developed a pivaloylamino-directed catalytic C-H activation/arylation reaction using aryl iodides as coupling partners.[243] $Pd(OAc)_2$, AgOAc and TFA were employed as the catalyst, additive and solvent respectively. The presence of steric effects led to monoarylation products; otherwise, the formation of diarylated products was observed (Scheme 3.11). Bromo and iodo group tolerance was found in this reaction which, however, requires excess aryl iodides and 2-9 equiv of AgOAc employed. The simple AcNH group was also found to be a successful DG, but the yields of the *ortho* arylation products were reduced due to side reactions. Subsequently, Wu and co-workers reported the use of the $Me_3CCH_2C(O)NH$ as an efficient DG

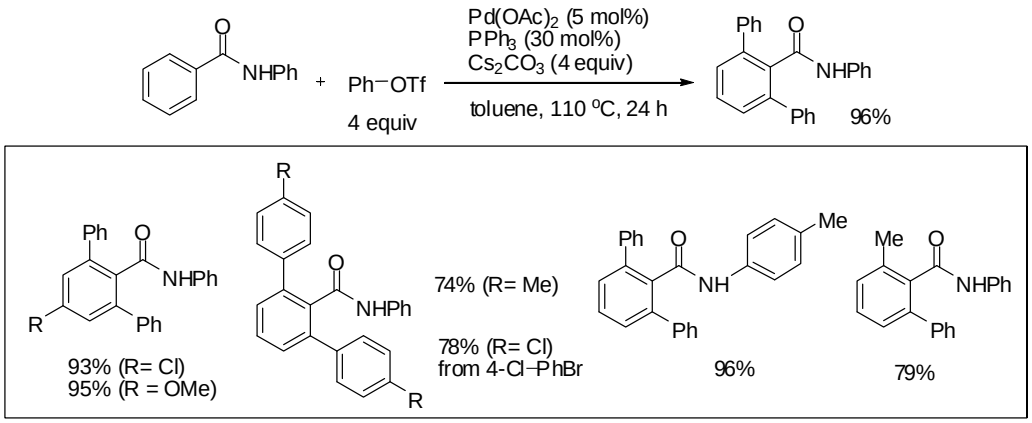
in the presence of K_3PO_4 and $PdCl_2$ as replacement for $Pd(OAc)_2$ for C-H activation/coupling reactions under prolonged reaction times.[241]



Scheme 3.11

Amide as a directing group

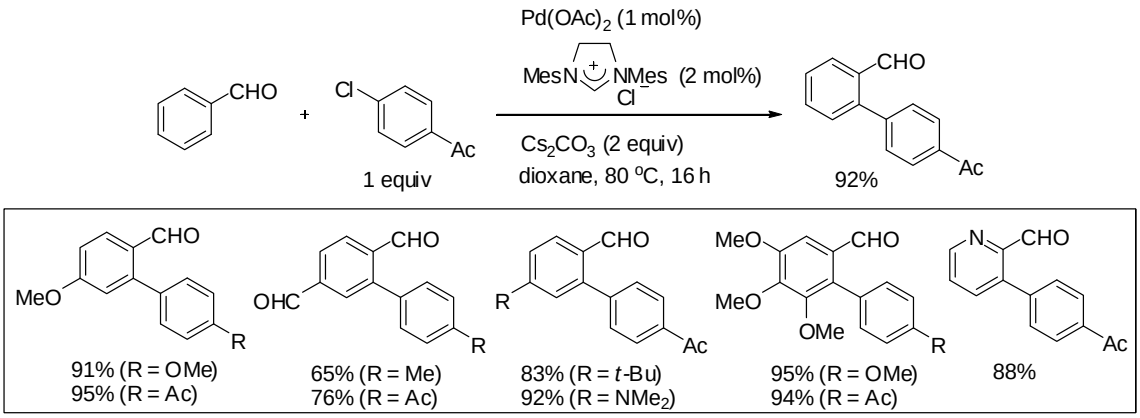
The first amide-directed catalytic arylation with aryl bromides or triflates was reported by Miura group in 2000, in which N-Ph benzamides underwent 2,6-diarylation in toluene under $Pd(OAc)_2/PPh_3/Cs_2CO_3$ catalytic conditions (Scheme 3.12).[244] Although the principle of a secondary amide DG was proved, the scope was not well established. It is of interest that N-arylation was not observed and N,N-dimethylbenzamides failed to give coupled products under these conditions. Later, Daugulis developed a different set of catalytic conditions ($Pd(OAc)_2$, AgOAc in TFA) for the N-isopropylamide-directed arylation with aryl iodides.[245] The N-isopropyl benzamides were arylated by electron-rich and electron-poor aryl iodides with good functional group tolerance.



Scheme 3.12

Aldehyde as a directing group

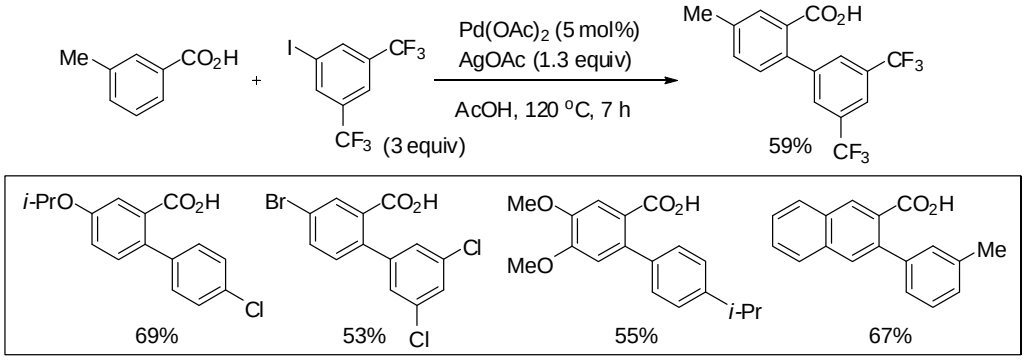
To develop an aldehyde DG is a challenging undertaking because a side reaction, decarbonylation, always occurs under the coupling reaction conditions. Examples of aldehyde DG C-H activation are rare in the literature. In 2005, Cetinkaya reported a highly selective aldehyde-directed C-H bond activation-arylation using aryl chlorides in which the catalyst $Pd(OAc)_2$, a bulky electron-rich N-heterocyclic carbene (NHC) ligand and Cs_2CO_3 were employed (Scheme 3.13).[246] Only monoarylation was observed. Electron-withdrawing and electron-donating groups on both substrates and aryl chlorides were tolerated. A pyridylaldehyde was also shown to give the coupled product in excellent yield. In addition, diarylated products were easily formed when 2 equivalents of aryl bromides were used.



Scheme 3.13

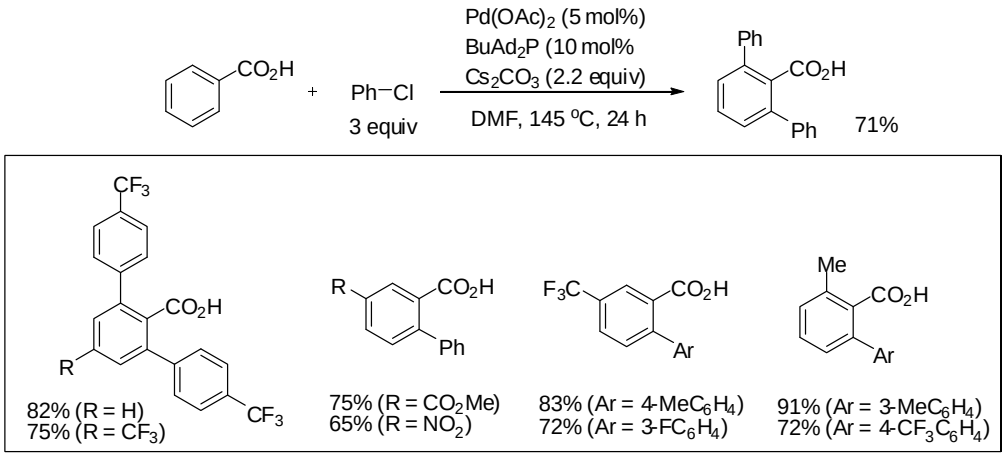
Carboxylic acid as a directing group

Two catalytic carboxylic acid-directed arylations of benzoic acids with aryl iodides were reported by Daugulis in 2007.[247] In the first arylation, $Pd(OAc)_2$ as catalyst under ligand-free conditions was used (Scheme 3.14). Only *meta*-substituted benzoic acids were examined and led to formation of monoarylated products selectively, again presumably due to steric effects. Br and Cl groups were tolerated on both substrates and coupling partners. Although the yields are modest at best, this work constituted the first successful use of the CO_2H as a DG. A $Pd^{II/IV}$ catalytic cycle involving CO_2H directing-coordination was suggested as a mechanism without evidence.



Scheme 3.14

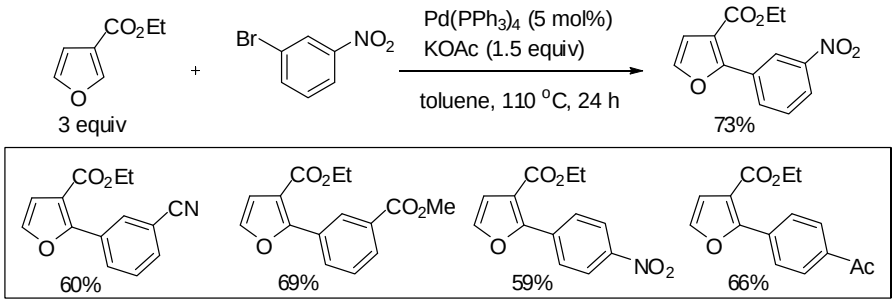
In the second CO_2H-directed arylation, less reactive aryl chlorides were employed as coupling partners under conditions of cesium carbonate and *n*-butyl-di-1-adamantylphosphine as base and ligand respectively (Scheme 3.15). Unsurprisingly, based on the above discussion, diarylation was found in some cases and steric effects induced selective monoarylation. In comparison with the previous reaction (Scheme 3.14), the current coupling shows improved yields of products.



Scheme 3.15

Ester as a directing group

In 2003, Sharp found that 3-ethoxycarbonyl furan underwent a selective 2-arylation with arylbromides under catalytic $Pd(PPh_3)_4$ conditions (Scheme 3.16).[248] A large excess of 3-ethoxycarbonyl furan was employed and only arylbromides with EWGs (electron-withdrawing groups) were effective as bromobenzene and 3-bromoanisole failed to give the expected products. Although a Heck-type mechanism was proposed without chelation assistance from the ester group, a chelation assisted $Pd^{0/II}$ catalytic pathway cannot be ruled out. This reaction was also successful on 3-methoxycarbonyl thiophene to give analogous products.



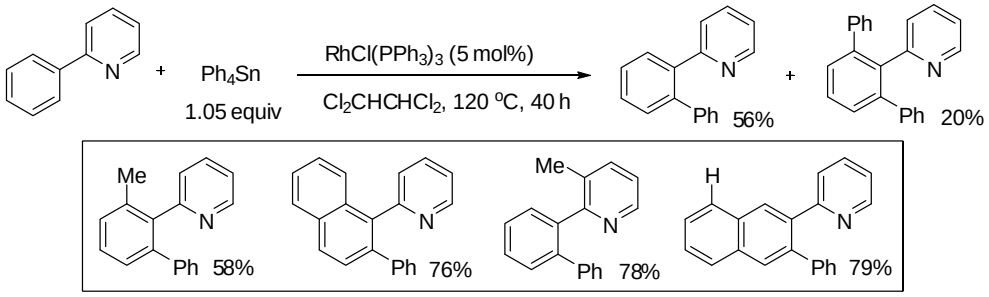
Scheme 3.16

3.1.1.2 Arylation with Organometallic Reagents

As described above, a large number of successful examples of directed C-H bond activation/cross coupling reactions have been described above which involve arylation using aryl halides. In contrast, studies on directed C-H bond activation arylation using organometallic reagents have been relatively limited until recently with several successful reports.

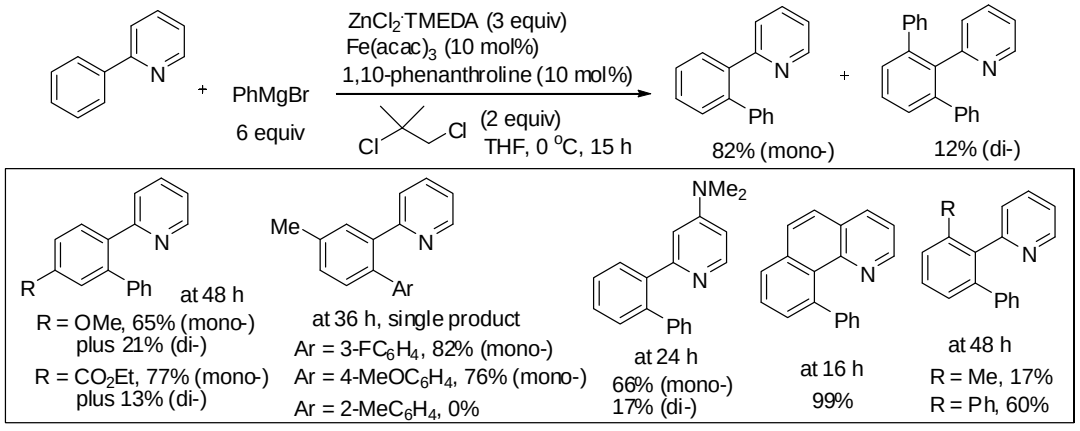
Pyridyl as a directing group

The first catalytic C-H bond directed arylation using organometallic coupling partners was reported by Oi and co-workers in 1998.[249] Using a 2-pyridyl DG substrate and tetraarylstannane (arylation reagent), a coupling reaction under Rh-catalyzed conditions was achieved (Scheme 3.17). Due to pyridine-N coordination potential to two C-H bond activation by phenyl-pyridyl bond rotation, the formation of a mixture of mono- and di-arylated products is not unexpected and was observed. Also as expected, single arylation proceeded when one C-H position was blocked by a substituent or steric hindrance was present. The reaction is inefficient since only one of four phenyl groups of an arylstannane is transferred in the reaction. The use of toxic arylstannanes is also a drawback of this coupling reaction.



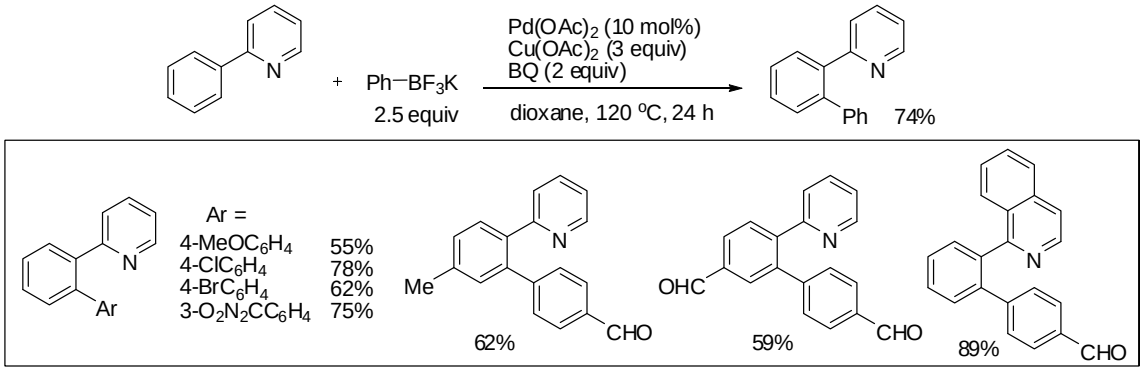
Scheme 3.17

A decade later, Nakamura reported a pyridyl-N-directed C-H activation/aryl-aryl cross coupling on the same substrate under new conditions (Scheme 3.18).[250] The conditions involve Fe^{3+} catalysis and excess of a Grignard reagent and $ZnCl_2$·TMEDA. As evidenced from the given examples and with reference to previously discussed reactions above, steric effects control the selectivity of the monoarylations. A noteworthy difference from the previous reactions, which are effected at > 80 °C, is that the reaction must be carried out at 0 °C since arylation yields are reduced at elevated temperature. The combination of Fe, Mg and Zn reagents, 1,10-phenanthroline, TMEDA, and 1,2-dichloro-2-methylpropane is important for the success of the reaction, but the mechanism is not clear. The use of three metal reagents and additives and a high excess amount of the Grignard reagent are drawbacks of this method.



Scheme 3.18

Most recently, the Wu group reported the use of potassium aryltrifluoroborates as coupling reagents in a pyridyl-N -directed C-H activation/arylation reaction, in the presence of $Pd(OAc)_2$, $Cu(OAc)_2$ and benzoquinone (BQ) as catalyst and oxidant respectively (Scheme 3.19).[251] The coupling reaction is tolerant of both EDGs (electron-donating groups) and EWGs and compatible with bromo substitution in the aryltrifluoroborate partner. Although more than 2 equivalents of aryltrifluoroborates were used, no diarylation products were reported. The excess amount of oxidant is a potential drawback of this reaction. Moreover, aryl boronic acids gave low yields of products. On the other hand, many aryltrifluoroborates are now commercial, albeit expensive commodities.

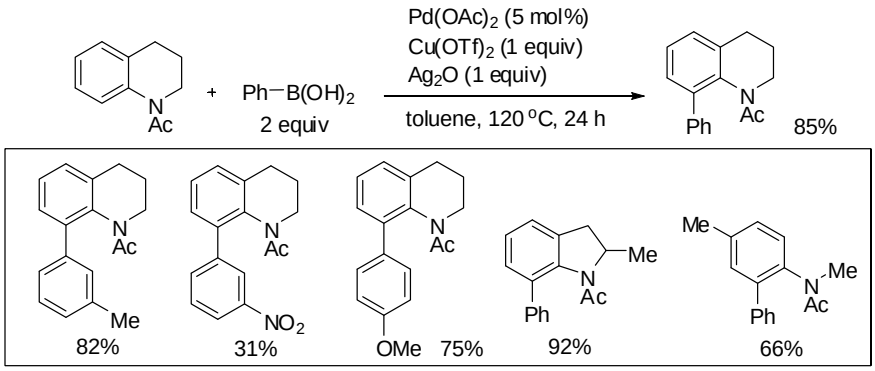


Scheme 3.19

Acetamino and urea as directing groups

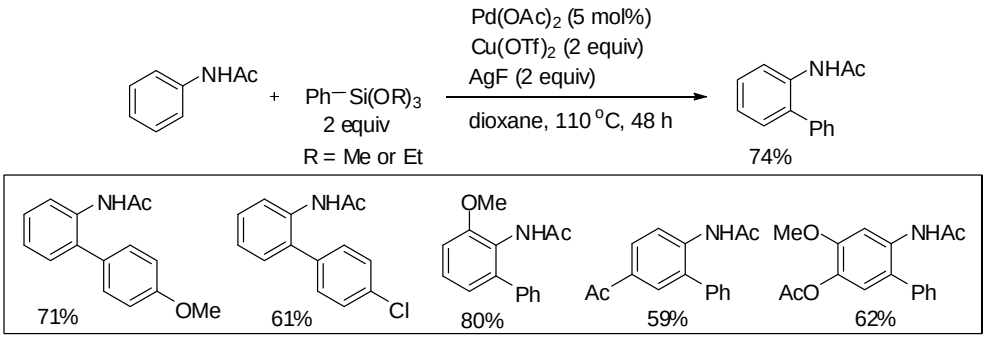
The first catalytic acetamino-directed arylation of a C-H bond for coupling with arylboronic acids was uncovered by the Shi group in 2007.[252] $Cu(OTf)_2$ as the oxidant and Ag_2O as an additive were combined with $Pd(OAc)_2$ as catalyst to effect this arylation (Scheme 3.20). While boronic acids with EDGs showed high efficiency, boronic acids bearing EWGs were found

to give decreased yields of products. As expected, the coupling reaction was suggested to be initiated by a coordination of Pd(II) with the acetamino group, but the detailed mechanism is not clear. An advantage of the reaction is using nontoxic boronic acids which are commercially available or easily prepared as arylating reagents.



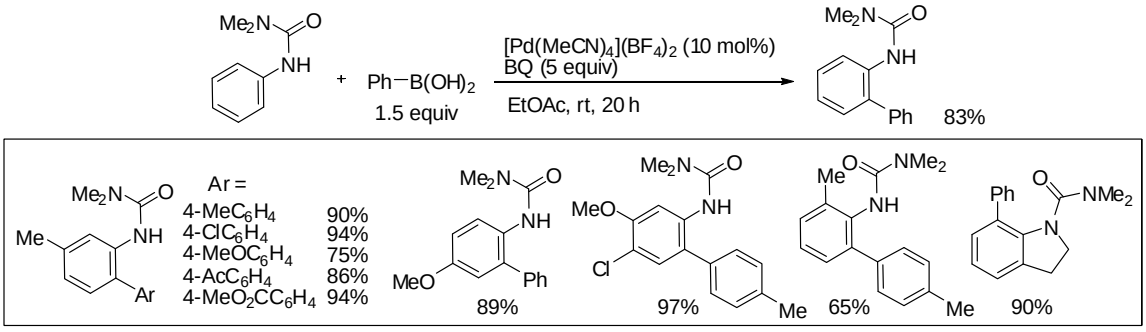
Scheme 3.20

Almost at the same time, the Shi group reported another Pd-catalyzed acetamino-directed C-H activation-arylation using trialkoxyarylsilane coupling partners under similar catalytic conditions in which, however, AgF as an additive and dioxane as the solvent were employed instead of Ag_2O and toluene (Scheme 3.21).[253] Under prolonged reaction times, the coupling proceeded in moderate to good yields. No observation of diarylation products was reported even when 2 equivalents of trialkoxyarylsilanes were used. A mechanism involving a $Pd^{II/0}$ catalytic cycle with acetamino-assisted C-H activation and fluoride-assisted transmetalation (silicate intermediate formation) was suggested for the process without experimental evidence.



Scheme 3.21

In 2010, a Pd-catalyzed urea-directed C-H bond activation-arylation and arylboronic acid coupling was reported by the Lipshutz group.[254] This reaction, mediated by benzoquinone (BQ), proceeded at room temperature to give biaryl products in good yields (Scheme 3.22). Arylboronic acids bearing EDGs and EWGs were tolerated. It was found that monoarylation highly suppressed the formation of diarylated products and trace amounts of diarylated products were obtained in only a few cases. High regioselectivity and ambient temperature are important features here.

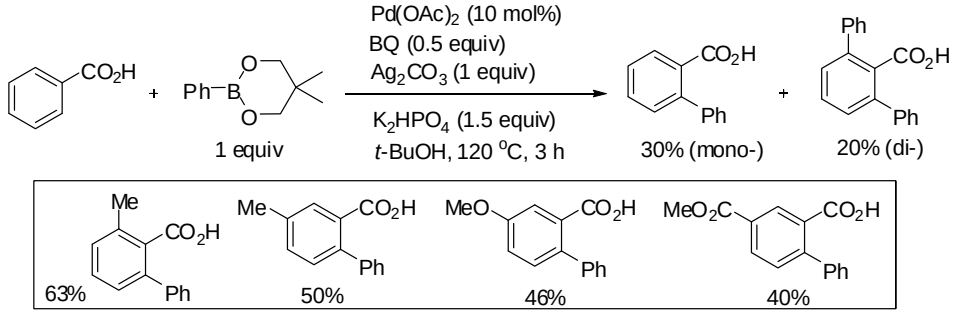


Scheme 3.22

Carboxylic acid as a directing group

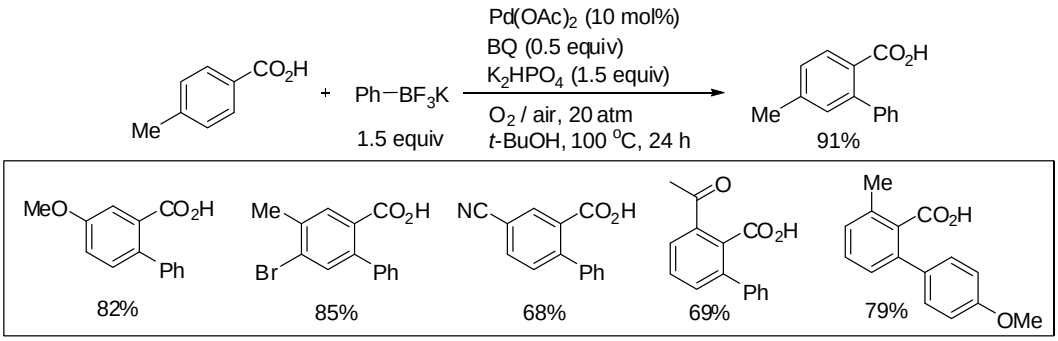
Although arylcarboxylic acids were developed as coupling partners for C-C bond formations via catalytic decarboxylative coupling since 2002,[255,256] their use as DGs for the synthesis of biaryls via C-H activation has been reported only recently.

In 2007, Yu group reported the first Pd-catalyzed COOH-directed C-H activation/cross coupling reaction which employs organoboronates as coupling partners and Ag_2CO_3 as an oxidant.[257] Although the arylation of simple benzoic acid afforded a mixture of mono- and diarylated products, *meta*-substituted benzoic acids led to regioselective *ortho*-arylation (Scheme 3.23). As reported, the yields of products were modest, the scope of benzoic acid was limited to a few substrates, and only the phenyl boroneopentylate was used as a coupling partner.



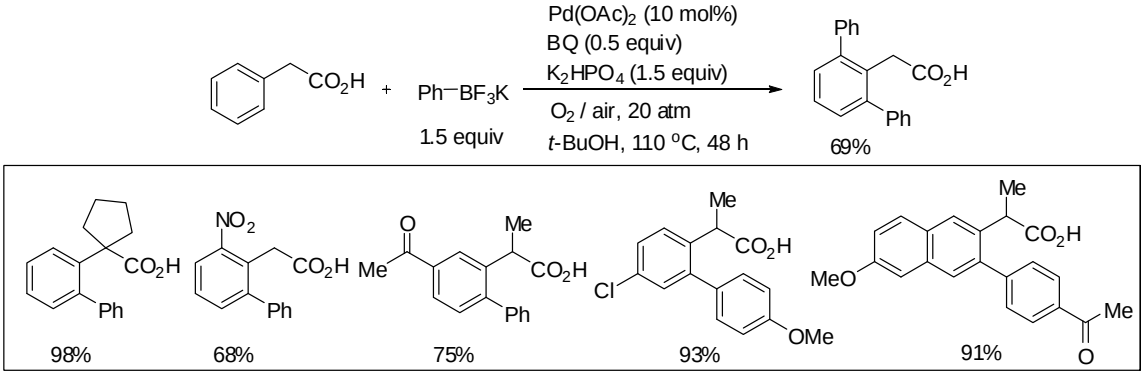
Scheme 3.23

In 2008, Yu reported a considerable improvement in the Pd-catalyzed arylation via COOH-directed C-H activation using aryltrifluoroborates as coupling partners.[258] The reaction proceeded under pressurized O_2/air conditions (20 atm) mostly in good yields (Scheme 3.24). Excellent tolerance of functionalities such as F, Cl, Br, CN and acetyl groups was reported. As expected from the previous discussion, the *meta*-substitution effect also controlled the regioselectivity of the arylation. On the other hand, perhaps surprisingly, monoarylated products were obtained in high yields when *para*-substituted benzoic acids were utilized.



Scheme 3.24

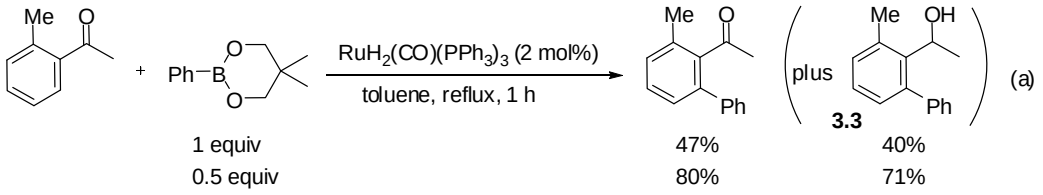
Furthermore, C-H activation/arylation of phenyl acetic acid, i.e. by an acetic acid DG, was demonstrated using aryltrifluoroborate coupling partners under the same conditions by the Yu group (Scheme 3.25).[258] An α-substituent was necessary to induce the mono arylation selectivity presumably by imparting a steric effect; its absence led to 2,6-diarylation in good yield. EWGs and EDGs in both acid substrates and organoborates were found to be compatible. A considerable limitation of these reactions for practical application is the requirement of high pressure.



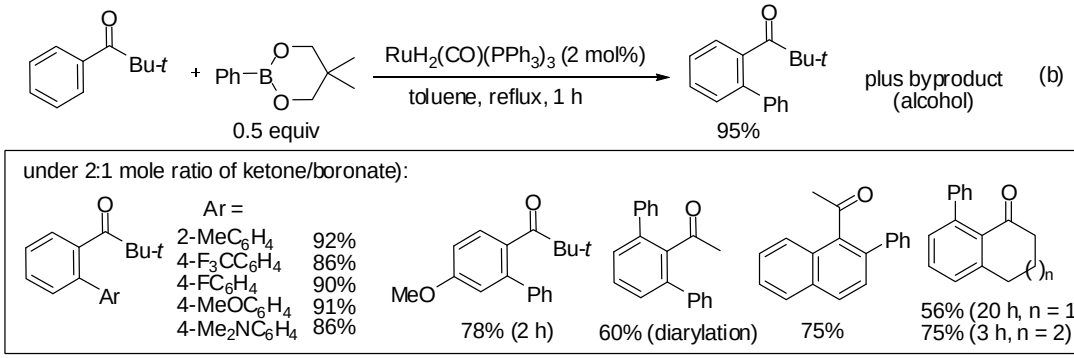
Scheme 3.25

Ketone as a directing group

In 2003, Murai, Chatani, Kakiuchi and co-workers reported a new type of C-H bond arylation in the Ru-catalyzed coupling of ketones with organoboronates to give biaryls in good yields (Scheme 3.26).[259] The catalyst ($RuH_2(CO)(PPh_3)_3$) and solvent (toluene) are the same as those used in previous directed C-H activation/olefin couplings reported by this excellent group (see Scheme 3.4). Both of the *ortho* C-H bonds are activated in the acetophenone substrate to give 2,6-diaryl products. On the other hand, only one C-H bond activation occurs in the reaction of phenyl pivaloyl ketone presumably due to inability to establish sufficient concentrations of the required rotamer for second coordination in the mono *ortho* arylated product (Scheme 3.26 (b)). As expected, the *ortho*-methyl acetophenone affords the monoarylated product (Scheme 3.26 (a)). EDGs and EWGs including Me, CF_3, F, NMe_2 and OMe in both of starting materials are tolerated. Increasing the amount of starting ketone to 2 equivalents leads to the formation of the coupled products in high yields compared to those obtained using 1 equiv of ketone. The isolation of the reduction byproduct **3.3** suggests the involvement of a hydride transfer and offers rationalization of the requirement for 2 equiv of ketone substrate for obtention of improved yields (Scheme 3.26 (a)).[260] Clearly, at least 2 : 1 ratio of ketone : organoboronate is required for high yield coupling due to the reduction reaction, a feature which obviously decreases the utility of the reaction for expensive and precious ketone substrates.

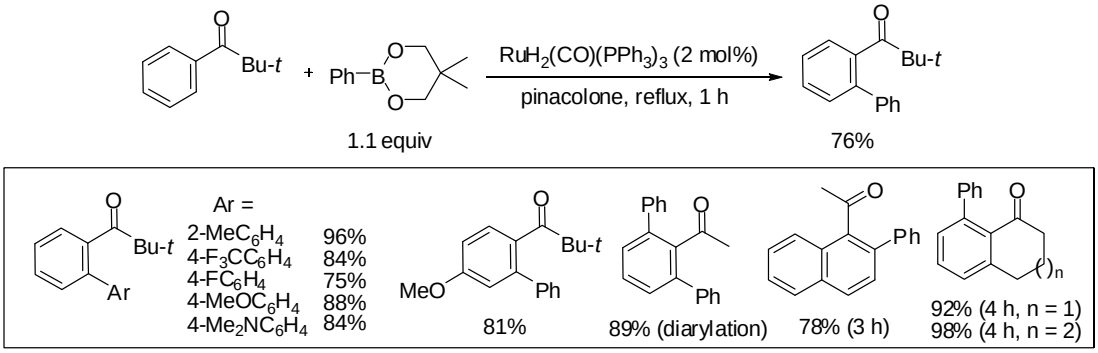


Scheme 3.26 (a)



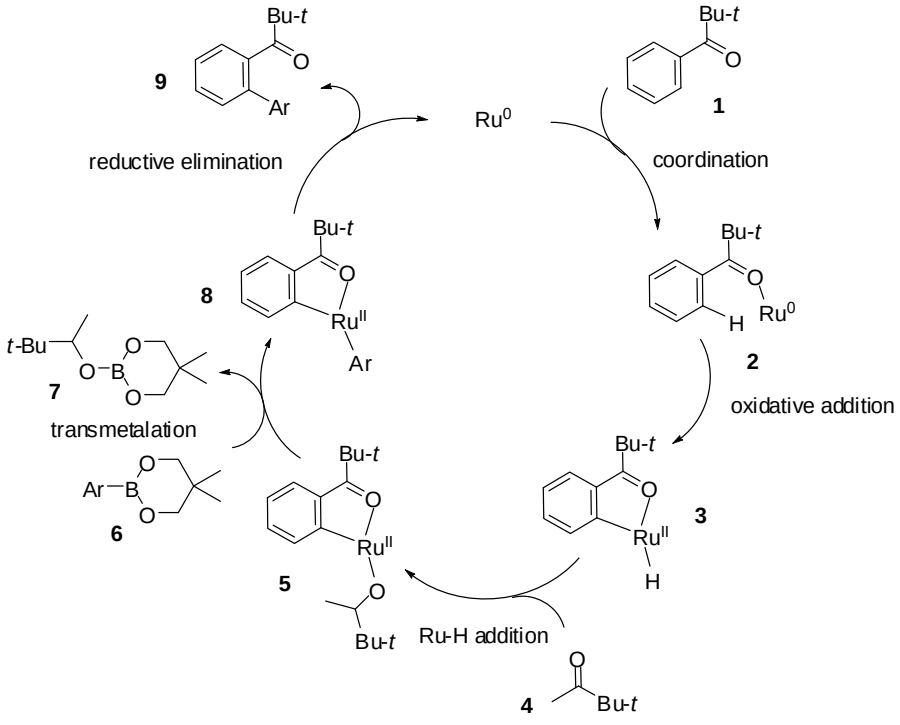
Scheme 3.26 (b)

To overcome the above deficiency, aliphatic ketones such as pinacolone and acetone, which are more reactive than aryl ketones, were introduced as solvent to act as hydride scavenger from Ru-H generated by Ru insertion into the *ortho*-C-H bond of aromatic ketones. After this inventive improvement, using an almost 1:1 ratio of aromatic ketone and organoboronate partners, the coupling reaction proceeded in good to excellent yields (Scheme 3.27).[260] Interestingly, fused aromatic ketones showed excellent yields of products under the new conditions. Moreover, among various screened phenylboronates including phenyl boropinacolate and boronic acid, it is found phenyl boroneopentylate exhibits the highest reactivity.[260]



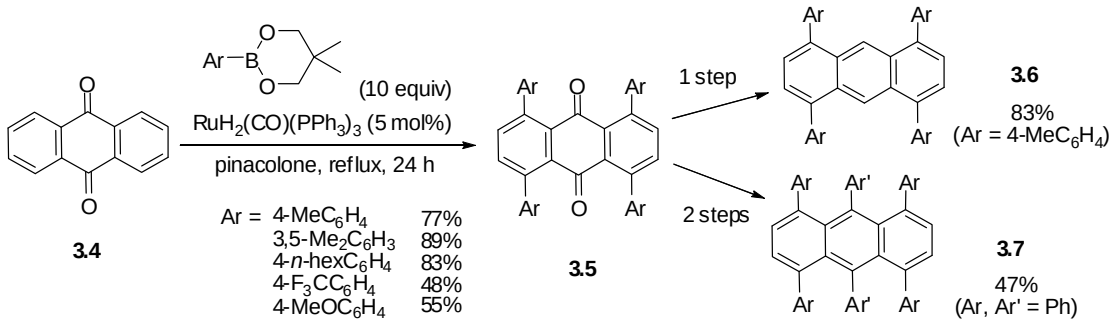
Scheme 3.27

A mechanism was proposed starting with the coordination (**2**) of ketone carbonyl with Ru(0), followed by C-H bond cleavage oxidative addition to yield an *ortho*-metalated ruthenacycle **3** which undergoes addition to pinacolone **4** to generate a Ru-OR intermediate **5**, followed by transmetalation and reductive elimination to provide the coupled product **9** with regeneration of the active Ru(0) species (Scheme 3.28).[260] A precoordination between the Ru catalyst and the oxygen of the ketone group was supported by deuterium-labeling studies on intra- and inter-molecular competition experiments.[260] As further evidence, the trialkyoxyborane **7**, generated after transmetalation, was detected by ^{1}H and ^{11}B NMR and GC/MS spectrometric studies.[260] The use of pinacolone as solvent and hydride acceptor is an important feature in this ketone directed C-H activation/cross coupling reaction.



Scheme 3.28

In 2009, the independent Kakiuchi group further extended the ketone directed C-H activation/arylation strategy to synthesize tetra- and hexa-arylanthracenes.[261] This is a short and straightforward process starting with inexpensive commercial anthraquinone **3.4** which undergoes direct C-H arylation with arylboronates employing $RuH_2(CO)(PPh_3)_3$ catalysis to yield tetraarylanthraquinones **3.5**, which upon reduction afford the tetraarylanthracenes **3.6**, or followed by addition of aryllithium reagents and further reductive aromatization furnish the hexaarylanthracenes **3.7** (Scheme 3.29). The ketone directed arylation of anthraquinone C-H bond using organoboronates is the key step in which four aryl groups are successfully introduced in a beautiful one-step operation.

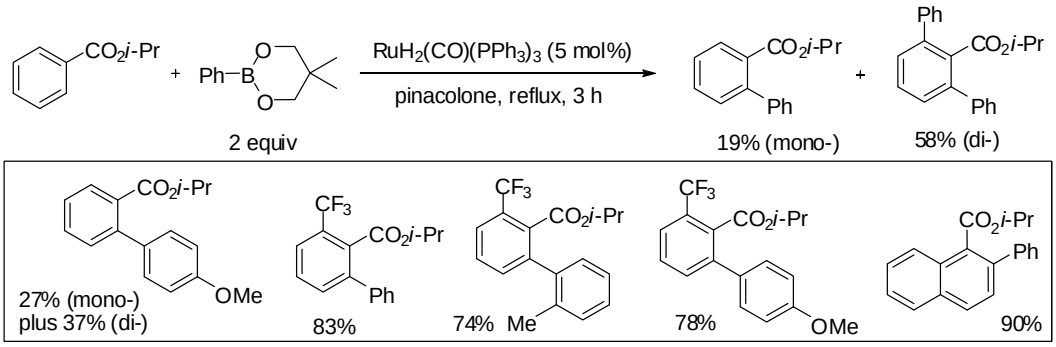


Scheme 3.29

Ester as a directing group

Most recently, in 2010, the ester group was also found by Kakiuchi group as a directing group to effect the Ru-catalyzed C-H activation/aryl-aryl cross coupling reaction (Scheme 3.30).[262] In particular, isopropyl benzoates showed high reactivity in this reaction after screening a variety of esters. When one of two *ortho* positions to the isopropyl ester is substituted by e.g. a Me or CF_3 group, the coupling reaction proceeds in good yields. Otherwise, to repeat, as observed in many of these C-H activation reactions of aryl DG systems, a mixture of mono- and,

predominantly, di-arylated products are obtained. A similar mechanism as that previously presented for arylation of aromatic ketones (Scheme 3.28) was proposed. These results demonstrate the viability of the ester to act as a DG for C-H bond activation-arylation with organoboronates. However, the scope and limitations for the reaction were inadequately investigated.



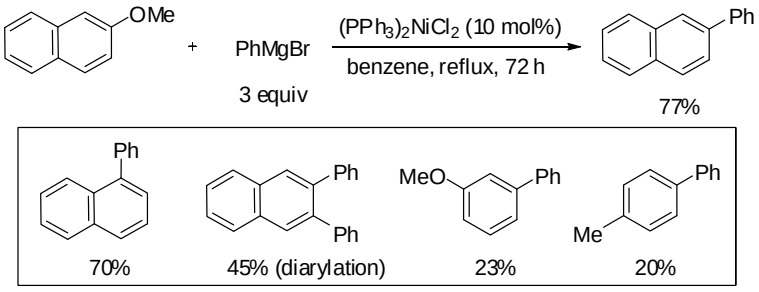
Scheme 3.30

3.1.2 C-O Bond Activation and Cross Coupling

Reductive aryl C-O bond cleavage in derivatives such as C-OTf,[53] C-OAc,[263] C-OPiv,[263-265] C-OCONEt$_2$,[64,63] C-OCO$_2$Bu-*t*[64] and C-OSO$_2$NMe$_2$,[64] are significant recent reactions in the organic chemist's tool box. Of these, the reductive C-OTf bond cleavage has received broad application.[53] Furthermore, these C-O functional groups serve as complementary cross coupling partners to aryl halides, allowing consideration of alternative phenol-derived processes to a halide, can directly undergo Suzuki cross coupling with organoboron partners. However, some drawbacks of these methodologies remain: i) all functional groups are characterized by at least modest or strong EWGs, e.g. Tf, Ac, Piv, CONEt$_2$, CO$_2$Bu-*t* and SO$_2$NMe$_2$, for assisting the oxidative addition by transition metal catalysts; ii) require expensive pre-preparation such as the synthesis of aryl triflates from phenols with triflic anhydride. Consideration of the broad and

commercial availability of aryl ethers, the discovery of a transition metal process for C-OMe bond cleavage would provide a convenient and powerful method for cross coupling.

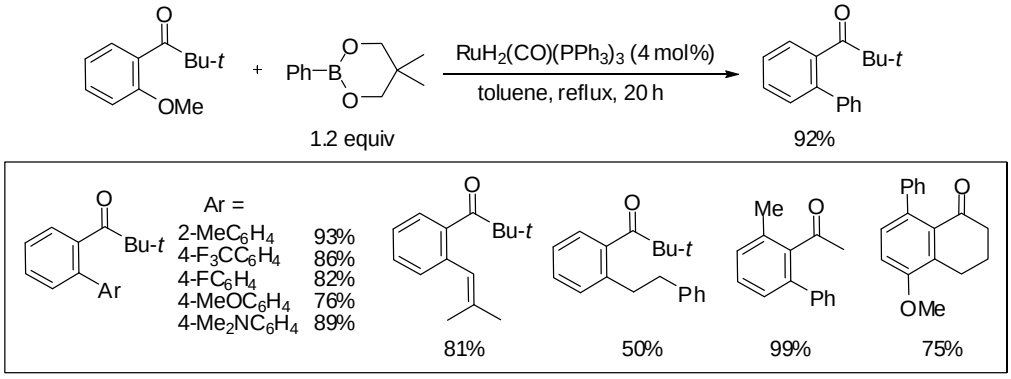
The aryl ether C-O bond is one of the most abundant and unreactive bonds in organic molecules. In view of the high bond dissociation energy[202] of the C-OMe bond (higher than C-Cl, see Table 3.1), finding an efficient C-O bond cleavage process in aryl ethers is a difficult and challenging order. However, already in 1979, Wenkert reported that aryl ethers undergo Kumada-Corriu cross coupling with Grignard reagents under Ni(0) catalysis to form biaryls in low to moderate yields (Scheme 3.31).[266,267] Although the yields of the coupled products were modest and the scope for substituent tolerance was shown to be poor, this constituted the first transition metal-catalyzed C-C bond formation via C-O bond cleavage of aryl ethers. Reaction of naphthyl ethers was found to be more efficient than that of phenyl ethers.



Scheme 3.31

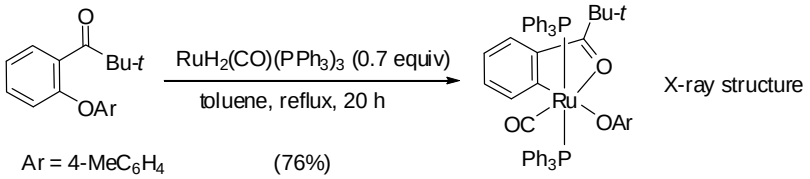
The area lay dormant until 2004 when the Kakiuchi-Chatani-Murai group discovered a new type of C-O bond cleavage of aryl ethers by Ru-catalysis under chelation assistance.[268] The new reaction involves Ru-catalyzed ketone-directed C-OMe bond activation and Suzuki-type C-C cross coupling with organoboronates (Scheme 3.32). It is found that phenyl boroneopentylate holds the highest reactivity among various screened phenylboronates including phenyl

boropinacolates. The scope for organoboroneopentylates was examined broadly (aryl, alkenyl and alkylboronates) and a variety of functional groups in the arylboronates (Me, vinyl, OMe, F and CF_3) were found to be compatible. Both C-H and C-O activation/coupling reactions occurred simultaneously when 2-methoxy acetophenone was employed.[269] In order to avoid the undesired C-H activation, the bulky *t*-butyl ketone has to be used to block the C-H activation by steric hindrance.



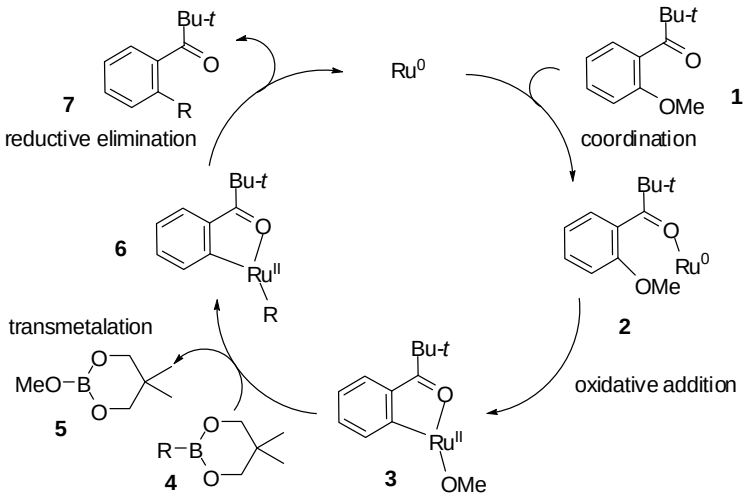
Scheme 3.32

Ru(0)–ketone carbonyl chelation was demonstrated to be required and confirmed by X-ray crystal structure analysis (Scheme 3.33).[270] This is the first direct evidence of the oxidative addition of a transition metal into an aryl C-OAr bond and constitutes the first efficient cross coupling reaction via unreactive C-O bond activation, avoiding consideration of necessary transformation to Ar-OTf.



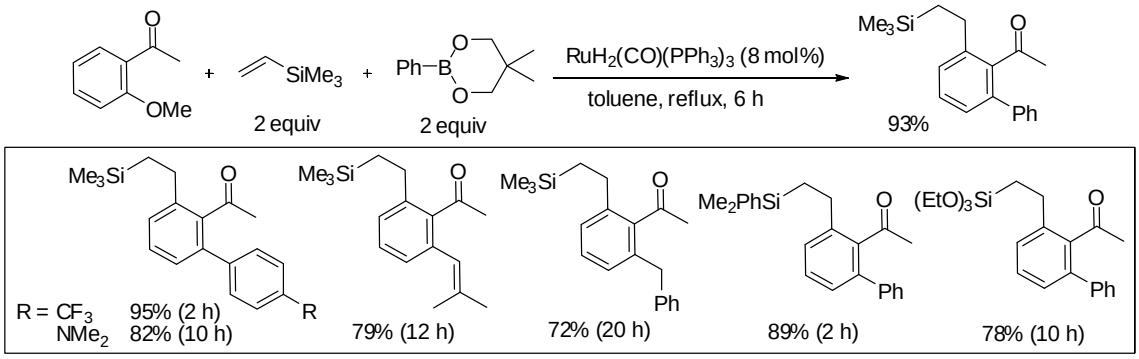
Scheme 3.33

The proposed mechanism for the ketone DG assisted C-OMe activation of aryl ethers involves four elementary steps (Scheme 3.34): i) coordination between Ru(0) and the ketone carbonyl **(2)**; ii) oxidative addition of Ru(0) into the aryl C-OMe with chelation assistance **(3)**; iii) transmetalation between the Ru(II)-OMe species **3** and the organoboronate **4** to form the Ar-Ru(II)-R intermediate **6**; and iv) reductive elimination of Ar-Ru(II)-R **6** to give the coupled product **7** with regeneration of the active Ru(0) to continue the catalytic cycle.[270] In this reaction, the nature of the aryl ketone substituent is very important for controlling the coupling selectivity since two different possible reaction sites, C-H and the C-OMe, are available for activation and coupling. As described above (Scheme 3.26 and 3.27),[259,260] ketone DG assisted aryl C-H/ArB$(OR)_2$ coupling is an established reaction. Thus, in the case of 2-methoxy acetophenone, non-regioselective C-H and C-OMe activations occur to form mixtures of mono- and di-coupled products.[269] Two solutions were found to avoid the di-coupling reactions: i) elimination of the C-H activation by incorporating an *ortho* methyl substituent and ii) as in previous similar problems (Scheme 3.26 and 3.27), choosing a bulky ketone such as pivaloyl to block the C-H activation by a steric effect. The results of the Chatani-Kakiuchi group have demonstrated that the aryl C-O/ArB$(OR)_2$ coupling proceeds without interference from C-H/ArB$(OR)_2$ coupling by using the *t*-butyl group as steric shield.[268] Although the solutions i) and ii) have efficiently solved the regioselectivity and di-coupling problems, they constitute special blocking and steric structural changes which will limit the application of this powerful methodology.



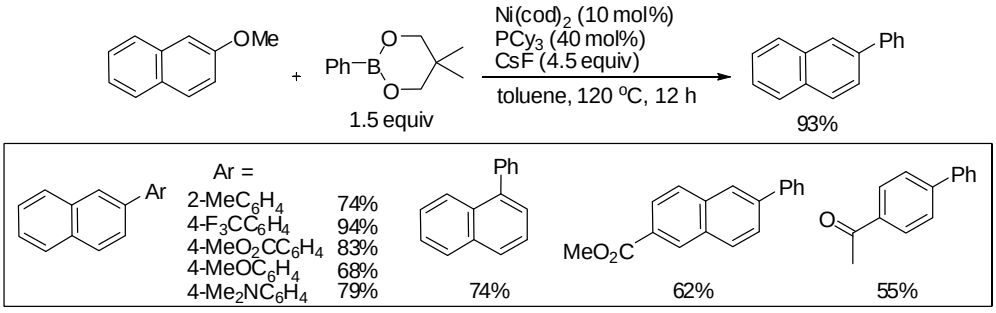
Scheme 3.34

Further studies concerning the reactivity of C-H and C-O bonds indicated that the C-H activation/olefin coupling proceeds faster than the C-H or C-O activation/$ArB(OR)_2$ coupling reaction. Based on this difference, a highly chemoselective process involving sequential C-C bond formations with vinylsilanes and organoboronates has been developed by the way of ketone-directed C-H and C-O activations (Scheme 3.35).[270] Thus, using a three-component reaction, two different C-C bond forming reactions, alkylation and arylation, are successfully achieved in one-pot. This is an important feature of the Ru-catalyzed ketone-directed coupling reaction.



Scheme 3.35

In 2008, Chatani and co-workers reported the direct C-OMe bond cross coupling reaction with organoboronates under Ni(0) catalysis without ketone DG assistance (Scheme 3.36).[271] This reaction constitutes another important development in the C-O bond activation/C-C bond cross coupling area. As also found in a Kumada-Corriu coupling process described before (Scheme 3.31),[266,267] naphthyl ethers performed better than phenyl ethers in this coupling process. However, the present Suzuki-type coupling reaction shows remarkable differences in high functional group tolerance and good yields. This reaction was suggested to proceed by a similar mechanism as that proposed for the Ru-catalyzed process with the obvious exception of the chelation step.

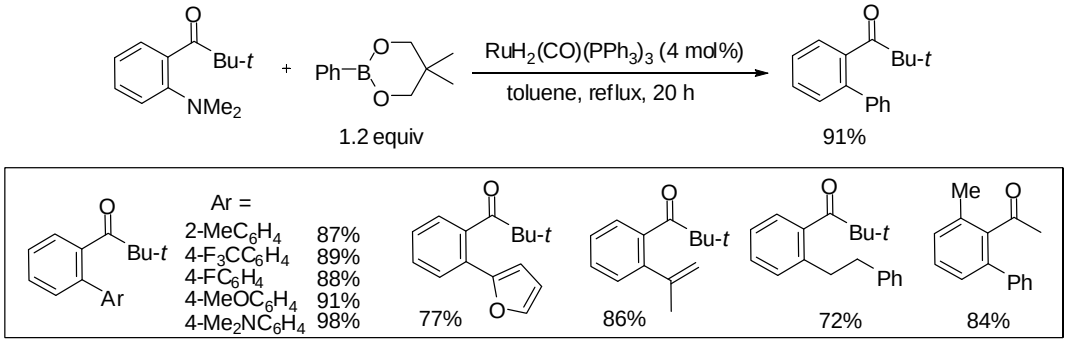


Scheme 3.36

3.1.3 C-N Bond Activation and Cross Coupling

Aryl C-N bonds have high bond dissociation enthalpies[202] (e.g. DH_{298} = 104 kcal/mol for the aniline C-NH_2 bond, in comparison, DH_{298} = 101 kcal/mol for C-OMe, and DH_{298} = 97 kcal/mol for C-Cl, see Table 3.1). Among the abundant bonds in organic molecules, the aromatic C-N bond is an unreactive or difficult-to-cleave bond for organic synthesis manipulation. Although aryl C-N bond activations by conversion of anilines to diazonium or ammonium salts for ANS (aromatic nucleophilic substitution) are well-known, catalytic C-N bond transformations

such as C-N bond activation/cross coupling remained unknown until 2007. As part of research in chelation-assisted reactions of aryl ketones with organoborates, Kakiuchi and co-workers discovered the Ru-catalyzed C-N bond activation/ Suzuki-type cross coupling reaction (Scheme 3.37).[272] The reaction is carried out under conditions similar to those used for the directed C-OMe bond activation/cross coupling reactions (Scheme 3.32).[270] The ketone DG and $RuH_2(CO)(PPh_3)_3$ catalysis still play the key role in the necessary C-NR_2 activation, in which the coordination of Ru(0) to the ketone carbonyl assists Ru(0) insertion into the C-NR_2 bond analogous to the C-OMe insertion process. Similarly, the bulky *t*-butyl is used to avoid the undesired C-H activation as in the C-OMe activation case. Aryl, heteroaryl, alkenyl and alkylboronates undergo the C-N cross coupling reaction to afford biaryls in good yields. Me, vinyl, TMS, OMe, F and CF_3 substituted arylboronates were tolerated and, perhaps surprisingly, *ortho*-primary, secondary and tertiary amino pivaloylphenones may be used in this reaction. This reaction constitutes a new Suzuki-type C-C bond cross coupling reaction via C-N activation.



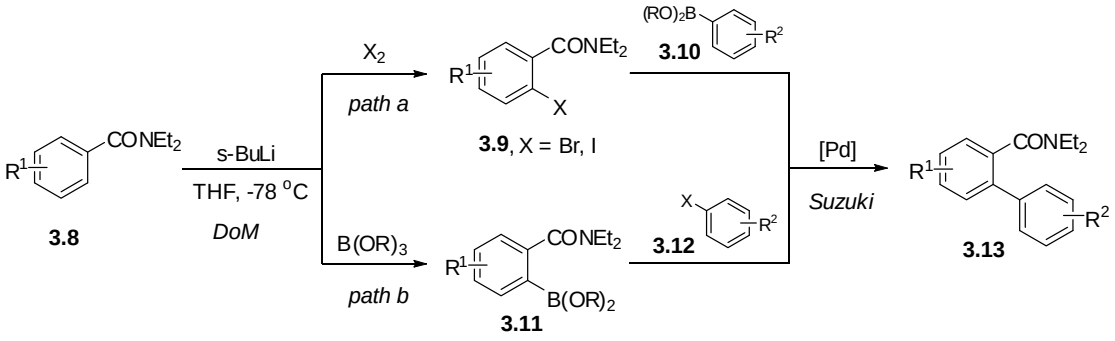
Scheme 3.37

As established by the work of Murai, Chatani, and Kakiuchi but also by other contributors and reviewed above, the use of a coordinating directing group to induce inert C-H,

C-O and C-N bond activation/C-C bond formation, especially in a Suzuki-type process, is a practical and promising methodology for the synthesis of biaryls. Of the methods discussed above, the ketone-directed Ru-catalyzed reaction is a simple and powerful process for unreactive bond functionalization, especially by way of cross coupling reactions to form biaryls.

3.2 Research Goals

As described in Chapter 1, the directed *ortho* metalation (DoM) reaction has become an important synthetic tool for aromatic ring C-H functionalization in organic synthesis and is now widely used in research and in industry.[4,3,1] Furthermore, the combined DoM-cross coupling strategy (Scheme 3.38) is playing an important role in C-C bond forming reactions via DoM chemistry.[60,51] This tactic has links to Suzuki-Miyaura, Kumada-Corriu, Negishi and Migita-Stille cross coupling processes, of which the DoM-Suzuki reaction is considered to be the most efficient and practical.



Scheme 3.38

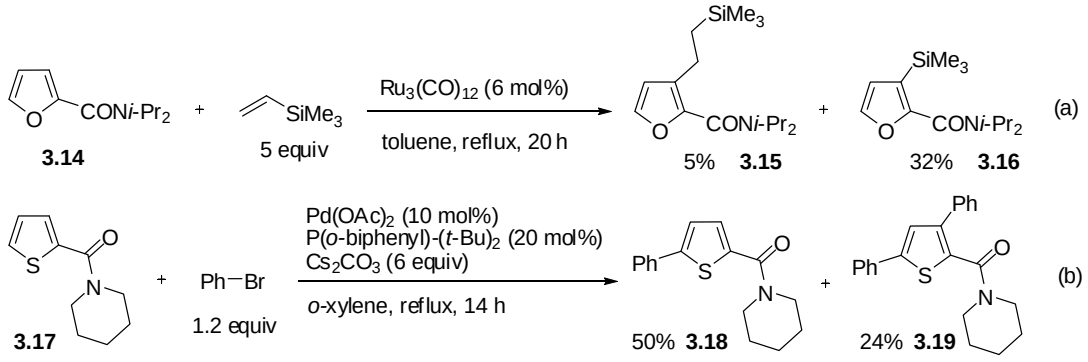
Harsh conditions (low temperature and strong base, usually -78 °C and BuLis) as a requisit has been limiting the applications of DoM. Recently, new milder bases such as TMPMgCl·LiCl by Knochel[273,274] and mixed lithium zincate and aluminum 'ate' complexes by

Uchiyama and Kondo,[275-277] have been developed for DoM at elevated temperatures even in presence of base-sensitive functional groups, e.g. Br, I, ketone, ester and nitrile. However, the necessity of stoichiometric or excess amounts of base is still a drawback in these reactions. Making DoM/functionalization in a catalytic way with/without base at elevated temperatures will be a challenge for future research.

