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DEVELOPMENT OF COPPER-CATALYZED SUZUKI-MIYAURA COUPLING USING ALKYLBORON REAGENTS AND NICKEL-CATALYZED ALKENE DICARBOFUNCTIONALIZATION REACTIONS

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by

PRAKASH BASNET

M.S., Organic Chemistry, Tribhuvan University, 2009

DISSERTATION

Submitted in Partial Fulfillment of the
Requirements for the Degree of

Doctor of Philosophy
Chemistry

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DEDICATION

To my parents, my wife Sheela and my son Sameep

For their love, support and encouragement

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There are several people who have helped and supported me in so may ways in my research careers to achieve this milestone.

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Abstract

This thesis is divided into two parts. The first part deals with the development of copper-catalyzed Suzuki-Miyaura coupling of alkylboron reagents for the first time. In the second part, we will discuss the development of novel nickel-catalyzed alkene dicarbofunctionalization reactions.

Part I. Cross-coupling reactions are versatile tools to form new carbon-carbon bonds and are widely used in the synthesis of various drug molecules, natural products and materials. However, these reactions are typically catalyzed by palladium, an expensive and rare metal which makes the reaction unsustainable in long-terms. Additionally, palladium-catalyzed cross-coupling reactions with alkylorganometallic reagents suffer from side reactions due to complications by β-hydride elimination and protodemetalation. The reactions also less

tolerate to heteroarenes as these substrates generally deactivate the catalysts. These problems are largely addressed by using sterically hindered, expensive and difficult-to-make ligands. Recently, copper, a cheap and highly abundant metal, has emerged as an alternative catalyst, and has been utilized increasingly in cross-coupling reactions. The rising use of copper in cross-coupling can be attributed to lower tendency of alkylcopper intermediates for β-hydride elimination than those of analogous alkylpalladium species. Additionally, copper catalysts are also known to tolerate heteroarenes much better than palladium catalysts. In this thesis, we present our results on the development of a copper-catalyzed Suzuki-Miyaura cross-coupling reaction of alkylboron reagents with aryl and heteroaryl iodides. This novel reaction works well with alkylboron reagents without any complication form β-hydride elimination and tolerates heteroarenes without requiring sterically hindered and expensive ligands. We also conducted mechanistic studies of this reaction through independent synthesis of pertinent reaction intermediates such as anionic dialkylborate complexes, radical clock experiment and a Hammett plot. The experimental results with discrete alkylboron intermediates indicate that anionic alkyl(alkoxy)borate complexes, which are generally accepted as active transmetalating species, undergo disproportionation into anionic dialkylborate intermediates prior to transmetalation to copper catalyst. Radical clock experiment and the Hammett plot indicate that the reaction proceeds through non-radical pathway.

Part II. In this part, we discuss the development of nickel-catalyzed regioselective alkene dicarbofunctionalization reactions by using the imines as a coordination group. These reactions that simultaneously form two carbon-carbon bonds across alkenes will offer a highly effective strategy for providing modular, convergent, and expedient routes to

generate complex bioactive molecules. However, the development of regioselective three-component dicarbofunctionalization of unactivated alkenes has remained a formidable challenge for more than three decades. These reactions are limited to difunctionalizing geometrically constrained norbornenes. Recent use of coordination approach brought some success in dicarbofunctionalization of unactivated alkenes. However, the current state of the coordination approach is also seriously limited as only alkenes proceeding via five-membered metallacycles or via stable and mostly planar six-membered metallacycles with vinylarenes can be utilized as substrates. Aliphatic γ,δ-alkenyl carbonyl compounds, which generate more challenging and less stable six-membered metallacycles, cannot be used as substrates. The use of these alkenes suffers from two key limitations: (1) formation of cross-coupling products caused by slow migratory insertion of alkenes due to weak binding, and (2) formation of Heck products caused by faster β-H elimination from metallacycles than competing transmetalation with organometallic reagents. These side reactions have seriously limited the generality of the coordination approach and the scope of alkene dicarbofunctionalization reactions. In this thesis, we will implement two novel strategies to difunctionalize unactivated alkenes regioselectively using organic halides and organometallic reagents. First, we will introduce a strategy of cationic catalysis, where cationic Ni(II) catalysts are generated *in situ* to address the key issues identified above. This process will enable us to perform regioselective γ,δ-difunctionalization of unactivated alkenes located at the γ,δ-position of carbonyl compounds. It is our observation that cationic Ni(II) promotes transmetalation faster than β-H elimination. This is unprecedented and will be of paramount fundamental significance in catalysis. Since this new cationic catalysis concept addresses two major issues that are common in alkene

difunctionalization, we also anticipate that this discovery will be widely applicable for a general class of alkene substrates. In our second strategy, we introduce a novel concept of metallacycle contraction process, a reaction that harnesses the potential of alkylmetal intermediates to undergo β-H elimination to contract a six-membered metallacycle to a five-membered metallacycle, and difunctionalizes unactivated alkenes at the unusual 1,3-position rather than the usual 1,2-position of alkenes. This unprecedented reaction allows us to create two new carbon-carbon bonds at the β- and δ-positions of carbonyl compounds containing γ,δ-alkenes.

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List of Abbreviations

Ac	acetyl, acetate
Aq.	Aqueous
Bn	benzyl
^{13}C NMR	carbon nuclear magnetic resonance
CDCl3	deuterated chloroform
cat.	catalyst
d	doublet
dd	doublet of doublet
dt	double of triplet
δ	chemical shift
dr	diastereomeric ratio
DCM	dichloromethane
DMA	dimethylacetamide
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
equiv	equivalents
EtOAc	ethyl acetate
Et2O	diethyl ether

GC	gas chromatography
GC-MS	gas chromatography mass spectrometry
g	gram
h	hours
HMPA	hexamethylphosphoramide
HOAc	acetic acid
1H NMR	proton nuclear magnetic resonance
HRMS	high resolution mass spectra
Hz	hertz
ipr	*isopropyl*
IR	infrared
J	*coupling constant*
m	*meta*
MeCN	acetonitrile
mg	milligram
m	multiplet
MHz	megahertz
min	minute
ml	milliliter

mmol	millimole
mol	mole
MS	mass spectrometry
M	transition metal
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
NMP	N-Methyl-2-pyrrolidone
o	*ortho*
p	*para*
ppm	parts per million
pent	pentet
q	quartet
rt	room temperature
s	singlet
sept	septet
TBS	*tert*-butyldimethylsilyl
THF	tetrahydrofuran
t	triplet
tt	triplet of triplet

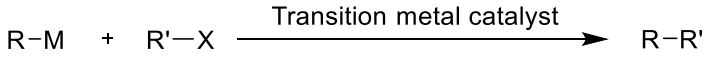
TEA	triethylamine
UV	ultraviolet

Chapter 1. Cross-Coupling Reaction

1.1. Introduction

Cross-coupling reactions are very efficient and powerful methods of forming new carbon-carbon bonds.[1,2] These reactions utilize organometallic reagent as a source of nucleophile and organic halide or pseudo-halide as a source of electrophile. Cross-coupling reactions are typically catalyzed by palladium. There are several named reactions for cross-coupling based on the types of organometallic reagents used. The commonly used organometallic reagents are organoboron (Suzuki-Miyaura),[3,4] organozinc (Negishi),[5,6] organosilicon (Hiyama),[7] organomagnesium (Kumada)[8,9] and organotin (stille).[10] The importance and usefulness of this transformation was recognized by the Nobel prize in chemistry awarded to pioneer scientists Richard Heck, Akira Suzuki and Ei-chi Negishi in 2010.[11]

Scheme 1.1. General cross-coupling reactions



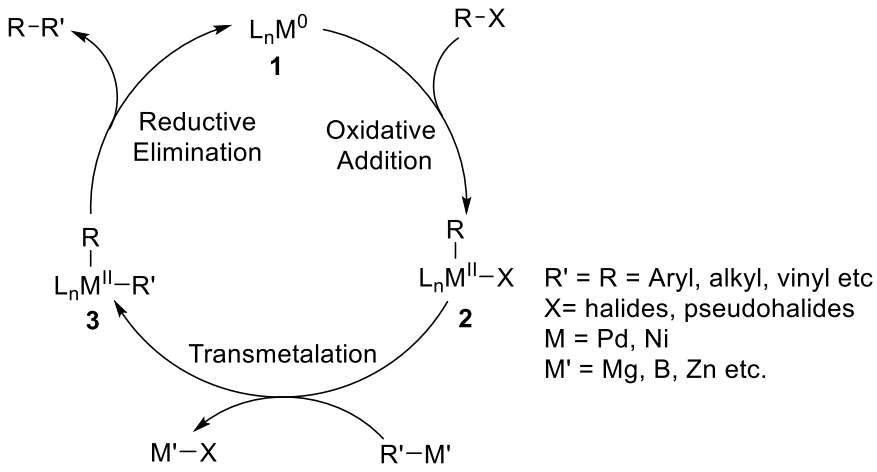
R- alkyl, aryl, vinyl, etc; R'- alkyl, aryl, vinyl, etc
M- B, Si, Sn, Zn, Mg, etc; X= halides, pseudohalides
Catalyst- Pd, Ni, Fe, Cu, Co, Pt, etc

The history of cross-coupling dates back to the 18th century when Glaser reported the first copper mediated homocoupling of phenylacetylene.[12] However, the use of homocoupling reaction was limited due to the requirement for a super stochiometric amount of metal and their low level of selectivity. The reaction was later made catalytic by Cadiot and Chodkiewicz.[13] Despite these early works, the field of cross-coupling only gained momentum after the discovery of palladium as a catalyst for the coupling of alkenes with

aryl halides by Mizoroki[14] and Heck,[15] a reaction now popularly known as Mizoroki-Heck reaction.

The general mechanism of transition metal-catalyzed cross-coupling reaction is represented by three elementary steps (Scheme 1.2). These steps are oxidative addition, transmetalation and reductive elimination. Generally, cross-coupling reaction with a palladium or nickel catalyst involves oxidative addition as the first step. In this step, an organic halide adds to a catalyst by a two-electron redox process. This step is followed by transmetalation, a process where ligand exchange takes place between the organometallic

Scheme 1.2. General catalytic cycle for cross-coupling reaction

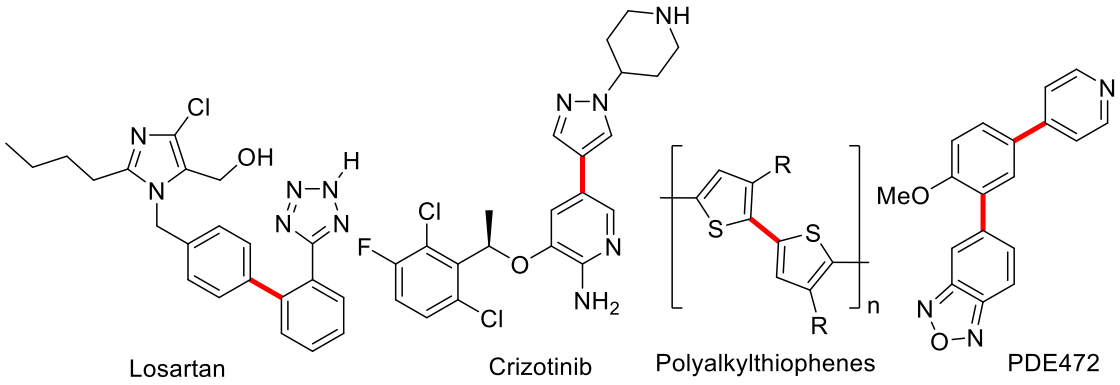


reagent and oxidative addition intermediate **2** with the transfer of the organic component to the transition metal. The final step is reductive elimination by which the two carbon moieties on the catalyst **3** are released with the formation of new carbon-carbon bond, and with concomitant two-electron reduction of the metal, regenerates the active catalyst 1.[16]

Cross-coupling reactions are one of the most versatile reactions known in organic chemistry, and are widely used in the synthesis of various natural products, drug molecules

and materials.[17] For example (Figure 1.1), Suzuki coupling was utilized for Merck's synthesis of Losartan, a drug for the treatment of high blood pressure.[18] Recently, a large scale reaction to synthesize Crizotinib was also reported in which Suzuki coupling was implemented.[19] Crizotinib, a potential drug for cancer treatment, and PDE472, a potential drug for the treatment of asthma, were also prepared using Corriu-Kumada and Negishi coupling.[20] Likewise, materials like polyalkylthiophenes, a polymer used in organic solar cells, was prepared by Kumada coupling.[21]

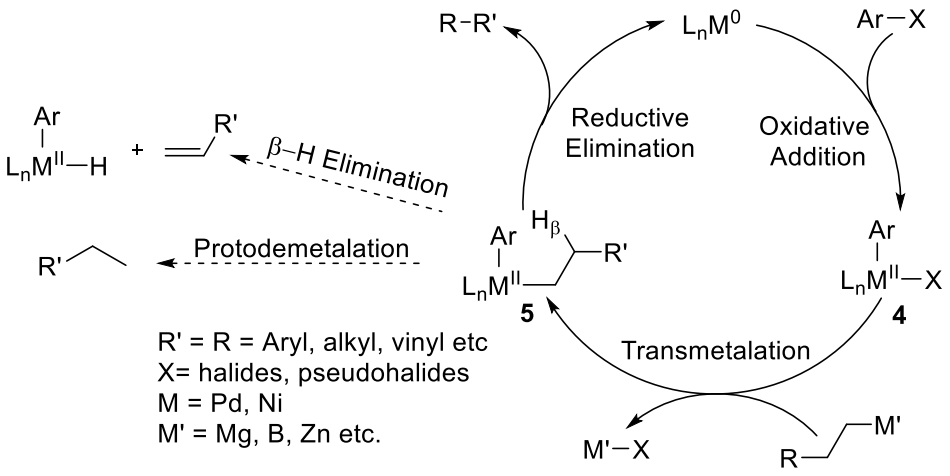
Figure 1.1. Different drug molecules and materials synthesized applying cross-coupling



1.2. Cross-Coupling Reaction with Alkyl Organometallic Reagents

Alkyl organometallic reagents refer to compounds containing sp^3 carbons bonded to a metal. The use of alkyl organometallic reagents in cross-coupling are still less common than aryl and vinyl organometallic reagents and remain underdeveloped. Synthetically, they are difficult to prepare and purify compared to aryl and vinyl organometallic reagents. They are also moisture sensitive and cannot be stored for long time. Therefore, they are generally generated *in-situ* prior to use. More critically, alkyl organometallic reagents are

Scheme 1.3. Catalytic cycle for cross-coupling reaction with C(sp^3) organometallics

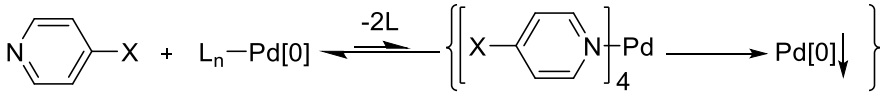


prone to undergo β-H elimination and protodemetalation after they are transmetalated to transition metals (Scheme 1.3).[22] It is also known that the alkyl organometallic reagent can also cause slow reductive elimination.[23] By comparison, similar reactions that involve alkyl halides have largely been solved using nickel as a catalyst. Although the alkyl-metal species generated from alkyl halides also have issues similar to those generated after transmetalation with alkyl organometallic reagents, the use of alkyl halides as a carbon source is known to cause less problems then alkyl organometallic reagents when nickel catalysts are used. This is because nickel usually reduces alkyl halides by a single electron transfer (SET) process, and therefore, generates alkyl radicals that do not undergo β-H elimination.[24,25] Recombination of these alkyl radicals with nickel and the subsequent reductive elimination are known to proceed fast with nickel catalysts.[26,27]

Cross-coupling of alkyl organometallic reagents with heteroaryl halides cause even further challenge in synthesis.[28] This is due to deactivation of catalysts by binding of heteroarenes

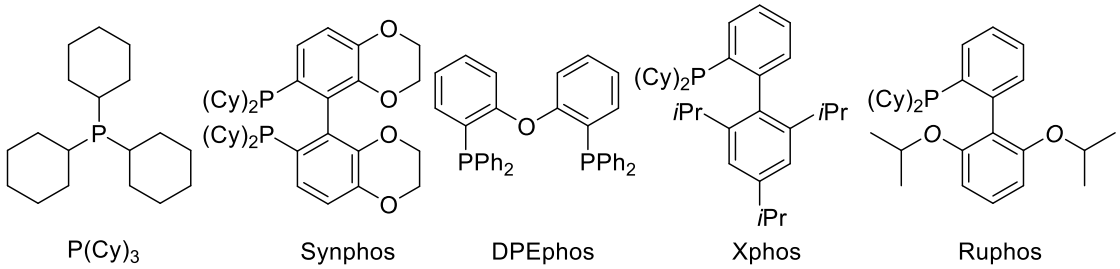
to transition metals and displacing ligands that are typically required for cross-coupling. The catalyst deactivation eventually leads to termination of the reaction (Scheme 1.4).[28,29]

Scheme 1.4. Deactivation of palladium catalyst by heteroarenes

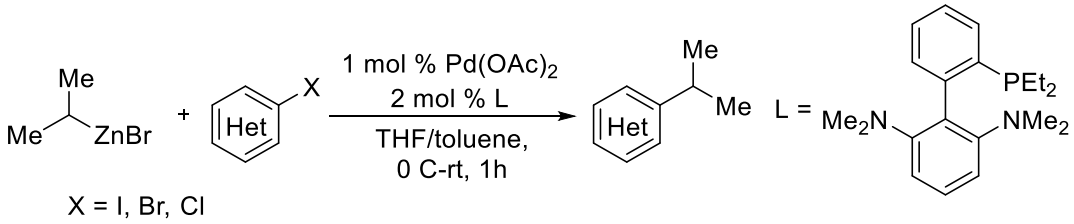


Both problems of β-H elimination with alkyl organometallic reagent and catalyst deactivation by heteroarenes are generally addressed in cross-coupling by the use of electron-rich and sterically hindered ligands (Figure 1.2).[29-32] For example, Buchwald and coworkers recently employed a sterically hindered and complex biaryl phosphine ligand, CPhos, to carry out Negishi coupling of secondary alkylzinc reagents with heteroaryl halides (Scheme 1.5).[33] These sterically hindered ligands prevent β-H elimination by forcing β-hydrogens out of syn co-planarity to transition metal catalysts. These ligands also prevent multiple coordination of heteroarenes that would generally displace the ligands. In addition, the sterically hindered ligands also help in promoting reductive elimination.

Figure 1.2. Sterically bulky and difficult-to-make ligands



Scheme 1.5. Palladium catalyzed cross-coupling of secondary-alkylzinc with heteroaryl halides



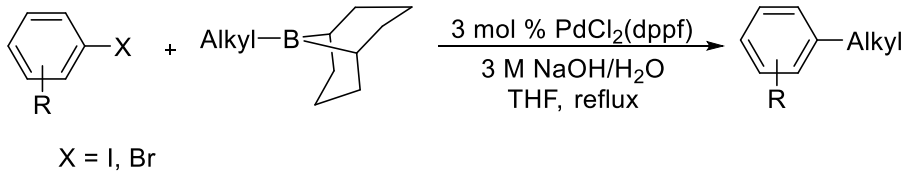
1.3. Suzuki-Miyaura Cross-Coupling of Alkylboron Reagents

The cross-coupling reaction that uses organoboron reagent as a nucleophilic coupling partner is called Suzuki-Miyaura coupling. Suzuki-Miyaura coupling is one of the most widely used cross-coupling reactions.[34] The popularity of Suzuki-Miyaura coupling stems from several advantages of organoboron compounds over other organometallic reagents. Organoboron reagents can be easily prepared and are readily available. Unlike organozinc[35] and organomagnesium[36] reagents, organoboron reagents are less moisture sensitive and bench stable. Compared to organotin reagents,[37] organoboron and its byproducts are also less toxic.[38] In some reactions, water can also be used as a solvent. Moreover, Suzuki coupling shows higher tolerance of sensitive functional groups than organomagnesium and organozinc reagents.[39] The high functional group tolerance and stability of organoboron reagents, however, come at the cost of their lower reactivity than organomagnesium and organozinc reagents.[40] Use of organoboron reagents is a preferred compromise between their reactivity and stability over more reactive organomagnesium and organozinc reagents, and less reactive organosilicon reagents, which exhibit even more stability, and therefore less reactive, than organoboron reagents. Due to the preferred balance between reactivity and stability, organoboron reagents are more desired and

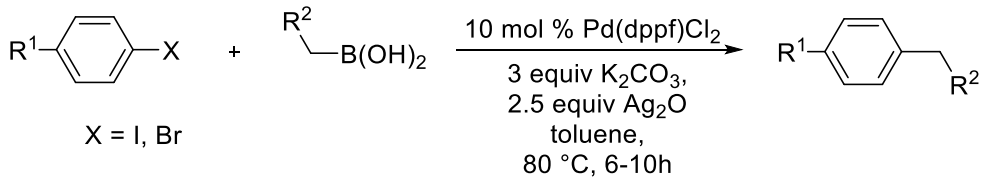
practical than other organometallic reagents.[41] Therefore, the Suzuki-Miyaura coupling reaction remains one of the most useful reactions in the synthetic chemistry.[42]

The Suzuki-Miyaura coupling of alkylboron reagents with organic halides is highly desirable cross-coupling. However, this reaction still remains underdeveloped. Known examples typically use primary alkylboron reagents with limited reports on the coupling of secondary alkylboron reagents. For example, in 1989 Suzuki and co-workers developed the first cross-coupling between alkylboron reagents and aryl halides (Scheme 1.6).[42] They also developed the cross-coupling between alkylboronic esters and aryl halides, but, the reaction requires toxic thallium hydroxide.[43] In 2001, Falck and coworkers successfully developed the cross-coupling between primary alkylboronic acids with aryl halides in presence of a palladium catalyst (Scheme 1.7). The significance of this reaction is that it used the air and moisture stable alkylboronic acids and avoided the use of toxic thallium compounds. However, the reaction require stoichiometric amount of silver oxide.[44] Similarly, Molander and coworkers also developed a palladium-catalyzed cross-coupling of potassium trifluoroboratohomoenolates with aryl halides (Scheme 1.8).[45] Fu and coworkers utilized a nickel catalyst, and developed alkyl-alkyl Suzuki-Miyaura coupling by using primary alkyl-9-BBN reagents in the presence of a diamine ligand (Scheme 1.9).[46]

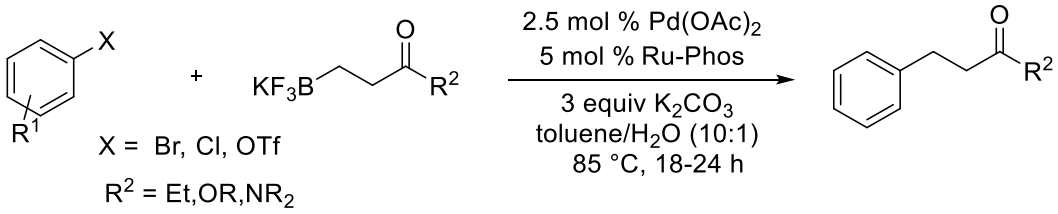
Scheme 1.6. Palladium catalyzed coupling of primary alkyl-9-BBN with aryl iodides



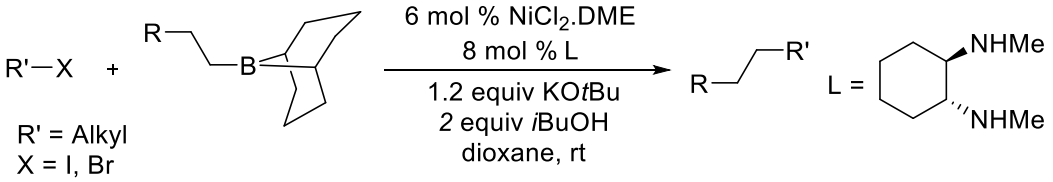
Scheme 1.7. Palladium catalyzed coupling of primary alkylboronic acid with aryl halides



Scheme 1.8. Palladium catalyzed cross-coupling with trifluoroboratohomoenolates



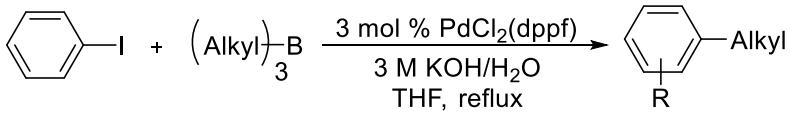
Scheme 1.9. Nickel-catalyzed alkyl-alkyl Suzuki-Miyaura coupling



In 1989 Suzuki and coworkers were also successful in cross-coupling secondary alkylboron reagent particularly, cyclobutane and cyclohexane with iodobenzene in moderate yields (Scheme 1.10).[42] In 2000, Fu and coworkers performed the palladium catalyzed cross-coupling between cyclopentylboronic acid and 4-chlorotoluene with 75% yield (Scheme 1.11).[47] In 2002, Wallace and coworkers successfully utilized a cyclopropylboronic acid for the Suzuki-Miyaura coupling to afford higher yields. In this reaction, palladium in combination with tricyclohexylphosphine was used as a catalyst (Scheme 1.12).[48] and they only used cyclopropylboronic acid. In 2008, Molander and coworkers developed a palladium-catalyzed Suzuki-Miyaura coupling using secondary alkylboron reagents

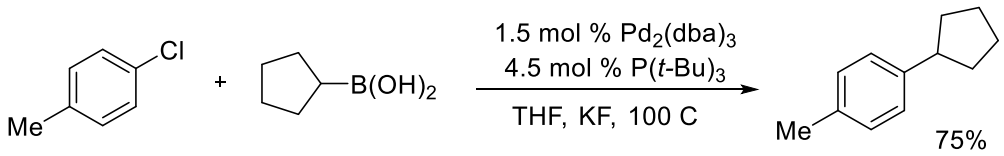
(Scheme 1.13).[49] The reaction generally worked well with cyclic secondary alkylboron reagents. Reaction with *iso*-propylboron reagent however, formed the branched product with linear product via a β-H elimination and reinsertion pathway as a side reaction.

Scheme 1.10. Pd-catalyzed cross-coupling of trialkylboranes with iodobenzene

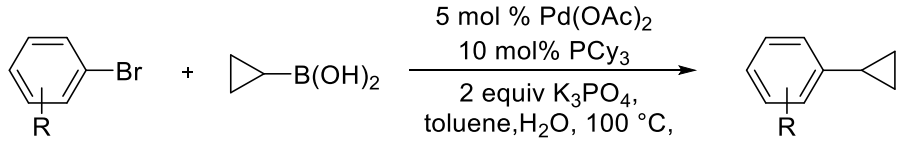


Alkyl = Cyclopentyl, Cyclohexyl

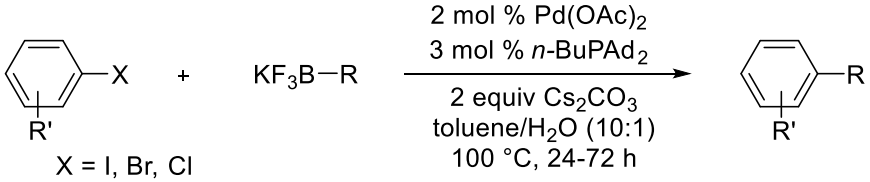
Scheme 1.11. Pd-catalyzed cross-coupling of cyclopentylboronic acid with 4-chlorotoluene



Scheme 1.12. Palladium catalyzed cross-coupling with cyclopropyl boronic acid



Scheme 1.13. Palladium catalyzed cross-coupling with cyclopentylboron reagent.



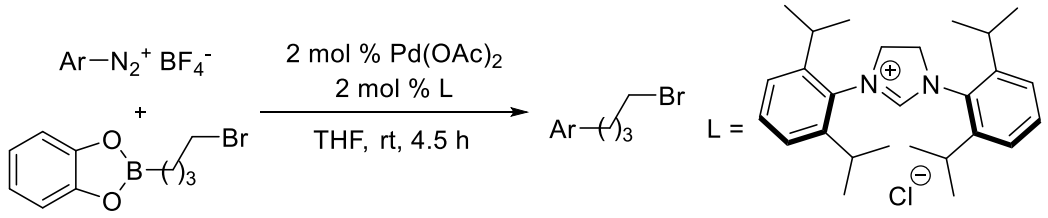
X = I, Br, Cl

R = Cyclopentyl, *i*Pr

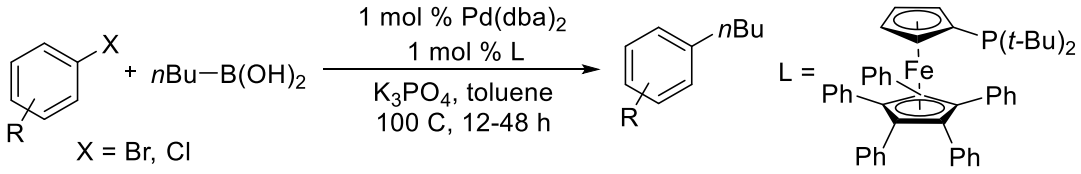
Despite significant progress, the development of the Suzuki-Miyaura coupling with alkylboron reagents still remains a major challenge. The problem is mostly generic and is related to β-H elimination from alkylmetal species generated after transmetalation. The alkylboron reagents also show low tendency for transmetalation due to their relatively higher stability than alkylmagnesium and alkylzinc reagents. In many cases, the most reactive alkylboron reagents are alkyl-9-BBN (BBN: 9-borabicyclo(3.3.1)nonane), which are prone to undergo dehydroboration to generate alkenes.[50,51]

The use of sterically hindered and electron-rich ligands have been very successful in addressing the problems with coupling alkylboron reagents much like the cross-coupling with any other alkyl organometallic reagents. For example, In 2001, Andrus and coworkers developed the palladium catalyzed cross-coupling between aryldiazonium tetrafluoroborate and alkylcatecholborane using a *N*,*N*-bis(2,6-diisopropylphenyl)dihydroimidazolium chloride as ligand (Scheme 1.14).[52] The reaction works at room temperature and base is not required. In 2002, Hartwig and coworkers developed a palladium catalyst with ferrocenylphosphine ligand which was able to cross-couple alkylboronic acid with aryl bromides and chlorides (Scheme 1.15).[53] Buchwald and coworkers developed in 2004 a highly efficient, electron-rich and sterically-hindered phosphine ligand for a palladium catalyst, and performed the Suzuki-Miyaura coupling between *n*-hexyl-9-BBN and aryl bromide, which furnished the coupling products in good yields (Scheme 1.16).[54]

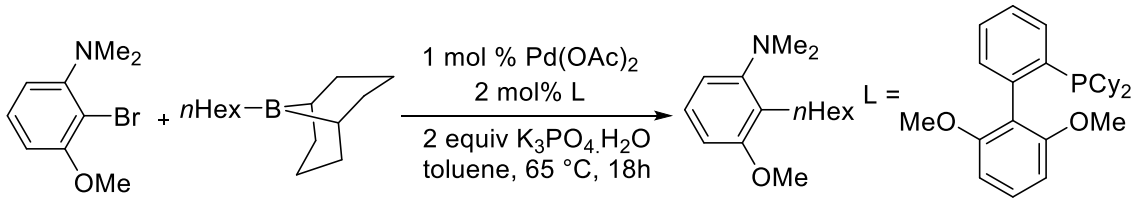
Scheme 1.14. Palladium catalyzed cross-coupling between alkylboron with N,N-bis(2,6-diisopropylphenyl)dihydroimidazolium chloride ligand



Scheme 1.15. Palladium catalyzed reaction between alkylboronic acid with bulky ferrocenylphosphine ligand



Scheme 1.16. Palladium catalyzed cross-coupling of primary alkylboranes with aryl bromides with bulky phosphine ligand



1.4. Conclusion

Cross-coupling reaction is a versatile tool to form new carbon-carbon bond. This reaction is typically catalyzed by palladium, but catalysts based on other metals (such as Ni, Fe and Co) are also on the rise. Among different cross-coupling reactions, the Suzuki-Miyaura coupling remains one of the most widely practiced in both small-scale and large-scale

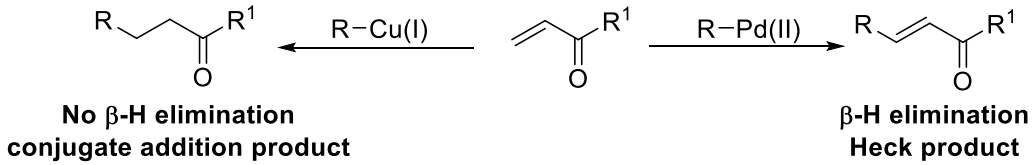
synthesis of natural products, bioactive molecules, pharmaceuticals and materials. While well-developed for the coupling of aryl and vinyl electrophiles and nucleophiles, the Suzuki-Miyaura coupling of alkylboron reagents, and of any alkyl organometallic reagents in general, has still remained underdeveloped. Palladium-catalyzed, and in many cases Ni, Fe and Co-catalyzed, cross-coupling reactions are less tolerant of heteroarenes and alkyl organometallic reagents. The low tolerance arises mainly due to the high propensity of alkylmetal species of these metals to undergo facile β-H elimination and catalyst deactivation by heteroarenes by displacing critically-needed ligands from the metal catalysts. These problems have generally been addressed by implementing sterically hindered and electron-rich ligands. However, identification of a proper ligand that works the best for a particular set of reactions usually requires extensive screening of several exotic ligands, the preparation of which usually requires a cumbersome multistep synthetic endeavor. Even if they are commercially available, the cost of these ligands is forbiddingly expensive, and unaffordable. Therefore, there is a clear need for the development of new metal-based catalysts, which can address these problems at the fundamental level without requiring assistance from exotic and expensive ligands.

Chapter 2. Copper-Catalyzed Suzuki-Miyaura Cross-Coupling Reactions

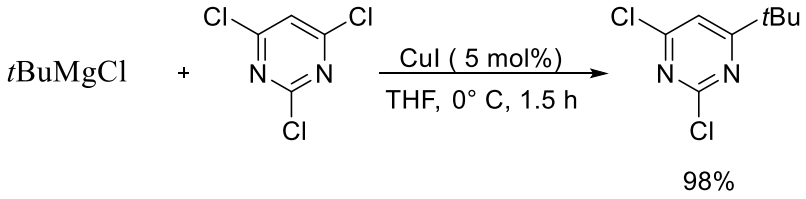
2.1. Introduction

Cross-coupling is very important tool in the synthesis of complex molecules to form new carbon-carbon bond. These transformations are typically catalyzed by palladium or nickel. Historically, copper was used prior to palladium or nickel in the formation of carbon-carbon bond. After the discovery of palladium-catalyzed reactions, copper received less attention mainly due to the requirement for stoichiometric amounts of copper salts, and the formation of products in low yields. The inefficiency of the reaction was mainly ascribed to instability of organocopper species generated as reaction intermediates. In addition, organocopper also form less reactive aggregates,[55,56] and undergo disproportionation by radical processes.[57,58] Nevertheless, copper has gained significant attention in the last few years as an alternative to palladium in cross-coupling reactions.[59,60] Copper is inexpensive, and also a sustainable metal, occurring naturally in higher abundance than palladium. More importantly, copper is known to be more tolerant of heteroatoms than palladium. In addition, alkylcopper species are also known to be less prone to undergo β-H elimination than analogous alkylpalladium species (Scheme 2.1). Examples from Cu-catalyzed conjugate addition, allylic substitution and cross-coupling have shown that alkylcopper species generally are reluctant to undergo β-H elimination.[61-63] In addition, prior examples have also shown that Cu can tolerate N, O, S-containing heteroarenes in copper-catalyzed cross-coupling reactions (Scheme 2.2).[64]

Scheme 2.1. Lower tendency of organocopper towards β-H elimination

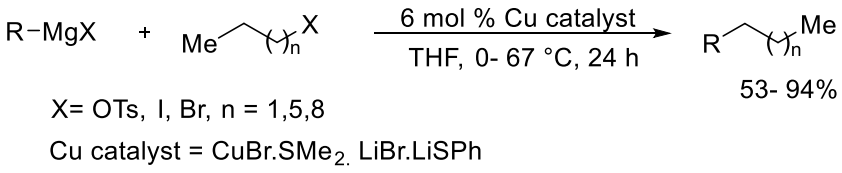


Scheme 2.2. Heteroarenes tolerance by copper-catalyzed cross-coupling

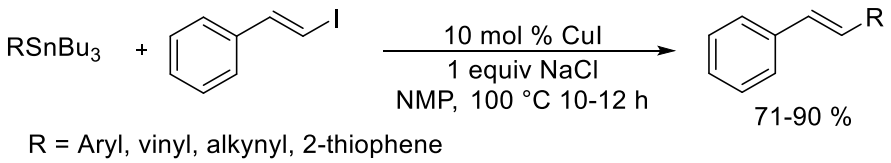


The first copper-catalyzed cross-coupling was developed using various alkyl, aryl and vinyl Grignard reagents with alkyl halides and pseudohalides. Burns and coworkers were successful in developing a highly soluble copper catalyst comprising equimolar amounts of CuBr.DMS, LiSPh and Lithium bromide. Using this copper catalyst, they were able to develop a cross-coupling reaction in 1997 with organomagnesium reagents, and alkyl, aryl, allyl and vinyl halides, and pseudohalides (Scheme 2.3).[65] Kang and coworkers also reported a copper-catalyzed cross-coupling reactions using organotin reagents with good to excellent yields. The reaction can be applied to the coupling of various organotin reagents like aryl, heteroaryl, vinyl and alkynyltin reagents with aryl and vinyl iodides (Scheme 2.4).[66]

Scheme 2.3. Copper-catalyzed cross-coupling of Grignard reagent with alkylhalides and pseudohalides

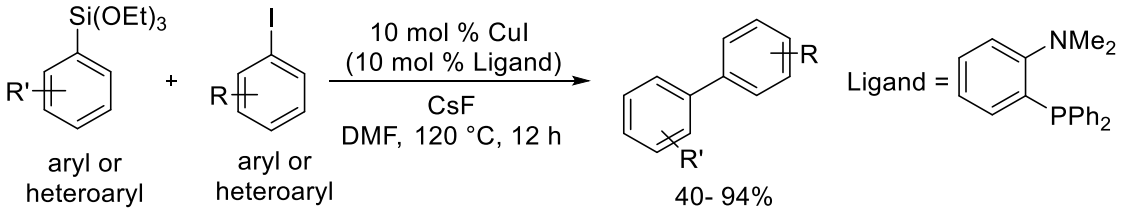


Scheme 2.4. Copper-catalyzed Stille coupling with vinyl iodides

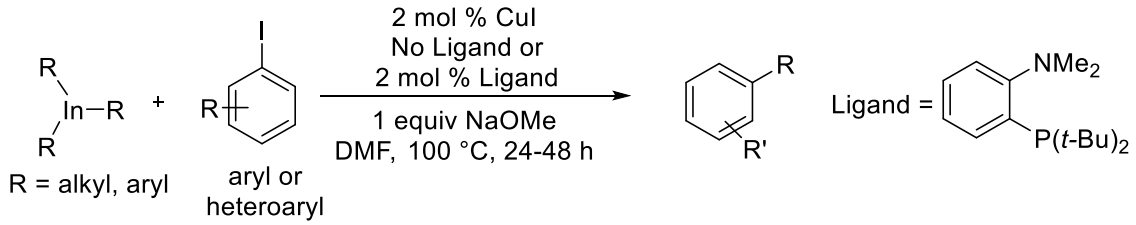


Our group has played a vital role in broadening the scope of copper-catalyzed cross-coupling reactions. Our group developed the first examples of copper-catalyzed Hiyama coupling of aryl or heteroaryltriethoxysilanes with aryl and heteroaryl halides. The reaction requires 2-(diphenylphosphino)-*N*,*N*-dimethylaniline as a ligand to promote the reaction. Interestingly, the reaction with heteroaryl iodides did not require any extra ligand (Scheme 2.5).[67] Our group also developed a copper-catalyzed cross-coupling between trialkyl- or triarylindium reagents and aryl or heteroaryl iodides in the presence of 2-(*tert*-butyl-phosphino)-*N*,*N*-dimethylaniline as a ligand with moderate to excellent yields (Scheme 2.6). The reaction with heteroaryl iodides produced cross-coupled products without the use of a ligand.[68] In the case of alkylindium reagents, the reaction gives products in good yields with primary, secondary and tertiary alkyl groups without any complications.