The ketone-directed catalytic C-H, C-O and C-N bond activation/cross coupling reactions carried out under the simple $RuH_2(CO)(PPh_3)_3$/solvent conditions shows considerable advantage in high regioselectivity, yields and operational simplicity. As described previously (Scheme 3.30), the $RuH_2(CO)(PPh_3)_3$ system is also suitable for ester-directed C-H activation/aryl-aryl cross coupling reactions. Stimulated by the Murai-Chatani-Kakiuchi discoveries, we proposed that $CONEt_2$, a powerful and widely used directed metalation group (DMG) in DoM chemistry,[4,3,1] may provide a chelating DG property for C-H, C-O and C-N bond activation/cross coupling reactions under similar conditions. The rationale for this proposal was based on the following considerations: i) ester and ketone DG activation for these bonds has been established and the tertiary amide, as known, should exhibit greater coordination ability; ii) the well-known steric bulk of the $CONEt_2$ in DoM chemistry, as evidenced in resistance to nucleophilic attack by organolithium bases compared to $CONMe_2$,[278,279] suggests that it would behave similarly to the *t*-butyl group of *ortho*-methoxyphenyl *t*-butyl ketone in preventing non-regioselective C-H and C-O activation and therefore diarylation (Scheme 3.32); iii) if *ortho* activation is achieved, the door would be opened to the development of new DoM–cross coupling chemistry which takes advantage of the scope of the regioselective DoM strategy for the synthesis of polysubstituted aromatics and heteroaromatics; iv) likewise, assuming *ortho* activation is achieved, new strategies

complementary to DoM would be offered which have advantages of non-cryogenic, strong base conditions compared to the latter and therefore would have value in synthetic aromatic chemistry.

To the best of our knowledge, only two examples of tertiary amide mediated C-H bond functionalization have been reported: the first case involves the $Ru_3(CO)_{12}$-catalyzed silylation of a C-H bond of furan 2-carboxamide **3.14** (Scheme 3.39 (a)).[280] This reaction was carried out to test the amide-directed C-H activation/olefin coupling reaction which did proceed to give **3.15** but in very low yield, the major product being the 3-TMS derivative **3.16**, a mechanistically interesting result. The second example is the $Pd(OAc)_2$-catalyzed C-H activation/arylation of the thiophene amide **3.17** which leads to products **3.18** and **3.19** whose formation evidently occurs by non-*ortho* and *ortho*-DG activation reactions (Scheme 3.39 (b)).[281] In addition, it has been reported that a tertiary benzamide was examined for a amide-directed C-H activation/arylation under $Pd(OAc)_2/PPh_3/Cs_2CO_3$ catalysis condition but that this reaction failed to give coupled product.[244]



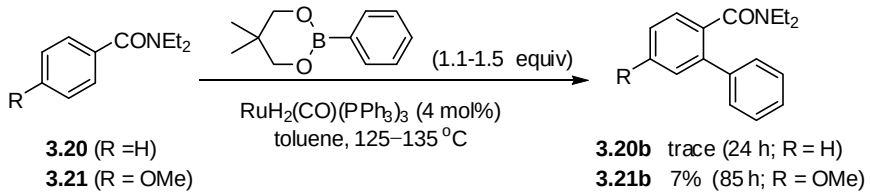
Scheme 3.39

The discovery of a tertiary amide-directed catalytic arylation reaction will achieve a dream: the catalytic base-free DoM-cross coupling process at non-cryogenic temperatures.

3.3 Results and Discussion

3.3.1 C-H Activation and C-C Bond Formation

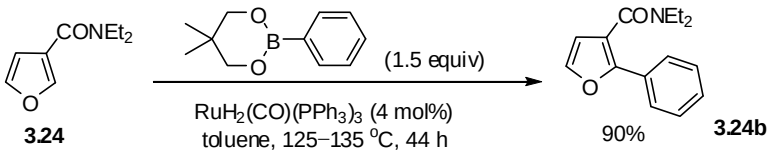
To initiate our study of tertiary amide-directed C-H activation, we chose N,N-diethylbenzamide **3.20** as substrate and placed reliance on the conditions of the Ru-catalyzed ketone-directed C-H activation/arylation reaction developed by Murai, Kakiuchi and co-workers.[259,260] In the first experiment (Scheme 3.40), treatment of **3.20** under the $RuH_2(CO)(PPh_3)_3$/toluene conditions with phenyl boroneopentylate and monitoring the reaction by GC-MS led only to the formation of trace amount of mono-phenylated product **3.20b** after 24 h reaction, the remainder being starting material **3.20** (Scheme 3.40). Furthermore, when 4-methoxybenzamide **3.21** was subjected to the same conditions, a very slow reaction proceeded to give, after 85 h, only a 7% isolated yield of *ortho*-arylated product **3.21b**. Therefore, it appears that $CONEt_2$ is not an effective DG for C-H activation of tertiary *benzamides*/arylation reaction under $RuH_2(CO)(PPh_3)_3$ catalysis. It may be surmised from the introduction to Chapter 3 that this is both a positive and negative result.



Scheme 3.40

The differences in bond dissociation enthalpies of heterocyclic vs aromatic C-H bonds (e.g. DH_{298} = 105, 112 kcal/mol for the pyridine C-H (2-position, 3-/4-position), in comparison, DH_{298} = 113 kcal/mol for the benzene C-H)[282] encouraged the examination of a variety of

heterocyclic tertiary amides. Treatment of N-$CONEt_2$ pyrrole, N-$CONEt_2$ indole, and N-$CONEt_2$ benzimidazole under the above conditions (Scheme 3.40) led to no reaction or trace amounts of arylated products (Table 3.2, entries 1, 10, and 14). For 4-$CONEt_2$ and 3-$CONEt_2$ pyridines (entries 8 and 7), trace amounts of a 1: 5 (GC-MS) mixtures of unknown regioisomeric products were observed. 2-$CONEt_2$ Pyridine and 2-$CONEt_2$ pyrazine showed reactivity to afford the *ortho*-arylated products in 7% and 12% yields respectively upon isolation. The yields of products were not improved even when the catalyst loading was increased to 10 mol% (entries 6 and 9). In indole cases, some encouraging results were obtained. Thus, although 2-$CONEt_2$ indole did not yield arylation products, 3-$CONEt_2$ indole led to the corresponding 2-arylated derivative **3.32b, 3.33b-c** in modest yields (entries 11-13). These results encouraged the exploration of additional heterocylic amides. In thiophene cases, although 2-$CONEt_2$ thiophenes generated only trace amounts of a phenylated product, 3-$CONEt_2$ thiophene led to the isolation of a mono-*ortho* arylated (2-phenylated) product in 21% yield (entries 4 and 5). A surprising result was obtained in the arylation reaction of furan amides. Although the 2-$CONEt_2$ furan afforded the 3-phenylated product in 13% yield, the 3-$CONEt_2$ isomer **3.24** furnished the 2-phenylated product **3.24b** in good to excellent yields as a function of equivalents of the phenylboronate used (entries 2 and 3). This is the first example of an efficient tertiary amide-directed C-H activation/arylation reaction (Scheme 3.41).

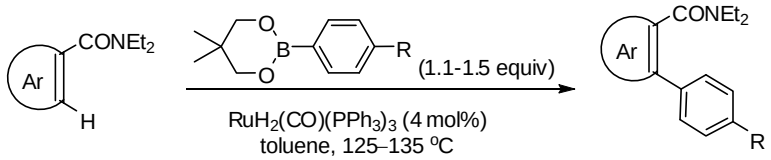


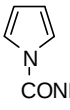
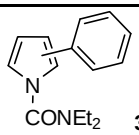
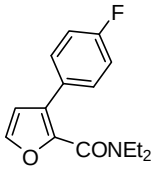
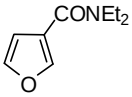
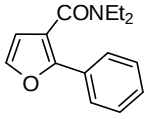
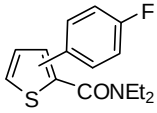
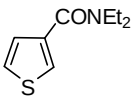
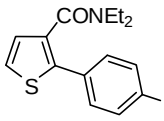
3.24 **3.24b**

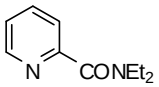
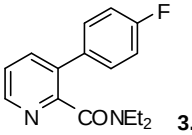
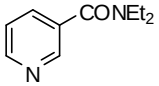
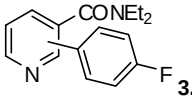
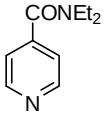
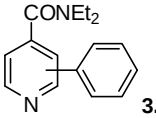
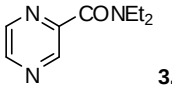
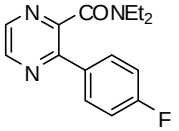
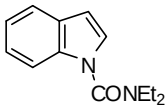
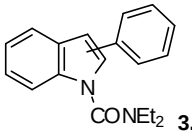
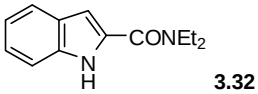
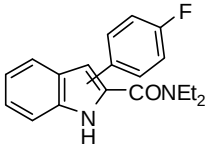
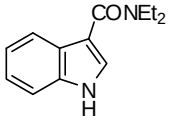
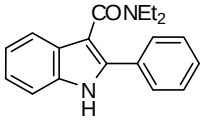
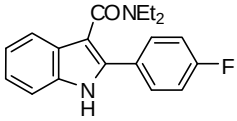
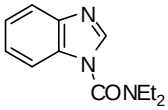
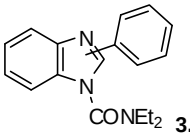
Scheme 3.41

Interestingly, ketone-directed C-H activation/arylation of furan systems has not been reported. A single example for C-H activation/*olefin coupling* of 2-acetyl furan has been achieved in quantitative yield (GC) by Murai, Kakiuchi and co-workers.[213]

Table 3.2 Screening for Amide-directed C-H Activation



Entry	Amide	(equiv)	Time (h)	Product	Yield (%)[a]
1	 **3.22**	R = H (1.5)	44	 **3.22b**	trace[b]
2	 **3.23**	R = F (1.5)	44	 **3.23b**	13 22[c]
3	 **3.24**	R = H (1.1) (1.5)	44 44	 **3.24b**	68 90
4	 **3.25**	R = F (1.5)	44	 **3.25b**	trace[b]
5	 **3.26**	R = F (1.5)	44	 **3.26b**	21

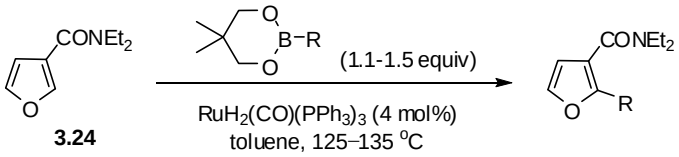
6	 **3.27**	R = F (1.5)	44	 **3.27b**	7 10[c]
7	 **3.28**	R = F (1.5)	44	 **3.28b**	trace[b,d]
8	 **3.29**	R = H (1.5)	20	 **3.29b**	n.d.
9	 **3.30**	R = F (1.5)	44	 **3.30b**	12 16[c]
10	 **3.31**	R = H (1.5)	20	 **3.31b**	trace[b]
11	 **3.32**	R = F (1.5)	44	 **3.32b**	n.d.
12	 **3.33**	R = H (1.5)	90	 **3.33b**	39
13		R = F (1.5)	44	 **3.33c**	45[c]
14	 **3.34**	R = H (1.5)	20	 **3.34b**	n.d.

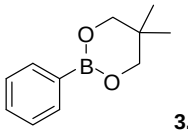
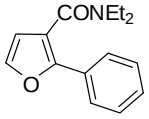
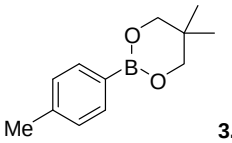
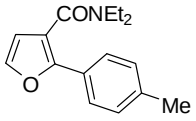
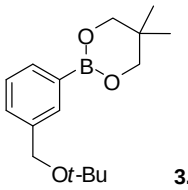
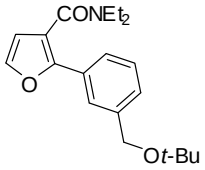
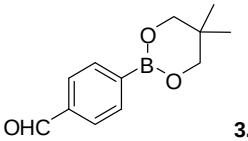
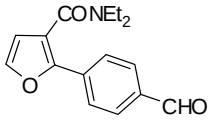
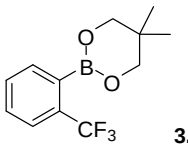
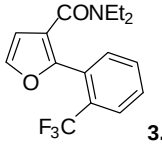
[a] Yields of isolated products.
[b] The product was not isolated due to low conversion (< 10% by GC-MS analysis)
[c] 10 mol% catalyst loading was used.
[d] Mixture of isomers in 1:5 ratio by GC-MS analysis.

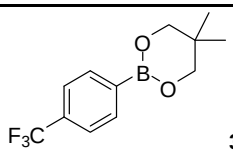
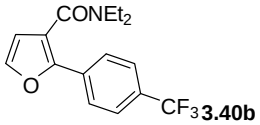
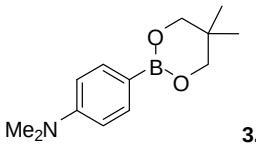
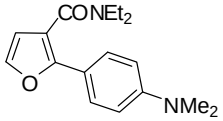
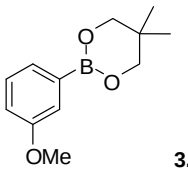
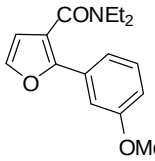
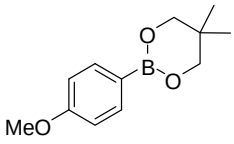
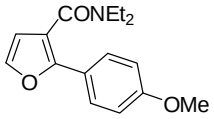
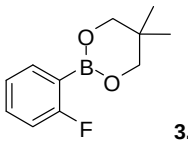
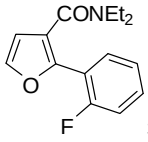
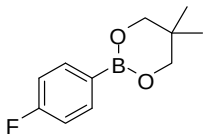
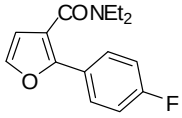
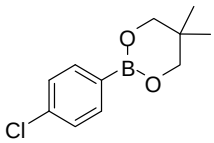
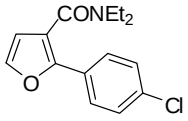
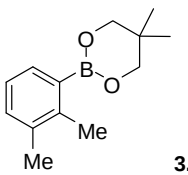
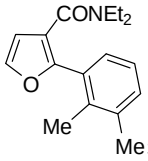
The discovery of the 3-$CONEt_2$ furan as an excellent substrate for the highly selective C-H activation/phenylation reaction motivated the further exploration of this substrate. Thus, a variety of arylboronates were investigated and the results are collected in Table 3.3. When arylboronates with EDGs such as Me, CH_2O*t*-Bu, NMe_2 and OMe were employed, high yields of products were obtained (entries 2, 3, 7-9). Similarly, the aryl boronates containing the EWGs, F and CF_3, underwent arylation in good yields (entries 6, 11 and 14). The 4-formyl phenyl boronate **3.38a** provided the 2-arylated product **3.38b** in low yield (entry 4). The 4-chlorophenyl boronate leads to inefficient coupling which may be due to a possible side reaction involving insertion of Ru into the C-Cl bond (see discussion in Section 3.3.7) (entry 12). The 2-naphthyl boronate was found to afford the corresponding phenylated product in good yield (entry 16). Then, a screening of the reaction of the furan 3-$CONEt_2$ **3.24** with a number of heterocyclic boronates was undertaken. An efficient coupling was observed between the furan amide and the 3-thiopheneboronate **3.52a** (entry 18). However, the coupling of **3.24** with furan and benzofuran boronates **3.51a** and **3.53a** afforded coupled products **3.51b** and **3.53b** in moderate yields due to deboronation as evidenced by total consumption of these boronates during the reaction (entries 17 and 19). Similar deboronation results also compromised the yields in other cases (entries 6, 10, 11 and 14). Increasing the amount of boronates may help solve this problem although this was not attempted. Steric hindrance was found to influence the coupling reaction. When a 2,3-dimethylphenyl boronate **3.47a** was employed, the coupling yield decreased to 50% (entry 13). When more bulky boronates **3.39a, 3.49a** were used, no coupled products were observed (entries 5 and 15). As a brief exploration of C-H activation/sp^2-sp^3 coupling, two alkyl boronates were also examined. The coupling of the phenyl cyclopropyl boronate **3.55a** with the furan amide **3.24** provided a low yield of product **3.55b** while the *n*-butyl boronate failed (entries 20 and 21).

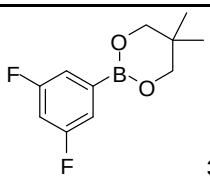
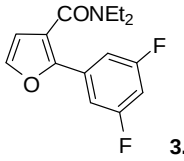
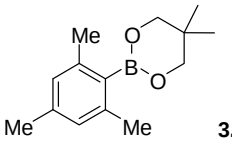
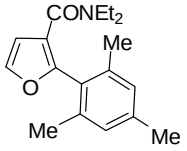
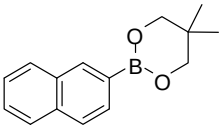
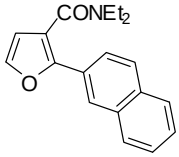
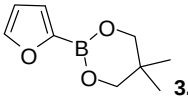
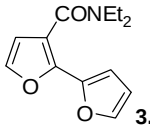
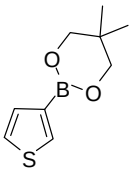
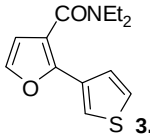
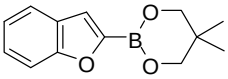
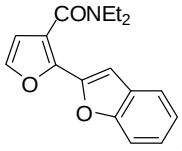
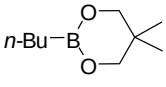
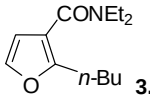
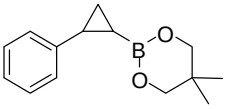
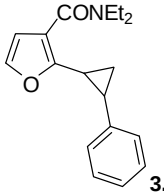
Although this is clearly an incomplete evaluation, it appears that alkylboronates are not suitable for this coupling reaction.

Table 3.3 Amide-directed C-H Activation and C-C Cross Coupling of N,N-Diethyl Furan-3-carboxamide



Entry	Boronate	Equiv. of Boronate	Time (h)	Product	Yield (%)[a]
1	 **3.35a**	1.1	44	 **3.24b**	68
		1.5	44		90
2	 **3.36a**	1.5	44	 **3.36b**	85
3	 **3.37a**	1.5	44	 **3.37b**	93
4	 **3.38a**	1.5	24	 **3.38b**	18[b]
5	 **3.39a**	1.5	24	 **3.39b**	n.d.

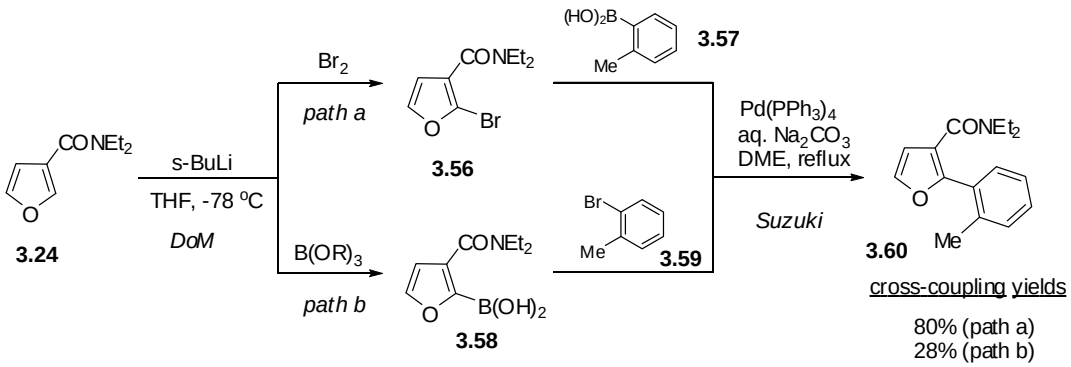
6	 **3.40a**	1.1	24	 **3.40b**	72[c]
		1.5	24		82
7	 **3.41a**	1.5	44	 **3.41b**	76
8	 **3.42a**	1.1	24	 **3.42b**	91
9	 **3.43a**	1.1	24	 **3.43b**	94
10	 **3.44a**	1.5	24	 **3.44b**	41[c]
11	 **3.45a**	1.1	24	 **3.45b**	80[c]
		1.5	24		92
12	 **3.46a**	1.5	24	 **3.46b**	18
13	 **3.47a**	1.5	44	 **3.47b**	50

14	 **3.48a**	1.1	24	 **3.48b**	60[c]
		1.5	24		87
15	 **3.49a**	1.5	24	 **3.49b**	n.d.
16	 **3.50a**	1.1	24	 **3.50b**	80
17	 **3.51a**	1.5	24	 **3.51b**	39[c]
18	 **3.52a**	1.5	44	 **3.52b**	72
19	 **3.53a**	1.5	24	 **3.53b**	37[c]
20	 **3.54a**	1.5	44	 **3.54b**	n.d
21	 **3.55a**	1.5	24	 **3.55b**	23[b]

[a] Yields of Isolated and purified products. [b] The catalyst loading: 10 mol%. [c] The boronate was totally consumed.

Of considerable significance is that amide reduction was not observed under the conditions of the cross coupling reaction. This suggests that, in contrast to the ketone-directed C-H activation/arylation reaction in which pinacolone solvent or 2 equivalents of a ketone substrate were required to act as hydride scavengers for the Ru-H species in order to maintain the catalytic cycle, the Ru-H cannot effect reduction of the amide group. Thus, the necessity for using pinacolone (or acetone) as solvent is eliminated and alternative solvents may be used. Toluene is an appropriate solvent for the reaction.

In general, the new Ru-catalyzed C-H activation/arylation method for the construction of a variety of heterobiaryls (Table 3.3) is complementary to the DoM–cross coupling strategy well known in our laboratories.[51,60,61] To cite a specific and, in view of the result obtained by the C-H activation route, appropriate comparison, the lithiation–cross coupling of 3-$CONEt_2$ furan was carried out by routes involving both possible combinations of partners, routes (a) and (b), **3.24** → **3.56** and **3.24** → **3.58** (Scheme 3.42) to afford the product **3.60** in excellent and poor yields respectively.[283] The poor yield in the (b) route is a reflection of the protodeboronation which is problematic in Suzuki-Miyaura reactions.[284] In contrast, the new C-H activation/arylation protocol affords a similar product **3.47b** (Table 3.3) in 50% yield. This example may be viewed as an indication of the potential complementary value of the C-H activation/arylation method as a simple, efficient and powerful complement of the DoM–cross coupling strategy. Furthermore, the heterobiaryl compounds are potential candidates for further D*o*M, D*re*M and cross coupling chemistry.[3]



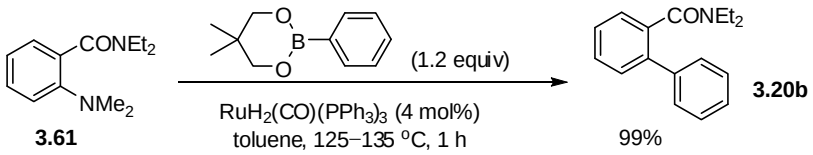
Scheme 3.42

With a focus on the most effective furan 3-$CONEt_2$ arylation results of the above studies (Scheme 3.41 and Table 3.3), we note: i) this is the first catalytic tertiary amide-directed C-H activation/arylation reaction; ii) it is under high regioselectivity control for the formation of 2-aryl 3-$CONEt_2$ furan products; iii) it provides a catalytic, base-free, one-step method for the formation of heterobiaryls which may also be obtained by the DoM–cross coupling regimen. Although inappropriate to evaluate at this time, based on the limited studies, the C-H activation route appears more efficient and will therefore complement and perhaps supercede the latter methodology.

3.3.2 C-N Activation and C-C Bond Formation

Catalytic C-N activation/C-C bond formation is fresh chemistry. To date, only the Ru-catalyzed ketone-directed C-N activation/C-C bond forming reaction was reported by Kakiuchi and co-workers as a part of the study of chelation-assisted reactions of aromatic ketones with organoboronates (Scheme 3.37).[272] This observation provided the impetus to test a catalytic *ortho*-amide-directed C-N activation/C-C bond forming process under $RuH_2(CO)(PPh_3)_3$/toluene conditions. Thus treatment of 2-Me_2N-N,N-diethylbenzamide **3.61** under the Kakiuchi conditions

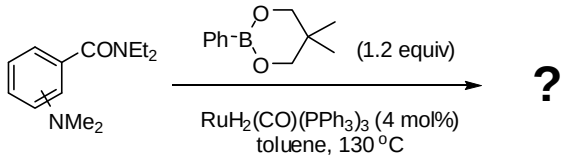
with phenyl boroneopentylate led in 1 h to the formation the diphenyl amide **3.20b** in almost quantitative yield with no observation of the alternative C-H activation/arylation product (Scheme 3.43).

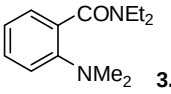
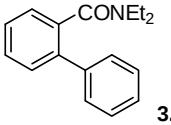
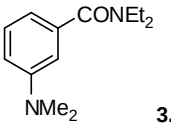
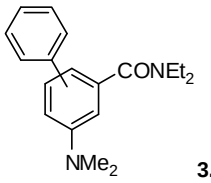
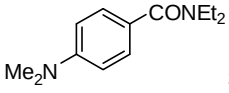


Scheme 3.43

To demonstrate the existence of the chelation assistance in the above reaction, 3-Me_2N-N,N-diethylbenzamide **3.62** and 4-Me_2N-N,N-diethylbenzamide **3.63** were tested under the same reaction conditions. As perhaps expected, no C-N/phenylation products were found in both experiments although, in the former case, a phenylated product was detected (GC-MS) in only 4% yield after 24 h reaction time (Table 3.4, entries2 and 3). The results strongly support the requirement of amide DG–Ru chelation to effect C-N bond oxidative addition. This is highly selective *ortho*-directed C-N activation/arylation reaction in which the amide directing is inert to the *ortho* C-H bond activation. This feature is quite different with the ketone directed C-N activation/C-C bond formation reaction in which both C-H and C-N can be activated via ketone group mediation and bulky ketone groups are always needed to prevent the C-H activation.[272]

Table 3.4 C-N Activation/C-C Cross Coupling of the Three Isomeric Dimethylamino Benzamides **3.61-3.63**

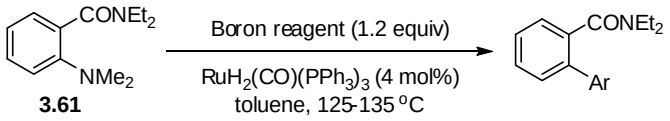


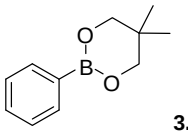
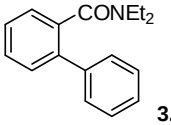
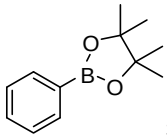
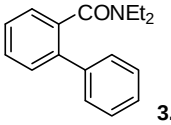
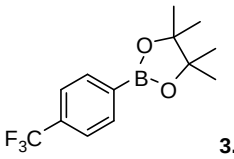
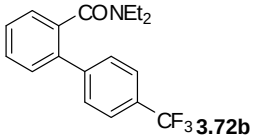
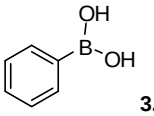
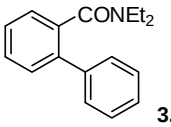
Entry	Amide	Time (h)	Product	Yield (%)
1	 **3.61**	1	 **3.20b**	99[a]
2	 **3.62**	20	 **3.62b**	(4)[b]
3	 **3.63**	20	n.d.[c]	--[c]

[a] Yield of isolated and purified product.
[b] Yield determined by GC-MS analysis (C-H activation occurred; single isomer was found) with 94% starting material recovery (amide).
[c] Recovery of starting material (99%).

The above excellent result of the amide-directed coupling using boroneopentylate (Table 3.4, entry 1) prompted the examination of other boron coupling reagents. Aryl boropinacolates **3.64a** and **3.65a** afforded the coupled products in only 8% yield (Table 3.5, entries 2 and 3) while phenyl boronic acid failed to give any product (entry 4). As originally recommended by Kakiuchi, the boroneopentylates are the best coupling partners.

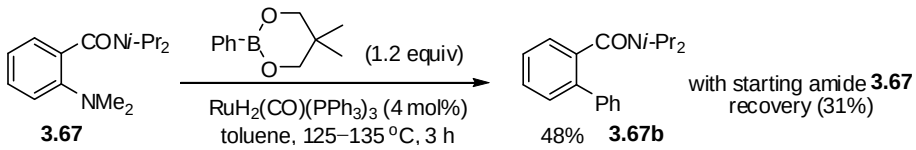
Table 3.5 Screening Boron Reagents for Cross Coupling of 2-Me_2N-N,N-diethylbenzamide **3.61**



Entry	Boron Reagent	Time (h)	Product	Yield (%)[a]
1	 **3.35a**	1	 **3.20b**	99
2	 **3.64a**	20	 **3.20b**	8[b]
3	 **3.65a**	20	 **3.72b**	8[c]
4	 **3.66a**	20	 **3.20b**	n.d.[d]

[a] Yields of isolated and purified products. [b] Starting amide recovered (92%).
[c] Starting amide recovered (91%). [d] No product; starting amide recovered (92%).

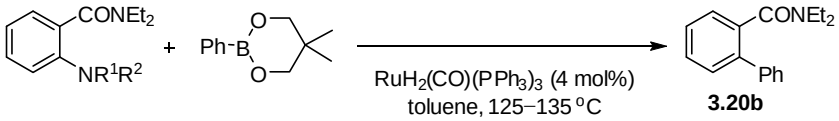
To obtain appreciation of the steric effects of the amide, the 2-Me_2N-N,N-diisopropyl benzamide **3.67** was tested and found that the reaction gave product **3.67b** in 48% decreased yield even in prolonged time (Scheme 3.44). Therefore, the N,N-diethyl benzamides were employed for further studies. The corresponding N,N-dimethyl amides were not considered in view of their ineffiency in DoM chemistry where alkyllithiums will mainly attack the N,N-dimethyl amide group.[278,279]



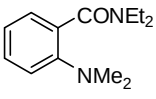
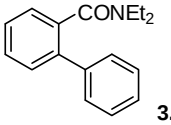
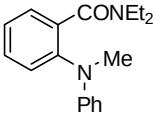
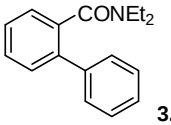
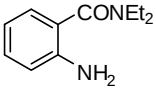
Scheme 3.44

We next examined the effect of amino N-substitution on the cross coupling efficiency. GC-MS analysis of results showed that the bulky N-methyl-N-phenyl group (**3.68**) inhibited the reaction leading to the coupled product **3.20b** in only 44% yield after 20 h (Table 3.6, entry 2). Moreover, a byproduct, PhNHMe, as direct evidence of reductive deamination was obtained in 11% yield. This observation deserves further investigation. When 2-aminobenzamide **3.69** was subjected to the coupling reaction conditions, starting material was recovered in quantitative yield (entry 3). This result is quite different with observations by Kakiuchi in ketone-directed C-N activation/coupling in which NH_2 and NHMe did not prevent efficient C-N activation. It appears that minimal steric hindrance and unavailability of N-H bonds are very important for a highly efficient amide-directed C-N activation/cross coupling result.

Table 3.6 Screening Substituted Amino Groups for the Cross Coupling Reaction of *ortho*-Amino N,N-Diethyl Benzamides



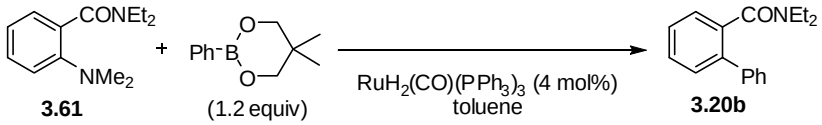
3.20b

Entry	Amide	Time (h)	Product	Yield (%)
1	 **3.61**	1	 **3.20b**	99[a]
2	 **3.68**	20	 **3.20b**	(44)[b]
3	 **3.69**	20	n.d.[c]	--[c]

[a] Yield of Isolated and purified product.
[b] Yield determined by GC-MS analysis; PhNHMe was also found in 11% yield (GC).
[c] No product; starting amide recovery (95%).

Next, screening of temperature effect on the cross coupling reaction of the chosen substrate **3.61** was carried out (Table 3.7). At 130 ^{o}C, an almost quantitative yield of coupled product **3.20b** was obtained (entry 3), but at 110 ^{o}C, a prolonged reaction time was needed to achieve a comparable yield (entry 2). Lowering the reaction temperature decreased the reaction efficiency. Thus, at 80 ^{o}C, only a 19% yield of coupled product **3.20b** was observed even after 44 h reaction time (entry 1). These experiments suggest that the higher temperature is required for the activation of the $RuH_2(CO)(PPh_3)_3$ catalyst, which was not indicated in Kakiuchi papers. Therefore, 130 ^{o}C was chosen as the optimized temperature for this C-N activation/coupling reaction.

Table 3.7 Temperature Screening Experiments for the Cross Coupling Reaction of 2-Me_2N-*N*,*N*-diethyl Benzamide **3.61**



3.61 (1.2 equiv) **3.20b**

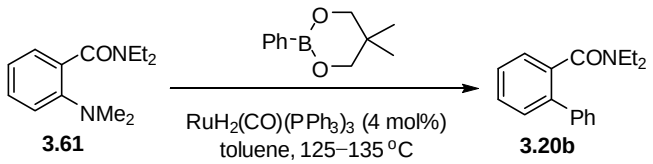
Entry	Temperature	Time	Isolated Yield (%)
1	80 ^{o}C	44 h	19*
2	110 ^{o}C	8 h	98
3	**130 ^{o}C**	**1 h**	**99**

* Starting amide recovery (81%)

Further, in screening the stoichiometry of the reaction, it was found that organoboronate equivalents can be reduced to 1.05 without loss of reaction efficiency (Table 3.8, entry 1). However, if a coupling reaction requires longer time for completion, excess organoboronates

have to be used to overcome the protodeboronation reaction which occurs under prolonged reaction conditions (see Table 3.10, entries 12, 13 and 16).

Table 3.8 Screening Boronate Equivalent Experiments for the Cross Coupling Reaction of 2-Me_2N-N,N-diethyl Benzamide **3.61**

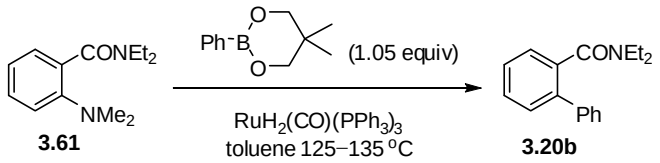


3.61 **3.20b**

Entry	Boranate (equiv)	Time	Isolated Yield (%)
1	**1.05**	**1 h**	**99**
2	1.2	1 h	99

To complete the screening experiments, the catalyst loading was investigated and the results are shown in Table 3.9. At 4% catalyst loading, the reaction proceeded in quantitative yield (entry 1). Reduction to 2 or 3 mol% did not affect the high yield of product significantly if the reaction time was somewhat prolonged (entries 2 and 3). However, when 1 mol% catalyst was employed, the yield decreased greatly even under prolonged reaction time (entry 4). Therefore, the 4 mol% was adopted as the optimized catalyst loading for the C-N activation/coupling reaction.

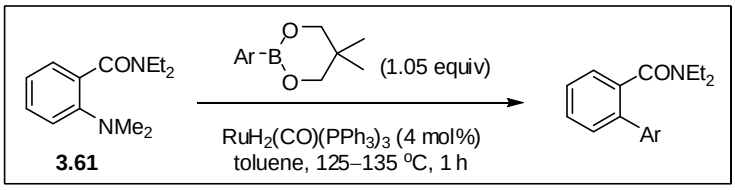
Table 3.9 Screening the Catalyst Loading for the Cross Coupling Reaction of 2-Me_2N-N,N-diethyl Benzamide **3.61**



Entry	Catalyst Loading (mol%)	Time	Isolated Yield (%)
1	**4**	**1 h**	**99**
2	3	3 h	96
3	2	5 h	92
4	1	20 h	31*

* Starting amide recovery (69%).

The above sets of screening experiments of reaction temperature, stoichiometry of coupling partners, and catalyst loading led to the establishment of the optimized C-N activation/ cross coupling conditions as shown in Scheme 3.45 which were employed for the further investigation of the reaction scope and limitations.



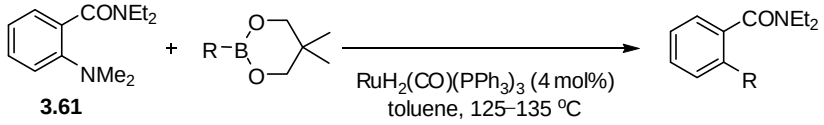
Scheme 3.45 Optimized Conditions for the Coupling Reaction of 2-Me_2N-*N*,*N*-diethyl Benzamide **3.61** with Aryl Boroneopentylates

Following the successful demonstration of the amide-directed C-N activation/coupling reaction for 2-Me_2N-*N*,*N*-diethyl benzamide **3.61**, we proceeded to test the generality of the

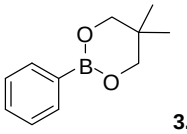
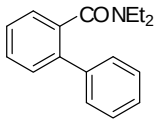
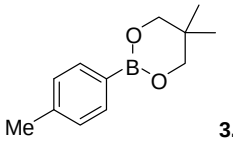
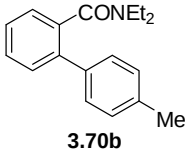
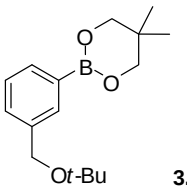
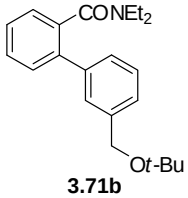
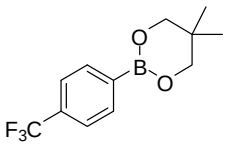
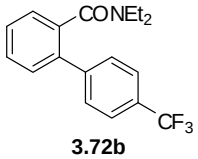
reaction with a variety of aryl boroneopentylates and the results shown in Table 3.10 deserve comment. First, the coupling reaction proceeds mostly with excellent yields for EDGs such as Me, CH_2O*t*-Bu, NMe_2 and OMe (**3.70b-3.71b, 3.73b-3.75b,** Table 3.10, entries 2, 3, 5-7). However, EWGs showed a range of effects. When aryl boroneopentylates with EWGs such as F and CF_3 were employed, the coupling reaction proceeded in high yields (**3.72b, 3.76b-3.78b,** entries 4, 8-10). However, when CHO, CN and NO_2 substituted aryl boroneopentylates were used, the arylation was completely inhibited even after a 20 h reaction time (Table 3.11, entries 2, 3 and 5). These trends are quite similar as those found in the amide-directed furan C-H activation/arylation reaction (Table 3.3). The unsuccessful cases contain strong EWGs which effect significant electron density changes at the C-B bond. This effect may be responsible for the failure of the C-N activation/coupling. Interestingly, Murai and Kakiuchi did not mention such examples.[259,260,272] Similar to our previous results of C-H activation/arylation (Table 3.3, entry 12), halogen groups except F were found to inhibit the reaction due to dehalogenation (Table 3.11, entries 6-8) (see Section 3.3.7 for discussion). Such side reactions were also not mentioned by Murai and Kakiuchi.[259,260,272] As also observed in the furan amide coupling reaction (Table 3.3, entry 16), the naphthyl boroneopentylate was found to afford the arylated product **3.79b** in high yield (Table 3.10, entry 11). In the study of heterocyclic boroneopentylates, good yields of products **3.80b-3.82b** were obtained for the thiophene, furan and benzofuran cases (Table 3.10, entries 12-14) but slight excess amounts of boronates and prolonged reaction time were always required. Steric hindrance was shown to greatly decrease the coupling efficiency. Thus, when sterically congested boroneopentylates were employed, the expected coupled products were not detected and deboronation and de-NMe_2 became the major reactions (Table 3.11, entries 4 and 9). An (*E*)-styrylboronate underwent arylation to give the stilbene product **3.83b** in modest yield and

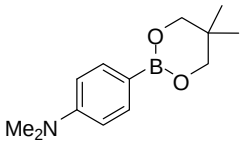
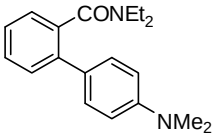
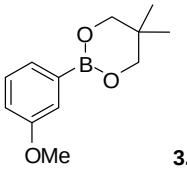
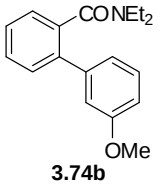
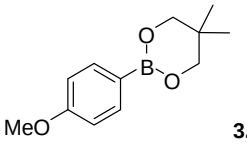
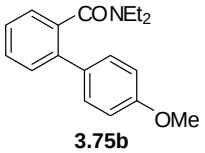
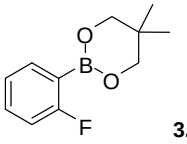
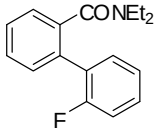
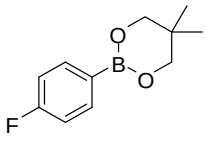
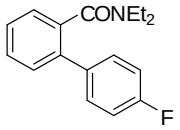
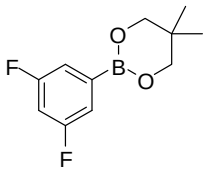
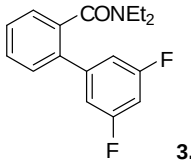
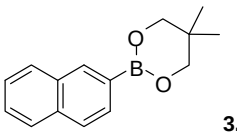
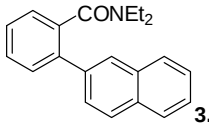
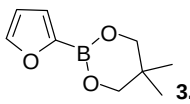
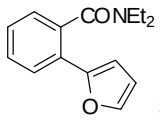
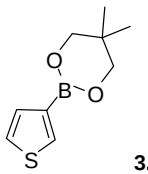
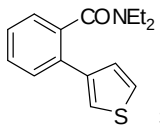
with retention of the *E*-stereochemistry (Table 3.10, entry 15). Two alkyl boroneopentylates were also chosen for testing the C-N activation/sp^2-sp^3 coupling reaction. *n*-Butyl boroneopentylates failed to undergo the coupling reaction (Table 3.11, entry 1) but a good yield of the interesting derivative **3.84b** was obtained from the coupling of a cyclopropyl boroneopentylates **3.55a** (Table 3.10, entry 16) which however may be considered to have the well-established C-sp^2 character.[285]

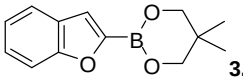
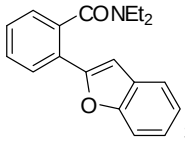
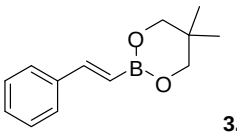
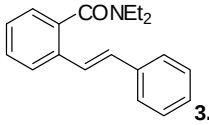
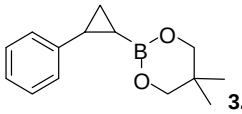
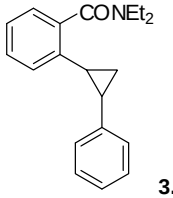
Table 3.10 Cross Coupling Reactions of 2-Me_2N-*N*,*N*-diethyl Benzamide **3.61** with Aryl Boroneopentylates



3.61

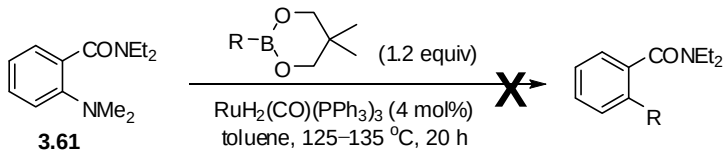
Entry	Boronate	Equiv. of boronate	Time (h)	Product	Yield (%)[a]
1	 **3.35a**	1.05	1	 **3.20b**	98
2	 **3.36a**	1.05	1	 **3.70b**	98
3	 **3.37a**	1.05	1	 **3.71b**	97
4	 **3.40a**	1.05	1	 **3.72b**	99

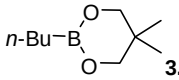
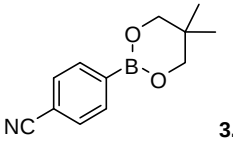
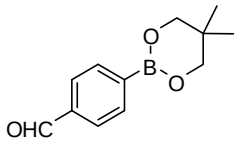
5	 **3.41a**	1.05	6	 **3.73b**	81
6	 **3.42a**	1.05	1	 **3.74b**	99
7	 **3.43a**	1.05	1	 **3.75b**	99
8	 **3.44a**	1.05	2	 **3.76b**	90
9	 **3.45a**	1.05	1	 **3.77b**	98
10	 **3.48a**	1.05	2	 **3.78b**	98
11	 **3.50a**	1.05	2	 **3.79b**	96
12	 **3.51a**	1.2	20	 **3.80b**	82
13	 **3.52a**	1.2	20	 **3.81b**	75

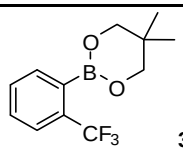
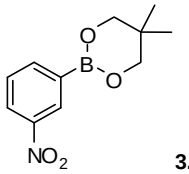
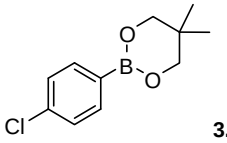
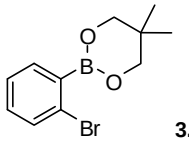
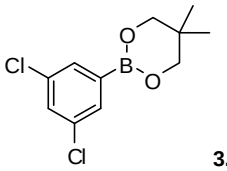
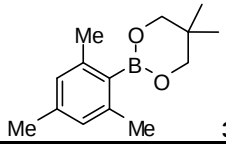
14	 **3.53a**	1.05	2	 **3.82b**	67[b]
15	 **3.83a**	1.05	3	 **3.83b**	56
16	 **3.55a**	1.2 1.5	20 20	 **3.84b**	49 88[c]

[a] Yields of isolated and purified products.
[b] Boronate has been totally consumed due to deboronation involved.
[c] The catalyst loading: 10 mol%.

Table 3.11 Unsuccessful Examples of the Cross Coupling Reactions of 2-Me_2N-*N*,*N*-diethyl Benzamide **3.61** with Aryl Boroneopentylates



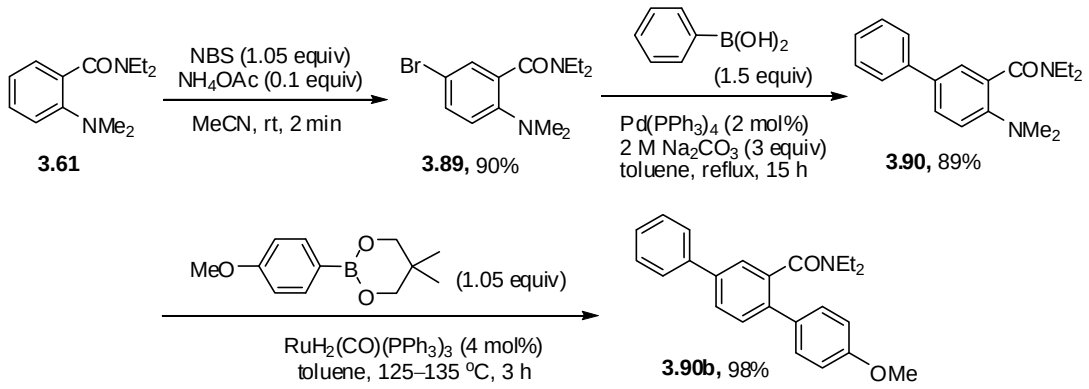
Entry	Boronate	GC-MS (ratio)						
		Amide :	Boronate :	de-B :	de-NMe_2 :	de-Cl :	de-Br :	Product
1	 **3.54a**	100	40	--[a]	1			--
2	 **3.85a**	100	29	13	--			2
3[b]	 **3.38a**	100	70	2	--			--

4	 **3.39a**	100	--	-- [a]	24			--
5	 **3.86a**	100	3	15	--			--
6	 **3.46a**	100	66	-- [a]	2	1		4
7	 **3.87a**	81	100	1	trace [c]		2	--
8	 **3.88a**	100	86	14	trace [c]	2		--
9	 **3.49a**	68	100	12	17			--

[a] The protodeboronation product was not detected (GC-MS).
[b] De-CHO exists.
[c] < 1% (GC-MS).

As evidenced by the collected data above, the new tertiary amide-directed Ru-catalyzed C-N activation/C-C bond forming reaction of 2-Me_2N-*N*,*N*-diethyl benzamide with aryl boroneopentylates is a general and highly efficient methodology for the synthesis or biaryls and heterobiaryls. It has the following advantages over the corresponding ketone-directed method: i) it is not compromised by competitive C-H activation and coupling reaction; ii) compared to the unproductive *t*-butylcarbonyl group, it presents the amide functional group for further manipulation as well as utility in D*o*M, D*re*M and related subsequent chemistry (Section 3.5 for further discussion).

As an application of this methodology, a C-N activated and standard Suzuki C-C cross coupling sequence was developed (Scheme 3.46). Taking advantage of the expected electrophilic reactivity of 2-Me_2N-N,N-diethylbenzamide, conversion into the bromobenzamide **3.89** was achieved in high yield. The subsequent standard Suzuki cross coupling gave the biaryl **3.90** which, upon C-N activated coupling with the anisyl boroneopentylate afforded the teraryl **3.90b** in 80% overall yield in three steps. Notably, the C-N activation/coupling step proceeded in almost quantitative yield.



Scheme 3.46 Bromination–Suzuki Coupling–C-N Activation/Coupling Sequence. Synthesis of the Teraryl **3.90b**

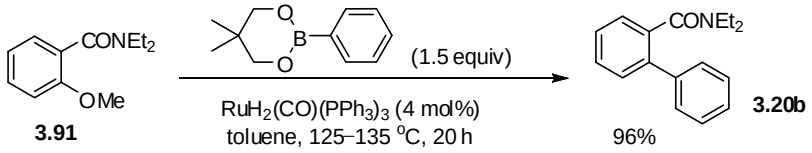
In summary, the described reaction constitutes the first catalytic amide-directed C-N activation/C-C bond forming reaction; it is general and proceeds with high efficiency and regiospecificity. It achieves the same result, the synthesis of biarylamides, in sequential two catalytic processes as that derived by the DoM–Suzuki coupling combination at non-cryogenic temperatures without the use of organolithium bases.

3.3.3 C-O Activation and C-C Bond Formation

3.3.3.1 C-O Activation of Benzamides and C-C Bond Formation

As previously summarized (Scheme 3.32), the first Ru-catalyzed C-O activation/coupling reaction using the ketone DG was developed by Murai, Kakiuchi and co-workers.[268] Limitations of this methodology involving competitive C-H activation, necessity for use of bulky synthetically inflexible ketones, and unavailability of ketone substrates were noted.

The achievement of the catalytic amide-directed unreactive C-H (Table 3.3) and C-N (Table 3.10) bond activations/C-C bond formation reactions prompted the exploration of the analogous C-O activation/cross coupling reaction with reference to the successful results achieved by Kakiuchi on ketonic materials.[268] In the initial test case, the simple 2-MeO-N,N-diethylbenzamide **3.91** was subjected to the previously developed conditions in toluene solution and afforded, to our excitement, the biaryl amide **3.20b** in 96% yield after a 20 h reaction time. Notably, as in the case of the analogous 2-Me_2N-*N*,*N*-diethyl benzamide **3.61** (Scheme 3.43), no C-H activation product was observed (GC-MS analysis) (Scheme 3.47).

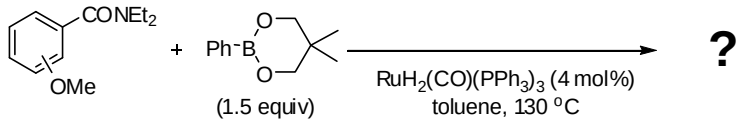


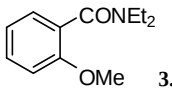
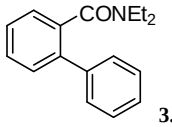
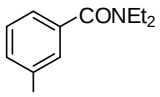
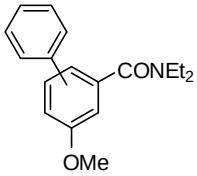
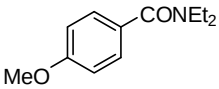
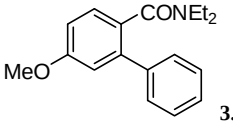
Scheme 3.47

As control reactions for the chelation requirement for C-O activation, 3-MeO-N,N-diethylbenzamide **3.92** and 4-MeO-N,N-diethylbenzamide **3.21** were examined. After 85 h reactions, only a trace amount (GC-MS) and 7% yield (isolated) of single C-H activation/phenylation were observed for the *meta*-anisamide **3.92b** and *para*-anisamide **3.21b**

respectively (Table 3.12, entries 2 and 3). C-O activation/arylation products were not detected (GC-MS) in both experiments. Similar observations were recorded for the amide-directed C-N activation/cross coupling reaction (Section 3.3.2). As also for the C-N activation reaction, these results strongly support the requirement for an *ortho*-DG to achieve the oxidative addition–cross coupling process. Paralleling also the C-N activation/cross coupling process, the corresponding selective C-O activation/arylation reaction is regioselective without interference from the *ortho* C-H bond activated reaction. As also for the C-N activation/cross coupling process, this feature distinguishes the new C-O activation/coupling reaction from that of the corresponding ketone directed reaction for which both *ortho* C-H and C-O bond are activated and require a bulky *t*-butyl ketone to inhibit C-H activation.[268]

Table 3.12 C-O Activation/Cross Coupling of Isomeric N,N-Diethyl Anisamides

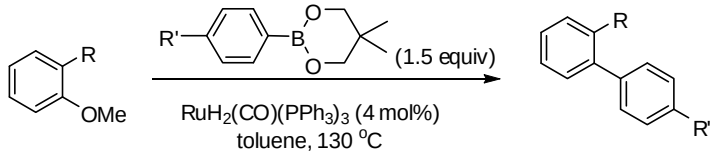


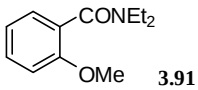
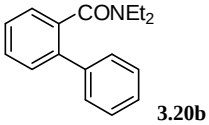
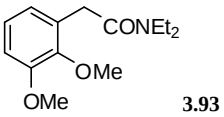
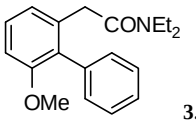
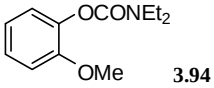
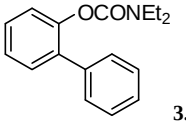
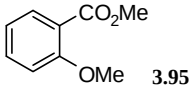
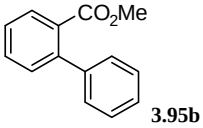
Entry	Amide	Time	Product	Yield (%)[a]
1	 **3.91**	20	 **3.20b**	96
2	 **3.92**	85	 **3.92b**	trace[b]
3	 **3.21**	85	 **3.21b**	7[c]

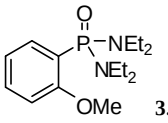
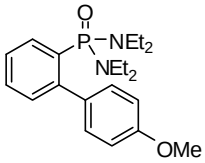
[a] Yields of isolated and purified products.
[b] C-H activated single isomeric product (1% yield, GC-MS) . Recovered starting amide (98%).
[c] Starting amide recovery (88%).

The discovery of the $CONEt_2$ C-O activation/coupling reaction led to examination of other DGs which may effect this process. As seen from Table 3.13, the results show that a variety of groups, including some strong DMGs in DoM chemistry, do not promote C-O activation/cross coupling reactions (entries 3 and 5). Only in the ester-directed case, trace amounts of expected product was observed by GC-MS analysis (entry 4). Rationalization of these results may involve the requirement for strong coordination and 5-member ring chelation as displayed by the $CONEt_2$ (entry 1) but not the CH_2CONEt_2 (entry 2) and $OCONEt_2$ (entry 3) groups. Two possible reasons may be forwarded for the failure of the phosphoramidate (entry 5) to serve as a DG: Ru-O=P coordination strength and steric hindrance.

Table 3.13 Screening of Directing Groups for the C-O Activation/ C-C Cross Coupling Reaction



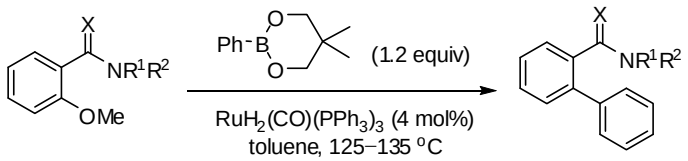
Entry	Substrate	Product	Yield (%)[a]
1	 **3.91**	 **3.20b**	96
2	 **3.93**	 **3.93b**	n.d.[b]
3	 **3.94**	 **3.94b**	n.d.[b]
4	 **3.95**	 **3.95b**	(4)[c]

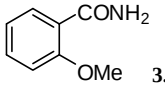
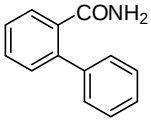
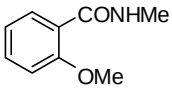
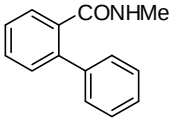
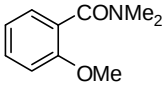
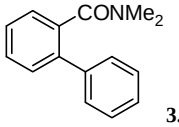
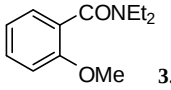
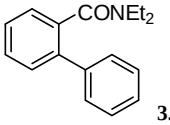
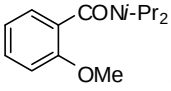
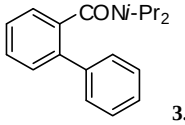
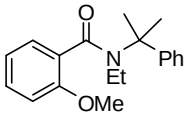
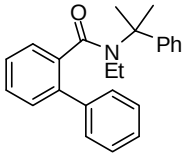
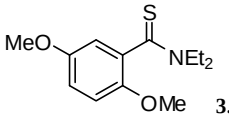
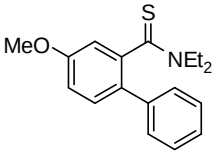
5	 **3.96**	 **3.96b**	n.d.[b]

[a] Yield of isolated and purified product.
[b] Starting amide recovery: 99% (entry 2), 98% (entry 3) and 99% (entry 5).
[c] Yield from GC.

With reference to the studies of $CONEt_2$ amide substitution effects in the C-N activation/cross coupling reactions (Scheme 3.44), we undertook to determine such effects in the corresponding C-O activation/coupling reactions and the results are given in Table 3.14. Thus, primary and secondary amides **3.97, 3.98** failed to give coupled products (entries 1 and 2) suggesting that free N-H functionality inhibits the reaction. In tertiary amide cases, less hindered amides **3.99, 3.91** afford the expected products **3.99b, 3.20b** in excellent yields (entries 3 and 4). However, bulky amides **3.100-3.101** greatly decreased the yields of coupled products **3.67b, 3.101b** (entries 5 and 6), indicating the operation of steric effects. When a thioamide **3.102** was employed, only 14% yield of coupled product **3.102b** was obtained (entry 7). In comparison with the $CONEt_2$ case (entry 4), a weaker coordination between C=S and Ru metal may be cause of the low efficiency of the latter reaction. We conclude that less hindered tertiary amides are important for a successful and efficient C-O activation/coupling reaction.

Table 3.14 Amide Substitution Effects on the C-O Activation/Coupling



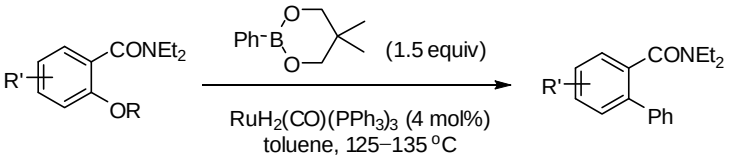
Entry	Substrate	Product	Yield (%)[a]
1	 **3.97**	 **3.97b**	n.d.[b]
2	 **3.98**	 **3.98b**	n.d.[b]
3	 **3.99**	 **3.99b**	92
4	 **3.91**	 **3.20b**	96
5	 **3.100**	 **3.67b**	33[b]
6	 **3.101**	 **3.101b**	50[b]
7	 **3.102**	 **3.102b**	14[b]

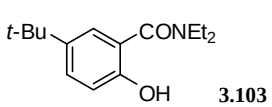
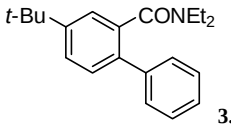
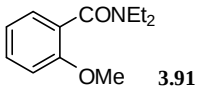
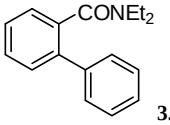
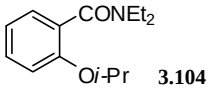
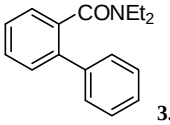
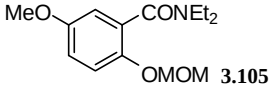
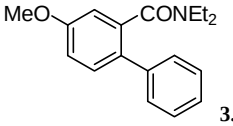
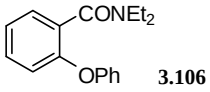
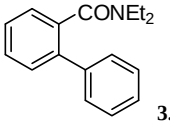
[a] Yields of isolated and purified products.
[b] Starting amide recovery: 96% (entry 1), 97% (entry 2), 66% (entry 5), 43% (entry 6), 83% (entry 7).

With the above preliminary studies in hand, a variety of *ortho*-OR benzamides were examined to test the scope of the C-O activation/cross coupling reaction. To begin, the salicylamide case **3.103** failed to afford coupled product with complete recovery of starting material (Table 3.15, entry 1). As noted above, the initially studied *ortho*-anisamide **3.91** gave the product **3.20b** in excellent yield (entry 2) while bulky OR group cases **3.104, 3.106** (entries 3 and

5) led to low yields of coupled products indicative of the operation of steric effects. Somewhat surprisingly, OMOM case **3.105** did not afford the expected coupled product (entry 4). A further contributing factor may be incomplete or different Ru-OMOM chelation. As perhaps expected and certainly synthetically advantageous, the *ortho* anisamide is the best choice for this C-O activation/coupling reaction.

Table 3.15 Screening of -OR Groups for the Cross Coupling with Phenyl Boroneopentylate

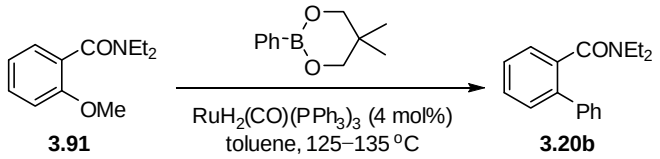


Entry	Substrate	Product	Yield (%)[a]
1	 **3.103**	 **3.103b**	n.d.[b]
2	 **3.91**	 **3.20b**	96
3	 **3.104**	 **3.20b**	14[b]
4	 **3.105**	 **3.120b**	n.d.[b]
5	 **3.106**	 **3.20b**	28[b]

[a] Yields of isolated and purified products.
[b] Starting amide recovery: 99% (entry 1), 85% (entry 3), 89% (entry 4), 72% (entry 5).

The boronate stoichiometry was next investigated and showed that 1.5 equivalents were required in long reaction times to obtain an excellent yield of biaryl product (Table 3.16, entry 3). Lower boronate equivalents resulted in incomplete reactions (entries 1 and 2).

Table 3.16 Variation of Boronate Stoichiometry in the Cross Coupling Reaction of the *ortho*-Anisamide **3.91** with Phenyl Boroneopentylate

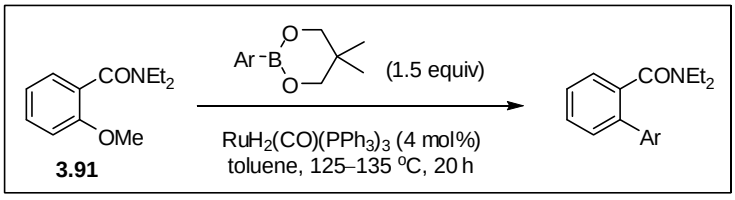


3.91 **3.20b**

Entry	Boranate (equiv)	Time	Isolated Yield (%)
1	1.05	2 h	66[a]
2	1.2	8 h	78[b]
3	**1.5**	**20 h**	**96**

[a] Boronate was fully consumed due to protodeboronation; Starting amide recovery (33%).
[b] Boronate was fully consumed due to protodeboranation; Starting amide recovery (22%).

The above screening results demonstrate the optimized C-O activation/C-C cross coupling conditions as shown in Scheme 3.48. These were therefore employed in the further investigation of the reaction scope and limitations.

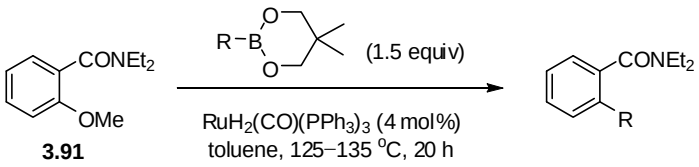


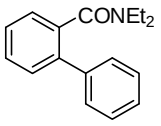
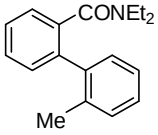
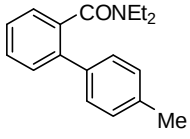
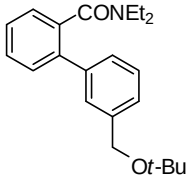
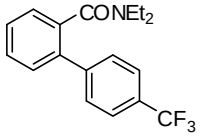
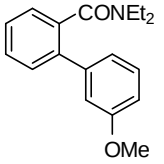
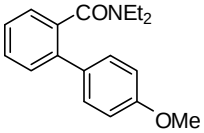
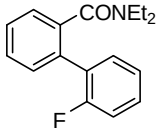
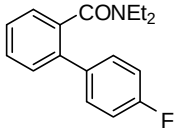
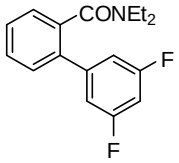
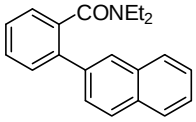
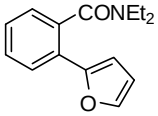
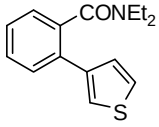
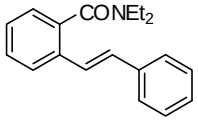
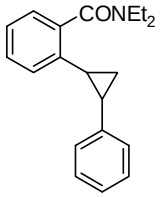
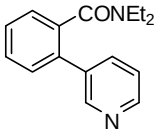
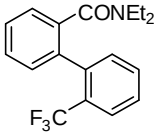
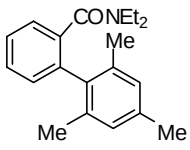
3.91

Scheme 3.48 Optimized Conditions for C-C Cross Coupling Reaction of *ortho*-Anisamide **3.91**

The results concerning the scope and limitations of the *ortho*-anisamide **3.91** with a variety of aryl boroneopentylates are summarized in Table 3.17. As expected, the coupling reaction proceeds in good yields for various aryl boroneopentylates bearing Me, CH_2O*t*-Bu and OMe EDGs (**3.70b-3.72b, 3.74b-3.75b**). Furthermore, arylboronates with F and CF_3 EWGs also give high yields of coupled products **3.72b, 3.76b-3.78b**. As also expected based on previous results in the C-N cross coupling studies (Table 3.11, entries 4 and 9), steric hindrance was found to decrease the coupling efficiency. Thus, a slightly reduced yield of biaryl product **3.107b** was obtained in the 2-methylphenyl boronate case but for when highly steric-congested boronates were employed, the expected coupled products **3.109b-3.110b** were not detected. The 2-naphthyl boronate was found to afford the arylated product **3.79b** in good yield. In studies of heterocyclic boronate, good yields of heterobiaryls **3.80b-3.81b** were obtained in the furan and thiophene boronate cases while a pyridine boronate failed to give a coupled product **3.108b**. Thus, electron-deficient heterocycles are inappropriate substrates for the reaction. An (*E*)-styrylboronate underwent the coupling reaction affording a moderate yield of **3.83b**. As expected from the C-N activation/cross coupling studies (Table 3.10, entry 16), a cyclopropyl boronate provided the coupled product **3.84b** in good yield.

Table 3.17 Scope of the Cross Coupling Reaction of the *ortho*-Anisamide **3.91** with Aryl Boroneopentylates



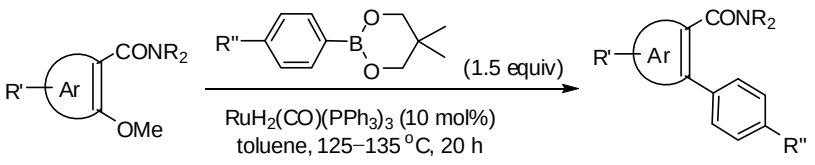
 **3.20b** 96%*	 **3.107b** 82%[a]	 **3.70b** 96%	 **3.71b** 93%	 **3.72b** 90%
 **3.74b** 93%	 **3.75b** 98%	 **3.76b** 87%	 **3.77b** 95%	 **3.78b** 91%
 **3.79b** 81%	 **3.80b** 84%[a]	 **3.81b** 67%[a]	 **3.83b** 58%[a]	 **3.84b** 83%[a]
 **3.108b** n.d.[b]	 **3.109b** n.d.[b]	 **3.110b** n.d.[b]		

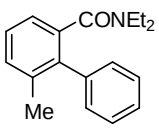
* Yields of isolated and purified products. [a] The catalyst loading: 10 mol%. [b] Monitored by GC-MS.

Next, the scope of substituted *ortho*-anisamides was investigated and the results are displayed in Table 3.18. *ortho*-Anisamides containing EDGs such as Me, *t*-Bu, OMe, OMOM and

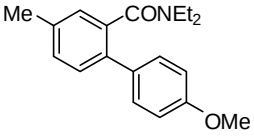
Ph were mostly well tolerated to give products **3.111b-3.122b, 3.90b, 3.21b**. However, when EWG (NO_2 and $CONEt_2$) -substituted *ortho*-anisamides were employed, the reactions failed to afford the coupled products **3.126b-3.127b** and resulted in almost complete recovery of starting materials. The decreased electron density at the DG and the C-O bond in these derivatives may be a reason of these failures. The bromo substituted *ortho*-anisamide does not participate in the coupling reaction to **3.125b** possibly due to a side reaction which involves oxidative addition of Ru metal to the C-Br bond (for discussion, see Section 3.3.7). Studies on sterically hindered *ortho*-anisamides led to some interesting results. Thus, the reactions of 6-substituted anisamides gave decreased yields of biaryl products **3.115b-3.117b, 3.124b**. Of them, in particular, the 6-Me anisamide led to almost complete recovery of starting material. This result may be rationalized by the inability of the amide C=O to bring coordinating Ru catalyst into proximity to achieve a proper angle for the C-O oxidative addition to occur. Surprisingly, the coupling reactions of 3-substituted and even 3,4-disubstituted 2-methoxybenzamides proceeded well to give products **3.111b, 3.118b-3.119b, 3.122b** in good yields although steric hindrance existed. Notably, in an indole case, the coupled product **3.123b** was formed in 60% yield. From these results, it can be inferred that free rotation of amide group is important for a highly efficient C-O bond activation/coupling reaction.

Table 3.18 Scope of the Cross Coupling Reaction of Substituted 2-Methoxybenzamide with Aryl Boroneopentylates

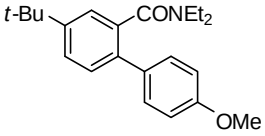




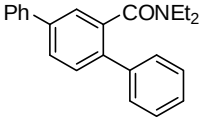
3.111b
85%*



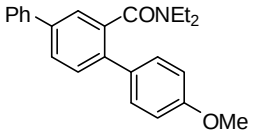
3.112b
92%



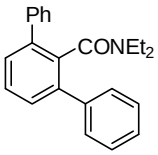
3.113b
94%



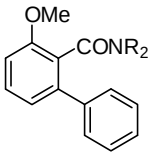
3.114b
98%
72%[a]



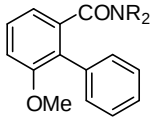
3.90b
97%[a]



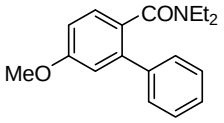
3.115b
31%
27%[a]



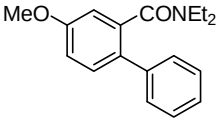
3.116b, 68%[a,b] (R = Me)
3.117b, 60%[a,b] (R = Et)



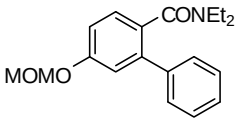
3.118b, 91%[a] (R = Me)
3.119b, 87%[a] (R = Et)



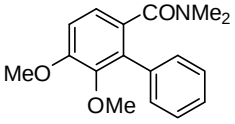
3.21b
89%[a]



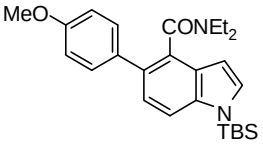
3.120b
75%
50%[a]



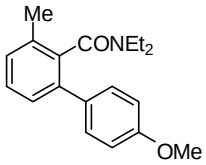
3.121b
98%[a]



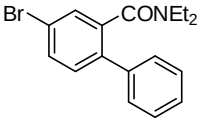
3.122b
90%[a]



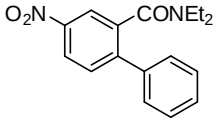
3.123b
60%



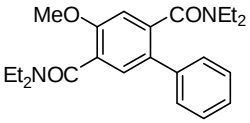
3.124b
trace[c]



3.125b
n.d.[d]



3.126b
n.d.[e]



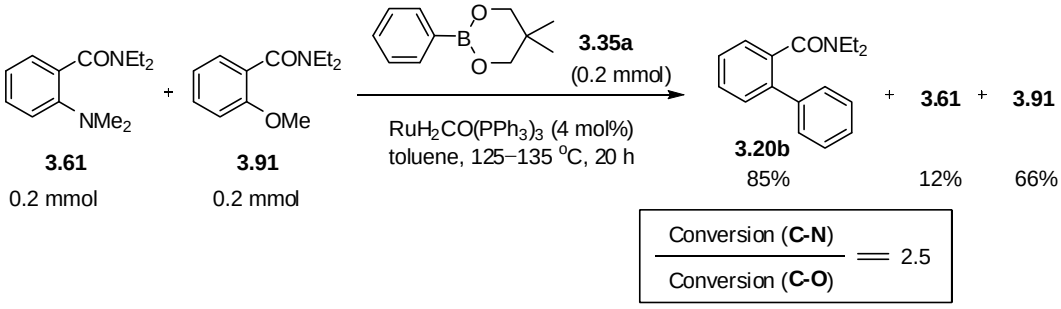
3.127b
trace[c]

* Yields of isolated and purified products.
[a] The catalyst loading: 4 mol%.
[b] Di- C-O activations were found: 22% (R = Me); 23% (R = Et).
[c] Less than 3% yields determined by GC-MS analysis; starting amide recovery: 97% and 91% respectively.
[d] De-Br in 3% yield from GC; starting amide recovery (93%).
[e] Starting amide recovery (95%).

The above results demonstrate the achievement of a highly efficient C-O activation/C-C bond formation reaction of *ortho*-anisamides with aryl boroneopentylates to give a variety of

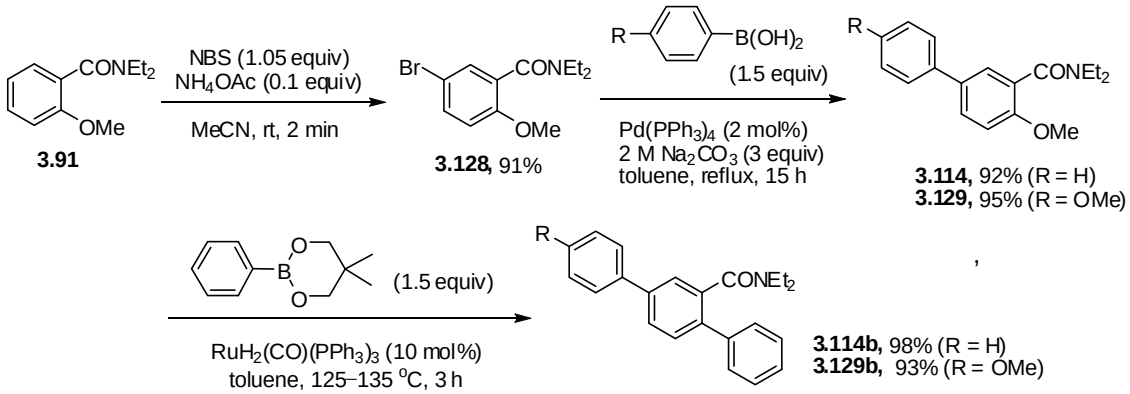
biaryl and heterobiaryl amides. The new methodology has the following advantages over the Kakiuchi ketone-directed C-O activation/coupling reaction: i) it is not compromised by a C-H activation cross coupling reaction; ii) compared to the intractable *t*-butyl ketone products, the resulting amides are potentially useful in further amide-related chemistry (for discussion, see Scheme 3.5). Therefore, as in the C-N activated cross coupling chemistry (Section 3.3.2), the corresponding C-O activated coupling reaction is a significant advance of the Ru-catalyzed ketone-directed C-O activation/coupling reaction developed by Murai, Kakiuchi, and co-workers.[268]

In order to qualitatively establish the relative rates of the C-N and C-O bond activation/cross coupling reactions, a competitive experiment was carried out using a 1:1:1 mixture of 2-Me_2N-N,N-diethylbenzamide **3.61**, 2-MeO-N,N-diethylbenzamide **3.91**, and phenyl boroneopentylate **3.35a**. The result, indicating that C-N activation is more efficient than C-O activation (Scheme 3.49) matches a feature in the C-N activation/coupling conditions compared to those of the corresponding C-O reaction, that of short reaction times being required for the former reaction.



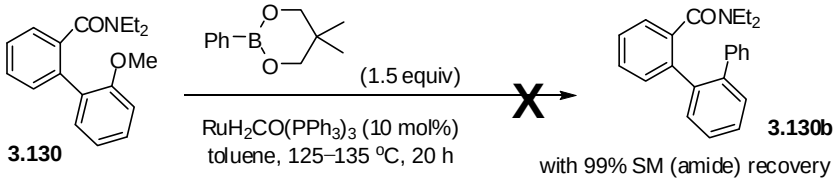
Scheme 3.49 Competition Experiment for the C-N and C-O Activation/Cross Coupling Processes

As an application of the above methodology and paralleling the application established in the C-N activation/cross coupling series (Scheme 3.46), a Ru-catalyzed C-O and normal Suzuki cross coupling sequence was developed for the synthesis of teraryls **3.114b** and **3.129b** (Scheme 3.50). The selective electrophilic bromination of 2-MeO-N,N-diethylbenzamide **3.91** afforded the expected aryl bromide **3.128**, which, upon Suzuki cross coupling with commercially available phenyl and 4-methoxyphenyl boronic acids furnished the biaryl amides **3.114** and **3.129** respectively. The subsequent Ru-catalyzed amide-directed C-O activation/coupling reaction with aryl boroneopentylates gave compounds **3.114b** and **3.129b**. The overall synthesis combines classical electrophilic substitution and two catalytic cross coupling reactions in an overall efficient synthesis of teraryls. The two routes according to C-N and C-O activation processes are comparable in efficiency and facility of operation: 80% overall yield in 3 steps. A complimentary route to the biaryl **3.114** is the Ir-catalyzed C-H activation/borylation recently established in our laboratories.[286]



Scheme 3.50 Bromination–Suzuki Coupling–C-O Activation/Coupling Sequence. Synthesis of the Teraryls **3.114b** and **3.129b**

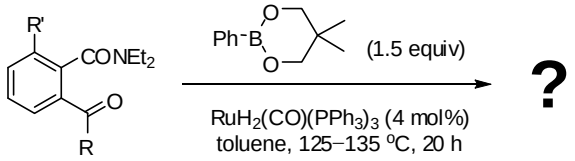
With the availability of a 2'-methoxy substituted biaryl amide **3.130** and with a reference to D*re*M reactivity (Chapter 1), a remote amide-directed C-O activation/coupling reaction was tested. However and unfortunately, treatment of biaryl amide **3.130** with phenyl boroneopentylate under the standard coupling conditions failed and resulted in the quantitative recovery of starting material (Scheme 3.51). Perhaps not surprisingly, in view of the preferred conformation of the hindered 2,2'-biaryl **3.130** and the necessity for large-ring coordination, C-O bond activation cannot be achieved. The alternative of *ortho*-amide C-H activation was, of course, not expected.

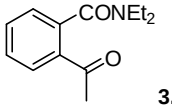
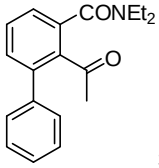
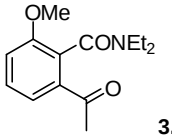
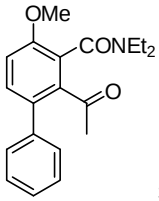
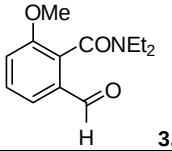


Scheme 3.51 Failure of an Amide-directed Remote C-O Activation

We next briefly examined cross coupling of substrates which combine amide and ketone directing groups in order to establish their relative DG abilities in C-H activation reactions. In the simple 2-acetylbenzamide **3.131**, the ketone-directed C-H activation/coupling reaction occurred in good yield of **3.131b** even if consideration is given that the presence of the $CONEt_2$ acts as a EWG and detrimental effect (Table 3.19, entry 1). The presence of the OMe substituent suppressed the amide-directed C-O activation/coupling to afford the C-H activation product **3.132b** in a modest 54% yield (entry 2). The aldehyde case **3.133** afforded no coupled product and led to decarbonylation as the major reaction (entry 3). Although rotational barriers undoubtedly play a role, the more powerful effect of the ketone C=O in a competitive amide-ketone C-H activation situation is apparent in the results of both entries 1 and 2.

Table 3.19 Comparison of C-O and C-H Activations by Amide- and Carbonyl-DGs

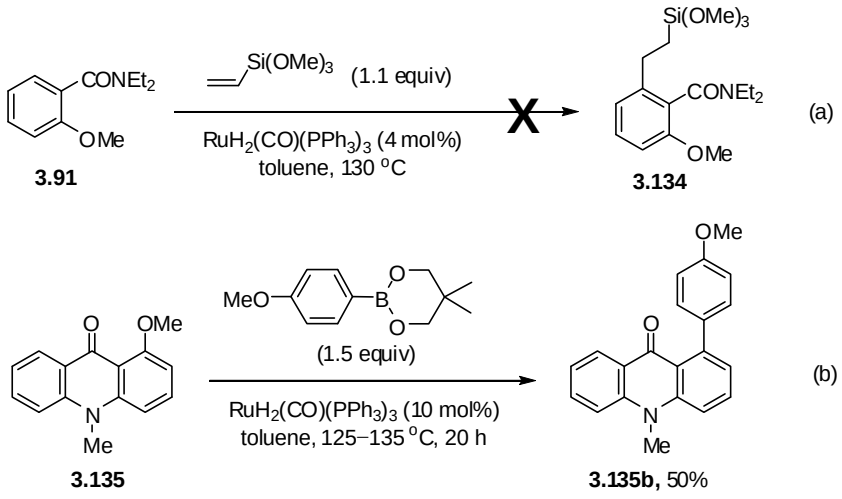


Entry	Substrate	Product	Yield (%)[a]
1	 **3.131**	 **3.131b**	81
2	 **3.132**	 **3.132b**	54
3	 **3.133**	--[b]	--[b]

[a] Yields of isolated and purified products.
[b] De-CHO in 16% yield determined by GC-MS analysis.

To extend the amide-directed C-O activation/coupling reaction, the original Murai-type coupling of 2-MeO-N,N-diethylbenzamide **3.91** with an olefin was tested but led only to recovery of starting material. Incidentally, C-H or C-O bond activation/coupling reactions were also not observed (Scheme 3.52 (a)). Hence, as opposed to ketone substrates, benzamides are not suitable substrates for the Murai reaction. The acridone substrate **3.135** available in our laboratories from the D*re*M chemistry research of Steve MacNeil,[287,288] was tested for ketone-directed C-O activation/coupling reaction (Scheme 3.52 (b)) and led, delightfully, to the expected product **3.135b** in 50% yield. This result is noteworthy in that C-H activation/coupling at the alternate *peri* position was not observed in direct contrast from the recent results of Kakiuchi in which a

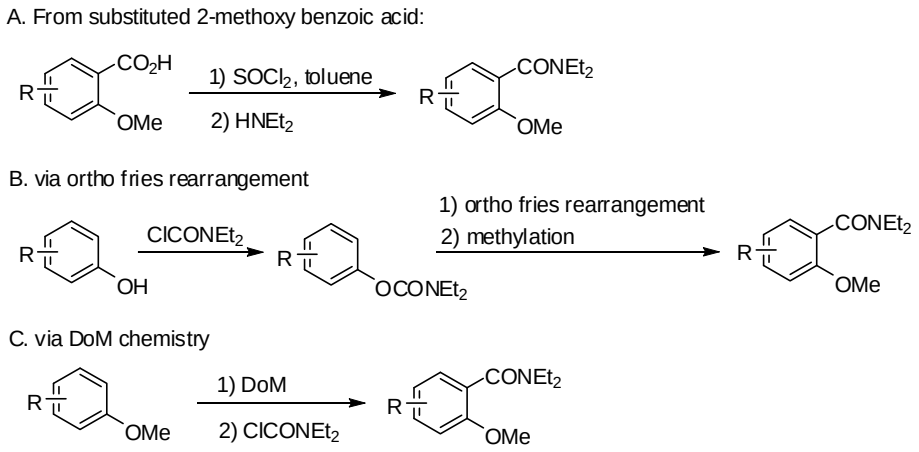
highly reactive ketone-directed C-H activation process of arthraquinone was uncovered involving four C-H bond activations to form 1,4,5,8-tetraarylanthracenes.[261] The selective C-O activation/coupling result indicates that valuable new synthetic chemistry may be established by connecting D*re*M and Ru-catalyzed C-O activation/coupling reactions.



Scheme 3.52 C-H or C-O Activation–Olefin Addition and *peri*-Substitution Results

Based on the results described above, a general and efficient amide-directed C-O activation/cross coupling methodology for the synthesis of biaryl and heterobiaryl amides has been developed. The methodology has high practical value in that, compared to the preparation of starting materials for our amide-directed C-N activation (Section 3.3.2) or the Kakiuchi ketone-directed coupling reactions (Scheme 3.32, 3.37), the substituted *ortho*-anisamides are readily available from simple and inexpensive commodity chemicals. Three common methods are shown in Scheme 3.53. Method A starts from substituted salicylic *ortho*-anisic acids to afford the corresponding amides in classical two-step one-pot sequence. Method B involves the anionic *ortho* Fries rearrangement[289,44,290] to lead to *ortho*-anisamides in three simple steps starting from commercially available phenols. This method also has the benefit of DoM chemistry to obtain

unusually substituted derivatives; Method C starts from substituted anisoles to afford the 2-MeO benzamides in a single step via DoM chemistry. The facile and multiple routes for the preparation of 2-MeO benzamides will make the amide-directed C-O activation/coupling reaction of practical interest.



Scheme 3.53 Methods for the Preparation of Substituted *ortho*-Anisamides

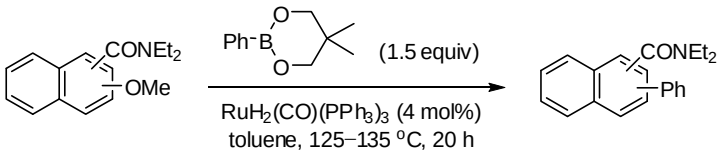
In summary, we have demonstrated the first catalytic amide-directed C-O activation/C-C cross coupling reaction. The reaction is efficient, highly regiospecific and has considerable practical potential. The catalytic reaction may be viewed as complementing or superceding the DoM-cross coupling strategy[51,60,61] with advantage of non-cryogenic temperatures and non-requirement of base.

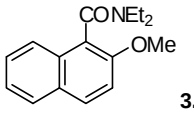
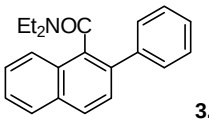
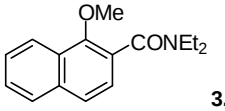
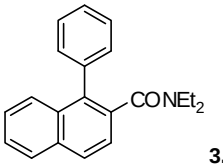
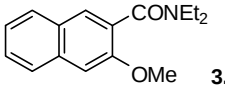
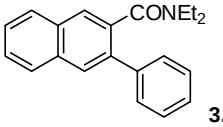
3.3.3.2 C-O Activation of Naphthamides and C-C Bond Formation

As demonstrated above, *ortho*-anisamides are highly reactive partners for the Ru-catalyzed amide-directed C-O activation/C-C cross coupling reaction with aryl boroneopentylates (Tables 3.17, 3.18). How about naphthamides? We turned our sights to this undertaking with the

examination of several *ortho*-MeO naphthamides and the initial results are given in Table 3.20. Yields of cross coupling products varied as a function of methoxy naphthamide isomers. Thus 2-MeO-1-naphthamide **3.136** and 1-MeO-2-naphthamide **3.137** underwent the C-O activation/cross coupling reaction to afford the biaryl products **3.136b-3.137b** in excellent yields (Table 3.20, entries 1 and 2) while the 3-MeO-2-naphthamide **3.138** gave product **3.138b** in much lower yield (entry 3). As also observed for the C-O cross coupling reactions of benzamides (Tables 3.17, 3.18), no C-H activation/coupling products were formed. To note again, in contrast to the Kakiuchi ketone-directed C-O activation/cross coupling reaction (Table 3.24, entry 2), the corresponding naphthamide coupling reaction is only for *ortho* C-O activation and is inert to the *ortho* C-H bond activation process.

Table 3.20 C-O Activation/Cross Coupling of Isomeric Naphthamide



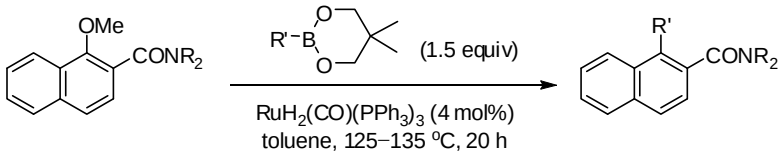
Entry	Substrate	Product	Yield (%)[a]
1	 **3.136**	 **3.136b**	97
2	 **3.137**	 **3.137b**	96
3	 **3.138**	 **3.138b**	30

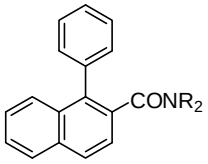
[a] Yields of isolated and purified products.

These exciting results motivated the investigation of the generality of the reaction with a variety of organoboronates and the results are shown in Table 3.21. In the initial study, 1-MeO-2-naphthamide was subjected to reaction with a variety of aryl boroneopentylates bearing Me, CH_2O*t*-Bu, NMe_2 and OMe EWGs and afforded biaryl products **3.140b-3.143b, 3.145b-3.147b** mostly with excellent yields. Likewise, aryl boroneopentylates with F and CF_3 EWGs gave the coupled products **3.144b, 3.148b-3.150b** in high yields. However and reminiscent of the results of the *ortho*-anisamide studies (Section 3.3.3.1), aryl boroneopentylates with CHO and NO_2 EWGs, no arylation occurred and starting materials were recovered in high yields (**3.156b-3.157b**). These observations may be rationalized as those obtained for the corresponding substrates in the *ortho*-anisamide studies (Section 3.3.3.1). Unsurprisingly and analogous for the observation made in the C-O activated coupling of benzamides with arylbromo boroneopentylates, the corresponding aryl chloro derivatives do not serve for this coupling reaction (**3.158b**) possibly due to dehalogenation (to be discussed in Section 3.3.7). In general, these trends are quite similar as those found in previously described amide-directed C-H, C-N and C-O activation/coupling reactions. Also not unexpectedly, steric hindrance was found to decrease the coupling efficiency. Thus the coupling of the N,N-diethyl 1-MeO-2-naphthamide with 2-methylphenyl boronate proceeded in somewhat lower yield of **3.141b**. However, the less sterically hindered N,N-dimethyl naphthamide gave the coupled product **3.140b** in excellent yield. Furthermore, the 2-naphthyl boroneopentylate afforded the coupled product **3.151b** in good yield. To mention again, as observed for *ortho*-anisamide cross coupling reactions, furan and thiophene boronates afforded the expected heterobiaryls **3.152b-3.153b** in good yields while the 3-pyridine boronate failed to give the coupled product **3.159b**. As observed in the *ortho*-anisamide coupling process (Table 3.17), electron-deficient heterocycles are inappropriate

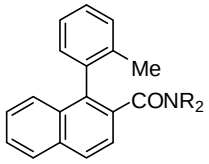
partners. The (*E*)-styrylboronate underwent the coupling reaction with both dimethyl and diethyl amides to afford the expected products **3.154b-3.155b** in high yields. These results establish a general, efficient, and potentially useful route for the preparation of 1-arylated naphthalenes. As indicated by the observed high yields in all reactions, no *peri*-hindrance effect inhibits the C-O activated coupling.[121,122]

Table 3.21 Cross Coupling of 1-MeO-2-naphthamide with Aryl Boroneopentylates

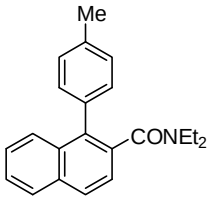




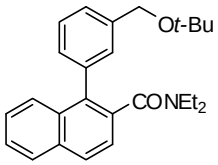
3.139b, 99%* (R = Me)
3.137b, 96% (R = Et)



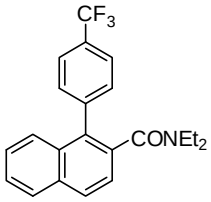
3.140b, 96% (R = Me)
3.141b, 79% (R = Et)



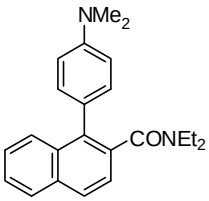
3.142b
99%



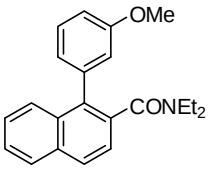
3.143b
97%



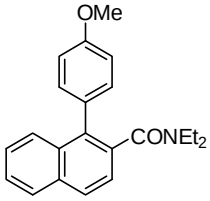
3.144b
95%



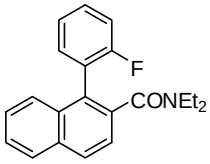
3.145b
90%



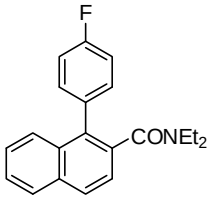
3.146b
96%



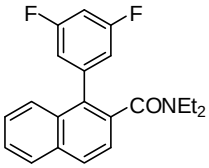
3.147b
99%



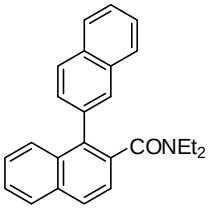
3.148b
97%



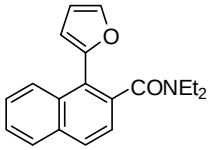
3.149b
96%



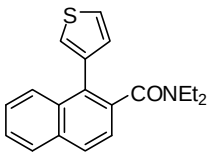
3.150b
99%



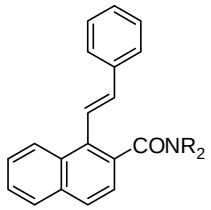
3.151b
82%



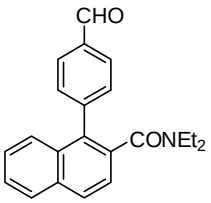
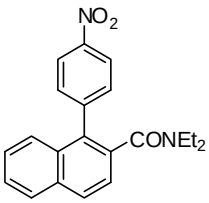
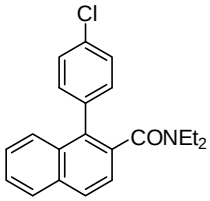
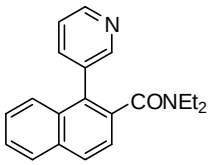
3.152b
99%



3.153b
67%



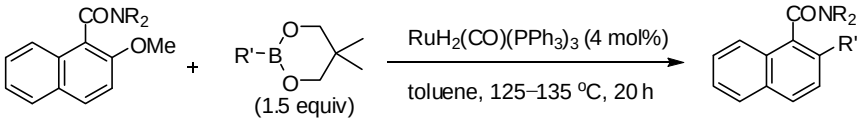
3.154b, 88% (R = Me)
3.155b, 88% (R = Et)

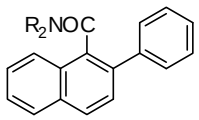
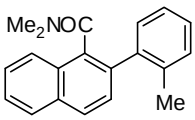
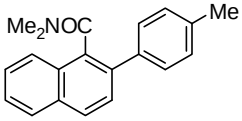
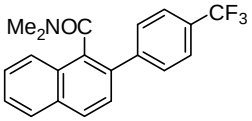
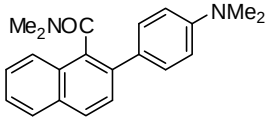
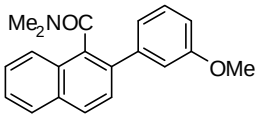
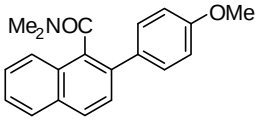
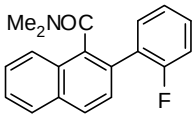
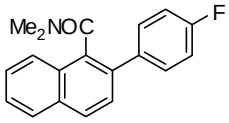
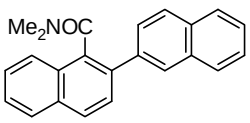
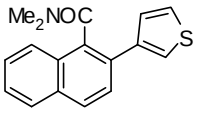
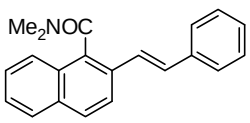
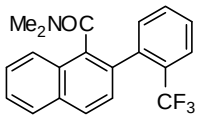
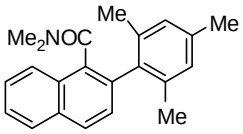
			
3.156b n.d.[a]	**3.157b** n.d.[a]	**3.158b** (7%)[a,b]	**3.159b** (4%)[a,b]

* Yields for isolated products. [a] Starting amide recovery (90%). [b] Yield determined by GC-MS analysis.

Next, we investigated the generality of the reaction of 2-MeO-1-naphthamides with a variety of organoboronates. Considering a possible steric conflict between the *peri*-hydrogen and an amide group, 2-MeO-N,N-dimethyl-1-naphthamide was employed in the initial study based on the previous experience of its smallest steric effect (Table 3.21, **3.140b**) to minimize problems of *peri* steric hindrance in coupling with *ortho*-substituted aryl boroneopentylates. The results are shown in Table 3.22. The tolerance of functional groups present in the boroneopentylates is quite similar to that observed in the previously investigated 1-MeO-2-naphthamide cases (Table 3.21). Me, NMe_2 and OMe EDGs and F and CF_3 EWGs are well tolerated to give high yields of biaryl products **3.161b-3.168b**. Furthermore, 2-naphthyl-, thiophen-3-yl- and styryl-boronates also afforded the expected heterobiaryls **3.169b-3.171b** in high yields. Similarly, steric hindrance decreased the coupling efficiency. Steric-congested boroneopentylates failed to afford any C-O activation/coupling products **3.172b-3.173b** although an excellent yield of **3.161b** was obtained in the coupling reaction with 2-methylphenyl boroneopentylate. Based on these results, the method may establish a useful route for making 2-arylated naphthalenes.

Table 3.22 Cross Coupling of 2-MeO-1-naphthamide with Aryl Boroneopentylates



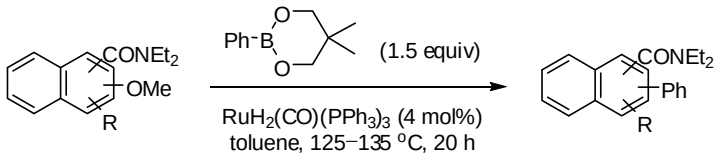
			
3.160b, 99%* (R = Me) **3.136b**, 97% (R = Et)	**3.161b** 98%	**3.162b** 99%	**3.163b** 99%
			
3.164b 89%	**3.165b** 99%	**3.166b** 98%	**3.167b** 99%
			
3.168b 99%	**3.169b** 88%	**3.170b** 96%[a]	**3.171b** 99%[a]
			
3.172b n.d.[a,b]	**3.173b** n.d.[a,b]		

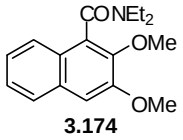
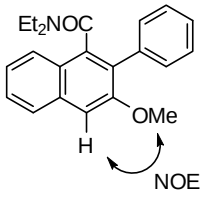
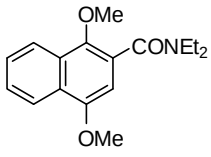
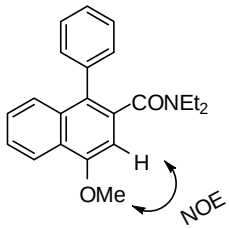
* Yields of isolated and purified products. [a] The catalyst loading: 10 mol%. [b] Monitored by GC-MS.

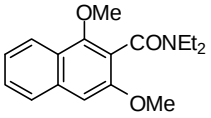
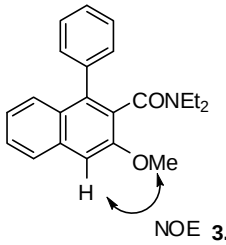
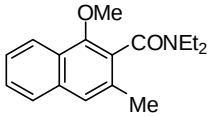
Having completed a study concerning the scope of the aryl boroneopentylates in the cross coupling reaction, we investigated the scope of the naphthamide coupling partners and the results are given in Table 3.23. Entries 1 and 2 demonstrate that selective *ortho* to amide C-O bond activation/cross coupling occurs to give the *ortho*-phenylated products **3.174b-3.175b** in quantitative yields, which reinforces the significance of amide directing and chelation assistance in the reaction. Interestingly, entry 3 shows that, in the presence of C-1- and C-3 C-O bonds, C-1 C-O activation/cross coupling selectivity is observed (**3.176b**). This exiting result confirms the higher C-1 compared to the C-3 C-O activation reactivity, which was also observed in studies of other isomeric methoxy naphthamides (Table 3.20). As gleaned from entry 4 (Table 3.23),

additional steric effect inhibited the reaction. Thus the 3-methyl naphthamide **3.177** failed to give the cross coupling product. Since the corresponding 3-methoxy naphthamide afforded a high yield of C-1 coupled product **3.176b**, this result cannot be rationalized simply by a steric effect and other possibly electronic factors play a role in this unexplained observation. Similar observations were made in the benzamide coupling studies (Table 3.18, **3.116b-3.117b, 3.124b**). Although we do not understand the failure, rationalization may be found in the requirement of proper transition state in which amide C=O–Ru coordination angle is appropriate for proximate C-O bond oxidative addition and the presence of a non-coordinating 3-methyl provides sufficient hindrance to prevent its formation. To repeat previous conclusions (Section 3.3.3.1), free rotation of the amide group is important for a successful highly efficient C-O bond activation/coupling reaction.

Table 3.23 Selectivity and Steric Effects in the Cross Coupling of Substituted Naphthamides

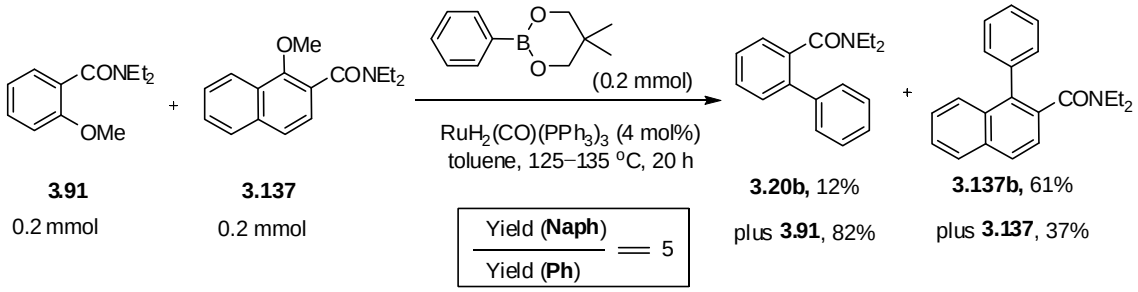


Entry	Substrate	Product	Yield (%)[a]
1	 **3.174**	 **3.174b**	99
2	 **3.175**	 **3.175b**	99

3	 **3.176**	 NOE **3.176b**	97
4	 **3.177**	n.d.[b]	--[b]

[a] Yields of isolated and purified products. [b] Starting amide recovery: 98%

A competition experiment between 2-MeO-N,N-diethylbenzamide and 1-MeO-N,N-diethyl-2-naphthamide in the C-O activation/cross coupling with phenyl neopentylboronate showed that naphthalene ring activation is significantly greater than that of the benzene ring (Scheme 3.54).

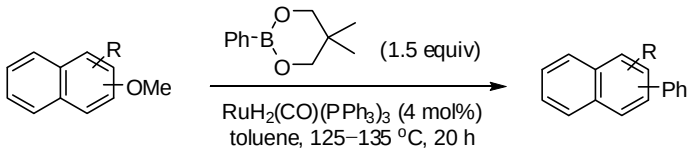


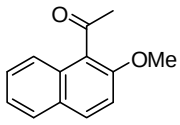
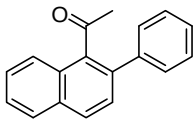
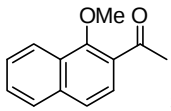
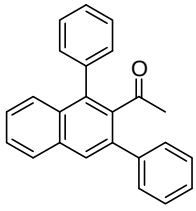
Scheme 3.54 Competition Experiment between 2-Methoxybenzamide and 1-Methoxy-2-Naphthamide in Cross Coupling with Phenyl Boroneopentylate

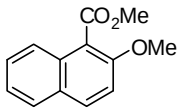
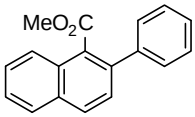
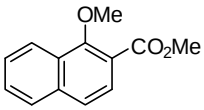
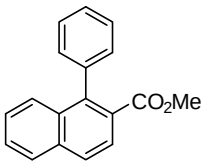
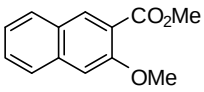
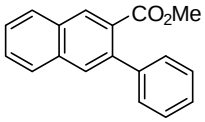
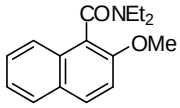
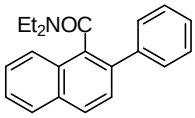
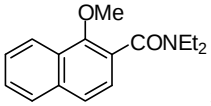
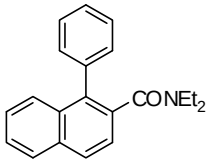
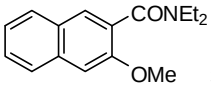
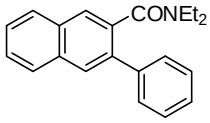
The observation of the higher cross coupling reactivity of the naphthamide prompted a study of the corresponding ketone and ester naphthalene systems and the results, including the previously obtained naphthamide-directed coupling data, are summarized in Table 3.24. Murai, Kakiuchi and co-workers previously established[268] that 1-methoxy-2-acetylnaphthalene undergoes cross coupling to give diaryl product **3.178b** in good yield (entry 1). We found that the

isomeric methoxy acetyl naphthalene **3.179** participates in both ketone-directed C-H and C-O activation/cross coupling reactions to afford the diarylated product **3.179b** in almost quantitative yield (entry 2). In comparison, the corresponding amides **3.137-3.138** (entries 7 and 8) and ester **3.181** (entry 4) undergo only the C-O activation/coupling reaction without detectable formation of the C-H activation/coupling products. Other than the amide cases in which all of three regioisomers **3.136-3.138** show reactivity for the C-O activation/coupling reaction (entries 6-8), only two regioisomers **3.180-3.181** in ester cases have the reactivity and one (**3.182**) does not have (entries 3-5). These studies establish the following order of relative reactivities of directing groups: ketone > amide > ester and suggest that amide controls the best selectivity and reactivity. Notably, they also indicate that the ester is an excellent DG for C-O activation/coupling reaction in one naphthalene series (entry 3).

Table 3.24 Comparison of Relative Cross Coupling Facility of Amide, Ester, and Ketone Directing Groups

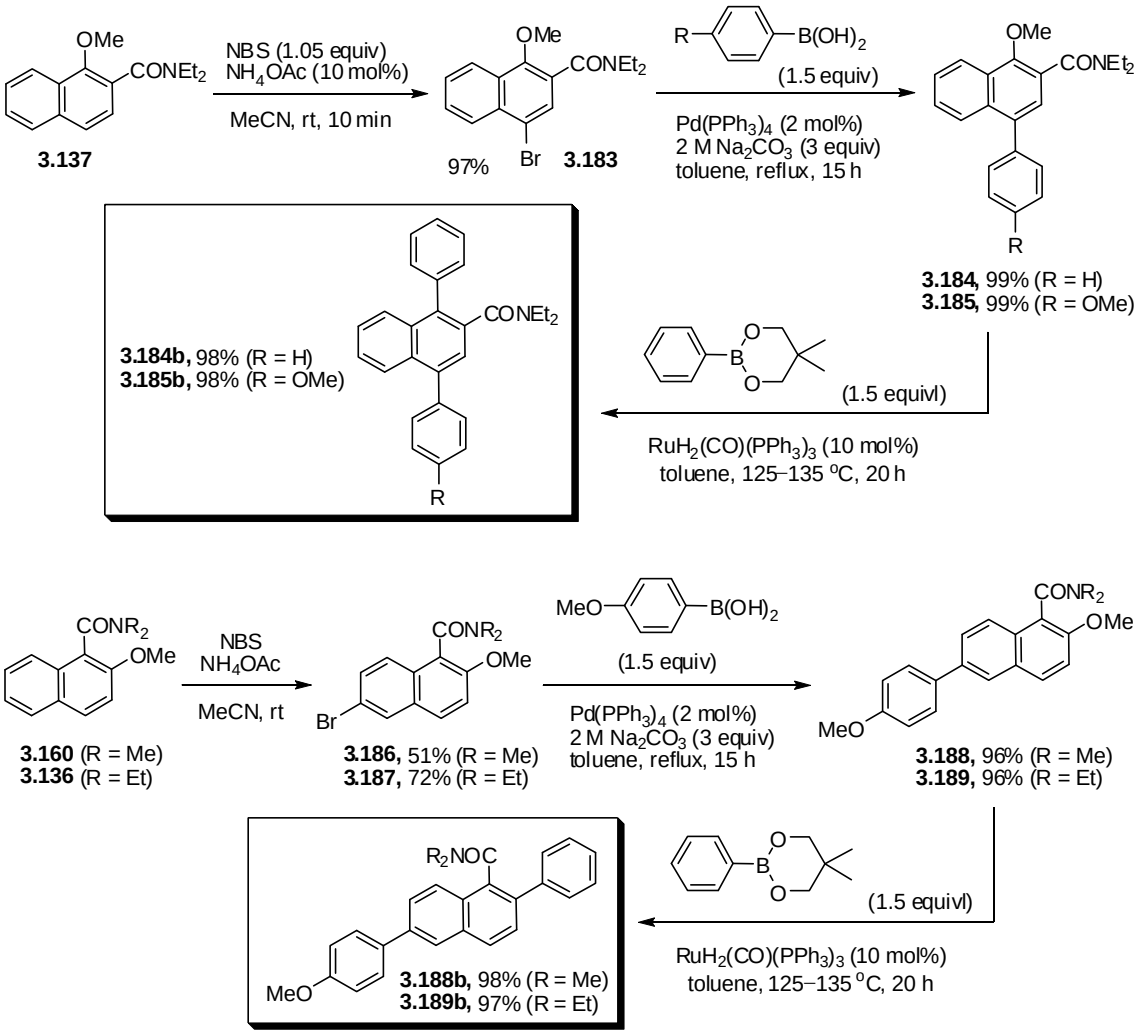


Entry	Substrate	Product	Yield (%)[a]
1	 **3.178**	 **3.178b**	84[b]
2	 **3.179**	 **3.179b**	99[c]

3	 **3.180**	 **3.180b**	96
4	 **3.181**	 **3.181b**	39[d]
5	 **3.182**	 **3.182b**	n.d.[d,e]
6	 **3.136**	 **3.136b**	97
7	 **3.137**	 **3.137b**	96
8	 **3.138**	 **3.138b**	30

[a] Yields of isolated and purified products. [b] See ref[268](1.2 equiv. boronate and reflux for 1 h).
[c] C-H activation involved; reduction of 50% SM (amide) was considered on yield calculation.
[d] The catalyst loading: 10 mol%. [e] De-ester in 23% yield determined by GC-MS analysis.

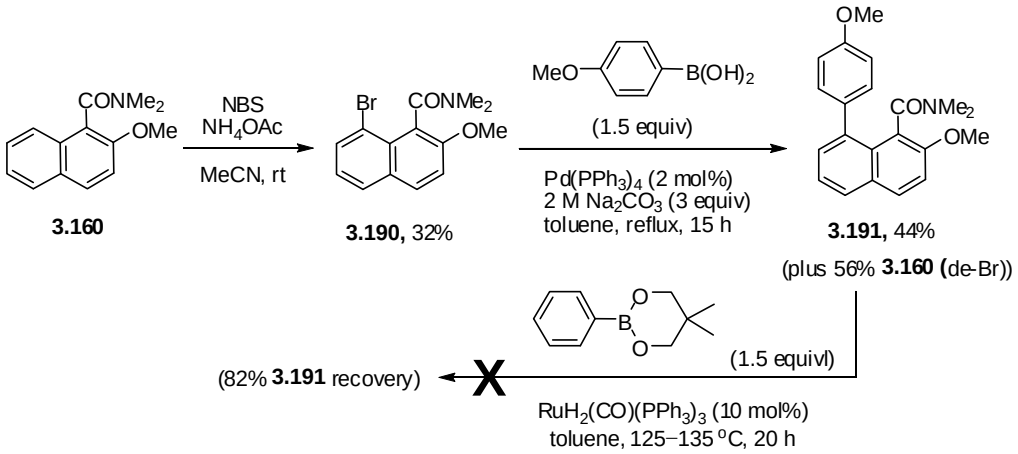
Analogous to the previous application studies concerning combined C-O and standard Suzuki cross coupling tactics (Scheme 3.50), a similar high yield process was developed which involved bromination, Suzuki coupling and the C-O activation/coupling for the construction of teraryls incorporating a functionalized central naphthalene ring (Scheme 3.55).



Scheme 3.55 Synthesis of Teraryls via Sequential Bromination, Standard Suzuki Cross Coupling and C-O Activation/Coupling Reactions

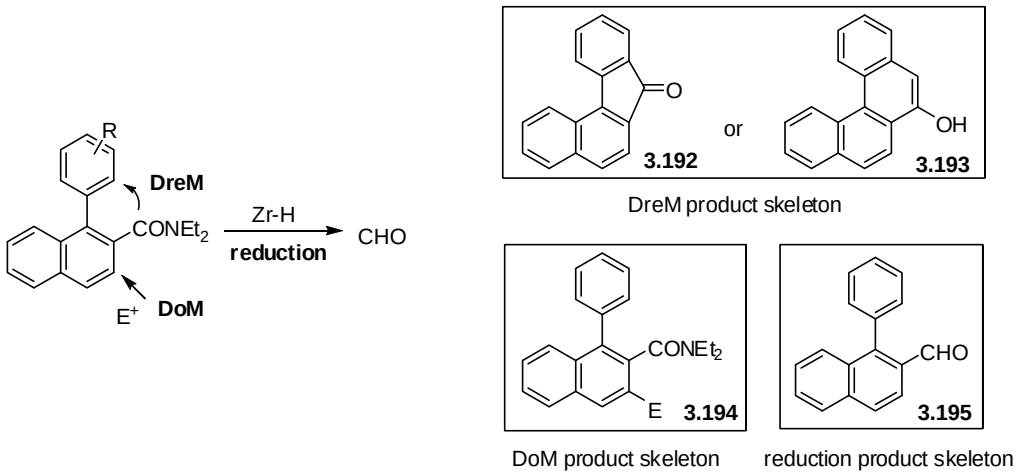
A further application using the 8-bromonaphthalene amide **3.190** was undertaken (Scheme 3.56). Compound **3.190** as byproduct of bromination of **3.186** was prepared by standard bromination. Upon treatment under standard Suzuki coupling conditions, it afforded the 8-aryl naphthamide **3.191** in low yield. The formation of debrominated product **3.160** in major amounts indicates that, although oxidative addition occurs, the cross coupling step is disfavoured,

presumably due to *peri* steric effects. Thus, the C-O activation/coupling reaction failed also due to steric effects on the amide C=O which is unable to assume the required geometry for Ru-coordination–C-O insertion although the less-hindered N,N-dimethyl amide was employed.



Scheme 3.56 Unsuccessful C-O Activated Cross Coupling of an 8-Aryl Naphthamide **3.191**

The utility of the synthesized naphthyl-aryl derivatives in further D*o*M and D*re*M processes to yield fused fluorenone **3.192** and phenanthrol **3.193** aromatics (Scheme 3.57) is evident from previous work in our laboratories.[49,50,1,3] Further synthetic application may be derived from application of the efficient amide to aldehyde *in situ* Schwartz reduction as demonstrated for several substrates (Chapter 2, Table 2.9, **2.51-2.52**).



Scheme 3.57 Links to D*o*M, D*re*M and Schwartz Reduction Processes

In summary, the efficient and highly regioselective Ru-catalyzed naphthamide coupling methodology established above constitutes the first catalytic amide-directed C-O activation of naphthamides/C-C bond cross coupling reaction. It complements and may supercede the DoM–Suzuki cross coupling strategy since it has the advantages of non-cryogenic and non-strong base conditions. In addition, it provides naphthamides which are difficult to prepare by the traditional DoM-Suzuki cross coupling sequence, e.g. **3.139b-3.155b** (Table 3.21).