Scheme 2.5. Copper-catalyzed aryl-aryl and aryl-heteroaryl Hiyama coupling

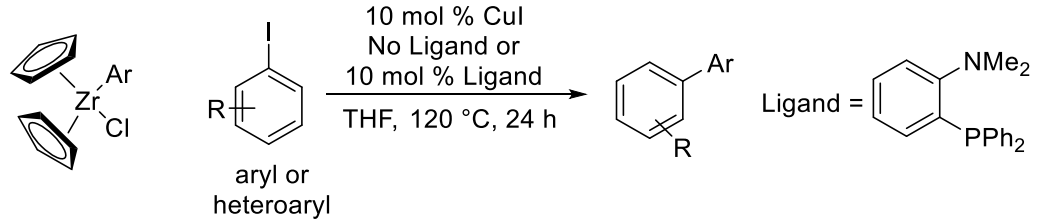


Scheme 2.6. Copper-catalyzed cross-coupling of organoindium with aryl iodides

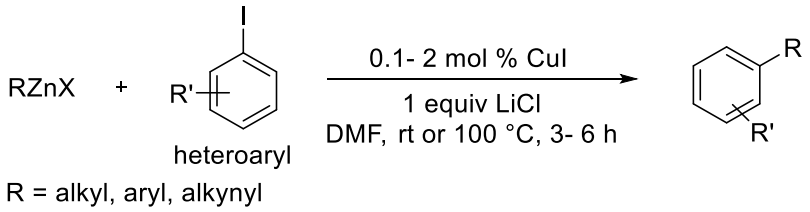


We also developed a copper-catalyzed cross-coupling reaction of arylzirconium reagents with aryl iodides in the presence of 2-(diphenylphosphino)-*N*,*N*-dimethylaniline as a ligand (Scheme 2.7).[69] Copper-catalyzed Negishi coupling of alkylzinc and arylzinc reagents with aryl and heteroaryl iodides was also developed (Scheme 2.8).[70] The reaction gave products in good yields with primary, secondary and tertiary alkylzinc reagents without any complications from β-H elimination. This reaction tolerated heteroaryl iodides without requiring a ligand. Similarly, our group developed the copper-catalyzed cross-coupling reaction using organoaluminium reagent and various electrophiles under otherwise similar reaction conditions.[71] This reaction also furnished products in moderate yields with heteroaryl bromides and chlorides.

Scheme 2.7. Copper-catalyzed cross-coupling of arylzirconium with aryl iodides



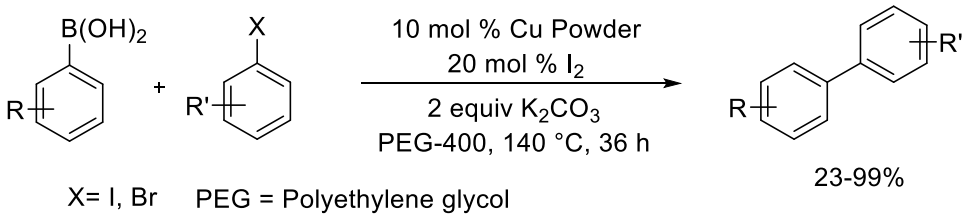
Scheme 2.8. Copper-catalyzed Negishi coupling with heteroaryl iodides



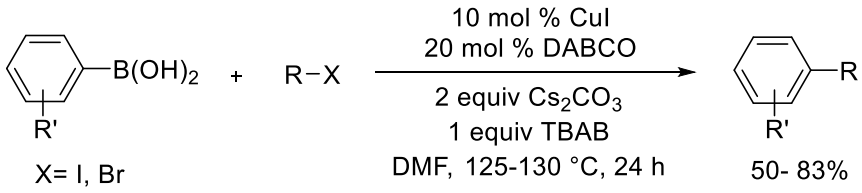
2.2. Copper-Catalyzed Suzuki-Miyaura Coupling

In 2002, Rothenberg and coworkers reported the first example of Cu-catalyzed Suzuki-Miyaura coupling of aryl boronic acids with aryl halides.[72] They utilized copper/noble metal mixed nanoclusters as catalysts. A similar reaction was also developed by Ji and coworkers by utilizing a copper(0) catalyst in PEG 400 (Scheme 2.9).[73] Hu and coworkers developed a copper-catalyzed cross-coupling of arylboronic acids with aryl and vinyl halides using DABCO as a ligand (Scheme 2.10).[74] This reaction works well with various aryl iodides and bromides.

Scheme 2.9. Copper-catalyzed Suzuki-Miyaura coupling with aryl bromides and iodides

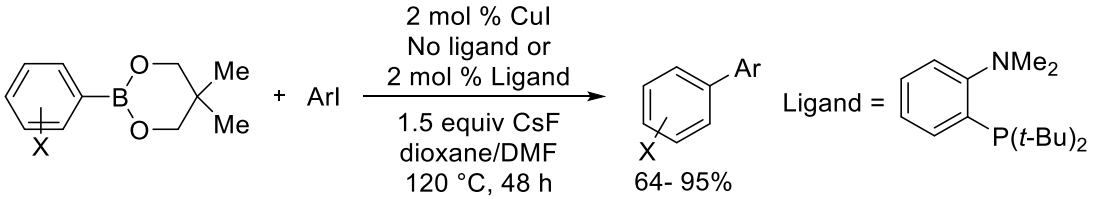


Scheme 2.10. Copper-catalyzed Suzuki-Miyaura coupling with aryl and vinyl iodides

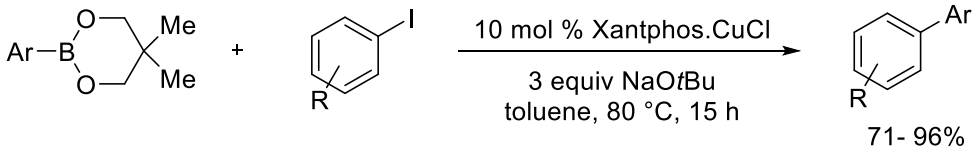


Recently, we developed a copper-catalyzed Suzuki-Miyaura cross-coupling of aryl and heteroaryl boronic esters with aryl and heteroaryl iodides employing o-(di-*tert*-butylphosphino)-*N*,*N*-dimethylaniline as a ligand (Scheme 2.11).[75] Interestingly, the reaction does not require any extra ligand with heteroaryl iodides. Brown and co-workers also developed a similar reaction using xantphos as a ligand for copper (Scheme 2.12).[76,77]

Scheme 2.11. Copper-catalyzed aryl-aryl and aryl-heteroaryl Suzuki-Miyaura coupling

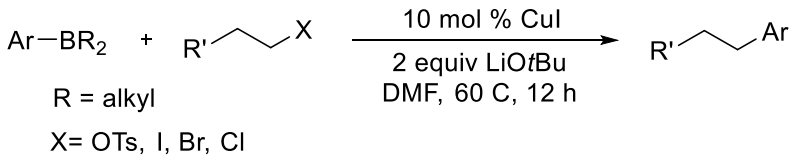


Scheme 2.12. Copper.xantphos catalyzed aryl-aryl Suzuki-Miyaura coupling



Liu and coworkers developed copper-catalyzed cross-coupling using aryl boronic esters and alkyl halides and pseudohalides (Scheme 2.13). In this case, arylcopper intermediates formed after transmetalation react with alkyl halides through an S_N2 process without requiring redox changes on copper.[78,79]

Scheme 2.13. Copper-catalyzed Suzuki-Miyaura coupling of aryl boron reagent and alkyl halides and pseudohalides



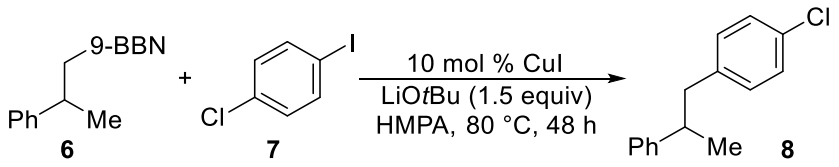
Although there has been a significant progress in developing Cu-catalyzed Suzuki-Miyaura coupling with aryl and vinylboron reagents, cross-coupling with alkylboron reagents still remains undeveloped. Development of such a reaction becomes formidably challenging due to the formation of alkylcopper intermediates that could undergo rapid β-H elimination. In addition, alkylcopper species can also undergo disproportionation reactions and derail the reaction to generate side products. Therefore, we show in the subsequent section our investigation and results on the development of Cu-catalyzed Suzuki-Miyaura coupling of alkylboron reagents.

2.3. Results and Discussion

We began our investigation by reacting *n*-butylboronic ester with 4-iodotoluene in the presence of CuI as a catalyst. The reaction produced no cross-coupled product. From our previous studies on copper-catalyzed alkyl-aryl cross-coupling reactions with other organometallic reagents, it was evident that the reaction would furnish cross-coupling products with aryl halides if alkylcopper intermediates were generated after transmetalation. Therefore, we assumed that transmetalation could be the problem. It is also known that the trivalent organoboron reagents are less nucleophilic and typically do not undergo transmetalation. Therefore, we made the more nucleophilic tetravalent alkylboronic ester by treating it with 1 equiv of *n*BuLi. Pleasingly, the alkylated

alkylboronic ester formed the cross-coupling product in 44% yield. We then examined the reaction using several bases and alkylboron reagents with different backbones. After examining various conditions, we found that the cross-coupled product was obtained in 90% GC yield when B-(2-phenylpropyl)- 9-BBN was treated with 4-iodo chlorobenzene in presence of 10 mol % CuI and 1.5 equivalent Li*O*t*Bu in HMPA at 80 ˚C for 24 h (Table 2.1, entry 1). The alkyl-9-BBN reagent was prepared *in-situ* by the hydroboration of α-methyl styrene. It was observed that both copper catalyst and base were indispensable for the reaction as there was no cross-coupled product formed in the absence of either of them. Other bases like LiOMe, K_3PO_4 and CsF also also formed the desired product albeit in moderate yields. When DMSO, NMP, DMPU or DMF was used as a solvent instead of HMPA, the product was formed in low yields. Reactions in toluene, dioxane, acetonitrile or THF did not form any desired product. When *n*-octylboronic acid and *n*-octylboronic acid neopentyl glycol esters were used instead of **6**, the reaction gave the product in 0% and 37% yields, respectively. 4-Bromobenzotrifluoride formed the product in 20% yield. The reaction can be run in a gram-scale (10 mmol) affording the expected product in 73% yield.

Table 2.1. Optimization of Reaction Conditions[a]



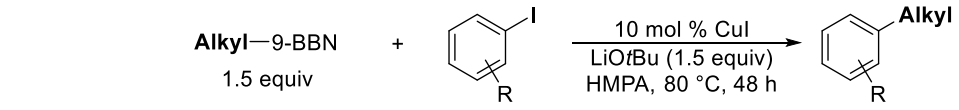
Entry	Variation from the standard conditions	Yield [%][b]
1	None	90 (85)
2	Without LiO*t*Bu or CuI	0
3	LiOMe, K_3PO_4 or CsF instead of LiO*t*Bu	38-52
4	DMSO, NMP, DMPU, DMF	13-34
5	toluene, dioxane, acetonitrile, THF	<1
6	*n*Oct-$B(OH)_2$ instead of **6**	0[c]
7	[d]*n*Oct-$B(OR)_2$ instead of **6**	37[c]
8	4-bromobenzotrifluoride instead of **7**	20[e]

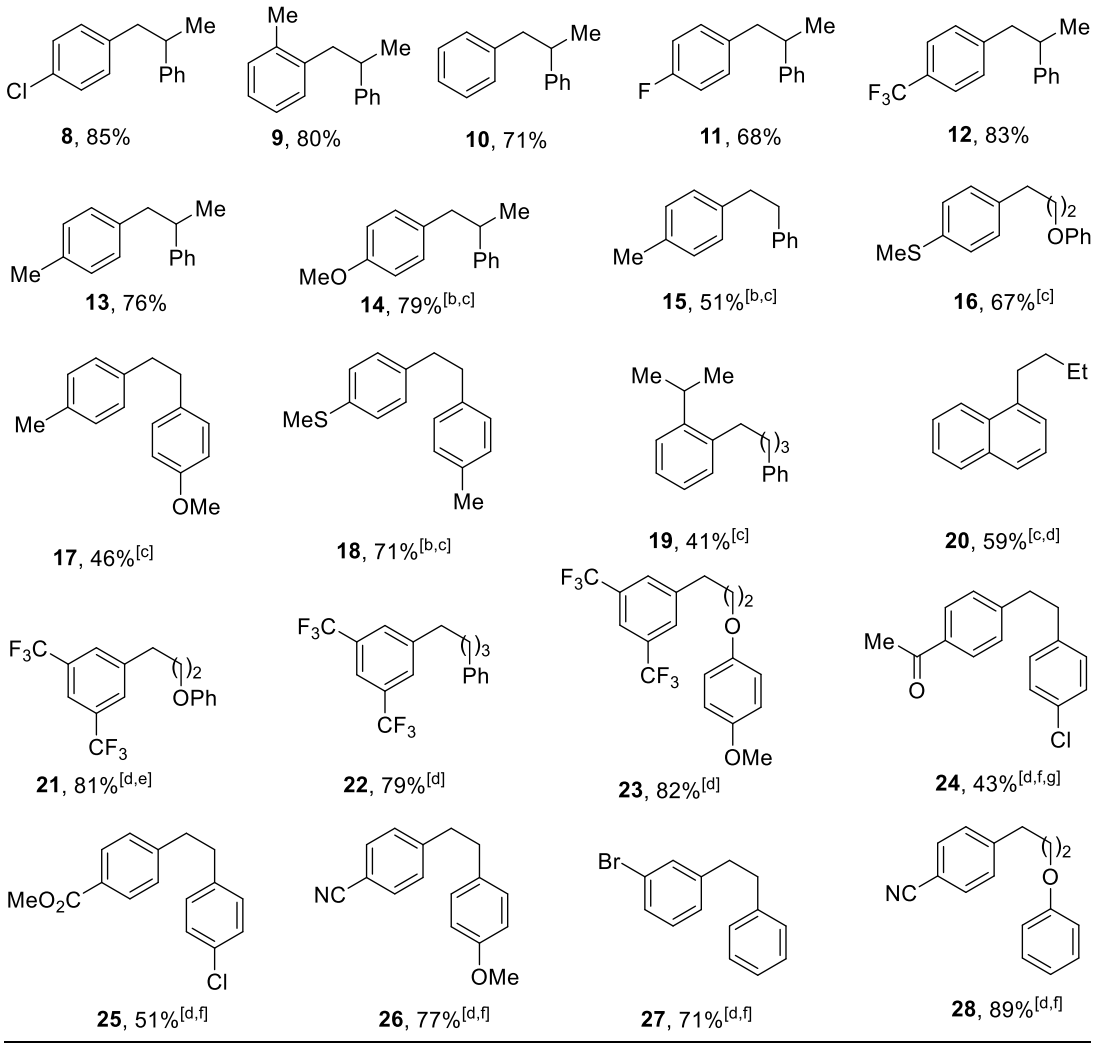
[a]0.1 mmol scale reactions in 0.5 mL solvent. [b] GC yields with pyrene as a standard. Value in parenthesis is the isolated yield (10.0 mmol scale reaction at 120 ˚C). [c] 4-Chlorophenyloctane as the product. [d] (OR)2 = neopentylglycol ester. [e] 4-(2-Phenylpropyl)benzotrifluoride as the product. 120 ˚C, 12 h.

With the optimized condition in hand, we then studied the substrate scope of the reaction. It was found that the reaction condition was applicable with different alkylboron reagent and aryl iodides to afford the desired cross-coupled product in good to excellent yields. However, some reactions required moist K_3PO_4 and DMF instead of Li*O*tBu and HMPA to give the products in best yields. In some reactions elevated temperature (100-120 ˚C) helped to produce best yields of the product. The reaction can be applied to variety of alkylboron reagents and aryl iodides (Table 2.2). The reaction was found to tolerate various functional groups like ketone, ester, nitrile, bromide, thioether and chloride with good to excellent yields. The reaction also tolerates *ortho*-substituents and sterically hindered groups. The reaction also works well with alkylboron reagent with β-branching.

To further broaden the substrate scope, the reaction condition was also investigated with nitrogen-containing heteroaryl iodides. The reaction gave products in good to excellent yields with different heteroaryl iodides (Table 2.3). Moist K_3PO_4 was required for the reaction to give best yield perhaps due to its solubility issue. Some reactions gave higher yield with the DMF instead of HMPA. The reaction was also found to tolerate β-branching in the alkylboron and functional groups like chlorides, bromides, olefins, monoprotected amines and thioethers.

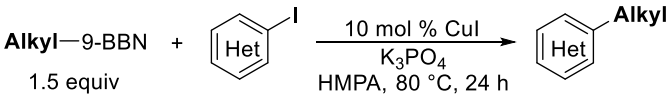
Table 2.2. Substrate scope of different alkylboron reagent and aryl iodide

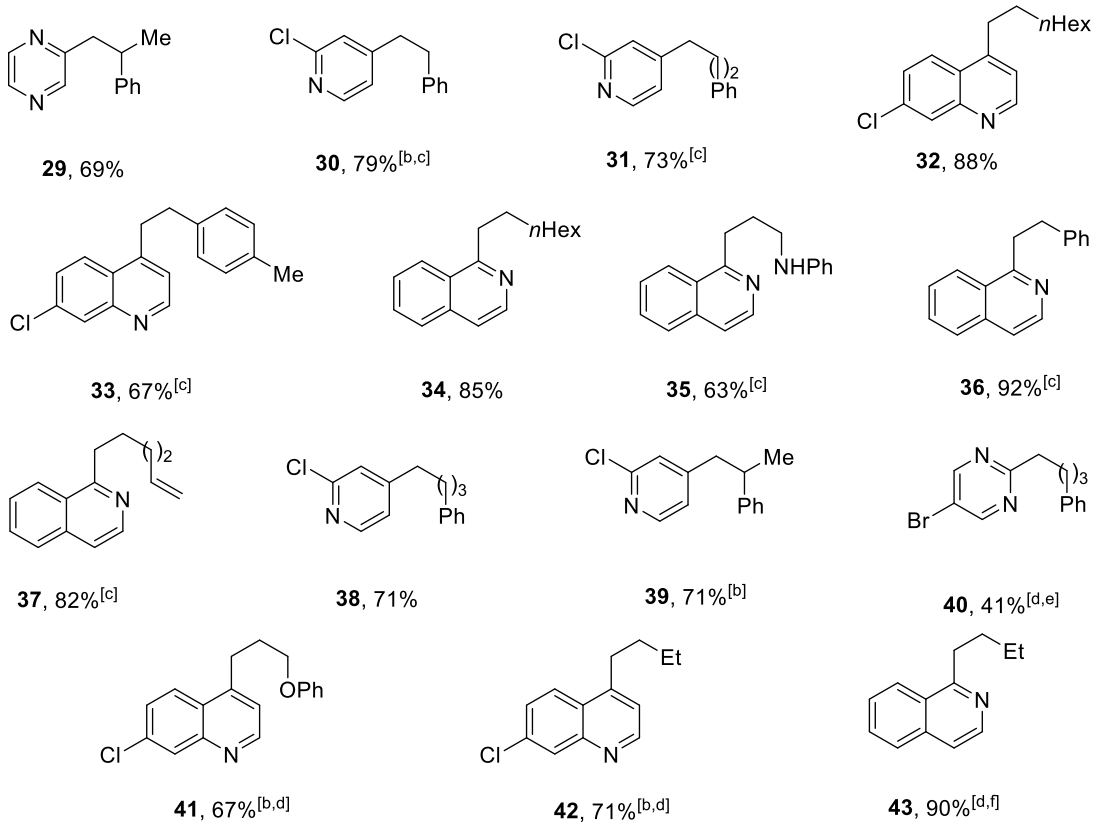




[a] Reactions were conducted in 1.0 mmol scale in 5 mL solvent. Values are isolated yields. [b] 2 equiv of alkyl-9-BBN was used. [c] 120 °C. [d] 3 equiv of K_3PO_4 used instead of LiO*t*Bu. [e] 36 h. [f] 100 °C. [g] 24 h.

Table 2.3. Substrate scope of different alkylboron reagent and heteroaryl iodides





[a] Reactions were conducted in 1.0 mmol scale in 5 mL solvent. Values are isolated yields. [b] 100 °C. [c] 48 h. [d] DMF used instead of HMPA. [e] 60 °C. [f] 12 h.

2.4. Mechanistic Studies

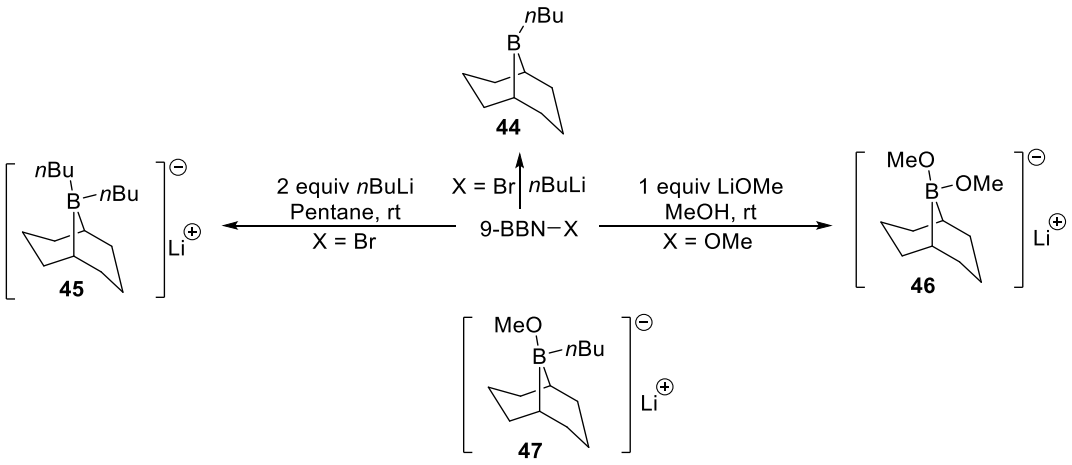
The copper mediated cross-coupling were discovered before the palladium catalyzed cross-coupling. However, less attention was given due to various challenges like lack of understanding of mechanism, possible disproportionation of organocopper species, difficulty in characterization of intermediates and formation of aggregates.[80] However,

mechanistic studies on copper-catalyzed coupling reaction have been done which were mainly focused on C-N and C-O bond formation.[21] In case of C-C bond, our group had done some mechanistic works on aryl-aryl Suzuki-Miyaura cross-coupling.

Metal catalyzed cross-coupling involves three elementary steps which are oxidative addition, transmetalation and reductive elimination. Our previous study on copper-catalyzed Suzuki-Miyaura cross-coupling, transmetalation was found to be the initial step which follows oxidative addition and reductive elimination is the final step. So, we began our mechanistic investigation and first focused on transmetalation step. It is believed that more nucleophilic organometallic species undergo faster transmetalation. Organozinc and organomagnesium are nucleophilic enough to undergo transmetalation. However, organoboron are mildly nucleophilic and therefore require base to transmetalate which is believed to be due to the formation of more nucleophilic anionic borate species. The control reaction shows that reaction did not proceed without base. This indicates the potential role of base in the formation of anionic borate species. So, we assume the anionic boron intermediate formed by the reaction between alkylboron and base should be the transmetalating species. To probe further detail in the transmetalation step, we attempted to prepare the potential transmetalating species by treating B-OMe 9-BBN with *n*BuLi in THF at room temperature. Generally, an anionic boron intermediate, (OMe)*n*Bu-9-BBN (**47**) was expected to form. However, two anionic borate species **45** and **46** were observed. This was believed to occur due to the disproportionation of the anionic (OMe)*n*Bu-9-BBN. Similar trend of disproportionation was also reported by Furstner and coworkers.[81] We independently synthesized the two anionic borate species. The dibutyl anionic borate was prepared by reacting Br-9-BBN with 2.0 equiv of *n*BuLi at room temperature in pentane

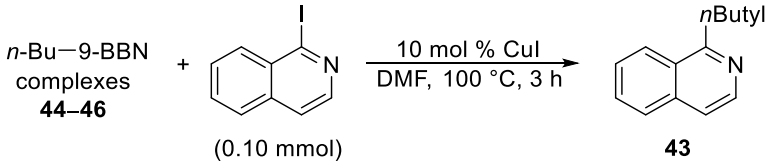
for 1 h while di-methoxy anionic borate was prepared by reacting 9-OMe-9-BBN with 1 equiv of lithium methoxide at room temperature in methanol for 2 h. We also obtained the crystal structure of these borate intermediates, **45** as a 12-crown-4 complex and **46** as a THF dimer.

Scheme 2.14. Independent synthesis of organoboron complexes



With these boron intermediate in hand, we conducted the reactivity study. First, we performed the reaction between 0.5 equiv of complex **45** and 1 equiv of 1-iodoisoquinoline without any base. The reaction gave 48% yield while when 0.5 equiv of lithium methoxide was added as a base in the reaction, it gave 95% yield of the product. This shows that complex **45** is also capable of transmetalating butyl group but it can only transmetalate one butyl group in absence of base. In the presence of base, complex **45** can transmetalates both butyl group. We performed another reaction using 0.5 equiv each of complex **45** and **46** in the reaction without the use of base, the reaction gave 97% yield. From this result, it shows that complex **45** and **46** comproportionates to give anionic borate species **47** and the potential role of these complexes in the reaction. Complex **47** was also believed to form when complex **45** was treated with base and when a complex **44** was treated with base.

Table 2.4. Reactivity of *n*-Butyl-9-BBN Species **44-46** with 1-iodoisoquioline



Entry	*n*-Bu-9-BBN complexes	Base	Yield [%]
1	*n*-Bu-9-BBN (1.0 equiv)	none	trace
2	*n*-Bu-9-BBN (1.0 equiv)	LiOMe (1 equiv)	94
3	Complex **45** (0.50 equiv)	none	48
4	Complex **45** (1.0 equiv)	none	95
5	Complex **45** (0.50 equiv)	LiOMe (0.5 equiv)	94
6	Complexes **45** + **46** (0.50 equiv each)	none	97

We also performed the experiment to show the disproportionation of the complex 47 through the proton and boron NMR spectroscopy. These NMR spectra also shows that the anionic borate intermediate **47** undergo disproportionation to give two anionic borate species **45** and **46** in the reactions (Tables 2.1, 2.2, 2.3).

Figure 2.1. ^{1}H NMR spectrum in DMSO-d_6 of the reaction mixture overlaid with the standard samples of the borate complexes **45** and **46**.

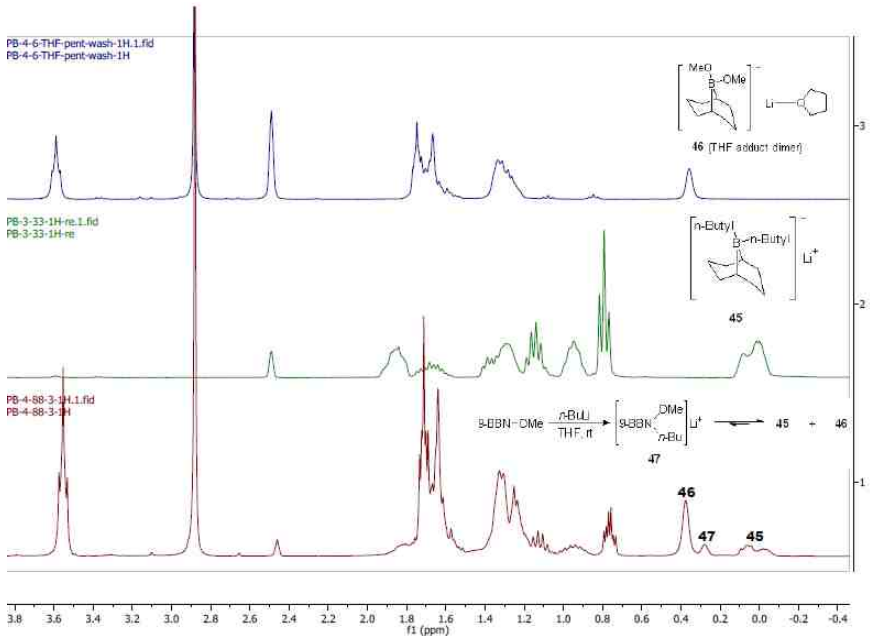


Figure 2.2. ^{11}B NMR spectrum in DMSO-d_6 of the reaction mixture overlaid with the standard samples of the borate complexes **45** and **46**.

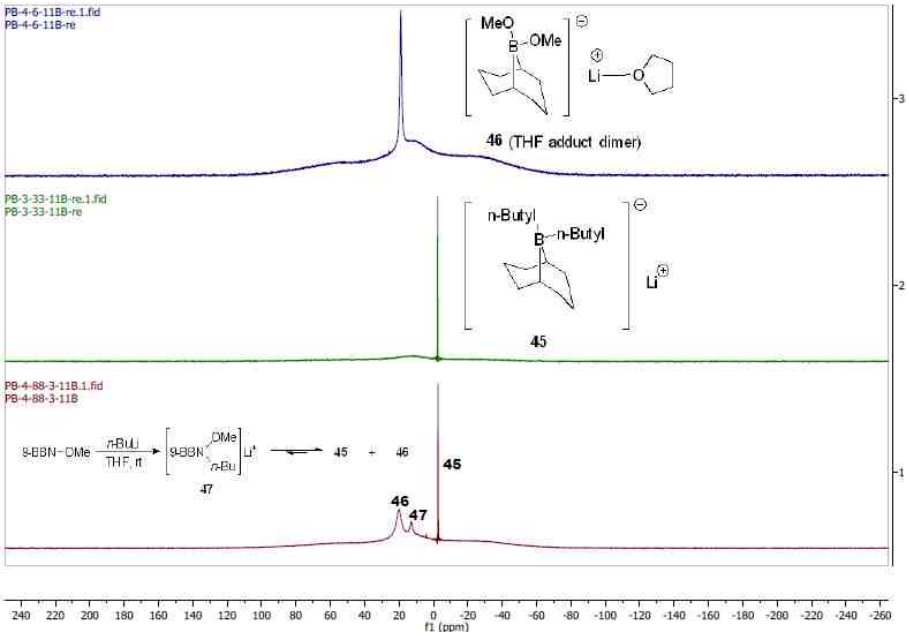
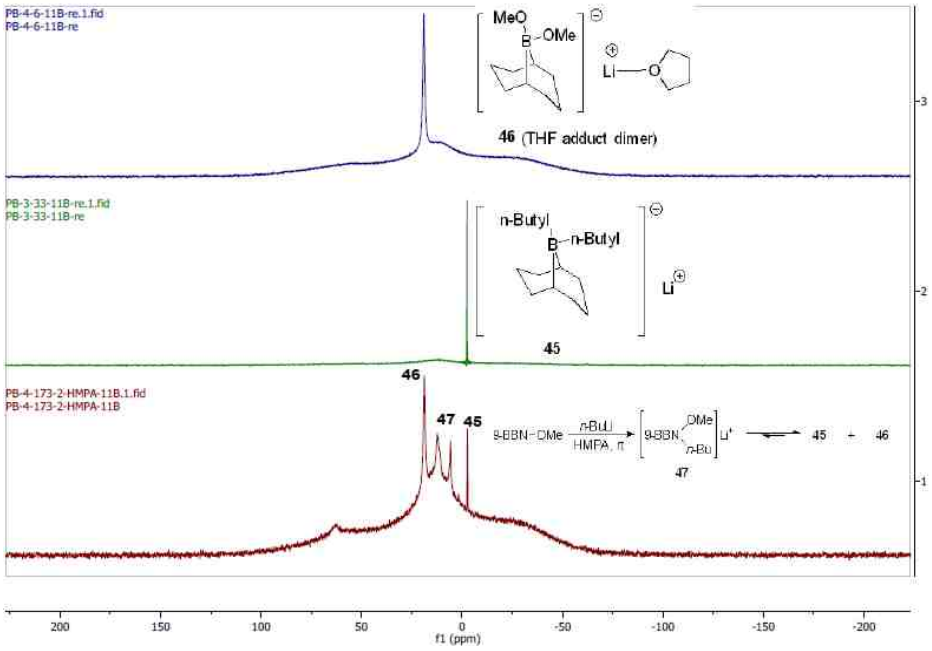


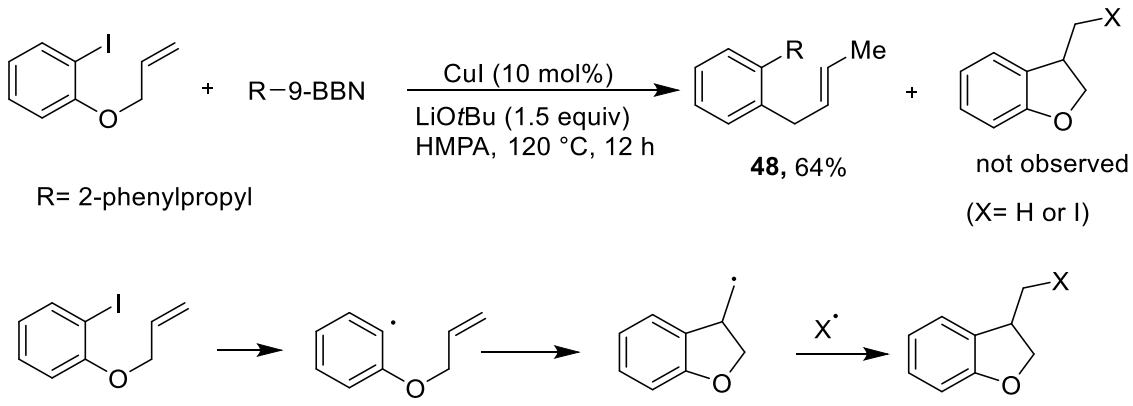
Figure 2.3. ^{11}B NMR spectrum in HMPA of the reaction mixture overlaid with the standard samples of the borate complexes **45** and **46**.



Radical probe experiment

Our next step was to examine the reaction of aryl halide with the transmetalated copper intermediate. Aryl halide is believed to react with two different routes. Either copper(I) intermediate undergo oxidative addition to aryl iodides to form a copper (III) complex or undergo single electron transfer (SET) or halogen atom transfer (HAT) to generate copper (II) complex and aryl radical. To probe the potential involvement of aryl radical in the reaction, we first conducted the radical probe experiment. In this experiment, *o*-allyloxyiodobenzene was used as a radical probe. It is reported that o-allyloxyiodobenzene undergoes cyclization protonation at the rate constant of 9.8×10^9 s^{-1}in DMSO at room temperature[82] when the corresponding aryl radical is generated by the cleavage of C-I bond

Scheme 2.15. Radical probe experiment

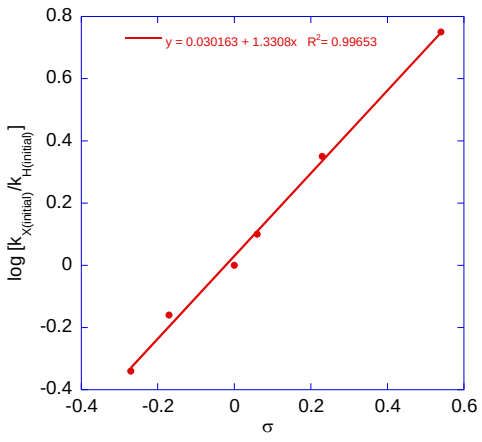


(Scheme 2.15). This radical probe has been widely used to test the involvement of radical in the reaction.[83,84] The reaction gave the cross-coupled product **48** in 64% yield without any observance of cyclized product. This result indicates that no free aryl radical is involved in this reaction.

Hammett plot

We also obtained the Hammett plot to further confirm non-radical pathway. We investigated the change in the rate of reaction of alkylboron reagent and aryl iodide in the

Figure 2.4. Hammett plot



standard reaction when electron withdrawing and electron donating substituents were used in the aryl iodides (Scheme 2.16). A linear curve ($R^2 = 0.99$) was obtained when the log value of the ratio of initial rate of substituted iodoarenes to initial rate of the iodoarene was plotted against substituent constant (σ). The reaction constant (ρ) equal to +1.33 was obtained (Figure 2.4). The result was consistent with the reaction of electron rich metals

Scheme 2.16. Reaction of alkylboron reagent with electronically different aryl iodides

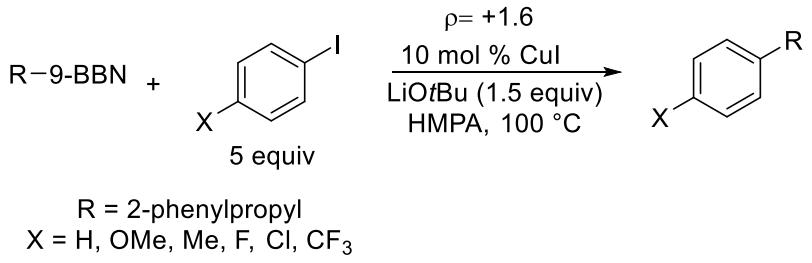


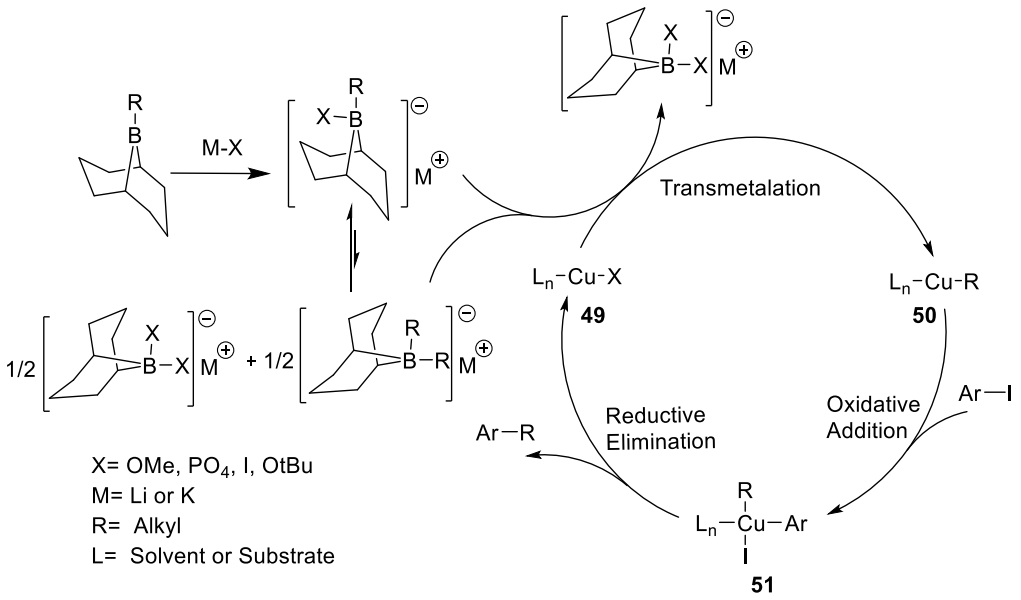
Table 2.5. Values used to Obtain the Hammett Plot

iodoarenes	$k_{X(initial)}$ (M s^{-1})	$\log[k_{X(initial)}/ k_{H(initial)}]$	σ
X = H	1.34×10^{-5}	0.00	0.00
X = OMe	0.61×10^{-5}	-0.34	-0.27
X = Me	0.92×10^{-5}	-0.16	-0.17
X = F	1.68×10^{-5}	0.10	0.06
X = Cl	3.02×10^{-5}	0.35	0.23
X = CF_3	7.58×10^{-5}	0.75	0.54

and aryl halides which proceeds through oxidative addition mechanism.[85,86] This result also rules out the possibility of involving free aryl radical in the reaction and indicates the oxidative addition-reductive elimination pathway.

We then proposed the possible catalytic cycle of our reaction. We believe that the anionic borate intermediate formed after complexation of alkylboron with base undergo disproportionation before transmetalation and forms the two anionic borate species. The two butyl containing borate species then undergo transmetalation with copper catalyst **49**

Scheme 2.17. Proposed catalytic cycle



to form alkylcopper species **50**. This species undergoes oxidative addition with aryl iodide and forms copper (III) intermediate **51**. The copper (III) species gives the desired product with the regeneration of active catalyst after reductive elimination.

2.5. Conclusion

We developed a novel copper-catalyzed Suzuki-Miyaura cross-coupling with alkylboron reagent and aryl or heteroaryl iodides without the use of any complex ligands. The reaction condition is applicable to various alkylboron reagent and tolerates sensitive functional groups and heteroarenes. Mechanistic studies showed that the anionic alkylborate intermediate prepared from alkyllithium and alkoxyboron reagent disproportionates to anionic dialkylborates and dialkoxyborates before transmetalation to copper catalyst. Radical clock experiment and Hammett plot obtained indicated that the reaction proceeds through non-radical pathway.

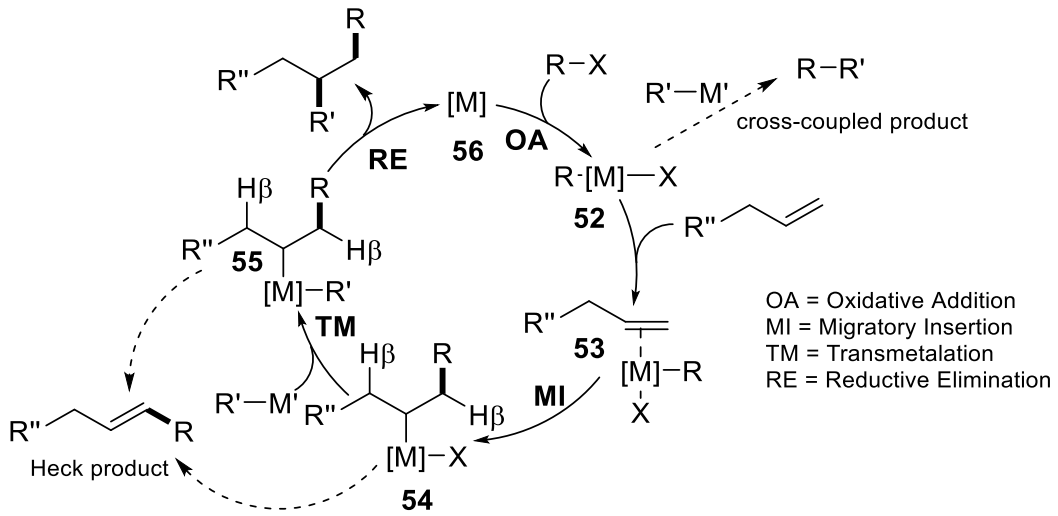
Chapter 3. Dicarbofunctionalization of Alkenes

3.1. Introduction

Transition metal-catalyzed dicarbofunctionalization is a versatile reaction to generate two new carbon-carbon bonds across an alkene in a single step.[87,88] The reaction is an extremely efficient process to build complex molecule since it reduces time and energy required for the isolation and purification of intermediates. In addition, this method utilizes highly abundant and inexpensive alkenes, which are usually generated as byproducts of petroleum industry. Sharpless' dihydroxylation is one of the early examples in which an alkene is difunctionalized and two new C-O bonds are generated.[89]

Dicarbofunctionalization through cross-coupling is one of the most useful ways to perform dicarbofunctionalization of alkenes. Herein, an alkene, organic halide and an organometallic reagent are used as reagents in presence of a transition metal catalyst. This process combines the elementary steps of the Heck process and a cross-coupling reaction to form two new carbon-carbon bonds across an alkene. The reaction can be anticipated to proceed with four basic steps – oxidative addition, migratory insertion, transmetalation and reductive elimination (Scheme 3.1). Initially, an organic halide oxidatively adds to a catalyst generally bound to the substrate alkene **53**. Upon migratory insertion of the bound alkene, a new alkylmetal species **54** is generated, which then undergoes transmetalation with nucleophilic organometallic reagents. The resulting intermediate **55** undergoes reductive elimination to form a dicarbofunctionalized product and regenerates the catalyst **56**.

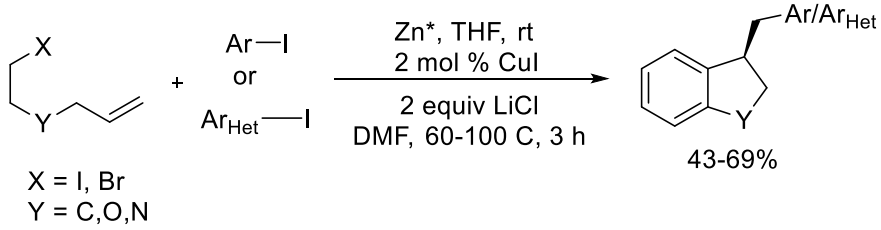
Scheme 3.1. General catalytic cycle for alkene difunctionalization through cross-coupling with fundamental issues



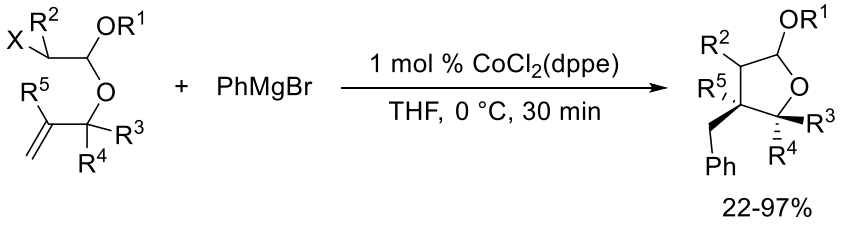
However, the development of alkene dicarbofunctionalization reactions by cross-coupling approach is not straightforward. The sequence of the four elementary steps required for dicarbofunctionalization is generally marred by two major side reactions – 1) direct cross-coupling between an organic halide and an organometallic reagent prior to alkene insertion, and 2) β-H elimination from the alkylmetal species after the alkene insertion.[90-92] Therefore, these two issues must be addressed in order to develop alkene dicarbofunctionalization reaction. Despite these two serious challenges, a few alkene dicarbofunctionalization reactions have been developed. Majority of these reactions, however, involve cyclization/coupling where an alkene is tethered either to organic halides or organometallic reagents.[93,94,95,96] These two component reactions are generally favored by the intramolecular nature of the alkene, which enables efficient alkene binding and promote migratory insertion faster than direct cross-coupling. In addition, the formation of

alkylmetal intermediates on the exocyclic backbone of a ring could also slow down the process of β-H elimination and promote the subsequent steps of transmetalation and reductive elimination. For example, our group developed copper-catalyzed cyclization cross- coupling using alkylzinc halides and arylzinc halides with aryl and heteroaryl iodides. The reaction involves the radical cyclization followed by interception of alkylcopper species by aryl and heteroaryl iodides (Scheme 3.2).[97] Oshima and coworkers in 2001 reported the development of dicarbofunctionalization reaction in which they were successful in forming a cyclized product using alkene tethered to alkyl halide and Grignard reagent in presence of cobalt catalyst and dppe as ligand. The reaction was believed to occur through the formation of alkyl radicals (Scheme 3.3).[98]

Scheme 3.2. Copper-catalyzed cyclization/ cross-coupling of Arylzinc halides



Scheme 3.3. Cobalt catalyzed cyclization/ cross-coupling with Grignard reagents

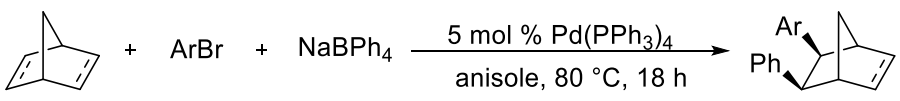


3.2. Three-Component Dicarbofunctionalization of Alkenes

In a three-component alkene dicarbofunctionalization reactions, separate entities of alkenes, organic halides and organometallic reagents are employed. Transition metal catalyzed three-component dicarbofunctionalization of alkenes is a very efficient method to build molecular complexity rapidly from readily available starting materials. However, development of these three-component reactions remains a formidable challenge especially when alkenes are unactivated. The issues of cross-coupling and β-H elimination are generally more pronounced in three-component reactions than in cyclization/coupling because of inefficient alkene binding and the lack of any stabilizing factors in alkylmetal species. Traditionally, three strategies were generally implemented to dicarbofunctionalize alkenes – the use of geometrically constrained alkenes to prevent β-H elimination, the use of additional alkene component in dienes or styrenes to intercept alkylmetal species as *p*-allyl and *p*-benzylmetal species, and the use of CO to intercept alkylmetal species as alkylacylmetal species.

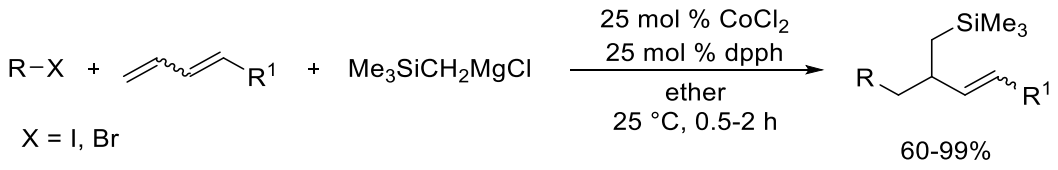
As a first strategy of using geometrically restricted alkenes, Chiusoli and Catellani reported in 1982 the dicarbofunctionalization of norbornene with alkyl halides and alkynes catalyzed by palladium.[99] In this reaction cis exocyclic products were formed without β-H elimination due to geometric restrictions. Dicarbofunctionalization of norbornadiene with aryl halides and Sodium tetraphenylborate was also successfully developed by Goodson and coworkers in presence of palladium catalyst (Scheme 3.4).[100]

Scheme 3.4. Palladium catalyzed diarylation of norbornadiene

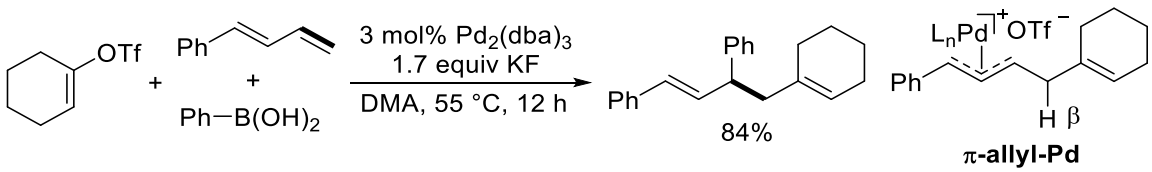


Takai and coworkers reported the second strategy of using an additional alkene in dienes to stabilize alkylmetal species by developing difunctionalization of 1,3-dienes with alkyl halides and aldehydes in presence of chromium chlorides.[101] This reaction required an excess amount of chromium salts to form products in good yields. In 2003, Oshima and coworkers reported the development of cobalt-catalyzed dicarbofunctionalization of 1,3-dienes with alkyl halides and Grignard reagents (Scheme 3.5).[102] In this case, β-H elimination was suppressed by the formation of π-allylcobalt intermediates. Sigman and coworkers also applied this strategy for palladium-catalyzed dicarbofunctionalization of dienes with arylboronic acids and vinyl triflates (Scheme 3.6).[103] Similarly, Gong and coworkers used this approach for enantioselective dicarbofunctionalization of dienes with aryl halides and dialkyl malonates in presence of a palladium catalyst and a H_8-BINOL based phosphoramadite ligand.[104,105]

Scheme 3.5. Cobalt catalyzed dicarbofunctionalization of dienes

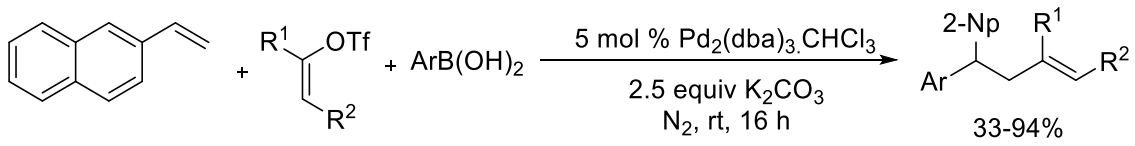


Scheme 3.6. Palladium catalyzed arylvinylation of dienes

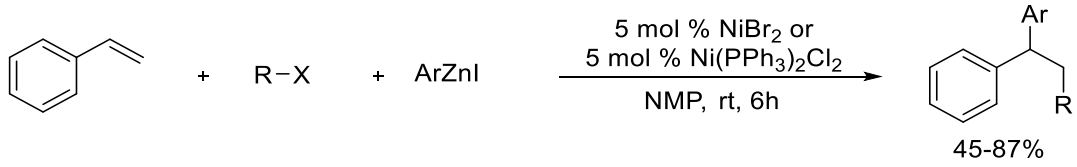


Like dienes, styrene derivatives can also be used as a source of alkenes where the alkylmetal species is stabilized as π-benzylmetal intermediates.[106] In 2010, Song and coworkers developed the vinylarylation of styrene derivatives using vinyl triflates and arylboronic acids in presence of palladium as a catalyst (Scheme 3.7).[107] Recently, our group also successfully developed alkylarylation of styrenes using nickel as a catalyst (Scheme 3.8).[108] The reaction condition are applicable to the use of various primary, secondary and tertiary alkyl halides. However, the reaction with tertiary alkyl halides required $Ni(PPh_3)_2Cl_2$ as the nickel catalyst to get higher yield of the desired product.

Scheme 3.7. Palladium catalyzed vinylarylation of styrenes



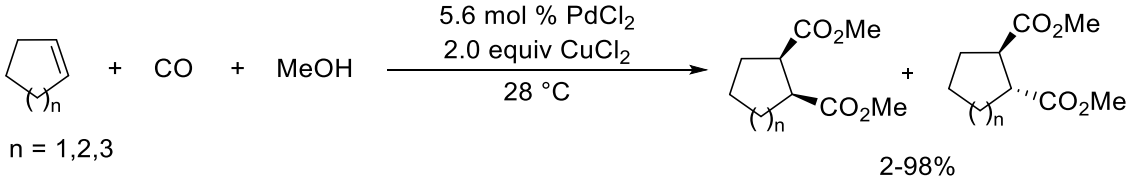
Scheme 3.8. Nickel-catalyzed alkylarylation of styrenes



Stille and coworkers utilized the third approach in which CO molecules would intercept alkylmetal species by CO insertion to generate alkylacylmetal intermediates, which would not undergo β-H elimination. Herein, Stille and coworkers developed dicarbofunctionalization of various alkenes using carbon monoxide and methanol in presence of palladium chloride and copper chloride (Scheme 3.9).[109] Although the reaction does not involve the pattern of cross-coupling approach for bond formation, the reaction

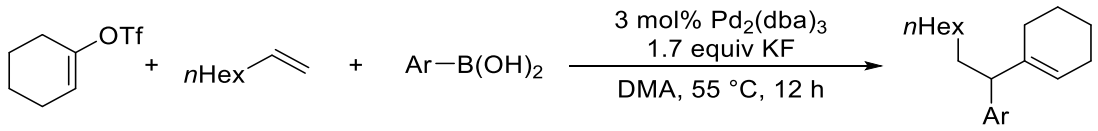
represents a powerful method to dicarbofunctionalize unactivated alkenes. In this method two alkoxy groups are simultaneously added to alkenes. Ishii and coworkers also developed later the dicarboalkoxylation of styrenes and unactivated alkenes using methanol in presence of palladium as a catalyst and molybdovanadophosphate as an oxidant.[110] In this reaction, they observed the formation of 1,2- and 1,3-difunctionalized product.

Scheme 3.9. Palladium catalyzed decarboxylation of unactivated alkenes



The use of unbiased alkenes generally leads to the formation of Heck products during alkene difunctionalization reactions. However, Sigman and coworkers demonstrated in some instances that the alkene products after β-H elimination could also undergo reinsertion of metal-hydrides (Pd-H) and furnish 1,1-dicarbofunctionalized products. For example, a Pd-catalyzed difunctionalization of unactivated alkenes with vinyl triflate and arylboronic acids formed 1,1-vinylarylated products (Scheme 3.10). [104]

Scheme 3.10. Palladium catalyzed 1,1-difunctionalization of simple alkene



3.3. Conclusion

Over the past few decades, significant progress has been made in the use of the combined alkyl-metal species and cross-coupling to difunctionalize unactivated alkenes with

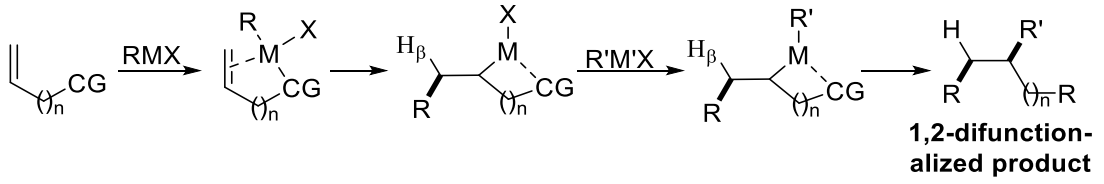
organohalides and organometallic reagents. Several strategies have been executed since its discovery. However, the strategies require the special substrates. These substrates help to prevent the formation of heck product from β-H elimination by the formation of geometrically constrained alkylmetal species, stable π-allyl metal, π-benzyl metal intermediates or intercepting the alkylmetal species with carbon monoxide. Using these strategies, various dicarbofunctionalization reactions involving three-component intermolecular and the two-component cyclization/cross-coupling processes were developed.

Chapter 4. Coordinating Group Approach for Dicarbofunctionalization of Alkene

4.1. Introduction

Heteroatom bearing groups such as pyridines and imines are among the best coordinating ligands for transition metals. Intramolecular chelation with these groups is thus utilized in organometallic chemistry to generate C(sp^3)-M metallacycles[111] that are stable towards β-H elimination.[112-117] C(sp^3)-M metallacycles are also routinely generated *in situ* during catalytic sp^3 C–H bond functionalization directed by heteroatoms that resist β-H elimination.[118,119] Metallacycles undergo decomposition by β-H elimination more slowly than their acyclic variants due to restricted rotations that prevent the attainment of favorable geometry for β-H elimination.[112-117] Even in metallacycles that contain exocyclic alkyl groups with β-H's that have greater freedom of rotation,[113] β-H elimination proceeds almost four orders of magnitude more slowly than in their acyclic counterparts.[112]

Scheme 4.1. Coordinating group approach in difunctionalization of alkene



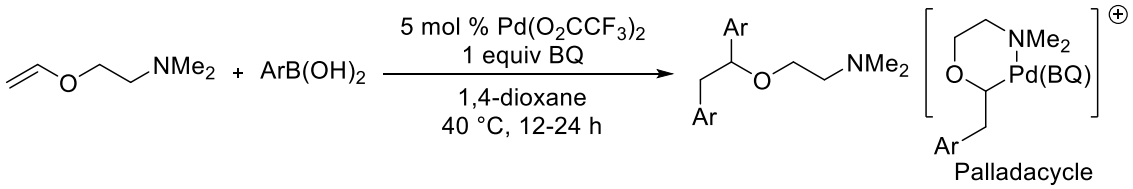
M=Pd, Ni etc; M'= Zn, Mg etc; X = halides; R, R' = alkyl, aryl, CG=Coordinating group

In coordination-assisted alkene difunctionalization, it could be envisioned that the substrates could function as bidentate ligands due to the presence of the heteroatom and the alkene, which could intercept the initial oxidative addition intermediates, R-[M]-X (Scheme 4.1).[120] This bidentate coordination could then enable the carbometalation of R-

[M]-X upon the coordinated alkene to proceed much faster than the direct cross-coupling between organohalides and organometallic reagents that usually operates as a serious side reaction.

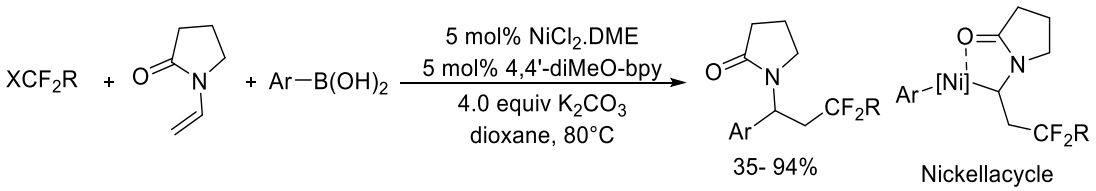
In 2009, Larhed and co-workers successfully developed the oxidative diarylation of vinyl ethers in presence of palladium catalyst. In this reaction, they proposed that β-H elimination in the alkylpalladium intermediate was prevented by the formation of palladacycle with amine as coordinating group (Scheme 4.2).[121] However, the alkene in this substrate is activated and same aryl groups are incorporated in the double bond.

Scheme 4.2. Palladium catalyzed coordination assisted diarylation of vinyl ethers



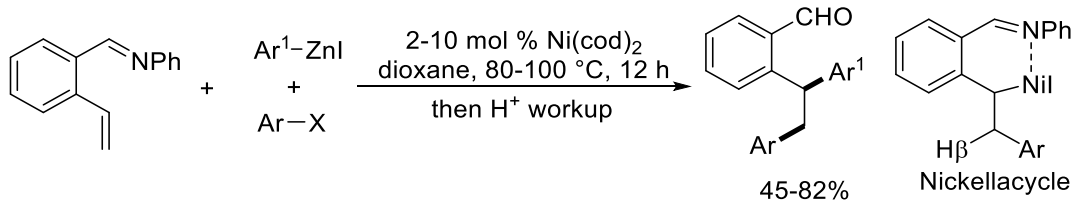
Zhang and coworkers in 2016 developed nickel-catalyzed difluoroalkylarylation of enamides where they showed the successful difluoroalkylarylation in the vinyl group of enamides using nickel catalyst. They proposed that nickellacyle formed between the oxygen in enamide as the coordinating group and alkene with catalyst is responsible to prevent the β-H elimination (Scheme 4.3).[122] Though, the reaction is a promising transformation, the difficulty in removal of coordinating group and activated alkene limits the scope.

Scheme 4.3. Nickel-catalyzed difluoroalkylarylation of enamides

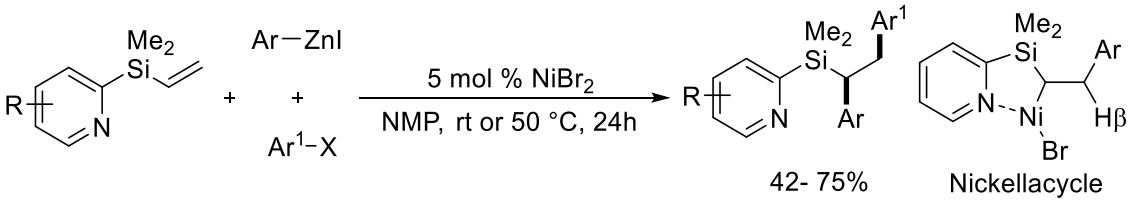


Our group used the coordinating group strategy to regioselectively diarylate vinylarene derivatives in presence of nickel catalyst and easily removable imine as a coordinating group. This reaction is believed to undergo diarylation without β-H elimination due to the formation of 6-membered nickellacycle (Scheme 4.4).[120] The reaction is highly promising as aryl iodide, bromides and triflates give the desired product in good yields. Similarly, our group also used pyridine as the coordinating group and developed the diarylation of pyridylvinyl silanes. In this reaction, the formation of 5-membered nickellacycle is believed to contribute in preventing β-H elimination (Scheme 4.5).[123] The removal of coordinating group through oxidation of the difunctionalized product affords the alcohols.

Scheme 4.4. Nickel-catalyzed 1,2-diarylation of vinylarenes through cocordinating group assisted formation of metallacycle

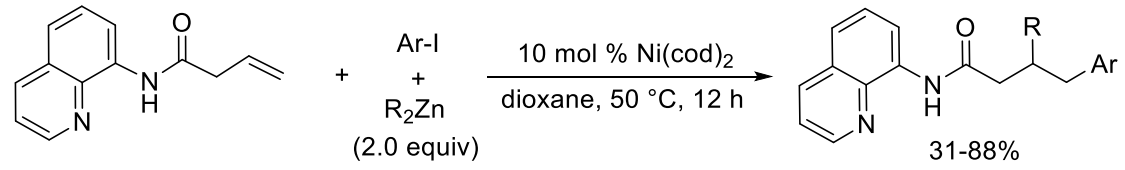


Scheme 4.5. Nickel-catalyzed 1,2-diarylation of vinylsilanes through pyridine assisted formation of metallacycle

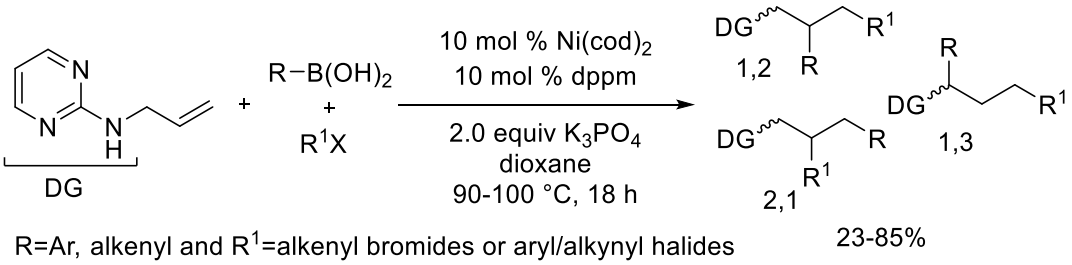


Engle and coworkers also developed the dicarbofunctionalization of alkene using 8-aminoquinolinamide as the coordinating group. The reaction is proposed to proceed by the formation of transient metallacycle which prevent the β-H elimination. Nevertheless, the coordination group require harsh condition to be removed (Scheme 4.6).[124] To remove the coordinating group from the product, it has to be refluxed in ethanol in presence of sodium hydroxide. Zhao and coworkers did the nickel-catalyzed dicarbofunctionalization of alkene using aminopyrimidine as the coordinating group. The reaction forms 1,2 or 2,1 or 1,3 dicarbofunctionalized product depending on the use of various electrophiles.[125] In this reaction as well the coordinating group is difficult to remove (Scheme 4.7).

Scheme 4.6. Nickel-catalyzed alkylarylation of 8-aminoquinolinamide

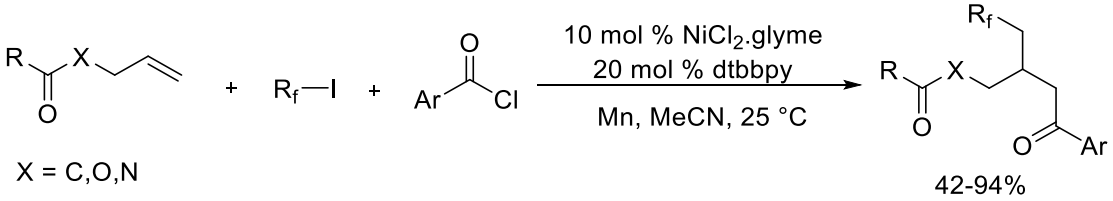


Scheme 4.7. Nickel-catalyzed difunctionalization of *N*-Allyl aminopyrimidines

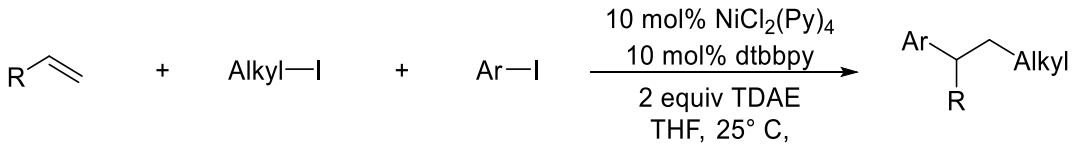


Chu and coworkers recently developed the carboacylation of alkenes using nickel catalyst. The reaction is proposed to undergo through the assistance of oxygen as the coordinating group. The reaction involves the formation of acyl radical and addition to alkene which then radically recombined with the alkyl radical to form the difunctionalized product (Scheme 4.8). [126] Similarly, Nevado and coworkers developed the reductive alkylarylation of alkenes using nickel catalyst.[126,127] The reaction is believed to involve radical mechanism. In this reaction alkenes are mildly activated and in some cases the reaction is believed to involve the coordination assisted stabilization of the alkylmetal intermediate. In some particular substrates, it was observed that in the absence of coordinating groups the reaction did not afford any dicarbofunctionalized product (Scheme 4.9).

Scheme 4.8. Nickel-catalyzed carboacylation of alkene



Scheme 4.9. Nickel-catalyzed reductive alkylarylation of alkenes

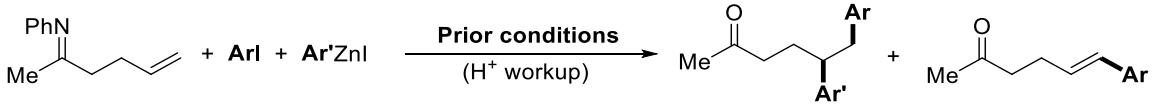


4.2. Nickel-catalyzed β, δ-Diarylation of Unactivated Alkene in Ketones

In our previous works on nickel-catalyzed diarylation of alkenes using a coordinating group strategy, we used the special substrates like N-phenyl-1-(2-vinylphenyl)methanimine and pyridylvinylsilanes which are mildly activated alkenes. In addition, alkene and coordinating group remain in syn co-planar. This will facilitate strong binding of catalyst to alkene and helps in the formation of a stable metallacycle. This in turn helps to prevent β-H elimination and therefore undergo transmetalation and reductive elimination to give the desired product.

In our continuous effort to broaden the scope of dicarbofunctionalization of alkenes using coordinating group strategy, we decided to use an alkene with an aliphatic backbone and imine as a coordinating group. For this we chose hex-5-en-2-one as a substrate. It has an unactivated alkene and the keto group that can be converted into ketimine. We first subjected *N*-phenylhex-5-en-2-imine to our previous reaction conditions (Scheme 4.10).

Scheme 4.10. Reaction of ketimine in previous conditions.

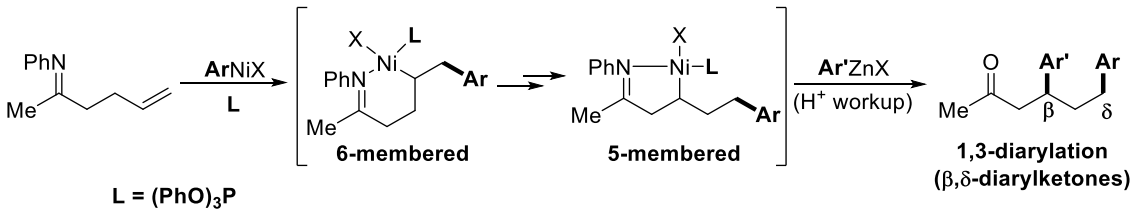


	Prior conditions:		
Ar = 4-MeC_6H_4	a) 5 mol % $Ni(cod)_2$, dioxane, 80 °C, 12 h	0	traces
Ar' = 4-$CF_3C_6H_4$	b) 5 mol% $NiBr_2$, NMP, 50 °C, 24 h	0	74%

Unfortunately, we found that the reaction only afforded heck product without any

observance of diarylated product.[128-130] We assumed that due to its aliphatic backbone, the transient metallacycle formed after the binding of coordinating group and alkene to the catalyst will be 6-membered which will be fluxional and unstable. Therefore, give a heck product by readily undergoing β-H elimination.[92,128,131,132] To stabilize the fluxional and unstable 6-membered metallacycle we planned to use a ligand. The ligand was expected to

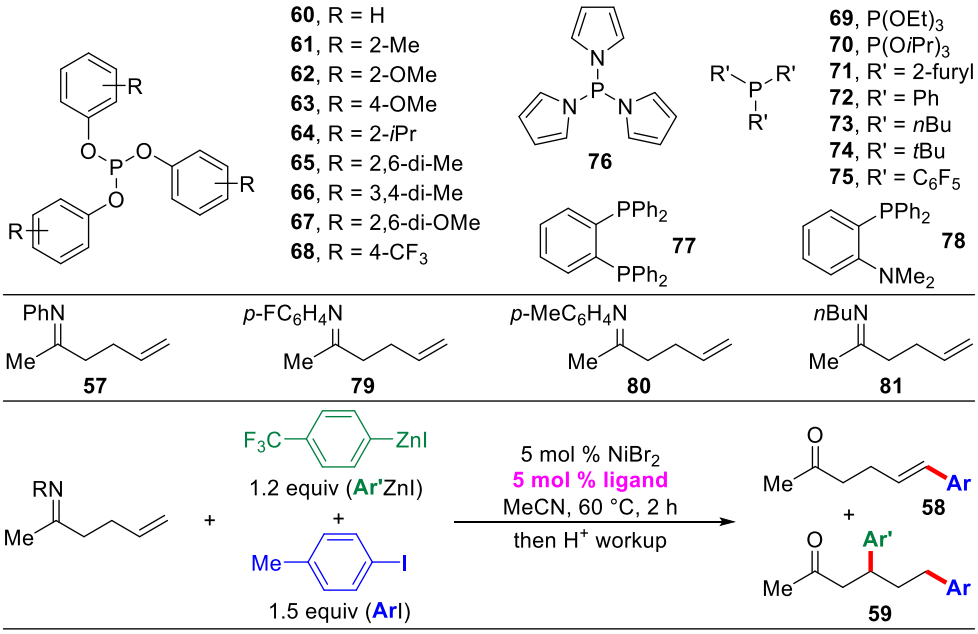
Scheme 4.11. Contraction of transient nickellacycles and their stabilization by $(PhO)_3P$



stabilize the metallacycle by occupying the coordination sites in the nickel catalyst. This in turn slows down the β-H elimination and forms heck product. As expected, we observed a formation of diarylated product when an electron deficient triphenylphospite was used as a ligand (Table 4.1). However, after a careful examination of the structure of product through the synthesis of 1,2-diarylated product and obtaining the x-ray crystal structure of the product, the product was found to be an unusual β, δ-diarylation instead of the regular γ, δ-diarylation of alkenyl ketones. We assumed that β, δ-diarylation product may be formed by the contraction of fluxional 6-membered nickellacycle to more stable 5-membered nickellacycle through the β-H elimination and reinsertion of Ni-H into the alkene (Scheme 4.11).[133-135]

During optimization of the reaction condition, it was found that the alkenyl ketimine when reacted with (4-(trifluoromethyl)phenyl)zinc iodide and 4-iodotoluene in presence of 5 mol % $NiBr_2$ and 5 mol % triphenylphosphite in acetonitrile at 60˚C for 2 h , 71% yield of -

Table 4.1. Optimization of reaction condition for β, δ-diarylation of alkene in ketones

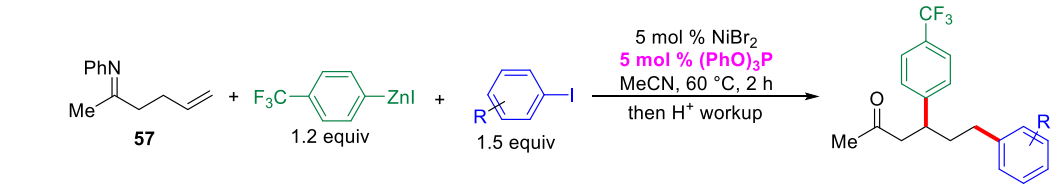


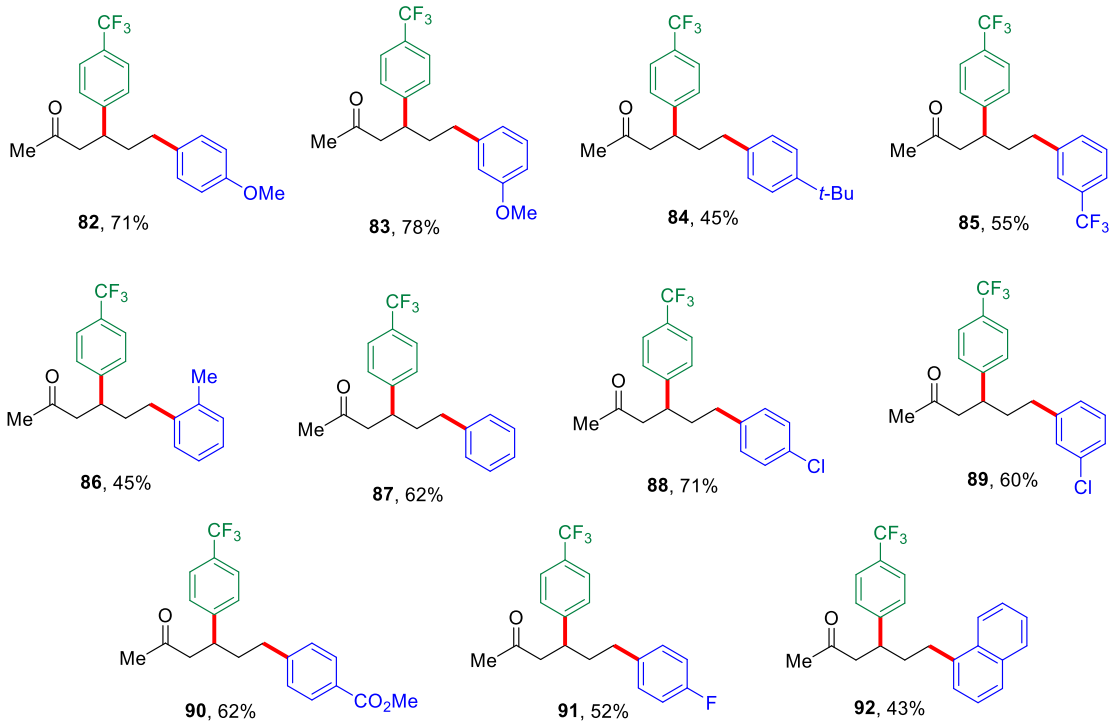
entry	reaction condition deviation	ligand	vinylimine	yields of **2** and **5** (%)[b]	
1	NMP instead of MeCN	**60**	**57**	12	54
2	none	**60**	**57**	6	78 (71)
3	toluene instead of MeCN	**60**	**57**	0	0
4	DMF or DMSO instead of MeCN	**60**	**57**	14-17	59-65
5	THF or dioxane instead of MeCN	**60**	**57**	<5	12-13
6	none	**61-64, 68**	**57**	10-13	30-42
7	none	**65-67, 71**	**57**	2-17	9-24
8	none	**76**	**57**	21	55
9	none	**69,70,72,75-78**	**57**	5-28	<5
10	none	**73, 74**	**57**	0	0
11	none	**none**	**57**	18	0[c]
12	no $NiBr_2$	**60**	**57**	0	0
13	none	**60**	**79**	17	31
14	none	**60**	**80**	31	53
15	none	**60**	**81**	6	24
16	12 h	**60**	**57**	13	41
17	Pd, Co, Fe or Cu-cat.[c] instead of $NiBr_2$	**60**	**57**	0	0
18	parent ketone instead of imine	**60**	**57**	0	0
19	parent ketone instead of imine	**none**	**57**	0	0

[a]0.1 mmol scale reactions in 0.5 mL solvent. [b]1H NMR yields using pyrene as an internal standard. Value in parenthesis is the isolated yield from 0.5 mmol. [c]Pd(OAc)2, CoCl2, FeCl2 or CuI.

β,δ-diarylation product was formed (Table 4.1, entry 1) The reaction did not give any desired product in absence of either $NiBr_2$ or triphenylphosphite. The yield of the desired product did not increase after using other substituted phosphites and phosphines. The ketimine formed from substituted aniline like 4-fluoroaniline, 4-methylaniline and butyl-

Table 4.2. Scope with aryl iodides[a]





[a]Isolated from 0.5 mmol. 5-10% Heck products observed.

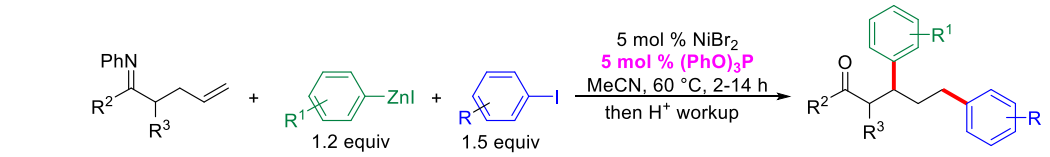
amine also unable to increase the yield of product. The reaction also gave moderate yield with the use of DMF or DMSO as solvent instead of MeCN. Low yield was obtained with

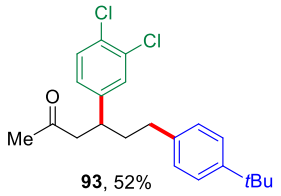
THF and dioxane while no product was observed with toluene as solvent. The use of salts of common transition metal catalyst like $Pd(OAc)_2$, $CoCl_2$, $FeCl_2$ or CuI instead of $NiBr_2$ in the standard reaction did not form any difunctionalized products. No product was observed with the use of parent ketone in the presence and absence of triphenylphosphite in the standard reaction condition which shows the importance of imine as a coordinating group in the reaction.

With the optimized condition, we examined the substrate scope of the reaction condition. We first studied the substrate scope with respect to various electronically biased aryl iodides with ketimine **57** (Table 4.2). It was found that reaction works well with moderate to good yields of the desired product. The reaction also tolerates sensitive functional groups like fluorides, chlorides, methoxy, nitriles and esters and ortho-substituted aryl iodides with moderate to good yields.

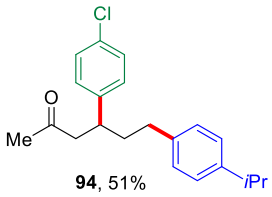
For further scope of β, δ-diarylation reaction, we also examined the reaction condition with various ketimines, arylzinciodides and aryl iodides and observed that reaction gave moderate to good yields (Table 4.3). The reaction tolerates various important functional groups like nitriles, fluoride, chlorides, trifluomethyl and methoxy. The reaction with various alpha substituted ketimines furnished the diarylation product in moderate to good yield with nearly 1:1 diastereoselectivity.