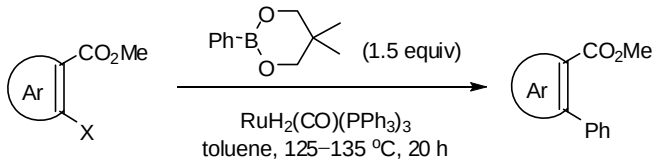
3.3.3.3 Ester-Directed C-O Activation and C-C Bond Formation

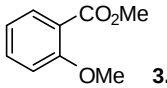
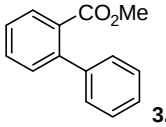
The first Ru-catalyzed ester-directed C-H activation/arylation was reported by Kakiuchi and co-workers.[262] The disadvantage of this method is that the formation of a mixture of mono- and di-arylated products cannot be avoided even when the required isopropyl ester is used as the directing group.

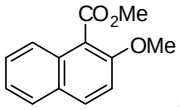
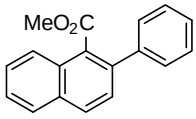
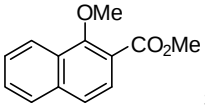
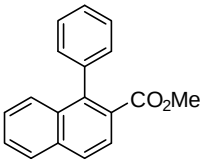
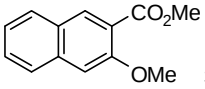
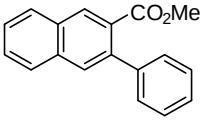
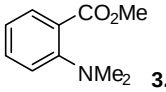
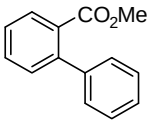
The ester-directed C-O activation/arylation reaction has not been reported to date. Based on the results in the naphthyl ester series (Table 3.24), we considered that the ester may have the

appropriate directing features for the C-O activation/C-C bond formating reaction. Several experiments were formulated to test this idea and the results are shown in Table 3.25. The commercially available *ortho*-anisic ester led to only trace amounts of C-O activation/cross coupling product **3.95b** (Table 3.25, entry 1). Thus, benzoates are not useful substrates for the C-O activation/coupling reaction. On the other hand, of the three regioisomeric naphthoates, as previously described, the 2-MeO-1-naphthoate **3.180** showed excellent reactivity for a C-O activation/phenylation reaction while the isomeric 1-methoxy ester **3.181** was modestly reactive and the 3-methoxy ester **3.182** was unreactive (entries 2-4). This constitutes the first examples of the ester-directed C-O activation/cross coupling reaction. Moreover, using the N,N-dimethyl anthranilate ester **3.196**, we found an ester-directed C-N activation/phenylation which proceeds in good yield and high selectivity without observed C-H activation/cross coupling product (entry 5). Therefore, the C-N activation is favored over the C-H activation process. A similar example was reported by Kakiuchi and co-workers in which, however, the presence of an *ortho*-Me group blocked C-H activation.[272]

Table 3.25 C-O and C-N Activation/C-C Cross Coupling Reactions of Ester Directing Group Substrates



Entry	Substrate	Catalyst loading (mol%)	Product	Yield (%)[a]
1	 **3.95**	10	 **3.95b**	--(4)[b]

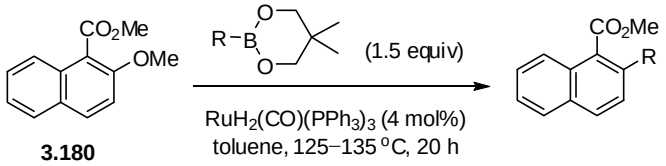
2	 **3.180**	4	 **3.180b**	96
3	 **3.181**	10	 **3.181b**	39
4	 **3.182**	10	 **3.182b**	n.d.[c]
5	 **3.196**	10	 **3.196b**	72[d]

[a] Yields of isolated and purified products.
[b] Yield determined by GC-MS analysis.
[c] De-ester was found in 23% yield determined by GC-MS analysis.
[d] 1.2 Equiv of boronate was used

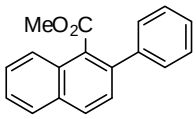
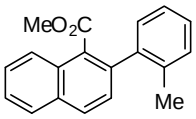
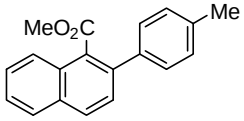
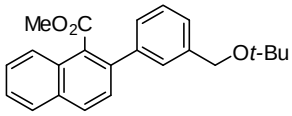
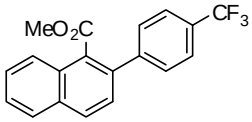
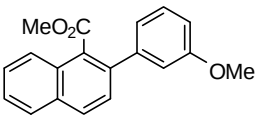
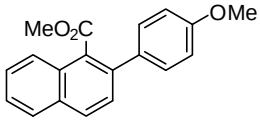
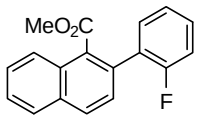
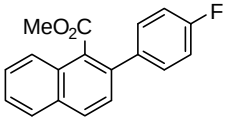
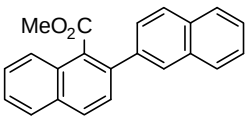
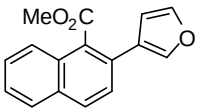
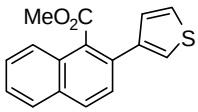
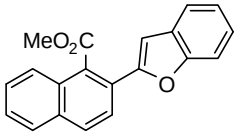
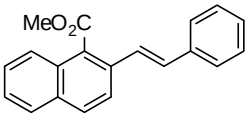
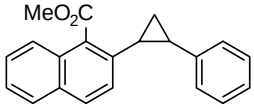
The recognition that the 2-MeO-1-naphthoate ester **3.180** has an excellent reactivity and selectivity for a C-O activation/phenylation reaction stimulated a study concerning the generalization of the reaction for a variety of aryl boroneopentylates and the results are shown in Table 3.26. As expected from previous studies on C-O coupling reactions of amides (Section 3.3.3.2), aryl boroneopentylates with Me, CH_2O*t*-Bu and OMe EDGs afforded arylation products **3.197b-3.199b, 3.201b-3.202b** in good yields. Similarly, aryl boroneopentylates with the EWGs F and CF_3 led to coupled products **3.200b, 3.203b-3.204b** in high yields. The modestly hindered 2-methylphenyl and the 2-naphthyl boronates underwent efficient coupling reactions (**3.197b** and **3.205b**). In the heterocyclic series, good yields were obtained for the thiophene and benzofuran boronate cases (**3.207b** and **3.208b**) but, unexpectedly, and in view of the previous result for the amide-directed C-O activation/coupling (**3.152b**, Table 3.21), the 3-furan boronate afforded a low yield of product **3.206b**. As in previous reaction scope examinations (Sections 3.3.3.1, 3.3.3.2),

(*E*)-styryl and cyclopropyl boronate were examined to furnish 73% and 43% yields of products **3.209b** and **3.210b** respectively, in which **3.209b** retained *E*-stereochemistry.

Table 3.26 C-OMe Activated Cross Coupling of Methyl 2-MeO-1-naphthoate **3.180** with Aryl Boroneopentylates



3.180

			
3.180b 96%*	**3.197b** 90%	**3.198b** 92%	**3.199b** 93%
			
3.200b 86%	**3.201b** 90%	**3.202b** 86%	**3.203b** 88%
			
3.204b 90%	**3.205b** 94%	**3.206b** 31%**	**3.207b** 73%**
			
3.208b 91%**	**3.209b** 73%**	**3.210b** 43%**	

* Yields of isolated and purified products.
** 10 mol% catalyst loading.

In summary, a highly efficient and regioselective Ru-catalyzed naphthoate ester-directed C-O activation/cross coupling methodology has been discovered and generalized. Together with the benzoate results, it constitutes a new reaction which extends the Murai, Kakiuchi chemistry from ketone- to ester-directed reactions.

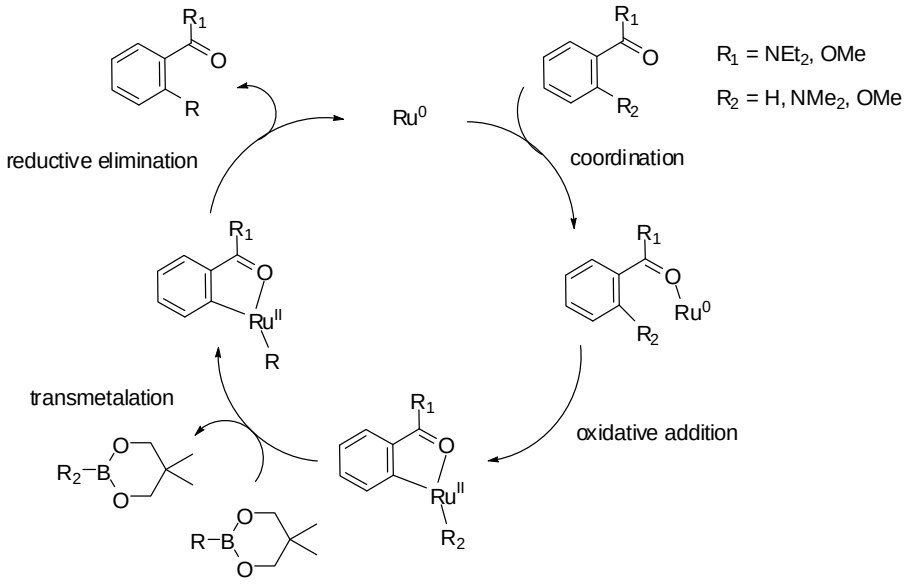
This method is the first catalytic ester-directed C-O activation/C-C bond formation reaction. It proceeds with high efficiency and regioselectivity and may be viewed as a complement and, in the future, perhaps a replacement of the DoM–Suzuki cross coupling strategy with advantages of non-cryogenic temperatures and strong base conditions. We suggest that this has the potential to become the most highly efficient and practical cross coupling route for the preparation of 2-aryl and heteroaryl naphthoate acids and esters from easily available or commercial 1-naphthoate ester derivatives.

3.3.4 Proposed Mechanism for Ru-Catalyzed Amide- and Ester-Directed C-H, C-N, C-O Activation/Cross Coupling Reactions

The Ru-catalyzed amide- and ester-directed C-H, C-N, C-O activation/cross coupling reactions, based on the results above, may be considered as an expansion of the corresponding Ru-catalyzed ketone-directed reaction developed by Murai, Kakiuchi, and co-workers[259,260,268,272] and therefore, likely follow a similar mechanism as that suggested by these workers (Scheme 3.28 and 3.34).

A mechanism involving amide- and ester-directing and chelation assistance is proposed and indicated in Scheme 3.58. The only exception is elimination of the carbonyl reduction step in the C-H activation/coupling process due to no carbonyl reduction of amide observed, which is different from the ketone-directed C-H activation/coupling reaction.

As direct evidence of reductive deamination, an amine byproduct was obtained in 11% yield in amide-directed C-N activation/coupling reaction (Table 3.6, entry 2).



Scheme 3.58

3.3.5 C-O Activation and Reduction (Hydrodemethoxylation)

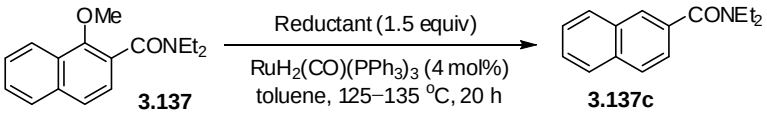
The current popular method for reductive removal of a phenol or alkoxy substituent from an aromatic substrate is via conversion into the C-OTf derivative and catalytic hydrodetriflation.[291-295] The requirement of preparation of the triflate using expensive triflic anhydride or $PhNTf_2$ represents a major limitation of this procedure. An available direct hydrodemethoxylation of aromatic C-OMe derivatives via a catalytic C-O cleavage would constitute a useful contribution to organic synthesis.

Based on the above studies of amide-directed C-O activation/cross coupling reactions, we considered that a hydrodemethoxylation reaction of aromatic OMe derivatives may be achieved

via a C-O activation/reduction by a hydride source. Mechanistically, this postulate requires that the coordinated Ru-OMe species (e.g. Scheme 3.58) undergoes, rather than transmetalation with organoboronate, formation of a Ru-H species which, by reductive elimination forms the hydrodemethoxylation product. An absolute requirement for the success of the proposed process is that the chosen hydride reagent does not reduce the amide group.

Initially, several reductants were tested for the hydrodemethoxylation reaction of 1-MeO-N,N-diethyl-2-naphthamide **3.137** using $RuH_2(CO)(PPh_3)_3$ catalysis and the results are tabulated in Table 3.27. To our delight, using Et_3SiH afforded the hydrodemethoxylation product in almost quantitative yield (entry 1) while DIBAL-H was somewhat less effective but still a suitable reagent to give product in 72% yield (entry 2). However, only trace amounts of the expected product was observed (GC-MS analysis) using $LiAlH(OBu\text{-}t)_3$ (entry 3) and a hydrogenation reaction led to complete recovery of starting material (entry 4).

Table 3.27 Initial Test for Reductant**s**

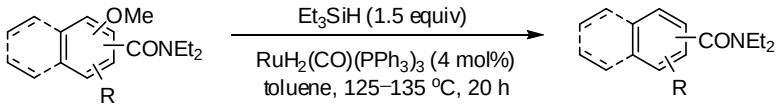


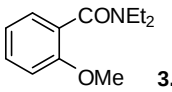
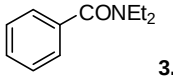
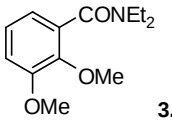
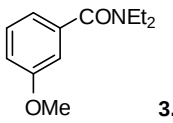
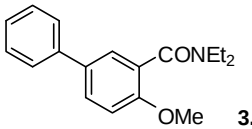
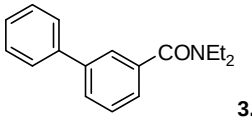
Entry	Reductant	Isolated Yield (%)
1	Et_3SiH	98
2	DIBAL-H	72
3	$LiAlH(OBu\text{-}t)_3$	-- (9)[a]
4	H_2	--[b]

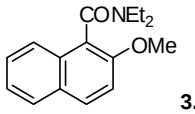
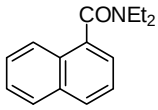
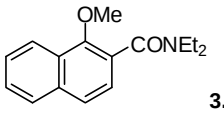
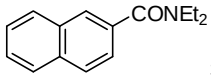
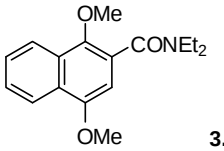
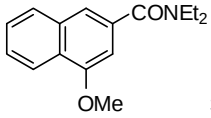
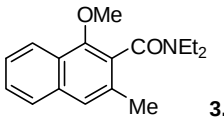
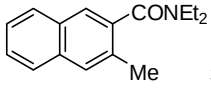
[a] Yield determined by GC-MS analysis
[b] 60 psi. Recovery of starting material (98%).

Having established the most effective hydride reagent, Et_3SiH, generalization of the discovered method was pursued and the results are shown in Table 3.28. Low reactivity was found in simple benzamide cases **3.91, 3.119** (entries 1 and 2) although, surprisingly, the 5-phenyl benzamide **3.114** led to hydrodemethoxylated product **3.114c** in 88% yield under higher catalyst loading (entry 3). On the other hand, all naphthamide cases **3.136-3.137, 3.175** (entries 4-6) proceeded well to the reduction products **3.136c-3.137c, 3.175c** with the exception of the 3-methyl naphthamide **3.177** which gave trace amounts of product **3.177c** (entry 7). A similar effect, attributed to inability to achieve an appropriate geometry for C-O activation was previously observed and discussed in amide-directed C-O activation of naphthamides/cross coupling reaction (Table 3.23). Clearly, based on these results, Et_3SiH is an efficient reductant for the hydrodemethoxylation of 2-naphthamides and the biaryl amide (entry 3) but not benzamide derivatives.

Table 3.28 Ru-catalyzed Hydrodemethoxylation Benzamides and Naphthamides Using Et_3SiH



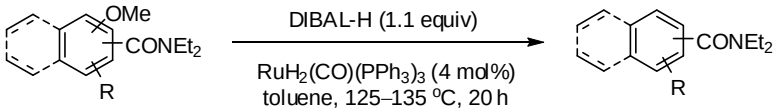
Entry	Substrate	Product	Yield (%)[a]
1	 **3.91**	 **3.20**	--(4)[b]
2	 **3.119**	 **3.119c**	--(12)[b]
3	 **3.114**	 **3.114c**	88[c]

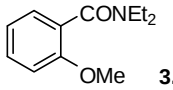
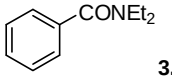
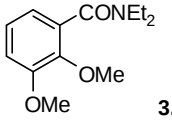
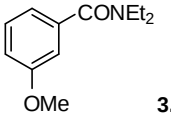
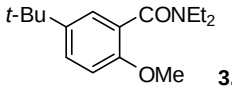
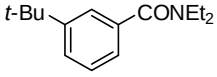
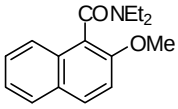
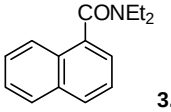
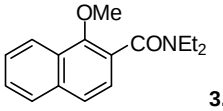
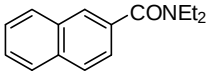
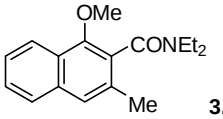
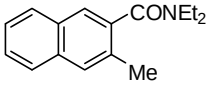
4	 **3.136**	 **3.136c**	87
5	 **3.137**	 **3.137c**	98
6	 **3.175**	 **3.175c**	93
7	 **3.177**	 **3.177c**	--(6)[b]

[a] Yields of isolated and purified products.
[b] Yield determined by GC-MS analysis
[c] The catalyst loading: 10 mol%

The successful albeit lower yielding hydrodemethoxylation established using DIBAL-H (Table 3.27) prompted further examination of this reagent for several aromatic amides and the results are listed in Table 3.29. Interestingly, in contrast to the results obtained using Et_3SiH (Table 3.28), reductions of benzamides **3.91, 3.119, 3.114** under DIBAL-H conditions proceeded smoothly to give hydrodemethoxylation products **3.20, 3.119c, 3.114c** in 51-68% yields (entries 1-3). In the naphthamide cases **3.136-3.137**, slightly higher yields (70-83%) of reduction products **3.136c-3.137c** were observed (entries 4 and 5). However, in comparison with Et_3SiH, the DIBAL-H has lower reactivity for the naphthalene series. Similarly, as observed in the reduction with Et_3SiH and perhaps for the same reasons, the 3-methyl-2-naphthamide **3.177** failed to undergo reduction and led to high recovery of starting material (entry 6). We conclude that DIBAL-H is also a useful reductant with a major difference to Et_3SiH in its ability to hydrodemethoxylate not only methoxy naphthamides but also the corresponding benzamides.

Table 3.29 Ru-catalyzed Hydrodemethoxylation Using DIBAL-H

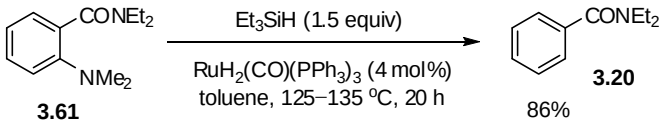


Entry	Substrate	Product	Yield (%)[a]
1	 **3.91**	 **3.20**	51
2	 **3.119**	 **3.119c**	68
3	 **3.114**	 **3.114c**	55[b]
4	 **3.136**	 **3.136c**	70[c]
5	 **3.137**	 **3.137c**	83 72[c]
6	 **3.177**	 **3.177c**	n.d.

[a] Yields of isolated and purified products
[b] The catalyst loading: 10 mol%
[c] 1.5 Equiv. of reductant is used

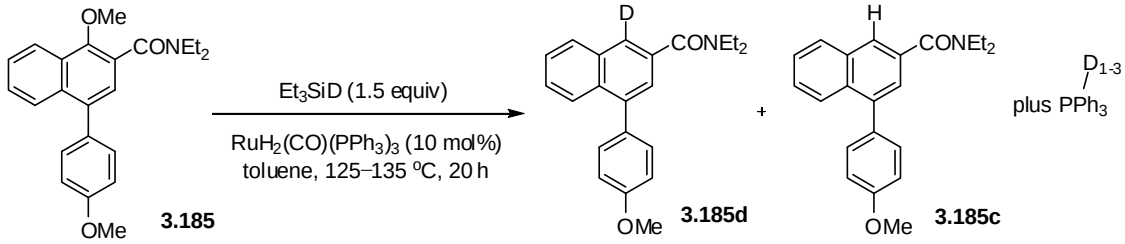
The above successful results and obvious mechanistic analogy led to the return of the N,N-dimethyl anthranilamides as substrates for the potential amide-directed C-N hydrodeamination. Treatment of the prototype substrate **3.61** under the $RuH_2(CO)(PPh_3)_3/Et_3SiH$ conditions resulted in smooth reduction to give diethyl benzamide **3.20** in 86% yield (Scheme

3.59). This result juxtaposed to the *ortho*-anisamide study (Table 3.28, entry 1) establishes the higher reactivity of the C-N bond compared to the C-O bond in the Ru-catalyzed process.



Scheme 3.59

In a brief mechanistic study, the 4-aryl naphthamide **3.185** was subjected to the Ru-catalyzed conditions in the presence of the same conditions but using Et_3SiD (Scheme 3.60) to afford a mixture of expected reduction products **3.185d** and **3.185c** in a D/H = 1 : 1.8 ratio and in 98% yield. Moreover, the formation of non-deuterated product may be via a D-H exchange between Et_3SiD and PPh_3 to generate Et_3SiH which effects the hydrodemethoxylation.

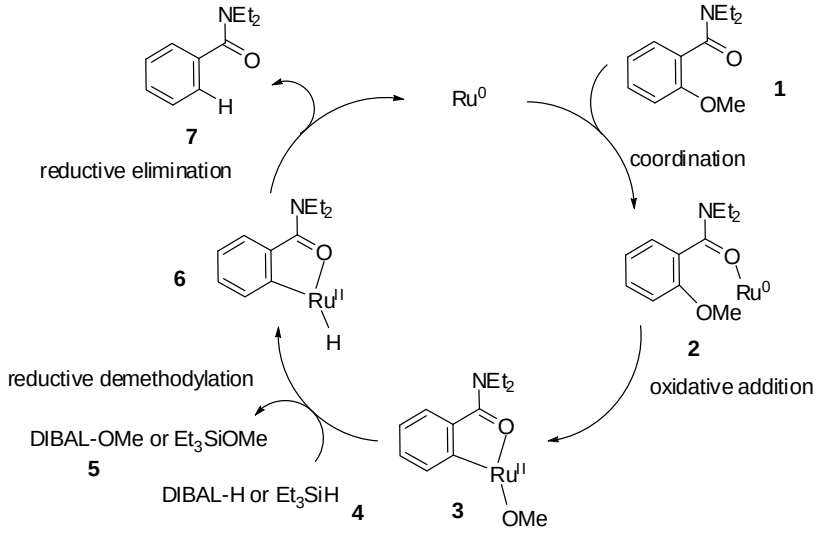


98% isolated yield for the mixture of above 2 compounds
Ratio: **D/H = 1/1.8** (calculated from HRMS)

Scheme 3.60 Hydrodemethoxylation of Naphthamide **3.185** using Et_3SiD

The above deuterium incorporation result and by analogy with the general Murai-Chatani-Kakiuchi mechanistic proposal,[270,268] the reaction path for the hydrodemethoxylation may be formulated (Scheme 3.61). Four elementary steps are involved: i) amide carbonyl-Ru(0)

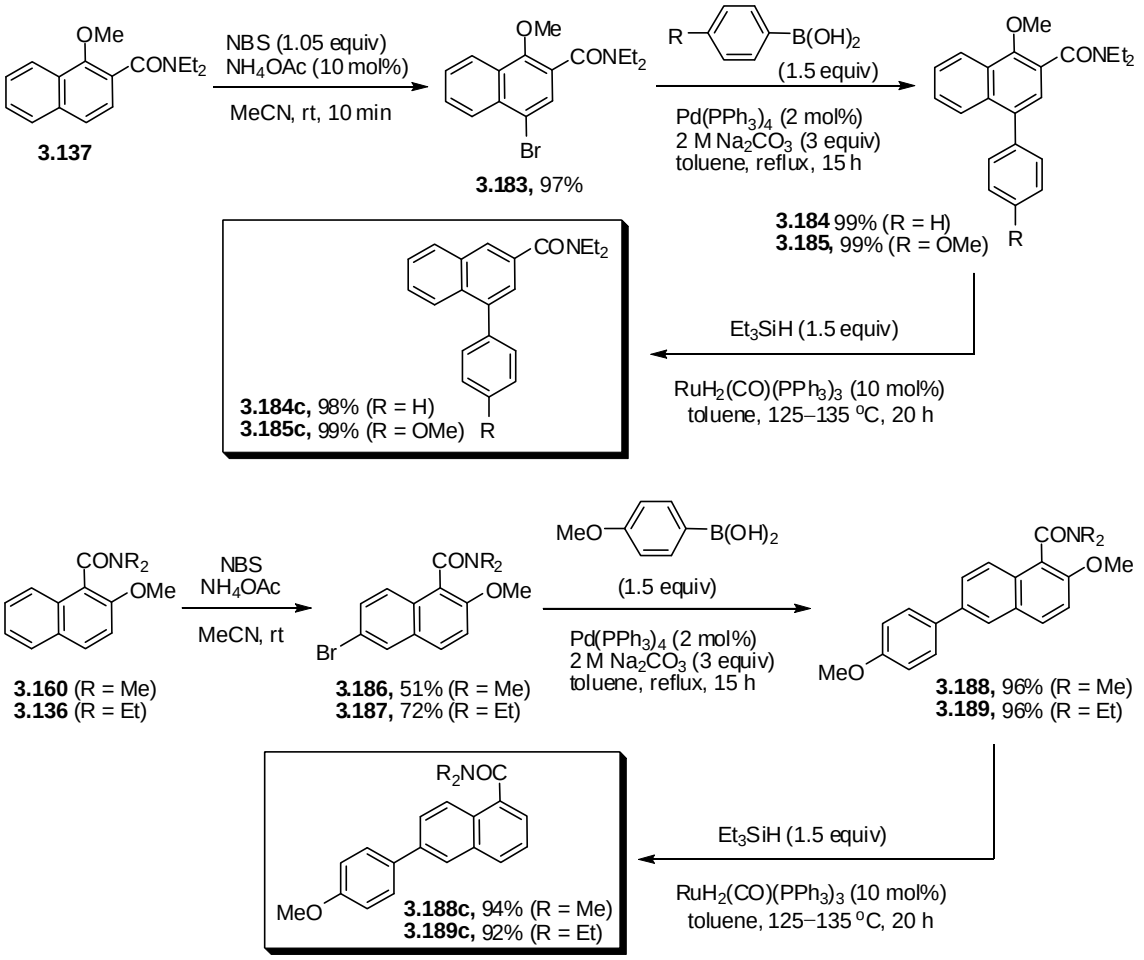
coordination; ii) with chelation assistance, oxidative addition of Ru(0) into the aryl C-OMe bond; iii) reductive demethoxylation of the Ru(II)-OMe species **3** by the hydride source **4** (Et_3SiH or DIBAL-H) to form the Ar-Ru(II)-H intermediate **6**; and iv) reductive elimination of Ar-Ru(II)-H **6** to give the hydrodemethoxylation product **7** with regeneration of the active Ru(0) to continue the catalytic cycle.



Scheme 3.61

To demonstrate application of the above hydrodemethoxylation methodology, the synthesis of aryl naphthamides **3.184c-3.185c, 3.188c-3.189c** was carried out (Scheme 3.62). In the first, the naphthamide **3.137** was converted by highly regioselective electrophilic bromination to give compound **3.183** which, upon Suzuki coupling with two aryl boronic acids, afforded the 4-aryl naphthamides **3.184-3.185** respectively in quantitative yields. Under the established Ru-catalyzed conditions, the hydrodemethoxylation was achieved to give **3.184c-3.185c** also in quantitative yields. In the second synthesis, the same bromination, Suzuki cross coupling, and hydrodemethoxylation starting from **3.136, 3.160** and proceeding via intermediates **3.186-3.187**

and **3.188-3.189** afforded the 6-aryl 2-naphthamides **3.188c-3.189c**. Thus, starting from simple naphthamides, two types of naphthyl-based biaryls were synthesized in three steps in 46-95% overall yields. These syntheses demonstrate the concept, perhaps of general value, of using the strong OMe-directed electrophilic substitution reaction to derive a Suzuki coupling partner, which after it has served such a purpose, is detached to derive a substance which is again primed for further regioselective DoM chemistry.



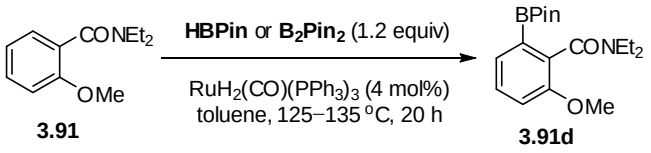
Scheme 3.62 Synthesis of Naphthyl-Based Biaryls via a Bromination-Suzuki Cross Coupling-Hydrodemethoxylation Sequence

In summary, the above studies show that the Ru-catalyzed amide-directed hydrodemethoxylation is a general method of significant potential in organic synthesis. To the best of our knowledge, this is the first catalytic hydrodemethoxylation reaction. In the course of the preparation of this thesis, a hydrodemethoxylation of simple aryl methyl ethers was reported.[296]

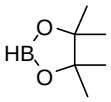
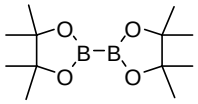
3.3.6 C-H Activation and C-B Bond Formation

The major part of this thesis has been concerned with the Ru-catalyzed amide-directed C-O activation for the discovery, generalization, and development of highly regioselective and efficient methods for the formation of C-C bonds. To test the idea that the Ru-catalytic conditions may also be applicable for amide-directed C-O activation/C-B bond formation, two experiments were carried out. The results are listed in Table 3.30. Surprisingly, instead of the expected C-O activation/C-B bond formation, a corresponding C-H activation/C-B formation was observed. B_2Pin_2 was found to show much higher reactivity than HBPin in the reaction. When B_2Pin_2 was employed, a 72% conversion as monitored by GC-MS after 20 h was established but led to the isolation of product in only 30% yield perhaps due to instability of the product to silica gel chromatography. This result demonstrates a new *ortho* C-H activation/borylation of tertiary benzamides under $RuH_2(CO)(PPh_3)_3$ catalysis, other than the failure of the C-H activation/C-C coupling of benzamides (Scheme 3.40).

Table 3.30 Test of C-H vs C-O Activation for C-B Formation of *ortho*-Anisamide **3.91**



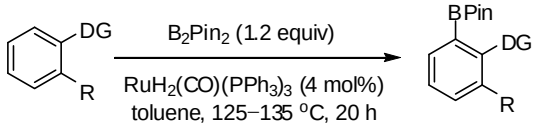
3.91 **3.91d**

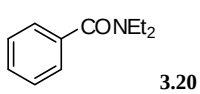
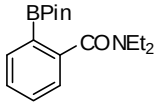
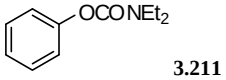
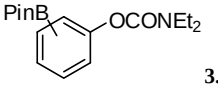
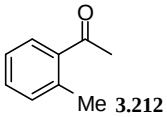
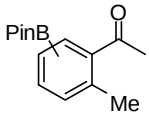
Entry	Borane		Yield*(%)
1		(HBPin)	--(11)
2		(B_2Pin_2)	30(72)

* Yield of isolated and (GC-determined) products

As mentioned several times in the above discussion, our laboratory has developed a general Ir-catalyzed *meta*-borylation strategy of DMG–bearing substrates which complements the DoM borylation reaction.[286] These results and the high reactivity of the Ru-catalysts in C-H, C-N, and C-O activation processes prompted the test of several unsubstituted substrates using Ru-catalysis. Thus, to our delight, the simple N,N-diethylbenzamide **3.20** underwent the C-H activation/borylation to afford the expected product **3.20d** in 75% yield (Table 3.31, entry 1). On the other hand, the phenyl *O*-carbamate **3.211** and the acetophenone **3.212** led only to low yields (GC-MS) of corresponding products **3.211d** and **3.212d** respectively (entries 2 and 3). Surprisingly, other than the reactivity order previously established (Section 3.3.3.2), the ketone appears to be a poor directing group for the borylation reaction.

Table 3.31 C-H Activation/C-B Formation for Benzamide, *O*-Carbamate and Acetophenone

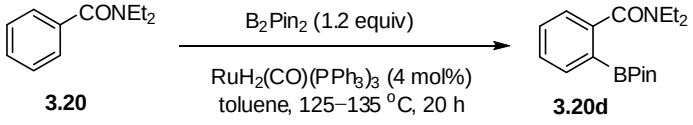


Entry	Substrate	Product	Yield (%)
1	 **3.20**	 **3.20d**	75[a](88)[b]
2	 **3.211**	 **3.211d**	-- (12)[b]
3	 **3.212**	 **3.212d**	-- (23)[b]

[a] Yields of isolated products. [b] Yields determined by GC-MS analysis.

The experimental data given in Table 3.32 (entry 4) established 20 h as the optimized reaction time for 95% conversion of benzamide **3.20** to borylated product **3.20d**. Shorter reaction times showed decreased yields of products (entries 1-3).

Table 3.32 Reaction Time Screening for C-H Activation and C-B Formation



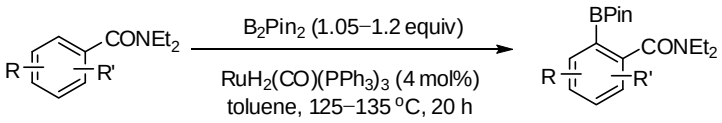
3.20 **3.20d**

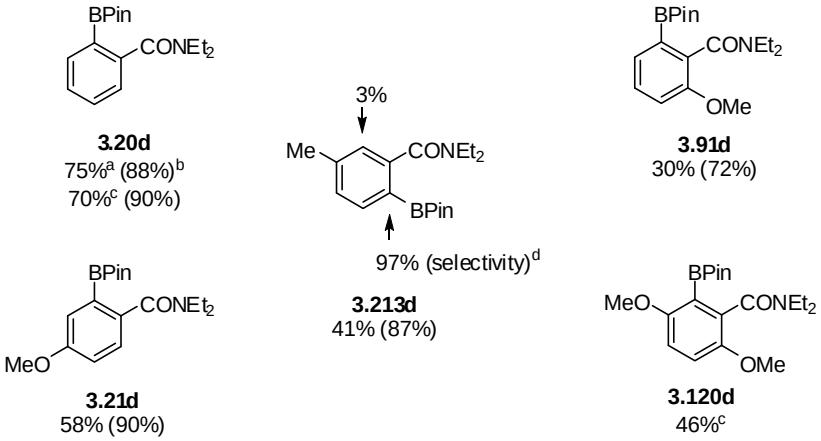
Entry	Time	SM : Product (GC-MS ratio)	Yield (%)[a]
1	2 h	1 : 2.1	66
2	5 h	1 : 3.7	79
3	10 h	1 : 7.1	88
4	**20 h**	**1 : 20.1**	**95**

[a] Yields determined by GC-MS analysis.

Several substituted benzamides were examined for the C-H activation/borylation reaction and results are summarized in Table 3.33. All substrates underwent the C-H activation/borylation reaction in good conversions as monitored by GC-MS but led to isolated products **3.21d, 3.91d, 3.120d, 3.213d** in much lower yields. It is very likely that products are unstable and undergo decomposition/deborylation during purification by flash SiO_2 column chromatography. Only monoborylation products were observed even when two *ortho* C-H bonds were present. The 3-methyl benzamide, underwent reaction to give *ortho*-BPin product **3.213d** complementing the highly *meta*-regioselective Ir-catalyzed borylation[286] and showing advantage over the DoM derived procedure which shows an approximate 2:1 C_2:C_6 regioselectivity at least as established by deuterium quench experiments.[278] On the other hand, all of the other BPin products **3.20d, 3.21d, 3.91d, 3.120d** are the same as those obtained by the DoM tactic.

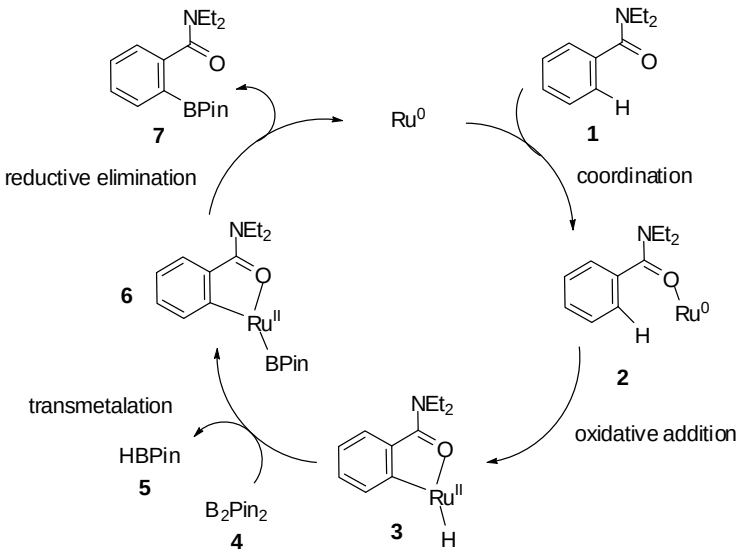
Table 3.33 C-H Activation and C-B Formation





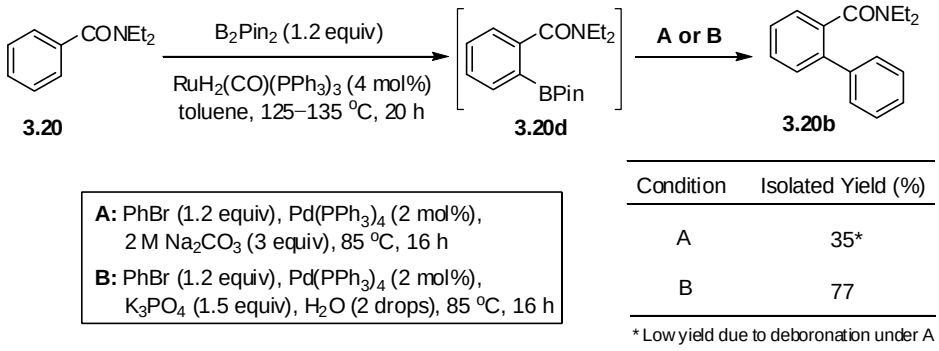
[a] Yields of isolated and purified products. [b] Yield determined by GC-MS analysis.
[c] Yield from neat condition without any solvent. [d] Isomers ratio on GC-MS.

A proposed mechanism analogous to that postulated by Kakiuchi and delineated for the C-H, C-N, C-O activation/C-C cross coupling reactions (Scheme 3.28, 3.34, 3.58) involves Ru(0)-amide carbonyl coordination **2,** chelation assisted oxidative addition **3**, and transmetalation to form the Ar-Ru(II)-BPin intermediate **6**, and reductive elimination of Ar-Ru(II)-BPin to give borylation product **7** with regeneration of the active Ru(0) catalyst.



Scheme 3.63

In order to ascertain that the decomposition of borylation products occurs during purification, a one-pot process of borylation and Suzuki cross coupling was examined (Scheme 3.64). Using two sets of conditions generally used in our laboratories,[51,286] condition A (aqueous) afforded the biaryl in unsatisfactory yield while condition B (non-aqueous) furnished the product in acceptable yield. However, in view of the high yield of the borylation step (Table 3.31, entry 1), protodeboronation still occurs under the latter conditions.



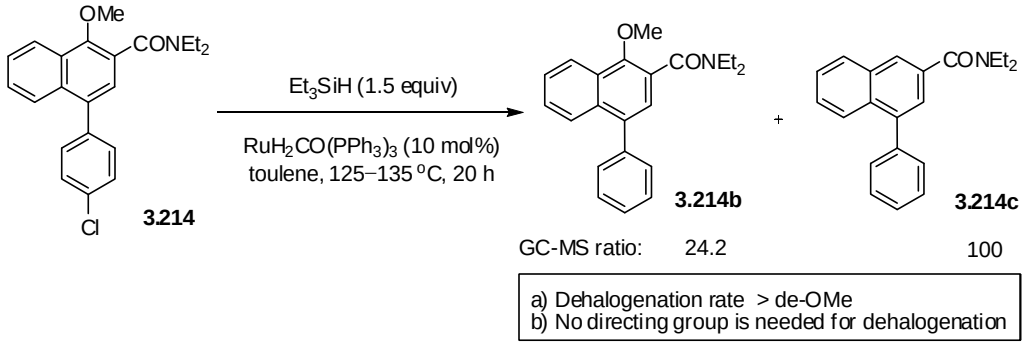
Condition	Isolated Yield (%)
A	35*
B	77

* Low yield due to deboronation under A

Scheme 3.64 One-pot Process of Borylation and C-C Suzuki Cross Coupling

3.3.7 Ru-Catalyzed Hydrodehalogenation of Aryl C-Cl, C-Br and C-I Bonds

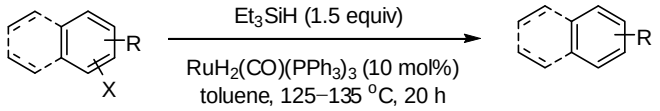
During investigation of Ru-catalyzed amide-directed C-O activation/ hydrodemethoxylation reaction, an interesting result attracted our attention (Scheme 3.65). When the chloroaryl **3.214** was subjected to the Ru-catalyzed reduction with Et_3SiH, only partial hydrodemethoxylation was observed while a dechlorination process occurred with full conversion. The result indicated that the rate of dechlorination is not only faster than hydrodemethoxylation but also non-chelative Ru insertion into C-Cl bond and reduction is more favorable than those into the C-O bond.

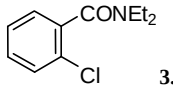
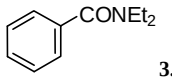
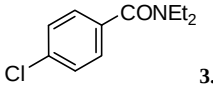
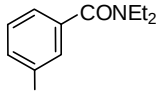
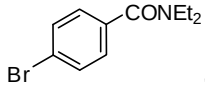
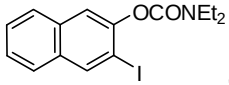
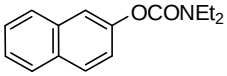


Scheme 3.65

A catalytic dehalogenation of aryl chlorides by $RuHCl(H_2)_2(PCy_3)_2$ under $NaOH/H_2O$/s-BuOH/80 °C conditions has been previously reported.[297] To confirm the existence of dehalogenation under $RuH_2(CO)(PPh_3)_3/Et_3SiH$ conditions, a number of halogenated benzamides and one *O*-carbamate were examined. The results, displayed in Table 3.34, show that de-Cl, de-Br and de-I occur in high yields (entries 1-5). Furthermore, in two control experiments using 4-Cl-N,N-diethylbenzamide and 3-Br-N,N-diethylbenzamide, the lack of reactivity under Et_3SiH/refluxing toluene (recovery of starting materials) clearly demonstrates the definite Ru-catalyzed nature of the dehalogenation reaction.

Table 3.34 Ru-Catalyzed Hydrodehalogenation Using Et_3SiH



Entry	Substrate	Product	Yield (%)[a]
1	 **3.215**	 **3.20**	92
2	 **3.216**	**3.20**	83
3	 **3.217**	**3.20**	89
4	 **3.218**	**3.20**	88
5	 **3.219**	 **3.219b**	87

[a] Yields of isolated and purified products

This result can explain the previous failure of amide-directed C-H, C-N or C-O activation/cross coupling reactions with halogenated substrates (see Tables 3.3, 3.11, 3.18, 3.22). The more favorable C-halogen bond insertion by Ru presumably prevents the C-H, C-N and C-O activations, so the C-H, C-N and C-O activation/coupling reactions cannot happen.

3.4 Conclusions

The simple $RuH_2(CO)(PPh_3)_3$/toluene catalytic system provides rich new chemistry based on tertiary amide-directed activation. This thesis has described a number of new reactions based on this conceptual framework inspired by the discoveries of Murai, Chatani, and Kakiuchi. The new chemistry first involves the highly efficient and regioselective Ru-catalyzed amide-directed C-H, C-N, C-O activation/C-C bond forming reactions. Of these, the amide-directed C-H activation/C-C bond cross coupling proceeds well on furan amides only, but the corresponding C-N and C-O reactions are broadly applicable to benzamides and naphthamides due to its inertness of benzamides and naphthamides to the C-H activation process. Thus, the major component of this work (see especially Tables 3.10, 3.17, 3.18, 3.21, 3.22) has established a chemoselective C-N and C-O activation/cross coupling reactions which significantly differ from the corresponding Kakiuchi ketone-directed reactions which are always accompanied by C-H activation processes when *ortho* C-H bonds are available.

These amide-directed C-H, C-N, C-O activation/cross coupling reactions complement and may, in the future, supercede the DoM-Suzuki cross coupling strategies especially since they present catalytic, base-free reaction, non-cryogenic temperature conditions.

In addition, this work has demonstrated the first catalytic hydrodemethoxylation reaction via a Ru-catalyzed amide-directed C-O activation/reduction process which establishes a new

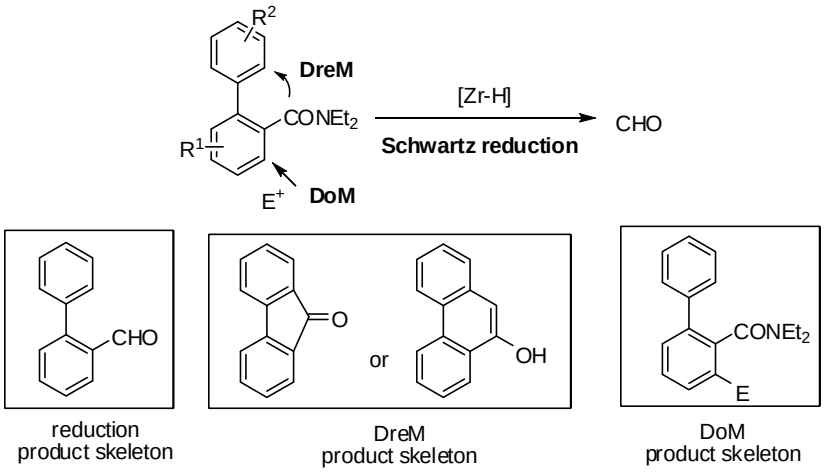
method for an aryl OMe ether group reductive cleavage. This process allows synthetic planning which involves utility of the *ortho*-OMe group for electrophilic bromination *meta* to the amide for subsequent Suzuki coupling and then its excision for potential further DoM chemistry.

In what we believe is the second most major contribution, this work has demonstrated the first catalytic ester-directed C-O activation/C-C bond forming reaction. Although low benzoate C-O ester-directed reactivity was observed, highly efficient corresponding reactions were demonstrated for the 2-MeO-1-naphthate ester. This reaction constitutes an additional complement to the DoM–Suzuki cross coupling combination but with ester rather than common amide DMG involvement, which proceeds without cryogenic conditions and strong alkyllithium or LDA bases. It may be called a catalytic DoM surrogate. Although work described in this thesis has also established a practical amide to aldehyde conversion using the Schwartz reagent (Chapter 2), this reaction provides the convenience of ester manipulation for other chemistry. Of specific general value is the fact that this method establishes the most efficient and practical cross coupling route to prepare 2-substituted-1-naphthoic acid derivatives from easily available or commercial naphthalene substrates. Complementary DoM chemistry with the ester DMG using mixed metal and turbo Grignard reagents are mentioned in this context.[273,274]

The new general Suzuki-type coupling reaction for C-N and C-O bonds, perhaps named the Chatani-Kakiuchi reaction, established by this work has the advantages of bypassing the requirement for halogenations or borylation by DoM (dependent on the substrate), convenience, perhaps economy, and, to highlight a highly abused term, provision of an alternative *green* methodology.

3.5 Utility of Products

Subsequent to the various Ru-catalyzed amide-directed C-H, C-N, C-O activation/arylation reactions, a rich chemistry of obtained 2-amide biaryls may be projected in Scheme 3.66: i) the amide to aldehyde reduction using the Schwartz reagent for the preparation of useful building blocks which has been developed as an efficient and powerful method in this thesis (Chapter 2, Table 2.9, **2.51-2.53**); ii) the link to D*re*M (directed *remote* metalation) to make fused complex aromatic systems, e.g. fluorenones and phenanthrols; iii) a large number of links to further DoM functionalization.



Scheme 3.66

3.6 Future Work and Outlook

In this thesis, work described has shown the achievement of a series of highly efficient Ru-catalyzed amide-directed C-H, C-N, C-O activation/coupling reactions and ester-directed C-O activation/couplings as well as amide-directed hydrodemethoxylation. Especially the amide and ester-directed C-O activation/arylation exhibit the potential to become powerful and practical methods in organic synthesis due to their high efficiency and the ease of availability of starting

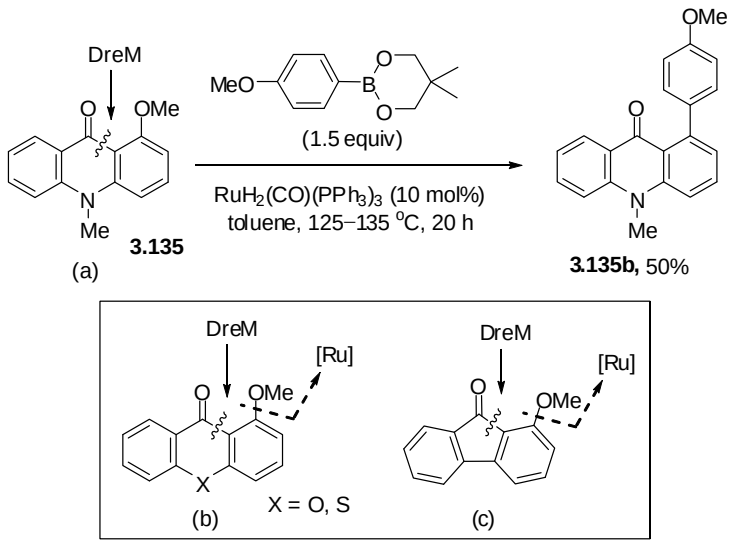
materials. Aside from the results of ketone[272,268,259] and amide directing groups, other groups such as 2-pyridyl, imine and oxazoline may be successful for the Ru-catalyzed C-H, C-N, C-O activation/cross coupling reactions and therefore should be tested.

As demonstrated in this thesis (Scheme 3.30), the isopropyl ester exhibits stronger directing ability than the corresponding methyl ester for Ru-catalyzed C-H activation/cross coupling[262] and the methyl ester has low directing activity for C-O activation of the benzene system (Table 3.25, entry 1). We therefore propose that isopropyl or *t*-butyl benzoate esters may improve the reactivity of C-O activation/cross coupling with good regioselectivity.

In a preliminary study (**3.196 → 3.196b**, Table 3.25), we have discovered an ester-directed C-N activation/arylation in good yield with high selectivity in which no C-H activition/coupling was observed. This reaction should be further investigated in terms of reaction scope and limitations.

The Ru-catalyzed amide-directed hydrodemethoxylation (Section 3.3.5) requires further study to confirm its position as a powerful methodology in synthetic chemistry.

The interesting highly selective ketone-directed C-O activation/cross coupling reaction (Scheme 3.67 (a)) has presented the possibility of D*re*M–Ru-catalyzed C-O activation/cross coupling connection. This result should serve the basis for expansion of the chemistry of some related ketone targets (Scheme 3.67 (b) and (c)). Alcides da Silva, my colleague, has initiated work on C-O activation/arylation on the fluorenone system (Scheme 3.67 (c)) and a number of expected but highly interesting results of C-O activation/arylation have been obtained.[298] This result further confirms that C-O activation is favoured over C-H activation for the fluorenone system. Therefore, new synthetic sequences connecting D*re*M and Ru-catalyzed C-O activation/coupling reactions may be established.



Scheme 3.67

3.7 Experimental Section

General Methods

Melting points were obtained on a Fisher Scientific Melting Point Apparatus and are uncorrected. IR spectra were recorded on a BOMEM FT-IR or Varian 1000 FT-IR spectrometers. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance-400 or 500 MHz spectrometers. The chemical shifts of ^{1}H and ^{13}C NMR signals are quoted relative to internal $CHCl_3$ (δ = 7.26) and $CDCl_3$ (δ =77.0) or tetramethylsilane (δ = 0.0). ^{1}H NMR data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet, etc.), coupling constant (Hz) and relative intensity. ^{13}C NMR data are reported as follows: chemical shift in ppm (δ). The GC-MS analyses were performed on an Agilent 6890 GC coupled with an agilent 5973 inert MS under EI conditions. High resolution mass spectra were

obtained on a GCT Mass Spectrometer (Waters, Micromass) and a QSTAR XL hybrid mass Spectrometer (Applied Biosystems/MDS Sciex).

All Ru-catalyzed experiments were carried out under nitrogen in dried and sealed vials. All Pd-catalyzed Suzuki cross coupling reactions were carried out under a nitrogen atmosphere in sealed vials (not dried). The temperatures shown in catalytic reaction conditions are recorded from oil bath. Amide and ester substrates were obtained from Snieckus group inventory or prepared from commercially available starting materials. All reactions involving alkyllithiums were carried out under an argon atmosphere in oven-dried glassware, using syringe-septum cap techniques. Alkyllithiums were purchased from Sigma-Aldrich Chemicals Co. and titrated biweekly against N-benzylbenzamide.[149] Anhydrous toluene and THF were obtained by treatment under the Pure-Solv SPS-4-4 solvent purification system (Innovative Technology, Inc.) and toluene was degassed before use. $RuH_2(CO)(PPh_3)_3$ and $Pd(PPh_3)_4$ were obtained from Strem Chemicals, Inc., USA. All purchased chemicals were used without further purification. Flash column chromatography was carried out using Silicycle Silia-P silica gel (particle size: 40-60 μm, 60A).

General Procedures

A. Preparation of Organoboronates

A THF solution of an organoboronic acid and 2,2-dimethylpropane-1,3-diol (neopentyl glycol) (1.03-1.20 equiv) was refluxed for 40 min under a Dean Stark apparatus, the reaction mixture was cooled and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes or CH_2Cl_2/hexanes) to yield the product.

B. Amide- , Ketone- and Ester-directed C-H, C-N and C-O Activation/C-C Bond Formation

A mixture of the substrate, the organoboronate (1.05-1.50 equiv) and $RuH_2(CO)(PPh_3)_3$ (4 mol%) in toluene was heated at 125-135 ^oC (oil bath temperature) in a sealed vial for 1 to 44 h. The reaction progress was monitored by GC-MS analysis. The reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes or EtOAc/CH_2Cl_2/hexanes) to yield the product.

C. Amide-directed C-O Activation/Reduction (Hydrodemethoxylation)

A mixture of the amide substrate, Et_3SiH or DIBAL-H (1.1-1.5 equiv) and $RuH_2(CO)(PPh_3)_3$ (4 mol%) in toluene was heated at 125-135 ^oC (oil bath temperature) in a sealed vial for 20 h. The reaction progress was monitored by GC-MS analysis. The reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes or EtOAc/CH_2Cl_2/hexanes) to yield the product.

D. Amide-directed C-H Activation/C-B Bond Formation

A mixture of an amide, B_2Pin_2 (1.05-1.20 equiv) and $RuH_2(CO)(PPh_3)_3$ (4 mol%) in toluene was heated at 125-135 ^oC (oil bath temperature) in a sealed vial for 20 h. The reaction progress was monitored by GC-MS analysis. The reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

E. Bromination of Amides

To a mixture of an amide and NH_4OAc (0.1 equiv) in MeCN at rt was added NBS (1.05 equiv) quickly. The reaction was stirred at rt for 2 min to 4 h and monitored by TLC analysis until the completion. After removal of the solvent, water and EtOAc were added to the residue, the layers were separated and the water layer was extracted with EtOAc. The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

F. Suzuki Cross Coupling Procedure

A mixture of a bromide substrate, a boronic acid (1.5 equiv), a degassed 2 M aqueous solution of Na_2CO_3 (3 equiv) and $Pd(PPh_3)_4$ (2 mol%) in toluene was heated at 120-130 ^oC (oil bath temperature) in a sealed vial for 15 h. The reaction progress was monitored by GC-MS analysis. The reaction mixture was cooled to rt and extracted with EtOAc. Then, the combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Finally, the residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes) to yield the product.

G. Aryl C-halo Dehalogenations via Ru Catalysis

A mixture of a halogen substrate, Et_3SiH (1.5 equiv) and $RuH_2(CO)(PPh_3)_3$ (10 mol%) in toluene was heated at 125-135 ^oC (oil bath temperature) in a sealed vial for 20 h. The reaction progress was monitored by GC-MS analysis. The reaction mixture was cooled to rt and concentrated *in vacuo*. The residue was subjected to flash SiO_2 column chromatography (eluent: EtOAc/hexanes or EtOAc/CH_2Cl_2/hexanes) to yield the product.

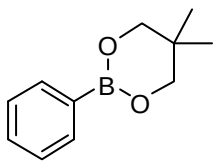
Experimental Procedures and Data

Preparation of Organoboronates

3.35a-3.55a, 3.83a, 3.85a-3.88a, 3.107a, 3.206a

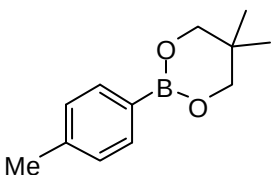
Following General Procedure A, all organoboronates were prepared as described below except 5,5-dimethyl-2-(pyridin-3-yl)-1,3,2-dioxaborinane which was purchased from Sigma-Aldrich Chemicals Co.

5,5-Dimethyl-2-phenyl-1,3,2-dioxaborinane (**3.35a**, Table 3.3, entry 1)



According to General Procedure A and using the following materials: phenylboronic acid (6.22 g, 50 mmol), neopentyl glycol (6.31 g, 60 mmol) and THF (60 mL), the compound **3.35a** (9.51 g, 99% yield) was obtained as a colorless solid. mp 62-63 ^{o}C (hexanes) (lit[299] mp 61-63 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.82 (d, *J* = 6.7 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 3.78 (s, 4H), 1.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 133.79 (2C), 130.63, 127.54 (2C), 72.29 (2C), 31.86, 21.89 (2C). The physical and spectral data were consistent with those previously reported.[299]

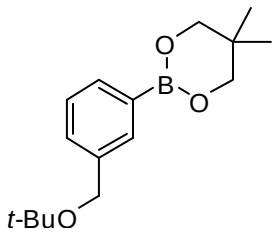
5,5-Dimethyl-2-(4-methylphenyl)-1,3,2-dioxaborinane (**3.36a**, Table 3.3, entry 2)



According to General Procedure A and using the following materials: 4-methylphenylboronic acid (0.69 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.36a** (0.90 g, 89% yield) was obtained as a colorless solid. mp 91-93 ^{o}C (hexanes) (lit[300] 92-95 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.71 (d, *J* = 7.7 Hz, 2H), 7.19 (d, *J* = 7.6 Hz, 2H), 3.77 (s, 4H), 2.37 (s, 3H), 1.03

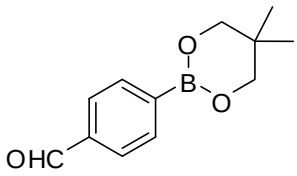
(s, 6H);[301] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 140.64, 133.86 (2C), 128.37 (2C), 72.24 (2C), 31.86, 21.89 (2C), 21.63. The physical and spectral data were consistent with those reported.[300,301]

2-(3-(*t*-Butoxymethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.37a**, Table 3.3, entry 3)



According to General Procedure A and using the following materials: 3-(*t*-butoxymethyl)phenylboronic acid (425 mg, 2.0 mmol), neopentyl glycol (253 mg, 2.4 mmol) and THF (15 mL), the title compound **3.37a** (536 mg, 97% yield) was obtained as a colorless solid. mp 74-75 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2970, 1478, 1431, 1415, 1377, 1362, 1342, 1320, 1250, 1221, 1195, 1129, 1065, 707 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (s, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 4.45 (s, 2H), 3.77 (s, 4H), 1.30 (s, 9H), 1.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 138.79, 132.95, 132.70, 130.06, 127.60, 73.29, 72.25 (2C), 64.27, 31.84, 27.70 (3C), 21.88 (2C). MS EI *m/z* (rel. int.) 276 (M^+, 6), 220 (18), 219 (48), 203 (100), 202 (19), 117 (18), 91 (14), 57 (17), 56 (19); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{25}BO_3$, 276.1897, found 276.1906.