Table 4.3. Substrate Scope of various ketone derivatives, aryl iodide and arylzinc reagents[a]

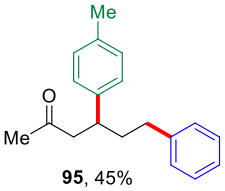




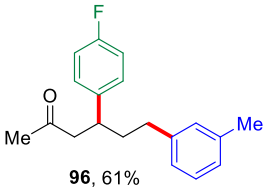
93, 52%



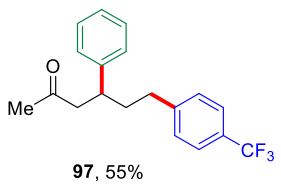
94, 51%



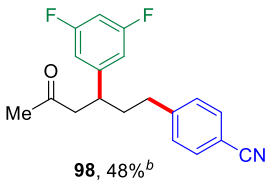
95, 45%



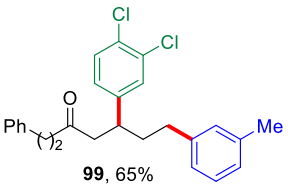
96, 61%



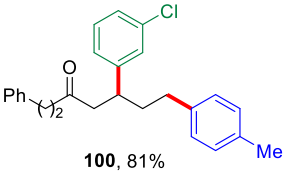
97, 55%



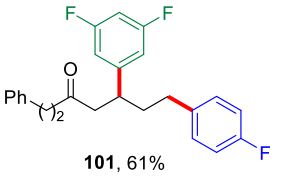
98, 48%[b]



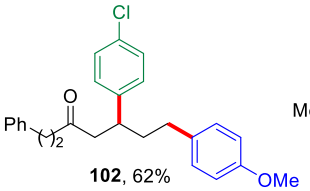
99, 65%



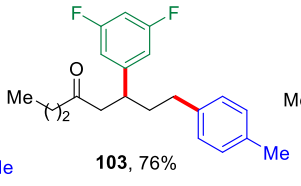
100, 81%



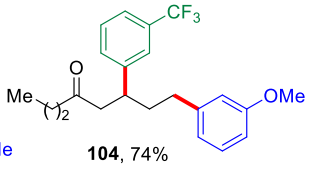
101, 61%



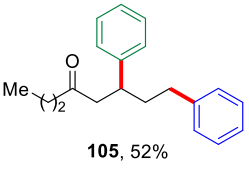
102, 62%



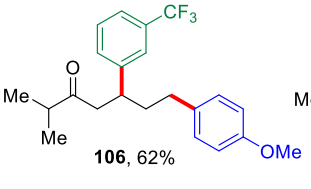
103, 76%



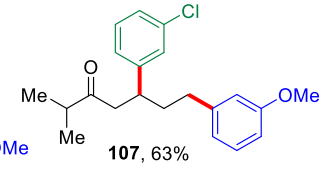
104, 74%



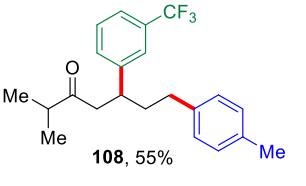
105, 52%



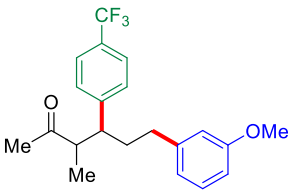
106, 62%



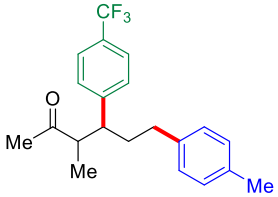
107, 63%



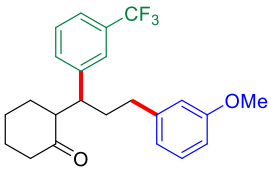
108, 55%



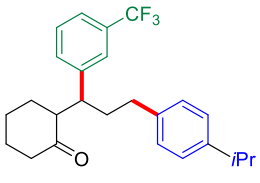
109, 45% (dr, 1:1)



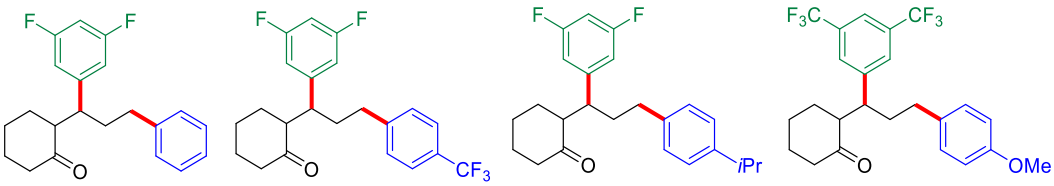
110, 54% (dr, 1:1.2)



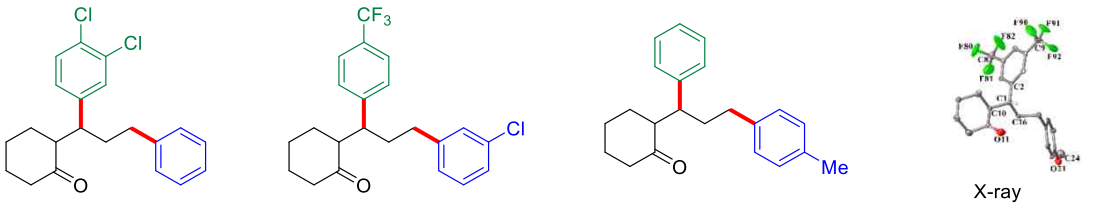
111, 61% (dr, 1:1.2)



112, 56% (dr, 1:1.2)



113, 62% (dr, 1:1) **114**, 58%, (dr, 1:1.5) **115**, 43%, (dr, 1:1.4) **116**, 62% (dr, 1:1)



117, 41% (dr, 1:1.3) **118**, 61% (dr, 1:1.3) **119**, 44% (dr, 1:1.3)

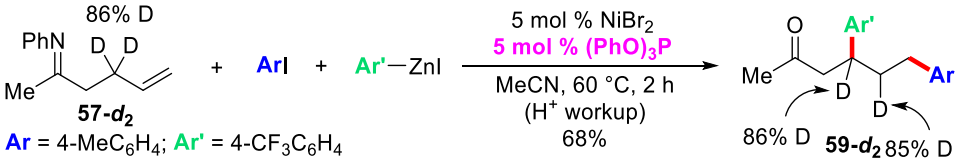
X-ray structure of compound **116**

[a]Isolated from 0.5 mmol. 5-10% Heck products observed.

Mechanistic Investigations

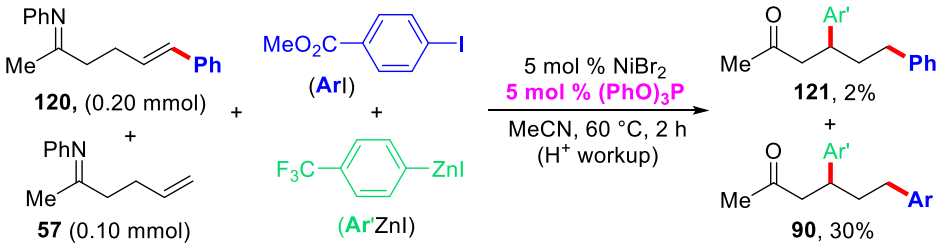
We also conducted experiments to know the actual pathway of reaction. At first, we performed the deuterium labelling experiment. We prepared the β-di-deuterium substituted ketimine **57-*d*$_2$** and subjected it to the standard reaction condition. The isolated product **59-*d*$_2$** showed that one of the deuterium from β- position had quantitatively migrated to the γ-position. This result supports the contraction of 6-membered metallacycle to more stable 5-membered metallacycle through β-H elimination and Ni-H reinsertion before transmetalation and reductive elimination. We also performed the cross-over experiment adding **120** in the standard reaction condition. The product **121** was observed in a trace

Scheme 4.12. Deuterium labelling experiment



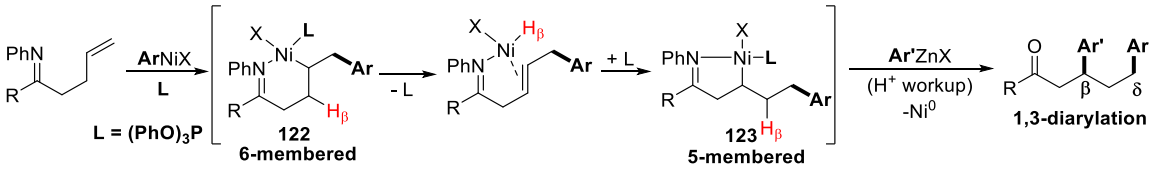
amount. This result indicates that nickel catalyst remained bound to alkene throughout the reaction.

Scheme 4.13. Cross-over experiment



Then, we proposed the possible pathway for β, δ-diarylation reaction. We believed that the metal catalyst first undergoes oxidative addition with aryl iodides. The resulting intermediate then migratory inserts into alkene and forms 6-membered nickellacycle **122**. Due to the fluxional and unstable nature, it will readily undergo β-H elimination. In the presence of ligand, Ni-H reinserts into alkene and forms a stable 5-membered nickellacycle **123**. This nickellacycle undergo transmetalation with organozinc and the resulting intermediate will give the desired product after reductive elimination.

Scheme 4.14. Possible pathway for β, δ-diarylation



4.3. Conclusion

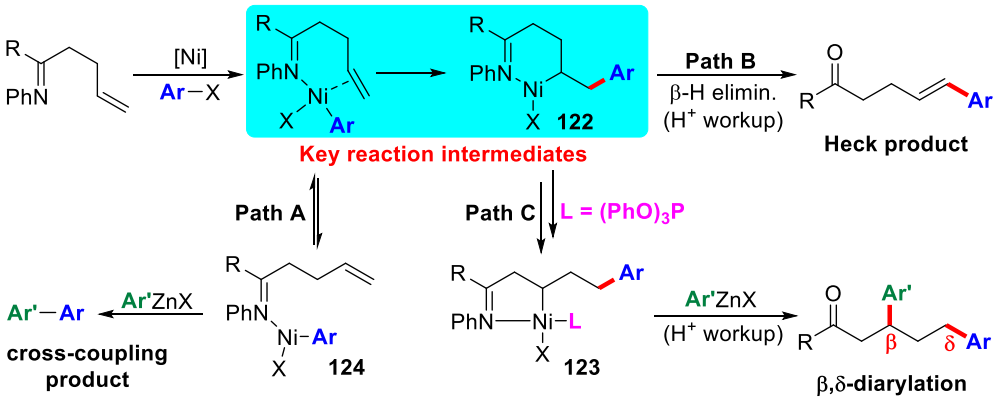
We developed a novel nickel-catalyzed regioselective β, δ-diarylation of unactivated alkene in ketimines with arylzinc reagents, aryliodides and $(PhO)_3P$ as ligand through the formation of transient nickellacycle. The deuterium labelling experiment shows that the

fluxional and less stable 6-membered nickellacycle undergo contraction to more stable 5-membered nickellacycle via β-H elimination followed by Ni-H reinsertion. Cross-over experiment indicates that nickel catalyst remains bound to the alkene throughout the reaction.

4.4. Nickel-catalyzed γ,δ-Diarylation of Unactivated Alkene in Ketimines

After the development of β, δ-diarylation of unactivated alkene in ketimine, we continued our efforts to develop γ,δ-diarylation reaction in ketimines. From the mechanistic works on β, δ-diarylation, we found that β-H elimination is faster than transmetalation in the fluxional and unstable nickellacycle **122.** Therefore, the major challenge is β-H elimination due to which contraction of metallacycle took place.

Scheme 4.15. Pathway for β,δ-diarylation and other side products

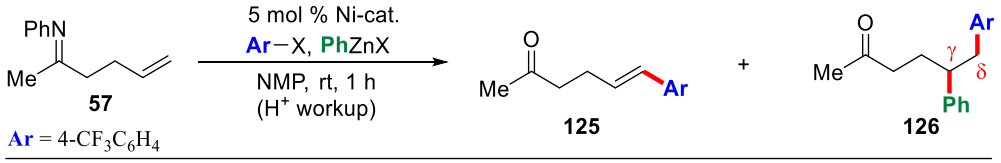


Therefore, we hypothesized that if we could promote transmetalation from 6-membered nickellacycle, there would be possibility of forming γ,δ-diarylation product. To promote transmetalation in the 6-membered nickellacycle, we planned to execute two ideas: Literature reports in the stille coupling reported that the rate of reaction is increased when a co-catalyst, usually copper salts are used. This is believed to be due to the faster

transmetalation of organocopper formed after transmetalation with organotin species with the palladium catalyst.[136-138] Therefore, we believed that using a co-catalyst in our reaction like copper salts, could form a more nucleophilic organometal species through the transmetalation with organozinc. The more nucleophilic organometal then could transmetalate faster with the 6-membered nickellacycle and give the desired 1,2 diarylation after reductive elimination.

Secondly, we planned to generate a cationic nickel species in the reaction. It is believed that transmetalation undergo faster in the cationic nickel species than the neutral nickel species.[139,140] We also assumed that the cationic nickel species will help to bind the alkene

Table 4.4. Optimization of reaction condition for γ,δ-diarylation[a]



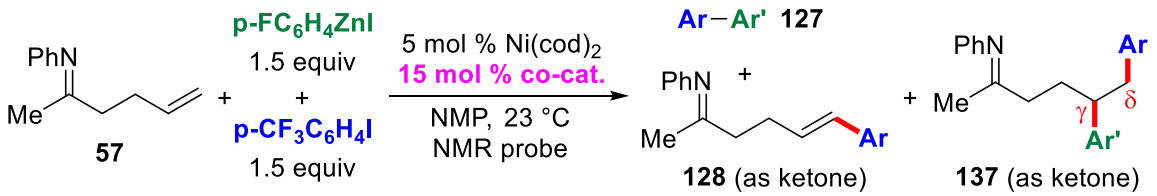
entry	reaction condition	% yield of **125**	% yield of **126**
1	$NiBr_2$, 15 mol % $AgBF_4$	7	39
2	$NiBr_2$, 15 mol % $Cu(MeCN)_4BF_4$	9	16
3	$Ni(cod)_2$, 15 mol % $AgBF_4$	11	80 (76, 72)[b]
4	$Ni(cod)_2$, 15 mol % $Cu(MeCN)_4BF_4$	20	65
5	$Ni(cod)_2$, 15 mol % $Cu(MeCN)_4OTf$	19	72
6	$Ni(cod)_2$, 15 mol % CuI	15	78 (73)[c]
7	$Ni(cod)_2$	22	38

[a]Reactions run in 0.1 mmol scale. Yields determined by 1H NMR with pyrene as a standard. Isolated yields in parenthesis. [b]Isolated from 0.5 mmol (76%) and 2.0 mmol (72%). [c]Isolated from 0.5 mmol(73%).

tightly and facilitate the faster migratory insertion. This will help in the reduction of the rate of forming cross-coupled product. From literature reports,[141] it was found that $AgBF_4$ is considered as a good halide abstracting agent. Therefore, we first examined our previous reaction of ketimine in NMP by adding CuI or $AgBF_4$ and indeed we found that 1,2 diarylation product was formed in significant amount when $NiBr_2$ was used as a catalyst. when Ni $(cod)_2$ was used as a catalyst instead of $NiBr_2$, the yield of the desired 1,2 diarylation increased upto 76%. We also performed the reaction with 15 mol % CuI and the reaction gave comparable yield. The yield of the product decreased to 38% when no additives were used (Table 4.4).

In-Situ Monitoring of the standard reaction

We also performed the reaction using 4-fluorophenylzinciodide and 4-iodo benzotrifluoride in presence of 15 mol % $AgBF_4$ or CuI in standard condition and monitored it by ^{19}F-NMR. It was found that the rate of reaction on the addition of $AgBF_4$ and CuI increased drastically with the significant reduction of cross-coupled product.



NMR yields (after hydrolysis): no additive, **137**, 29%; **127**, 32%; , **128,** 37%
with $AgBF_4$, **137**, 68%; **127**, 16%; **128**, 14%; with CuI, **137**, 61%; **127**, 25%; **128,** 21%

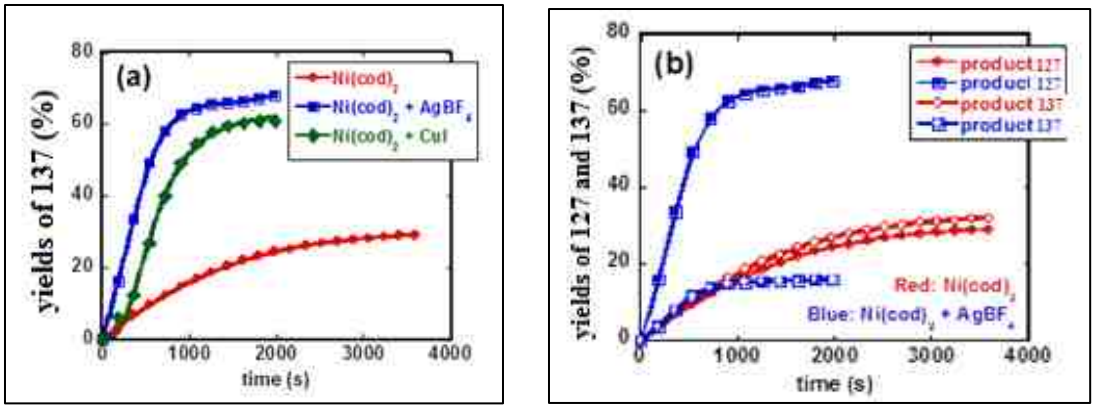


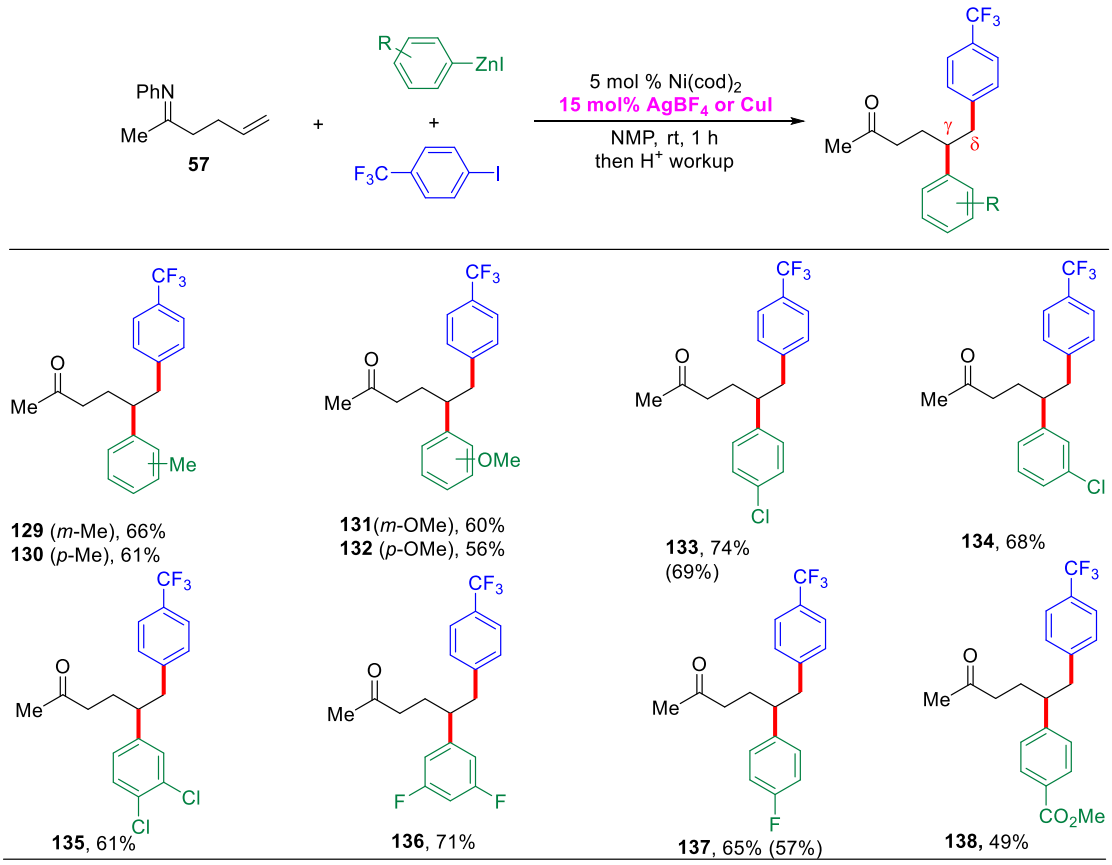
Figure 4.1. In situ ^{19}F NMR monitoring of reaction progress by generating cationic Ni-species for the reaction of alkenyl imine **57** with 4-FC_6H_4ZnI and 4-$CF_3C_6H_4I$. (a) Reaction profiles with and without $AgBF_4$ and CuI. Blue: with $AgBF_4$; green: with CuI; red: without $AgBF_4$ or CuI. (b) Comparison of reaction rates for the formation of diarylation product **137** and biaryl side product **127** by cross-coupling in the presence and absence of $AgBF_4$. Blue: with $AgBF_4$; red: without $AgBF_4$; hollow square and circle: cross-coupling (**127**); solid square and circle: alkene diarylation **(137**)

With optimized condition in hand, we examined the substrate scope of this reaction condition. We examined the scope of electronically different arylzinc reagents with 4-iodobenzotrifluoride as the aryl iodide with ketimine **57**. The reaction gave moderate to good yields with the tolerance of various sensitive functional groups like esters, methoxy, trifluoromethane, fluorides, methyl and chlorides.

To further broaden the substrate scope of this reaction, we applied this reaction method to various ketimines, arylzinc reagents and aryl iodides. The reaction gave moderate to good yields. The reaction was also found to tolerate various sensitive and important functional

groups like esters, nitrile, ketone, fluorides, chorides and methoxy with moderate to good yields.

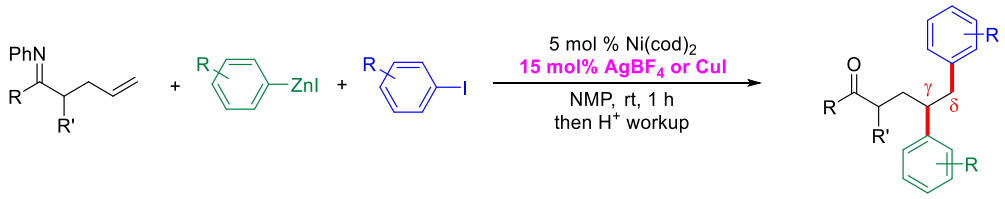
Table 4.5. Substrate scope of aryl zinciodides[a]

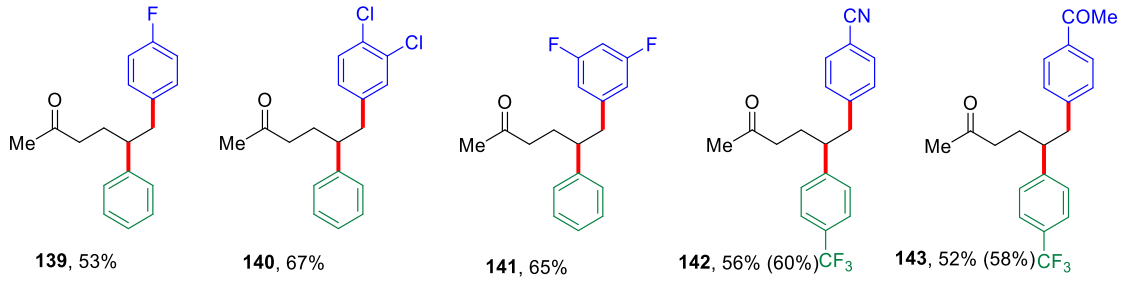


[a]Isolated from 0.5 mmol. ArZnI (1.5 equiv), ArI (1.5 equiv), NMP (2.5 mL). Yileds with CuI in parenthesis. [b]Single diastereomer observed by GC of crude reaction mixture and by ^{1}H and ^{13}C-NMR of isolated products.

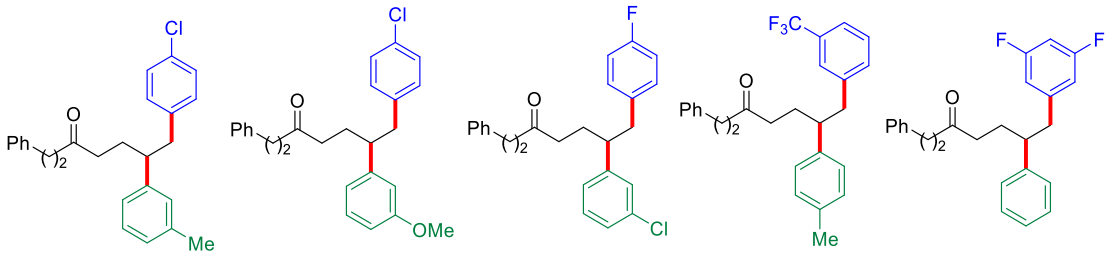
It was found that the reaction works well with heterocycle substituted ketimine. The reaction condition was also applicable to the alpha substituted ketimines as they gave moderate yields with single diastereomer.

Table 4.6. Substrate scope with various ketimines, ArZnI and Aryl iodides[a]

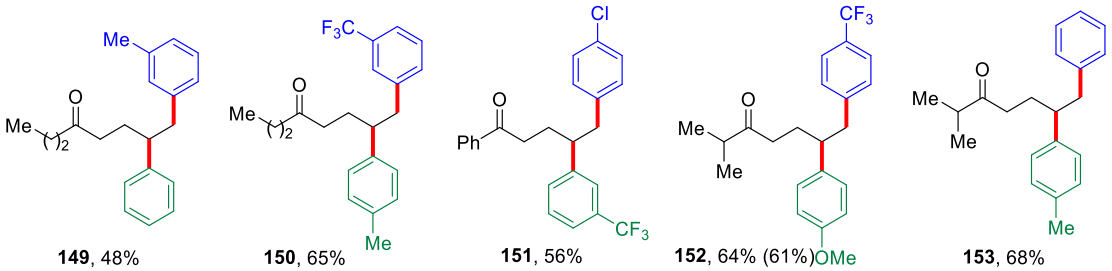




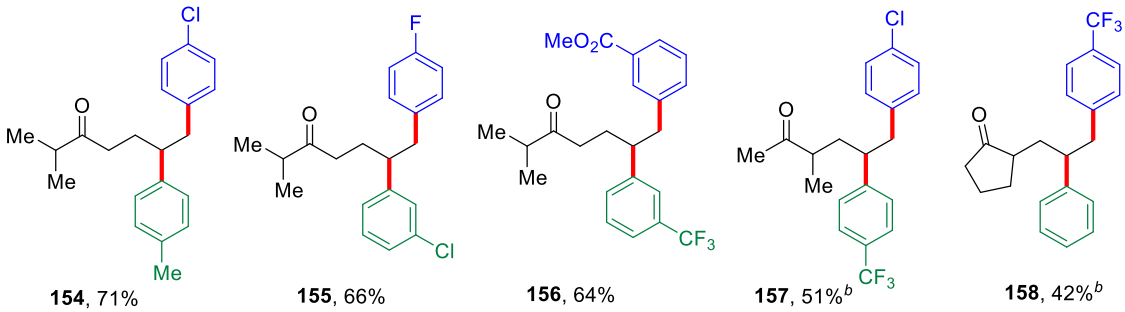
139, 53% **140**, 67% **141**, 65% **142**, 56% (60%) **143**, 52% (58%)



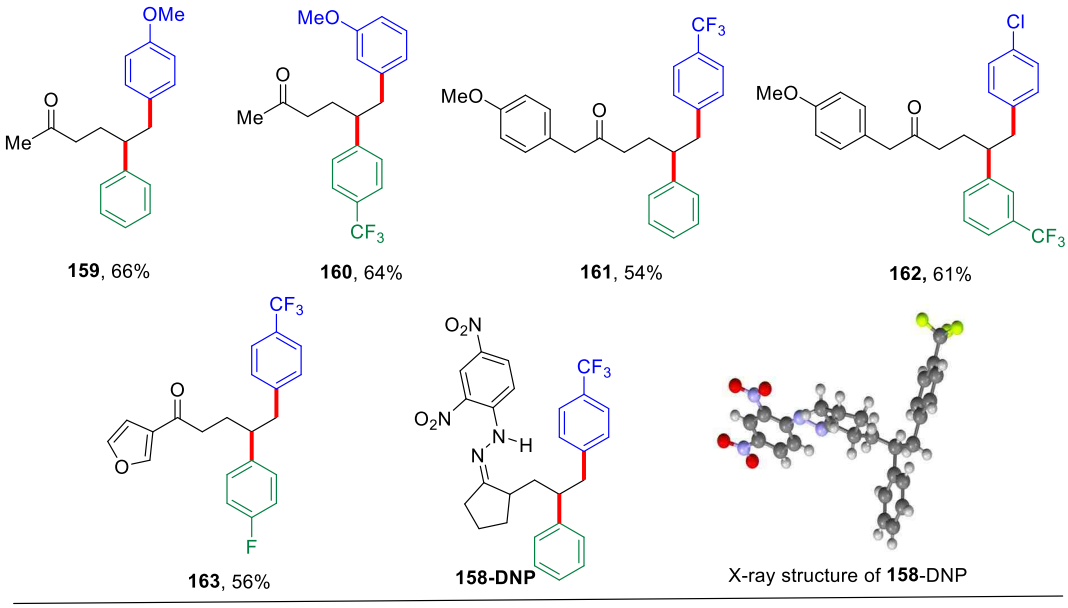
144, 65% **145**, 67% (71%) **146**, 61% **147**, 72% **148**, 56%



149, 48% **150**, 65% **151**, 56% **152**, 64% (61%) **153**, 68%



154, 71% **155**, 66% **156**, 64% **157**, 51%[b] **158**, 42%[b]



[a]Isolated from 0.5 mmol. ArZnI (1.5 equiv), ArI (1.5 equiv), NMP (2.5 mL). Yields with CuI in parenthesis. [b]Single diastereomer observed by GC of crude reaction mixture and by 1H and ^{13}C-NMR of isolated products.

Mechanistic Study

We hypothesized that a more nucleophilic organocopper species was formed by the transmetalation of organozinc with copper iodide. This organocopper undergo transmetalation with the alkene and coordinating group bound 6-membered nickellacycle. To test this hypothesis and know the actual role of $AgBF_4$ and CuI in our reaction, we performed a reaction between *p*-fluorophenylzinciodide and $AgBF_4$ which was monitored by ^{19}F-NMR. The reaction was monitored for 30 min. ^{19}F-NMR spectrum shows no any new peaks. Similarly, we also performed the reaction between *p*-fluorophenylzinciodide and CuI and monitored the reaction by ^{19}F-NMR. The ^{19}F-NMR spectrum shows no any new peak. So, these resulst indicate that there was no formation of any organocopper or organosilver species during our reaction and in fact, there was no reaction took place in

Scheme 4.16. ^{19}F-NMR monitoring of reaction between ArZnI and $AgBF_4$

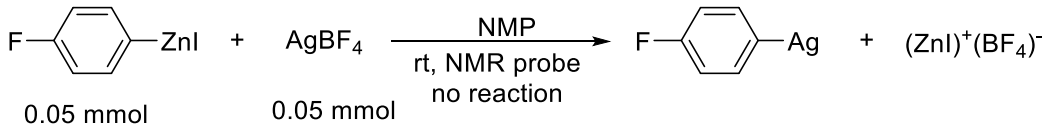
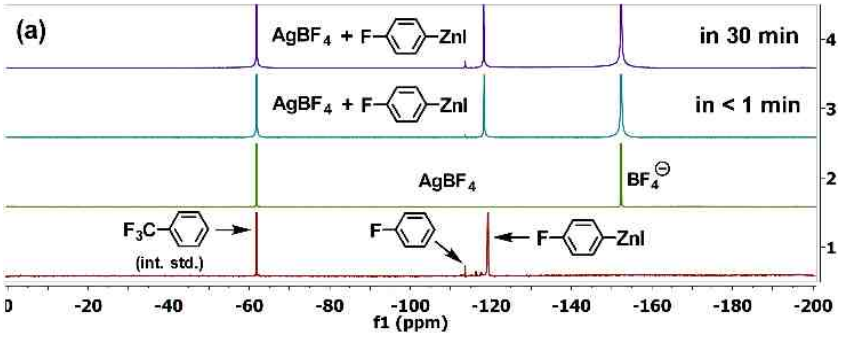
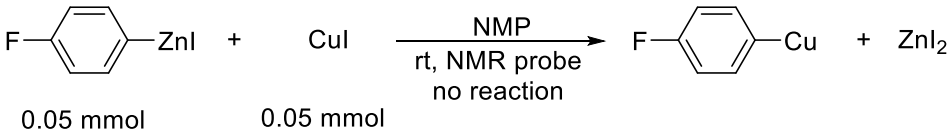


Figure 4.2. ^{19}F-NMR monitoring of reaction between ArZnI and $AgBF_4$

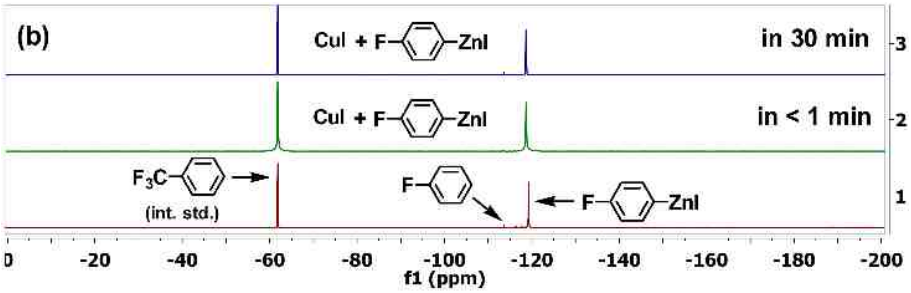


Scheme 4.17. ^{19}F-NMR monitoring of reaction between ArZnI and CuI



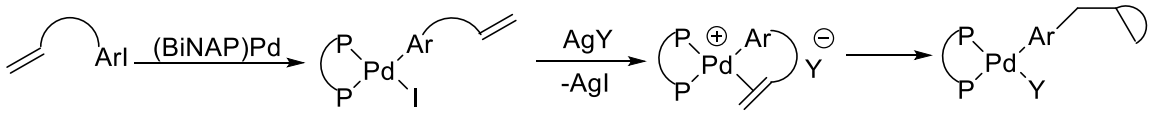
both reactions and hence rule out the possibility of forming any organosilver or organocopper in our reaction.

Figure 4.3. ^{19}F-NMR monitoring of reaction between ArZnI and CuI

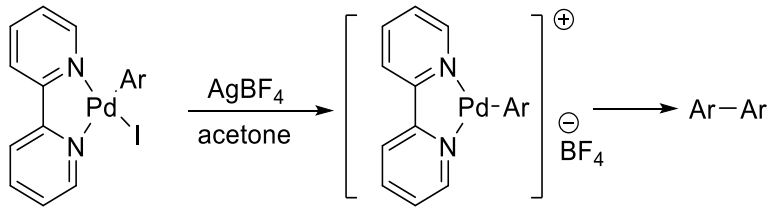


Literature reports by Overman and coworkers used $AgBF_4$ in their reaction and proposed the formation of cationic palladium species which is believed to bind alkene strongly and helps in the migratory insertion of aryl group to alkenes.[142] Similarly, Suzaki and coworkers proposed the formation of cationic palladium species when $AgBF_4$ was used in their reaction.[143]

Scheme 4.18. Formation of cationic palladium species by silver salts



Scheme 4.19. Formation of cationic palladium species by $AgBF_4$



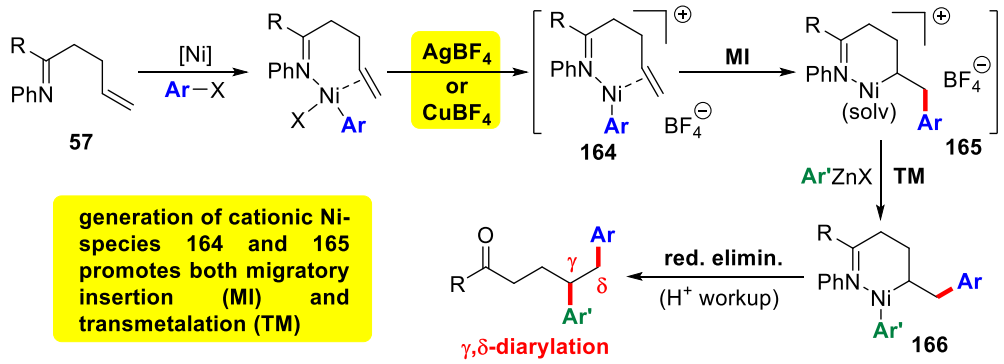
From these literature reports, we believe that $AgBF_4$ was involved in the formation of cationic nickel species in the reaction which is responsible for increase in rate of transmetalation of organozinc reagent to nickel catalyst. The resulting intermediate then further undergo reductive elimination to give the desired 1,2-diarylation product.

Proposed Catalytic cycle

The nickel catalyst first undergo oxidative addition with aryl iodides and $AgBF_4$ then abstracts halide from the resulting intermediate to form a cationic nickel species **164**. This then migratory inserts into alkene to give **165**. This intermediate undergo transmetalation

with organozinc and forms **166**. The resulting intermediate then gives the desired product with the regeneration of catalyst after reductive elimination.

Scheme 4.20. Possible pathway for γ,δ-diarylation of ketimine.



4.4. Conclusion

We developed a novel nickel-catalyzed γ,δ-diarylation of unactivated alkene in ketimines with arylzinc reagents and aryl iodides. Reaction between arylzinc iodide and $AgBF_4$ or CuI monitored by ^{19}F-NMR rules out the possibility of formation of organocopper or organosilver species and literature report supports the possibility of *in-situ* generation of cationic nickel species in the reaction which helped to promote transmetalation of organozinc with six-membered nickellacycle.

Chapter 5. Experimental

5.1. Copper-catalyzed Suzuki-Miyaura Coupling of Alkylboron reagents with Aryl halides.

5.1.1. General Information

Reactions were set up in a nitrogen-filled glovebox unless stated otherwise. All glassware were properly dried in an oven before use. Bulk solvents were obtained from EMD. Anhydrous solvents (DMF, DMSO, NMP, toluene, dioxane) were obtained from Sigma-Aldrich and were used directly without further purification. HMPA was dried over CaH_2 followed by distillation and stored under N_2 in 4 Å molecular sieves. Deuterated solvents were purchased from Cambridge Isotope. 9-BBN (0.50 M solution in THF), B-methoxy-9-BBN (1.0 M solution in hexanes) and B-Br-9-BBN (1.0 M Solution in CH_2Cl_2) were obtained in SureSeal bottles from Sigma-Aldrich. Aryl halides and olefins were purchased from Acros, Sigma-Aldrich, Oakwood, TCI-America, Matrix and Alfa-Aesar. CuI (99.999%) was procured from Sigma-Aldrich. *o*-Allyloxyiodobenzene was synthesized following a literature procedure.[144] ^{1}H, ^{13}C, ^{19}F and ^{11}B NMR spectra were recorded on a Bruker instrument (300, 75, 282, and 96 MHz, respectively) and internally referenced to the residual solvent signals of $CDCl_3$ for ^{1}H and ^{13}C NMR at 7.26 and 77.16 ppm, respectively, C_6F_6 for ^{19}F NMR at −164.9 ppm, and boric acid for ^{11}B NMR at 36.0 ppm. NMR chemical shifts and the coupling constants (*J*) for ^{1}H, ^{13}C, ^{19}F and ^{11}B NMR are reported in parts per million (ppm) and in Hertz, respectively. The following conventions are used for multiplicities: s, singlet; d, doublet; t, triplet; p, pentate; m, multiplet; dd, doublet of doublet. High resolution mass and NMR spectra of new compounds were recorded at the Mass Spectrometry and NMR Facilities, Department of Chemistry and

Chemical Biology, University of New Mexico (UNM). X-ray diffraction was performed on Bruker Kappa APEX II CCD diffractometer at the Department of Chemistry and Chemical Biology, UNM.

5.1.2. Experimental section

Generation of B-alkyl-9-BBN Reagents

In an oven-dried 15 mL pressure tube, olefin (1.5 mmol) was added to a solution of 9-BBN in THF (3 mL, 0.5 M in THF). The pressure tube was tightly capped and heated at 60 °C for 2 hours. The reaction mixture was then cooled to room temperature and the solvent was removed under vacuum. The B-alkyl-9-BBN generated *in situ* was directly used for subsequent reactions without further purification.

Procedure for Screening Reaction Conditions

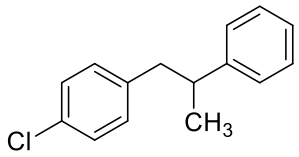
B-(2-phenylpropyl)-9-BBN (36.0 mg, 0.15 mmol), 1-chloro-4-iodobenzene (23.8 mg, 0.10 mmol), LiOtBu (12 mg, 0.15 mmol) or other bases (0.15 mmol), and CuI (1.9 mg, 0.010 mmol) were weighed in a 1-dram vial and dissolved in HMPA or other solvents (0.5 mL). The vial was then tightly capped and placed in a hotplate pre-heated to 80 °C with vigorous stirring. After 48 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock solution) as an internal standard was added, diluted with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC.

General Procedure for Tables 2.2 and 2.3

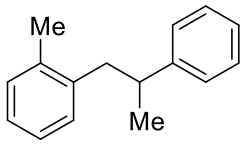
In an oven-dried 15 mL pressure tube, B-alkyl-9-BBN reagent (1.5 – 2.0 mmol), aryl iodide (1.0 mmol), LiO*t*Bu (120.0 mg, 1.5 mmol) or K_3PO_4 (636 mg, 3 mmol) and CuI (19 mg,

0.10 mmol) were weighed and dissolved in HMPA or DMF (5 mL). The pressure vessel was then tightly capped and placed in an oil bath pre-heated to 60 – 120 °C with vigorous stirring. After 12-48 h, the reaction mixture was cooled to room temperature, diluted with ethyl acetate (15 mL) and washed with H_2O (5 mL × 3). The aqueous fraction was extracted back with ethyl acetate (5 mL × 3) and combined with the first ethyl acetate fraction. The combined ethyl acetate fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The non-heterocyclic products were purified by silica gel column chromatography using hexanes as an eluting solvent. Heterocyclic products were purified by silica gel column chromatography using 10–20% ethyl acetate/hexanes.

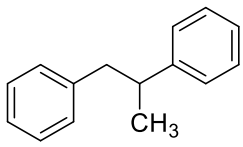
5.1.3. Characterization data for compounds



*1-Chloro-4-(2-phenylpropyl)benzene (**8**)*:[145] Reaction was conducted in 10.0 mmol scale in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound **8** was obtained as yellow oil (1684 mg, 73%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (d, *J* = 6.0 Hz, 3H), 2.76-2.83 (m, 1H), 2.89-3.06 (m, 2H), 7.01 (dd, *J*= 6.0 Hz, 3.0 Hz, 2H), 7.17-7.24 (m, 5H), 7.29-7.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 41.9, 44.5, 126.3, 127.2, 128.3, 128.5, 130.6, 131.7, 139.3, 146.5; GCMS (m/z) 230.1.

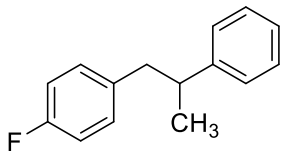


*1-Methyl-2-(2-phenylpropyl)benzene (**9**)*: Reaction was conducted in 5.0 mmol scale in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **9** obtained as colorless oil (747 mg, 71%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (d, *J* = 6.0 Hz, 3H), 2.32 (s, 3H), 2.80-2.87 (m, 1H), 2.95-3.08 (m, 2H), 7.05-7.18 (m, 4H), 7.22-7.26 (m, 3H), 7.31-7.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.6, 21.2, 40.8, 42.5, 125.7, 126.1, 126.2, 127.1, 128.4, 130.2, 130.3, 136.3, 139.2, 147.3; IR (neat) cm^{-1} 2958, 1510, 1243, 1035; HRMS (TOF) Calcd for $C_{16}H_{18}$ (M^+) 210.1409, found 210.1416.

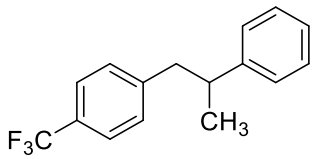


*Propane-1,2-diyldibenzene (**10**)*:[2] Reaction was conducted in 5.0 mmol scale in HMPA at 120 °C for 24 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **10** obtained as yellow oil (716 mg, 73%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (d, *J* = 6.0 Hz, 3H), 2.78-

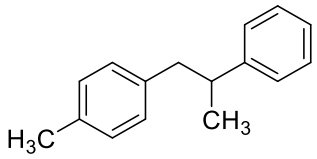
2.86 (m, 1H), 2.97-3.09 (m, 2H), 7.12-7.15 (m, 2H), 7.21-7.35 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 42.0, 45.2, 126.0, 126.1, 127.2, 128.2, 128.4, 129.3, 140.9, 147.1; GCMS (m/z) 196.1.



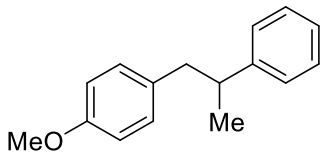
*1-Fluoro-4-(2-phenylpropyl)benzene (**11**)*: Reaction was conducted in 5.0 mmol scale in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **11** obtained as yellow oil (621 mg, 58%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, J = 6.0 Hz, 3H), 2.74-2.81 (m, 1H), 2.87-3.01 (m, 2H), 6.89-6.94 (m, 2H), 6.99-7.03 (m, 2H), 7.15-7.22 (m, 3H), 7.26-7.31 (m, 2H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 21.3, 42.1, 44.3, 114.9 (d, J_{CF} = 79.0 Hz), 126.2, 127.2, 128.5, 130.6 (d, J_{CF} = 28.2 Hz), 136.5 (d, J_{CF} = 11.3 Hz), 146.7, 159.8, 163.1; ^{19}FNMR (282 MHz, $CDCl_3$) δ -116.1; IR (neat) cm^{-1} 2930, 1602, 1508, 1452, 1219, 1157, 1014; HRMS (TOF) Calcd for $C_{15}H_{15}F$ (M^+) 214.1158, found 214.1148.



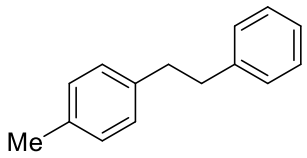
*1-(2-Phenylpropyl)-4-(trifluoromethyl)benzene (**12**)*: Reaction was conducted in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **12** obtained as colorless oil (214 mg, 81%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, J = 6.0 Hz, 3H), 2.81-2.91 (m, 1H), 2.95-3.06 (m, 2H), 7.15-7.23 (m, 5H), 7.26-7.32 (m, 2H), 7.48 (d, J = 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 41.8, 44.9, 125.1 (q, J_{CF} = 16.9 Hz), 126.4, 127.1, 128.6, 129.5, 145.0, 146.3; ^{19}FNMR (282 MHz, $CDCl_3$) δ -60.7; IR (neat) cm^{-1} 2948, 1322, 1112, 1066; HRMS (TOF) Calcd for $C_{16}H_{15}F_3$ (M^+) 264.1126, found 264.1139.



*1-Methyl-4-(2-phenylpropyl)benzene (**13**)*: Reaction was conducted in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **13** obtained as yellow oil (164 mg, 78%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, J = 6.0 Hz, 3H), 2.33 (s, 3H), 2.71-2.81 (m, 1H), 2.92-3.07 (m, 2H), 7.00-7.09 (m, 4H), 7.18-7.24 (m, 3H), 7.28-7.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 21.3, 42.0, 44.7, 126.1, 127.2, 128.4, 128.9, 129.2, 135.4, 137.9, 147.3; IR (neat) cm^{-1} 2921, 1515, 1451; HRMS (TOF) Calcd for $C_{16}H_{18}$ (M^+) 210.1409, found 210.1408.

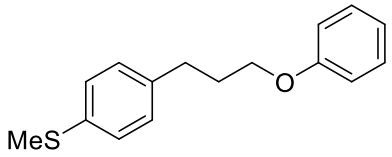


*1-Methoxy-4-(2-phenylpropyl)benzene(**14**)* :[146] Reaction was conducted in HMPA at 120 °C for 48 h with 2.0 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **14** obtained as yellow oil (179 mg, 79%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, *J* = 6.0 Hz, 3H), 2.70-2.77 (m, 1H), 2.88-3.04 (m, 2H), 3.79(s, 3H), 6.81 (d, *J* = 9.0 Hz, 2H), 7.1 (d, *J* = 6.0 Hz, 2H), 7.18-7.22 (m, 3H), 7.27-7.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 42.2, 44.3, 55.3, 113.6, 126.1, 127.2, 128.4, 130.2, 133.0, 147.2, 157.9; HRMS (APCI) Calcd for $C_{16}H_{19}O$ $(MH)^+$ 227.1436, found 227.1431.

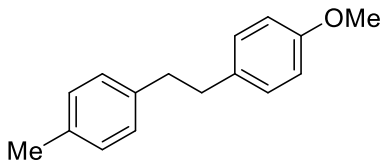


*1-Methyl-4-phenethylbenzene (**15**)* :[147] Reaction was conducted in HMPA at 120 °C for 48 h with 2.0 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound was **15** obtained as yellow oil (100 mg, 51%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.93, (s, 4H), 7.13 (s, 4H),

7.21-7.25 (m, 3H), 7.30-7.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 37.7, 38.2, 126.0, 128.4, 128.6, 129.2, 135.5, 138.9, 142.1; GCMS (m/z) 196.1.

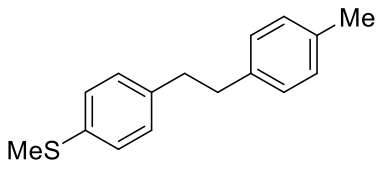


Methyl(4-(3-phenoxypropyl)phenyl)sulfane (**16**): Reaction was conducted in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **16** was obtained as white solid (173 mg, 67%) after purification by silica gel column chromatography.^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05-2.14 (m, 2H), 2.48 (s, 3H), 2.80 (t, *J* = 7.5 Hz, 2H), 3.97 (t, *J* = 6.0 Hz, 2H), 6.90-6.98 (m, 3H), 7.14-7.33 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4, 31.0, 31.7, 66.7, 114.6, 120.7, 127.3, 129.2, 129.6, 135.6, 138.8, 159.1; IR (neat) cm^{-1} 2918, 1489, 1238, 1174, 1042; HRMS (ESI) Calcd for $C_{16}H_{18}NaOS$ $(MNa)^+$ 281.0976, found 281.0974.

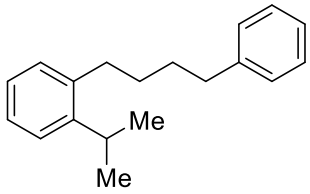


*1-Methoxy-4-(4-methylphenethyl)benzene (**17**)*: Reaction was conducted in HMPA at 120°C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound **17** was obtained as yellow oil (104 mg, 46%) after purification by silica gel

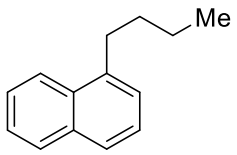
column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.85 (s, 4H), 3.79 (s, 3H), 6.80-6.85 (m, 2H), 7.08 (s, 5H), 7.12 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 37.3, 37.9, 55.4, 113.9, 128.5, 129.1, 129.5, 134.2, 135.4, 138.9, 157.9; IR (neat) cm^{-1} 2918, 1509, 1241, 1030; HRMS (APCI) Calcd for $C_{16}H_{19}O$ $(MH)^+$ 227.1436, found 227.1438.



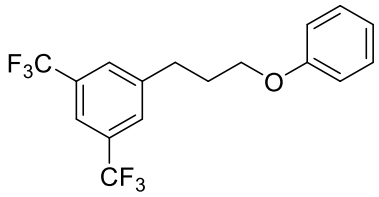
*Methyl(4-(4-methylphenethyl)phenyl)sulfane (**18**)* : Reaction was conducted in HMPA at 120 °C for 48 h with 2.0 equiv of alkylboron reagent using Li*O*t*Bu as a base. The title compound **18** was obtained as yellow oil (172 mg, 71%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.52 (s, 3H), 2.91 (s, 4H), 7.13 (s, 4H), 7.17 (s, 2H), 7.23 (s, 1H), 7.26 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4, 21.2, 37.5, 37.6, 127.2, 128.4, 129.1, 135.5, 138.6, 139.1; IR (neat) cm^{-1} 2916, 2850, 1419, 1091; HRMS (APCI) Calcd for $C_{16}H_{19}S$ $(MH)^+$ 243.1207, found 243.1212.



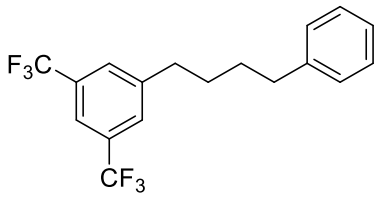
*1-Isopropyl-2-(4-phenylbutyl)benzene (**19**)* : Reaction was conducted in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using LiO*t*Bu as a base. The title compound **19** was obtained as yellow oil (103 mg, 41%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (dd, *J* = 6.0 Hz, 3.0 Hz, 6H), 1.58-1.76 (m, 4H), 2.67 (t, *J* = 7.5 Hz, 4H), 3.09-3.19 (m, 1H), 7.11-7.30 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 28.7, 31.5, 31.6, 33.0, 36.0, 125.4, 125.6, 125.8, 126.3, 128.4, 128.6, 129.5, 139.4, 142.7, 146.6; IR (neat) cm^{-1} 2929, 1489, 1453, 1032; HRMS (TOF) Calcd for $C_{19}H_{24}$ (M^+) 252.1878, found 252.1898.



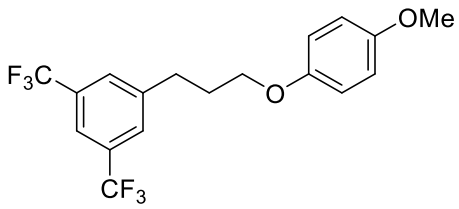
*1-Butylnaphthalene **(20)***:[148] Reaction was conducted in HMPA at 120 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **20** was obtained as yellow oil (108 mg, 59%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.5 Hz, 3H), 1.42-1.54 (m, 2H), 1.71-1.81 (m, 2H), 3.09 (t, *J* = 7.5 Hz, 2H), 7.33-7.43 (m, 2H), 7.47-7.53 (m, 2H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.85-7.88 (m, 1H), 8.05-8.09 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.0, 33.0, 33.2, 124.1, 125.5, 125.7, 125.8, 126.0, 126.5, 128.9, 132.1, 134.0, 139.1; HRMS (APPI) Calcd for $C_{14}H_{16}$ $(M)^+$ 184.1252, found 184.1259.



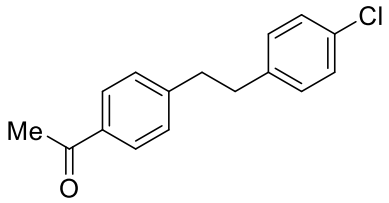
*1-(3-Phenoxypropyl)-3,5-bis(trifluoromethyl)benzene (**21**)*: Reaction was conducted in HMPA at 80 °C for 36 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **21** was obtained as yellow oil (281 mg, 81%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.11-2.20 (m, 2H), 2.98 (t, J = 7.5 Hz, 2H), 4.01 (t, J = 6.0 Hz, 2H), 6.88-6.99 (m, 3H), 7.27-7.33 (m, 2H), 7.68 (s, 2H), 7.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.7, 32.3, 66.5, 114.6, 120.2 (t, J_{CF} = 14.1 Hz), 121.1, 121.8, 125.4, 128.8, 129.7, 131.6 (q, J_{CF} = 124.1 Hz), 144.2, 158.9; ^{19}FNMR (282 MHz, $CDCl_3$) δ -61.3; IR (neat) cm^{-1} 2925, 1601, 1275, 1124; HRMS (APPI) Calcd for $C_{17}H_{14}F_6O$ $(M)^+$ 348.0949, found 348.0948.



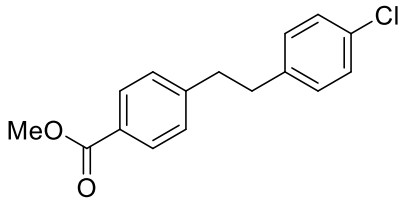
*1-(4-Phenylbutyl)-3,5-bis(trifluoromethyl)benzene (**22**)*:[149] Reaction was conducted in HMPA at 80 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **22** was obtained as yellow oil (273 mg, 79%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70-1.75 (m, 4H), 2.69 (t, *J* = 6.0 Hz, 2H), 2.78 (t, *J* = 7.5 Hz, 2H), 7.19-7.24 (m, 3H), 7.29-7.35 (m, 2H), 7.63 (s, 2H), 7.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.7, 31.0, 35.6, 35.8, 120.0 δ t, J_{CF} = 14.1 Hz), 121.8, 125.4, 126.0, 128.5, 128.6, 131.5 (q, J_{CF} = 124.1 Hz), 142.2, 145.0; ^{19}FNMR (282 MHz, $CDCl_3$) δ -61.3; HRMS (APCI) Calcd for $C_{18}H_{16}F_6$ $(M)^+$ 346.1156, found 346.1157.



*1-(3-(4-Methoxyphenoxy)propyl)-3,5-bis(trifluoromethyl)benzene (**23**)*: Reaction was conducted in HMPA at 80 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **23** was obtained as colorless oil (310 mg, 82%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08-2.17 (m, 2H), 2.96 (t, *J* = 7.5 Hz, 2H), 3.78 (s, 3H), 3.95 (t, *J* = 6.0 Hz, 2H), 6.84 (s, 4H), 7.67 (s, 2H), 7.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8, 32.3, 55.9, 67.3, 114.9, 115.6, 120.2 (br d, J_{CF} = 16.9 Hz), 125.4, 128.8, 131.8 (q, J_{CF} = 126.9 Hz), 144.3, 153.0, 154.1; ^{19}FNMR (282 MHz, $CDCl_3$) δ -61.2 ; IR (neat) cm^{-1} 2927, 1508, 1276, 1126; HRMS (ESI) Calcd for $C_{18}H_{17}F_6O_2$ $(MH)^+$ 379.1133, found 379.1141.

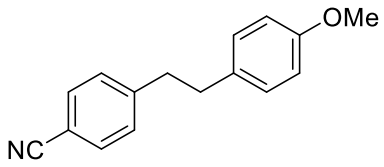


*1-(4-(4-Chlorophenethyl)phenyl)ethan-1-one (**24**)*: Reaction was conducted in HMPA at 100°C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **24** was obtained as light yellow solid (111 mg, 43%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.57 (s, 3H), 2.86-2.98 (m, 4H), 7.05 (d, *J* = 9.0 Hz, 2H), 7.20-7.24 (m, 4H), 7.87 (d, *J*= 6.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.6, 36.7, 37.7, 128.5, 128.6, 128.8, 129.9, 131.9, 135.3, 139.5, 147.0, 197.8; IR (neat) cm^{-1} 2916, 1674, 1360, 1264, 1090; HRMS (ESI) Calcd for $C_{16}H_{16}{}^{35}ClO$ $(MH)^+$ 259.0890, found 259.0881.

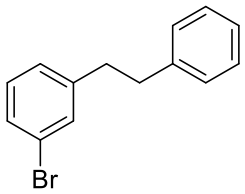


*Methyl 4-(4-chlorophenethyl)benzoate (**25**)*: Reaction was conducted in HMPA at 100 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound

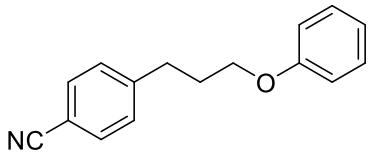
25 was obtained as white solid (140 mg, 51%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.88-2.97 (m, 4H), 3.90 (s, 3H), 7.05 (d, *J* = 9.0 Hz, 2H), 7.18-7.24 (m, 4H), 7.95 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.9, 37.9, 52.2, 128.2, 128.6, 128.7, 129.9, 130.0, 132.0, 139.6, 146.8, 167.2; IR (neat) cm^{-1} 2922, 1711, 1507, 1279, 1096; HRMS (ESI) Calcd for $C_{16}H_{16}{}^{35}ClO_2$ $(MH)^+$ 275.0839, found 275.0834.



*4-(4-Methoxyphenethyl)benzonitrile (**26**)*:[150] Reaction was conducted in HMPA at 100 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **26** was obtained as yellow oil (182 mg, 77%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.83-2.98 (m, 4H), 3.79 (s, 3H), 6.79-6.84 (m, 2H), 7.01-7.06 (m, 2H), 7.21 (s, 1H), 7.24 (s, 1H), 7.53-7.56 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.5, 38.3, 55.4, 109.9, 113.9, 119.2, 129.5, 132.2, 132.8, 147.4, 158.1; HRMS (ESI) Calcd for $C_{16}H_{16}NO$ $(MH)^+$ 238.1232, found 238.1227.

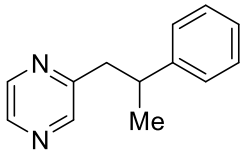


*1-Bromo-3-phenethylbenzene (**27**)*:[151] Reaction was conducted in HMPA at 100 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound was **27** obtained as yellow oil (184 mg, 71%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.92 (s, 4H), 7.09-7.26 (m, 5H), 7.29-7.37 (m, 4H); ^{13}C NMR (75 MHz, CDCl3) δ 37.7, 37.8, 122.5, 126.2, 127.3, 128.5, 129.2, 130.0, 131.6, 141.3, 144.2; GCMS (m/z) 260.0.

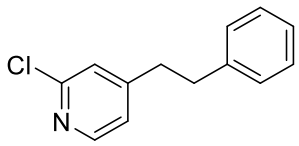


*4-(3-Phenoxypropyl)benzonitrile (**28**)*: Reaction was conducted in HMPA at 100 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **28** was obtained as colorless oil (211 mg, 89%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06-2.17 (m, 2H), 2.89 (t, *J* = 7.5 Hz, 2H), 3.96 (t, *J* = 6.0 Hz, 2H), 6.8 (d, *J* = 6.0 Hz, 2H), 6.95 (t, *J* = 7.5 Hz, 1H), 7.27-7.33 (m, 4H), 7.58 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.5, 32.6, 66.4, 110.0, 114.6, 119.2, 120.9, 129.5, 129.6, 132.4, 147.4, 158.9; IR (neat) cm^{-1} 2928, 2227, 1733,

1600, 1496, 1241, 1042; HRMS (ESI) Calcd for $C_{16}H_{16}NO$ $(MH)^+$ 238.1232, found 238.1226.

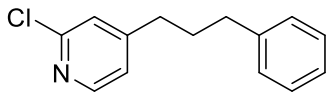


*2-(2-Phenylpropyl)pyrazine (**29**)*: Reaction was conducted in DMF at 80 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **29** was obtained as yellow oil (137 mg, 69%) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (d, *J* = 6.0 Hz, 3H), 3.01-3.10 (m, 2H), 3.23-3.35 (m, 1H), 7.15-7.19 (m, 3H), 7.24-7.29 (m, 2H), 8.20 (s, 1H), 8.35 (d, *J* = 2.4 Hz, 1H), 8.49 (t, *J* = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 40.3, 44.3, 126.5, 127.0, 128.6, 142.3, 144.2, 145.3, 145.9, 156.4; IR (neat) cm^{-1} 2923, 2854, 1454, 1403, 1017; HRMS (ESI) Calcd for $C_{13}H_5N_2$ $(MH)^+$ 199.1235, found 199.1233.

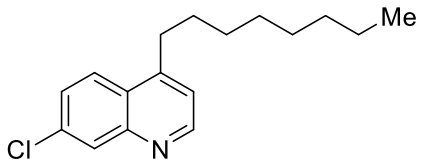


*2-Chloro-4-phenethylpyridine (**30**)*: Reaction was conducted in HMPA at 100 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **30** was obtained as colorless solid (172 mg, 79%) after purification by silica gel column

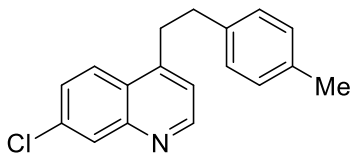
chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.92 (s, 4H), 6.99 (dd, *J* = 6.0 Hz, 3.0 Hz, 1H), 7.12-7.15 (m, 3H), 7.19-7.32 (m, 3H), 8.25 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.5, 36.9, 122.9, 124.4, 126.6, 128.5, 128.7, 140.3, 149.6, 151.8, 154.0; IR (neat) cm^{-1} 2932, 1591, 1546, 1385, 1085; HRMS (ESI) Calcd for $C_{13}H_{13}{}^{35}ClN$ $(MH)^+$ 218.0737, found 218.0739.



*2-Chloro-4-(3-phenylpropyl)pyridine (**31**)*: Reaction was conducted in HMPA at 80 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **31** was obtained as yellow oil (169 mg, 73%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.91-2.02 (m, 2H), 2.60-2.69 (m, 4H), 7.03 (dd, *J* = 6.0 Hz, 3.0 Hz, 1H), 7.15-7.23 (m, 4H), 7.27-7.33 (m, 2H), 8.26 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, CDCl3) δ 31.6, 34.4, 35.3, 122.8, 124.3, 126.2, 128.5, 128.6, 141.4, 149.6, 151.7, 154.7; IR (neat) cm^{-1} 2931, 1591, 1545, 1385, 1085; HRMS (ESI) Calcd for $C_{14}H_{15}{}^{35}ClN$ $(MH)^+$ 232.0893, found 232.0895.

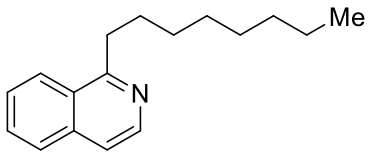


*7-Chloro-4-octylquinoline (**32**)*:[71] Reaction was conducted in HMPA at 80 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **32** was obtained as yellow oil (242 mg, 88%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.5 Hz, 3H), 1.26-1.43 (m, 10H), 1.68-1.78 (m, 2H), 3.03 (t, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 3.0 Hz, 1H), 7.50 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 7.97 (d, *J* = 9.0 Hz, 1H) 8.09 (s, 1H), 8.79 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.8, 29.3, 29.5, 29.8, 30.2, 31.9, 32.2, 121.0, 125.1, 126.1, 127.2, 129.2, 134.9, 149.0, 151.3; HRMS (ESI) Calcd for $C_{17}H_{23}{}^{35}ClN$ $(MH)^+$ 276.1519, found 276.1515.

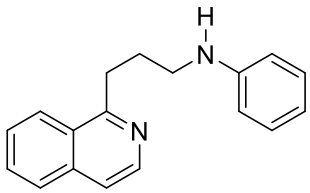


*7-Chloro-4-(4-methylphenethyl)quinoline (**33**)*: Reaction was conducted in HMPA at 80 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **33** was obtained as white solid (188 mg, 67%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.01 (t, *J* = 7.5 Hz, 2H), 3.34 (t, *J* = 7.5 Hz, 2H), 7.06-7.13 (m, 4H), 7.17 (d, *J* = 3.0 Hz, 1H), 7.51 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 7.99 (d, *J* = 9.0 Hz, 1H), 8.13 (d, *J* = 3.0 Hz, 1H), 8.78 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz,$CDCl_3$) δ 21.2, 34.2, 35.8, 121.2, 125.0, 126.0, 127.5, 128.3, 129.3, 129.4,

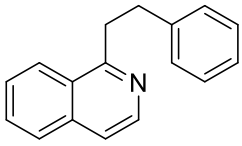
135.0, 136.1, 137.7, 147.8, 149.0, 151.4; IR (neat) cm^{-1} 2919, 1598, 1515, 1417, 1095; HRMS (ESI) Calcd for $C_{18}H_{17}{}^{35}ClN$ $(MH)^+$ 282.1050, found 282.1046.



*1-Octylisoquinoline (**34**)*:[9] Reaction was conducted in HMPA at 80 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **34** was obtained as yellow oil (205 mg, 85%) after purification by silica gel column chromatography. ^1H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6.0 Hz, 3H), 1.25-1.32 (m, 8H), 1.42-1.52 (m, 2H), 1.80-1.91 (m, 2H), 3.28 (t, *J* = 9.0 Hz, 2H), 7.47 (d, *J* = 6.0 Hz, 1H), 7.53-7.66 (m, 2H), 7.78 (d, *J* = 6.0 Hz, 1H), 8.15 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 8.42 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.8, 29.4, 29.6, 29.9, 30.0, 32.0, 35.7, 119.2, 125.5, 127.0, 127.5, 129.8, 136.4, 142.0, 162.6; HRMS (ESI) Calcd for $C_{17}H_{24}N$ $(MH)^+$ 242.1909, found 242.1907.

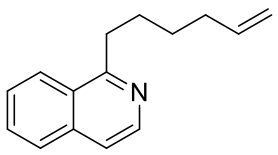


*N-(3-(isoquinolin-1-yl)propyl)aniline (**35**)*: Reaction was conducted in HMPA at 80 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **35** was obtained as white solid (165 mg, 63%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.18-2.28 (m, 2H), 3.28 (t, *J* = 7.5 Hz, 2H), 3.43 (t, *J* = 7.5 Hz, 2H), 3.97 (s, 1H), 6.63 (d, *J* = 9.0 Hz, 2H), 6.69 (t, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 9.0 Hz, 2H), 7.52-7.60 (m, 2H), 7.64-7.70 (m, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 8.14 (d, *J* = 9.0 Hz, 1H), 8.45 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 32.7, 43.7, 112.9, 117.2, 119.5, 125.2, 127.1, 127.2, 127.5, 129.3, 130.0, 136.3, 141.9, 148.5, 161.3; IR (neat) cm^{-1} 3735, 3628, 2924, 2308, 1457, 1010; HRMS (ESI) Calcd for $C_{18}H_{19}N_2$ $(MH)^+$ 263.1548, found 263.1547.

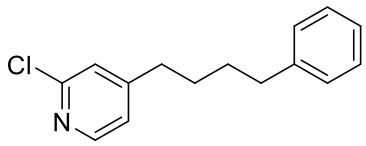


*1-Phenethylisoquinoline (**36**)*:[152] Reaction was conducted in HMPA at 80°C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **36** was obtained as yellow oil (215 mg, 92%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.19-3.24 (m, 2H), 3.59-3.64 (m, 2H), 7.24 (t, *J* = 6.5 Hz, 1H), 7.33 (d, *J* = 6.0 Hz, 4H), 7.54 (d, *J* = 6.0 Hz, 1H), 7.60 (dd, *J*= 6.0 Hz, 3.0Hz, 1H), 7.65-7.70 (m, 1H), 7.83 (d, *J* = 6.0 Hz, 1H), 8.16 (d, *J* = 6.0 Hz, 1H), 8.49 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.6, 37.4, 119.5, 125.2, 126.2, 127.0, 127.2, 127.5, 128.5,

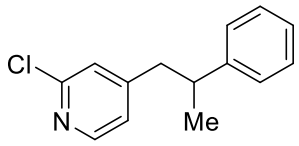
128.6,128.6, 129.9, 136.4, 142.0, 161.1; HRMS (ESI) Calcd for $C_{17}H_{16}N$ $(MH)^+$ 234.1283, found 234.1280.



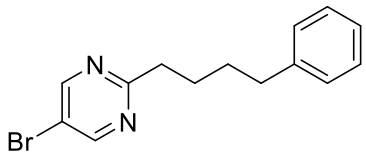
*1-(Hex-5-en-1-yl)isoquinoline (**37**)*:[153] Reaction was conducted in HMPA at 80 °C for 48 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **37** was obtained as yellow oil (173 mg, 82%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53-1.63 (m, 2H), 1.83-1.94 (m, 2H), 2.14 (q, *J* = 7.5 Hz, 2H), 3.30 (t, *J* = 7.5 Hz, 2H), 4.92-5.05 (m, 2H), 5.75-5.89 (m, 1H), 7.49 (d, *J* = 6.0 Hz, 1H), 7.55-7.67 (m, 2H), 7.80 (d, *J* = 9.0 Hz, 1H), 8.15 (d, *J* = 9.0 Hz, 1H), 8.43 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.2, 29.3, 33.8, 35.5, 114.6, 119.3, 125.4, 127.0, 127.5, 129.9, 136.4, 138.9, 142.0, 162.3; HRMS (ESI) Calcd for $C_{15}H_{18}N$ $(MH)^+$ 212.1439, found 212.1441.



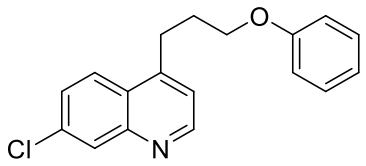
*2-Chloro-4-(4-phenylbutyl)pyridine (**38**)*: Reaction was conducted in HMPA at 80 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **38** was obtained as yellow oil (174 mg, 71%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64-1.69 (m, 4H), 2.58-2.68 (m, 4H), 7.00 (d, *J* = 6.0 Hz, 1H), 7.13-7.22 (m, 4H), 7.26-7.31 (m, 2H), 8.25 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.7, 30.9, 34.9, 35.7, 122.8, 124.2, 126.0, 128.5, 142.0 149.5, 151.7, 154.9; IR (neat) cm^{-1} 2932, 1591, 1545, 1385, 1085; HRMS (ESI) Calcd for $C_{15}H_{17}{}^{35}ClN$ $(MH)^+$ 246.1050, found 246.1046.



*2-Chloro-4-(2-phenylpropyl)pyridine (**39**)*: Reaction was conducted in HMPA at 100 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **39** was obtained as colorless oil (164 mg, 71%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (d, *J* = 6.0 Hz, 3H), 2.76-2.92 (m, 2H), 2.96-3.07 (m, 1H), 6.86 (dd, *J* = 6.0 Hz, 3.0 Hz, 1H), 7.02 (s, 1H), 7.10-7.14 (m, 2H), 7.17-7.23 (m, 1H), 7.25-7.31 (m, 2H), 8.19 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 41.1, 44.0, 123.4, 124.9, 126.7, 127.0, 128.7, 145.3, 149.3, 151.5, 153.2; IR (neat) cm^{-1} 2963, 1591, 1385, 1086; HRMS (ESI) Calcd for $C_{14}H_{15}{}^{35}ClN$ $(MH)^+$ 232.0893, found 232.0888.

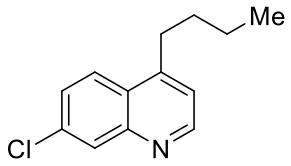


*5-Bromo-2-(4-phenylbutyl)pyrimidine (**40**)*: Reaction was conducted in DMF at 60 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **40** was obtained as colorless oil (119 mg, 41%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.67-1.75 (m, 2H), 1.81-1.92 (m, 2H), 2.66 (t, *J* = 7.5 Hz, 2H), 2.95 (t, *J* = 7.5 Hz, 2H), 7.15-7.19 (m, 3H), 7.24-7.30 (m, 2H), 8.69 (s, 2H); ^{13}CNMR (75 MHz, $CDCl_3$) δ 28.3, 31.2, 35.8, 38.7, 117.7, 125.8, 128.4, 128.5, 142.4, 157.7, 169.7; IR (neat) cm^{-1} 2930, 1537, 1421, 1116, 1010; HRMS (ESI) Calcd for $C_{14}H_{16}BrN_2$ $(MH)^+$ 291.0497, found 291.0500.

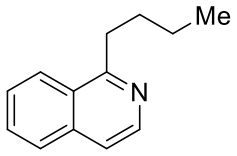


*7-Chloro-4-(3-phenoxypropyl)quinoline (**41**)*: Reaction was conducted in DMF at 100°C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **41** was obtained as yellow oil (199 mg, 67%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17-2.26 (m, 2H), 3.26 (t, *J* = 7.5 Hz, 2H), 4.02 (t, *J* = 6.0 Hz, 2H), 6.90-7.00 (m, 3H), 7.24-7.33 (m, 3H), 7.48 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 8.00 (d, *J* = 9.0 Hz, 1H), 8.12 (d, *J* = 3.0 Hz, 1H), 8.79 (d, *J* = 6.0 Hz, 1H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 28.6, 29.7, 66.5, 114.6, 121.0, 121.3, 125.1, 126.1, 127.5, 129.2, 129.6, 135.1, 147.9, 148.9, 151.3, 158.8; IR (neat) cm^{-1} 2930, 1584, 1496, 1238, 1055; HRMS (ESI) Calcd for $C_{18}H_{17}{}^{35}ClNO$ $(MH)^+$ 298.0999, found 298.0993.



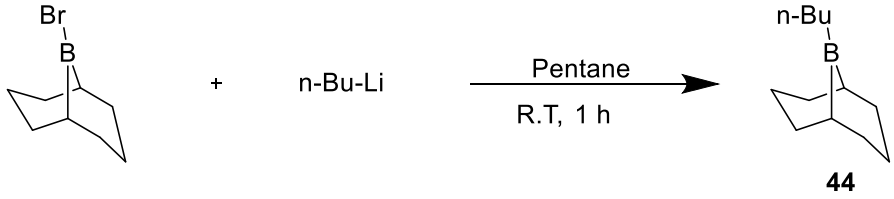
*4-Butyl-7-chloroquinoline **(42)***: Reaction was conducted in DMF at 100 °C for 24 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **42** was obtained as white solid (156 mg, 71%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, *J* = 6.0 Hz, 3H), 1.36-1.48 (m, 2H), 1.64-1.74 (m, 2H), 2.99 (t, *J* = 6.0 Hz, 2H), 7.18 (d, *J* = 3.0 Hz, 1H), 7.45 (dd, *J* = 9.0 Hz, 3.0 Hz, 1H), 7.92 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 3.0 Hz, 1H), 8.76 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.8, 31.9, 32.2, 121.0, 125.1, 126.1, 127.2, 129.2, 134.8, 148.9, 151.3; IR (neat) cm^{-1} 2929; 1590, 1458, 1278, 1091; HRMS (ESI) Calcd for $C_{13}H_{15}{}^{35}ClN$ $(MH)^+$ 220.0893, found 220.0895.



*1-Butylisoquinoline **(43)***:[9] Reaction was conducted in DMF at 80 °C for 12 h with 1.5 equiv of alkylboron reagent using K_3PO_4 as a base. The title compound **43** was obtained as yellow oil (167 mg, 90%) after purification by silica gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, *J* = 9.0 Hz, 3H), 1.43-1.56 (m, 2H), 1.79-1.90 (m, 2H), 3.29 (t, *J* = 9.0 Hz, 2H), 7.48 (d, *J* = 6.0 Hz, 1H), 7.54-7.65 (m, 2H), 7.66 (d, *J* = 3.0 Hz, 1H), 8.15 (d, *J* = 6.0 Hz, 1H), 8.43 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 23.1, 32.0, 35.4, 119.2, 125.5, 126.9, 127.5, 129.8, 136.4, 142.1, 162.5; HRMS (ESI) Calcd for $C_{13}H_{16}N$ $(MH)^+$ 186.1283, found 186.1281.

Synthesis of Boron complexes

Synthesis of B-*n*Butyl-9-BBN (44)[153]

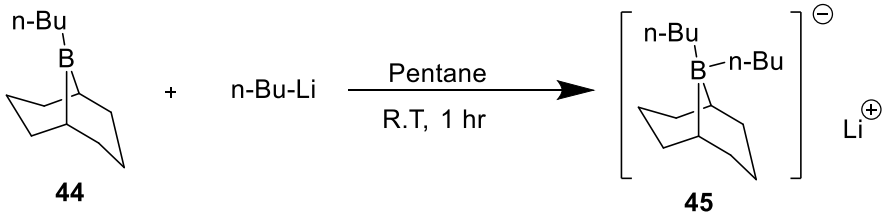


44

*n*Butyllithium (1.0 mmol, 0.625 mL from a 1.6 M solution in hexanes) was added dropwise to a solution of B-Br-9-BBN (1.0 mL from a 1.0 M solution in CH_2Cl_2) in pentane (1 mL) at room temperature. Immediately after the addition, lithium bromide precipitated as white solid. After stirring for 1 h, the reaction mixture was filtered through Celite. Solvent was removed under vacuum to obtain the title compound **44** as a colorless oil (170 mg, 96%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.5 Hz, 3H), 1.19-1.27 (m, 3H), 1.29-1.40 (m,

4H), 1.43-1.52 (m, 2H), 1.66-1.72 (m, 6H), 1.81-1.88 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 23.4, 26.1, 26.9, 31.1, 33.3; ^{11}BNMR (96 MHz, $CDCl_3$) δ 103.6.

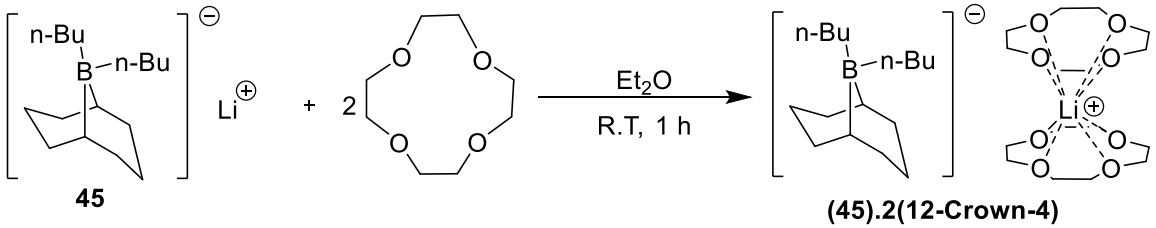
Synthesis of Lithium B-di-*n*butyl-9-BBN (45)[154]



44 **45**

To a solution of B-*n*butyl-9-BBN **44** (178 mg, 1.0 mmol) in pentane (3 mL), *n*BuLi (1.0 mmol, 0.625 mL from a 1.6 M solution in hexanes) was added dropwise at room temperature. Immediately after the addition, a white solid precipitated out of the solution. After stirring for 1 h, the suspension was filtered through a frit funnel and the residue was washed with pentane (2 mL × 3). The residue was then dried under vacuum to obtain the title compound **45** as a white solid (220 mg, 91%). ^{1}H NMR (300 MHz, DMSO) δ 0.04-0.10 (m, 6H), 0.79 (t, J = 6.0 Hz, 6H), 0.89-1.00 (m, 4H), 1.08-1.19 (m, 4H), 1.23-1.41 (m, 6H), 1.57-1.75 (m, 2H), 1.80-1.92 (m, 4H); ^{13}C NMR (75 MHz, DMSO) δ 14.9, 23.9 (q, J_{BC} = 52.8 Hz), 26.8 (q, J_{BC} = 49.0 Hz), 27.0, 28.1 (apparent d, J_{BC} = 3.8 Hz), 29.2, 32.9; ^{11}BNMR (96 MHz, DMSO) δ -2.50.