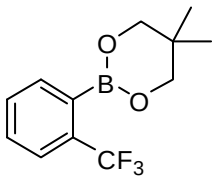
4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)benzaldehyde (**3.38a**, Table 3.3, entry 4)



According to General Procedure A and using the following materials: 4-formylphenylboronic acid (0.77 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.38a** (1.00 g, 92% yield) was obtained as a colorless solid. mp 67-69 °C (EtOAc/hexanes) (lit[302] mp 68-68.5°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 10.04 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.1 Hz, 2H), 3.79 (s, 4H), 1.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 192.78, 137.73, 134.28 (2C),

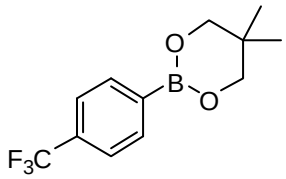
128.61 (2C), 72.38 (2C), 31.86, 21.83 (2C). The physical and spectral data were consistent with those previously reported.[302]

5,5-Dimethyl-2-(2-(trifluoromethyl)phenyl)-1,3,2-dioxaborinane (**3.39a**, Table 3.3, entry 5)



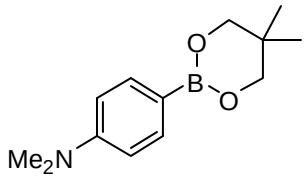
According to General Procedure A and using the following materials: 2-(trifluoromethyl)phenylboronic acid (0.58 g, 3.0 mmol), neopentyl glycol (0.38 g, 3.6 mmol) and THF (25 mL), the title compound **3.39a** (0.71 g, 92% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.69 (d, J = 6.9 Hz, 1H), 7.65 (d, J = 7.1 Hz, 1H), 7.55-7.37 (m, 2H), 3.80 (s, 4H), 1.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 133.87, 133.10 (q, $^{2}J_{C\text{-}F}$ = 31.0 Hz), 130.67, 129.23, 125.26 (q, $^{3}J_{C\text{-}F}$ = 4.9 Hz), 124.61 (q, $^{1}J_{C\text{-}F}$ = 273.2 Hz), 72.62 (2C), 31.76, 21.84 (2C). The physical and spectral data were consistent with those previously reported.[303]

5,5-Dimethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborinane (**3.40a**, Table 3.3, entry 6)



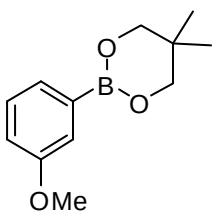
According to General Procedure A and using the following materials: 4-(trifluoromethyl)phenylboronic acid (0.98 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.40a** (1.21 g, 94% yield) was obtained as a colorless solid. mp 108-110 ^{o}C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, J = 7.7 Hz, 2H), 7.60 (d, J = 7.8 Hz, 2H), 3.79 (s, 4H), 1.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 134.09 (2C), 132.25 (q, $^{2}J_{C\text{-}F}$ = 31.7 Hz), 124.30 (q, $^{1}J_{C\text{-}F}$ = 272.2 Hz), 124.14 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz, 2C), 72.37 (2C), 31.88, 21.82 (2C). The physical and spectral data were consistent with those previously reported.[304]

4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)-N,N-dimethylaniline (**3.41a**, Table 3.3, entry 7)



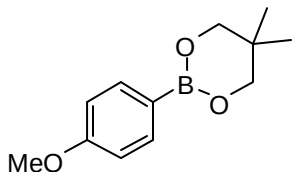
According to General Procedure A and using the following materials: 4-(dimethylamino)phenylboronic acid (495 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (25 mL), the title compound **3.41a** (383 mg, 55% yield) was obtained as a pale solid. mp 156-158 ^{o}C (EtOAc/hexanes) (lit[303] mp 155 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.70 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 8.7 Hz, 2H), 3.76 (s, 4H), 2.99 (s, 6H), 1.02 (s, 6H);[301] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 152.21, 135.10 (2C), 111.26 (2C), 72.17 (2C), 40.14 (2C), 31.87, 21.91 (2C). The physical and spectral data were consistent with those previously reported.[303,301]

2-(3-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.42a**, Table 3.3, entry 8)



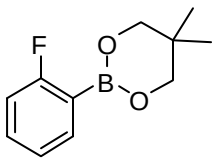
According to General Procedure A and using the following materials: 3-methoxyphenylboronic acid (0.78 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.42a** (1.08 g, 98% yield) was obtained as a colorless solid. mp 68-69 ^{o}C (EtOAc/hexanes) (lit[305] mp 68-71 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.41 (d, *J* = 7.1 Hz, 1H), 7.35 (d, *J* = 2.1 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 6.99 (dd, *J* = 7.8, 2.1 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 4H), 1.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 159.01, 128.72, 126.23, 117.91, 117.21, 72.29 (2C), 55.13, 31.85, 21.88 (2C). The physical and spectral data were consistent with those previously reported.[305]

2-(4-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.43a**, Table 3.3, entry 9)



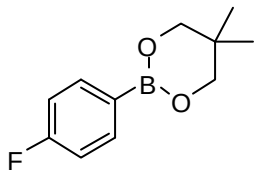
According to General Procedure A and using the following materials: 4-methoxyphenylboronic acid (1.57 g, 10 mmol), neopentyl glycol (1.26 g, 12 mmol) and THF (50 mL), the title compound **3.43a** (2.20 g, 99% yield) was obtained as colorless solid. mp 55-56 ^{o}C (EtOAc/hexanes) (lit[306] mp 59-60 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 3.83 (s, 3H), 3.76 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 161.69, 135.46, 113.09, 72.19, 54.98, 31.83, 21.87. The physical and spectral data were consistent with those previously reported.[306]

2-(2-Fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.44a**, Table 3.3, entry 10)



According to General Procedure A and using the following materials: 2-fluorophenylboronic acid (428 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (20 mL), the title compound **3.44a** (590 mg, 95% yield) was obtained as a colorless solid. mp 39-40 ^{o}C (hexanes) (lit[148] mp 40 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75-7.70 (m, 1H), 7.43-7.34 (m, 1H), 7.12 (t, J = 7.3 Hz, 1H), 7.01 (t, J = 9.0 Hz, 1H), 3.80 (s, 4H), 1.04 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.09 (d, $^{1}J_{C\text{-}F}$ = 249.7 Hz), 136.12 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz), 132.46 (d, $^{3}J_{C\text{-}F}$ = 8.8 Hz), 123.42 (d, $^{4}J_{C\text{-}F}$ = 3.1 Hz), 115.28 (d, $^{2}J_{C\text{-}F}$ = 24.6 Hz), 72.41 (2C), 31.78, 21.82 (2C). The physical and spectral data were consistent with those previously reported.[148]

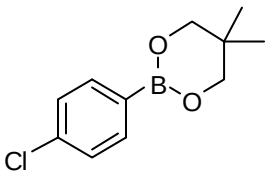
2-(4-Fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.45a**, Table 3.3, entry 11)



According to General Procedure A and using the following materials: 4-fluorophenylboronic acid (0.98 g, 7.0 mmol), neopentyl glycol (0.76 g,

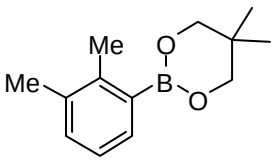
7.2 mmol) and THF (50 mL), the title compound **3.45a** (1.43 g, 99% yield) was obtained as a colorless solid. mp 65-66 °C (EtOAc/hexanes) (lit[307] mp 64-67 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.79 (dd, J = 8.2, 6.4 Hz, 2H), 7.03 (t, J = 8.9 Hz, 2H), 3.76 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 164.81 (d, $^{1}J_{C\text{-}F}$ = 249.0 Hz), 135.96 (d, $^{3}J_{C\text{-}F}$ = 8.0 Hz, 2C), 114.56 (d, $^{2}J_{C\text{-}F}$ = 20.0 Hz, 2C), 72.28 (2C), 31.86, 21.86 (2C). The physical and spectral data were consistent with those previously reported.[307]

2-(4-Chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.46a**, Table 3.3, entry 12)



According to General Procedure A and using the following materials: 4-chlorophenylboronic acid (0.81 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.46a** (1.12 g, 99% yield) was obtained as a colorless solid. mp 91-92 °C (EtOAc/hexanes) (lit[300] mp 95-96 °C); IR (KBr) ν_{max} 2959, 1592, 1481, 1423, 1376, 1345, 1322, 1296, 1251, 1134, 1086, 1016, 826, 638 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.73 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 3.76 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 136.84, 135.23 (2C), 127.78 (2C), 72.29 (2C), 31.85, 21.86 (2C). MS EI *m/z* (rel. int.) 224 (M^+, 100), 181 (21), 139 (18), 56 (83); HRMS *m/z* (EI, M^+) calcd for $C_{11}H_{14}BClO_2$, 224.0775, found 224.0772.

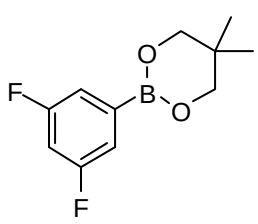
2-(2,3-Dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.47a**, Table 3.3, entry 13)



According to General Procedure A and using the following materials: 2,3-dimethylphenylboronic acid (0.77 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.47a** (0.99 g, 91% yield) was obtained as a colorless solid. mp 46-47 °C (hexanes). IR (KBr) ν_{max} 2962, 2933,

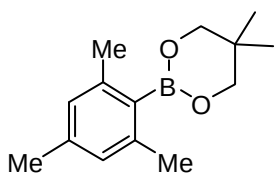
2889, 1477, 1426, 1409, 1377, 1333, 1305, 1276, 1244, 1241, 1219, 1174, 1149, 1089, 728, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.56 (d, *J* = 7.2 Hz, 1H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 3.80 (s, 4H), 2.46 (s, 3H), 2.29 (s, 3H), 1.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 141.75, 136.35, 132.27, 131.47, 124.75, 72.31 (2C), 31.58, 21.86 (2C), 20.49, 18.41. MS EI *m/z* (rel. int.) 218 (M^+, 100), 161 (29), 132 (28), 117 (22), 56 (27); HRMS *m/z* (EI, M^+) calcd for $C_{13}H_{19}BO_2$, 218.1478, found 218.1477.

2-(3,5-Difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.48a**, Table 3.3, entry 14)



According to General Procedure A and using the following materials: 3,5-difluorophenylboronic acid (484 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (15 mL), the title compound **3.48a** (678 mg, 99% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 2965, 2939, 2894, 2876, 1588, 1481, 1433, 1379, 1352, 1333, 1256, 1118, 1002, 976, 873, 701, 691 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.34-7.19 (m, 2H), 6.83 (tt, *J* = 9.0, 2.4 Hz, 1H), 3.76 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 162.75 (dd, $^{1,3}J_{C\text{-}F}$ = 248.7, 11.0 Hz, 2C), 115.86 (dd, $^{2,4}J_{C\text{-}F}$ = 16.9, 5.5 Hz, 2C), 105.82 (t, $^{2}J_{C\text{-}F}$ = 25.2 Hz), 72.37 (2C), 31.87, 21.80 (2C). MS EI *m/z* (rel. int.) 226 (M^+, 51), 183 (14), 56 (100); HRMS *m/z* (EI, M^+) calcd for $C_{11}H_{13}BF_2O_2$, 226.0977, found 226.0977.

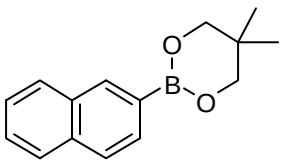
2-Mesityl-5,5-dimethyl-1,3,2-dioxaborinane (**3.49a**, Table 3.3, entry 15)



According to General Procedure A and using the following materials: mesitylboronic acid (502 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (20 mL), the title compound **3.49a** (522 mg, 75%

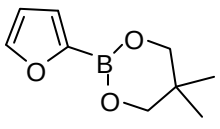
yield) was obtained as a colorless solid. mp 46-47 °C (hexanes) (lit[308] mp 47 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 6.79 (s, 2H), 3.79 (s, 4H), 2.38 (s, 6H), 2.26 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 140.65 (2C), 137.99, 127.27 (2C), 72.19 (2C), 31.58, 22.21 (2C), 22.12 (2C), 21.14. The physical and spectral data were consistent with those previously reported.[308]

2-(Naphthalen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.50a**, Table 3.3, entry 16)



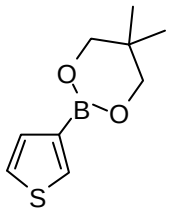
According to General Procedure A and using the following materials: naphthalene-2-ylboronic acid (0.86 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (30 mL), the title compound **3.50a** (1.11 g, 93% yield) was obtained as a colorless solid. mp 103-104 °C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.38 (s, 1H), 7.96-7.76 (m, 4H), 7.57-7.40 (m, 2H), 3.85 (s, 4H), 1.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 135.01, 134.83, 132.87, 129.90, 128.63, 127.62, 126.75, 126.58, 125.55, 72.38 (2C), 31.92, 21.91 (2C). The physical and spectral data were consistent with those previously reported.[304]

2-(Furan-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.51a**, Table 3.3, entry 17)



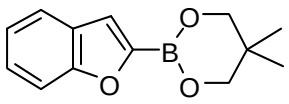
According to General Procedure A and using the following materials: furan-2-ylboronic acid (0.58 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.51a** (0.84 g, 93% yield) was obtained as a colorless solid. mp 87-88 °C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.61 (d, J = 2.0 Hz, 1H), 6.97 (d, J = 3.3 Hz, 1H), 6.41 (dd, J = 3.2, 1.6 Hz, 1H), 3.75 (s, 4H), 1.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 146.56, 121.41, 110.13, 72.23 (2C), 32.05, 21.82 (2C). The physical and spectral data were consistent with those previously reported.[272]

2-(Thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.52a**, Table 3.3, entry 18)



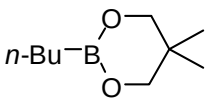
According to General Procedure A and using the following materials: thiophen-3-ylboronic acid (0.94 g, 7.0 mmol), neopentyl glycol (0.88 g, 8.4 mmol) and THF (35 mL), the title compound **3.52a** (1.26 g, 92% yield) was obtained as a pale solid. mp 96-98 ^{o}C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.84 (dd, *J* = 2.6, 0.8 Hz, 1H), 7.38 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.31 (dd, *J* = 4.8, 2.7 Hz, 1H), 3.75 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 134.83, 131.62, 124.95, 72.19 (2C), 31.90, 21.89 (2C). The physical and spectral data were consistent with those previously reported.[304]

2-(Benzofuran-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.53a**, Table 3.3, entry 19)



According to General Procedure A and using the following materials: benzofuran-2-ylboronic acid (501 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (20 mL), the title compound **3.53a** (622 mg, 90% yield) was obtained as a light yellow solid. mp 115-117 ^{o}C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.62 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.37-7.28 (m, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 3.82 (s, 4H), 1.05 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 157.26, 127.71, 125.46, 122.52, 121.68, 117.79, 111.79, 72.43 (2C), 32.10, 21.84 (2C). The physical and spectral data were consistent with those previously reported.[304]

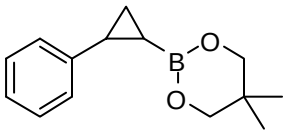
2-*n*-Butyl-5,5-dimethyl-1,3,2-dioxaborinane (**3.54a**, Table 3.3, entry 20)



According to General Procedure A and using the following materials: *n*-butylboronic acid (316 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol)

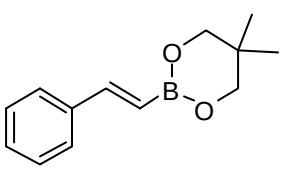
and THF (25 mL), the title compound **3.54a** (474 mg, 93% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 3.57 (s, 4H), 1.41-1.20 (m, 4H), 0.94 (s, 6H), 0.86 (t, *J* = 7.1 Hz, 3H), 0.69 (t, *J* = 7.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 71.94 (2C), 31.58, 26.36, 25.49, 21.81 (2C), 13.94. The physical and spectral data were consistent with those previously reported.[299]

2-(2-Phenylcyclopropyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.55a**, Table 3.3, entry 21)



According to General Procedure A and using the following materials: *trans*-2-phenylcyclopropylboronic acid (512 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (15 mL), the title compound **3.55a** (488 mg, 71% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 2962, 2932, 2886, 1477, 1418, 1397, 1341, 1286, 1256, 1232, 1197, 1089, 765, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.22 (t, *J* = 7.4 Hz, 2H), 7.16-6.99 (m, 3H), 3.58 (s, 4H), 2.03 (dt, *J* = 8.0, 5.3 Hz, 1H), 1.10 (ddd, *J* = 8.0, 6.9, 3.5 Hz, 1H), 1.02-0.87 (m, 7H), 0.18 (ddd, *J* = 9.7, 6.8, 5.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 143.95, 128.15 (2C), 125.57 (2C), 125.27, 72.07 (2C), 31.77, 21.78 (2C), 21.56, 14.74. MS EI *m/z* (rel. int.) 230 (M^+, 100), 229 (17), 157 (18), 144 (17), 143 (12), 130 (13), 129 (14), 117 (23), 116 (72), 115 (23); HRMS *m/z* (EI, M^+) calcd for $C_{14}H_{19}BO_2$, 230.1478, found 230.1479.

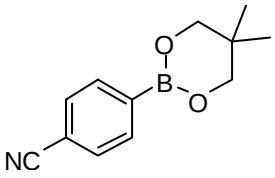
(*E*)-5,5-Dimethyl-2-styryl-1,3,2-dioxaborinane (**3.83a**, Table 3.10, entry 15)



According to General Procedure A and using the following materials: (*E*)-styrylboronic acid (0.91 g, 6.0 mmol), neopentyl glycol (0.70 g, 6.6 mmol) and THF (15 mL), the title compound **3.83a** (1.27 g, 98% yield)

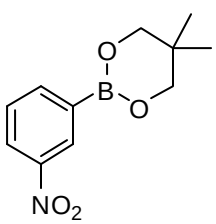
was obtained as a colorless solid. mp 46-47 °C (hexanes) (lit[299] mp 41-44°C); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.48 (d, *J* = 7.2 Hz, 2H), 7.40-7.16 (m, 4H), 6.11 (d, *J* = 18.3 Hz, 1H), 3.69 (s, 4H), 1.00 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 147.09, 137.77, 128.47 (3C), 126.96 (2C), 72.16 (2C), 31.83, 21.84 (2C). The physical and spectral data were consistent with those previously reported.[299]

4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)benzonitrile (**3.85a**, Table 3.11, entry 2)



According to General Procedure A and using the following materials: 4-cyanophenylboronic acid (249 mg, 2.0 mmol), neopentyl glycol (253 mg, 2.4 mmol) and THF (20 mL), the title compound **3.85a** (346 mg, 81% yield) was obtained as a colorless solid. mp 116-118 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2962, 2228, 1487, 1477, 1425, 1341, 1319, 1293, 1254, 1129, 842, 813, 757, 739, 639 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.87 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 3.78 (s, 4H), 1.02 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 134.19 (2C), 130.98 (2C), 119.09, 113.88, 72.39 (2C), 31.87, 21.81 (2C); MS EI *m/z* (rel. int.) 215 (M^+, 40), 172 (27), 171 (19), 144 (20), 130 (22), 129 (29), 116 (22), 102 (15), 76 (24), 56 (100), 55 (22); HRMS *m/z* (EI, M^+) calcd for $C_{12}H_{14}BNO_2$, 215.1118, found 215.1127.

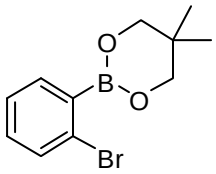
2-(3-Nitrophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.86a**, Table 3.11, entry 5)



According to General Procedure A and using the following materials: 3-nitrophenylboronic acid (0.85 g, 5 mmol), neopentyl glycol (0.63 g, 6 mmol) and THF (25 mL), the title compound **3.86a** (1.16 g, 99% yield) was obtained as a light yellow solid. mp 72-73 °C (EtOAc/hexanes) (lit[306] mp 77-78 °C);

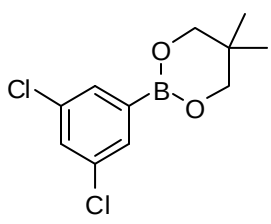
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.62 (d, *J* = 1.6 Hz, 1H), 8.24 (ddd, *J* = 8.2, 2.4, 1.2 Hz, 1H), 8.08 (d, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 1H), 3.79 (s, 4H), 1.03 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 147.84, 139.79, 128.55, 128.47, 125.27, 72.41 (2C), 31.91, 21.80 (2C). The physical and spectral data were consistent with those previously reported.[306]

2-(2-Bromophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.87a**, Table 3.11, entry 7)



According to General Procedure A and using the following materials: 2-bromophenylboronic acid (603 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (25 mL), the title compound **3.87a** (751 mg, 93% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.56 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.52 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.26 (td, *J* = 7.3, 1.1 Hz, 1H), 7.20 (td, *J* = 7.7, 1.9 Hz, 1H), 3.80 (s, 4H), 1.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 135.35, 132.59, 131.05, 127.02, 126.24, 72.45 (2C), 31.70, 21.86 (2C). The physical and spectral data were consistent with those previously reported.[309]

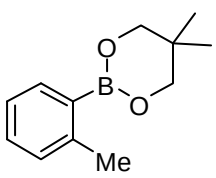
2-(3,5-Dichlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.88a**, Table 3.11, entry 8)



According to General Procedure A and using the following materials: 3,5-dichlorophenylboronic acid (573 mg, 3.0 mmol), neopentyl glycol (379 mg, 3.6 mmol) and THF (25 mL), the title compound **3.88a** (753 mg, 97% yield) was obtained as a colorless solid. mp 65-66 ^{o}C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.64 (d, *J* = 2.0 Hz, 2H), 7.39 (t, *J* = 2.0 Hz, 1H), 3.76 (s, 4H), 1.01 (s, 6H);[310] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 134.50 (2C), 131.91

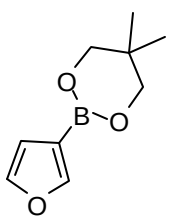
(2C), 130.44, 72.40 (2C), 31.89, 21.79 (2C). The physical and spectral data were consistent with those previously reported.[310]

5,5-Dimethyl-2-(2-methylphenyl)-1,3,2-dioxaborinane (**3.107a**, Table 3.17)



To a solution of 2-methylphenyl bromide (864 mg, 5.0 mmol) in THF (8 mL) at -78 ^{o}C was added *n*-BuLi (2.7 mL, 5.3 mmol, 1.94 M in hexanes) slowly. After 5 min, B(O*i*-Pr)$_3$ (1.3 mL, 5.5 mmol) was added at -78 ^{o}C and the cooling bath was removed to allow the mixture to warm to 0 ^{o}C. Neopentyl glycol (632 mg, 6.0 mmol) in THF (8 mL) was added at 0 ^{o}C. The mixture was allowed to warm to rt and stirred at rt for 30 min before treatment with saturated aq. NH_4Cl (5 mL) and water (10 mL). The resultant mixture was extracted with EtOAc (3 x 20 mL) and the combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. After purification of the residue via flash SiO_2 column chromatography (eluent: EtOAc/hexanes), the compound **3.107a** (884 mg, 87% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.75 (d, *J* = 7.1 Hz, 1H), 7.30 (t, *J* = 6.8 Hz, 1H), 7.22-7.11 (m, 2H), 3.79 (s, 4H), 2.54 (s, 3H), 1.05 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 143.90, 134.78, 129.99, 129.91, 124.63, 72.23 (2C), 31.61, 22.36, 21.86 (2C). The physical and spectral data were consistent with those previously reported.[304]

2-(Furan-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (**3.206a**, Table 3.26, entry 12 sm)

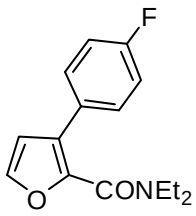


According to General Procedure A and using the following materials: furan-3-ylboronic acid (0.80 g, 7.0 mmol), neopentyl glycol (0.88 g, 8.4 mmol) and THF (35 mL), the title compound **3.206a** (0.91 g, 75% yield) was obtained as a

colorless solid. mp 75-76 °C (EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.76-7.64 (m, 1H), 7.49-7.38 (m, 1H), 6.59-6.48 (m, 1H), 3.71 (s, 4H), 1.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 150.16, 142.69, 112.78, 72.10 (2C), 31.93, 21.88 (2C). The physical and spectral data were consistent with those reported.[272]

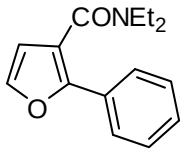
Amide-Directed C-H Activation/C-C Bond Formation Reactions. Synthesis of Compounds 3.23b-3.24b, 3.26b-3.27b, 3.30b, 3.33b, 3.33c, 3.36b-3.38b, 3.40b-3.48b, 3.50b-3.53b, 3.55b

N,N-Diethyl-3-(4-fluorophenyl)furan-2-carboxamide (**3.23b**, Table 3.2, entry 2)



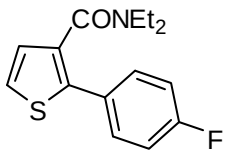
According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-2-carboxamide (50 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (28 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.23b** (17 mg, 22% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2977, 1634, 1516, 1433, 1223, 1158, 856, 839 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.54-7.46 (m, 2H), 7.44 (d, J = 1.8 Hz, 1H), 7.10-7.01 (m, 2H), 6.60 (d, J = 1.8 Hz, 1H), 3.59-3.40 (m, 2H), 3.25-3.12 (m, 2H), 1.23-1.16 (m, 3H), 1.11-0.98 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 162.28 (d, $^{1}J_{C-F}$ = 247.1 Hz), 161.79, 142.80, 142.26, 129.49 (d, $^{3}J_{C-F}$ = 8.0 Hz, 2C), 128.04 (d, $^{4}J_{C-F}$ = 3.4 Hz), 125.47, 115.48 (d, $^{2}J_{C-F}$ = 21.5 Hz, 2C), 111.43, 43.01, 39.83, 14.25, 12.54. MS EI *m/z* (rel. int.) 261 (M^+, 27), 190 (30), 189 (100), 162 (14), 133 (17); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{16}FNO_2$, 261.1165, found 261.1166.

N,N-Diethyl-2-phenylfuran-3-carboxamide (**3.24b**, Table 3.2, entry 3)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (86 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.5 mL), the title compound **3.24b** (66 mg, 90% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 2935, 1631, 1491, 1430, 1295, 1216, 1061, 775, 758, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.66 (d, *J* = 7.3 Hz, 2H), 7.46 (d, *J* = 1.8 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.32-7.25 (m, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 3.58 (q, *J* = 7.1 Hz, 2H), 3.20 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.21, 149.26, 141.62, 130.00, 128.59 (2C), 128.03, 125.06 (2C), 116.90, 111.59, 43.03, 39.17, 14.05, 12.53. MS EI *m/z* (rel. int.) 243 (M^+, 25), 214 (10), 171 (100), 115 (10); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{17}NO_2$, 243.1259, found 243.1261.

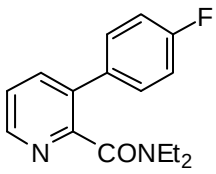
N,N-Diethyl-2-(4-fluorophenyl)thiophene-3-carboxamide (**3.26b**, Table 3.2, entry 6)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylthiophene-3-carboxamide (55 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.26b** (17 mg, 21% yield) was obtained as a light yellow solid. mp 62-63 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2975, 2935, 1626, 1505, 1435, 1286, 1234, 1099, 839 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.56-7.44 (m, 2H), 7.29 (d, *J* = 5.2 Hz, 1H), 7.10-6.98 (m, 3H), 3.48 (q, *J* = 7.1 Hz, 2H), 2.99 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.36, 162.63 (d, $^1J_{C\text{-}F}$ = 248.5 Hz), 138.84, 133.53, 129.70 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, 2C), 129.44 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 127.68, 125.18, 115.76 (d, $^2J_{C\text{-}F}$ = 21.7 Hz, 2C), 42.75, 39.01, 13.78, 12.3. MS

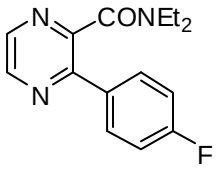
EI *m/z* (rel. int.) 277 (M^+, 24), 244 (12), 205 (100), 133 (25); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{16}FNOS$, 277.0937, found 277.0934.

N,N-Diethyl-3-(4-fluorophenyl)picolinamide (**3.27b**, Table 3.2, entry 7)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylpicolinamide (54 mg, 0.03 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (28 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.27b** (8 mg, 10% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2977, 1636, 1513, 1223, 1103, 798 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.62 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.52-7.44 (m, 2H), 7.38 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.15-7.01 (m, 2H), 3.42 (q, *J* = 7.1 Hz, 2H), 2.89 (q, *J* = 7.1 Hz, 2H), 1.01 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.07, 162.84 (d, $^1J_{C\text{-}F}$ = 248.3 Hz), 153.73, 148.34, 137.24, 133.28, 133.21 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 130.63 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, 2C), 123.61, 115.57 (d, $^2J_{C\text{-}F}$ = 21.5 Hz, 2C), 42.46, 38.72, 13.50, 12.21. MS EI *m/z* (rel. int.) 272 (M^+, 7), 173 (13), 172 (23), 72 (100); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{17}FN_2O$, 272.1325, found 272.1319.

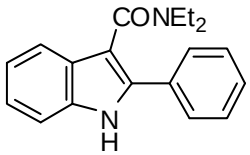
N,N-Diethyl-3-(4-fluorophenyl)pyrazine-2-carboxamide (**3.30b**, Table 3.2, entry 10)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylpyrazine-2-carboxamide (54 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (28 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.30b** (13 mg, 16% yield) was obtained as a yellow oil. IR (KBr) ν_{max} 2978, 2936, 1638, 1513, 1382, 1227,

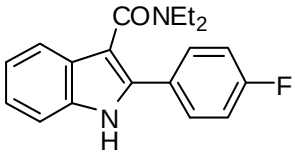
1161, 1111, 848 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.67 (d, *J* = 2.4 Hz, 1H), 8.54 (d, *J* = 2.4 Hz, 1H), 7.88-7.77 (m, 2H), 7.14 (t, *J* = 8.6 Hz, 2H), 3.50 (q, *J* = 7.1 Hz, 2H), 2.92 (q, *J* = 7.1 Hz, 2H), 1.14 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.08, 163.82 (d, $^1J_{C\text{-}F}$ = 250.4 Hz), 149.82, 148.89, 144.09, 142.06, 132.54 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 130.82 (d, $^3J_{C\text{-}F}$ = 8.5 Hz, 2C), 115.71 (d, $^2J_{C\text{-}F}$ = 21.7 Hz, 2C), 42.66, 39.15, 13.42, 12.14. MS EI *m/z* (rel. int.) 273 (M^+, 6), 173 (18), 72 (100); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{16}FN_3O$, 273.1277, found 273.1277.

N,N-Diethyl-2-phenyl-1*H*-indole-3-carboxamide (**3.33b**, Table 3.2, entry 13)



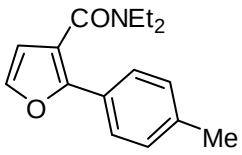
According to General Procedure B and using the following materials refluxed in 90 h: N,N-diethyl-1*H*-indole-3-carboxamide (65 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (86 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.5 mL), the title compound **3.33b** (34 mg, 39% yield) was obtained as a light yellow solid. mp 224-226 °C (EtOAc/hexanes); IR (KBr) ν_{max} 3143, 2976, 2930, 1594, 1574, 1543, 1495, 1457, 1420, 1320, 1274, 1235, 1124, 1048, 743, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 9.11 (s, 1H), 7.61-7.49 (m, 3H), 7.30-7.24 (m, 4H), 7.18-7.05 (m, 2H), 3.81-3.43 (m, 2H), 3.24-3.02 (m, 2H), 1.25 (t, *J* = 6.3 Hz, 3H), 0.77 (t, *J* = 6.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.82, 135.79, 134.70, 131.62, 128.75 (2C), 128.08, 127.47, 126.90 (2C), 122.72, 120.55, 119.33, 111.17, 109.74, 43.13, 38.99, 14.03, 12.74. MS EI *m/z* (rel. int.) 292 (M^+, 25), 221 (61), 220 (100); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{20}N_2O$, 292.1576, found 292.1582.

N,N-Diethyl-2-(4-fluorophenyl)-1*H*-indole-3-carboxamide (**3.33c**, Table 3.2, entry 14)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethyl-1*H*-indole-3-carboxamide (65 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (28 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.33c** (42 mg, 45% yield) was obtained as a light yellow solid. mp 192-193 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 3212, 3184, 1601, 1556, 1507, 1476, 1456, 1447, 1284, 1235, 1162, 836, 805, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.05 (s, 1H), 7.52-7.39 (m, 1H), 7.27-7.17 (m, 2H), 7.16-7.02 (m, 3H), 6.63 (t, *J* = 8.7 Hz, 2H), 3.80-3.53 (m, 2H), 3.34-3.08 (m, 2H), 1.31 (t, *J* = 6.6 Hz, 3H), 0.86 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.32, 162.36 (d, $^1J_{C-F}$ = 248.0 Hz), 135.73, 134.52, 128.62 (d, $^3J_{C-F}$ = 8.2 Hz, 2C), 127.64 (d, $^4J_{C-F}$ = 3.1 Hz), 126.95, 122.43, 120.44, 118.89, 115.59 (d, $^2J_{C-F}$ = 21.8 Hz, 2C), 111.52, 108.95, 43.26, 39.13, 14.15, 12.86. MS EI *m/z* (rel. int.) 310 (M^+, 31), 238 (100), 211 (32), 183 (33); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{19}FN_2O$, 310.1481, found 310.1466.

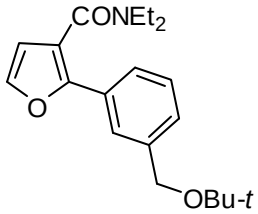
N,N-Diethyl-2-(*p*-tolyl)furan-3-carboxamide (**3.36b**, Table 3.3, entry 2)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 5,5-dimethyl-2-(4-methylphenyl)-1,3,2-dioxaborinane (92 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.36b** (66 mg, 85% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 1934, 1630, 1496, 1429, 1294, 1069, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.54 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 1.8 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.47 (d, *J* = 1.8 Hz, 1H), 3.57 (q, *J* = 7.1 Hz, 2H), 3.19 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101

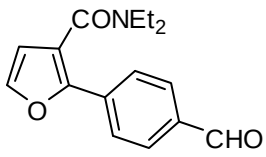
MHz, $CDCl_3$) δ ppm 166.32, 149.49, 141.26, 137.97, 129.28 (2C), 127.29, 125.01 (2C), 116.16, 111.51, 43.00, 39.13, 21.23, 14.06, 12.52. MS EI *m/z* (rel. int.) 257 (M^+, 35), 228 (10), 185 (100); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{19}NO_2$, 257.1416, found 257.1417.

N,N-Diethyl-2-(3-(*t*-butoxymethyl)phenyl)furan-3-carboxamide (**3.37b**, Table 3.3, entry 3)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(3-(*t*-butoxymethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (124 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.37b** (91 mg, 93% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 1633, 1482, 1459, 1431, 1363, 1194, 1064, 794 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.62 (s, 1H), 7.54 (d, *J* = 7.2 Hz, 1H), 7.44 (d, *J* = 1.7 Hz, 1H), 7.37-7.27 (m, 2H), 6.48 (d, *J* = 1.7 Hz, 1H), 4.44 (s, 2H), 3.57 (q, *J* = 7.1 Hz, 2H), 3.18 (q, *J* = 7.1 Hz, 2H), 1.29 (s, 9H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.22, 149.26, 141.56, 140.37, 129.93, 128.63, 127.20, 124.05, 123.91, 116.81, 111.62, 73.49, 63.96, 43.05, 39.17, 27.65 (3C), 14.09, 12.59. MS EI *m/z* (rel. int.) 329 (M^+, 100), 257 (26), 201 (64), 199 (27), 185 (65), 184 (45), 183 (77), 92 (24), 57 (24); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{27}NO_3$, 329.1991, found 329.1988.

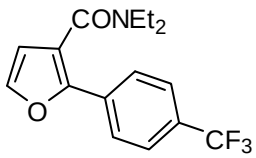
N,N-Diethyl-2-(4-formylphenyl)furan-3-carboxamide (**3.38b**, Table 3.3, entry 4)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (17 mg, 0.10 mmol), 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)benzaldehyde (33 mg, 0.15

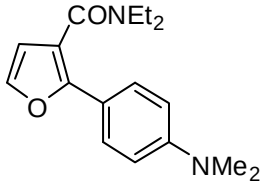
mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.38b** (5 mg, 18% yield) was obtained as a light yellow solid. mp 64-66 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 1699, 1628, 1608, 1493, 1432, 1309, 1294, 1214, 1172, 1070, 832 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 10.00 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.54 (d, *J* = 1.8 Hz, 1H), 6.54 (d, *J* = 1.8 Hz, 1H), 3.61 (q, *J* = 7.1 Hz, 2H), 3.23 (q, *J* = 7.1 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 191.49, 165.67, 147.88, 143.01, 135.32, 135.25, 130.16 (2C), 125.18 (2C), 119.74, 112.03, 43.14, 39.36, 14.19, 12.60. MS EI *m/z* (rel. int.) 271 (M^+, 2), 199 (20), 171 (26), 115 (100), 56 (32); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{17}NO_3$, 271.1208, found 271.1215.

N,N-Diethyl-2-(4-trifluoromethylphenyl)furan-3-carboxamide (**3.40b**, Table 3.3, entry 6)



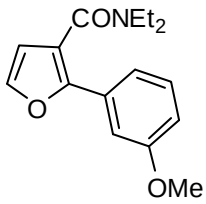
According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 5,5-dimethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborinane (116 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.40b** (76 mg, 82% yield) was obtained as a light yellow solid. mp 45-48 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2977, 2937, 1634, 1621, 1497, 1432, 1326, 1294, 1167, 1125, 1067, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 1.8 Hz, 1H), 6.51 (d, *J* = 1.8 Hz, 1H), 3.58 (q, *J* = 7.1 Hz, 2H), 3.22 (q, *J* = 7.1 Hz, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.69, 147.83, 142.55, 133.13, 129.63 (q, $^2J_{C\text{-}F}$ = 32.6 Hz), 125.63 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, 2C), 125.05 (2C), 123.98 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 118.84, 111.78, 43.11, 39.32, 14.16, 12.59. MS EI *m/z* (rel. int.) 311 (M^+, 22), 282 (15), 239 (100); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{16}F_3NO_2$, 311.1133, found 311.1131.

N,N-Diethyl-2-(4-(dimethylamino)phenyl)furan-3-carboxamide (**3.41b**, Table 3.3, entry 7)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-N,N-dimethylaniline (105 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.41b** (65 mg, 76% yield) was obtained as a light yellow solid. mp 73-74 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1625, 1618, 1528, 1500, 1429, 1362, 1199, 1065, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.53 (d, *J* = 8.9 Hz, 2H), 7.36 (d, *J* = 1.8 Hz, 1H), 6.69 (d, *J* = 8.9 Hz, 2H), 6.44 (d, *J* = 1.8 Hz, 1H), 3.56 (q, *J* = 7.1 Hz, 2H), 3.20 (q, *J* = 7.1 Hz, 2H), 2.97 (s, 6H), 1.25 (t, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.75, 150.39, 150.05, 140.27, 126.31 (2C), 118.45, 113.91, 111.95, 111.48 (2C), 42.98, 40.23 (2C), 39.11, 14.09, 12.61. MS EI *m/z* (rel. int.) 286 (M^+, 80), 214 (100), 158 (23), 106 (18); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{22}N_2O_2$, 286.1681, found 286.1680.

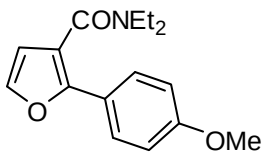
N,N-Diethyl-2-(3-methoxyphenyl)furan-3-carboxamide (**3.42b**, Table 3.3, entry 8)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(3-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (73 mg, 0.33 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.42b** (74 mg, 91% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 2936, 1630, 1578, 1492, 1460, 1433, 1293, 1271, 1220, 1043, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.45 (d, *J* = 1.8 Hz, 1H), 7.32-7.17 (m, 3H), 6.89-6.78 (m, 1H), 6.49 (d, *J* = 1.8 Hz, 1H), 3.82 (s, 3H), 3.57 (q, *J* = 7.1 Hz, 2H), 3.21 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.1

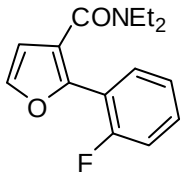
Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.18, 159.78, 149.09, 141.60, 131.22, 129.66, 117.60, 117.13, 114.21, 111.61, 110.18, 55.23, 43.08, 39.25, 14.08, 12.63. MS EI *m/z* (rel. int.) 273 (M^+, 38), 202 (58), 201 (100), 174 (14); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{19}NO_3$, 273.1365, found 273.1362.

N,N-Diethyl-2-(4-methoxyphenyl)furan-3-carboxamide (**3.43b**, Table 3.3, entry 9)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (73 mg, 0.33 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.43b** (77 mg, 94% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2935, 1629, 1599, 1520, 1497, 1460, 1431, 1296, 1254, 1180, 1068, 1033, 835 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.59 (d, *J* = 8.9 Hz, 2H), 7.39 (d, *J* = 1.8 Hz, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 6.45 (d, *J* = 1.8 Hz, 1H), 3.81 (s, 3H), 3.56 (q, *J* = 7.0 Hz, 2H), 3.19 (q, *J* = 7.0 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.41, 159.47, 149.53, 140.95, 126.64 (2C), 122.98, 115.38, 114.03 (2C), 111.48, 55.22, 43.02, 39.16, 14.08, 12.58. MS EI *m/z* (rel. int.) 273 (M^+, 38), 201 (100); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{19}NO_3$, 273.1365, found 273.1360.

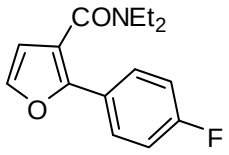
N,N-Diethyl-2-(2-fluorophenyl)furan-3-carboxamide (**3.44b**, Table 3.3, entry 10)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(2-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11

mg, 4 mol%) and toluene (0.4 mL), the title compound **3.44b** (32 mg, 41% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2975, 2936, 1632, 1598, 1494, 1457, 1430, 1294, 1220, 1064, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.65 (td, *J* = 7.6, 1.6 Hz, 1H), 7.51 (d, *J* = 1.8 Hz, 1H), 7.34-7.27 (m, 1H), 7.17 (td, *J* = 7.6, 1.0 Hz, 1H), 7.13-7.04 (m, 1H), 6.53 (d, *J* = 1.8 Hz, 1H), 3.51 (q, *J* = 7.1 Hz, 2H), 3.26 (q, *J* = 7.1 Hz, 2H), 1.20 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.63, 158.82 (d, $^1J_{C-F}$ = 251.5 Hz), 145.48 (d, $^4J_{C-F}$ = 1.9 Hz), 142.23, 130.04 (d, $^3J_{C-F}$ = 8.3 Hz), 128.94 (d, $^4J_{C-F}$ = 2.8 Hz), 124.23 (d, $^3J_{C-F}$ = 3.5 Hz), 119.81 (d, $^3J_{C-F}$ = 2.1 Hz), 118.18 (d, $^2J_{C-F}$ = 13.5 Hz), 116.10 (d, $^2J_{C-F}$ = 21.8 Hz), 111.47, 42.84, 38.91, 13.86, 12.42. MS EI *m/z* (rel. int.) 261 (M^+, 30), 232 (15), 190 (15), 189 (100); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{16}FNO_2$, 261.1165, found 261.1167.

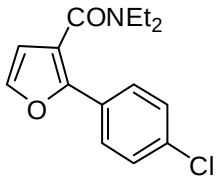
N,N-Diethyl-2-(4-fluorophenyl)furan-3-carboxamide (**3.45b**, Table 3.3, entry 11)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.45b** (72 mg, 92% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2975, 2936, 1630, 1601, 1518, 1496, 1460, 1431, 1295, 1234, 1159, 1068, 839,755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.70-7.58 (m, 2H), 7.43 (d, *J* = 1.8 Hz, 1H), 7.11-6.98 (m, 2H), 6.47 (d, *J* = 1.8 Hz, 1H), 3.56 (q, *J* = 7.0 Hz, 2H), 3.20 (q, *J* = 7.0 Hz, 2H), 1.24 (t, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.07, 162.45 (d, $^1J_{C-F}$ = 248.3 Hz), 148.63, 141.56, 127.04 (d, $^3J_{C-F}$ = 8.1 Hz, 2C), 126.36 (d, $^4J_{C-F}$ = 3.3 Hz), 116.65, 115.68 (d, $^2J_{C-F}$ = 21.8 Hz, 2C), 111.53, 43.06,

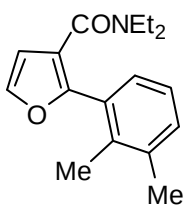
39.23, 14.11, 12.59. MS EI *m/z* (rel. int.) 261 (M^+, 27), 232 (11), 189 (100), 133 (10); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{16}FNO_2$, 261.1165, found 261.1160.

N,N-Diethyl-2-(4-chlorophenyl)furan-3-carboxamide (**3.46b**, Table 3.3, entry 12)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (101 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.46b** (15 mg, 18% yield) was obtained as a light yellow solid (with 63% recovery of N,N-diethylfuran-3-carboxamide). mp 64-66 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2975, 1630, 1489, 1431, 1295, 1094, 1068, 832 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.61 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 1.8 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 2H), 6.49 (d, *J* = 1.8 Hz, 1H), 3.57 (q, *J* = 7.0 Hz, 2H), 3.20 (q, *J* = 7.0 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.97, 148.35, 141.88, 133.89, 128.89 (2C), 128.49, 126.33 (2C), 117.38, 111.66, 43.09, 39.27, 14.17, 12.61. MS EI *m/z* (rel. int.) 277 (M^+, 28), 248 (19), 207 (30), 205 (100), 170 (15), 149 (14); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{16}ClNO_2$, 277.0870, found 277.0869.

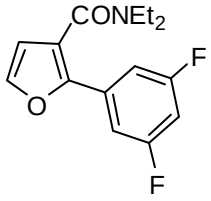
N,N-Diethyl-2-(2,3-dimethylphenyl)furan-3-carboxamide (**3.47b**, Table 3.3, entry 13)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(2,3-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (98 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.47b** (41 mg, 50% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2935, 1631,

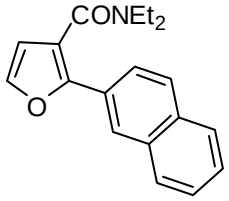
1478, 1458, 1433, 1062, 788 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.48 (d, *J* = 1.8 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.57 (d, *J* = 1.8 Hz, 1H), 3.42 (q, *J* = 7.0 Hz, 2H), 3.10 (q, *J* = 7.0 Hz, 2H), 2.31 (s, 3H), 2.22 (s, 3H), 1.08 (t, *J* = 6.9 Hz, 3H), 0.76 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.72, 151.58, 141.68, 137.40, 135.57, 130.72, 129.87, 127.96, 125.42, 118.74, 111.23, 42.90, 38.91, 20.46, 16.76, 13.61, 12.49. MS EI *m/z* (rel. int.) 271 (M^+, 4), 199 (100), 198 (50), 171 (22), 143 (14), 128 (23), 72 (16); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{21}NO_2$, 271.1572, found 271.1567.

N,N-Diethyl-2-(3,5-difluorophenyl)furan-3-carboxamide (**3.48b**, Table 3.3, entry 14)



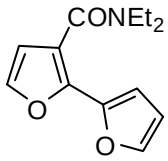
According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(3,5-difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (102 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.48b** (73 mg, 87% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2976, 2937, 1626, 1583, 1506, 1481, 1432, 1321, 1290, 1216, 1121, 1083, 983, 866, 823 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.47 (d, *J* = 1.8 Hz, 1H), 7.24-7.14 (m, 2H), 6.72 (tt, *J* = 8.7, 2.3 Hz, 1H), 6.50 (d, *J* = 1.8 Hz, 1H), 3.59 (q, *J* = 7.1 Hz, 2H), 3.22 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.43, 163.22 (dd, $^{1,3}J_{C\text{-}F}$ = 247.8, 13.0 Hz, 2C), 147.01 (t, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 142.44, 132.63 (t, $^{3}J_{C\text{-}F}$ = 10.6 Hz), 118.89, 111.76, 107.68 (dd, $^{2,4}J_{C\text{-}F}$ = 27.7, 8.0 Hz, 2C), 103.23 (t, $^{2}J_{C\text{-}F}$ = 25.5 Hz), 43.10, 39.35, 14.16, 12.48. MS EI *m/z* (rel. int.) 279 (M^+, 24), 250 (10), 207 (100), 151 (12); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{15}F_2NO_2$, 279.1071, found 279.1064.

N,N-Diethyl-2-(naphthalen-2-yl)furan-3-carboxamide (**3.50b**, Table 3.3, entry 16)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(naphthalen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (79 mg, 0.33 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.50b** (71 mg, 81% yield) was obtained as a pale solid. mp 92-93 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 1627, 1478, 1430, 1294, 832, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.14 (s, 1H), 7.91-7.73 (m, 4H), 7.51 (d, *J* = 1.6 Hz, 1H), 7.50-7.39 (m, 2H), 6.55 (d, *J* = 1.6 Hz, 1H), 3.62 (q, *J* = 7.0 Hz, 2H), 3.21 (q, *J* = 7.0 Hz, 2H), 1.32 (t, *J* = 7.0 Hz, 3H), 0.94 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.26, 149.24, 141.88, 133.27, 132.84, 128.35, 128.27, 127.65, 127.42, 126.46, 126.33, 124.09, 122.86, 117.35, 111.81, 43.09, 39.28, 14.09, 12.62. MS EI *m/z* (rel. int.) 293 (M^+, 35), 222 (64), 221 (100), 165 (28); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{19}NO_2$, 293.1416, found 293.1417.

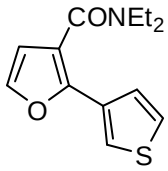
N,N-Diethyl-2-(furan-2-yl)furan-3-carboxamide (**3.51b**, Table 3.3, entry 17)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(furan-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (81 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.51b** (27 mg, 39% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2975, 1629, 1487, 1462, 1430, 1293, 1068, 1008, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.42 (d, *J* = 1.7 Hz, 1H), 7.39 (d, *J* = 1.7 Hz, 1H), 6.64 (d, *J* = 3.4 Hz, 1H), 6.48 (d, *J* = 1.8 Hz, 1H), 6.44 (dd, *J* = 3.3, 1.8 Hz, 1H), 3.64-3.50 (m, 2H), 3.35-3.16 (m, 2H), 1.26 (t, *J* = 6.4 Hz, 3H), 1.01 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

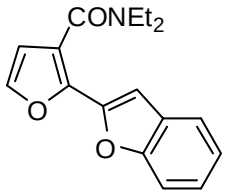
ppm 164.98, 145.07, 142.57, 142.51, 141.54, 116.35, 111.47, 111.11, 107.54, 43.02, 39.17, 14.08, 12.68. MS EI *m/z* (rel. int.) 233 (M^+, 28), 161 (100), 105 (20); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{13}H_{16}NO_3$, 234.1130, found 234.1126.

N,N-Diethyl-2-(thiophen-3-yl)furan-3-carboxamide (**3.52b**, Table 3.3, entry 18)



According to General Procedure B and using the following materials refluxed in 44 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (88 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.52b** (54 mg, 72% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 1627, 1492, 1435, 1291, 1067, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.59 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.38 (d, *J* = 1.8 Hz, 1H), 7.37 (dd, *J* = 5.9, 1.2 Hz, 1H), 7.31 (dd, *J* = 5.1, 3.0 Hz, 1H), 6.45 (d, *J* = 1.8 Hz, 1H), 3.64-3.44 (m, 2H), 3.35-3.17 (m, 2H), 1.26 (t, *J* = 6.9 Hz, 3H), 1.00 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.95, 147.27, 140.83, 131.15, 126.00, 125.11, 121.35, 115.86, 111.01, 43.11, 39.29, 14.20, 12.77. MS EI *m/z* (rel. int.) 249 (M^+, 33), 178 (42), 177 (100), 121 (33); HRMS *m/z* (EI, M^+) calcd for $C_{13}H_{15}NO_2S$, 249.0824, found 249.0814.

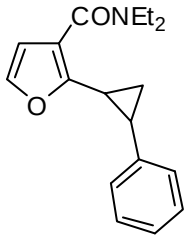
N,N-Diethyl-2-(benzofuran-2-yl)furan-3-carboxamide (**3.53b**, Table 3.3, entry 19)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (50 mg, 0.30 mmol), 2-(benzofuran-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (104 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.53b** (32 mg, 37% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974,

1630, 1493, 1455, 1430, 1254, 1076, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.58 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 1.7 Hz, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.33-7.18 (m, 2H), 7.02 (s, 1H), 6.56 (d, *J* = 1.7 Hz, 1H), 3.70-3.56 (m, 2H), 3.37-3.21 (m, 2H), 1.36 (t, *J* = 6.9 Hz, 3H), 1.03 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 164.71, 154.68, 146.58, 142.75, 141.97, 128.31, 124.81, 123.25, 121.28, 118.81, 111.48, 111.19, 103.41, 43.12, 39.26, 14.12, 12.70. MS EI *m/z* (rel. int.) 283 (M^+, 27), 212 (30), 211 (100), 155 (72), 126 (20), 57 (29), 56 (29); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{17}NO_3$, 283.1208, found 283.1221.

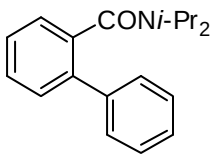
N,N-Diethyl-2-(2-phenylcyclopropyl)furan-3-carboxamide (**3.55b**, Table 3.3, entry 21)



According to General Procedure B and using the following materials refluxed in 24 h: N,N-diethylfuran-3-carboxamide (17 mg, 0.1 mmol), 2-(2-phenylcyclopropyl)-5,5-dimethyl-1,3,2-dioxaborinane (35 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.55b** (7 mg, 23% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2934, 1623, 1496, 1477, 1459, 1433, 1380, 1297, 1215, 1138, 1055, 752, 735, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.27 (t, *J* = 7.4 Hz, 2H), 7.20 (d, *J* = 1.9 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 2H), 6.36 (d, *J* = 1.9 Hz, 1H), 3.55-3.27 (m, 4H), 2.48 (dt, *J* = 8.8, 5.3 Hz, 1H), 2.42 (dt, *J* = 9.0, 5.3 Hz, 1H), 1.61 (ddd, *J* = 8.9, 5.6, 5.0 Hz, 1H), 1.40 (ddd, *J* = 9.0, 6.0, 5.0 Hz, 1H), 1.22-1.04 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 165.74, 154.72, 141.24, 139.49, 128.38 (2C), 125.97 (3C), 116.12, 110.18, 43.05 (br), 39.19 (br), 25.18, 20.25, 16.44, 14.12 (br), 13.05 (br). MS EI *m/z* (rel. int.) 283 (M^+, 6), 192 (44), 153 (64), 152 (60), 128 (37), 115 (48), 104 (100), 103 (32), 91 (71), 78 (55), 77 (66), 56 (45), 51 (49); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1566.

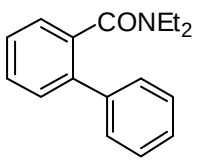
Amide-Directed C-N Activation/C-C Bond Formation. Synthesis of Compounds 3.67b, 3.20b, 3.70b-3.84b, 3.89-3.90, 3.90b

N,N-Diisopropyl-2-phenylbenzamide (**3.67b**, Scheme 3.44)



According to General Procedure B and using the following materials refluxed in 3 h: N,N-diethyl-2-(diisopropylamino)benzamide (50 mg, 0.20 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (40 mg, 0.21 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.67b** (27 mg, 47% yield) was obtained as a light yellow solid. mp 107-109 ^oC (EtOAc/hexanes) (lit[276] 107-108 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.60-7.52 (m, 2H), 7.45-7.27 (m, 7H), 3.43 (sept., *J* = 6.7 Hz, 1H), 3.22 (sept., *J* = 6.8 Hz, 1H), 1.52 (d, *J* = 6.8 Hz, 3H), 1.28 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.33 (d, *J* = 6.6 Hz, 3H);[276] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.24, 139.80, 137.93, 137.67, 129.30 (2C), 129.20, 128.42, 128.23 (2C), 127.53, 127.47, 126.54, 50.47, 45.53, 20.79, 20.70, 19.44, 19.39. The physical and spectral data were consistent with those reported.[276]

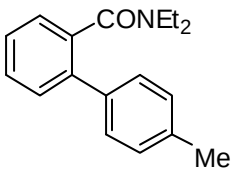
N,N-Diethyl-2-phenylbenzamide (**3.20b**, Table 3.10, entry 1)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (60 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.20b** (75 mg, 98% yield) was obtained as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ ppm 7.50-7.45 (m, 2H), 7.45-7.28 (m, 7H), 3.80-3.68 (m, 1H), 3.05-2.82 (m, 2H), 2.69-2.57 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H), 0.72 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.49, 139.78, 138.33, 136.34,

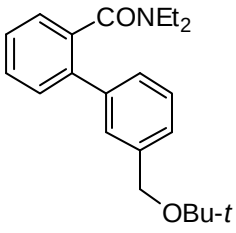
129.36, 128.87, 128.83 (2C), 128.24 (2C), 127.50, 127.48, 126.94, 42.18, 38.26, 13.32, 11.89. The physical and spectral data were consistent with those previously reported.[311]

N,N-Diethyl-2-(4-methylphenyl)benzamide (**3.70b**, Table 3.10, entry 2)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(4-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (64 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.70b** (78 mg, 98% yield) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46-7.31 (m, 6H), 7.17 (d, *J* = 7.7 Hz, 2H), 3.80-3.64 (m, 1H), 3.14-2.84 (m, 2H), 2.76-2.55 (m, 1H), 2.36 (s, 3H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.74 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.63, 138.31, 137.21, 136.89, 136.27, 129.33, 128.92 (2C), 128.82, 128.66 (2C), 127.21, 126.95, 42.21, 38.31, 21.08, 13.34, 11.96. The physical and spectral data were consistent with those previously reported.[312]

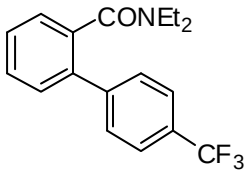
N,N-Diethyl-2-(3-*t*-butoxymethylphenyl)benzamide (**3.71b**, Table 3.10, entry 3)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(3-*t*-butoxymethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.71b** (99 mg, 97% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2933, 1630, 1470, 1459, 1431, 1363, 1290, 1195, 1090, 1071, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46-7.39 (m, 3H), 7.38-7.31 (m, 5H), 4.46 (s, 2H), 3.81-3.65 (m, 1H), 3.07-

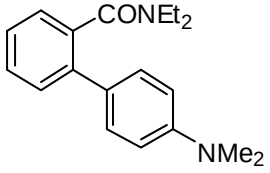
2.90 (m, 2H), 2.74-2.58 (m, 1H), 1.28 (s, 9H), 0.90 (t, J = 7.1 Hz, 3H), 0.74 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.50, 140.00, 139.64, 138.43, 136.29, 129.46, 128.82, 128.24, 127.69, 127.58, 127.39, 126.93, 126.47, 73.41, 63.94, 42.33, 38.38, 27.64 (3C), 13.39, 11.99. MS EI *m/z* (rel. int.) 339 (M^+, 15), 209 (24), 194 (45), 193 (100), 181 (48), 152 (30), 72 (39); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{29}NO_2$, 339.2198, found 339.2205.

N,N-Diethyl-2-((4-trifluoromethyl)phenyl)benzamide (**3.72b**, Table 3.10, entry 4)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-((4-trifluoromethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (81 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.72b** (95 mg, 99% yield) was obtained as a light yellow solid. mp 81-82 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2977, 1628, 1430, 1326, 1290, 1165, 1125, 1109, 1069, 767 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.68-7.57 (m, 4H), 7.51-7.33 (m, 4H), 3.83-3.62 (m, 1H), 3.13-2.83 (m, 2H) 2.77-2.58 (m, 1H), 0.88 (t, J = 7.1 Hz, 3H), 0.78 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.99, 143.39, 136.88, 136.41, 129.70 (q, $^2J_{C\text{-}F}$ = 32.7 Hz), 129.36, 129.20 (2C), 129.08, 128.32, 126.96, 125.17 (q, $^3J_{C\text{-}F}$ = 3.7 Hz, 2C), 124.13 (q, $^1J_{C\text{-}F}$ = 271.9 Hz), 42.29, 38.37, 13.42, 11.85. MS EI *m/z* (rel. int.) 321 (M^+, 31), 320 (52), 249 (100), 201 (33), 152 (18); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{18}F_3NO$, 321.1340, found 321.1334.

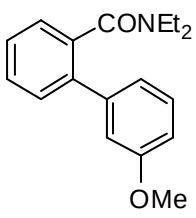
N,N-Diethyl-2-(4-(dimethylamino)phenyl)benzamide (**3.73b**, Table 3.10, entry 5)



According to General Procedure B and using the following materials refluxed in 6 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30

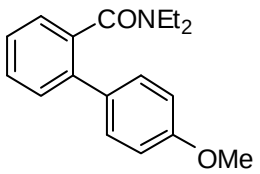
mmol), 2-(4-(dimethylamino)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (74 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.73b** (71 mg, 81% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2933, 2875, 2803, 1625, 1613, 1527, 1484, 1443, 1429, 1356, 1288, 1223, 783 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.42-7.26 (m, 6H), 6.72 (d, *J* = 8.8 Hz, 2H), 3.81-3.64 (m, 1H), 3.15-3.02 (m, 1H), 3.00-2.87 (m, 7H), 2.72-2.59 (m, 1H), 0.98 (t, *J* = 7.1 Hz, 3H), 0.73 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.05, 149.98, 138.45, 135.97, 129.49 (2C), 128.99, 128.74, 127.92, 127.05, 126.38, 112.21 (2C), 42.18, 40.46 (2C), 38.38, 13.33, 12.18. MS EI *m/z* (rel. int.) 296 (M^+, 100), 295 (24), 224 (88); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{24}N_2O$, 296.1889, found 296.1885.

N,N-Diethyl-2-(3-methoxyphenyl)benzamide (**3.74b**, Table 3.10, entry 6)



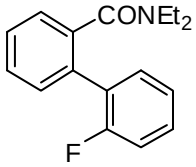
According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(3-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (69 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.74b** (85 mg, 99% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2972, 2935, 1627, 1602, 1581, 1464, 1429, 1318, 1291, 1221, 1094, 1053, 783, 761, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.46-7.32 (m, 4H), 7.27 (t, *J* = 8.1 Hz, 1H), 7.10-6.99 (m, 2H), 6.87 (dd, *J* = 8.2, 2.4 Hz, 1H), 3.81 (s, 3H), 3.78-3.68 (m, 1H), 3.09-2.89 (m, 2H), 2.74-2.59 (m, 1H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.45, 159.35, 141.16, 138.23, 136.35, 129.26, 129.24, 128.82, 127.56, 126.91, 121.21, 114.11, 113.44, 55.22, 42.24, 38.26, 13.38, 11.92. MS EI *m/z* (rel. int.) 283 (M^+, 46), 282 (45), 211 (100), 168 (18), 72 (17); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1574.

N,N-Diethyl-2-(4-methoxyphenyl)benzamide (**3.75b**, Table 3.10, entry 7)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (69 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.75b** (85 mg, 99% yield) was obtained as light yellow solid. mp 46-47 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2935, 1626, 1518, 1485, 1458, 1428, 1289, 1244, 1180, 1035, 836, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.46-7.29 (m, 6H), 6.90 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 3.78-3.66 (m, 1H), 3.10-2.86 (m, 2H), 2.71-2.59 (m, 1H), 0.93 (t, *J* = 7.1 Hz, 3H), 0.73 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.68, 159.16, 137.90, 136.20, 132.31, 129.94 (2C), 129.23, 128.82, 127.05, 126.94, 113.66 (2C), 55.25, 42.19, 38.33, 13.36, 12.08; MS EI *m/z* (rel. int.) 283 (M^+, 36), 282 (30), 211 (100), 168 (19); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1572.

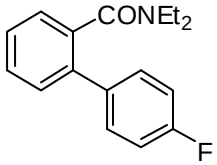
N,N-Diethyl-2-(2-fluorophenyl)benzamide (**3.76b**, Table 3.10, entry 8)



According to General Procedure B and using the following materials refluxed in 2 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(2-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.76b** (73 mg, 90% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 2935, 1632, 1482, 1456, 1426, 1290, 1221, 1090, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.49-7.35 (m, 5H), 7.34-7.27 (m, 1H), 7.18-7.04 (m, 2H), 4.01-3.53 (m, 1H), 3.30-2.56 (m, 3H), 0.86 (t, *J* = 7.1 Hz, 3H), 0.80 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.85, 159.44 (d, $^1J_{C\text{-}F}$ = 246.0 Hz), 137.19,

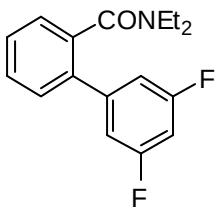
132.31, 132.09 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 130.63 (d, $^4J_{C\text{-}F}$ = 2.1 Hz), 129.43 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 128.34, 128.02, 127.09 (d, $^2J_{C\text{-}F}$ = 15.0 Hz), 126.58, 123.85 (d, $^3J_{C\text{-}F}$ = 3.6 Hz), 115.34 (d, $^2J_{C\text{-}F}$ = 22.3 Hz), 42.14, 38.04, 13.50, 11.80. MS EI *m/z* (rel. int.) 271 (M^+, 42), 270 (58), 199 (100), 170 (25); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{18}FNO$, 271.1372, found 271.1368.

N,N-Diethyl-2-(4-fluorophenyl)benzamide (**3.77b**, Table 3.10, entry 9)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.77b** (80 mg, 98% yield) was obtained as a light yellow solid. mp 57-59 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2975, 2935, 1627, 1515, 1485, 1470, 1458, 1428, 1290, 1223, 1161, 1097, 840, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.50-7.30 (m, 6H), 7.05 (t, *J* = 8.6 Hz, 2H), 3.83-3.63 (m, 1H), 3.12-2.84 (m, 2H), 2.75-2.57 (m, 1H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.31, 162.43 (d, $^1J_{C\text{-}F}$ = 247.0 Hz), 137.19, 136.32, 135.83 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 130.49 (d, $^3J_{C\text{-}F}$ = 8.0 Hz, 2C), 129.33, 128.91, 127.61, 126.87, 115.14 (d, $^2J_{C\text{-}F}$ = 21.4 Hz, 2C), 42.22, 38.32, 13.39, 12.00. MS EI *m/z* (rel. int.) 271 (M^+, 24), 270 (50), 199 (100), 171 (18), 170 (28); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{18}FNO$, 271.1372, found 271.1382.

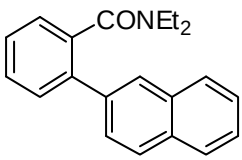
N,N-Diethyl-2-(3,5-difluorophenyl)benzamide (**3.78b**, Table 3.10, entry 10)



According to General Procedure B and using the following materials refluxed in 2 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(3,5-difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (71 mg,

0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.78b** (85 mg, 98% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2976, 2935, 1625, 1592, 1433, 1414, 1338, 1292, 1120, 1093, 988, 864, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.49-7.32 (m, 4H), 7.07-6.96 (m, 2H), 6.78 (tt, *J* = 8.9, 2.3 Hz, 1H), 3.98-3.66 (m, 1H), 3.16-2.86 (m, 2H), 2.84-2.65 (m, 1H), 0.97 (t, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.78, 162.70 (dd, $^{1,3}J_{C\text{-}F}$ = 248.7, 12.9 Hz, 2C), 142.93 (t, $^3J_{C\text{-}F}$ = 9.6 Hz), 136.29, 135.99 (t, $^4J_{C\text{-}F}$ = 2.3 Hz), 129.14, 129.11, 128.50, 127.00, 111.82 (dd, $^{2,4}J_{C\text{-}F}$ = 25.8 Hz, 7.17 Hz, 2C), 102.85 (t, $^2J_{C\text{-}F}$ = 25.2 Hz), 42.39, 38.44, 13.49, 11.82. MS EI *m/z* (rel. int.) 289 (M^+, 27), 288 (50), 217 (100), 189 (18), 188 (28); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{17}F_2NO$, 289.1278, found 289.1278.

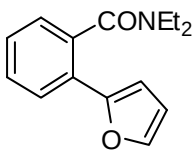
N,N-Diethyl-2-(naphthalen-2-yl)benzamide (**3.79b**, Table 3.10, entry 11)



According to General Procedure B and using the following materials refluxed in 2 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(naphthalen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (76 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.79b** (88 mg, 96% yield) was obtained as a light yellow solid. mp 52-53 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2933, 1625, 1474, 1458, 1424, 1290, 1089, 774, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.96 (s, 1H), 7.90-7.79 (m, 3H), 7.63 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.55-7.45 (m, 4H), 7.44-7.39 (m, 2H), 3.82-3.58 (m, 1H), 3.09-2.84 (m, 2H), 2.71-2.52 (m, 1H), 0.80 (t, *J* = 7.1 Hz, 3H), 0.71 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.57, 138.19, 137.21, 136.52, 133.15, 132.54, 129.70, 128.98, 128.21, 127.92, 127.74, 127.60, 127.54, 127.16, 126.96, 126.19, 126.07, 42.36, 38.47, 13.41, 12.00. MS EI *m/z* (rel. int.) 303 (M^+, 30), 232 (48), 231

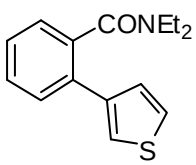
(100), 203 (21), 202 (54), 72 (21); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{21}NO$, 303.1623, found 303.1624.

N,N-Diethyl-2-(furan-2-yl)benzamide (**3.80b**, Table 3.10, entry 12)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(furan-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (65 mg, 0.36 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.80b** (60 mg, 82% yield) was obtained as a yellow oil. IR (KBr) ν_{max} 2974, 2935, 1631, 1460, 1428, 1381, 1292, 1272, 1222, 1094, 1011, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.71 (dd, *J* = 7.9, 0.6 Hz, 1H), 7.44 (dd, *J* = 1.7, 0.6 Hz, 1H), 7.38 (td, *J* = 7.9, 1.6 Hz, 1H), 7.29 (td, *J* = 7.4, 1.2 Hz, 1H), 7.24 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.64 (dd, *J* = 3.4, 0.6 Hz, 1H), 6.42 (dd, *J* = 3.4, 1.8 Hz, 1H), 3.75 (q, *J* = 7.0 Hz, 1H), 3.38 (q, *J* = 7.0 Hz, 1H), 3.12-2.91 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.61, 151.61, 142.25, 133.85, 128.62, 127.47, 127.09, 126.81, 126.09, 111.64, 108.16, 42.59, 38.72, 13.34, 12.28. MS EI *m/z* (rel. int.) 243 (M^+, 78), 171 (100), 143 (28), 115 (45); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{17}NO_2$, 243.1259, found 243.1253.

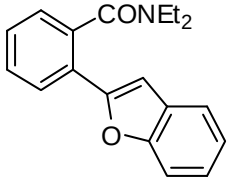
N,N-Diethyl-2-(thiophen-3-yl)benzamide (**3.81b**, Table 3.10, entry 13)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (71 mg, 0.36 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.81b** (58 mg, 75%

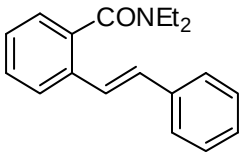
yield) was obtained as a yellow oil. IR (KBr) ν_{max} 2973, 2933, 1625, 1459, 1428, 1291, 1089, 860, 801, 774, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.51-7.29 (m, 6H), 7.27 (dd, *J* = 5.0, 1.3 Hz, 1H), 3.81-3.66 (m, 1H), 3.22-3.08 (m, 1H), 3.02-2.87 (m, 1H), 2.82-2.68 (m, 1H), 1.04 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.68, 140.11, 136.08, 132.84, 128.86, 128.75, 128.19, 127.39, 126.80, 125.44, 123.17, 42.34, 38.48, 13.29, 12.18. MS EI *m/z* (rel. int.) 259 (M^+, 29), 258 (15), 188 (36), 187 (100), 160 (19), 115 (48); HRMS *m/z* (EI, M^+) calcd for $C_{15}H_{17}NOS$, 259.1031, found 259.1035.

N,N-Diethyl-2-(benzofuran-2-yl)benzamide (**3.82b**, Table 3.10, entry 14)



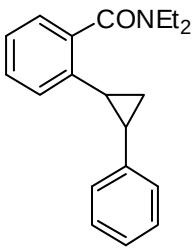
According to General Procedure B and using the following materials refluxed in 2 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), 2-(benzofuran-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (73 mg, 0.32 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.82b** (59 mg, 67% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 1632, 1491, 1472, 1455, 1427, 1290, 1258, 1088, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.92 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.51-7.43 (m, 2H), 7.40 (td, *J* = 7.5, 1.2 Hz, 1H), 7.35-7.18 (m, 3H), 7.05 (s, 1H), 3.88-3.73 (m, 1H), 3.46-3.32 (m, 1H), 3.15-2.92 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.44, 154.69, 153.51, 135.02, 129.01, 128.77, 128.58, 127.18, 126.98, 126.85, 124.52, 122.89, 121.19, 111.10, 104.76, 42.74, 38.87, 13.49, 12.41. MS EI *m/z* (rel. int.) 293 (M^+, 66), 222 (47), 221 (100), 193 (17), 165 (36); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{19}NO_2$, 293.1416, found 293.1416.

(*E*)-N,N-Diethyl-2-styrylbenzamide (**3.83b**, Table 3.10, entry 15)



According to General Procedure B and using the following materials refluxed in 3 h: N,N-diethyl-2-(dimethylamino)benzamide (44 mg, 0.20 mmol), (*E*)-2-styryl-5,5-dimethyl-1,3,2-dioxaborinane (45 mg, 0.21 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.83b** (31 mg, 56% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 1628, 1598, 1495, 1485, 1469, 1458, 1449, 1428, 1381, 1285, 1075, 963, 762, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.70 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.3 Hz, 2H), 7.40-7.18 (m, 6H), 7.13 (d, *J* = 16.7 Hz, 1H), 7.09 (d, *J* = 17.7 Hz, 1H), 4.05-3.68 (m, 1H), 3.56-3.22 (m, 1H), 3.10 (q, *J* = 7.0 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.35, 137.01, 136.35, 133.63, 130.82, 128.75, 128.65 (2C), 127.84, 127.53, 126.56 (2C), 126.18, 125.25, 125.02, 42.82, 38.89, 13.87, 12.96. MS EI *m/z* (rel. int.) 279 (M^+, 22), 208 (27), 207 (49), 179 (40), 178 (100), 177 (21), 176 (25), 152 (21), 77 (20), 57 (31), 56 (40); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{21}NO$, 279.1623, found 279.1639.

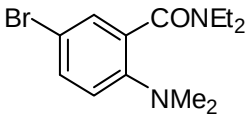
N,N-Diethyl-2-(2-phenylcyclopropyl)benzamide (**3.84b**, Table 3.10, entry 16)



According to General Procedure B and using the following materials refluxed in 1 h: N,N-diethyl-2-(dimethylamino)benzamide (44 mg, 0.2 mmol), 2-(2-phenylcyclopropyl)-5,5-dimethyl-1,3,2-dioxaborinane (69 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.84b** (52 mg, 88% yield) was obtained as a yellow solid. mp 52-53 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2933, 1631, 1602, 1494, 1472, 1459, 1428, 1291, 1072, 755, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.39-6.87 (m, 9H), 3.90-3.64 (m, 1H), 3.40-2.68 (m, 3H), 2.37-1.29

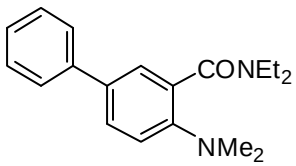
(m, 4H), 1.14-0.78 (m, 6H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.62, 142.11, 141.94, 137.89, 137.71, 128.75, 128.31, 128.24, 128.11, 126.16, 126.00, 125.75, 125.73, 125.54, 125.43, 125.18, 124.94, 123.04, 42.53, 42.45, 38.43, 28.83, 26.08, 25.15, 24.31, 17.25, 17.12, 13.90, 13.64, 12.45, 12.28 (atropisomers involved). MS EI *m/z* (rel. int.) 293 (M^+, 2), 189 (100), 160 (29), 132 (13), 91 (14); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{23}NO$, 293.1780, found 293.1780.

5-Bromo-2-(dimethylamino)-N,N-diethylbenzamide (**3.89**, Scheme 3.46)



According to General Procedure E and using the following materials stirred in 2 min: N,N-diethyl-2-(dimethylamino)benzamide (221 mg, 1.00 mmol), NH_4OAc (8 mg, 0.10 mmol), NBS (189 mg, 1.05 mmol) and MeCN (5 mL), the title compound **3.89b** (268 mg, 90% yield) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.33 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.26 (d, *J* = 2.3 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 1H), 3.83-3.62 (m, 1H), 3.43-3.26 (m, 1H), 3.25-2.98 (m, 2H), 2.77 (s, 6H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.67, 148.27, 132.18, 131.08, 118.62, 112.74, 43.31 (2C), 42.75, 38.89, 13.69, 12.50 (1C not observed). The physical and spectral data were consistent with those previously reported.[313]

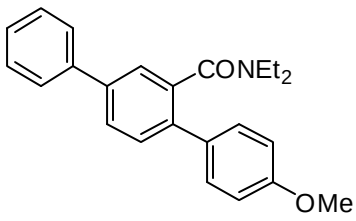
2-(Dimethylamino)-5-phenyl-N,N-diethylbenzamide (**3.90**, Scheme 3.46)



According to General Procedure F and using the following materials: 5-bromo-2-(dimethylamino)-N,N-diethylbenzamide (180 mg, 0.6 mmol), phenylboronic acid (110 mg, 0.9 mmol), a degassed 2 M aqueous solution of Na_2CO_3 (0.9 mL, 1.8 mmol) and $Pd(PPh_3)_4$ (14 mg, 2 mol%) and toluene (1

mL), the title compound **3.90** (157 mg, 89% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2936, 1625, 1515, 1486, 1458, 1432, 1378, 1320, 1263, 1137, 1081, 763, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.56 (d, *J* = 7.3 Hz, 2H), 7.51 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.43 (d, *J* = 2.0 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 3.90-3.71 (m, 1H), 3.42-3.31 (m, 1H), 3.30-3.19 (m, 1H), 3.18-3.06 (m, 1H), 2.85 (s, 6H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.25, 148.50, 140.22, 133.06, 129.52, 128.65 (2C), 127.89, 127.05, 126.64, 126.46 (2C), 117.15, 43.38 (2C), 42.75, 38.81, 13.75, 12.55. MS EI *m/z* (rel. int.) 296 (M^+, 38), 224 (100), 223 (50), 196 (25), 181 (47), 180 (36), 167 (38), 153 (42), 152 (75), 72 (41), 58 (48), 57 (38), 56 (66); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{19}H_{25}N_2O$, 297.1966, found 297.1979.

N,N-Diethyl-2-(4-methoxyphenyl)-5-phenylbenzamide (**3.90b**, Scheme 3.46)

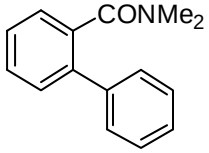


According to General Procedure B and using the following materials refluxed in 3 h: 2-(dimethylamino)-5-phenyl-N,N-diethylbenzamide (30 mg, 0.100 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (23 mg, 0.105 mmol), $RuH_2(CO)(PPh_3)_3$ (4 mg, 4 mol%) and toluene (0.5 mL), the title compound **3.90b** (35 mg, 98% yield) was obtained as a pale solid. mp 139-141 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2934, 1626, 1522, 1473, 1459, 1433, 1295, 1272, 1256, 1244, 1180, 1036, 829, 767, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.70-7.61 (m, 3H), 7.59 (d, *J* = 1.3 Hz, 1H), 7.51-7.40 (m, 5H), 7.36 (t, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 2H), 3.83 (s, 3H), 3.79-3.67 (m, 1H), 3.17-2.91 (m, 2H), 2.78-2.62 (m, 1H), 0.98 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.66, 159.26, 139.99, 139.90, 136.85, 136.60, 131.92, 129.95 (2C), 129.74,

128.81 (2C), 127.52, 127.48, 126.96 (2C), 125.61, 113.76 (2C), 55.28, 42.32, 38.45, 13.46, 12.14. MS EI *m/z* (rel. int.) 359 (M^+, 50), 358 (36), 288 (30), 287 (100), 216 (28), 215 (79), 77 (32), 72 (39), 57 (30), 56 (51); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{24}H_{26}NO_2$, 360.1963, found 360.1979.

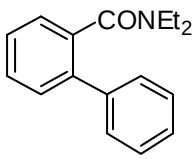
Amide-Directed C-O Activation of Benzamides/C-C Bond Formation. Synthesis of Compounds 3.99b, 3.20b, 3.67b, 3.101b-3.102b, 3.107b, 3.70b-3.72b, 3.74b-3.81b, 3.83b-3.84b, 3.111b-3.123b, 3.90b, 3.21b, 3.128, 3.114, 3.129, 3.129b, 3.131b-3.132b, 3.135b

N,N-Dimethyl-2-phenylbenzamide (**3.99b**, Table 3.14, entry 3)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxybenzamide (54 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.99b** (62 mg, 92% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.53-7.29 (m, 9H), 2.84 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.27, 139.90, 138.63, 135.73, 129.27, 129.26, 128.44 (2C), 128.33 (2C), 127.65, 127.55, 127.37, 37.91, 34.49. The physical and spectral data were consistent with those previously reported.[314]

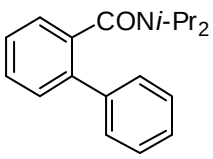
N,N-Diethyl-2-phenylbenzamide (**3.20b**, Table 3.14, entry 4)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.20b** (73 mg, 96% yield) was obtained as a

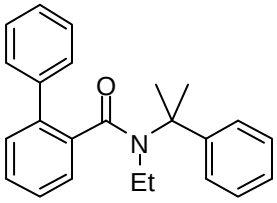
yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diisopropyl-2-phenylbenzamide (**3.67b**, Table 3.14, entry 5)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diisopropyl-2-methoxybenzamide (118 mg, 0.5 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (114 mg, 0.6 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 4 mol%) and toluene (1 mL), the title compound **3.67b** (46 mg, 33% yield) was obtained as a light yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

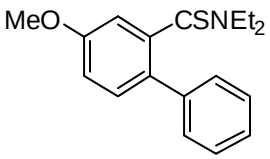
N-Ethyl-N-cumyl-2-phenylbenzamide (**3.101b**, Table 3.14, entry 6)



According to General Procedure B and using the following materials refluxed in 20 h: N-ethyl-N-cumyl-2-methoxybenzamide (45 mg, 0.15 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (43 mg, 0.23 mmol), $RuH_2(CO)(PPh_3)_3$ (6 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.101b** (26 mg, 51% yield) was obtained as a pale solid. mp 121-122 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2980, 1638, 1395, 1287, 748, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.56-7.28 (m, 9H), 7.27-7.18 (m, 2H), 7.15 (t, *J* = 6.7 Hz, 1H), 7.01 (d, *J* = 6.5 Hz, 2H), 3.05 (m, 2H), 1.65 (s, 3H), 1.61 (s, 3H), 0.86 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.99, 148.43, 140.16, 138.02, 137.94, 129.63, 129.36, 128.38, 128.36, 128.05, 127.41, 127.15, 127.09, 125.69, 124.32, 61.74, 41.30, 29.55, 26.91, 16.61. MS EI *m/z* (rel. int.)

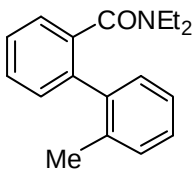
343 (M^+, 7), 238 (25), 224 (75), 181 (100), 153 (17), 152 (25), 119 (20); HRMS *m/z* (EI, M^+) calcd for $C_{24}H_{25}NO$, 343.1936, found 343.1935.

N,N-Diethyl-4-methoxybiphenyl-2-carbothioamide (**3.102b**, Table 3.14, entry 7)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2,5-dimethoxybenzothioamide (25 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.102b** (4 mg, 14% yield) was obtained as a yellow solid. mp 104-107 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2970, 2931, 1605, 1496, 1484, 1462, 1441, 1430, 1314, 1290, 1271, 1236, 1225, 1140, 1130, 1150, 770, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.55 (d, *J* = 7.1 Hz, 2H), 7.38-7.27 (m, 3H), 7.22 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 2.4 Hz, 1H), 6.92 (dd, *J* = 8.4, 2.6 Hz, 1H), 4.68-4.48 (m, 1H), 3.85 (s, 3H), 3.43-3.19 (m, 2H), 2.91-2.71 (m, 1H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 198.54, 158.81, 142.74, 139.51, 130.98, 129.10 (2C), 128.63, 128.08 (2C), 127.08, 114.82, 112.48, 55.45, 47.21, 45.33, 13.11, 10.06. MS EI *m/z* (rel. int.) 299 (M^+, 89), 298 (75), 227 (71), 222 (53), 195 (100), 184 (95), 152 (78), 139 (54), 72 (64), 61 (46), 56 (63); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{18}H_{22}NOS$, 300.1422, found 300.1432.

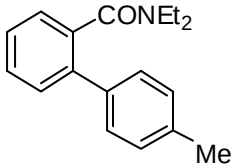
N,N-Diethyl-2-(*o*-tolyl)benzamide (**3.107b**, Table 3.17)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (42 mg, 0.2 mmol), 2-(2-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg, 0.3 mmol),

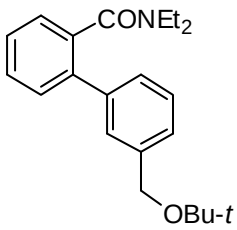
$RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.107b** (44 mg, 82% yield) was obtained as a yellow solid. mp 64-65 ^oC (EtOAc/hexanes) (lit[315] mp 67-68 ^oC); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.62-6.86 (m, 8H), 4.02-3.42 (m, 1H), 3.40-2.44 (m, 3H), 2.22 (s, 3H), 1.14-0.51 (m, 6H) (atropisomers involved);[315] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.03, 137.14 (brs), 130.69 (brs), 130.22 (brs), 130.02, 128.13 (brs), 127.61, 127.32, 126.38 (brs), 125.07 (brs), 42.26 (brs), 37.80, 20.22, 13.65, 11.73 (atropisomers involved). The physical and spectral data were consistent with those reported.[315]

N,N-Diethyl-2-(4-methylphenyl)benzamide (**3.70b**, Table 3.17)



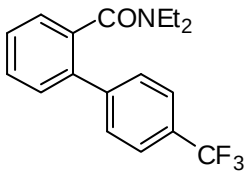
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(4-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (92 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.70b** (77 mg, 96% yield) was obtained as a yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(3-*t*-butoxymethylphenyl)benzamide (**3.71b**, Table 3.17)



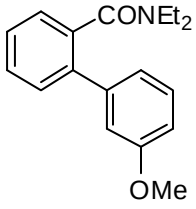
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(3-*t*-butoxymethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (124 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.71b** (95 mg, 93% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-((4-trifluoromethyl)phenyl)benzamide (**3.72b**, Table 3.17)



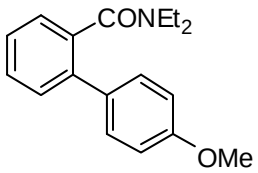
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-((4-trifluoromethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (116 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.72b** (86 mg, 90% yield) was obtained as a light yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(3-methoxyphenyl)benzamide (**3.74b**, Table 3.17)



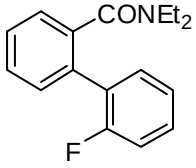
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(3-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (91 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.74b** (79 mg, 93% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(4-methoxyphenyl)benzamide (**3.75b**, Table 3.17)



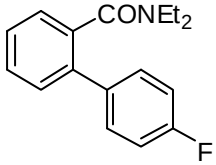
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (99 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.75b** (83 mg, 98% yield) was obtained as light yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(2-fluorophenyl)benzamide (**3.76b**, Table 3.17)



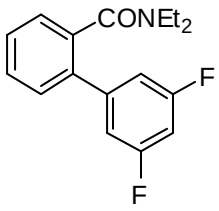
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(2-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.76b** (70 mg, 87% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(4-fluorophenyl)benzamide (**3.77b**, Table 3.17)



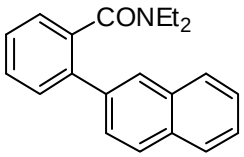
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (94 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.77b** (77 mg, 95% yield) was obtained as a light yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(3,5-difluorophenyl)benzamide (**3.78b**, Table 3.17)



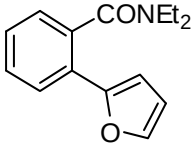
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(3,5-difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (102 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.78b** (79 mg, 91% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(naphthalen-2-yl)benzamide (**3.79b**, Table 3.17)



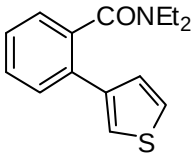
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(naphthalen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (108 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.79b** (73 mg, 81% yield) was obtained as a light yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(furan-2-yl)benzamide (**3.80b**, Table 3.17)



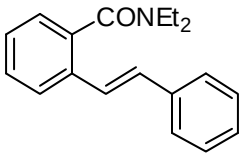
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.3 0mmol), 2-(furan-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (81 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.80b** (41 mg, 84% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(thiophen-3-yl)benzamide (**3.81b**, Table 3.17)



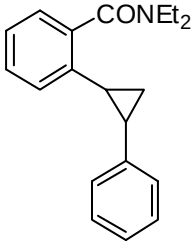
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (62 mg, 0.30 mmol), 2-(thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (88 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.81b** (35 mg, 67% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

(*E*)-N,N-Diethyl-2-styrylbenzamide (**3.83b**, Table 3.17)



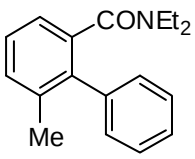
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (42 mg, 0.2 mmol), (*E*)-2-styryl-5,5-dimethyl-1,3,2-dioxaborinane (65 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.83b** (32 mg, 58% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-(2-phenylcyclopropyl)benzamide (**3.84b**, Table 3.17)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (42 mg, 0.2 mmol), 2-(2-phenylcyclopropyl)-5,5-dimethyl-1,3,2-dioxaborinane (69 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.84b** (48 mg, 83% yield) was obtained as a yellow solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

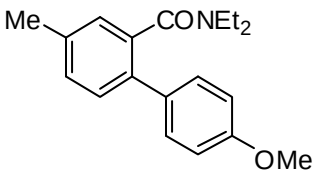
3-Methyl-2-phenyl-N,N-diethylbenzamide (**3.111b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-3-methylbenzamide (44 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.111b** (45 mg, 85% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2932, 1633, 1478, 1456, 1441, 1426, 1330, 1315, 1291, 1122, 796, 773, 749, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.45-

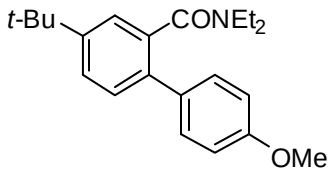
7.23 (m, 6H), 7.22-7.13 (m, 2H), 3.86-3.67 (m, 1H), 3.20-3.02 (m, 1H), 2.82-2.61 (m, 2H), 2.15 (s, 3H), 0.91 (t, J = 7.1 Hz, 3H), 0.59 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.22, 138.39, 137.78, 137.43, 136.37, 130.25, 128.60 (br), 128.37 (br), 127.46, 127.33 (br, 2C), 127.14, 123.17, 42.17, 37.57, 20.50, 13.57, 11.52. MS EI *m/z* (rel. int.) 267 (M^+, 25), 266 (51), 195 (95), 166 (32), 165 (100), 152 (61), 56 (34); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{18}H_{22}NO$, 268.1701, found 268.1692.

N,N-Diethyl-5-methyl-2-(4-methoxyphenyl)benzamide (**3.112b**, Table 3.18)



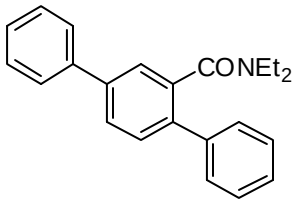
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-5-methylbenzamide (57 mg, 0.2 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.112b** (55 mg, 92% yield) was obtained as a light yellow solid. mp 113-114 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2934, 1627, 1520, 1474, 1461, 1437, 1293, 1247, 1180, 1091, 1038, 821 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.40 (d, J = 8.8 Hz, 2H), 7.29-7.19 (m, 2H), 7.15 (s, 1H), 6.89 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H), 3.78-3.65 (m, 1H), 3.12-2.88 (m, 2H), 2.75-2.58 (m, 1H), 2.38 (s, 3H), 0.95 (t, J = 7.1 Hz, 3H), 0.73 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.88, 158.99, 136.88, 136.04, 135.03, 132.32, 129.88 (2C), 129.61, 129.13, 127.51, 113.63 (2C), 55.25, 42.20, 38.28, 20.94, 13.37, 12.12. MS EI *m/z* (rel. int.) 297 (M^+, 32), 296 (29), 225 (100), 182 (20), 165 (16), 153 (24), 152 (17); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{19}H_{24}NO_2$, 298.1807, found 298.1823.

N,N-Diethyl-5-*tert*-butyl-2-(4-methoxyphenyl)benzamide (**3.113b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-5-*t*-butylbenzamide (53 mg, 0.2 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.113b** (65 mg, 94% yield) was obtained as a light yellow solid. mp 89-92 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2965, 1629, 1610, 1522, 1489, 1474, 1461, 1434, 1294, 1261, 1248, 1180, 1138, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.45-7.36 (m, 3H), 7.34 (d, *J* = 2.0 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 2H), 3.81 (s, 3H), 3.80-3.69 (m, 1H), 3.08-2.87 (m, 2H), 2.75-2.57 (m, 1H), 1.34 (s, 9H), 0.95 (t, *J* = 7.1 Hz, 3H), 0.74 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.22, 159.01, 150.00, 135.74, 135.01, 132.29, 129.89 (2C), 128.91, 125.90, 123.86, 113.64 (2C), 55.24, 42.22, 38.40, 34.53, 31.22, 13.38, 12.14. MS EI *m/z* (rel. int.) 339 (M^+, 32), 267 (67), 211 (39), 165 (26), 72 (43), 57 (100); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{29}NO_2$, 339.2198, found 339.2179.

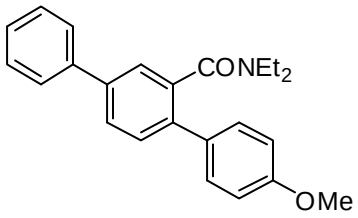
N,N-Diethyl-2,5-diphenylbenzamide (**3.114b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-5-phenyl-2-methoxybenzamide (57 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.114b** (65 mg, 98% yield) was obtained as a light yellow solid. mp 128-130 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2933, 1627, 1473, 1458, 1433, 1272, 1093, 758, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.74-7.63 (m, 3H), 7.62 (d, *J* = 1.5 Hz, 1H), 7.54 (d, *J* = 6.8 Hz, 2H), 7.51-7.43 (m, 3H), 7.43-7.30 (m, 4H), 3.87-3.70 (m, 1H), 3.13-2.90 (m, 2H), 2.79-

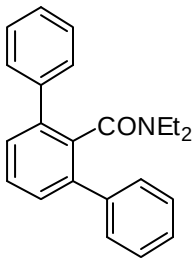
2.61 (m, 1H), 0.93 (t, J = 7.1 Hz, 3H), 0.74 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.42, 140.37, 139.94, 139.38, 137.22, 136.77, 129.88, 128.83 (2C), 128.81 (2C), 128.32 (2C), 127.61, 127.57, 127.52, 127.01 (2C), 125.60, 42.27, 38.34, 13.42, 11.96. MS EI *m/z* (rel. int.) 329 (M^+, 37), 328 (40), 257 (100), 228 (25); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{23}NO$, 329.1780, found 329.1783.

N,N-Diethyl-2-(4-methoxyphenyl)-5-phenylbenzamide (**3.90b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-5-phenyl-2-methoxybenzamide (57 mg, 0.2 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.90b** (70 mg, 97% yield) was obtained as a pale solid. The physical and spectral data were consistent with those reported for this compound as prepared previously.

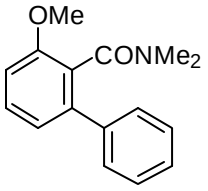
N,N-Diethyl-2,6-diphenylbenzamide (**3.115b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-6-phenyl-2-methoxybenzamide (28 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (4 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.115b** (9 mg, 27% yield) was obtained as a light yellow solid. mp 82-83 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2361, 2341, 1628, 1458, 1440, 1285, 768, 755, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.56-7.42 (m, 5H), 7.41-7.28 (m, 8H), 3.10 (q, J = 7.1 Hz, 2H),

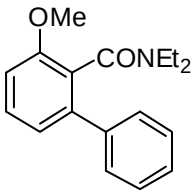
2.79 (q, J = 7.1 Hz, 2H), 0.64 (t, J = 7.1 Hz, 3H), 0.47 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.62, 140.20 (2C), 139.27 (2C), 135.33, 129.32 (4C), 129.02 (2C), 128.34, 127.94 (4C), 127.34 (2C), 42.22, 37.52, 12.84, 11.41. MS EI *m/z* (rel. int.) 329 (M^+, 15), 258 (15), 257 (100), 252 (49), 228 (18); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{23}NO$, 329.1780, found 329.1790.

N,N-Dimethyl-2-methoxy-6-phenylbenzamide (**3.116b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2,6-dimethoxybenzamide (42 mg, 0.20 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (42 mg, 0.22 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.116b** (35 mg, 68% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2935, 1639, 1593, 1583, 1570, 1500, 1466, 1429, 1394, 1309, 1270, 1256, 1123, 1098, 1059, 1019, 761, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.50-7.42 (m, 2H), 7.41-7.28 (m, 4H), 6.99 (dd, J = 7.7, 0.6 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 3.87 (s, 3H), 2.86 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.59, 155.79, 140.21, 139.74, 129.62, 128.52 (2C), 128.17 (2C), 127.48, 125.06, 122.01, 109.84, 55.89, 37.63, 34.26. MS EI *m/z* (rel. int.) 255 (M^+, 8), 211 (100), 168 (29), 152 (29), 139 (44), 72 (16); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{17}NO_2$, 255.1259, found 255.1257.

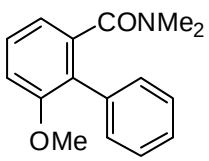
N,N-Diethyl-2-methoxy-6-phenylbenzamide (**3.117b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2,6-dimethoxybenzamide (71 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11

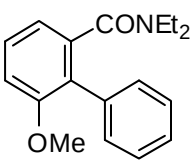
mg, 4 mol%) and toluene (0.4 mL), the title compound **3.117b** (51 mg, 60% yield) was obtained as a pale solid. mp 79-80 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2975, 2935, 1632, 1583, 1569, 1465, 1423, 1283, 1265, 761, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.48 (d, *J* = 6.7 Hz, 2H), 7.41-7.27 (m, 4H), 6.97 (d, *J* = 7.7 Hz, 1H), 6.92 (d, *J* = 8.3 Hz, 1H), 3.85 (s, 3H), 3.84-3.73 (m, 1H), 3.05-2.87 (m, 2H), 2.77-2.63 (m, 1H), 0.84-0.72 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.59, 155.75, 140.03, 139.61, 129.31, 128.92 (2C), 128.01 (2C), 127.38, 125.56, 121.96, 109.78, 55.69, 42.14, 37.88, 13.26, 11.85. MS EI *m/z* (rel. int.) 283 (M^+, 8), 211 (100), 206 (18); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1570.

N,N-Dimethyl-2-phenyl-3-methoxybenzamide (**3.118b**, Table 3.18)



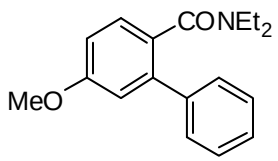
According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2,3-dimethoxybenzamide (63 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.118b** (70 mg, 91% yield) was obtained as a light yellow solid. mp 83-84 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2936, 1635, 1579, 1502, 1466, 1455, 1433, 1395, 1257, 1053, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.45-7.28 (m, 6H), 6.99 (dd, *J* = 8.4, 2.3 Hz, 2H), 3.76 (s, 3H), 2.73 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.63, 156.32, 138.19, 135.29, 129.98 (2C), 129.02, 127.64 (2C), 127.45, 127.34, 119.02, 111.55, 55.81, 38.05, 34.23. MS EI *m/z* (rel. int.) 255 (M^+, 48), 211 (100), 196 (24); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{17}NO_2$, 255.1259, found 255.1267.

N,N-Diethyl-2-phenyl-3-methoxybenzamide (**3.119b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2,3-dimethoxybenzamide (71 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.119b** (74 mg, 87% yield) was obtained as a light yellow solid. mp 79-80 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2934, 1629, 1459, 1426, 1297, 1255, 1059, 801, 744, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.44-7.27 (m, 6H), 6.97 (t, *J* = 7.9 Hz, 2H), 3.80-3.67 (m, 4H), 3.13-2.99 (m, 1H), 2.86-2.72 (m, 1H), 2.71-2.56 (m, 1H), 0.84 (t, *J* = 7.1 Hz, 3H), 0.66 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.70, 156.36, 138.62, 135.22, 130.16 (2C), 128.92, 127.64 (2C), 127.24, 127.20, 118.51, 111.22, 55.78, 42.04, 37.74, 13.50, 11.64. MS EI *m/z* (rel. int.) 283 (M^+, 64), 282 (69), 212 (13), 211 (100), 196 (35), 168 (15); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1563.

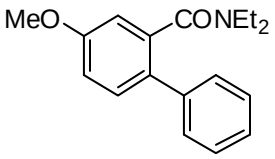
N,N-Diethyl-2-phenyl-4-methoxybenzamide (**3.21b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2,4-dimethoxybenzamide (71 mg, 0.3 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.8 mL), the title compound **3.21b** (76 mg, 89% yield) was obtained as a light yellow solid. mp 64-65 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2935, 1625, 1468, 1428, 1290, 1271, 1036, 772, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.47 (d, *J* = 6.6 Hz, 2H), 7.40-7.27 (m, 4H), 6.96-6.85 (m, 2H), 3.84 (s, 3H), 3.79-3.63 (m, 1H), 3.16-2.78 (m, 2H), 2.73-2.48 (m, 1H), 0.86 (t, *J* = 7.1 Hz, 3H), 0.72 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.52, 159.70, 139.97, 139.76, 129.02, 128.70 (2C), 128.44, 128.24

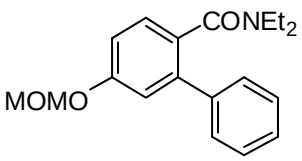
(2C), 127.59, 114.62, 112.97, 55.33, 42.23, 38.29, 13.35, 11.90. MS EI *m/z* (rel. int.) 283 (M^+, 11), 282 (16), 211 (100); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1574.

N,N-Diethyl-2-phenyl-3-methoxylbenzamide (**3.120b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2,5-dimethoxybenzamide (62 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (28 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.120b** (64 mg, 75% yield) was obtained as a light yellow solid. mp 55-56 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2935, 1628, 1608, 1478, 1433, 1315, 1291, 1269, 1230, 1086, 1047, 830, 773, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.47-7.40 (m, 2H), 7.37-7.27 (m, 4H), 6.97 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.89 (d, *J* = 2.6 Hz, 1H), 3.84 (s, 3H), 3.80-3.69 (m, 1H), 3.06-2.89 (m, 2H), 2.71-2.56 (m, 1H), 0.89 (t, *J* = 7.1 Hz, 3H), 0.73 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.21, 158.96, 139.47, 137.27, 130.88, 130.65, 128.77 (2C), 128.20 (2C), 127.05, 115.04, 111.93, 55.42, 42.17, 38.25, 13.35, 11.88; MS EI *m/z* (rel. int.) 283 (M^+, 41), 282 (38), 211 (100), 168 (17); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1564.

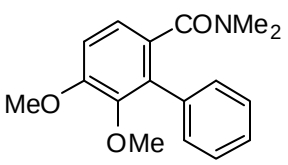
N,N-Diethyl-4-methoxymethoxy-2-phenylbenzamide (**3.121b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-4-methoxymethoxy-2-methoxy-benzamide (54 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.121b** (61 mg, 98% yield) was obtained as a light yellow solid. mp 63-64 ^oC

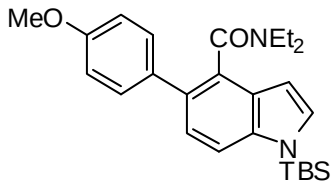
(EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2934, 1626, 1468, 1430, 1314, 1289, 1220, 1184, 1154, 1095, 1079, 996, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.47 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.39-7.27 (m, 4H), 7.08-7.02 (m, 2H), 5.21 (s, 2H), 3.85-3.63 (m, 1H), 3.49 (s, 3H), 3.15-2.84 (m, 2H), 2.74-2.49 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H), 0.72 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.45, 157.44, 139.98, 139.60, 130.10, 128.72 (2C), 128.41, 128.25 (2C), 127.61, 116.96, 115.18, 94.40, 56.07, 42.25, 38.32, 13.36, 11.90. MS EI *m/z* (rel. int.) 313 (M^+, 24), 312 (50), 241 (100), 211 (65), 168 (28), 139 (33); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{19}H_{24}NO_3$, 314.1756, found 314.1760.

N,N-Dimethyl-2-phenyl-3,4-dimethoxybenzamide (**3.122b**, Table 3.18)



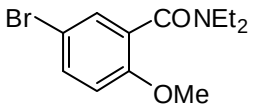
According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2,3,4-trimethoxybenzamide (48 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.122b** (51 mg, 90% yield) was obtained as a colorless solid. mp 101-102 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2936, 1633, 1596, 1479, 1450, 1394, 1296, 1273, 1258, 1122, 1021, 767, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.43 (d, *J* = 6.8 Hz, 2H), 7.39-7.28 (m, 3H), 7.11 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 3.90 (s, 3H), 3.45 (s, 3H), 2.71 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.65, 153.43, 146.17, 135.14, 133.25, 130.16, 129.77 (2C), 127.69 (2C), 127.46, 122.79, 111.72, 60.47, 55.91, 38.11, 34.34. MS EI *m/z* (rel. int.) 285 (M^+, 39), 241 (100), 226 (47); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{19}NO_3$, 285.1365, found 285.1360.

1-(*tert*-Butyldimethylsilyl)-N,N-diethyl-5-(4-methoxyphenyl)-1*H*-indole-4-carboxamide (**3.123b**, Table 3.18)



According to General Procedure B and using the following materials refluxed in 20 h: 1-(*t*-butyldimethylsilyl)-N,N-diethyl-5-methoxy-1*H*-indole-4-carboxamide (36 mg, 0.10 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (33 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.123b** (26 mg, 60% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2957, 2932, 1626, 1521, 1464, 1424, 1288, 1247, 1150, 839, 809, 789, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.54-7.43 (m, 3H), 7.20 (d, *J* = 3.2 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 2.7 Hz, 1H), 3.83 (s, 3H), 3.78-3.66 (m, 1H), 3.33-3.17 (m, 1H), 3.05-2.93 (m, 1H), 2.78-2.66 (m, 1H), 1.03 (t, *J* = 7.1 Hz, 3H), 0.94 (s, 9H), 0.65 (t, *J* = 7.1 Hz, 3H), 0.64 (s, 3H), 0.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.17, 158.56, 140.26, 133.58, 131.94, 130.29 (2C), 129.36, 129.30, 127.41, 122.98, 114.10, 113.53 (2C), 104.05, 55.27, 42.35, 38.19, 26.23 (3C), 19.43, 13.65, 12.37, -3.96, -4.02. MS EI *m/z* (rel. int.) 436 (M^+, 38), 364 (100), 321 (16), 258 (17), 73 (31), 57 (16); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{26}H_{37}N_2O_2Si$, 437.2624, found 437.2626.

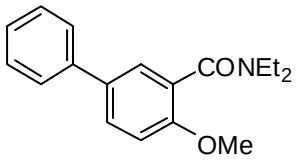
5-Bromo-N,N-diethyl-2-methoxybenzamide (**3.128**, Scheme 3.50)



According to General Procedure E and using the following materials stirred in 10 min: N,N-diethyl-2-methoxybenzamide (622 mg, 3.0 mmol), NH_4OAc (23 mg, 0.3 mmol), NBS (567 mg, 3.2 mmol) and MeCN (15 mL), the title compound **3.128** (781 mg, 91% yield) was obtained as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.37 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.26 (d, *J* = 2.4 Hz, 1H), 6.75 (d, *J* =

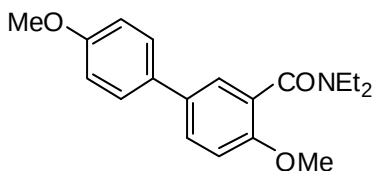
8.8 Hz, 1H), 3.76 (s, 3H), 3.56-3.45 (m, 2H), 3.15-3.05 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.01 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 166.84, 154.22, 132.41, 130.02, 128.71, 112.77, 112.68, 55.69, 42.72, 38.81, 13.84, 12.71. The physical and spectral data were consistent with those previously reported.

N,N-Diethyl-2-methoxy-5-phenylbenzamide (**3.114**, Scheme 3.50)



According to General Procedure F and using the following materials: 5-bromo-2-methoxy-N,N-diethylbenzamide (229 mg, 0.8 mmol), phenylboronic acid (146 mg, 1.2 mmol), a degassed 2 M aqueous solution of Na_2CO_3 (1.2 mL, 2.4 mmol) and $Pd(PPh_3)_4$ (19 mg, 2 mol%) and toluene (1.2 mL), the title compound **3.114** (208 mg, 92% yield) was obtained as a light yellow solid. mp 85-87 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2935, 1633, 1485, 1475, 1461, 1436, 1275, 1251, 1087, 1020, 763, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.60-7.49 (m, 3H), 7.48-7.36 (m, 3H), 7.31 (t, *J* = 7.3 Hz, 1H), 6.97 (d, *J* = 8.6 Hz, 1H), 3.85 (s, 3H), 3.66-3.52 (m, 2H), 3.25-3.11 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.53, 154.67, 140.11, 133.82, 128.70 (2C), 128.34, 127.25, 126.87, 126.66 (2C), 126.07, 111.27, 55.65, 42.79, 38.81, 13.98, 12.88. MS EI *m/z* (rel. int.) 283 (M^+, 24), 282 (23), 211 (100); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{21}NO_2$, 283.1572, found 283.1575.

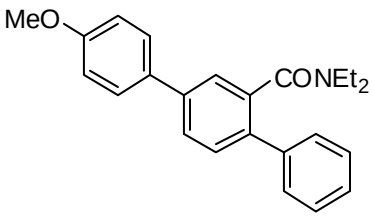
N,N-Diethyl-2-methoxy-5-(4-methoxyphenyl)benzamide (**3.129**, Scheme 3.50)



According to General Procedure F and using the following materials: 5-bromo-2-methoxy-N,N-diethylbenzamide (100 mg, 0.35 mmol), 4-methoxyphenylboronic acid (80 mg, 0.53

mmol), a degassed 2 M aqueous solution of Na_2CO_3 (0.55 mL, 1.05 mmol) and $Pd(PPh_3)_4$ (8 mg, 2 mol%) and toluene (0.55 mL), the title compound **3.129** (104 mg, 95% yield) was obtained as a colorless solid. mp 58-60 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2971, 2936, 1633, 1609, 1494, 1474, 1462, 1438, 1276, 1244, 1181, 1087, 1051, 1021, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.54-7.41 (m, 3H), 7.38 (d, *J* = 2.2 Hz, 1H), 7.01-6.85 (m, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.64-3.50 (m, 2H), 3.24-3.11 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.62, 158.82, 154.21, 133.54, 132.74, 127.88, 127.69 (2C), 127.19, 125.66, 114.15 (2C), 111.27, 55.65, 55.29, 42.79, 38.79, 13.98, 12.88. MS EI *m/z* (rel. int.) 313 (M^+, 32), 312 (25), 241 (100), 183 (15), 139 (26); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{19}H_{24}NO_3$, 314.1756, found 314.1746.

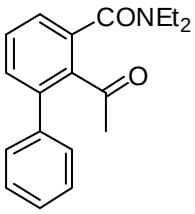
N,N-Diethyl-2-phenyl-5-(4-methoxyphenyl)benzamide (**3.129b**, Scheme 3.50)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-5-(4-methoxyphenyl)benzamide (31 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.129b** (33 mg, 93% yield) was obtained as a light yellow solid. mp 117-118 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2933, 1627, 1521, 1473, 1460, 1439, 1317, 1290, 1272, 1245, 1181, 1093, 826, 773, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.63 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.61-7.48 (m, 5H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.42-7.29 (m, 3H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 3H), 3.81-3.69 (m, 1H), 3.11-2.89 (m, 2H), 2.76-2.58 (m, 1H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.74 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.54, 159.38, 139.97, 139.45, 136.67, 136.56, 132.40, 129.82,

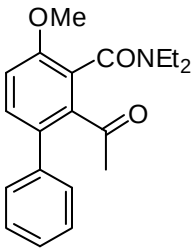
128.78 (2C), 128.29 (2C), 128.02 (2C), 127.47, 127.05, 125.08, 114.27 (2C), 55.31, 42.26, 38.32, 13.39, 11.94. MS EI *m/z* (rel. int.) 359 (M^+, 54), 358 (47), 287 (100), 216 (29), 215 (71), 72 (28), 56 (37); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{24}H_{26}NO_2$, 360.1963, found 360.1955.

N,N-Diethyl-2-acyl-3-phenylbenzamide (**3.131b**, Table 3.19, entry 1)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-acylbenzamide (66 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.131b** (36 mg, 81% yield based on consideration of 50% ketone substrate reduced) was obtained as a light yellow solid. mp 58-59 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2975, 2935, 1697, 1631, 1478, 1438, 1424, 1348, 1296, 1247, 765, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.49-7.37 (m, 5H), 7.34 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 1H), 3.52 (q, *J* = 7.0 Hz, 2H), 3.36 (q, *J* = 7.0 Hz, 2H), 1.96 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 205.99, 170.19, 139.80, 139.68, 139.58, 136.40, 130.04, 128.95, 128.81 (2C), 128.73 (2C), 128.08, 124.62, 43.36, 38.86, 31.60, 13.73, 12.35; MS EI *m/z* (rel. int.) 295 (M^+, 1), 280 (7), 224 (13), 223 (100), 152 (11), 72 (30); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{21}NO_2$, 295.1572, found 295.1575.

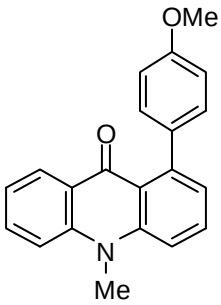
N,N-Diethyl-2-acyl-3-phenyl-6-methoxybenzamide (**3.132b**, Table 3.19, entry 2)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-acyl-6-methoxybenzamide (75 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (87 mg, 0.45 mmol),

$RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.132b** (26 mg, 54% yield based on consideration of 50% ketone substrate reduced) was obtained as a pale solid. mp 100-103 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2976, 2936, 1699, 1629, 1582, 1469, 1438, 1274, 1047, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.41-7.27 (m, 6H), 6.99 (d, *J* = 8.5 Hz, 1H), 3.85 (s, 3H), 3.70 (q, *J* = 6.8 Hz, 1H), 3.42-3.20 (m, 3H), 1.95 (s, 3H), 1.23-1.11 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 205.54, 166.99, 154.28, 140.72, 139.50, 131.61, 130.91, 128.80 (2C), 128.64 (2C), 127.59, 125.09, 111.62, 55.69, 43.03, 38.40, 31.74, 13.27, 12.24; MS EI *m/z* (rel. int.) 325 (M^+, 8), 254 (24), 253 (100), 72 (24); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{23}NO_3$, 325.1678, found 325.1664.

1-(4-Methoxyphenyl)-10-methylacridin-9(10*H*)-one (**3.135b**, Scheme 3.52)

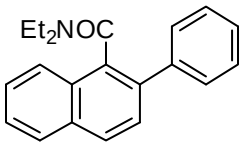


According to General Procedure B and using the following materials refluxed in 20 h: 1-methoxy-10-methylacridin-9(10*H*)-one (24 mg, 0.10 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (33 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.135b** (16 mg, 50% yield) was obtained as a yellow solid. mp 215-216 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1635, 1602, 1513, 1492, 1460, 1369, 1288, 1243, 1173, 1031, 782, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.40 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.73-7.61 (m, 2H), 7.52 (d, *J* = 8.7 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.24-7.17 (m, 1H), 7.06 (dd, *J* = 7.2, 0.9 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.92 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 178.22, 158.31, 144.60, 144.14, 142.18, 136.05, 133.36, 132.19, 129.22 (2C), 127.95, 125.17, 124.03, 121.13, 120.07, 114.34, 114.12, 113.02

(2C), 55.18, 34.63. MS/MS ESI *m/z* (rel. int.) 316 ($[M+1]^+$, 100), 301 (36), 300 (50), 284 (14), 273 (32), 272 (18); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{21}H_{18}NO_2$, 316.1337, found 316.1328.