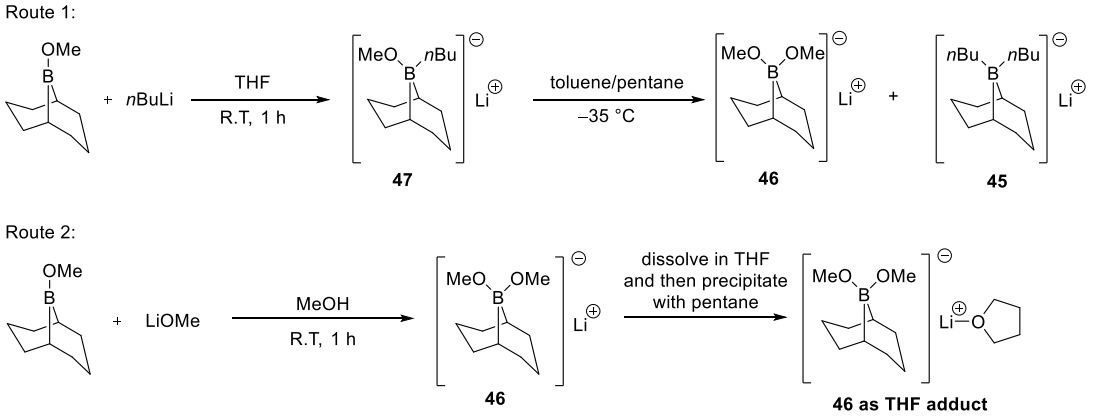
Synthesis of Lithium B-di-*n*butyl-9-BBN (45)•2(12-Crown-4) Complex



45 **(45).2(12-Crown-4)**

A solution of 12-Crown-4 (0.32 mL, 2.0 mmol) in diethyl ether (1 mL) was added dropwise to a solution of lithium B-di-*n*butyl-9-BBN **45** (242 mg, 1.0 mmol) in diethyl ether (2 mL) at room temperature. After stirring for 1 h, the solvent was removed under vacuum to obtain a white residue. The residue was washed with pentane (2 mL × 3) and dried under vacuum to obtain the title compound **(45)•2(12-Crown-4)** as a white solid (540 mg, 91%). ^{1}H NMR (300 MHz, DMSO) δ 0.04-0.09 (m, 6H), 0.79 (t, J = 6.0 Hz, 6H), 0.90-1.00 (m, 4H), 1.06-1.21 (m, 4H), 1.25-1.41 (m, 6H), 1.60-1.76 (m, 2H), 1.80-1.92 (m, 4H), 3.54 (s, 32H); ^{13}C NMR (75 MHz, DMSO) δ 14.8, 23.8 (q, J_{BC} = 52.8 Hz), 26.7 (q, J_{BC} = 49.0 Hz), 27.0, 28.1 (apparent d, J_{BC} = 4.8 Hz), 29.2, 32.9, 69.9; ^{11}BNMR (96 MHz, DMSO) δ -2.50. The title compound **(45)•2(12-Crown-4)** was crystallized by slow evaporation of a pentane/THF solution of **(45)•2(12-Crown-4)** under N_2 atmosphere.

Synthesis of Lithium B-dimethoxy-9-BBN (46)



*n*BuLi (1.0 mmol, 0.625 mL from a 1.6 M solution in hexanes) was added dropwise to a solution of B-methoxy-9-BBN (1.0 mmol, 1.0 mL from a 1.0 M solution in hexanes) in THF (2 mL). After stirring for 1 h, the solvent was removed under vacuum to obtain a white residue. ^{1}H and ^{11}B NMR of the white solid in DMSO-d_6 reveals the formation of three compounds **45-47** (see the overlaid ^{1}H and ^{11}B NMR spectra below). The white residue was then dissolved in minimum toluene, layered with pentane and placed in a freeze at -35 °C. Colorless crystals of the title compound **46** were formed in one week.

The title compound **46** was also synthesized independently as follows: B-methoxy-9-BBN (1.0 mmol, 1 mL from a 1.0 M solution in hexanes) was added dropwise to a solution of LiOMe (38 mg, 1.0 mmol) in methanol. After stirring the clear reaction solution for 1 h, the solvent was removed under vacuum to obtain a white residue. The residue was then dissolved in THF (2 mL) and precipitated with excess pentane. The precipitate was washed with pentane (2 mL × 5) and dried under vacuum to obtain the THF adduct of the title compound **46** as a white solid (177 mg, 93%). ^{1}H NMR (300 MHz, DMSO) δ 0.36 (s, 2H), 1.26-1.34 (m, 6H), 1.65-1.77 (m, 10H), 2.88 (s, 6H), 3.57-3.61 (m, 4H); ^{13}C NMR (75 MHz, DMSO) δ 25.1, 26.4, 32.7, 47.2, 67.0; ^{11}BNMR (96 MHz, DMSO) δ -19.0; IR (neat) cm^{-1} 2821, 1202, 1065, 1043.

Reaction in HMPA and in situ formation of compounds 45-47: *n*BuLi (0.10 mmol, 0.062 mL from a 1.6 M solution in hexanes) was added dropwise to a solution of B-methoxy-9-BBN (0.10 mmol, 0.10 mL from a 1.0 M solution in hexanes) in HMPA (1 mL). After stirring for 0.5 h, ^{11}B NMR was acquired which revealed the formation of three compounds **45-47** (see the overlaid ^{11}B NMR spectra).

Mechanistic studies

Reactivity of n-Butyl-9-BBN Complexes with 1-Iodoisoquinoline

*Reaction of n-butyl-9-BBN (**44**) with 1-iodoisoquinoline (Table 4, entry 1):* n-butyl-9-BBN (**44**) (17.8 mg, 0.10 mmol), 1-iodoisoquinoline (25.5 mg, 0.10 mmol), and CuI (1.9 mg, 0.010 mmol) were dissolved with DMF in a 1 dram vial and heated at 100 °C. After 3 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock solution) as an internal standard was added, diluted with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC. The butylated product **43** was formed only in trace amounts.

*Reaction of n-butyl-9-BBN (**44**) with 1-iodoisoquinoline (Table 4, entry 2):* n-butyl-9-BBN (**44**) (17.8 mg, 0.10 mmol), 1-iodoisoquinoline (25.5 mg, 0.10 mmol), LiOMe (3.8 mg, 0.10 mmol), and CuI (1.9 mg, 0.010 mmol) were dissolved with DMF in a 1 dram vial and heated at 100 °C. After 3 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock solution) as an internal standard was added, diluted with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC. The butylated product **43** was formed in 94% yield.

*Reaction of the complex **45** with 1-iodoisoquinoline (Table 4, entry 3):* complex **45** (12.1 mg, 0.050 mmol), 1-iodoisoquinoline (25.5 mg, 0.10 mmol), and CuI (1.9 mg, 0.010 mmol) were dissolved with DMF in a 1-dram vial and heated at 100 °C. After 3 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock

solution) as an internal standard was added, diluted with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC. The butylated product **43** was formed in 48% yield.

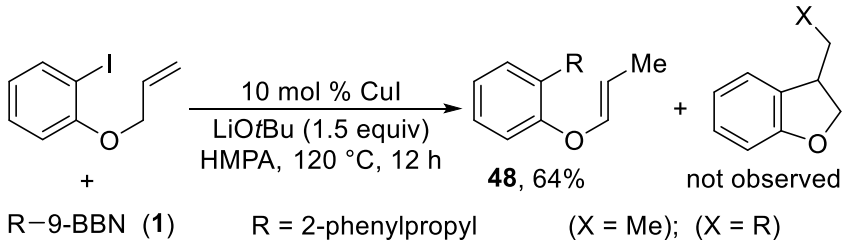
*Reaction of the complex **45** with 1-iodoisoquinoline (Table 4, entry 4):* complex **45** (24.2 mg, 0.10 mmol), 1-iodoisoquinoline (25.5 mg, 0.10 mmol), and CuI (1.9 mg, 0.010 mmol) were dissolved with DMF in a 1-dram vial and heated at 100 °C. After 3 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock solution) as an internal standard was added, diluted with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC. The butylated product **43** was formed in 95% yield.

*Reaction of the complex **45** with 1-iodoisoquinoline (Table 4, entry 5):* complex **45** (12.1 mg, 0.050 mmol), 1-iodoisoquinoline (25.5 mg, 0.10 mmol), LiOMe (1.9 mg, 0.050 mmol), and CuI (1.9 mg, 0.010 mmol) were dissolved with DMF in a 1-dram vial and heated at 100 °C. After 3 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock solution) as an internal standard was added, diluted with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC. The butylated product **43** was formed in 94% yield.

*Reaction of the complexes **45** and **46** with 1-iodoisoquinoline (Table 4, entry 6):* complex **45** (12.1 mg, 0.050 mmol), complex **46** (9.5 mg, 0.050 mmol), 1-iodoisoquinoline (25.5 mg, 0.10 mmol), and CuI (1.9 mg, 0.010 mmol) were dissolved with DMF in a 1-dram vial and heated at 100 °C. After 3 h, the reaction mixture was cooled to room temperature, 20 µL of pyrene (0.010 mmol, 0.5 M stock solution) as an internal standard was added, diluted

with EtOAc (1 mL) and filtered through a short pad of silica gel in a pipette. The reaction mixture was then analyzed by GC. The butylated product **43** was formed in 97% yield.

Reaction of B-(2-Phenylpropyl)-9-BBN (1) with *o*-Allyloxyiodobenzene



o-Allyloxyiodobenzene (260.0 mg, 1.0 mmol), LiO*t*Bu (120 mg, 1.5 mmol), and CuI (19.0 mg, 0.10 mmol) were weighed in a 15 mL pressure tube and dissolved in HMPA (5 mL). B-(2-Phenylpropyl)-9-BBN (**1**) (360.0 mg, 1.5 mmol) was then added to the reaction mixture and tightly capped. The reaction mixture was placed in an oil bath pre-heated to 120 °C with vigorous stirring. After 24 h, reaction mixture was cooled to room temperature. An aliquot of the reaction mixture was analyzed by GC and GC-MS. Only the cross-coupled product **48** was formed. The cyclized product and the cyclized-coupled product were not detected.

The remainder of the reaction mixture was diluted with ethyl acetate (15 mL) and washed with H_2O (5 mL × 3). The aqueous fraction was extracted back with ethyl acetate (5 mL × 3) and combined with the first ethyl acetate fraction. The combined ethyl acetate fraction was dried over Na_2SO_4 and the solvent was removed in a rotary evaporator. The title compound (**48**) was obtained as yellow oil (161 mg, 64%) after purification by silica gel column chromatography using 5% ethyl acetate in hexanes. ^{1}H NMR (300 MHz, $CDCl_3$)

δ 1.26 (d, *J* = 6.0Hz, 3H), 1.77 (dd, *J* = 6.0 Hz, 3.0Hz, 3H), 2.81-3.15 (m, 3H), 4.86 (p, *J* = 6.0 Hz, 1H), 6.34 (d, *J* = 6.0 Hz, 1H), 6.92 (q, *J* = 3.0 Hz, 2H), 7.03 (d, *J* = 6.0 Hz, 1H), 7.12-7.31 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.6, 21.1, 39.6, 40.5, 106.7, 114.8, 122.2, 126.0, 127.1, 127.3, 128.4, 130.4, 131.4, 141.6, 147.6, 155.8; GCMS (m/z) 252.2.

Hammett Plot

α-Methylstyrene (1.536 g, 13.0 mmol) and 9-BBN (10 mmol, 20 mL from a 0.5 M solution in THF) were mixed in a sealed tube, tightly capped and heated at 60 °C. After 4 h, the reaction mixture was transferred to a round-bottom flask, and subjected to high vacuum at room temperature until THF was removed and then at 40 °C for 2 h to remove excess □-methylstyrene. The alkyl-9-BBN thus obtained was directly used for the following kinetic experiment.

CuI (38.0 mg, 0.20 mmol) was weighed in a 1.0 mL volumetric flask and dissolved with HMPA to obtain a stock solution (0.20 M).

Alkyl-9-BBN (480.4 mg, 2.0 mmol) was weighed in a 1.0 mL volumetric flask and dissolved with HMPA to obtain a stock solution (2.0 M).

LiOtBu (300.2 mg, 3.75 mmol) was weighed in a 5.0 mL volumetric flask and dissolved with HMPA by stirring with a magnetic stirrer for 8 h to obtain a stock solution (0.75 M).

ArI (5.0 mmol) was weighed in a 2.0 mL volumetric flask and dissolved with HMPA to obtain a stock solution (2.50 M).

CuI (50 μL, 0.010 mmol), LiOtBu (200 μL, 0.150 mmol), alkyl-9-BBN (**1**) (50 μL, 0.10 mmol) and *p*-XC_6H_4I (X = H, OMe, Me, F, Cl, CF_3) (200 μL, 0.50 mmol) were mixed in a

1-dram vial (total volume: 0.50 mL). The reaction mixture was then tightly capped and placed in a hotplate pre-heated to 100 °C. A total of 6 to 9 reactions were setup for each *p*-XC_6H_4I and were stopped at 6-9 time intervals. At least a duplicate reaction was setup for each of the data point to take an average. Product yields at different time points for the reaction of *p*-XC_6H_4I with alkyl-9-BBN (**1**) were determined by GC using pyrene as a standard. The product yields were then plotted against the corresponding reaction times and the slope of the linear portion of the curve (for less than 30% yield) was used to determine the initial rates of the reactions.

The initial rates of the reactions ($k_{X(initial)}$), $\log[k_{X(initial)}/k_{H(initial)}]$ and □-values used to obtain the Hammett plot are given below:

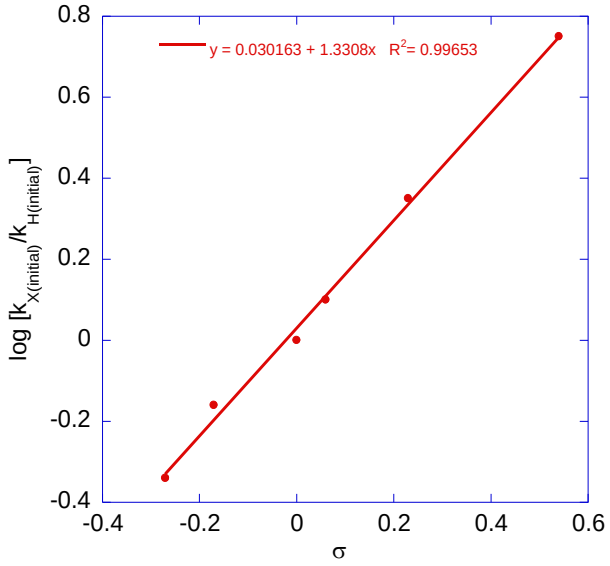


Figure 5.1. The Hammett plot for the reaction of alkyl-9-BBN (**1**) with 5.0 equivalents of *p*-XC_6H_4I (X = H, OMe, Me, F, Cl, CF_3). The curve depicts the result of an unweighted least-square fit to y = a*x + b (a = +1.33, b = 3.01×10^{-2}, R^2 = 0.99). Substituent constants

(σ values) were adopted from C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165-195.

5.1.8. X-ray Crystallographic Data for Complex 45

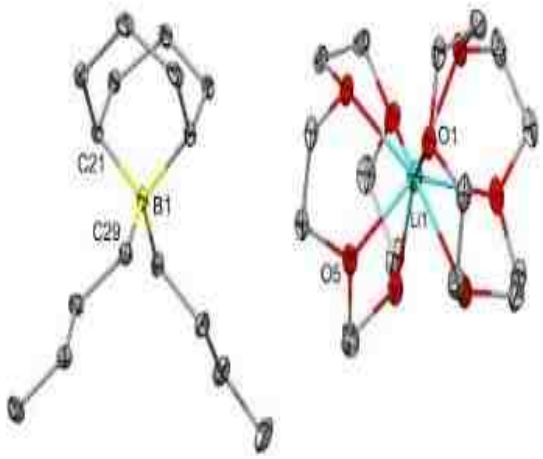


Table 5.1. Crystal data and structure refinement for complex 45.

Identification code	rgpb3_33_0m
Empirical formula	$C_{32}H_{64}BLiO_8$
Formula weight	594.58
Temperature/K	99.51
Crystal system	monoclinic
Space group	$P2_1/n$

a/Å	10.6109(3)
b/Å	22.4723(6)
c/Å	14.5753(4)
α/°	90
β/°	92.6743(15)
γ/°	90
Volume/Å^3	3471.71(17)
Z	4
ρ_{calc}g/cm^3	1.138
μ/mm^{-1}	0.078
F(000)	1312.0
Crystal size/mm^3	0.841 × 0.315 × 0.216
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.334 to 55.016
Index ranges	-13 ≤ h ≤ 12, -29 ≤ k ≤ 29, -18 ≤ l ≤ 18
Reflections collected	33894

Independent reflections	7967 [R_{int} = 0.0277, R_{sigma} = 0.0244]
Data/restraints/parameters	7967/0/448
Goodness-of-fit on F^2	1.065
Final R indexes [I>=2σ (I)]	R_1 = 0.0487, wR_2 = 0.1242
Final R indexes [all data]	R_1 = 0.0610, wR_2 = 0.1321
Largest diff. peak/hole / e $Å^{-3}$	0.70/-0.40

Table 5.2. Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for complex 45. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	***x***	***y***	***z***	**U(eq)**
O1	1689.2(10)	6948.3(5)	9325.2(7)	22.16(19)
O2	4212.2(10)	6752.1(5)	9433.5(7)	23.4(2)
O3	3762.5(10)	5552.4(5)	9690.1(7)	25.3(2)
O4	1182.8(10)	5751.3(5)	9562.7(7)	25.8(2)
O5	900.4(10)	6225.2(5)	7605.0(7)	21.3(2)
O6	2498.6(10)	5263.7(5)	7817.5(7)	22.3(2)

O7	4520.5(10)	6023.4(5)	7768.0(7)	21.6(2)
O8	2924.7(10)	6971.2(5)	7546.9(7)	20.1(2)
C1	2559.6(14)	7419.6(7)	9577.7(10)	22.16(19)
C2	3734.0(15)	7177.4(7)	10044.5(11)	24.9(3)
C3	5133.1(14)	6355.7(8)	9864.8(11)	28.5(4)
C4	4513.0(15)	5863.2(7)	10357.2(11)	27.1(3)
C5	2860.4(17)	5148.4(7)	10078.5(11)	29.0(4)
C6	1701.6(15)	5468.2(7)	10361.6(11)	25.9(3)
C7	276.4(13)	6211.1(7)	9751.8(11)	24.5(3)
C8	916.1(14)	6777.3(7)	10046.5(10)	24.0(3)
Li1	2715(2)	6215.9(11)	8566.6(17)	21.3(5)
C9	3690(5)	5064(2)	7535(3)	26.7(9)
C10	4384(3)	5561.0(14)	7087(2)	25.8(7)
C11	4895(3)	6586.6(18)	7361(3)	22.0(7)
C12	3811(3)	6904.2(13)	6882(2)	20.4(6)
C13	1647(3)	7121.6(14)	7129(2)	20.0(7)

C14	911(3)	6578.2(16)	6835(2)	20.3(6)
C15	453(3)	5614.9(13)	7419(2)	23.1(7)
C16	1532(5)	5242(2)	7099(3)	24.4(9)
C9A	3474(5)	5143(2)	7195(4)	23.2(10)
C10A	4672(3)	5391.5(15)	7610(3)	21.9(8)
C11A	4720(4)	6385.4(19)	7023(3)	22.3(8)
C12A	4285(4)	6994.6(15)	7285(3)	20.3(8)
C13A	2096(4)	7021.2(16)	6816(3)	19.4(8)
C14A	864(3)	6825.2(19)	7173(3)	19.0(8)
C15A	869(3)	5773.8(15)	6924(3)	24.3(9)
C16A	1246(5)	5223(2)	7429(4)	25.4(11)
C17	2953.3(12)	6624.7(6)	4370.5(9)	15.1(3)
C18	2704.6(13)	7300.2(6)	4416.6(10)	18.8(3)
C19	3022.2(13)	7658.0(6)	3553.4(10)	19.3(3)
C20	2675.5(13)	7352.5(6)	2628.1(9)	16.1(3)
C21	2971.9(11)	6683.3(6)	2604.5(9)	12.0(2)

C22	4399.5(12)	6554.4(6)	2650.9(9)	14.2(3)
C23	5089.1(12)	6670.4(6)	3588.1(9)	16.7(3)
C24	4369.4(13)	6473.3(6)	4428.9(9)	17.6(3)
C25	2511.3(12)	5610.6(6)	3370.8(9)	14.8(3)
C26	2026.1(14)	5229.3(6)	4151.9(10)	19.1(3)
C27	2492.0(14)	4588.0(7)	4167.6(11)	22.8(3)
C28	1931.9(19)	4207.3(8)	4907.8(12)	35.3(4)
C29	732.0(12)	6468.8(6)	3413.7(9)	14.2(3)
C30	-17.6(12)	6329.4(6)	2515.8(9)	14.7(3)
C31	-1435.2(12)	6433.8(6)	2560.9(9)	15.0(3)
C32	-2194.8(13)	6287.8(7)	1677.7(10)	19.9(3)
B1	2263.4(13)	6334.7(7)	3435.2(10)	12.4(3)

Table 5.3. Anisotropic Displacement Parameters ($Å^2×10^3$) for complex 45. The Anisotropic displacement factor exponent takes the form: -

$2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	**U_{11}**	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**

O1	29.6(4)	23.1(4)	13.8(4)	-0.5(3)	1.7(3)	3.0(3)
O2	26.9(5)	30.2(6)	12.8(5)	-1.1(4)	-1.3(4)	1.2(4)
O3	31.2(6)	30.0(6)	14.6(5)	-3.3(4)	1.0(4)	6.4(5)
O4	29.1(6)	32.1(6)	16.1(5)	0.5(4)	0.9(4)	0.6(5)
O5	27.1(5)	20.8(5)	15.9(5)	-1.5(4)	-1.2(4)	1.8(4)
O6	25.7(5)	24.5(5)	16.7(5)	0.4(4)	1.6(4)	2.8(4)
O7	28.8(5)	20.2(5)	16.4(5)	-0.3(4)	5.8(4)	0.6(4)
O8	26.8(5)	21.9(5)	11.8(5)	-0.1(4)	4.5(4)	1.9(4)
C1	29.6(4)	23.1(4)	13.8(4)	-0.5(3)	1.7(3)	3.0(3)
C2	30.7(8)	24.9(8)	18.8(7)	-3.5(6)	-0.7(6)	-3.5(6)
C3	17.6(7)	48.5(10)	19.1(7)	-1.1(7)	-3.8(6)	5.6(7)
C4	28.7(8)	33.2(9)	18.9(7)	-1.7(6)	-5.5(6)	9.4(7)
C5	49.4(10)	16.8(7)	20.7(8)	2.2(6)	1.0(7)	6.6(7)
C6	34.4(8)	24.6(8)	18.8(7)	4.5(6)	2.2(6)	-1.1(6)
C7	16.6(7)	37.2(9)	20.2(7)	1.7(6)	4.5(5)	1.8(6)
C8	25.3(7)	30.1(8)	17.1(7)	1.7(6)	5.2(6)	8.7(6)

Li1	23.3(12)	23.3(12)	17.4(12)	0.4(10)	2.2(9)	1.4(10)
C9	36(2)	20.1(18)	25(2)	1.1(18)	5.7(19)	10.9(14)
C10	29.2(15)	27.7(16)	21.1(17)	-4.4(13)	7.9(12)	8.1(12)
C11	22.5(15)	26(2)	18.1(17)	0.0(13)	7.8(13)	-6.3(14)
C12	26.4(16)	22.8(15)	12.4(14)	1.4(11)	5.4(12)	-4.3(12)
C13	24.1(17)	20.2(15)	15.7(16)	3.3(12)	0.3(12)	8.2(13)
C14	23.1(14)	22.6(17)	15.0(15)	2.8(13)	-1.7(11)	2.7(12)
C15	23.7(14)	24.2(15)	21.2(16)	0.2(12)	-2.0(12)	-9.1(12)
C16	34(2)	20.7(16)	18(2)	-6.5(17)	-2.6(16)	-2.3(15)
C9A	34(3)	15(2)	20(3)	-3.3(19)	6(2)	4.9(16)
C10A	28.2(17)	19.1(16)	18.8(19)	1.7(13)	5.2(14)	11.2(13)
C11A	29(2)	18(2)	21(2)	1.6(15)	13.0(16)	1.8(15)
C12A	22.1(18)	18.5(17)	21(2)	1.9(14)	9.4(15)	-4.5(14)
C13A	27(2)	17.6(17)	13.3(18)	3.1(13)	1.4(15)	2.0(14)
C14A	23.1(17)	18.4(18)	14.9(18)	-0.4(14)	-3.7(13)	5.9(15)
C15A	27.0(17)	22.6(17)	22.7(19)	-3.8(14)	-6.5(15)	-4.3(14)

C16A	28(3)	20.2(19)	28(3)	-6(2)	-1(2)	-4.7(17)
C17	15.9(6)	20.3(7)	9.3(6)	-0.9(5)	2.2(5)	-3.9(5)
C18	18.6(6)	22.5(7)	15.4(7)	-8.0(5)	2.5(5)	-3.8(5)
C19	21.8(7)	15.9(7)	20.4(7)	-4.5(5)	1.2(5)	-2.0(5)
C20	17.0(6)	16.5(6)	14.9(6)	0.7(5)	1.1(5)	-1.5(5)
C21	11.8(6)	14.9(6)	9.4(6)	-0.9(5)	0.4(4)	-1.4(5)
C22	12.5(6)	19.1(6)	11.0(6)	-0.1(5)	2.4(5)	-1.6(5)
C23	11.9(6)	24.1(7)	14.1(6)	-0.1(5)	-1.2(5)	-2.4(5)
C24	17.7(6)	23.8(7)	11.0(6)	0.4(5)	-2.2(5)	-3.1(5)
C25	16.1(6)	16.6(6)	11.7(6)	0.4(5)	1.7(5)	-1.3(5)
C26	23.9(7)	17.9(7)	15.9(7)	1.7(5)	4.0(5)	-2.4(5)
C27	26.2(7)	19.8(7)	22.5(7)	5.6(6)	2.3(6)	0.1(6)
C28	56.6(11)	23.4(8)	26.4(9)	9.1(7)	7.4(8)	-3.4(8)
C29	13.9(6)	16.7(6)	12.3(6)	-2.1(5)	3.0(5)	-1.9(5)
C30	12.1(6)	17.8(6)	14.3(6)	-2.3(5)	2.8(5)	-1.6(5)
C31	12.9(6)	16.3(6)	15.9(6)	-0.4(5)	2.5(5)	0.6(5)

C32	13.9(6)	24.7(7)	20.9(7)	-1.8(6)	-0.8(5)	-0.2(5)
B1	12.8(6)	15.0(7)	9.6(6)	-1.0(5)	2.0(5)	-1.3(5)

Table 5.4. Bond Lengths for complex 45.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C1	1.4416(19)	O8	C13A	1.353(4)
O1	C8	1.4165(18)	C1	C2	1.494(2)
O1	Li1	2.287(3)	C3	C4	1.489(2)
O2	C2	1.4165(18)	C5	C6	1.499(2)
O2	C3	1.4444(19)	C7	C8	1.496(2)
O2	Li1	2.321(3)	C9	C10	1.503(6)
O3	C4	1.4124(19)	C11	C12	1.498(5)
O3	C5	1.453(2)	C13	C14	1.501(5)
O3	Li1	2.443(3)	C15	C16	1.510(6)
O4	C6	1.4156(18)	C9A	C10A	1.490(7)
O4	C7	1.4469(19)	C11A	C12A	1.500(5)

O4	Li1	2.462(3)	C13A	C14A	1.495(5)
O5	Li1	2.328(3)	C15A	C16A	1.486(7)
O5	C14	1.375(3)	C17	C18	1.543(2)
O5	C15	1.472(3)	C17	C24	1.5391(18)
O5	C14A	1.488(4)	C17	B1	1.6510(19)
O5	C15A	1.418(3)	C18	C19	1.544(2)
O6	Li1	2.408(3)	C19	C20	1.5425(19)
O6	C9	1.421(5)	C20	C21	1.5371(18)
O6	C16	1.432(5)	C21	C22	1.5406(17)
O6	C9A	1.434(6)	C21	B1	1.6522(19)
O6	C16A	1.423(6)	C22	C23	1.5415(18)
O7	Li1	2.328(3)	C23	C24	1.5390(19)
O7	C10	1.440(3)	C25	C26	1.5331(18)
O7	C11	1.461(4)	C25	B1	1.652(2)
O7	C10A	1.449(3)	C26	C27	1.523(2)
O7	C11A	1.381(4)	C27	C28	1.520(2)

O8	Li1	2.274(3)	C29	C30	1.5319(18)
O8	C12	1.390(3)	C29	B1	1.6515(19)
O8	C13	1.499(3)	C30	C31	1.5268(17)
O8	C12A	1.511(4)	C31	C32	1.5224(19)

Table 5.5. Bond Angles for complex 45.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C1	O1	Li1	109.78(11)	O5	Li1	O3	138.29(12)
C8	O1	C1	113.34(11)	O5	Li1	O4	78.95(8)
C8	O1	Li1	117.96(11)	O5	Li1	O6	71.12(8)
C2	O2	C3	113.42(11)	O5	Li1	O7	112.18(11)
C2	O2	Li1	115.89(11)	O6	Li1	O3	78.02(8)
C3	O2	Li1	110.41(11)	O6	Li1	O4	80.73(8)
C4	O3	C5	113.66(12)	O7	Li1	O3	82.10(9)
C4	O3	Li1	112.57(11)	O7	Li1	O4	142.89(12)
C5	O3	Li1	110.80(11)	O7	Li1	O6	70.83(8)

C6	O4	C7	113.63(12)	O8	Li1	O1	80.91(9)
C6	O4	Li1	115.69(11)	O8	Li1	O2	83.28(9)
C7	O4	Li1	105.82(10)	O8	Li1	O3	146.96(12)
C14	O5	Li1	117.27(15)	O8	Li1	O4	142.13(12)
C14	O5	C15	113.7(2)	O8	Li1	O5	72.74(8)
C15	O5	Li1	110.67(14)	O8	Li1	O6	112.16(11)
C14A	O5	Li1	105.49(17)	O8	Li1	O7	72.79(8)
C15A	O5	Li1	113.98(16)	O6	C9	C10	110.6(3)
C15A	O5	C14A	110.6(2)	O7	C10	C9	105.8(3)
C9	O6	Li1	110.2(2)	O7	C11	C12	112.6(3)
C9	O6	C16	113.2(3)	O8	C12	C11	104.9(3)
C16	O6	Li1	114.3(2)	O8	C13	C14	112.4(2)
C9A	O6	Li1	113.5(2)	O5	C14	C13	105.1(3)
C16A	O6	Li1	107.8(2)	O5	C15	C16	109.3(3)
C16A	O6	C9A	115.1(3)	O6	C16	C15	106.5(3)
C10	O7	Li1	114.85(15)	O6	C9A	C10A	107.4(4)

C10	O7	C11	111.4(2)	O7	C10A	C9A	109.5(3)
C11	O7	Li1	106.74(16)	O7	C11A	C12A	106.1(3)
C10A	O7	Li1	111.20(16)	C11A	C12A	O8	110.0(3)
C11A	O7	Li1	116.35(18)	O8	C13A	C14A	104.4(3)
C11A	O7	C10A	115.5(2)	O5	C14A	C13A	114.1(3)
C12	O8	Li1	117.71(15)	O5	C15A	C16A	104.7(3)
C12	O8	C13	111.7(2)	O6	C16A	C15A	111.6(4)
C13	O8	Li1	108.66(16)	C18	C17	B1	110.75(11)
C12A	O8	Li1	108.35(16)	C24	C17	C18	112.55(11)
C13A	O8	Li1	119.77(18)	C24	C17	B1	110.65(11)
C13A	O8	C12A	113.0(3)	C17	C18	C19	115.65(11)
O1	C1	C2	111.06(12)	C20	C19	C18	115.38(11)
O2	C2	C1	105.97(12)	C21	C20	C19	114.47(11)
O2	C3	C4	111.28(12)	C20	C21	C22	112.63(10)
O3	C4	C3	106.46(12)	C20	C21	B1	110.30(10)
O3	C5	C6	111.80(12)	C22	C21	B1	111.02(10)

O4	C6	C5	106.36(13)	C21	C22	C23	115.61(11)
O4	C7	C8	111.43(12)	C24	C23	C22	115.11(11)
O1	C8	C7	106.77(12)	C17	C24	C23	114.32(11)
O1	Li1	O2	72.07(8)	C26	C25	B1	116.65(11)
O1	Li1	O3	109.09(10)	C27	C26	C25	114.82(12)
O1	Li1	O4	71.20(8)	C28	C27	C26	113.95(13)
O1	Li1	O5	83.43(9)	C30	C29	B1	116.74(10)
O1	Li1	O6	145.21(12)	C31	C30	C29	113.89(11)
O1	Li1	O7	142.83(13)	C32	C31	C30	114.47(11)
O2	Li1	O3	70.94(8)	C17	B1	C21	102.62(10)
O2	Li1	O4	110.68(10)	C17	B1	C25	111.72(11)
O2	Li1	O5	148.11(13)	C17	B1	C29	109.97(10)
O2	Li1	O6	139.17(12)	C25	B1	C21	110.27(10)
O2	Li1	O7	79.07(9)	C25	B1	C29	109.75(10)
O3	Li1	O4	68.79(8)	C29	B1	C21	112.37(10)

Table 5.6. Torsion Angles for complex 45.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
O1	C1	C2	O2	55.27(15)	C12	O8	C13	C14	85.5(3)
O2	C3	C4	O3	60.07(16)	C13	O8	C12	C11	-163.8(3)
O3	C5	C6	O4	58.32(16)	C14	O5	C15	C16	83.3(3)
O4	C7	C8	O1	58.47(15)	C15	O5	C14	C13	-168.0(3)
O5	C15	C16	O6	58.5(4)	C16	O6	C9	C10	84.5(4)
O5	C15A	C16A	O6	-63.0(5)	C9A	O6	C16A	C15A	-81.4(5)
O6	C9	C10	O7	59.2(4)	C10A	O7	C11A	C12A	169.8(3)
O6	C9A	C10A	O7	-58.2(4)	C11A	O7	C10A	C9A	-84.5(4)
O7	C11	C12	O8	56.4(4)	C12A	O8	C13A	C14A	165.1(3)
O7	C11A	C12A	O8	-56.6(5)	C13A	O8	C12A	C11A	-85.9(4)
O8	C13	C14	O5	54.4(4)	C14A	O5	C15A	C16A	165.6(3)
O8	C13A	C14A	O5	-54.6(4)	C15A	O5	C14A	C13A	-77.6(4)
C1	O1	C8	C7	-168.26(11)	C16A	O6	C9A	C10A	162.0(4)
C2	O2	C3	C4	81.59(16)	C17	C18	C19	C20	39.64(17)

C3	O2	C2	C1	-163.60(12)	C18	C17	C24	C23	-68.08(15)
C4	O3	C5	C6	81.06(16)	C18	C17	B1	C21	62.07(13)
C5	O3	C4	C3	-166.03(12)	C18	C17	B1	C25	-179.81(10)
C6	O4	C7	C8	79.58(16)	C18	C17	B1	C29	-57.68(14)
C7	O4	C6	C5	-163.59(13)	C18	C19	C20	C21	-41.45(16)
C8	O1	C1	C2	84.67(15)	C19	C20	C21	C22	-68.49(14)
Li1	O1	C1	C2	-49.59(15)	C19	C20	C21	B1	56.17(14)
Li1	O1	C8	C7	-37.99(15)	C20	C21	C22	C23	71.62(14)
Li1	O2	C2	C1	-34.35(16)	C20	C21	B1	C17	-64.29(12)
Li1	O2	C3	C4	-50.39(15)	C20	C21	B1	C25	176.57(10)
Li1	O3	C4	C3	-39.02(15)	C20	C21	B1	C29	53.79(14)
Li1	O3	C5	C6	-46.88(15)	C21	C22	C23	C24	40.84(16)
Li1	O4	C6	C5	-40.86(16)	C22	C21	B1	C17	61.29(13)
Li1	O4	C7	C8	-48.42(14)	C22	C21	B1	C25	-57.85(13)
Li1	O5	C14	C13	-36.6(3)	C22	C21	B1	C29	179.36(10)
Li1	O5	C15	C16	-51.2(3)	C22	C23	C24	C17	-42.51(17)

Li1	O5	C14A	C13A	46.2(4)	C24	C17	C18	C19	72.13(15)
Li1	O5	C15A	C16A	46.9(4)	C24	C17	B1	C21	-63.45(13)
Li1	O6	C9	C10	-44.9(4)	C24	C17	B1	C25	54.67(14)
Li1	O6	C16	C15	-37.7(4)	C24	C17	B1	C29	176.80(11)
Li1	O6	C9A	C10A	37.1(4)	C25	C26	C27	C28	-176.15(13)
Li1	O6	C16A	C15A	46.4(4)	C26	C25	B1	C17	60.62(15)
Li1	O7	C10	C9	-44.3(3)	C26	C25	B1	C21	174.07(11)
Li1	O7	C11	C12	-47.4(3)	C26	C25	B1	C29	-61.63(14)
Li1	O7	C10A	C9A	50.9(4)	C29	C30	C31	C32	-179.09(11)
Li1	O7	C11A	C12A	36.7(4)	C30	C29	B1	C17	169.42(11)
Li1	O8	C12	C11	-37.1(3)	C30	C29	B1	C21	55.78(15)
Li1	O8	C13	C14	-46.0(3)	C30	C29	B1	C25	-67.29(14)
Li1	O8	C12A	C11A	49.3(4)	B1	C17	C18	C19	-52.31(15)
Li1	O8	C13A	C14A	35.6(4)	B1	C17	C24	C23	56.41(15)
C9	O6	C16	C15	-164.9(3)	B1	C21	C22	C23	-52.64(15)
C10	O7	C11	C12	78.7(3)	B1	C25	C26	C27	-168.62(12)

C11	O7	C10	C9	-165.9(3)	B1	C29	C30	C31	177.02(11)

Table 5.7. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for complex 45.

Atom	***x***	***y***	***z***	**U(eq)**
H1A	2152	7701	9994	27
H1B	2780	7641	9020	27
H2A	4356	7499	10167	30
H2B	3541	6988	10635	30
H3A	5685	6583	10305	34
H3B	5668	6187	9391	34
H4A	5154	5595	10649	33
H4B	3983	6024	10840	33
H5A	3263	4946	10620	35
H5B	2616	4840	9619	35
H6A	1089	5183	10606	31

H6B	1922	5766	10843	31
H7A	-270	6074	10242	29
H7B	-267	6286	9193	29
H8A	283	7090	10156	29
H8B	1434	6714	10621	29
H9A	3568	4730	7096	32
H9B	4199	4917	8075	32
H10A	5221	5424	6900	31
H10B	3898	5707	6536	31
H11A	5552	6509	6915	26
H11B	5269	6847	7849	26
H12A	4080	7297	6652	24
H12B	3461	6666	6358	24
H13A	1748	7382	6589	24
H13B	1167	7346	7581	24
H14A	42	6687	6623	24

H14B	1324	6370	6331	24
H15A	-240	5621	6941	28
H15B	124	5440	7984	28
H16A	1254	4827	6988	29
H16B	1847	5405	6522	29
H9AA	3271	5332	6593	28
H9AB	3557	4709	7101	28
H10C	4890	5188	8198	26
H10D	5367	5325	7191	26
H11C	4232	6241	6472	27
H11D	5626	6392	6888	27
H12C	4368	7271	6762	24
H12D	4820	7145	7810	24
H13C	2345	6762	6306	23
H13D	2046	7438	6596	23
H14C	596	7119	7631	23

H14D	221	6824	6659	23
H15C	1468	5864	6442	29
H15D	11	5733	6635	29
H16C	656	5152	7924	30
H16D	1187	4880	7003	30
H17	2564	6438	4912	18
H18A	3203	7465	4949	23
H18B	1802	7362	4532	23
H19A	2577	8045	3569	23
H19B	3939	7742	3582	23
H20A	1762	7409	2484	19
H20B	3137	7553	2140	19
H21	2616	6523	2007	14
H22A	4798	6802	2183	17
H22B	4527	6132	2484	17
H23A	5910	6461	3601	20

H23B	5266	7102	3643	20
H24A	4466	6038	4504	21
H24B	4761	6665	4984	21
H25A	2113	5465	2785	18
H25B	3431	5544	3343	18
H26A	2284	5419	4744	23
H26B	1092	5227	4102	23
H27A	2285	4405	3561	27
H27B	3422	4589	4263	27
H28A	1012	4197	4813	53
H28B	2156	4377	5513	53
H28C	2267	3802	4875	53
H29A	364	6235	3911	17
H29B	610	6895	3557	17
H30A	308	6580	2020	18
H30B	127	5908	2351	18

H31A	-1756	6189	3064	18
H31B	-1579	6857	2717	18
H32A	-1936	6552	1185	30
H32B	-3095	6344	1773	30
H32C	-2042	5873	1506	30

Table 5.8. Atomic Occupancy for complex 45.

Atom	***Occupancy***	**Atom**	***Occupancy***	**Atom**	***Occupancy***
C9	0.541(4)	H9A	0.541(4)	H9B	0.541(4)
C10	0.541(4)	H10A	0.541(4)	H10B	0.541(4)
C11	0.541(4)	H11A	0.541(4)	H11B	0.541(4)
C12	0.541(4)	H12A	0.541(4)	H12B	0.541(4)
C13	0.541(4)	H13A	0.541(4)	H13B	0.541(4)
C14	0.541(4)	H14A	0.541(4)	H14B	0.541(4)
C15	0.541(4)	H15A	0.541(4)	H15B	0.541(4)
C16	0.541(4)	H16A	0.541(4)	H16B	0.541(4)

C9A	0.459(4)	H9AA	0.459(4)	H9AB	0.459(4)
C10A	0.459(4)	H10C	0.459(4)	H10D	0.459(4)
C11A	0.459(4)	H11C	0.459(4)	H11D	0.459(4)
C12A	0.459(4)	H12C	0.459(4)	H12D	0.459(4)
C13A	0.459(4)	H13C	0.459(4)	H13D	0.459(4)
C14A	0.459(4)	H14C	0.459(4)	H14D	0.459(4)
C15A	0.459(4)	H15C	0.459(4)	H15D	0.459(4)
C16A	0.459(4)	H16C	0.459(4)	H16D	0.459(4)

5.1.9. X-ray Crystallographic Data for Complex 46

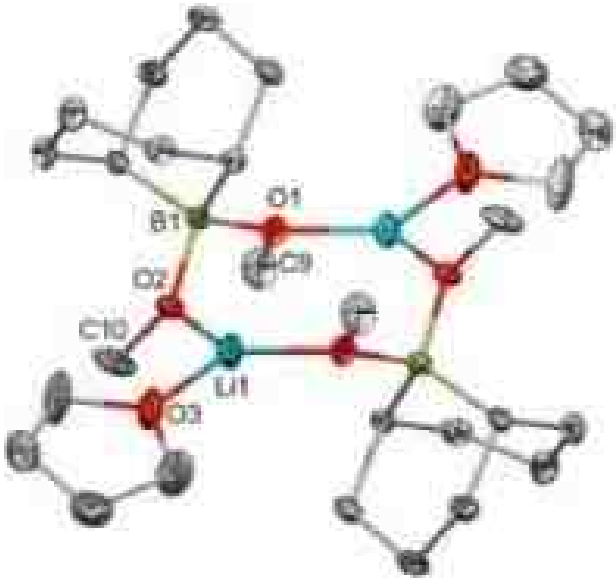


Table 5.9. Sample and crystal data for complex 46.

Identification code	rgpb2_287	
Chemical formula	$C_{28}H_{56}B_2Li_2O_6$	
Formula weight	524.22 g/mol	
Temperature	101(2) K	
Wavelength	0.71073 Å	
Crystal size	0.429 x 0.482 x 0.536 mm	
Crystal habit	colorless block	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 8.3308(4) Å	α = 98.430(2)°
	b = 9.3831(5) Å	β = 106.326(2)°
	c = 10.3351(5) Å	γ = 90.671(2)°
Volume	765.74(7) $Å^3$	
Z	1	

Density (calculated)	1.137 g/cm^3
Absorption coefficient	0.074 mm^{-1}
F(000)	288

Table 5.10. Data collection and structure refinement for complex 46.

Diffractometer	Bruker Kappa APEX II CCD
Radiation source	fine-focus tube, Mo Kα
Theta range for data collection	2.20 to 26.42°
Index ranges	-10<=h<=10, -11<=k<=11, -8<=l<=12
Reflections collected	16573
Independent reflections	3134 [R(int) = 0.0187]
Coverage of independent reflections	99.6%
Absorption correction	Multi-Scan

Max. and min. transmission	0.9690 and 0.9610	
Structure solution technique	direct methods	
Structure solution program	XT, VERSION 2014/4	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)	
Function minimized	$\Sigma\, w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	3134 / 4 / 184	
Goodness-of-fit on F^2	1.032	
Δ/σ_{max}	0.001	
Final R indices	2814 data; $I>2\sigma(I)$	R1 = 0.0530, wR2 = 0.1448
	all data	R1 = 0.0576, wR2 = 0.1492

Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0745P)^2+0.5935P]$ where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter	0.0(2)
Largest diff. peak and hole	0.561 and -0.448 eÅ^{-3}
R.M.S. deviation from mean	0.053 eÅ^{-3}

Table 5.11. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for complex 46.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
B1	0.47622(19)	0.57092(17)	0.30244(16)	0.0138(3)
O1	0.65189(12)	0.59106(11)	0.39875(10)	0.0172(3)
O2	0.41479(13)	0.41488(10)	0.28563(10)	0.0169(3)
O3	0.86952(15)	0.77137(14)	0.66953(11)	0.0300(3)

	x/a	y/b	z/c	U(eq)
Li1	0.6796(3)	0.6374(3)	0.5846(3)	0.0234(6)
C1	0.35809(18)	0.66972(15)	0.37579(14)	0.0157(3)
C2	0.4244(2)	0.82837(16)	0.40416(15)	0.0200(3)
C3	0.4461(2)	0.88905(16)	0.27956(16)	0.0235(3)
C4	0.5258(2)	0.78653(16)	0.18794(16)	0.0211(3)
C5	0.45935(17)	0.62777(15)	0.15862(14)	0.0151(3)
C6	0.27561(19)	0.60278(17)	0.07020(15)	0.0213(3)
C7	0.14488(19)	0.66845(18)	0.13730(16)	0.0239(4)
C8	0.17471(18)	0.64691(16)	0.28675(16)	0.0197(3)
C9	0.7859(2)	0.5337(2)	0.35341(18)	0.0300(4)
C10	0.4606(2)	0.30831(17)	0.1932(2)	0.0302(4)
C11	0.9612(3)	0.7951(3)	0.81120(19)	0.0469(6)
C12	0.1017(3)	0.9019(2)	0.8296(2)	0.0476(6)
C13	0.0654(5)	0.9640(5)	0.7096(5)	0.0386(8)

	x/a	y/b	z/c	U(eq)
C13A	0.1092(7)	0.9063(6)	0.6775(6)	0.0386(8)
C14	0.9392(3)	0.8682(2)	0.6011(2)	0.0412(5)

Table 5.12. Bond lengths (Å) for complex 46.

B1-O1	1.5125(18)	B1-O2	1.5145(18)
B1-C5	1.622(2)	B1-C1	1.624(2)
O1-C9	1.4104(18)	O1-Li1	1.854(3)
O2-C10	1.4112(18)	O2-Li1	1.853(3)
O3-C11	1.431(2)	O3-C14	1.438(2)
O3-Li1	1.924(3)	Li1-O2	1.853(3)
C1-C2	1.5391(19)	C1-C8	1.540(2)
C1-H1A	1.0	C2-C3	1.536(2)
C2-H2A	0.99	C2-H2B	0.99
C3-C4	1.538(2)	C3-H3A	0.99

C3-H3B	0.99	C4-C5	1.5399(19)
C4-H4A	0.99	C4-H4B	0.99
C5-C6	1.541(2)	C5-H5A	1.0
C6-C7	1.537(2)	C6-H6A	0.99
C6-H6B	0.99	C7-C8	1.538(2)
C7-H7A	0.99	C7-H7B	0.99
C8-H8A	0.99	C8-H8B	0.99
C9-H9A	0.98	C9-H9B	0.98
C9-H9C	0.98	C10-H10A	0.98
C10-H10B	0.98	C10-H10C	0.98
C11-C12	1.484(3)	C11-H11A	0.99
C11-H11B	0.99	C12-C13	1.406(5)
C12-C13A	1.598(6)	C12-H12A	0.99
C12-H12B	0.99	C12-H13D	1.17(3)
C13-C14	1.480(5)	C13-H13A	0.99

C13-H13B	0.99	C13A-C14	1.426(5)
C13A-H13C	1.006(19)	C13A-H13D	0.722(15)
C14-H14A	0.99	C14-H14B	0.99

Table 5.13. Bond angles (°) for complex 46.

O1-B1-O2	108.83(11)	O1-B1-C5	113.52(11)
O2-B1-C5	113.42(11)	O1-B1-C1	106.97(11)
O2-B1-C1	107.74(11)	C5-B1-C1	105.97(11)
C9-O1-B1	119.30(11)	C9-O1-Li1	119.11(13)
B1-O1-Li1	118.84(12)	C10-O2-B1	120.54(11)
C10-O2-Li1	120.42(13)	B1-O2-Li1	117.63(12)
C11-O3-C14	108.64(14)	C11-O3-Li1	126.03(13)
C14-O3-Li1	125.29(13)	O2-Li1-O1	138.60(16)
O2-Li1-O3	110.51(14)	O1-Li1-O3	110.78(13)
C2-C1-C8	112.99(12)	C2-C1-B1	109.34(11)

C8-C1-B1	109.66(11)	C2-C1-H1A	108.2
C8-C1-H1A	108.2	B1-C1-H1A	108.2
C3-C2-C1	115.15(12)	C3-C2-H2A	108.5
C1-C2-H2A	108.5	C3-C2-H2B	108.5
C1-C2-H2B	108.5	H2A-C2-H2B	107.5
C2-C3-C4	114.39(12)	C2-C3-H3A	108.7
C4-C3-H3A	108.7	C2-C3-H3B	108.7
C4-C3-H3B	108.7	H3A-C3-H3B	107.6
C3-C4-C5	115.45(12)	C3-C4-H4A	108.4
C5-C4-H4A	108.4	C3-C4-H4B	108.4
C5-C4-H4B	108.4	H4A-C4-H4B	107.5
C4-C5-C6	113.93(12)	C4-C5-B1	108.91(11)
C6-C5-B1	108.72(11)	C4-C5-H5A	108.4
C6-C5-H5A	108.4	B1-C5-H5A	108.4
C7-C6-C5	115.56(12)	C7-C6-H6A	108.4

C5-C6-H6A	108.4	C7-C6-H6B	108.4
C5-C6-H6B	108.4	H6A-C6-H6B	107.5
C6-C7-C8	114.42(12)	C6-C7-H7A	108.7
C8-C7-H7A	108.7	C6-C7-H7B	108.7
C8-C7-H7B	108.7	H7A-C7-H7B	107.6
C7-C8-C1	115.31(12)	C7-C8-H8A	108.4
C1-C8-H8A	108.4	C7-C8-H8B	108.4
C1-C8-H8B	108.4	H8A-C8-H8B	107.5
O1-C9-H9A	109.5	O1-C9-H9B	109.5
H9A-C9-H9B	109.5	O1-C9-H9C	109.5
H9A-C9-H9C	109.5	H9B-C9-H9C	109.5
O2-C10-H10A	109.5	O2-C10-H10B	109.5
H10A-C10-H10B	109.5	O2-C10-H10C	109.5
H10A-C10-H10C	109.5	H10B-C10-H10C	109.5
O3-C11-C12	107.55(16)	O3-C11-H11A	110.2

C12-C11-H11A	110.2	O3-C11-H11B	110.2
C12-C11-H11B	110.2	H11A-C11-H11B	108.5
C13-C12-C11	106.1(2)	C11-C12-C13A	103.6(2)
C13-C12-H12A	110.5	C11-C12-H12A	110.5
C13-C12-H12B	110.5	C11-C12-H12B	110.5
H12A-C12-H12B	108.7	C11-C12-H13D	121.5(11)
C13A-C12-H13D	24.5(9)	C12-C13-C14	108.5(3)
C12-C13-H13A	110.0	C14-C13-H13A	110.0
C12-C13-H13B	110.0	C14-C13-H13B	110.0
H13A-C13-H13B	108.4	C14-C13A-C12	101.4(3)
C14-C13A-H13C	111.(3)	C12-C13A-H13C	108.(3)
C14-C13A-H13D	142.(2)	C12-C13A-H13D	42.(3)
H13C-C13A-H13D	94.(4)	C13A-C14-O3	108.7(3)
O3-C14-C13	106.0(2)	O3-C14-H14A	110.5
C13-C14-H14A	110.5	O3-C14-H14B	110.5

C13-C14-H14B	110.5	H14A-C14-H14B	108.7

Table 5.14. Torsion angles (°) for complex 46.

O2-B1-O1-C9	72.71(16)	C5-B1-O1-C9	-54.62(17)
C1-B1-O1-C9	-171.15(13)	O2-B1-O1-Li1	-88.38(15)
C5-B1-O1-Li1	144.29(14)	C1-B1-O1-Li1	27.76(17)
O1-B1-O2-C10	-81.95(16)	C5-B1-O2-C10	45.44(18)
C1-B1-O2-C10	162.40(13)	O1-B1-O2-Li1	84.54(15)
C5-B1-O2-Li1	-148.08(13)	C1-B1-O2-Li1	-31.11(16)
C9-O1-Li1-O2	-119.3(2)	B1-O1-Li1-O2	41.8(3)
C9-O1-Li1-O3	56.3(2)	B1-O1-Li1-O3	-142.55(13)
O1-B1-C1-C2	59.08(14)	O2-B1-C1-C2	175.95(11)
C5-B1-C1-C2	-62.34(14)	O1-B1-C1-C8	-176.52(11)
O2-B1-C1-C8	-59.65(14)	C5-B1-C1-C8	62.06(14)
C8-C1-C2-C3	-68.54(16)	B1-C1-C2-C3	53.88(17)

C1-C2-C3-C4	-43.17(19)	C2-C3-C4-C5	43.47(19)
C3-C4-C5-C6	67.38(17)	C3-C4-C5-B1	-54.17(17)
O1-B1-C5-C4	-54.87(15)	O2-B1-C5-C4	-179.77(11)
C1-B1-C5-C4	62.24(14)	O1-B1-C5-C6	-179.54(11)
O2-B1-C5-C6	55.56(15)	C1-B1-C5-C6	-62.43(14)
C4-C5-C6-C7	-67.07(17)	B1-C5-C6-C7	54.59(16)
C5-C6-C7-C8	-43.35(19)	C6-C7-C8-C1	42.28(19)
C2-C1-C8-C7	69.26(16)	B1-C1-C8-C7	-52.99(16)
C14-O3-C11-C12	-4.8(3)	Li1-O3-C11-C12	177.24(18)
O3-C11-C12-C13	14.5(3)	O3-C11-C12-C13A	-14.2(3)
C11-C12-C13-C14	-18.4(4)	C11-C12-C13A-C14	27.9(4)
C12-C13A-C14-O3	-31.9(4)	C11-O3-C14-C13A	24.7(3)
Li1-O3-C14-C13A	-157.2(3)	C11-O3-C14-C13	-6.3(3)
Li1-O3-C14-C13	171.8(2)	C12-C13-C14-O3	15.7(4)

Table 5.15. Anisotropic atomic displacement parameters (Å^2) for complex 46.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
B1	0.0142(7)	0.0138(7)	0.0141(7)	0.0018(6)	0.0052(6)	-0.0003(6)
O1	0.0130(5)	0.0235(5)	0.0155(5)	0.0024(4)	0.0050(4)	0.0015(4)
O2	0.0213(5)	0.0128(5)	0.0186(5)	0.0010(4)	0.0100(4)	0.0004(4)
O3	0.0275(6)	0.0410(7)	0.0180(6)	0.0084(5)	-0.0004(5)	-0.0167(5)
Li1	0.0230(13)	0.0300(14)	0.0170(12)	0.0039(10)	0.0055(10)	-0.0072(11)
C1	0.0179(7)	0.0151(7)	0.0152(7)	0.0022(5)	0.0067(5)	0.0002(5)
C2	0.0251(8)	0.0151(7)	0.0200(7)	-0.0024(5)	0.0093(6)	0.0003(6)
C3	0.0326(9)	0.0141(7)	0.0253(8)	0.0014(6)	0.0115(7)	-0.0019(6)
C4	0.0290(8)	0.0170(7)	0.0196(7)	0.0027(6)	0.0110(6)	-0.0038(6)
C5	0.0171(7)	0.0143(7)	0.0141(7)	0.0003(5)	0.0057(5)	-0.0006(5)
C6	0.0209(8)	0.0251(8)	0.0157(7)	0.0015(6)	0.0024(6)	0.0007(6)
C7	0.0172(7)	0.0294(8)	0.0229(8)	0.0040(6)	0.0021(6)	0.0033(6)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C8	0.0156(7)	0.0202(7)	0.0247(8)	0.0026(6)	0.0085(6)	0.0023(5)
C9	0.0166(8)	0.0447(10)	0.0282(9)	0.0003(7)	0.0084(7)	0.0067(7)
C10	0.0402(10)	0.0153(7)	0.0428(10)	-0.0022(7)	0.0279(8)	0.0011(7)
C11	0.0395(11)	0.0719(15)	0.0212(9)	0.0113(9)	-0.0054(8)	-0.0242(10)
C12	0.0451(12)	0.0393(11)	0.0417(12)	0.0010(9)	-0.0114(9)	-0.0113(9)
C13	0.0336(19)	0.029(2)	0.051(2)	0.0086(17)	0.0088(13)	-0.0103(14)
C13A	0.0336(19)	0.029(2)	0.051(2)	0.0086(17)	0.0088(13)	-0.0103(14)
C14	0.0390(11)	0.0512(12)	0.0331(10)	0.0150(9)	0.0068(8)	-0.0212(9)

Table 5.16. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for complex 46.

	x/a	y/b	z/c	U(eq)
H1A	0.3653	0.6375	0.4652	0.019
H2A	0.3464	0.8883	0.4422	0.024
H2B	0.5341	0.8379	0.4749	0.024

	x/a	y/b	z/c	U(eq)
H3A	0.5166	0.9801	0.3118	0.028
H3B	0.3348	0.9126	0.2241	0.028
H4A	0.6482	0.7905	0.2316	0.025
H4B	0.5076	0.8225	0.0998	0.025
H5A	0.5308	0.5693	0.1102	0.018
H6A	0.2645	0.6433	-0.0149	0.026
H6B	0.2492	0.4975	0.0443	0.026
H7A	0.0328	0.6249	0.0836	0.029
H7B	0.1442	0.7732	0.1332	0.029
H8A	0.1339	0.5477	0.2879	0.024
H8B	0.1065	0.7146	0.3286	0.024
H9A	0.7778	0.5585	0.2630	0.045
H9B	0.7806	0.4285	0.3479	0.045
H9C	0.8923	0.5743	0.4178	0.045

	x/a	y/b	z/c	U(eq)
H10A	0.5268	0.2378	0.2435	0.045
H10B	0.5274	0.3538	0.1445	0.045
H10C	0.3594	0.2594	0.1275	0.045
H11A	1.0049	0.7036	0.8399	0.056
H11B	0.8875	0.8325	0.8672	0.056
H12A	1.1102	0.9766	0.9099	0.057
H12B	1.2090	0.8538	0.8433	0.057
H13A	1.1685	0.9756	0.6816	0.046
H13B	1.0211	1.0604	0.7256	0.046
H13C	1.142(6)	1.008(3)	0.672(5)	0.046
H13D	1.167(3)	0.907(3)	0.744(2)	0.046
H14A	0.8507	0.9251	0.5501	0.049
H14B	0.9924	0.8136	0.5362	0.049

5.2. Nickel-catalyzed β,δ-Diarylation of Unactivated Alkene in Ketimines

5.2.1. General Information

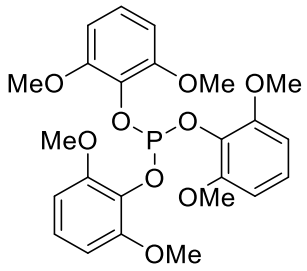
All the reactions were set up inside a nitrogen-filled glovebox and all the chemicals were handled under nitrogen atmosphere unless stated otherwise. All the glassware including the 4-dram and 1-dram borosilicate (Kimble-Chase) vials, and pressure vessels were properly dried in an oven before use. Bulk solvents were obtained from EMD and anhydrous solvents (DMF, DMA, DMSO, NMP, dioxane, toluene, MeCN) were obtained from Sigma-Aldrich, and were used directly without further purification. Deuterated solvents were purchased from Sigma-Aldrich. $NiBr_2$ was purchased from Alfa-Aesar. Aryl halides were purchased from Acros, Sigma-Aldrich, Oakwood, TCI-America, Matrix and Alfa-Aesar. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on a Bruker instrument (500 or 300, 75 or 126, 282 and 121.5 MHz respectively) and internally referenced to the residual solvent signals of $CDCl_3$ for ^{1}H and ^{13}C NMR, ^{19}F NMR and ^{31}P NMR at 7.26 ppm, 77.16 ppm, −164.9 ppm and 0 respectively. The chemical shifts of NMR and the coupling constants (*J*) for ^{1}H, ^{13}C, ^{19}F NMR and ^{31}P NMR are reported in δ parts per millions (ppm) and in Hertz, respectively. The following conventions are used for multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublet. High resolution mass of new compounds were recorded at the Mass Spectrometry, Department of Chemistry and Chemical Biology, University of New Mexico (UNM) and University of Texas at Austin. All NMR spectra were collected at Department of Chemistry and Chemical Biology, University of New Mexico (UNM). X-ray diffraction was performed on Bruker Kappa APEX II CCD diffractometer at the Department of Chemistry and Chemical Biology, UNM. Infrared (IR) spectra were recorded on Bruker Alpha-P ATR-IR at UNM and ν_{max} is reported in cm^{-1}.

Note for Acknowledgement: Sandia National Laboratories is a multi-mission laboratory managed and operated by National Technology and Engineering Solutions of Sandia, LLC., a wholly owned subsidiary of Honeywell International, Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525.

5.2.2. Experimental Section

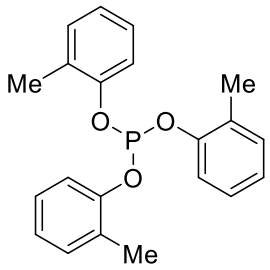
Ligand Preparation

Tris(2,6-dimethylphenyl) phosphite ,[155] tris(4-methoxyphenyl) phosphite ,[156] tris(4-(trifluoromethyl)phenyl) phosphite [157] and tri(1H-pyrrol-1-yl)phosphane [158] were prepared following the literature procedure.



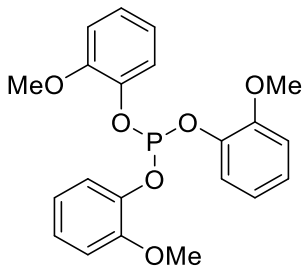
Tris(2,6-dimethoxyphenyl) phosphite : To a well stirred solution of 2,6 dimethoxyphenol (16.0 mmol) in THF (100 ml) under nitrogen at 0 °C, Et_3N (20.0 mmol) was added dropwise freshly distilled PCl_3 (5.0 mmol). The reaction mixture was stirred for 16h at room temperature. After the reaction was complete, the reaction mixture was filtered through fret funnel and the filtrate obtained was concentrated on rotavapor. The crude reaction mixture obtained was then purified by flash chromatography on a silica-gel column to obtain white solid (71% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.62 (s, 18H), 6.54 (d, *J*=9.0 Hz, 6H), 6.92 (t, *J*=7.5 Hz, 3H) ;**^{13}C NMR (75 MHz, $CDCl_3$):** δ 56.4, 105.8, 122.8, 132.6, 152.3; **^{31}P NMR (121.5 MHz, $CDCl_3$)** δ 146.6.



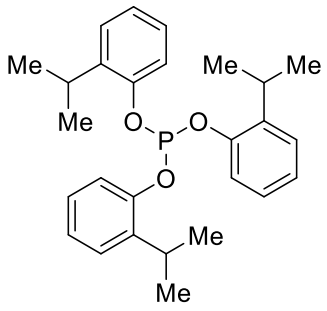
Tris(2-methoxyphenyl) phosphite : Prepared following the same procedure as for the synthesis of tris(2,6-dimethoxyphenyl) phosphite (colorless liquid, 81% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.27 (s, 9H), 7.08 (t, *J*=6.0 Hz, 3H), 7.18 (t, *J*=7.5 Hz, 3H), (d, *J*=9.0 Hz, 6H) ;**^{13}C NMR (75 MHz, $CDCl_3$):** 16.7, 120.4, 124.2, 126.9, 130.0, 131.4, 150.4; **^{31}P NMR (121.5 MHz, $CDCl_3$)** δ 131.3



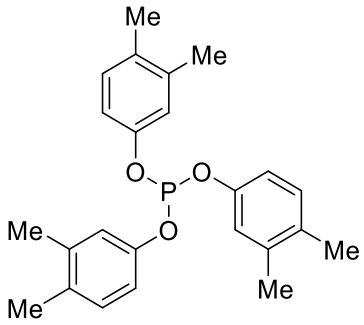
Tris(2-methoxyphenyl) phosphite : Prepared following the same procedure as for the synthesis of tris(2,6-dimethoxyphenyl) phosphite. (colorless liquid, 84% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.73 (s, 9H), 6.86- 6.93 (m, 6H), 7.07 (t, *J*=7.5 Hz, 3H), 7.25 (d, *J*=9.0 Hz, 3H) ;**^{13}C NMR (75 MHz, $CDCl_3$):** δ 56.0, 112.6, 120.9, 122.6, 122.7, 124.5, 141.7, 151.2; **^{31}P NMR (121.5 MHz, $CDCl_3$)** δ 134.9.



Tris(2-isopropylphenyl) phosphite : Prepared following the same procedure as for the synthesis of tris(2,6-dimethoxyphenyl) phosphite (colorless liquid, 76% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.17 (d, *J*=6.0 Hz, 18H), 3.26-3.35 (m, 3H), 7.11-7.16 (m, 6H), 7.21-7.24 (m, 3H), 7.29-7.32 (m, 3H) ;**^{13}C NMR (75 MHz, $CDCl_3$):** δ 23.1, 27.0, 120.3, 120.5, 124.4, 126.6, 126.9, 140.2, 149.3; **^{31}P NMR (121.5 MHz, $CDCl_3$)** δ 131.5.

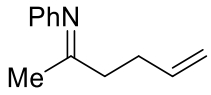


Tris(3,4-dimethylphenyl) phosphite : Prepared following procedure reported in literature.[159]

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.23 (s, 9H), 2.25 (s, 9H), 6.89-6.96 (m, 6H), 7.08 (d, *J*=9.0 Hz, 3H) ;**^{13}C NMR (75 MHz, $CDCl_3$):** δ 19.2, 20.0, 118.0, 118.1, 122.0, 122.1, 130.6, 132.3, 138.1, 149.7, 149.7; **^{31}P NMR (121.5 MHz, $CDCl_3$)** δ 129.2.

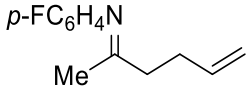
General Procedure for the Preparation of Ketimine

To a mixture of ketone (1.0 equiv) and aniline (2.0 equiv) in anhydrous toluene under nitrogen, molecular sieves 4 Å (1.0 gm/mmol) was added and heated at 80-120 °C for 24-36h. After the reaction was complete, the reaction mixture was filtered through a filter paper. Solvent was removed from the filtrate using rotavapor. The residue obtained was then purified by distillation or flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes).



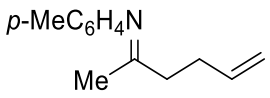
Hex-5-en-2-one was prepared following literature procedure.[160] N-Phenylhex-5-en-2-imine was then prepared following the general procedure using hex-5-en-2-one and aniline at 80 °C for 24h. The crude was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid (72% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78 (s, 0.80×3H), 2.17 (s, 0.20×3H), 2.23-2.24 (m, 0.20×4H), 2.43-2.55 (m, 0.80×4H), 4.94-5.14 (m, 2H), 5.61-5.70 (m, 0.20×1H), 5.85-5.99 (m, 0.80×1H), 6.69 (d, *J*=9.0 Hz, 2H), 7.03 (t, *J*=9.0 Hz, 1H), 7.28 (t, *J*=7.5 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 19.8, 26.1, 30.4, 31.0, 33.4, 40.7, 115.2, 115.6, 119.5, 123.1, 128.9, 136.9, 137.7, 151.0, 151.6, 171.1, 171.7 ; **IR (neat):** 3004, 2926, 1715, 1323, 1110, 1016.



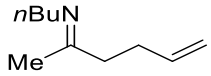
N-(4-Fluorophenyl) hex-5-en-2-imine was prepared following the general procedure using hex-5-en-2-one and 4-fluoroaniline at 80 °C for 24h. The crude was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid (75% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.77 (s, 0.80×3H), 2.15 (s, 0.20×3H), 2.21-2.22 (m, 0.20×4H), 2.41-2.52 (m, 0.80×4H), 4.94-5.12 (m, 2H), 5.58-5.70 (m, 0.20×1H), 5.83-5.96 (m, 0.80×1H), 6.60-6.65 (m, 2H), 6.94-6.99 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 19.8, 26.1, 30.4, 30.9, 33.3, 40.7, 115.2, 115.5, 115.8, 120.7, 120.8, 120.9, 136.7, 137.6, 147.6, 159.3 (d, *J*=239.3 Hz), 172.1, 172.7; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -121.6 ; **IR (neat):** 2968, 1658, 1593, 1484, 1363.



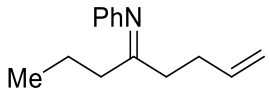
N-(*p*-Tolyl)hex-5-en-2-imine was prepared following the general procedure using hex-5-en-2-one and *p*-toluidine at 80 °C for 24h. The crude was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid (64% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78 (s, 0.80×3H), 2.15 (s, 0.20×3H), 2.23-2.31 (m, 0.20×4H), 2.31 (s, 3H), 2.43-2.52 (m, 0.80×4H), 4.94-5.13 (m, 2H), 5.57-5.72 (m, 0.20×1H), 5.85-5.98 (m, 0.80×1H), 6.59 (d, *J*=9.0 Hz, 2H), 7.09 (d, *J*=9.0 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 19.7, 20.9, 26.1, 30.5, 31.0, 33.2, 40.8, 115.1, 115.2, 119.4, 119.5, 129.5, 132.3, 136.9, 137.8, 148.4, 149.0, 171.1, 171.7 ; **IR (neat):** 3026, 1654, 1593, 1495, 1483.



N-Butylhex-5-en-2-imine was prepared following the general procedure using hex-5-en-2-one and *n*-butylamine at 80 °C for 24h. The crude was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid (61% yield).

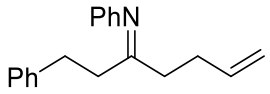
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, *J*=6.0 Hz, 3H), 1.27-1.39 (m, 2H), 1.51-1.62 (m, 2H), 1.78 (s, 0.80×3H), 1.97 (s, 0.20×3H), 2.20-2.34 (m, 4H), 3.20 (t, *J*=7.5 Hz, 2H), 4.90-5.06 (m, 2H), 5.74-5.87 (m, 1H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 14.1, 17.2, 20.8, 27.1, 30.5, 31.0, 31.5, 33.1, 33.4, 42.0, 50.1, 51.2, 114.8, 115.4, 137.3, 138.1, 168.8, 169.3 ; **IR (neat):** 2956, 2928, 1661, 1640, 1434, 1364.



Oct-7-en-4-one was prepared following a procedure described in the literature.[161] N-Phenyloct-7-en-4-imine was then prepared using the general procedure using oct-7-en-4-one and aniline at 120 °C for 24h. The crude was purified by distillation under vacuum at 90 °C (0.3 torr) in which impurities were distilled out. The remaining light reddish liquid was the desired imine. (74% yield).

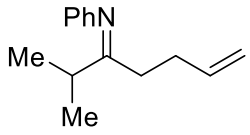
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (t, *J*=9.0 Hz, 0.6×3H), 1.01 (t, *J*= 9.0 Hz, 0.4×3H), 1.44-1.52 (m, 0.6×2H), 2.10 (t, *J*= 9.0 Hz, 0.6×2H), 2.17-2.22 (m, 0.4×4H), 2.39 (t, *J*= 9.0 Hz, 0.40×2H), 2.43-2.51 (m, 0.60×4H), 4.91-5.13 (m, 2H), 5.57-5.71 (m, 0.40×1H), 5.85-5.99 (m, 0.60×1H), 6.63-6.68 (m, 2H), 7.00 (t, *J*=7.5 Hz, 1H), 7.26 (t, *J*=7.5 Hz, 2H) ; **^{13}C**

NMR (75 MHz, $CDCl_3$): δ 14.0, 14.3, 19.8, 20.4, 30.5, 31.1, 32.4, 35.4, 37.5, 40.7, 115.0, 115.5, 119.5, 122.8, 122.9, 128.9, 137.1, 138.1, 151.5, 174.3 ; **IR (neat):** 2960, 1654, 1593, 1447, 1166.



1-Phenylhept-6-en-3-one was prepared following a literature procedure.[162] N,1-Diphenylhept-6-en-3-imine was then prepared following the general procedure using 1-phenylhept-6-en-3-one and aniline at 120 °C for 36h. The crude was purified by distillation under vacuum at 120 °C (0.3 torr) in which impurities were distilled out. The remaining light reddish liquid was the desired imine (68% yield).

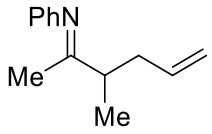
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.19-2.28 (m, 2H), 2.45-2.56 (m, 2H), 2.57-2.61 (m, 0.50×2H), 2.74-2.80 (m, 2H), 3.04-3.09 (m, 0.50×2H), 4.94-5.19 (m, 2H), 5.59-5.72 (m, 0.50×1H), 5.90-6.04 (m, 0.50×1H), 6.61 (d, *J*=9.0 Hz, 0.50×2H), 6.70 (d, *J*=9.0 Hz, 0.50×2H), 7.01-7.08 (m, 2H), 7.20-7.37 (m, 6H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.4, 30.9, 32.4, 32.9, 33.1, 35.3, 37.9, 40.0, 115.2, 115.6, 119.3, 119.3, 122.9, 126.0, 126.3, 128.2, 128.4, 128.5, 128.6, 128.6, 128.9, 128.9, 136.9, 137.9, 140.6, 141.9, 151.2, 173.1 ; **IR (neat):** 3026, 1654, 1593, 1483, 1452, 1070.



2-Methylhept-6-en-3-one was prepared following a literature procedure.[163] 2-Methyl-N-phenylhept-6-en-3-imine was then prepared following general procedure using 2-

methylhept-6-en-3-one and aniline at 80 °C for 24h. The crude was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid (74% yield).

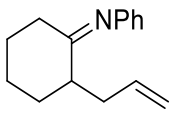
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 (d, *J*=9.0 Hz, 0.40×6H), 1.21 (d, *J*=9.0 Hz, 0.60×6H), 2.10-2.18 (m, 0.60×2H), 2.22-2.29 (m, 0.40×2H), 2.62-2.81 (m, 1H), 4.88-5.13 (m, 2H), 5.55-5.69 (m, 0.60×1H), 5.87-5.98 (m, 0.40×1H), 6.63-6.67 (m, 2H), 6.99 (t, *J*=7.5 Hz, 1H), 7.26 (t, *J*=6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 20.1, 20.5, 30.5, 31.2, 31.3, 31.6, 32.0, 36.1, 114.8, 115.3, 119.1, 119.2, 122.6, 122.7, 128.8, 128.9, 137.2, 138.5, 151.5, 177.6, 178.5 ; **IR (neat):** 2965, 1653, 1576, 1465, 1203.



3-Methylhex-5-en-2-one was prepared following a literature procedure.[164] 3-Methyl-N-phenylhex-5-en-2-imine was then prepared following the general procedure using 3-methylhex-5-en-2-one and aniline at 80 °C for 24h. The crude was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid (63% yield).

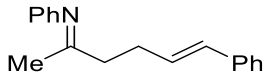
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.05 (d, *J*=6.0 Hz, 0.15×3H), 1.21 (d, *J*=6.0 Hz, 0.85×3H), 1.74 (s, 0.85×3H), 2.08 (s, 0.15×3H), 2.19-2.29 (m, 1H), 2.42-2.52 (m, 1H), 2.55-2.64 (m, 1H), 4.99-5.14 (m, 2H), 5.51-5.65 (m, 0.15×1H), 5.80-5.94 (m, 0.85×1H), 6.68 (d, *J*=9.0 Hz, 2H), 7.03 (t, *J*=7.5 Hz, 1H), 7.29 (t, *J*=7.5 Hz, 2H) ; **^{13}C NMR (75**

MHz, $CDCl_3$): δ 17.6, 17.8, 18.3, 21.1, 37.3, 38.8, 38.8, 44.3, 116.3, 116.7, 119.4, 122.8, 123.0, 128.9, 135.8, 136.6, 151.7, 175.0, 175.2 ; **IR (neat):** 2968, 1658, 1593, 1484, 1363.



2-Allylcyclohexan-1-one was prepared following a literature procedure.[165] 2-Allyl-N-phenylcyclohexan-1-imine was then prepared following the general procedure using 2-allylcyclohexan-1-one and aniline at 120 °C for 24h. The crude was purified by distillation under vacuum at 100 °C (.3 torr) in which impurities were distilled out. The remaining yellow liquid was the desired imine (71% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.47- 2.76 (m, 11H), 4.97-5.12 (m, 2H), 5.43-5.57 (m, 0.15×1H), 5.85-5.99 (m, 0.85×1H), 6.59-6.75 (m, 2H), 7.03 (t, *J*=7.5 Hz, 0.85× 1H), 7.17 (t, *J*=7.5 Hz, 0.85×1H), 7.29 (t, *J*=7.5 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 20.2, 24.5, 28.4, 30.9, 31.0, 33.5, 35.6, 35.8, 38.9, 40.4, 46.9, 115.9, 116.7, 119.7, 119.7, 122.9, 122.9, 128.9, 135.8, 137.5, 151.4, 176.1, 177.5 ; **IR (neat):** 2968, 1658, 1593, 1484, 1363.



(E)-6-Phenylhex-5-en-2-one was prepared following a literature procedure.[166] (5E)-N,6-Diphenylhex-5-en-2-imine was then prepared following the general procedure using (E)-6-phenylhex-5-en-2-one and aniline at 80 °C for 24h. The crude was purified by distillation under vacuum at 100 °C (.3 torr) in which impurities were distilled out. The remaining yellow liquid was the desired imine (66% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.82 (s, 0.80×3H), 2.22 (s, 0.20×3H), 2.33-2.43 (m, 0.20×4H), 2.59-2.65 (m, 0.80×4H), 6.00-6.06 (m, 0.20×1H), 6.29-6.38 (m, 0.80×1H), 6.50 (d, *J*=18.0 Hz, 1H), 6.71 (d, *J*=9.0 Hz, 2H), 7.05 (t, *J*=7.5 Hz, 1H), 7.20- 7.40 (m, 7H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 20.0, 26.2, 29.7, 30.3, 33.8, 41.1, 119.6, 123.1, 126.1, 127.1, 127.3, 128.6, 129.0, 129.7, 130.7, 130.9, 137.7, 151.6, 171.0.

General Procedure for the preparation of organozinc reagents (Knochel's Method)[167]

Under nitrogen, anhydrous LiCl (1.0 equiv) and zinc powder (1.5 equiv) were transferred to a Schlenk flask and dried under high vacuum at 150°C to 170°C for 2 h. The mixture was cooled to room temperature and then taken to a glovebox. Anhydrous THF (1ml/mmol) was added and stirred at room temperature. The reaction mixture was stirred for 5 min after the zinc was activated by adding 5 mol% of 1,2 dibromoethane and 3 mol% of TMSCl to the zinc/THF suspension. To this stirred solution was added corresponding aryl iodides (neat) dropwise and the reaction mixture was refluxed for 24h. The final concentration of the arylzinc reagent was determined by titration with molecular iodine in THF.[168]

General procedure for screening reaction conditions

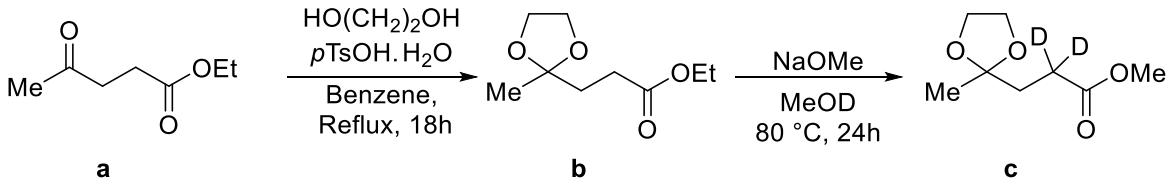
In a glovebox, 4-(trifluoromethyl) phenyl)zinc iodide solution in THF (0.12 mmol) was taken in a 1-dram vial and the solvent was removed under vacuum. To the residue, $NiBr_2$ (1.1 mg, 0.005 mmol, 5 mol%), triphenyl phosphite (1.6 mg, 0.005 mmol, 5 mol%), 4-iodotoluene (32.7 mg, 0.15 mmol) and N-phenylhex-5-en-2-imine (17.6 mg, 0.10 mmol) were added. The mixture was then dissolved in 0.5 ml of MeCN. The vial was capped

tightly and placed in a hotplate preheated to 60 °C with vigorous stirring. After 2h, the reaction mixture was cooled to room temperature. 1 mL of 6N HCl was added and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (1 mL × 3), 50 µL of pyrene (0.010 mmol, 0.20 M stock solution) as an internal standard was added and the solvent was removed in a rotary evaporator. The residue was dissolved in $CDCl_3$ and NMR spectrum was acquired. The yield was determined by integrating a product peak at 3.25 ppm against the pyrene peak at 8.06 ppm.