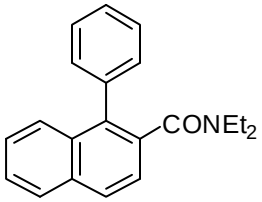
Amide-Directed C-O Activation of Naphthamides/C-C Bond Formation. Synthesis of Compounds 3.136b-3.138b, 3.139b-3.155b, 3.160b-3.171b, 3.174b-3.176b, 3.179b, 3.183-3.191, 3.184b-3.185b, 3.188b-3.189b

N,N-Diethyl-2-phenyl-1-naphthamide (**3.136b**, Table 3.20, entry 1)



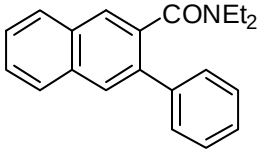
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-1-naphthamide (77 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (86 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.136b** (88 mg, 97% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 1625, 1480, 1429, 1285, 818, 749, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.96-7.81 (m, 3H), 7.62 (d, *J* = 7.0 Hz, 2H), 7.57-7.46 (m, 3H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 3.90-3.71 (m, 1H), 3.29-3.11 (m, 1H), 3.02-2.86 (m, 1H), 2.75-2.57 (m, 1H), 0.98 (t, *J* = 7.1 Hz, 3H), 0.62 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.23, 140.05, 135.29, 132.82, 132.57, 130.11, 129.26 (2C), 128.62, 128.19 (2C), 127.91, 127.46, 127.32, 126.99, 126.19, 125.56, 42.36, 38.22, 13.54, 12.07. MS EI *m/z* (rel. int.) 303 (M^+, 27), 232 (12), 231 (100), 203 (13), 202 (32); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{21}NO$, 303.1623, found 303.1624.

N,N-Diethyl-1-phenyl-2-naphthamide (**3.137b**, Table 3.20, entry 2)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (77 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (86 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.137b** (88 mg, 96% yield) was obtained as a light yellow solid. mp 121-122 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2933, 1629, 1478, 1428, 1380, 1286, 1103, 818, 763, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.60-7.29 (m, 8H), 3.90-3.75 (m, 1H), 3.26-3.03 (m, 1H), 2.91-2.61 (m, 2H), 0.89 (t, *J* = 7.1 Hz, 3H), 0.68 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.20, 137.13, 135.47, 134.22, 133.38, 131.96, 131.20, 129.69, 128.61, 128.20, 128.02, 127.62, 127.28, 126.54, 126.47, 126.21, 123.35, 42.25, 37.76, 13.71, 11.70. MS EI *m/z* (rel. int.) 303 (M^+, 28), 302 (26), 232 (15), 231 (100), 203 (12), 202 (38); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{21}NO$, 303.1623, found 303.1635.

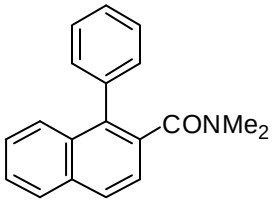
N,N-Diethyl-3-phenyl-2-naphthamide (**3.138b**, Table 3.20, entry 3)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-3-methoxy-2-naphthamide (39 mg, 0.15 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (43 mg, 0.23 mmol), $RuH_2(CO)(PPh_3)_3$ (6 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.138b** (14 mg, 30% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 2932, 1626, 1478, 1442, 1423, 1286, 1086, 893, 775, 751, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.93-7.84 (m, 4H), 7.58 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.55-7.49 (m, 2H), 7.45-7.34 (m, 3H), 3.89-3.75 (m, 1H), 3.10-2.91 (m, 2H), 2.73-2.58 (m, 1H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz,

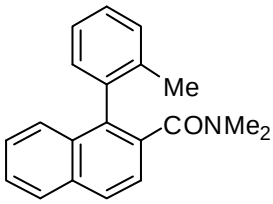
$CDCl_3$) δ ppm 170.38, 139.79, 136.48, 135.02, 133.27, 132.16, 129.09 (2C), 128.44, 128.29 (2C), 127.85 (2C), 127.53, 126.88, 126.52, 126.37, 42.27, 38.32, 13.34, 11.93. MS EI *m/z* (rel. int.) 303 (M^+, 44), 302 (38), 232 (14), 231 (100), 203 (20), 202 (41); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{21}NO$, 303.1623, found 303.1624.

N,N-Dimethyl-1-phenyl-2-naphthamide (**3.139b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-1-methoxy-2-naphthamide (46 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.139b** (55 mg, 99% yield) was obtained as a light yellow solid. mp 86-87 °C (EtOAc/hexanes); IR (KBr) ν_{max} 3065, 2927, 1635, 1502, 1493, 1443, 1396, 1264, 1095, 822, 763, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.62-7.48 (m, 2H), 7.48-7.29 (m, 6H), 2.79 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.08, 137.26, 135.84, 133.82, 133.59, 131.84, 130.78, 129.82, 128.67, 128.32, 128.06, 127.74, 127.40, 126.61, 126.51, 126.33, 123.63, 38.32, 34.24. MS EI *m/z* (rel. int.) 275 (M^+, 32), 232 (18), 231 (100), 203 (18), 202 (80), 201 (22), 200 (21), 72 (19); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{17}NO$, 275.1310, found 275.1310.

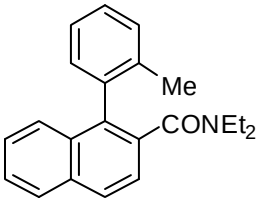
N,N-Dimethyl-1-*o*-tolyl-2-naphthamide (**3.140b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-1-methoxy-2-naphthamide (46 mg, 0.2 mmol), 2-(2-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg,

0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.140b** (56 mg, 96% yield) was obtained as a light yellow solid. mp 95-97 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 3055, 2926, 1637, 1503, 1445, 1397, 1379, 1111, 1082, 822, 759, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.53-7.48 (m, 1H), 7.47-7.01 (m, 7H), 2.83 (s, 3H), 2.81-2.60 (m, 3H), 2.04 (s, 3H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.79, 136.93 (brs), 135.79 (brs), 133.83 (brs), 133.15, 132.04 (brs), 129.97 (brs), 128.79 (brs), 128.07, 128.03, 127.99, 127.15 (brs), 126.68, 126.41, 126.32, 125.07 (brs), 123.46 (brs), 38.58 (brs), 34.29, 20.13 (atropisomers involved). MS EI *m/z* (rel. int.) 289 (M^+, 14), 246 (20), 245 (100), 244 (46), 216 (25), 215 (94), 213 (25), 202 (56), 189 (19), 72 (32); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{19}NO$, 289.1467, found 289.1455.

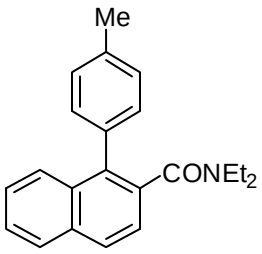
N,N-Diethyl-1-(*o*-tolyl)-2-naphthamide (**3.141b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (39 mg, 0.15 mmol), 2-(2-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (46 mg, 0.23 mmol), $RuH_2(CO)(PPh_3)_3$ (6 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.141b** (38 mg, 79% yield) was obtained as a pale solid. mp 150-152 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2933, 1631, 1489, 1477, 1457, 1428, 1379, 1285, 1115, 1098, 818, 758, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.99-7.79 (m, 2H), 7.58-6.93 (m, 8H), 3.94-3.57 (m, 1H), 3.46-2.63 (m, 3H), 2.18-1.82 (m, 3H), 1.17-0.80 (m, 3H), 0.67 (t, *J* = 7.0 Hz, 3H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.02, 138.74, 137.05, 136.08, 135.53, 134.00, 133.13, 132.19, 131.98, 130.01, 129.50, 128.72, 128.03, 127.90, 126.63, 126.48, 126.21, 125.71, 124.71, 123.57, 122.94, 42.55, 42.10, 37.65, 20.22, 20.07, 13.87, 11.70

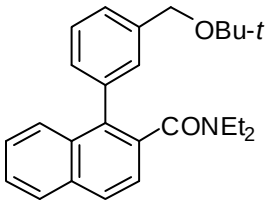
(atropisomers involved). MS EI *m/z* (rel. int.) 317 (M^+, 31), 316 (24), 245 (100), 244 (31), 215(27), 202 (26); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO$, 317.1780, found 317.1790.

N,N-Diethyl-1-(4-methylphenyl)-2-naphthamide (**3.142b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(4-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.142b** (63 mg, 99% yield) was obtained as a light yellow solid. mp 181-183 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2932, 1629, 1477, 1427, 1285, 1102, 817 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, *J* = 8.2 Hz, 2H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.49-7.37 (m, 3H), 7.33-7.18 (m, 3H), 3.95-3.71 (m, 1H), 3.25-3.06 (m, 1H), 2.98-2.82 (m, 1H), 2.81-2.65 (m, 1H), 2.44 (s, 3H), 0.91 (t, *J* = 7.0 Hz, 3H), 0.74 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.34, 137.28, 135.59, 134.24, 134.11, 133.40, 132.10, 131.03, 129.55, 129.22, 127.98 (3C), 126.55, 126.43, 126.14, 123.40, 42.26, 37.78, 21.24, 13.72, 11.71. MS EI *m/z* (rel. int.) 317 (M^+, 38), 316 (31), 246 (20), 245 (100), 215 (14), 202 (36); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO$, 317.1780, found 317.1786.

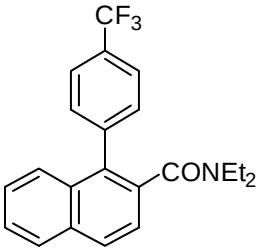
1-(3-(*t*-Butoxymethyl)phenyl)-N,N-diethyl-2-naphthamide (**3.143b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.20 mmol), 2-(3-(*t*-butoxymethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (76 mg, 0.27 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene

(0.6 mL), the title compound **3.143b** (76 mg, 97% yield) was obtained as a light yellow solid. mp 117-119 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2933, 1631, 1477, 1428, 1378, 1363, 1285, 1195, 1103, 1070, 819, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.96-7.84 (m, 2H), 7.71 (t, *J* = 7.9 Hz, 1H), 7.56-7.15 (m, 7H), 4.59-4.40 (m, 2H), 3.88-3.69 (m, 1H), 3.26-3.07 (m, 1H), 2.94-2.60 (m, 2H), 1.28 (d, 9H), 0.89 (m, 3H), 0.70 (t, *J* = 7.0 Hz, 3H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.24, 140.32, 139.25, 137.01, 136.80, 135.72, 135.54, 134.19, 134.05, 133.39, 133.32, 132.04, 131.93, 130.06, 129.83, 128.51, 128.41, 128.38, 128.13, 128.07, 127.93, 127.37, 126.68, 126.60, 126.46, 126.43, 126.18, 123.44, 123.21, 73.35, 63.96, 63.90, 42.42, 42.38, 37.96, 37.76, 27.64, 13.73, 13.71, 11.76, 11.71 (atropisomers involved). MS EI *m/z* (rel. int.) 389 (M^+, 25), 315 (14), 244 (31), 243 (100); HRMS *m/z* (EI, M^+) calcd for $C_{26}H_{31}NO_2$, 389.2355, found 389.2368.

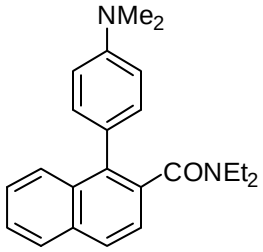
N,N-Diethyl-1-(4-trifluoromethylphenyl)-2-naphthamide (**3.144b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(4-trifluoromethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (77 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.144b** (71 mg, 95% yield) was obtained as a pale solid. mp 111-112 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2977, 2935, 1630, 1478, 1430, 1326, 1166, 1126, 1106, 1067, 818 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.95 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.79-7.64 (m, 3H), 7.59 (d, *J* = 8.3 Hz, 1H), 7.54 (d, *J* = 7.3 Hz, 1H), 7.50-7.39 (m, 3H), 3.91-3.69 (m, 1H), 3.21-3.02 (m, 1H), 2.93-2.63 (m, 2H), 0.92 (t, *J* = 7.0 Hz, 3H), 0.67 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.72, 141.09, 134.37, 133.95, 133.33, 131.77 (brs),

131.56, 130.03 (brs), 129.96 (q, $^{2}J_{C\text{-}F}$ = 32.5 Hz), 128.88, 128.23, 126.99, 126.49, 125.95, 125.56 (brs), 124.27 (brs), 124.15 (q, $^{1}J_{C\text{-}F}$ = 272.2 Hz), 123.17, 42.33, 37.86, 13.75, 11.55. MS EI *m/z* (rel. int.) 371 (M^+, 61), 370 (71), 300 (21), 299 (100), 251 (21), 202 (47); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{20}F_3NO$, 371.1497, found 371.1513.

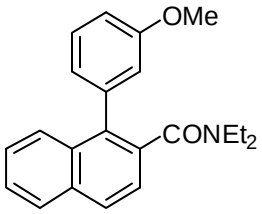
N,N-Diethyl-1-(4-(dimethylamino)phenyl)-2-naphthamide (**3.145b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(4-(dimethylamino)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (70 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.145b** (62 mg, 90% yield) was obtained as a pale solid. mp 140-141 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2932, 1627, 1612, 1523, 1477, 1428, 1380, 1349, 1282, 817 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.92-7.77 (m, 3H), 7.49 (t, *J* = 7.3 Hz, 1H), 7.46-7.35 (m, 3H), 7.20 (d, *J* = 8.1 Hz, 1H), 6.80 (t, *J* = 9.5 Hz, 2H), 3.92-3.71 (m, 1H), 3.21-3.06 (m, 1H), 2.99 (s, 6H), 2.94-2.84 (m, 1H), 2.77-2.64 (m, 1H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.78 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.76, 150.05, 135.93, 134.28, 133.52, 132.41, 131.83, 130.54, 127.93, 127.50, 126.79, 126.22, 126.02, 125.03, 123.60, 112.53, 111.44, 42.20, 40.61, 37.84, 13.71, 12.03. MS EI *m/z* (rel. int.) 346 (M^+, 84), 275 (18), 274 (100), 202 (14); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{26}N_2O$, 346.2045, found 346.2049.

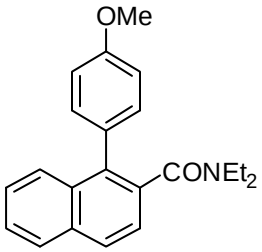
N,N-Diethyl-1-(3-methoxyphenyl)-2-naphthamide (**3.146b**, Table 3.21)

According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(3-methoxyphenyl)-5,5-dimethyl-1,3,2-



dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.146b** (64 mg, 96% yield) was obtained as a colorless solid. mp 91-93 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2934, 1629, 1578, 1478, 1463, 1429, 1378, 1285, 1251, 1047, 819 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.98-7.81 (m, 2H), 7.75 (t, *J* = 7.1 Hz, 1H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.47-7.28 (m, 3H), 7.19-7.08 (m, 1H), 7.01-6.83 (m, 2H), 3.93-3.73 (m, 4H), 3.25-3.05 (m, 1H), 2.91-2.63 (m, 2H), 0.96-0.82 (m, 3H), 0.73 (t, *J* = 6.9 Hz, 3H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.22, 170.16, 159.55, 158.68, 138.41, 135.41, 135.24, 134.11, 133.36, 131.82, 129.62, 128.30, 128.23, 127.99, 126.55, 126.52, 126.48, 126.22, 123.80, 123.37, 123.30, 122.12, 115.75, 115.67, 114.30, 112.76, 55.28, 42.41, 42.37, 37.89, 37.79, 13.76, 11.72 (atropisomers involved). MS EI *m/z* (rel. int.) 333 (M^+, 39), 332 (39), 262 (26), 261 (100), 246 (18), 218 (22), 189 (23); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO_2$, 333.1729, found 333.1726.

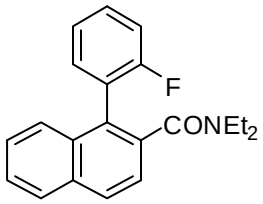
N,N-Diethyl-1-(4-methoxyphenyl)-2-naphthamide (**3.147b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.147b** (66 mg, 99% yield) was obtained as a pale solid. mp 114-116 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2933, 1628, 1514, 1477, 1429, 1380, 1286, 1246, 1178, 1102, 1034, 819, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.88 (d, *J* = 7.9 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.57-7.35 (m, 4H), 7.25 (d, *J* = 7.8 Hz, 1H), 6.98 (t, *J* = 8.4 Hz, 2H), 3.86 (s,

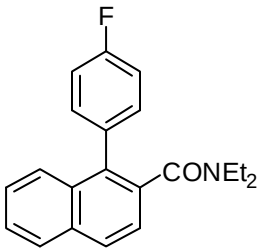
3H), 3.84-3.73 (m, 1H), 3.21-3.03 (m, 1H), 2.95-2.80 (m, 1H), 2.78-2.65 (m, 1H), 0.88 (t, J = 6.5 Hz, 3H), 0.75 (t, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.39, 159.15, 135.20, 134.39, 133.42, 132.35, 132.23, 130.82, 129.38, 128.01, 127.96, 126.48, 126.46, 126.14, 123.40, 113.41, 113.39, 55.31, 42.24, 37.82, 13.73, 11.92. MS EI *m/z* (rel. int.) 333 (M^+, 32), 332 (27), 262 (23), 261 (100), 218 (23), 189 (25); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO_2$, 333.1729, found 333.1721.

N,N-Diethyl-1-(2-fluorophenyl)-2-naphthamide (**3.148b**, Table 3.21)



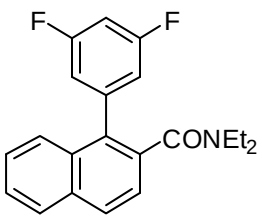
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(2-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.148b** (62 mg, 97% yield) was obtained as a pale solid. mp 137-140 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2934, 1630, 1492, 1478, 1449, 1429, 1286, 1233, 1094, 819, 758, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.01-7.83 (m, 2H), 7.59-7.36 (m, 6H), 7.32-7.09 (m, 2H), 3.94-3.72 (m, 1H), 3.37-3.10 (m, 1H), 3.04-2.68 (m, 2H), 1.08-0.80 (m, 3H), 0.68 (t, J = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.77, 159.98 (d, $^1J_{C\text{-}F}$ = 245.8 Hz), 135.15, 133.54, 132.95, 131.81, 129.96 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 129.73, 128.99, 128.14, 126.89, 126.40, 126.00, 124.52 (d, $^2J_{C\text{-}F}$ = 17.4 Hz), 124.27, 123.23, 114.89 (d, $^2J_{C\text{-}F}$ = 21.9 Hz), 41.95, 37.77, 13.77, 11.74. MS EI *m/z* (rel. int.) 321 (M^+, 31), 320 (34), 249 (100), 221 (14), 220 (35); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{20}FNO$, 321.1529, found 321.1528.

N,N-Diethyl-1-(4-fluorophenyl)-2-naphthamide (**3.149b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.149b** (62 mg, 96% yield) was obtained as a pale solid. mp 103-104 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2975, 2934, 1628, 1512, 1478, 1429, 1381, 1287, 1222, 1159, 1103, 819, 756, 728 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.98-7.83 (m, 2H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.60-7.49 (m, 2H), 7.48-7.40 (m, 2H), 7.36-7.27 (m, 1H), 7.22-7.07 (m, 2H), 3.90-3.71 (m, 1H), 3.20-3.03 (m, 1H), 2.94-2.64 (m, 2H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.06, 162.43 (d, $^1J_{C-F}$ = 246.9 Hz), 134.47, 134.35, 133.37, 133.05 (d, $^3J_{C-F}$ = 8.2 Hz), 133.04 (d, $^4J_{C-F}$ = 3.6 Hz) 132.01, 131.25 (d, $^3J_{C-F}$ = 7.9 Hz), 128.42, 128.13, 126.73, 126.31, 126.17, 123.25, 115.50 (d, $^2J_{C-F}$ = 21.2 Hz), 114.42 (d, $^2J_{C-F}$ = 21.6 Hz), 42.30, 37.88, 13.75, 11.84. MS EI *m/z* (rel. int.) 321 (M^+, 38), 320 (36), 249 (100), 220 (36); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{20}FNO$, 321.1529, found 321.1533.

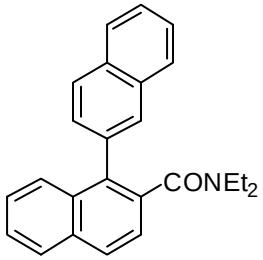
1-(3,5-Difluorophenyl)-N,N-diethyl-2-naphthamide (**3.150b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(3,5-difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (68 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.150b** (68 mg, 99% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2975, 1624, 1588, 1481, 1432, 1386, 1285, 1119, 987, 819, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.94 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.54 (t, *J* = 7.1

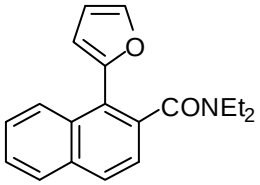
Hz, 1H), 7.51-7.41 (m, 2H), 7.13 (m, 1H), 6.92-6.83 (m, 2H), 3.96-3.80 (m, 1H), 3.25-3.03 (m, 1H), 2.97-2.74 (m, 2H), 0.96 (t, J = 7.0 Hz, 3H), 0.83 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.56, 162.94 (d, $^1J_{C\text{-}F}$ = 246.2 Hz), 162.13 (d, $^1J_{C\text{-}F}$ = 248.6 Hz), 140.49 (t, $^3J_{C\text{-}F}$ = 9.6 Hz, 1C), 134.25, 133.31, 133.02, 131.36, 129.04, 128.24, 127.10, 126.55, 125.80, 123.11, 114.60 (d, $^2J_{C\text{-}F}$ = 22.7 Hz, 1C), 112.62 (d, $^2J_{C\text{-}F}$ = 22.7 Hz, 1C), 103.17 (t, $^2J_{C\text{-}F}$ = 25.1 Hz), 42.49, 38.00, 13.80, 11.75. MS EI *m/z* (rel. int.) 339 (M^+, 32), 338 (30), 267 (100), 238 (31); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{19}F_2NO$, 339.1435, found 339.1420.

N,N-Diethyl-1-(2-naphthyl)-2-naphthamide (**3.151b**, Table 3.21)



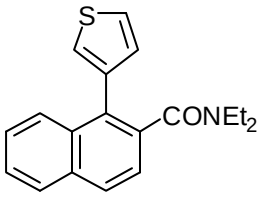
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (39 mg, 0.15 mmol), 2-(2-naphthyl)-5,5-dimethyl-1,3,2-dioxaborinane (54 mg, 0.23 mmol), $RuH_2(CO)(PPh_3)_3$ (6 mg, 4 mol%) and toluene (0.3 mL), the title compound **3.151b** (44 mg, 82% yield) was obtained as a pale solid. mp 159-161 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 1625, 1480, 1429, 1285, 1119, 1099, 921, 909, 819, 749, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.12-7.86 (m, 5H), 7.85-7.36 (m, 8H), 3.82-3.64 (m, 1H), 3.38-3.06 (m, 1H), 2.90-2.55 (m, 2H), 0.99-0.78 (m, 3H), 0.64-0.32 (m, 3H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.21, 135.54, 135.19, 135.06, 134.56, 134.52, 134.35, 133.44, 132.77, 132.61, 132.56, 132.19, 131.98, 130.30, 129.19, 128.51, 128.48, 128.39, 128.24, 128.08, 127.95, 127.87, 127.71, 127.42, 126.91, 126.63, 126.58, 126.27, 126.22, 126.13, 126.09, 123.59, 123.31, 42.46, 42.38, 37.90, 37.80, 13.77, 11.71, 11.50 (atropisomers involved). MS EI *m/z* (rel. int.) 353 (M^+, 28), 282 (46), 281 (100), 252 (41), 126 (14); HRMS *m/z* (EI, M^+) calcd for $C_{25}H_{23}NO$, 353.1780, found 353.1776.

N,N-Diethyl-1-(furan-2-yl)-2-naphthamide (**3.152b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(furan-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (54 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.152b** (58 mg, 99% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 2934, 1629, 1479, 1429, 1287, 820, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.08-7.98 (m, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.89-7.81 (m, 1H), 7.60 (brs, 1H), 7.57-7.47 (m, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 6.70 (d, *J* = 3.0 Hz, 1H), 6.55 (brs, 1H), 3.90-3.71 (m, 1H), 3.21-3.00 (m, 2H), 2.97-2.78 (m, 1H), 1.08 (t, *J* = 7.0 Hz, 3H), 0.84 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.26, 149.91, 142.61, 135.39, 133.34, 131.74, 129.45, 128.12, 127.08, 126.48, 126.23, 124.90, 123.58, 111.91, 111.20, 42.44, 38.40, 13.45, 12.30. MS EI *m/z* (rel. int.) 293 (M^+, 31), 220 (98), 193 (59), 164 (78), 138 (15), 100 (19); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{19}NO_2$, 293.1416, found 293.1429.

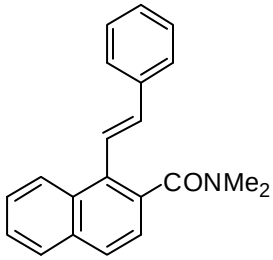
N,N-Diethyl-1-(thiophen-3-yl)-2-naphthamide (**3.153b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), 2-(thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (59 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.153b** (41 mg, 67% yield) was obtained as a light yellow solid. mp 71-73 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2932, 1626, 1478, 1429, 1285, 1101, 818, 755, 653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.92 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.61-7.36 (m, 5H), 7.26 (brs, 1H), 3.97-3.78 (m, 1H), 3.19-3.03 (m, 1H), 3.02-2.87 (m, 1H), 2.85-2.69 (m,

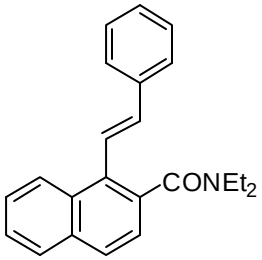
1H), 0.96-0.80 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.37, 136.99, 134.74, 133.32, 132.18, 130.58, 129.78 (brs), 128.34, 128.07, 126.68, 126.30, 126.29, 125.35 (brs), 124.88, 123.39, 42.29, 38.04, 13.70, 12.02; MS EI *m/z* (rel. int.) 309 (M^+, 17), 238 (37), 237 (100), 208 (64), 165 (32), 57 (35), 56 (40); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{19}H_{20}NOS$, 310.1265, found 310.1248.

(*E*)-N,N-Dimethyl-1-styryl-2-naphthamide (**3.154b**, Table 3.21)



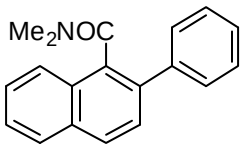
According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-1-methoxy-2-naphthamide (46 mg, 0.2 mmol), (*E*)-2-styryl-5,5-dimethyl-1,3,2-dioxaborinane (65 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.154b** (55 mg, 88% yield) was obtained as a pale solid. mp 114-116 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 3056, 2925, 1628, 1496, 1448, 1396, 1256, 1108, 1059, 975, 820, 751, 732, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.26-8.17 (m, 1H), 7.92-7.85 (m, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 16.4 Hz, 1H), 7.58-7.50 (m, 4H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.40 (t, *J* = 8.1 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.02 (d, *J* = 16.4 Hz, 1H), 3.07 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.69, 137.20, 136.01, 133.50, 132.94, 131.61, 131.42, 128.74 (2C), 128.44, 128.19, 128.10, 126.73, 126.63 (2C), 126.47, 125.23, 124.09, 123.33, 38.16, 34.75. MS EI *m/z* (rel. int.) 301 (M^+, 55), 257 (65), 256 (65), 229 (39), 228 (100), 227 (36), 226 (49), 105 (36), 77 (71), 72 (65); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{19}NO$, 301.1467, found 301.1452.

(*E*)-N,N-Diethyl-1-styryl-2-naphthamide (**3.155b**, Table 3.21)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.2 mmol), (*E*)-2-styryl-5,5-dimethyl-1,3,2-dioxaborinane (65 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.155b** (58 mg, 88% yield) was obtained as a pale solid. mp 86-89 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2361, 2341, 1624, 1479, 1449, 1427, 1379, 1286, 1115, 975, 816, 750, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.25-8.15 (m, 1H), 7.92-7.85 (m, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.64-7.46 (m, 5H), 7.44-7.34 (m, 3H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 16.4 Hz, 1H), 4.00-3.79 (m, 1H), 3.30-3.10 (m, 2H), 3.09-2.95 (m, 1H), 1.10 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.85, 137.06, 136.15, 133.44, 133.35, 131.49, 131.28, 128.67 (2C), 128.41, 128.03, 128.00, 126.68, 126.59 (2C), 126.35, 125.26, 124.00, 123.36, 42.61, 38.73, 13.86, 12.64. MS EI *m/z* (rel. int.) 329 (M^+, 40), 258 (27), 257 (53), 256 (39), 229 (62), 228 (100), 227 (51), 226 (59), 105 (40), 78 (31), 77 (43), 57 (47), 56 (70); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{23}NO$, 329.1780, found 329.1770.

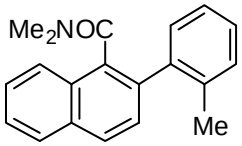
N,N-Dimethyl-2-phenyl-1-naphthamide (**3.160b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (69 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (86 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.160b** (82 mg, 99% yield) was obtained as a light yellow solid. mp 133-134 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1634, 1495, 1398, 765, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.97-7.83 (m, 3H), 7.59 (d, *J* = 7.1 Hz, 2H), 7.57-7.48 (m, 3H), 7.44 (t, *J* = 7.3 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 2.98 (s,

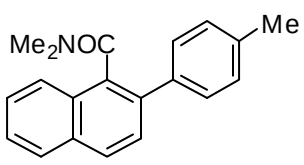
3H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.14, 140.14, 135.70, 132.60, 132.35, 129.91, 128.93, 128.86 (2C), 128.32 (2C), 127.95, 127.56, 127.28, 127.17, 126.29, 125.50, 37.68, 34.43. MS EI *m/z* (rel. int.) 275 (M^+, 22), 231 (100), 203 (13), 202 (31); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{17}NO$, 275.1310, found 275.1309.

2-(2-Methylphenyl)-N,N-dimethyl-1-naphthamide (**3.161b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(2-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.161b** (57 mg, 98% yield) was obtained as a light yellow solid. mp 108-109 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2926, 1637, 1508, 1494, 1448, 1400, 1264, 1193, 1124, 830, 762, 729 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.08-6.93 (m, 10H), 3.02-2.84 (m, 3H), 2.82-2.46 (m, 3H), 2.35-2.12 (m, 3H) (atropisomers involved); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.73, 169.60, 140.06, 138.77, 137.39, 136.40, 135.19, 134.81, 133.39, 133.29, 132.50, 132.39, 130.73, 130.20, 129.42, 128.20, 128.15, 128.00, 127.80, 127.69, 127.19, 127.05, 126.30, 126.21, 125.66, 125.56, 125.01, 124.69, 38.27, 37.72, 34.36, 34.12, 20.35, 20.25 (atropisomers involved). MS EI *m/z* (rel. int.) 289 (M^+, 5), 245 (91), 244 (64), 216 (34), 215 (100), 202 (65), 72 (35); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{19}NO$, 289.1467, found 289.1463.

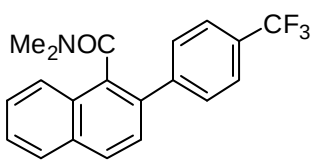
2-(4-Methylphenyl)-N,N-dimethyl-1-naphthamide (**3.162b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg,

0.2 mmol), 2-(4-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.162b** (57 mg, 99% yield) was obtained as a light yellow solid. mp 145-146 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2923, 1634, 1506, 1448, 1399, 1264, 1194, 1124, 812, 748, 730 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (d, *J* = 8.6 Hz, 1H), 7.88-7.83 (m, 2H), 7.58-7.44 (m, 5H), 7.24 (d, *J* = 7.9 Hz, 1H), 3.00 (s, 3H), 2.44 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.32, 137.32, 137.26, 135.75, 132.52, 132.18, 129.99, 129.09 (2C), 128.87, 128.74 (2C), 127.95, 127.42, 127.11, 126.16, 125.47, 37.71, 34.49, 21.18. MS EI *m/z* (rel. int.) 289 (M^+, 28), 245 (100), 215 (49), 202 (91); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{19}NO$, 289.1467, found 289.1465.

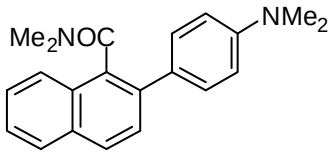
2-(4-(Trifluoromethyl)phenyl)-N,N-dimethyl-1-naphthamide (**3.163b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(4-(trifluoromethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (77 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.163b** (68 mg, 99% yield) was obtained as a light yellow solid. mp 184-186 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2931, 1635, 1619, 1507, 1402, 1325, 1166, 1125, 1082, 1062, 1019, 820, 754, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.94 (d, *J* = 8.5 Hz, 1H), 7.92-7.82 (m, 2H), 7.75-7.65 (m, 4H), 7.61-7.52 (m, 2H), 7.50 (d, *J* = 8.5 Hz, 1H), 3.00 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.74, 143.83, 134.15, 132.91, 132.89, 129.77, 129.72 (q, $^2J_{C-F}$ = 32.49 Hz), 129.27 (2C), 129.22, 128.08, 127.54, 126.83, 126.82, 125.52, 125.29 (q, $^3J_{C-F}$ = 3.69 Hz, 2C), 121.46 (q, $^1J_{C-F}$ = 272.03 Hz), 37.73, 34.49. MS EI *m/z* (rel. int.) 343 (M^+,

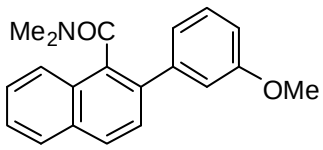
31), 299 (100), 251 (37), 202 (67), 69 (42); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{16}F_3NO$, 343.1184, found 343.1172.

2-(4-(Dimethylamino)phenyl)-N,N-dimethyl-1-naphthamide (**3.164b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(4-(dimethylamino)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (70 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.164b** (57 mg, 89% yield) was obtained as a light yellow solid. mp 156-157 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2923, 2890, 1633, 1610, 1527, 1506, 1445, 1398, 1360, 1199, 1125, 815, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.92-7.80 (m, 3H), 7.57-7.42 (m, 5H), 6.79 (d, J = 8.8 Hz, 2H), 3.03 (s, 3H), 3.01 (s, 6H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.74, 149.83, 135.97, 132.15, 131.37, 130.18, 129.65 (2C), 128.75, 127.97, 127.85, 127.45, 126.91, 125.71, 125.31, 112.18 (2C), 40.37, 37.67, 34.51. MS EI *m/z* (rel. int.) 318 (M^+, 68), 274 (100), 230 (25), 203 (28), 202 (87), 201 (22), 200 (20), 189 (23); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{22}N_2O$, 318.1732, found 318.1737.

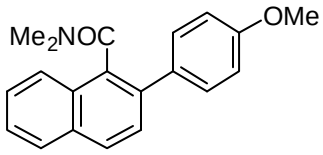
2-(3-Methoxyphenyl)-N,N-dimethyl-1-naphthamide (**3.165b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(3-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.165b** (61 mg, 99% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2933,

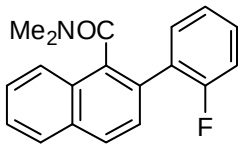
1633, 1611, 1596, 1581, 1509, 1490, 1465, 1399, 1290, 1261, 1222, 1046, 784, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, *J* = 8.5 Hz, 1H), 7.89-7.83 (m, 2H), 7.58-7.47 (m, 3H), 7.34 (t, *J* = 8.1 Hz, 1H), 7.19-7.13 (m, 2H), 6.96-6.89 (m, 1H), 3.85 (s, 3H), 3.00 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.17, 159.43, 141.57, 135.60, 132.66, 132.36, 129.90, 129.34, 128.91, 127.96, 127.21, 127.18, 126.32, 125.49, 121.27, 114.05, 113.66, 55.31, 37.76, 34.50. MS EI *m/z* (rel. int.) 305 (M^+, 28), 261 (100), 218 (27), 202 (32), 189 (71), 72 (17); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{19}NO_2$, 305.1416, found 305.1429.

2-(4-Methoxyphenyl)-N,N-dimethyl-1-naphthamide (**3.166b**, Table 3.22)



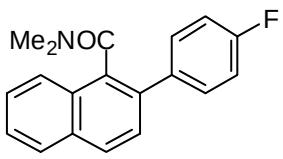
According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.166b** (60 mg, 98% yield) was obtained as a light yellow solid. mp 194-195 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2932, 1633, 1610, 1517, 1462, 1399, 1291, 1251, 1181, 1125, 1031, 821, 749, 730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.89 (d, *J* = 8.8 Hz, 1H), 7.87-7.82 (m, 2H), 7.55-7.46 (m, 5H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H), 3.00 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.39, 159.16, 135.39, 132.59, 132.42, 132.04, 130.07 (2C), 130.02, 128.87, 127.94, 127.36, 127.12, 126.09, 125.41, 113.81 (2C), 55.25, 37.68, 34.48. MS EI *m/z* (rel. int.) 305 (M^+, 36), 262 (31), 261 (100), 218 (23), 202 (25), 190 (28), 189 (87), 72 (29); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{19}NO_2$, 305.1416, found 305.1429.

2-(2-Fluorophenyl)-N,N-dimethyl-1-naphthamide (**3.167b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(2-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.167b** (58 mg, 99% yield) was obtained as a light yellow solid. mp 105-106 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2927, 1637, 1496, 1450, 1400, 1261, 1206, 1195, 806, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.93-7.87 (m, 2H), 7.87-7.80 (m, 1H), 7.60-7.46 (m, 4H), 7.41-7.31 (m, 1H), 7.24-7.12 (m, 2H), 2.96 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.50, 159.57 (d, $^1J_{C\text{-}F}$ = 246.3 Hz), 133.74, 132.87, 131.92 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 130.01, 129.88, 129.70 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 128.20, 128.08, 127.97 (d, $^4J_{C\text{-}F}$ = 2.3 Hz), 127.36 (d, $^2J_{C\text{-}F}$ = 14.9 Hz), 127.15, 126.61, 125.45, 124.00 (d, $^3J_{C\text{-}F}$ = 3.6 Hz), 115.49 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 37.76, 34.39. MS EI *m/z* (rel. int.) 293 (M^+, 28), 249 (96), 221 (38), 220 (100), 219 (20), 218 (22); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{16}FNO$, 293.1216, found 293.1230.

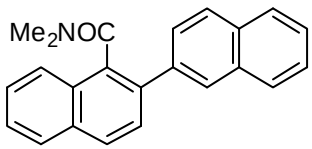
2-(4-Fluorophenyl)-N,N-dimethyl-1-naphthamide (**3.168b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.168b** (58 mg, 99% yield) was obtained as a light yellow solid. mp 103-104 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 3058, 2928, 1633, 1605, 1509, 1400, 1225, 1161, 823, 749, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, *J* = 8.5 Hz, 1H), 7.89-7.82 (m, 2H), 7.60-7.50 (m, 4H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.18-7.08 (m, 2H), 3.00 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm

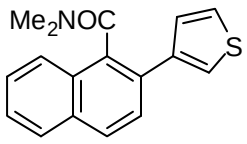
170.06, 162.43 (d, $^{1}J_{C\text{-}F}$ = 247.2 Hz), 136.19 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 134.61, 132.61, 132.48, 130.60 (d, $^{3}J_{C\text{-}F}$ = 8.1 Hz, 2C), 129.86, 129.02, 128.00, 127.33, 127.13, 126.43, 125.44, 115.42, 115.32 (d, $^{2}J_{C\text{-}F}$ = 21.4 Hz, 2C), 37.68, 34.46. MS EI *m/z* (rel. int.) 293 (M^+, 22), 249 (79), 221 (35), 220 (100), 219 (19), 218 (24); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{16}FNO$, 293.1216, found 293.1216.

2-(Naphthalen-2-yl)-N,N-dimethyl-1-naphthamide (**3.169b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.20 mmol), 2-(naphthalen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (64 mg, 0.26 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.169b** (57 mg, 88% yield) was obtained as a light yellow solid. mp 168-169 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 3055, 2938, 1631, 1504, 1400, 1265, 1194, 1125, 909, 819, 744, 731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.07 (d, *J* = 0.8 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.94-7.85 (m, 5H), 7.75 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.61-7.49 (m, 4H), 2.94 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.21, 137.66, 135.58, 133.29, 132.67, 132.66, 132.59, 130.03, 129.01, 128.32, 128.00, 127.96 (2C), 127.60, 127.54, 127.24, 126.94, 126.39, 126.25, 126.24, 125.56, 37.74, 34.49. MS EI *m/z* (rel. int.) 325 (M^+, 34), 282 (28), 281 (100), 253 (28), 252 (77), 250 (32), 72 (20); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{19}NO$, 325.1467, found 325.1468.

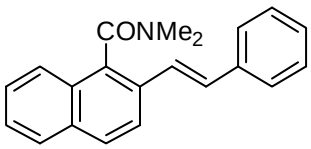
N,N-Dimethyl-2-(thiophen-3-yl)-1-naphthamide (**3.170b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2

mmol), 2-(thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (59 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.170b** (54 mg, 96% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2926, 1630, 1508, 1399, 1263, 1194, 1125, 1017, 800, 784, 748, 641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.88 (d, *J* = 8.5 Hz, 1H), 7.87-7.77 (m, 2H), 7.58 (d, *J* = 8.5 Hz, 1H), 7.56-7.46 (m, 3H), 7.41-7.34 (m, 2H), 3.08 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.50, 140.35, 132.54, 131.84, 130.30, 129.95, 128.87, 128.04, 127.97, 127.22, 126.72, 126.25, 125.65, 125.36, 123.45, 37.70, 34.59. MS EI *m/z* (rel. int.) 281 (M^+, 35), 238 (29), 237 (100), 209 (30), 208 (90), 165 (53), 164 (31), 163 (40); HRMS *m/z* (EI, M^+) calcd for $C_{17}H_{15}NOS$, 281.0874, found 281.0871.

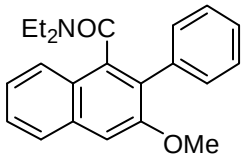
(*E*)-N,N-Dimethyl-2-styryl-1-naphthamide (**3.171b**, Table 3.22)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-2-methoxy-1-naphthamide (46 mg, 0.2 mmol), (*E*)-2-styryl-5,5-dimethyl-1,3,2-dioxaborinane (65 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.171b** (60 mg, 99% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 3057, 2928, 1633, 1510, 1496, 1449, 1399, 1263, 1190, 1123, 1023, 959, 909, 814, 742, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.87-7.79 (m, 3H), 7.71 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.57-7.44 (m, 4H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.27 (d, *J* = 16.4 Hz, 1H), 7.21 (d, *J* = 16.2 Hz, 1H), 3.33 (s, 3H), 2.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.22, 137.01, 132.95, 132.76, 131.54, 130.81, 129.75, 128.77, 128.68 (2C), 128.08, 128.03, 127.28, 126.76 (2C), 126.29, 125.13, 124.99, 122.57, 38.02, 34.62. MS EI *m/z* (rel. int.) 301 (M^+, 43), 257 (81), 256 (59), 229

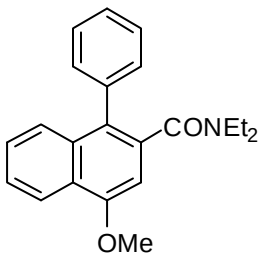
(70), 228 (100), 227 (51), 226 (78), 202 (35), 105 (70), 77 (67), 72 (33), 51 (38); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{19}NO$, 301.1467, found 301.1478.

N,N-Diethyl-3-methoxy-2-phenyl-1-naphthamide (**3.174b**, Table 3.23, entry 1)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-2,3-dimethoxy-1-naphthamide (58 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.174b** (66 mg, 99% yield) was obtained as a pale solid. mp 106-107 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2935, 1629, 1595, 1456, 1423, 1294, 1263, 1224, 1189, 1059, 762, 736, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.76 (t, *J* = 9.0 Hz, 2H), 7.60-7.43 (m, 3H), 7.42-7.30 (m, 4H), 7.23 (s, 1H), 3.87 (s, 3H), 3.86-3.77 (m, 1H), 3.16-2.90 (m, 2H), 2.78-2.59 (m, 1H), 0.74 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.33, 154.71, 135.69, 135.26, 134.23, 130.34, 128.49, 127.62 (2C), 127.44, 126.71 (3C), 125.50, 125.31, 124.50, 106.02, 55.70, 42.27, 37.70, 13.72, 11.76. MS EI *m/z* (rel. int.) 333 (M^+, 50), 332 (21), 262 (26), 261 (100), 246 (34), 189 (19); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO_2$, 333.1729, found 333.1732.

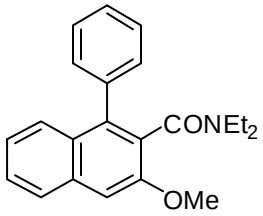
N,N-Diethyl-4-methoxy-1-phenyl-2-naphthamide (**3.175b**, Table 3.23, entry 2)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1,4-dimethoxy-2-naphthamide (58 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.175b** (66 mg, 99% yield) was obtained as a colorless oil. IR (KBr) ν_{max} 2971, 2934,

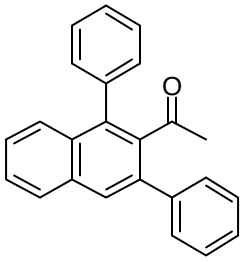
1630, 1593, 1477, 1459, 1431, 1375, 1344, 1272, 1104, 772, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.33 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.58-7.47 (m, 2H), 7.47-7.28 (m, 5H), 6.81 (s, 1H), 4.05 (s, 3H), 3.91-3.78 (m, 1H), 3.27-3.11 (m, 1H), 2.87-2.62 (m, 2H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.67 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.30, 155.19, 137.20, 134.03, 132.93, 131.48, 130.14, 128.58, 127.73, 127.32, 127.21, 126.97, 126.18, 125.51, 125.48, 121.90, 101.50, 55.64, 42.20, 37.69, 13.78, 11.65. MS EI *m/z* (rel. int.) 333 (M^+, 51), 318 (38), 262 (23), 261 (100), 246 (26), 189 (19); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO_2$, 333.1729, found 333.1720.

N,N-Diethyl-3-methoxy-1-phenyl-2-naphthamide (**3.176b**, Table 3.23, entry 3)



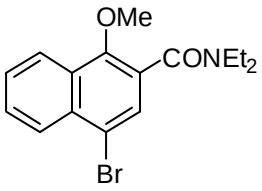
According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-1,3-dimethoxy-2-naphthamide (58 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.176b** (65 mg, 97% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2976, 2535, 1633, 1597, 1478, 1461, 1419, 1295, 1233, 1161, 1087, 754, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.78 (d, *J* = 8.1 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.47-7.42 (m, 2H), 7.41-7.35 (m, 2H), 7.30-7.22 (m, 2H), 7.21 (s, 1H), 3.97 (s, 3H), 3.93-3.80 (m, 1H), 3.24-3.10 (m, 1H), 2.86-2.70 (m, 2H), 0.93 (t, *J* = 7.1 Hz, 3H), 0.60 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.09, 153.35, 137.51, 136.71, 134.40, 131.10, 129.37, 128.46, 127.86, 127.59 (2C), 127.13, 126.78, 126.64, 126.50, 124.04, 105.39, 55.46, 42.20, 37.37, 13.27, 11.56. MS EI *m/z* (rel. int.) 333 (M^+, 22), 302 (15), 262 (18), 261 (100), 256 (14), 189 (12); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO_2$, 333.1729, found 333.1718.

1-(1,3-Diphenylnaphthalen-2-yl)ethanone (**3.179b**, Table 3.24, entry 2)



According to General Procedure B and using the following materials refluxed in 20 h: 1-(1-methoxynaphthalen-2-yl)ethanone (60 mg, 0.30 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (86 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.179b** (48 mg, 99% yield based on consideration of 50% ketone substrate reduced) was obtained as a colorless solid. mp 117-119 ^oC (EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.92 (d, *J* = 8.1 Hz, 1H), 7.87 (s, 1H), 7.62-7.32 (m, 13H), 1.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 206.07, 140.42, 140.04, 137.52, 136.13, 135.87, 133.04, 131.43, 130.61 (2C), 129.26 (2C), 128.77, 128.45 (2C), 128.18 (2C), 128.00, 127.83, 127.57, 126.93, 126.81, 126.64, 32.88. The physical and spectral data were consistent with those previously reported.[260]

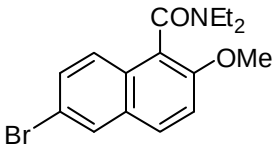
4-Bromo-N,N-diethyl-1-methoxy-2-naphthamide (**3.183**, Scheme 3.55)



According to General Procedure E and using the following materials stirred in 10 min: N,N-diethyl-1-methoxy-2-naphthamide (515 mg, 2.0 mmol), NH_4OAc (15 mg, 0.2 mmol), NBS (378 mg, 2.1 mmol) and MeCN (10 mL), the title compound **3.183** (650 mg, 97% yield) was obtained as a yellow oil.IR (KBr) ν_{max} 2973, 2935, 1634, 1592, 1476, 1454, 1429, 1361, 1324, 1278, 1255, 1220, 1132, 1083, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.20 (d, *J* = 9.1 Hz, 1H), 8.18 (d, *J* = 9.1 Hz, 1H), 7.68-7.51 (m, 3H), 4.00 (s, 3H), 3.86-3.69 (m, 1H), 3.53-3.35 (m, 1H), 3.32-3.08 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.49, 151.45, 132.97, 128.95, 128.19, 128.15, 127.41, 127.11, 126.25, 122.87, 117.54, 62.77, 43.15, 39.18,

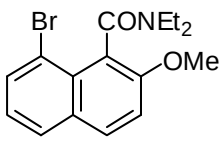
14.02, 12.74. MS EI *m/z* (rel. int.) 337 ($[M+2]^+$, 14), 335 (M^+, 17), 265 (89), 263 (87), 250 (24), 248 (25), 194 (26), 192 (30), 156 (23), 155 (24), 128 (30), 127 (23), 126 (65), 113 (62), 72 (31), 58 (34), 57 (100), 56 (100); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{16}H_{19}$ Br NO_2, 336.0599, found 336.0590.

6-Bromo-2-methoxy-N,N-diethyl-1-naphthamide (**3.187**, Scheme 3.55)



According to General Procedure E and using the following materials stirred in 3 h: N,N-diethyl-2-methoxy-1-naphthamide (258 mg, 1.00 mmol), NH_4OAc (7.7 mg, 0.10 mmol), NBS (189 mg, 1.05 mmol) and MeCN (5 mL), the title compound **3.187** as major isomer (241 mg, 72% yield) was obtained as a pale solid. mp 109-110 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2935, 1629, 1586, 1498, 1473, 1459, 1435, 1334, 1282, 1264, 1251, 1075, 887 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.94 (s, 1H), 7.75 (d, *J* = 9.1 Hz, 1H), 7.55-7.47 (m, 2H), 7.28 (d, *J* = 9.1 Hz, 1H), 3.93 (s, 3H), 3.86-3.72 (m, 1H), 3.70-3.53 (m, 1H), 3.18-2.98 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.23, 152.65, 130.52, 129.90, 129.78, 129.48, 129.16, 125.59, 120.69, 117.62, 113.95, 56.32, 42.79, 38.90, 13.99, 13.00. MS EI *m/z* (rel. int.) 337 ($[M+2]^+$, 22), 335 (M^+, 25), 265 (96), 263 (100), 126 (52), 113 (40), 57 (62), 56 (68); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{18}BrNO_2$, 335.0521, found 335.0525.

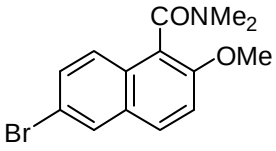
8-Bromo-2-methoxy-N,N-diethyl-1-naphthamide (**3.187i**, Scheme 3.55)



As minor isomer in the above reaction, the title compound **3.187i** (59 mg, 18% yield) was obtained as a pale solid. mp 86-88 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2934, 1634, 1595, 1506, 1459, 1429, 1263, 1090, 837, 824

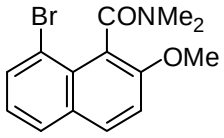
cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 (d, *J* = 9.0 Hz, 1H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 9.0 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 3.93 (s, 3H), 3.81-3.67 (m, 1H), 3.64-3.46 (m, 1H), 3.27-3.05 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.80, 155.01, 133.85, 131.29, 130.88, 129.05, 128.74, 124.12, 120.96, 117.96, 113.56, 56.56, 43.28, 39.09, 12.92, 11.94. MS EI *m/z* (rel. int.) 337 ($[M+2]^+$, 13), 335 (M^+, 11), 265 (100), 263 (96), 256 (83), 220 (27), 127 (25), 126 (23), 113 (25), 56 (40); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{18}BrNO_2$, 335.0521, found 335.0541.

6-Bromo-2-methoxy-N,N-dimethyl-1-naphthamide (**3.186**, Scheme 3.55)



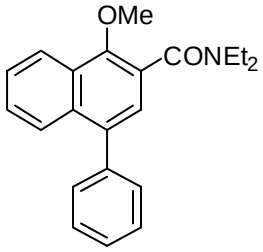
According to General Procedure E and using the following materials stirred in 4 h: N,N-dimethyl-2-methoxy-1-naphthamide (459 mg, 2.0 mmol), NH_4OAc (15 mg, 0.2 mmol), NBS (378 mg, 2.1 mmol) and MeCN (10 mL), the title compound **3.186** as major isomer (314 mg, 51% yield) was obtained as a pale solid. mp 124-125 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2936, 1636, 1586, 1499, 1411, 1391, 1352, 1333, 1274, 1253, 1186, 1176, 1133, 1073, 1019, 903, 818 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.94 (s, 1H), 7.76 (d, *J* = 9.1 Hz, 1H), 7.56-7.45 (m, 2H), 7.29 (d, *J* = 9.1 Hz, 1H), 3.94 (s, 3H), 3.24 (s, 3H), 2.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.09, 152.81, 130.64, 129.94, 129.81, 129.42, 129.28, 125.67, 120.18, 117.69, 113.90, 56.44, 37.75, 34.61. MS EI *m/z* (rel. int.) 309 ($[M+2]^+$, 22), 307 (M^+, 28), 265 (100), 263 (100), 222 (17), 220 (15), 194 (19), 192 (15), 126 (65), 114 (24), 113 (52), 72 (51); HRMS *m/z* (EI, M^+) calcd for $C_{14}H_{14}BrNO_2$, 307.0208, found 307.0202.

8-Bromo-2-methoxy-N,N-dimethyl-1-naphthamide (**3.190**, Scheme 3.56)



As minor isomer in the above reaction, the title compound **3.190** (196 mg, 32% yield) was obtained as a light yellow solid. mp 125-126 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2936, 1638, 1613, 1595, 1506, 1457, 1429, 1395, 1331, 11263, 1187, 1129, 1089, 1050, 1017, 824 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 (d, *J* = 9.1 Hz, 1H), 7.80 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.32 (d, *J* = 9.1 Hz, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 3.95 (s, 3H), 3.16 (s, 3H), 2.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.58, 154.80, 133.85, 131.44, 130.87, 129.03, 128.75, 124.20, 120.27, 117.38, 113.59, 56.82, 38.40, 35.04. MS EI *m/z* (rel. int.) 309 ($[M+2]^+$, 6), 307 (M^+, 6), 265 (79), 263 (80), 228 (100), 220 (23), 126 (44), 113 (38), 72 (33); HRMS *m/z* (EI, M^+) calcd for $C_{14}H_{14}BrNO_2$, 307.0208, found 307.0202.

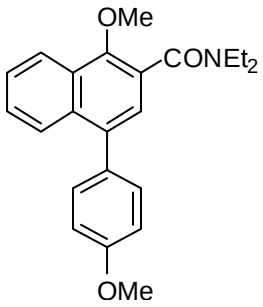
N,N-Diethyl-1-methoxy-4-phenyl-2-naphthamide (**3.184**, Scheme 3.55)



According to General Procedure F and using the following materials: 4-bromo-N,N-diethyl-1-methoxy-2-naphthamide (135 mg, 0.4 mmol), phenylboronic acid (73 mg, 0.6 mmol), a degassed 2 M aqueous solution of Na_2CO_3 (0.6 mL, 1.2 mmol) and $Pd(PPh_3)_4$ (9 mg, 2 mol%) and toluene (0.6 mL), the title compound **3.184** (133 mg, 99% yield) was obtained as a colorless solid. mp 102-103 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2935, 1631, 1476, 1457, 1429, 1369, 1271, 1221, 1082, 777, 755, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.26 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.52-7.37 (m, 6H), 7.29 (s, 1H), 4.07 (s, 3H), 3.89-3.70 (m, 1H), 3.57-3.41 (m, 1H), 3.40-3.15 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.86, 151.11, 139.84, 136.61, 132.94, 130.02 (2C), 128.22 (2C), 127.97, 127.30, 126.81, 126.33, 126.16, 125.49, 125.25, 122.61, 62.70,

43.16, 39.09, 14.08, 12.80. MS EI *m/z* (rel. int.) 333 (M^+, 28), 261 (100), 202 (32), 190 (27), 189 (71), 57 (32); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{23}NO_2$, 333.1729, found 333.1737.

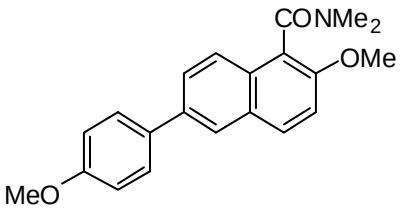
N,N-Diethyl-1-methoxy-4-(4-methoxyphenyl)-2-naphthamide (**3.185**, Scheme 3.55)



According to General Procedure F and using the following materials: 4-bromo-N,N-diethyl-1-methoxy-2-naphthamide (135 mg, 0.4 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol), a degassed 2 M aqueous solution of Na_2CO_3 (0.6 mL, 1.2 mmol) and $Pd(PPh_3)_4$ (9 mg, 2 mol%) and toluene (0.6 mL), the title compound **3.185** (143 mg, 99% yield) was obtained as a light yellow solid. mp 129-130 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2972, 2935, 1632, 1610, 1515, 1476, 1458, 1430, 1370, 1272, 1248, 1222, 1177, 1062, 1033, 839, 773 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.23 (d, *J* = 8.3 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 8.6 Hz, 2H), 7.25 (s, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 4.05 (s, 3H), 3.88 (s, 3H), 3.85-3.73 (m, 1H), 3.57-3.39 (m, 1H), 3.37-3.11 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.07 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.95, 158.97, 150.88, 136.34, 133.18, 132.22, 131.10 (2C), 128.02, 126.73, 126.41, 126.13, 125.42, 125.35, 122.61, 113.71 (2C), 62.74, 55.32, 43.17, 39.09, 14.11, 12.83. MS EI *m/z* (rel. int.) 363 (M^+, 36), 291 (100), 205 (24), 189 (47), 177 (27), 176 (33), 56 (33); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{25}NO_3$, 363.1834, found 363.1834.

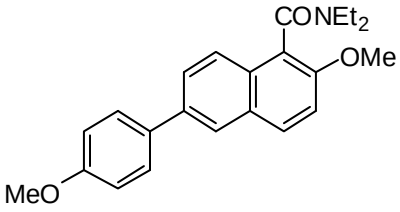
2-Methoxy-6-(4-methoxyphenyl)-N,N-dimethyl-1-naphthamide (**3.188**, Scheme 3.55)

According to General Procedure F and using the following materials: 6-bromo-N,N-dimethyl-2-methoxy-1-naphthamide (123 mg, 0.4 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol),



a degassed 2 M aqueous solution of Na_2CO_3 (0.6 mL, 1.2 mmol) and $Pd(PPh_3)_4$ (9 mg, 2 mol%) and toluene (0.6 mL), the title compound **3.188** (129 mg, 96% yield) was obtained as a light yellow solid. mp 187-188 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1621, 1503, 1455, 1394, 1284, 1258, 1190, 1136, 1071, 1043, 1029, 841, 817, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (s, 1H), 7.89 (d, *J* = 9.0 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 3.96 (s, 3H), 3.86 (s, 3H), 3.28 (s, 3H), 2.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.66, 159.12, 152.45, 136.36, 133.27, 130.44, 129.60, 129.14, 128.16 (2C), 126.94, 125.02, 124.34, 119.88, 114.27 (2C), 113.28, 56.46, 55.32, 37.82, 34.58. MS EI *m/z* (rel. int.) 335 (M^+, 41), 291 (100), 233 (22), 189 (24), 176 (23); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{21}H_{22}NO_3$, 336.1599, found 336.1588.

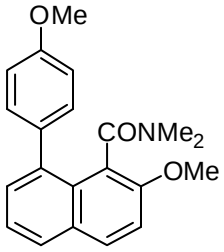
2-Methoxy-6-(4-methoxyphenyl)-N,N-diethyl-1-naphthamide (**3.189**, Scheme 3.55)



According to General Procedure F and using the following materials: 6-bromo-N,N-diethyl-2-methoxy-1-naphthamide (123 mg, 0.4 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol), a degassed 2 M aqueous solution of Na_2CO_3 (0.6 mL, 1.2 mmol) and $Pd(PPh_3)_4$ (9 mg, 2 mol%) and toluene (0.6 mL), the title compound **3.189** (139 mg, 96% yield) was obtained as a light yellow solid. mp 118-120 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2936, 1630, 1519, 1499, 1461, 1439, 1285, 1255, 1177, 1075, 1033, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (s, 1H), 7.88 (d, *J* = 9.0 Hz, 1H), 7.76-7.66 (m, 2H), 7.63 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 3.95 (s, 3H), 3.92-

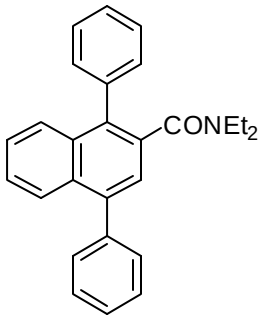
3.80 (m, 1H), 3.87 (s, 3H), 3.67-3.55 (m, 1H), 3.21-3.06 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.80, 159.12, 152.32, 136.30, 133.33, 130.18, 129.83, 129.13, 128.17 (2C), 126.86, 125.00, 124.30, 120.43, 114.28 (2C), 113.33, 56.36, 55.35, 42.83, 38.83, 14.04, 13.08. MS EI *m/z* (rel. int.) 363 (M^+, 39), 291 (100), 276 (15), 233 (24), 189 (25); HRMS *m/z* (EI, M^+) calcd for $C_{23}H_{25}NO_3$, 363.1834, found 363.1830.

2-Methoxy-8-(4-methoxyphenyl)-N,N-dimethyl-1-naphthamide (**3.191**, Scheme 3.56)



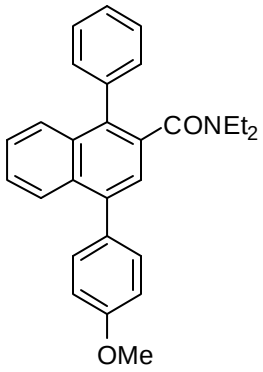
According to General Procedure F and using the following materials: 8-bromo-N,N-dimethyl-2-methoxy-1-naphthamide (123 mg, 0.4 mmol), 4-methoxyphenylboronic acid (91 mg, 0.6 mmol), a degassed 2 M aqueous solution of Na_2CO_3 (0.6 mL, 1.2 mmol) and $Pd(PPh_3)_4$ (9 mg, 2 mol%) and toluene (0.6 mL), the title compound **3.191** (60 mg, 44% yield) was obtained as a light yellow solid. mp 96-98 ^{o}C (EtOAc/hexanes); IR (KBr) ν_{max} 2933, 1635, 1611, 1593, 1509, 1457, 1439, 1432, 1397, 1289, 1259, 1244, 1183, 1117, 1090, 1047, 1034, 1022, 829, 730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (d, *J* = 9.0 Hz, 1H), 7.78 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.47 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.33 (dd, *J* = 8.0, 7.1 Hz, 1H), 7.28 (d, *J* = 9.0 Hz, 1H), 7.22 (dd, *J* = 7.0, 1.3 Hz, 1H), 7.08 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.96 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.86 (dd, *J* = 8.3, 2.72 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 2.64 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 167.74, 158.58, 154.03, 138.41, 133.74, 132.40, 131.11, 131.10, 129.97, 129.65, 129.30, 128.13, 123.12, 120.55, 113.03, 112.26, 112.21, 56.79, 55.28, 37.82, 33.68. MS EI *m/z* (rel. int.) 335 (M^+, 36), 291 (100), 276 (50), 205 (49), 189 (33), 176 (34), 72 (60); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{21}NO_3$, 335.1521, found 335.1504.

N,N-Diethyl-1,4-diphenyl-2-naphthamide (**3.184b**, Scheme 3.55)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-4-phenyl-1-methoxy-2-naphthamide (33 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.184b** (37 mg, 98% yield) was obtained as a light yellow solid. mp 111-113 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2932, 1631, 1475, 1460, 1430, 1380, 1272, 1106, 772, 754, 733, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.96 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.76 (dd, *J* = 7.1, 1.9 Hz, 1H), 7.61 (d, *J* = 7.3 Hz, 1H), 7.58-7.32 (m, 12H), 3.88-3.70 (m, 1H), 3.31-3.12 (m, 1H), 2.94-2.68 (m, 2H), 0.91 (t, *J* = 7.1 Hz, 3H), 0.71 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.07, 140.47, 140.07, 137.23, 134.97, 133.82, 132.40, 131.69, 131.28, 130.04 (2C), 129.81, 128.65, 128.31 (2C), 127.66, 127.49, 127.35, 126.85, 126.34, 126.27, 126.18, 124.20, 42.39, 37.86, 13.80, 11.76. MS EI *m/z* (rel. int.) 379 (M^+, 32), 378 (22), 308 (33), 307 (100), 278 (35), 277 (43), 276 (59), 202 (30), 77 (50), 57 (46), 56 (65); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{27}H_{26}NO$, 380.2014, found 380.1997.

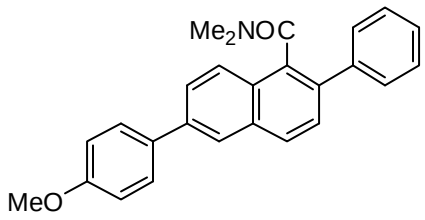
N,N-Diethyl-4-(4-methoxyphenyl)-1-phenyl-2-naphthamide (**3.185b**, Scheme 3.55)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-4-(4-methoxyphenyl)-1-methoxy-2-naphthamide (36 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.185b** (40 mg, 98% yield) was obtained as a light yellow solid. mp 126-128 ^oC (EtOAc/hexanes); IR

(KBr) ν_{max} 2972, 1631, 1610, 1515, 1505, 1475, 1460, 1433, 1380, 1290, 1272, 1247, 1178, 1107, 1033, 838, 771, 733, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.99 (d, *J* = 7.4 Hz, 1H), 7.75 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.55-7.30 (m, 9H), 7.06 (d, *J* = 8.5 Hz, 2H), 3.91 (s, 3H), 3.85-3.71 (m, 1H), 3.33-3.11 (m, 1H), 2.94-2.67 (m, 2H), 0.91 (t, *J* = 7.0 Hz, 3H), 0.70 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.14, 159.11, 140.15, 137.29, 134.64, 133.84, 132.44, 132.41, 131.89, 131.29, 131.12 (2C), 129.83, 128.64, 127.61, 127.33, 126.83, 126.27, 126.22, 126.16, 124.16, 113.78 (2C), 55.33, 42.37, 37.83, 13.79, 11.75. MS/MS ESI *m/z* (rel. int.) 410 ($[M+1]^+$, 100), 337 (77), 100 (49), 72 (19); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{28}H_{28}NO_2$, 410.2120, found 410.2109.

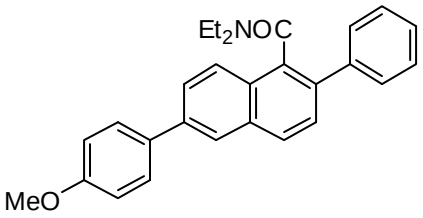
2-Phenyl-6-(4-methoxyphenyl)-N,N-dimethyl-1-naphthamide (**3.188b**, Scheme 3.55)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-dimethyl-6-(4-methoxyphenyl)-2-methoxy-1-naphthamide (34 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.188b** (37 mg, 98% yield) was obtained as a light yellow solid. mp 171-173 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2931, 1632, 1609, 1519, 1463, 1445, 1401, 1285, 1247, 1182, 1028, 826, 789, 761, 730, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.03 (s, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 7.1 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 8.6 Hz, 2H), 3.88 (s, 3H), 3.00 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.17, 159.38, 140.18, 138.59, 135.47, 133.10, 133.02, 132.23, 129.08, 128.86 (2C), 128.82, 128.36 (4C),

127.69, 127.57, 126.68, 126.05, 124.95, 114.35 (2C), 55.36, 37.72, 34.48. MS EI *m/z* (rel. int.) 381 (M^+, 60), 338 (28), 337 (100), 319 (25), 276 (25), 265 (37), 263 (43), 239 (24), 169 (21), 132 (24), 77 (32), 72 (27); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{26}H_{24}NO_2$, 382.1807, found 382.1822.

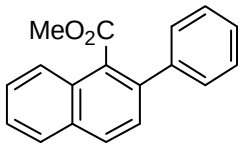
2-Phenyl-6-(4-methoxyphenyl)-N,N-diethyl-1-naphthamide (**3.189b**, Scheme 3.55)



According to General Procedure B and using the following materials refluxed in 20 h: N,N-diethyl-6-(4-methoxyphenyl)-2-methoxy-1-naphthamide (36 mg, 0.10 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.189b** (40 mg, 97% yield) was obtained as a light yellow solid. mp 147-148 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2973, 2933, 1625, 1519, 1494, 1460, 1440, 1284, 1269, 1248, 1181, 1034, 836, 825, 789, 760, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.02 (s, 1H), 7.94 (d, *J* = 7.4 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.1 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.42 (t, *J* = 7.0 Hz, 2H), 7.36(t, *J* = 7.0 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 3.88 (s, 1H), 3.86-3.75 (m, 1H), 3.33-3.12 (m, 1H), 3.04-2.87 (m, 1H), 2.75-2.59 (m, 1H), 1.00 (t, *J* = 7.0 Hz, 3H), 0.65 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.29, 159.36, 140.11, 138.46, 135.07, 133.11, 133.00, 132.70, 129.28 (2C), 129.04, 128.79, 128.33 (2C), 128.24 (2C), 127.75, 127.48, 126.52, 126.11, 124.91, 114.33 (2C), 55.36, 42.43, 38.30, 13.62, 12.12. MS EI *m/z* (rel. int.) 409 (M^+, 46), 338 (32), 337 (100), 265 (41), 263 (38), 239 (41), 202 (45), 77 (40), 72 (47), 56 (42); HRMS *m/z* (EI, M^+) calcd for $C_{28}H_{27}NO_2$, 409.2042, found 409.2018.

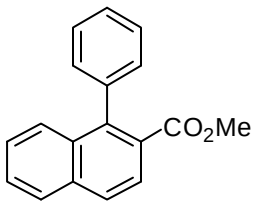
Ester-Directed C-O Activation/C-C Bond Formation. Synthesis of Compounds 3.180b-3.181b, 3.196b-3.210b

Methyl 2-phenyl-1-naphthoate (**3.180b**, Table 3.25, entry 2)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.180b** (50 mg, 96% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.03-7.94 (m, 2H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.64-7.31 (m, 8H), 3.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.00, 140.86, 138.01, 132.26, 129.92, 129.89, 128.46 (2C), 128.40 (2C), 128.09, 127.56, 127.43, 127.37, 126.30, 125.03, 52.15 (1C not observed). MS EI *m/z* (rel. int.) 262 (M^+, 62), 232 (24), 231 (100), 230 (21), 203 (26), 202 (72), 201 (22). The physical and spectral data were consistent with those previously reported.[258]

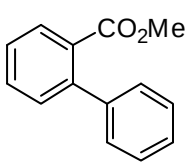
Methyl 1-phenyl-2-naphthoate (**3.181b**, Table 3.25, entry 3)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 1-methoxy-2-naphthoate (43 mg, 0.2 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (57 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.181b** (20 mg, 39% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.97-7.86 (m, 3H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.56 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.52-7.39 (m, 4H), 7.31 (dd, *J* = 7.7, 1.5 Hz, 2H), 3.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm

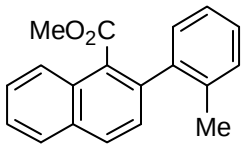
168.68, 141.53, 138.96, 134.72, 132.55, 129.54 (2C), 127.98, 127.84 (3C), 127.77, 127.68, 127.41, 127.29, 126.54, 125.40, 51.91. The physical and spectral data were consistent with those previously reported.[316]

Methyl biphenyl-2-carboxylate (**3.196b**, Table 3.25, entry 5)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-(dimethylamino)benzoate (36 mg, 0.20 mmol), 2-phenyl-5,5-dimethyl-1,3,2-dioxaborinane (40 mg, 0.21 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.196b** (30 mg, 72% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.82 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.53 (td, *J* = 7.5, 1.2 Hz, 1H), 7.44-7.29 (m, 7H), 3.63 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.12, 142.44, 141.27, 131.22, 130.83, 130.67, 129.73, 128.27, 128.01 (2C), 127.19 (2C), 127.12, 51.90. The physical and spectral data were consistent with those reported.[317]

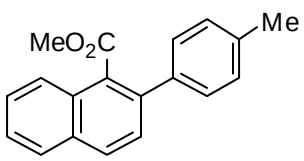
Methyl 2-*o*-tolyl-1-naphthoate (**3.197b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(2-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.197b** (50 mg, 90% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2949, 1727, 1492, 1435, 1279, 1256, 1234, 1137, 1031, 1018, 827, 760, 728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.97 (d, *J* = 7.8 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.92 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.62-7.51 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.32-7.26 (m, 2H), 7.25-7.17 (m, 2H), 3.59 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (101

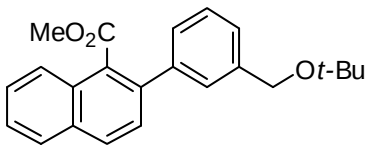
MHz, $CDCl_3$) δ ppm 169.41, 140.19, 138.30, 136.02, 132.26, 130.54, 129.88, 129.83, 129.42, 129.12, 128.13, 127.75, 127.46, 127.32, 126.26, 125.24, 125.11, 51.85, 20.16. MS EI *m/z* (rel. int.) 276 (M^+, 40), 245 (71), 244 (24), 217 (28), 216 (51), 215 (100), 213 (24), 202 (41), 189 (19); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{16}O_2$, 276.1150, found 276.1150.

Methyl 2-*p*-tolyl-1-naphthoate (**3.198b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(4-methylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (61 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.198b** (51 mg, 92% yield) was obtained as a colorless solid. mp 109-111 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2948, 1725, 1504, 1435, 1286, 1234, 1148, 1137, 1032, 813, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.94 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 7.8 Hz, 1H), 7.59-7.46 (m, 3H), 7.38 (d, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 3.73 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.17, 137.93, 137.89, 137.34, 132.17, 129.98, 129.85, 129.76, 129.17 (2C), 128.34 (2C), 128.08, 127.50, 127.35, 126.18, 124.98, 52.17, 21.19. MS EI *m/z* (rel. int.) 276 (M^+, 75), 245 (100), 244 (29), 215 (50), 202 (81); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{16}O_2$, 276.1150, found 276.1165.

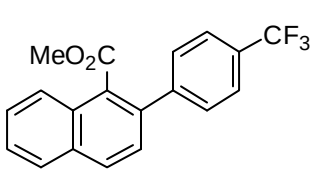
Methyl 2-(3-(*tert*-butoxymethyl)phenyl)-1-naphthoate (**3.199b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (22 mg, 0.10 mmol), 2-(3-(*t*-butoxymethyl)phenyl)-5,5-dimethyl-

1,3,2-dioxaborinane (42 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (4 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.199b** (33 mg, 93% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 1724, 1435, 1363, 1235, 1193, 1138, 1072, 1032, 790, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.97 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.90 (dd, *J* = 7.8, 1,0 Hz, 1H), 7.61-7.50 (m, 3H), 7.49 (s, 1H), 7.45-7.33 (m, 3H), 4.51 (s, 2H), 3.72 (s, 3H), 1.32 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.05, 140.73, 140.25, 138.04, 132.27, 129.98, 129.87, 128.38, 128.09, 127.56, 127.47, 127.38, 127.27, 126.62, 126.25, 125.05, 73.51, 63.99, 52.24, 27.69 (3C) (1C not observed). MS EI *m/z* (rel. int.) 348 (M^+, 28), 275 (23), 245 (36), 231 (54), 215 (44), 203 (30), 202 (100), 201 (29), 200 (33), 189 (25), 57 (50); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{12}O_3$, 348.1725, found 348.1730.

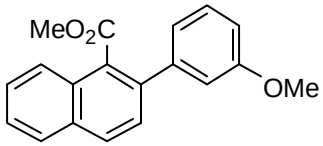
Methyl 2-(4-(trifluoromethyl)phenyl)-1-naphthoate (**3.200b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(4-(trifluoromethyl)phenyl)-5,5-dimethyl-1,3,2-dioxaborinane (77 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.200b** (57 mg, 86% yield) was obtained as a colorless solid. mp 74-76 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1728, 1325, 1237, 1167, 1125, 1114, 1085, 1064, 1022, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.04-7.95 (m, 2H), 7.92 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.71 (d, *J* = 8.1 Hz, 2H), 7.65-7.54 (m, 4H), 7.49 (d, *J* = 8.5 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.55, 144.57, 144.56, 136.52, 132.60, 130.25, 129.89, 129.76 (q, $^2J_{C-F}$ = 32.52 Hz), 128.90, 128.18, 127.75, 126.84, 126.79, 125.35 (q, $^3J_{C-F}$ = 3.74 Hz, 2C), 125.17, 124.17 (q,

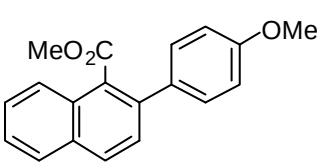
$^1J_{C\text{-}F}$ = 272.07 Hz), 52.28. MS EI *m/z* (rel. int.) 330 (M^+, 62), 299 (100), 251 (29), 202 (65), 69 (65); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{13}F_3O_2$, 330.0868, found 330.0848.

Methyl 2-(3-methoxyphenyl)-1-naphthoate (**3.201b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(3-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.201b** (53 mg, 90% yield) was obtained as a colorless viscous oil. IR (KBr) ν_{max} 1723, 1608, 1595, 1582, 1466, 1435, 1293, 1236, 1138, 1047, 1032, 787 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.96 (d, *J* = 8.1 Hz, 2H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.63-7.48 (m, 3H), 7.36 (t, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.05 (s, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 3.85 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.00, 159.55, 142.22, 137.82, 132.32, 129.89 (3C), 129.43, 128.09, 127.43, 127.26, 126.33, 125.02, 120.95, 113.86, 113.45, 55.25, 52.23. MS EI *m/z* (rel. int.) 292 (M^+, 75), 261 (94), 260 (29), 218 (28), 202 (34), 190 (25), 189 (100), 188 (25); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{16}O_3$, 292.1099, found 292.1092.

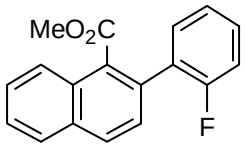
Methyl 2-(4-methoxyphenyl)-1-naphthoate (**3.202b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (66 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.202b** (51 mg, 86% yield) was obtained as a light yellow solid. mp 115-116 ^oC

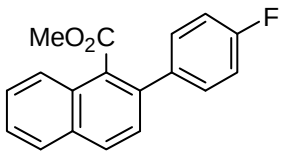
(EtOAc/hexanes); IR (KBr) ν_{max} 1724, 1610, 1518, 1504, 1463, 1435, 1292, 1242, 1180, 1137, 1032, 821, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.94 (d, *J* = 8.3 Hz, 2H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.61-7.47 (m, 3H), 7.43 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.24, 159.19, 137.54, 133.20, 132.06, 129.99, 129.82, 129.63 (3C), 128.07, 127.51, 127.36, 126.11, 124.90, 113.91 (2C), 55.27, 52.20. MS EI *m/z* (rel. int.) 292 (M^+, 55), 261 (93), 260 (28), 218 (21), 202 (19), 190 (31), 189 (100); HRMS *m/z* (EI, M^+) calcd for $C_{19}H_{16}O_3$, 292.1099, found 292.1089.

Methyl 2-(2-fluorophenyl)-1-naphthoate (**3.203b**, Table 3.26)



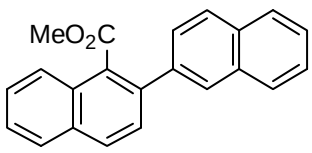
According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(2-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.5 mL), the title compound **3.203b** (50 mg, 88% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 1725, 1497, 1464, 1450, 1435, 1276, 1236, 1213, 1139, 1034, 1018, 827, 809, 759 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.06 (d, *J* = 7.9 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.91 (dd, *J* = 7.4, 1.73 Hz, 1H), 7.64-7.53 (m, 2H), 7.51 (dd, *J* = 8.5, 1.34 Hz, 1H), 7.43-7.32 (m, 2H), 7.24-7.12 (m, 2H), 3.70 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.17, 159.56 (d, J_{C-F}= 247.0 Hz, 1C), 132.67, 132.56, 131.05 (d, J_{C-F} = 3.1 Hz, 1C), 130.71, 130.04, 129.87, 129.63 (d, J_{C-F} = 8.0 Hz, 1C), 128.36 (d, J_{C-F} = 15.7 Hz, 1C), 128.14, 127.75 (d, J_{C-F} = 1.4 Hz, 1C), 127.44, 126.61, 125.31, 123.96 (d, J_{C-F} = 3.7 Hz, 1C), 115.64 (d, J_{C-F} = 22.1 Hz, 1C), 52.07. MS EI *m/z* (rel. int.) 280 (M^+, 69), 249 (99), 221 (37), 220 (100); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{13}FO_2$, 280.0900, found 280.0907.

Methyl 2-(4-fluorophenyl)-1-naphthoate (**3.204b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(4-fluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (62 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.204b** (51 mg, 90% yield) was obtained as a light yellow solid. mp 113-114 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 1726, 1606, 1514, 1505, 1435, 1266, 1235, 1161, 1138, 1032, 1020, 852, 844, 821, 809, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.02-7.93 (m, 2H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.63-7.52 (m, 2H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.47-7.41 (m, 2H), 7.14 (t, *J* = 8.7 Hz, 2H), 3.73 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.88, 162.44 (d, J_{C-F} = 247.1 Hz,1C), 136.87, 136.84, 132.28, 130.17 (d, J_{C-F} = 8.1 Hz,1C),130.03, 129.98, 129.89, 128.12, 127.55, 127.22, 126.43, 125.01, 115.38 (d, J_{C-F} = 21.5 Hz,1C), 52.21. MS EI *m/z* (rel. int.) 280 (M^+,62), 249 (100), 221 (36), 220 (93); HRMS *m/z* (EI, M^+) calcd for $C_{18}H_{13}FO_2$, 280.0900, found 280.0887.

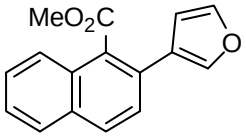
Methyl 2-(naphthalen-2-yl)-1-naphthoate (**3.205b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(naphthalen-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (72 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.5 mL), the title compound **3.205b** (59 mg, 94% yield) was obtained as a pale solid. mp 139-140 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 3056, 1724, 1504, 1434, 1238, 1137, 1032, 820, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.03 (d, *J* = 7.5 Hz, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 1.2 Hz, 1H), 7.96-7.87 (m, 4H), 7.68-7.49 (m, 6H), 3.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.03,

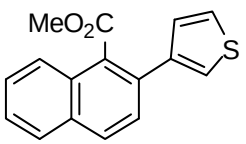
138.31, 137.93, 133.32, 132.58, 132.33, 130.15, 130.04, 129.99, 128.18, 128.14, 128.08, 127.68, 127.59, 127.50 (2C), 126.60, 126.38 (2C), 126.23, 125.08, 52.21. MS EI *m/z* (rel. int.) 312 (M^+, 78), 282 (20), 281 (94), 280 (24), 253 (36), 252 (100), 250 (53), 126 (37), 125 (20); HRMS *m/z* (EI, M^+) calcd for $C_{22}H_{16}O_2$, 312.1150, found 312.1156.

Methyl 2-(furan-3-yl)-1-naphthoate (**3.206b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), 2-(furan-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (54 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.206b** (16 mg, 31% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2951, 1769, 1726, 1605, 1509, 1435, 1238, 1152, 1139, 1033, 1019, 829, 752, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.91 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.67 (s, 1H), 7.59-7.46 (m, 4H), 6.64 (d, *J* = 0.8 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.35, 143.34, 140.11, 132.19, 129.93, 129.84, 129.42, 128.08, 127.91, 127.42, 126.54, 126.26, 124.90, 124.79, 110.56, 52.50. MS EI *m/z* (rel. int.) 252 (M^+, 93), 224 (51), 221 (25), 181 (25), 165 (100), 164 (61), 163 (69), 153 (48), 152 (41), 139 (40), 87 (28), 63 (36), 50 (35); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{12}O_3$, 252.0786, found 252.0786.

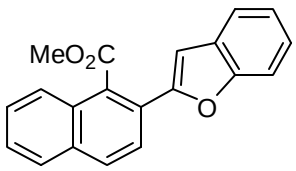
Methyl 2-(thiophen-3-yl)-1-naphthoate (**3.207b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (22 mg, 0.10 mmol), 2-(thiophen-3-yl)-5,5-dimethyl-1,3,2-dioxaborinane (29 mg, 0.15 mmol),

$RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.207b** (20 mg, 73% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 1725, 1435, 1280, 1236, 1137, 1031, 798, 780, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (d, *J* = 8.5 Hz, 1H), 7.91-7.84 (m, 2H), 7.61-7.49 (m, 3H), 7.45-7.38 (m, 2H), 7.28 (dd, *J* = 4.6, 1.7 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.29, 140.94, 132.26, 132.16, 129.91, 129.82, 129.69, 128.10, 127.98, 127.46, 126.99, 126.31, 125.92, 124.92, 123.01, 52.41. MS EI *m/z* (rel. int.) 268 (M^+, 43), 237 (56), 209 (24), 208 (83), 165 (66), 164 (47), 163 (100), 162 (25), 152 (25), 151 (31), 150 (30), 139 (36), 126 (22), 87 (23), 86 (21), 75 (22), 74 (23), 63 (27); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{12}O_2S$, 268.0558, found 268.0561.

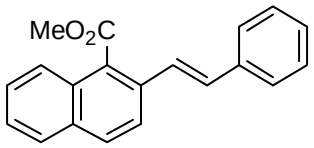
Methyl 2-(benzofuran-2-yl)-1-naphthoate (**3.208b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (22 mg, 0.10 mmol), 2-(benzofuran-2-yl)-5,5-dimethyl-1,3,2-dioxaborinane (35 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.4 mL), the title compound **3.208b** (28 mg, 91% yield) was obtained as a light yellow solid. mp 111-112 °C (EtOAc/hexanes); IR (KBr) ν_{max} 1731, 1449, 1434, 1278, 1257, 1238, 1176, 1138, 1079, 1032, 809, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.96 (d, *J* = 8.7 Hz, 1H), 7.93-7.83 (m, 3H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.61-7.49 (m, 3H), 7.33 (td, *J* = 7.7, 1.30 Hz, 1H), 7.27 (td, *J* = 7.4, 0.9 Hz, 1H), 7.10 (s, 1H), 4.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.01, 155.16, 154.19, 132.92, 129.98, 129.90, 128.79, 128.62, 128.13, 127.70, 126.97, 125.20, 125.15, 124.88, 124.11, 123.15, 121.29, 111.17, 104.85, 52.74. MS EI *m/z* (rel. int.) 302 (M^+, 92), 271 (44), 231 (31), 215

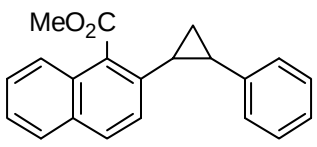
(75), 214 (28), 213 (100), 202 (34), 189 (29), 187 (33), 163 (26), 126 (47), 63 (30); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{14}O_3$, 302.0943, found 302.0930.

(*E*)-Methyl 2-styryl-1-naphthoate (**3.209b**, Table 3.26)



According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (43 mg, 0.2 mmol), (*E*)-2-styryl-5,5-dimethyl-1,3,2-dioxaborinane (65 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.5 mL), the title compound **3.209b** (42 mg, 73% yield) was obtained as a light yellow solid. mp 68-71 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 3058, 2950, 1726, 1509, 1448, 1435, 1283, 1251, 1229, 1215, 1160, 1136, 1035, 957, 8133, 741, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.90 (d, *J* = 8.7 Hz, 1H), 7.86-7.79 (m, 3H), 7.58-7.47 (m, 4H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 16.0 Hz, 1H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.24 (d, *J* = 16.3 Hz, 1H), 4.11 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 169.89, 136.98, 132.54, 132.51, 132.02, 130.12, 129.97, 129.83, 128.73 (2C), 128.14, 128.09, 127.37, 126.79 (2C), 126.28, 125.47, 125.07, 122.66, 52.46. MS EI *m/z* (rel. int.) 288 (M^+, 58), 257 (25), 256 (38), 229 (80), 228 (100), 227 (48), 226 (79), 202 (29), 126 (25); HRMS *m/z* (EI, M^+) calcd for $C_{20}H_{16}O_2$, 288.1150, found 288.1153.

Methyl 2-(2-phenylcyclopropyl)-1-naphthoate (**3.210b**, Table 3.26)

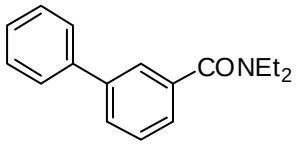


According to General Procedure B and using the following materials refluxed in 20 h: Methyl 2-methoxy-1-naphthoate (22 mg, 0.10 mmol), 2-(2-phenylcyclopropyl)-5,5-dimethyl-1,3,2-dioxaborinane (35 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.4 mL), the title

compound **3.210b** (13 mg, 43% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 1725, 1603, 1510, 1498, 1435, 1273, 1231, 1136, 1035, 817, 751, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.86 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 9.2 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 1H), 7.23-7.15 (m, 3H), 3.74 (s, 3H), 2.48 (dt, *J* = 8.9, 5.6 Hz, 1H), 2.22 (dt, *J* = 9.0, 5.4 Hz, 1H), 1.58 (dt, *J* = 8.9, 5.7 Hz, 1H), 1.46 (dt, *J* = 8.9, 5.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.00, 142.17, 136.94, 131.83, 131.46, 130.01, 129.83, 128.38 (2C), 128.02, 127.22, 125.89, 125.82 (2C), 125.75, 124.41, 123.77, 52.18, 26.67, 26.26, 16.78. MS EI *m/z* (rel. int.) 302 (M^+, 2), 196 (28), 183 (89) (25), 165 (50), 152 (41), 139 (58), 127 (48), 126 (44), 115 (70), 104 (100), 103 (39), 91 (93), 89 (37), 78 (82), 77 (73), 63 (34), 51 (36); HRMS *m/z* (EI, M^+) calcd for $C_{21}H_{18}O_2$, 302.1307, found 302.1315.

C-O Activation/Reduction (Hydrodemethoxylation). Synthesis of Compounds 3.114c, 3.136c-3.137c, 3.175c, 3.20, 3.119c, 3.185d, 3.184c-3.185c, 3.188c-3.189c

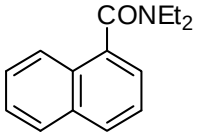
N,N-Diethyl-3-phenylbenzamide (**3.114c**, Table 3.28, entry 3)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-5-phenylbenzamide (28 mg, 0.10 mmol), Et_3SiH (18 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.114c** (22 mg, 88% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2973, 2934, 1632, 1484, 1456, 1431, 1316, 1272, 1101, 760, 745, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.68-7.53 (m, 4H), 7.50-7.40 (m, 3H), 7.39-7.30 (m, 2H), 3.75-3.09 (m, 4H), 1.37-1.01 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.14,

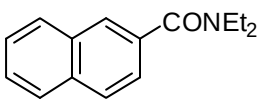
141.40, 140.42, 137.78, 128.82, 128.80 (2C), 127.77, 127.57, 127.10 (2C), 125.01, 124.98, 43.30, 39.21, 14.24, 12.89. MS EI *m/z* (rel. int.) 253 (M^+, 34), 252 (48), 181 (100), 153 (48), 152 (83), 151 (22); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{17}H_{20}NO$, 254.1544, found 254.1555.

N,N-Diethyl-1-naphthamide (**3.136c**, Table 3.28, entry 4)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-1-naphthamide (77 mg, 0.30 mmol), Et_3SiH (54 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.136c** (59 mg, 87% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.89-7.75 (m, 3H), 7.55-7.42 (m, 3H), 7.39 (d, *J* = 6.8 Hz, 1H), 3.99-3.74 (m, 1H), 3.62-3.40 (m, 1H), 3.21-2.97 (m, 2H), 1.37 (t, *J* = 7.11 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.14, 135.11, 133.36, 129.51, 128.61, 128.22, 126.74, 126.22, 125.01, 124.66, 123.07, 42.98, 38.90, 14.17, 12.99. The physical and spectral data were consistent with those reported.[318]

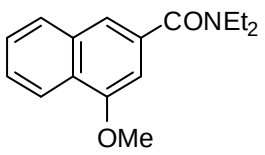
N,N-Diethyl-2-naphthamide (**3.137c**, Table 3.28, entry 5)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (77 mg, 0.30 mmol), Et_3SiH (54 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.137c** (67 mg, 98% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.93-7.79 (m, 4H), 7.57-7.49 (m, 2H), 7.47 (dd, *J* = 8.4, 1.3 Hz, 1H), 3.74-3.47 (m, 2H), 3.43-3.16 (m, 2H), 1.42-1.21 (m, 3H), 1.20-0.99 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.21, 134.57, 133.31, 132.72, 128.23, 128.18, 127.71, 126.68, 126.51, 125.67,

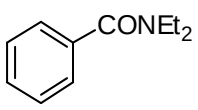
123.87, 43.32, 39.23, 14.20, 12.93. The physical and spectral data were consistent with those previously reported.[319]

N,N-Diethyl-4-methoxy-2-naphthamide (**3.175c**, Table 3.28, entry 6)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-1,4-dimethoxy-2-naphthamide (58 mg, 0.2 mmol), Et_3SiH (36 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.175c** (49 mg, 93% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2971, 2935, 1627, 1597, 1577, 1478, 1459, 1422, 1397, 1372, 1293, 1266, 1235, 1111, 1095, 818, 779 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.25 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.79 (dd, *J* = 6.8, 2.1 Hz, 1H), 7.59-7.46 (m, 2H), 7.41 (s, 1H), 6.81 (s, 1H), 4.02 (s, 3H), 3.70-3.15 (m, 4H), 1.41-1.08 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.34, 155.65, 134.57, 133.64, 127.80, 127.00, 125.96, 125.60, 121.91, 117.66, 102.16, 55.60, 43.03, 39.00, 14.10, 12.82. MS EI *m/z* (rel. int.) 257 (M^+, 85), 242 (40), 186 (32), 185 (100), 158 (32), 157 (47), 114 (22); HRMS *m/z* (EI, M^+) calcd for $C_{16}H_{19}NO_2$, 257.1416, found 257.1424.

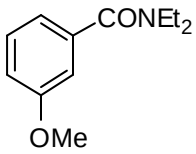
N,N-Diethylbenzamide (**3.20**, Table 3.29, entry 1)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (104 mg, 0.50 mmol), DIBAL-H (0.55 mL, 0.55 mmol, 1 M in THF), $RuH_2(CO)(PPh_3)_3$ (19 mg, 4 mol%) and toluene (1.5 mL), the title compound **3.20** (45 mg, 51% yield) was obtained as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.44-7.28 (m, 5H), 3.65-3.42 (m, 2H), 3.34-3.13 (m, 2H), 1.35-0.99 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.22, 137.25, 129.01, 128.32 (2C), 126.21 (2C),

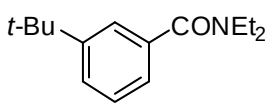
43.22, 39.17, 14.19, 12.89. The physical and spectral data were consistent with those previously reported.[320]

N,N-Diethyl-3-methoxybenzamide (**3.119c**, Table 3.29, entry 2)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-2,3-dimethoxybenzamide (48 mg, 0.20 mmol), DIBAL-H (0.22 mL, 0.22 mmol, 1 M in THF), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.119c** (28 mg, 68% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.30 (t, *J* = 7.9 Hz, 1H), 6.98-6.84 (m, 3H), 3.82 (s, 3H), 3.54 (m, 2H), 3.26 (m, 2H), 1.25 (m, 3H), 1.12 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.94, 159.48, 138.48, 129.47, 118.34, 114.94, 111.61, 55.26, 43.20, 39.14, 14.19, 12.84. The physical and spectral data were consistent with those previously reported.[321]

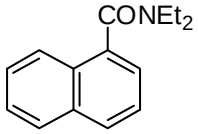
3-*tert*-Butyl-N,N-diethylbenzamide (**3.114c**, Table 3.29, entry 3)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-5-*t*-butyl-2-methoxybenzamide (26 mg, 0.10 mmol), DIBAL-H (0.11 mL, 0.11 mmol, 1 M in THF), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.114c** (13 mg, 55% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2966, 2936, 2872, 1635, 1473, 1459, 1431, 1414, 1380, 1365, 1293, 1261, 1100, 1088, 806, 707; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.46-7.35 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.17 (dt, *J* = 7.4, 1.2 Hz, 1H), 3.74-3.40 (m, 2H), 3.38-3.07 (m, 2H), 1.32 (s, 9H), 1.29-1.19 (m, 3H), 1.17-1.02 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.80, 151.28, 136.91, 128.03, 126.05, 123.30, 123.23, 43.25, 39.17, 34.74, 31.24 (3C), 29.68, 14.22, 12.91. MS

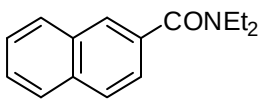
EI *m/z* (rel. int.) 233 (M^+, 33), 232 (58), 161 (100), 91 (19); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{15}H_{24}NO$, 234.1857, found 234.1854.

N,N-Diethy-1-naphthamide (**3.136c**, Table 3.29, entry 4)



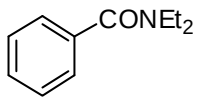
According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxy-1-naphthamide (52 mg, 0.2 mmol), DIBAL-H (0.3 mL, 0.3 mmol, 1 M in THF), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.136c** (32 mg, 70% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-2-naphthamide (**3.137c**, Table 3.29, entry 5)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-1-methoxy-2-naphthamide (52 mg, 0.20 mmol), DIBAL-H (0.22 mL, 0.22 mmol, 1 M in THF), $RuH_2(CO)(PPh_3)_3$ (7 mg, 4 mol%) and toluene (0.6 mL), the title compound **3.137c** (38 mg, 83% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

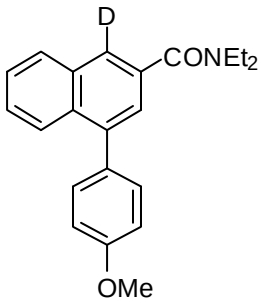
N,N-Diethylbenzamide (**3.20**, Scheme 3.59)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-2-(dimethylamino)benzamide (66 mg, 0.30 mmol), Et_3SiH (54 mg, 0.45 mmol), $RuH_2(CO)(PPh_3)_3$ (11 mg, 4 mol%) and toluene (0.6 mL), the title

compound **3.20** (46 mg, 86% yield) was obtained as a colorless oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

N,N-Diethyl-4-(4-methoxyphenyl)-1-D-2-naphthamide (**3.185d**, Scheme 3.60)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-4-(4-methoxyphenyl)-1-methoxy-2-naphthamide (36 mg, 0.10 mmol), Et_3SiH (18 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.185d** as a 1:2 (D/H) mixture (calculation shown below) with N,N-diethyl-4-(4-methoxyphenyl)-2-naphthamide was obtained as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 8.2 Hz, 1H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.40 (s, 1H), 7.03 (d, *J* = 8.6 Hz, 2H), 3.89 (s, 3H), 3.71-3.15 (m, 4H), 1.44-1.00 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.17, 159.11, 140.42, 134.10, 133.22, 132.34, 131.86, 131.04 (2C), 128.58, 126.74, 126.35, 126.02, 124.77, 113.76 (2C), 55.33, 43.38, 39.25, 14.35, 12.94 (1C not observed). HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{22}H_{23}DNO_2$, 335.1870, found 335.1854. The yield of products (the isotope mixture) is 98%. Based on MS (ESI) results, the D/H ratio in the mixture is calculated below:

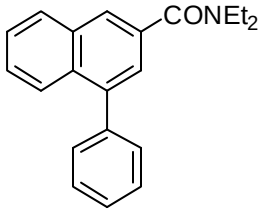
$$\text{Compound ratio (D/H)} = \frac{\text{peak area of m/z 335.1854 (D)} - 25.27\% \times \text{peak area of m/z 334.1829 (H)}}{\text{peak area of m/z 334.1829 (H)}}$$

(percentage (D/H) from isotope model of compounds)

$$= \frac{17.20 - 25.27\% \times 21.01}{21.01}$$

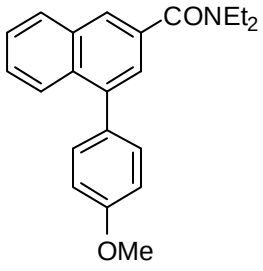
$$= \mathbf{0.566} \quad \text{(close to } \mathbf{1.1 : 2}\text{)}$$

N,N-Diethyl-4-phenyl-2-naphthamide (**3.184c**, Scheme 3.62)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-4-phenyl-1-methoxy-2-naphthamide (33 mg, 0.10 mmol), Et_3SiH (18 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.184c** (30 mg, 98% yield) was obtained as a light yellow solid. mp 123-124 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2934, 1631, 1476, 1462, 1428, 1381, 1271, 1096, 787, 755, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.92 (t, *J* = 7.0 Hz, 2H), 7.88 (s, 1H), 7.57-7.40 (m, 8H), 3.76-3.51 (m, 2H), 3.47-3.22 (m, 2H), 1.41-1.23 (m, 3H), 1.21-1.05 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.09, 140.74, 139.98, 134.18, 133.25, 131.64, 129.95 (2C), 128.63, 128.29 (2C), 127.49, 126.84, 126.42, 125.98, 125.23, 124.80, 43.39, 39.33, 14.30, 12.97. MS EI *m/z* (rel. int.) 303 (M^+, 38), 302 (31), 232 (19), 231 (79), 203 (53), 202 (100), 201 (21), 200 (21); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{21}H_{22}NO$, 304.1701, found 304.1688.

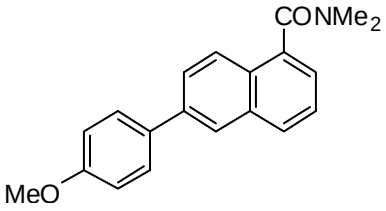
N,N-Diethyl-4-(4-methoxyphenyl)-2-naphthamide (**3.185c**, Scheme 3.62)



According to General Procedure C and using the following materials refluxed in 26 h: N,N-diethyl-4-(4-methoxyphenyl)-1-methoxy-2-naphthamide (36 mg, 0.10 mmol), Et_3SiH (18 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.185c** (32 mg, 99% yield) was obtained as a light yellow solid. mp 147-149 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2974, 2935, 1631, 1515, 1500, 1476, 1462, 1430, 1382, 1287, 1271, 1247, 1178, 1096, 1033, 836, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.93 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.84 (s, 1H), 7.52 (t, *J* = 7.3 Hz, 1H),

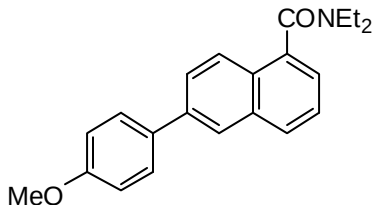
7.46 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.40 (s, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 3.89 (s, 3H), 3.70-3.49 (m, 2H), 3.44-3.26 (m, 2H), 1.38-1.21 (m, 3H), 1.20-1.04 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.17, 159.10, 140.41, 134.20, 133.29, 132.33, 131.85, 131.04 (2C), 128.63, 126.74, 126.35, 126.02, 124.90, 124.76, 113.75 (2C), 55.34, 43.40, 39.26, 14.34, 12.93. MS EI *m/z* (rel. int.) 333 (M^+, 52), 332 (39), 262 (28), 261 (100), 218 (24), 202 (35), 190 (41), 189 (72); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{22}H_{24}NO_2$, 334.1807, found 334.1797.

6-(4-Methoxyphenyl)-N,N-dimethyl-1-naphthamide (**3.188c**, Scheme 3.62)



According to General Procedure C and using the following materials refluxed in 26 h: N,N-dimethyl-6-(4-methoxyphenyl)-2-methoxy-1-naphthamide (34 mg, 0.10 mmol), Et_3SiH (18 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.188c** (29 mg, 94% yield) was obtained as a light yellow solid. mp 113-116 °C (EtOAc/hexanes); IR (KBr) ν_{max} 2932, 1635, 1504, 1461, 1395, 1288, 1249, 1179, 1124, 1026, 825, 802, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.00 (d, *J* = 1.5 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.7 Hz, 1H), 7.75 (dd, *J* = 8.7, 1.8 Hz, 4H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.49 (dd, *J* = 8.1, 7.1 Hz, 1H), 7.39 (dd, *J* = 7.0, 1.0 Hz, 4H), 7.02 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H), 3.27 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.83, 159.38, 138.60, 134.56, 133.82, 133.07, 129.11, 128.38 (2C), 128.33, 126.45, 125.56, 125.36 (2C), 123.59, 114.34 (2C), 55.35, 38.88, 34.86. MS EI *m/z* (rel. int.) 305 (M^+, 68), 262 (19), 261 (100), 233 (40), 218 (18), 190 (35), 189 (57); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{20}H_{20}NO_2$, 306.1494, found 306.1481.

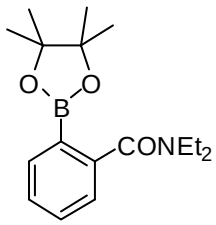
6-(4-Methoxyphenyl)-N,N-diethyl-1-naphthamide (**3.189c**, Scheme 3.62)



According to General Procedure C and using the following materials refluxed in 20 h: N,N-diethyl-6-(4-methoxyphenyl)-2-methoxy-1-naphthamide (36 mg, 0.10 mmol), Et_3SiH (18 mg, 0.15 mmol), $RuH_2(CO)(PPh_3)_3$ (9 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.189c** (31 mg, 92% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2974, 2934, 1630, 1519, 1501, 1460, 1439, 1426, 1289, 1248, 1181, 1031, 825, 799, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 8.00 (d, *J* = 1.6 Hz, 1H), 7.92-7.82 (m, 2H), 7.75 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 2H), 7.51-7.44 (m, 1H), 7.38 (dd, *J* = 6.9, 0.89 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 4.01-3.75 (m, 1H), 3.87 (s, 3H) 3.65-3.43 (m, 1H), 3.23-3.01 (m, 2H), 1.39 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 170.20, 159.35, 138.57, 135.01, 133.81, 133.10, 128.81, 128.44, 128.35 (2C), 126.35, 125.49, 125.29, 125.24, 122.88, 114.32 (2C), 55.34, 43.09, 38.98, 14.29, 13.08. MS EI *m/z* (rel. int.) 333 (M^+, 68), 332 (45), 262 (23), 261 (100), 233 (40), 218 (24), 190 (38), 189 (56); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{22}H_{24}NO_2$, 334.1087, found 334.1797.

Amide-Directed C-H Activation/C-B Bond Formation. Synthesis of Compounds 3.20d, 3.21d, 3.91d, 3.120d, 3.213d

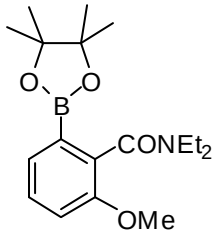
N,N-Diethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (**3.20d**, Table 3.33)



According to General Procedure D and using the following materials refluxed in 20 h: N,N-diethylbenzamide (71 mg, 0.40 mmol), B_2Pin_2 (107 mg, 0.42 mmol), $RuH_2(CO)(PPh_3)_3$ (15 mg, 4 mol%) without solvent, the

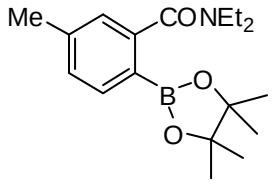
title compound **3.20d** (84 mg, 70% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.80 (dd, *J* = 7.3, 0.7 Hz, 1H), 7.42 (td, *J* = 7.5, 1.4 Hz, 1H), 7.35 (td, *J* = 7.4, 1.2 Hz, 1H), 7.27 (d, *J* = 7.0 Hz, 1H), 3.57 (q, *J* = 7.1 Hz, 2H), 3.21 (q, *J* = 7.1 Hz, 2H), 1.40-1.26 (m, 15H), 1.06 (t, *J* = 7.1 Hz, 3H);[311] ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.62, 142.45, 135.03, 130.46, 128.13, 125.40, 83.40 (2C), 42.97, 39.69, 24.88 (4C), 13.68, 12.48. The physical and spectral data were consistent with those previously reported.[311]

N,N-Diethyl-2-methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (**3.91d**, Table 3.33)



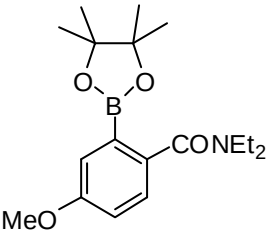
According to General Procedure D and using the following materials refluxed in 20 h: N,N-diethyl-2-methoxybenzamide (83 mg, 0.40 mmol), B_2Pin_2 (124 mg, 0.48 mmol), $RuH_2(CO)(PPh_3)_3$ (15 mg, 4 mol%) and toluene (0.2 mL), the title compound **3.91d** (39 mg, 30% yield) was obtained as a light yellow oil. IR (KBr) ν_{max} 2978, 2935, 1634, 1484, 1455, 1425, 1380, 1352, 1321, 1281, 1258, 1142, 1050 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.39 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.28 (dd, *J* = 8.1, 7.4 Hz, 1H), 6.97 (dd, *J* = 8.2, 0.7 Hz, 1H), 3.78 (s, 3H), 3.57 (q, *J* = 7.1 Hz, 2H), 3.09 (q, *J* = 7.2 Hz, 2H), 1.31-1.25 (m, 15H), 0.99 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.62, 154.86, 132.75, 128.62, 127.65, 113.65, 83.79 (2C), 55.57, 42.73, 38.64, 24.77 (4C), 13.40, 12.58; MS EI *m/z* (rel. int.) 333 (M^+, 12), 332 (38), 302 (26), 276 (20), 275 (100), 274 (39), 202 (32), 188 (47), 179 (88), 178 (25), 161 (58), 160 (39), 84 (52); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{18}H_{29}BNO_4$, 334.2189, found 334.2201.

N,N-Diethyl-5-methyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (**3.213d**, Table 3.33)



According to General Procedure D and using the following materials refluxed in 20 h: N,N-diethyl-3-methylbenzamide (77 mg, 0.40 mmol), B_2Pin_2 (107 mg, 0.42 mmol), $RuH_2(CO)(PPh_3)_3$ (15 mg, 4 mol%) and toluene (0.4 mL), the title compound **3.213d** (52 mg, 41% yield) was obtained as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.70 (d, *J* = 7.60 Hz, 1H), 7.15 (dd, *J* = 7.5, 0.6 Hz, 1H), 7.05 (s, 1H), 3.56 (q, *J* = 7.1 Hz, 2H), 3.15 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.32-1.24 (m, 15H), 1.02 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.76, 143.50, 141.04, 135.51, 128.48, 126.17, 83.53 (2C), 42.87, 39.06, 24.84 (4C), 21.56, 13.69, 12.51. The physical and spectral data were consistent with those previously reported.[322]

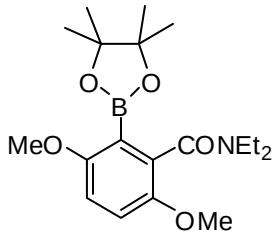
N,N-Diethyl-4-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (**3.21d**, Table 3.33)



According to General Procedure D and using the following materials refluxed in 20 h: N,N-diethyl-4-methoxybenzamide (83 mg, 0.40 mmol), B_2Pin_2 (107 mg, 0.42 mmol), $RuH_2(CO)(PPh_3)_3$ (15 mg, 4 mol%) without solvent, the title compound **3.21d** (77 mg, 58% yield) was obtained as light yellow oil. IR (KBr) ν_{max} 2976, 2937, 1630, 1590, 1462, 1444, 1380, 1371, 1362, 1341, 1323, 1287, 1233, 1179, 1147, 1109, 1057, 1034, 882, 852, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.36 (d, *J* = 8.6 Hz, 1H), 7.20 (d, *J* = 2.5 Hz, 1H), 6.83 (dd, *J* = 8.6, 2.6 Hz, 1H), 3.85 (s, 3H), 3.70-3.47 (m, 4H), 1.30 (s, 12H), 1.29-1.22 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 171.33, 161.68, 128.85, 126.81, 116.16, 115.64, 81.48 (2C), 55.25, 43.53, 43.41,

25.08 (4C), 13.63, 12.47; MS EI *m/z* (rel. int.) 333 (M^+, 7), 332 (33), 276 (16), 275 (100), 274 (44), 188 (33), 179 (30), 161 (35), 160 (37), 135 (19), 83 (28); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{18}H_{29}BNO_4$, 334.2189, found 334.2204.

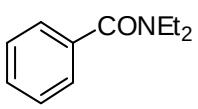
N,N-Diethyl-3,6-dimethoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (**3.120d**, Table 3.33)



According to General Procedure D and using the following materials refluxed in 20 h: N,N-diethyl-2,5-dimethoxybenzamide (95 mg, 0.40 mmol), B_2Pin_2 (124 mg, 0.48 mmol), $RuH_2(CO)(PPh_3)_3$ (15 mg, 4 mol%) and toluene (0.2 mL), the title compound **3.120d** (66 mg, 46% yield) was obtained as light yellow solid. mp 97-98 ^oC (EtOAc/hexanes); IR (KBr) ν_{max} 2978, 2936, 1630, 1596, 1475, 1464, 1421, 1372, 1360, 1333, 1314, 1282, 1251, 1146, 1052, 854, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm 6.82 (d, *J* = 8.9 Hz, 1H), 6.74 (d, *J* = 8.9 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.51 (q, *J* = 7.1 Hz, 2H), 3.14 (q, *J* = 7.1 Hz, 2H), 1.30 (s, 12H), 1.22 (t, *J* = 6.7 Hz, 3H), 1.04 (t, *J* = 7.10 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 168.10, 157.22, 149.17, 132.46, 113.43, 111.19, 83.77 (2C), 56.44, 56.29, 42.78, 38.51, 24.67 (4C), 13.36, 12.78; MS EI *m/z* (rel. int.) 363 (M^+, 7), 362 (16), 332 (20), 305 (18), 263 (18), 262 (100), 261 (25), 191 (22), 165 (23); HRMS *m/z* (ESI, $[M+1]^+$) calcd for $C_{19}H_{31}BNO_5$, 364.2295, found 364.2300.

Ru-catalyzed Dehalogenation of Aryl C-halo Bonds. . Synthesis of Compounds 3.20, 3.219b

N,N-Diethylbenzamide (**3.20**, Table 3.34, entries 1-4)



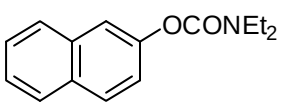
According to General Procedure G and using the following materials refluxed in 20 h: N,N-diethyl-2-chlorobenzamide (42 mg, 0.2 mmol), Et_3SiH (35 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.20** (33 mg, 92% yield) was obtained as a light yellow oil. The physical and spectral data were consistent with those reported for this compound as prepared previously.

According to General Procedure G and using the following materials refluxed in 20 h: N,N-diethyl-4-chlorobenzamide (42 mg, 0.2 mmol), Et_3SiH (35 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.20** (29 mg, 83% yield) was obtained as a light yellow oil.

According to General Procedure G and using the following materials refluxed in 20 h: N,N-diethyl-3-bromobenzamide (51 mg, 0.2 mmol), Et_3SiH (35 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.20** (31 mg, 89% yield) was obtained as a light yellow oil.

According to General Procedure G and using the following materials refluxed in 20 h: N,N-diethyl-4-bromobenzamide (51 mg, 0.2 mmol), Et_3SiH (35 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.20** (31 mg, 88% yield) was obtained as a light yellow oil.

Naphthalen-2-yl diethylcarbamate (**3.219b**, Table 3.34, entry 5)



According to General Procedure G and using the following materials refluxed in 20 h: 3-iodonaphthalen-2-yl diethylcarbamate (74 mg, 0.2 mmol), Et_3SiH (35 mg, 0.3 mmol), $RuH_2(CO)(PPh_3)_3$ (19 mg, 10 mol%) and toluene (0.6 mL), the title compound **3.219** (42 mg, 87% yield) was obtained as a light yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.84 (d, *J* = 8.7 Hz, 2H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 1.6 Hz, 1H), 7.52-7.40 (m, 2H), 7.30 (dd, *J* = 8.8, 2.1 Hz, 1H), 3.63-3.30 (m, 4H), 1.41-1.12 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 154.27, 149.15, 133.80, 131.08, 129.02, 127.62, 127.47, 126.24, 125.21, 121.62, 118.33, 42.22, 41.89, 14.24, 13.37. The physical and spectral data were consistent with those previously reported.[63]

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