General procedure for large scale reactions

In a glovebox, stock solution of arylzinc in THF (0.60 mmol) was taken in a 15 mL sealed tube and the solvent was removed under vacuum. To the residue of arylzinc, $NiBr_2$ (5.5 mg, 0.025 mmol, 5.0 mol%), triphenyl phosphite (7.8 mg, 0.025 mmol, 5.0 mol %), aryl iodides (0.75 mmol) and ketimine (0.5 mmol) were added. The mixture was then dissolved in MeCN (2.5 mL). The sealed tube was capped tightly, and placed in an oil-bath preheated to 60 °C with vigorous stirring. After 2-14h, the reaction mixture was cooled to room temperature, 5 mL of 6N HCl was added and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (3 mL × 4) and the combined ethyl acetate fraction was dried over Na_2SO_4 and solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using diethyl ether/hexanes as eluent.

Preparation of deuterated imine

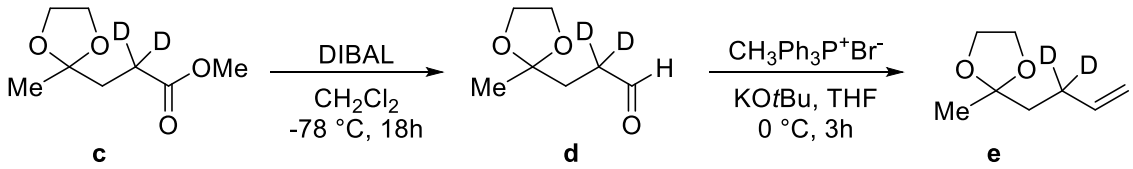


Ethyl 3-(2-methyl-1,3-dioxolan-2-yl) propanoate **b** was prepared following a literature procedure.[169]

Deuterium labelling performed according to a literature procedure.[170] Sodium methoxide (324 mg, 6.0 mmol) was added to a MeOD (16 ml) solution of **b** (752.8 mg, 4.0 mmol) under nitrogen and the mixture was refluxed at 80 °C for 24 h. After the reaction was complete, reaction mixture was cooled to room temperature and D_2O (8 ml) was added. The mixture was then extracted with dichloromethane. Organic layer was dried over Na_2SO_4 and concentrated in vacuum to get (methyl 3-(2-methyl-1,3-dioxolan-2-yl) propanoate-2,2-d_2 as a colorless liquid (61 % yield).

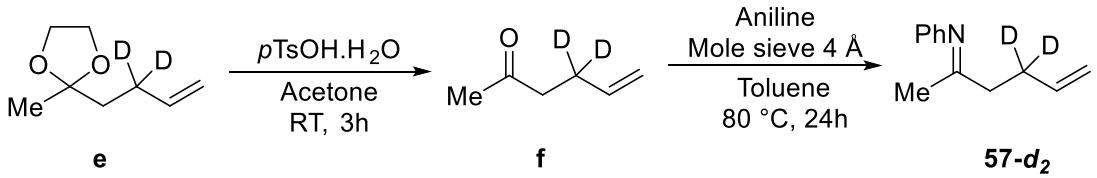
^{1}H NMR (300 MHz, $CDCl_3$): 1.31 (s, 3H), 2.01 (s, 2H), 3.66 (s, 3H), 3.92-3.94 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 28.7, 34.0, 51.7, 64.9, 109.3, 174.2.



3-(2-Methyl-1,3-dioxolan-2-yl) propanal-2,2-d_2 **d** was prepared from (methyl 3-(2-methyl-1,3-dioxolan-2-yl) propanoate-2,2-d_2 following literature procedure.[169] The crude product obtained was used without further purification in the next step. To a well stirred solution

of $CH_3Ph_3P^+Br^-$ (785.8 mg, 2.2 mmol) and KO*t*Bu (224 mg, 2.0 mmol) in THF (5 ml), **d** was added dropwise at 0 °C. After 3h the reaction mixture was filtered through a short pad of silica and the filtrate was concentrated carefully in rotavapor. The crude mixture was then partially purified by flash column chromatography using hexanes. The olefin **e** obtained as a colorless liquid was used in the next step without further purification.[170]



e **f** **57-*d*$_2$**

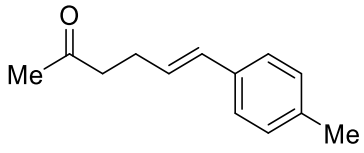
To a well- stirred solution of *p*TsOH.H_2O (14.2 mg, 5 mol%) in acetone (2 ml), 2-(but-3-en-1-yl-2,2-d_2)-2-methyl-1,3-dioxolane **e** was added at room temperature and the reaction mixture was left stirring for 4 h. The reaction mixture was then distilled to get hex-5-en-2-one-4,4-d_2 (**f**) [171] as a colorless liquid (65% yield).

^{1}H NMR (300 MHz, $CDCl_3$): 2.15 (s, 3H), 2.52 (s, 2H), 4.94-5.04 (m, 2H), 5.74-5.82 (m,1H).

N-phenylhex-5-en-2-imine-4,4-d_2 **57-*d*$_2$** was prepared following the general procedure for the preparation of imine using aniline and hex-5-en-2-one-4,4-d_2 at 80 °C for 24h. Then the reaction mixture was cooled to room temperature and filtered through a filter paper. Filtrate was concentrated in vacuum and the residue was purified by flash chromatography on a silica-gel column (deactivated by 10% TEA in hexanes) using hexanes as an eluent to get a yellow liquid with 86% deuterium incorporated in the imine.

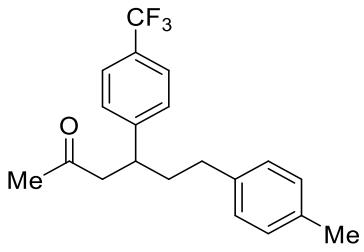
^{1}H NMR (300 MHz, $CDCl_3$): 1.78 (s, 0.80×3H), 2.17 (s, 0.20×3H), 2.23 (m, 0.20×2H), 2.50 (s, 0.80×2H), 4.94-5.14 (m, 2H), 5.61-5.69 (m, 0.20×1H), 5.90-5.96 (m, 0.80×1H), 6.69 (d, *J*=9.0 Hz, 2H), 7.03 (t, *J*=7.5 Hz, 1H), 7.28 (t, *J*=9.0 Hz, 2H).

5.2.2. Characterization data for new compounds



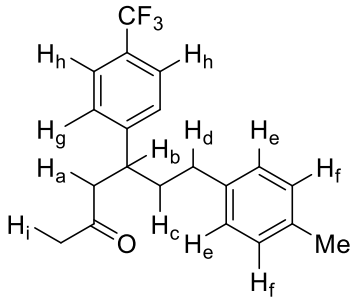
*6-(p-Tolyl)hex-5-en-2-one (**58**)***:** The title compound **58** was obtained as a colorless oil (69.6 mg, 74% yield) in 2h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 3H), 2.32 (s, 3H), 2.48 (t, *J*=6.0 Hz, 2H), 2.61 (t, *J*=7.5 Hz, 2H), 6.09-6.19 (m, 1H), 6.38 (d, , *J*=15.0 Hz, 1H), 7.10 (d, *J*=9.0 Hz, 2H), 7.23 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 21.3, 27.3, 30.2, 43.4, 126.0, 127.9, 129.3, 130.7, 134.8, 137.0, 208.2 ; **IR (neat):** 2920, 1713, 1512, 1360, 1159 ; **HRMS (ESI):** Calcd for $C_{13}H_{17}O$ $(M+H)^+$ 189.1279, found 189.1272.

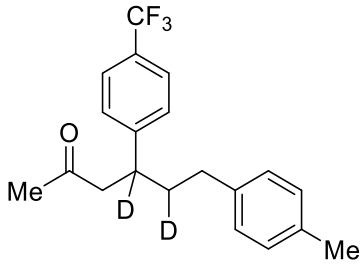


*6-(p-Tolyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**59**)*: The title compound **59** was obtained as a yellow oil (117 mg, 70% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.82-2.01 (m, 2H), 2.03 (s, 3H), 2.32 (s, 3H), 2.41 (t, *J*=7.5 Hz, 2H), 2.77 (d, *J*=6.0 Hz, 2H), 3.22-3.32 (m, 1H), 6.99 (d, *J*=9.0 Hz, 2H), 7.09 (d, *J*=9.0 Hz, 2H), 7.34 (d, *J*=9.0 Hz, 2H), 7.59 (d, *J*=9.0 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 21.1, 30.7, 33.2, 38.0, 40.6, 50.6, 124.4 (q, J_{CF}= 272.2 Hz), 125.6 (q, J_{CF}= 3.8 Hz), 128.1, 128.3, 128.9 (q, J_{CF}= 32.8 Hz), 129.2, 135.5, 138.5, 148.5, 207.0; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6; **IR (neat):** 3004, 2926, 1715, 1323, 1110, 1016; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO$ $(M+Na)^+$ 357.1442, found 357.1432.

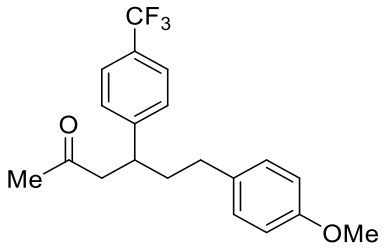


	H_b NOE Correlations	H_g NOE Correlations
	H_a 3.5 %	H_h 3.8 %
	H_c 2.6 %	H_b 1.5 %
	H_d 1.9 %	H_a 0.9 %
	H_g 3.2 %	H_c 1.2 %



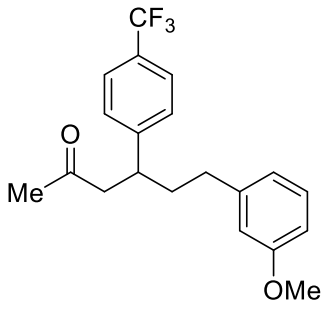
6-(p-Tolyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one-4,5-d_2 ***(59-d_2)*****:** The title compound ***59-d_2*** was obtained as a yellow oil (45.6 mg, 68% yield) in 2h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93-1.95 (m, 1H), 2.03 (s, 3H), 2.30 (s, 3H), 2.39 (d, *J*=9.0 Hz 2H), 2.75 (s, 2H), 6.97 (d, *J*=6.0 Hz, 2H), 7.07 (d, *J*=6.0 Hz, 2H), 7.32 (d, *J*=6.0 Hz, 2H), 7.57 (d, *J*=6.0 Hz, 2H).



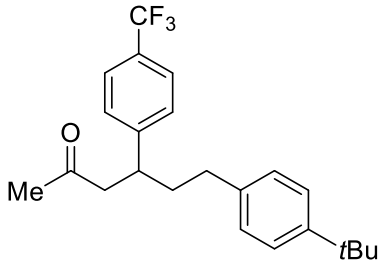
6-(4-Methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one ***(82)*****:** The title compound **82** was obtained as a yellow oil (120.9 mg, 69% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 10:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.83-1.91 (m, 1H), 1.94-2.01 (m, 1H), 2.03 (s, 3H), 2.39 (t, *J*=7.5 Hz, 2H), 2.76 (d, *J*=5.0 Hz, 2H), 3.22-3.28 (m, 1H), 3.78 (s, 3H), 6.81 (d, *J*=10.0 Hz, 2H), 7.0 (d, *J*=10.0 Hz, 2H), 7.33 (d, *J*=5.0 Hz, 2H), 7.58 (d, *J*=5.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 32.7, 38.1, 40.5, 50.6, 55.3, 113.9, 124.4 (q, J_{CF}= 272.2 Hz), 125.6 (q, J_{CF}= 3.8 Hz), 128.1, 128.9 (q, J_{CF}= 31.5 Hz), 129.3, 133.6, 148.5, 158.0, 207.0 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.4 ; **IR (neat):** 2934, 1715, 1616, 1322, 1244, 1111 ; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO_2$ $(M+Na)^+$ 373.1391, found 373.1380.



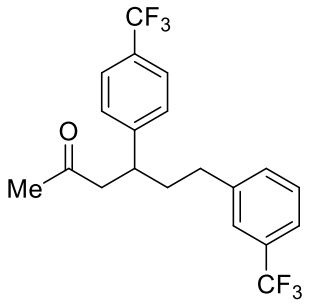
*6-(3-Methoxyphenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**83**)*: The title compound **83** was obtained as a yellow oil (136.6 mg, 78% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85-2.01 (m, 2H), 2.03 (s, 3H), 2.42 (t, *J*=7.5 Hz, 2H), 2.77 (d, *J*=9.0 Hz, 2H), 3.24-3.31 (m, 1H), 3.78 (s, 3H), 6.63-6.74 (m, 3H), 7.18 (d, *J*=7.5 Hz, 1H), 7.33 (d, *J*=9.0 Hz, 2H), 7.58 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.7, 33.7, 37.7, 40.5, 50.6, 55.2, 111.3, 114.3, 120.8, 124.4 (q, J_{CF}= 270.0 Hz), 125.7 (q, J_{CF}= 3.8 Hz), 128.1, 128.9 (q, J_{CF}= 32.3 Hz), 129.5, 143.2, 148.4, 159.8, 206.9 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.5 ; **IR (neat):** 3004, 2926, 1715, 1323, 1110, 1016; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO_2$ $(M+Na)^+$ 373.1391, found 373.1380.



*6-(4-(tert-Butyl)phenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**84**)***:** The title compound **84** was obtained as a yellow oil (86.6 mg, 46% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 20:1).

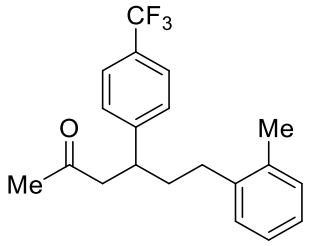
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (s, 9H), 1.87-2.07 (m, 2H), 2.02 (s, 3H), 2.38-2.44 (m, 2H), 2.76 (d, *J*=6.0 Hz, 2H), 3.22-3.32 (m, 1H), 7.02 (d, *J*=9.0 Hz, 2H), 7.28 (d, *J*=9.0 Hz, 2H), 7.33 (d, *J*=9.0 Hz, 2H), 7.57 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 31.5, 33.1, 34.5, 37.9, 40.7, 50.7, 124.3 (q, J_{CF}= 252.0 Hz), 125.4, 125.6 (q, J_{CF}= 3.8 Hz), 128.0, 128.1, 128.9 (q, J_{CF}= 31.5 Hz),138.5, 148.5, 148.9, 207.0 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.2; **IR (neat):** 2962, 1716, 1618, 1323, 1161, 1117 ; **HRMS (ESI):** Calcd for $C_{23}H_{27}F_3NaO$ $(M+Na)^+$ 399.1912, found 399.1904.



*6-(3-(Trifluoromethyl)phenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**85**)***:** The title compound **85** was obtained as a yellow oil (102.9 mg, 53% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 20:1).

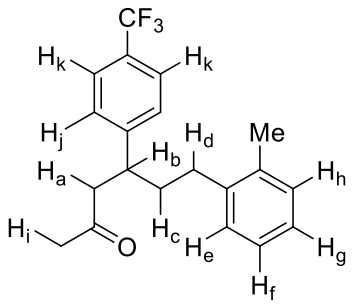
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.83-2.03 (m, 2H), 2.04 (s, 3H), 2.46-2.53 (m, 2H), 2.78 (d, *J*=6.0 Hz, 2H), 3.21-3.30 (m, 1H), 7.26 (d, *J*=6.0 Hz, 1H), 7.32 (d, *J*=6.0 Hz, 3H), 7.37 (d, *J*=6.0 Hz, 1H), 7.43 (d, *J*=6.0 Hz, 1H), 7.58 (d, *J*=6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.6, 33.5, 37.4, 40.5, 50.6, 123.0 (q, J_{CF}= 3.8 Hz), 124.3 (q, J_{CF}= 270.0 Hz), 125.1 (q, J_{CF}= 3.8 Hz), 125.8 (q, J_{CF}= 3.8 Hz), 128.1, 128.9, 129.1 (q, J_{CF}= 30.8 Hz), 130.8 (q, J_{CF}= 31.5 Hz), 131.9, 142.5, 148.1, 206.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.7, -

62.8 ; **IR (neat):** 2928, 1716, 1618, 1322, 1110 ; **HRMS (ESI):** Calcd for $C_{20}H_{18}F_6NaO$ $(M+Na)^+$ 411.1160, found 411.1147.



*6-(o-Tolyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**86**)***:** The title compound **86** was obtained as a colorless oil (75.2 mg, 45% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 10:1).

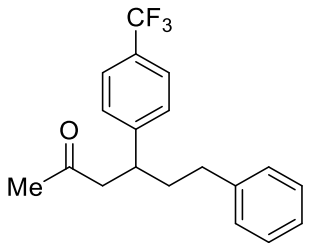
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79-2.01 (m, 2H), 2.05 (s, 3H), 2.16 (s, 3H), 2.31-2.53 (m, 2H), 2.79 (d, *J*=9.0 Hz, 2H), 3.27-3.37 (m, 1H), 7.02-7.04 (m, 1H), 7.08-7.14 (m, 3H), 7.36 (d, *J*=6.0 Hz, 2H), 7.59 (d, *J*=6.0 Hz, 2H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 19.2, 30.8, 31.3, 36.8, 41.0, 50.6, 124.4 (q, J_{CF}= 272.2 Hz), 125.7 (q, J_{CF}= 3.8 Hz), 126.1, 126.2, 128.1, 128.8, 129.0 (q, J_{CF}= 31.5 Hz), 130.4, 135.8, 139.9, 148.5, 206.9 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.0 ; **IR (neat):** 3016, 1716, 1322, 1113, 1067, 1016 ; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO$ $(M+Na)^+$ 357.1442, found 357.1431.



H_b NOE Correlations	H_j NOE Correlations
H_a 3.0 %	H_k 2.9 %
H_d 1.7 %	H_b 1.6 %

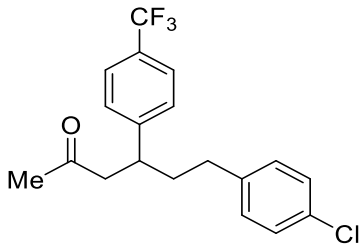
H_c 2.2 % H_a 0.9 %

H_j 2.9 % H_c 1.3 %



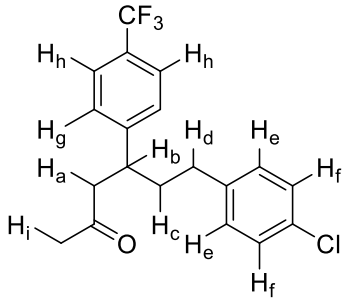
*6-Phenyl-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**87**)***:*** The title compound **87** was obtained as a colorless oil (96.1 mg, 60% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85-2.07 (m, 2H), 2.03 (s, 3H), 2.44 (t, *J*=9.0 Hz, 2H), 2.77 (d, *J*=6.0 Hz, 2H), 3.22-3.31 (m, 1H), 7.09 (d, *J*=9.0 Hz, 2H), 7.14-7.20 (m, 1H), 7.26 (t, *J*=7.5 Hz, 2H), 7.33 (d, *J*=6.0 Hz, 2H), 7.58 (d, *J*=6.0 Hz, 2H), ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 33.6, 37.9, 40.6, 50.6, 124.4 (q, J_{CF}= 272.2 Hz), 125.7 (q, J_{CF}= 3.8 Hz), 126.1, 128.1, 128.4, 128.5, 128.9 (q, J_{CF}= 32.8 Hz), 141.6, 148.5, 206.9 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6 ; **IR (neat):** 2927, 1715, 1322, 1160, 1109, 1067 ; **HRMS (ESI):** Calcd for $C_{19}H_{19}F_3NaO$ $(M+Na)^+$ 343.1286, found 343.1276.



*6-(4-Chlorophenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**88**)***:** The title compound **88** was obtained as a yellow oil (124.2 mg, 70% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.81-2.02 (m, 2H), 2.04 (s, 3H), 2.40 (t, *J*=7.5 Hz, 2H), 2.76 (d, *J*=6.0 Hz, 2H), 3.19-3.28 (m, 1H), 7.00 (d, *J*=6.0 Hz, 2H), 7.22 (d, *J*=9.0 Hz, 2H), 7.31 (d, *J*=9.0 Hz, 2H), 7.58 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 33.0, 37.6, 40.4, 50.6, 124.3 (q, J_{CF}= 272.2 Hz), 125.7 (q, J_{CF}= 3.8 Hz), 128.1, 128.6,, 129.1(q, J_{CF}= 32.8 Hz), 129.8, 131.8, 140.0, 148.2, 206.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.5 ; **IR (neat):** 2928, 1715, 1322, 1160, 1110, 1068 ; **HRMS (ESI):** Calcd for $C_{19}H_{18}ClF_3NaO$ $(M+Na)^+$ 377.0896, found 377.0882.



H_e NOE correlations

H_f 4.9 %

H_d 0.93 %

H_c 0.64 %

H_g NOE correlations

H_h 3.6 %

H_b 1.7 %

H_a 1.0 %

H_a NOE correlations

H_b 0.9 %

H_d 0.4 %

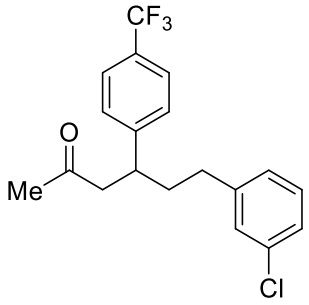
H_c 1.4 %

H_d 0.5 %

H_c 1.5 %

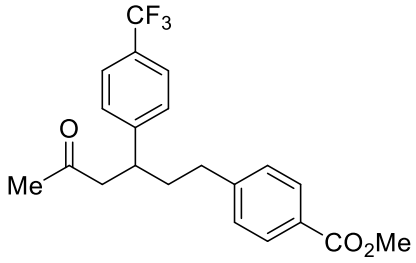
H_i 0.9 %

H_g 1.2 %



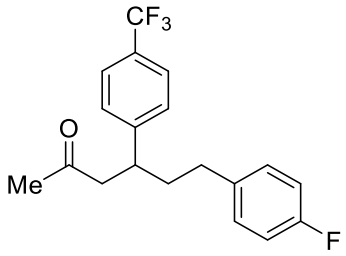
*6-(3-Chlorophenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**89**)***:** The title compound **89** was obtained as a yellow oil (106.2 mg, 60% yield) in 2h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.80-2.01 (m, 2H), 2.04 (s, 3H), 2.37-2.46 (m, 2H), 2.77 (d, *J*=6.0 Hz, 2H), 3.20-3.30 (m, 1H), 6.95 (d, *J*=6.0 Hz, 1H), 7.06 (s, 1H), 7.13 - 7.20 (m, 2H), 7.32 (d, *J*=9.0 Hz, 2H), 7.58 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.7, 33.4, 37.5, 40.5, 50.6, 124.3(q, J_{CF}= 270.0 Hz), 125.7 (q, J_{CF}= 4.5 Hz), 126.3, 126.6, 128.1, 128.5, 128.9, 129.1(q, J_{CF}= 32.3 Hz), 134.3, 143.7, 148.2, 206.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.9 ; **IR (neat):** 2928, 1771, 1322, 1160, 1110, 1068 ; **HRMS (ESI):** Calcd for $C_{19}H_{18}ClF_3NaO$ $(M+Na)^+$ 377.0896, found 377.0884.



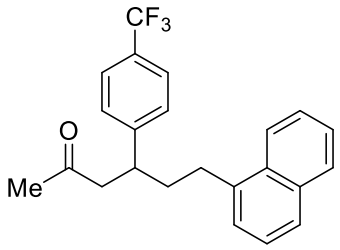
*Methyl 4-(5-oxo-3-(4-(trifluoromethyl)phenyl)hexyl)benzoate (**90**)***:** The title compound **90** was obtained as a yellow oil (113.5 mg, 60% yield) in 2h after purification by silica gel column chromatography (Hex : Et_2O = 5:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.85-2.08 (m, 2H), 2.03 (s, 3H), 2.48 (t, *J*=9.0 Hz, 2H), 2.77 (d, *J*=9.0 Hz, 2H), 3.20-3.28 (m, 1H), 3.89 (s, 3H), 7.14 (d, *J*=9.0 Hz, 2H), 7.32 (d, *J*=9.0 Hz, 2H), 7.58 (d, *J*=9.0 Hz, 2H), 7.93 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 33.7, 37.3, 40.5, 50.6, 52.1, 124.3 (q, J_{CF}= 272.2 Hz), 125.7 (q, J_{CF}= 3.8 Hz), 128.1, 128.5, 129.1 (q, J_{CF}= 32.8 Hz), 129.9, 147.1, 148.2, 167.2, 206.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.2 ; **IR (neat):** 2920, 1713, 1512, 1409, 1159 ; **HRMS (ESI):** Calcd for $C_{21}H_{22}F_3O_3$ $(M+H)^+$ 379.1521, found 379.1515.



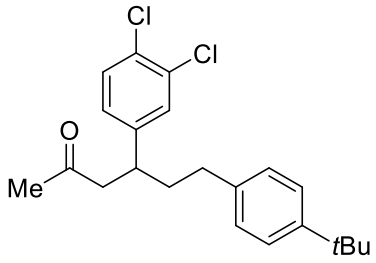
*6-(4-Fluorophenyl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**91**)***:** The title compound **91** was obtained as a yellow oil (93.0 mg, 55% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84-2.02 (m, 2H), 2.03 (s, 3H), 2.41 (t, *J*= 7.5 Hz, 2H), 2.77 (d, *J*=9.0 Hz, 2H), 3.19-3.28 (m, 1H), 6.90-6.96 (m, 2H), 6.99 - 7.05 (m, 2H), 7.32 (d, *J*=9.0 Hz, 2H), 7.58 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 32.8, 37.9, 40.4, 50.6, 115.2 (d, J_{CF}= 21.4 Hz), 124.3(q, J_{CF}= 272.2 Hz), 125.7 (q, J_{CF}= 3.8 Hz), 128.1, 129.3 (q, J_{CF}= 31.5 Hz),129.7 (d, J_{CF}= 7.6 Hz), 137.2 (d, J_{CF}= 2.5 Hz 148.3, 161.4 (d, J_{CF}= 243.2 Hz), 206.9 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -116.3, -61.2 ; **IR (neat):** 2928, 1715, 1652, 1508, 1322, 1110 ; **HRMS (ESI):** Calcd for $C_{19}H_{18}F_4NaO$ $(M+Na)^+$ 361.1191 found 361.1197.



*6-(Naphthalen-1-yl)-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**92**)***:*** The title compound **92** was obtained as a yellow oil (75.9 mg, 41% yield) in 2h after purification by silica gel column chromatography (Hex : Ether = 20:1).

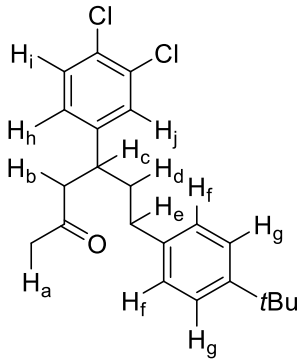
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.96-2.19 (m, 2H), 2.03 (s, 3H), 2.80 (d, *J*=9.0 Hz, 2H), 2.85-2.98 (m, 2H), 3.35-3.45 (m, 1H), 7.22 (d, *J*=6.0 Hz, 1H), 7.36 (d, *J*=9.0 Hz, 1H), 7.41 (d, *J*=6.0 Hz, 2H), 7.47 (dd, *J*=3.0 Hz, 6.0 Hz, 2H), 7.63 ((d, *J*=9.0 Hz, 2H), 7.71 (d, *J*=9.0 Hz, 1H), 7.78 (dd, *J*=3.0 Hz, 6.0 Hz, 1H), 7.85 (dd, *J*=3.0 Hz, 6.0 Hz, 1H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.7, 31.0, 37.4, 41.1, 50.6, 123.6, 124.4 (q, J_{CF}= 270.9 Hz), 125.6, 125.6, 125.7(q, J_{CF}= 3.8 Hz), 126.0, 126.0, 126.9, 128.2, 128.9 (q, J_{CF}= 28.9 Hz), 129.0, 131.7, 134.0, 137.9, 148.5, 206.9 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6 ; **IR (neat):** 3046, 2935, 1714, 1261, 1066, 1015; **HRMS (ESI):** Calcd for $C_{23}H_{21}F_3NaO$ $(M+Na)^+$ 393.1442, found 393.1436.



*6-(4-(tert-Butyl)phenyl)-4-(3,4-dichlorophenyl)hexan-2-one (**93**)***:** The title compound **93** was obtained as a colorless oil (98.1 mg, 52% yield) in 4h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 9H), 1.78-2.00 (m, 2H), 2.03 (s, 3H), 2.41 (t, *J*=9.0 Hz, 2H), 2.72 (d, *J*=6.0 Hz, 2H), 3.11-3.21 (m, 1H), 7.00-7.06 (m, 3H), 7.28 (d, *J*=6.0 Hz, 3H), 7.37 (d, *J*=9.0 Hz, 1H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.8, 31.5, 33.1, 34.5, 37.8, 40.1, 50.6, 125.4, 127.4, 128.1, 129.7, 130.6, 132.7, 138.4, 144.8, 148.9, 206.8 ; **IR (neat):** 2960, 1716, 1470, 1361, 1109, 1029 ; **HRMS (ESI):** Calcd for $C_{22}H_{26}Cl_2NaO$ $(M+Na)^+$ 399.1258, found 399.1258.

H_c NOE correlations



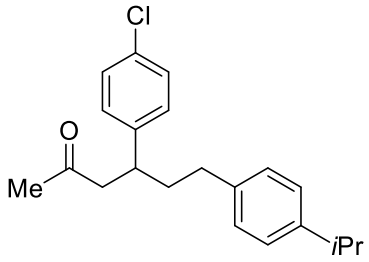
H_b 2.1 %

H_e 0.9 %

H_d 1.5 %

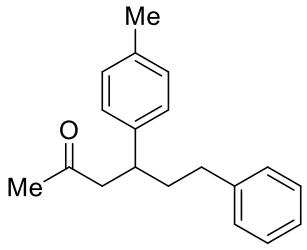
H_j 1.3 %

H_h 1.5 %



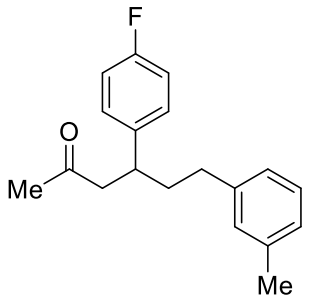
*4-(4-Chlorophenyl)-6-(4-isopropylphenyl)hexan-2-one (**94**)***:** The title compound **94** was obtained as a yellow oil (83.6 mg, 51% yield) in 4h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (d, *J*=6.0 Hz, 6H), 1.79-1.97 (m, 2H), 2.00 (s, 3H), 2.40 (t, *J*=7.5 Hz, 2H), 2.72 (d, *J*=9.0 Hz, 2H), 2.82-2.91 (m, 1H), 3.11-3.21 (m, 1H), 7.01(d, *J*=9.0 Hz, 2H), 7.13 (d, *J*=9.0 Hz, 4H), 7.29 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.2, 30.8, 33.2, 33.8, 38.1, 40.4, 50.9, 126.5, 128.3, 128.8, 129.1, 132.2, 139.1, 142.8, 146.6, 207.4 ; **IR (neat):** 2958, 1714, 1491, 1359, 1061, 1013 ; **HRMS (ESI):** Calcd for $C_{21}H_{25}ClNaO$ $(M+Na)^+$ 351.1492, found 351.1473.



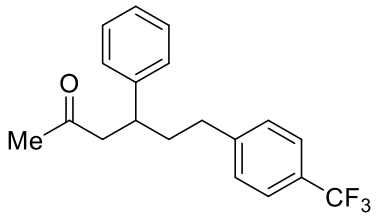
*6-Phenyl-4-(p-tolyl) hexan-2-one (**95**)***:** The title compound was obtained as a yellow oil (55.9 mg, 42% yield) in 2h after purification by silica gel column chromatography (Hex: Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.81-1.97 (m, 2H), 2.00 (s, 3H), 2.35 (s, 3H), 2.46 (t, *J*=9.0 Hz, 2H), 2.73 (d, *J*=9.0 Hz, 2H), 3.09-3.19 (m, 1H), 7.10-7.17 (m, 7H), 7.24-7.29 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 21.2, 30.7, 33.8, 38.2, 40.7, 51.2, 125.9, 127.6, 128.4, 128.5, 129.4, 136.1, 141.0, 142.2, 207.9 ; **IR (neat):** 2928, 1771, 1652, 1540, 1507 ; **HRMS (ESI):** Calcd for $C_{19}H_{23}O$ $(M+H)^+$ 267.1749, found 267.1726.



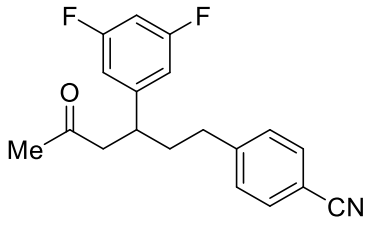
*4-(4-Fluorophenyl)-6-(m-tolyl)hexan-2-one (**96**)***:** The title compound **96** was obtained as a yellow oil (86.7 mg, 61% yield) in 4h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79-1.97 (m, 2H), 2.01 (s, 3H), 2.31 (s, 3H), 2.40 (t, *J*=9.0 Hz, 2H), 2.72 (d, *J*=6.0 Hz, 2H), 3.12-3.22 (m, 1H), 6.89 (d, *J*=9.0 Hz, 2H), 6.98-7.04 (m, 3H), 7.12-7.20 (m, 3H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 21.5, 30.8, 33.6, 38.3, 40.3, 51.1, 115.5 (d, J_{CF}= 20.3 Hz), 125.4, 126.7, 129.1, 129.2 (d, J_{CF}= 6.0 Hz), 138.0, 139.9, 141.9, 161.6 (d, J_{CF}= 243.0 Hz), 207.6 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -115.1 ; **IR (neat):** 2922, 1715, 1604, 1508, 1221, 1158 ; **HRMS (ESI):** Calcd for $C_{19}H_{21}FNaO$ $(M+Na)^+$ 307.1474, found 307.1461.



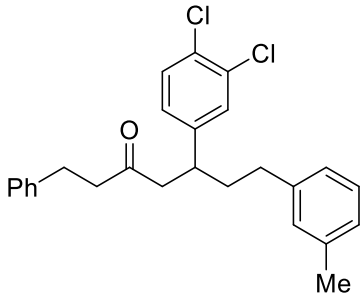
*4-Phenyl-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**97**)***:** The title compound **97** was obtained as a yellow oil (81.7 mg, 51% yield) in 4h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84-2.07 (m, 2H), 2.01 (s, 3H), 2.50 (t, *J*=7.5 Hz, 2H), 2.68-2.82 (m, , 2H), 3.12-3.21 (m, 1H), 7.18-7.26 (m, 5H), 7.30-7.36 (m, 2H), 7.50 (d, *J*=9.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 30.8, 33.6, 37.7, 40.9, 51.0, 124.5 (q, J_{CF}= 272.2 Hz), 125.3 (q, J_{CF}= 3.8 Hz), 126.8, 127.7, 128.3 (q, J_{CF}= 31.5 Hz), 128.8, 128.8, 143.8, 146.2, 207.6; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.3;**IR (neat):** 2928, 1714, 1617, 1322, 1108 ; **HRMS (ESI):** Calcd for $C_{19}H_{19}F_3NaO$ $(M+Na)^+$ 343.1286, found 343.1275.



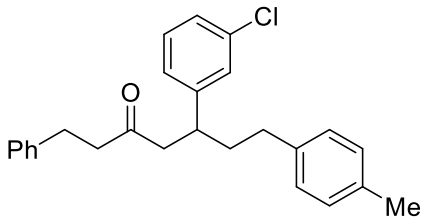
*4-(3-(3,5-Difluorophenyl)-5-oxohexyl)benzonitrile (**98**)***:** The title compound was obtained as a yellow oil (75.2 mg, 48% yield) in 4h after purification by silica gel column chromatography (Hex: DCM = 3:2).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74-1.87 (m, 1H), 1.93- 2.04 (m, 1H), 2.07 (s, 3H), 2.50 (t, *J*=9.0 Hz, 2H), 2.73 (d, *J*=6.0 Hz, 2H), 3.12-3.21 (m, 1H), 6.65-6.74 (m, 3H), 7.19 (d, *J*=6.0 Hz, 2H), 7.55 (d, *J*=6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.7, 33.8, 36.9, 40.3, 50.3, 102.4 (t, J_{CF}= 25.1 Hz), 110.1, 110.5 (dd, J_{CF}= 7.5, 16.5 Hz), 119.1, 129.2, 132.3, 147.1, 148.0 (t, J_{CF}= 8.3 Hz), 163.3 (dd, J_{CF}= 13.1, 247.5 Hz), 206.3 ; ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -107.9 ; **IR (neat):** 2929, 1714, 1594, 1416, 1115 ; **HRMS (ESI):** Calcd for $C_{19}H_{18}F_2NO$ $(M+H)^+$ 314.1356, found 314.1361.



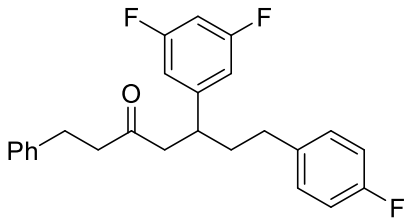
*5-(3,4-Dichlorophenyl)-1-phenyl-7-(m-tolyl)heptan-3-one (**99**)***:** The title compound was obtained as a yellow oil (137.8 mg, 65% yield) in 6h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.73-1.98 (m, 2H), 2.32 (s, 3H), 2.39 (t, *J*=7.5 Hz, 2H), 2.49-2.63 (m, 2H), 2.67 (d, *J*=6.0 Hz, 2H), 2.81 (t, *J*=7.5 Hz, 2H), 3.11-3.21 (m, 1H), 6.89 (s, 1H), 7.01 (t, *J*=9.0 Hz, 2H), 7.09 (d, *J*=6.0 Hz, 2H), 7.13-7.20 (m, 3H), 7.23-7.28 (m, 3H), 7.37 (d, *J*=9.0 Hz, 1H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 21.5, 29.7, 33.6, 37.8, 40.0, 45.0, 50.0, 125.4, 126.3, 126.8, 127.3, 128.4, 128.4, 128.6, 129.2, 129.7, 130.5, 130.6, 132.6, 138.0, 140.9, 141.4, 144.7, 208.0 ; **IR (neat):** 2924, 1712, 1468, 1363, 1092 ; **HRMS (ESI):** Calcd for $C_{26}H_{26}Cl_2ONa$ $(M+Na)^+$ 447.1258, found 447.1252.



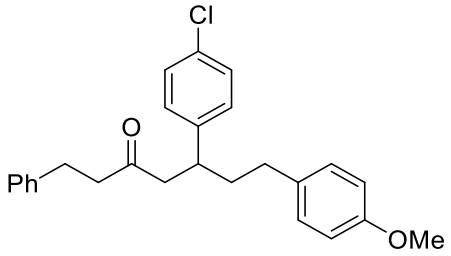
*5-(3-Chlorophenyl)-1-phenyl-7-(p-tolyl)heptan-3-one (**100**)***:** The title compound **100** was obtained as a yellow oil (158.0 mg, 81% yield) in 6h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79-2.01 (m, 2H), 2.35 (s, 3H), 2.43 (t, *J*=7.5 Hz, 2H), 2.50-2.67 (m, 2H), 2.71 (d, *J*=6.0 Hz, 2H), 2.81-2.86 (m, 2H), 3.16-3.25 (m, 1H), 7.01 (d, *J*=6.0 Hz, 2H), 7.09-7.14 (m, 5H), 7.21-7.31 (m, 6H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 21.1, 29.6, 33.2, 37.9, 40.5, 45.0, 50.1, 126.1, 126.2, 126.8, 127.7, 128.3, 128.4, 128.6, 129.1, 129.9, 134.5, 135.4, 138.6, 141.0, 146.5, 208.2 ; **IR (neat):** 2922, 1712, 1453, 1080, 1030 ; **HRMS (ESI):** Calcd for $C_{26}H_{28}ClO$ $(M+H)^+$ 391.1829, found 391.1830.



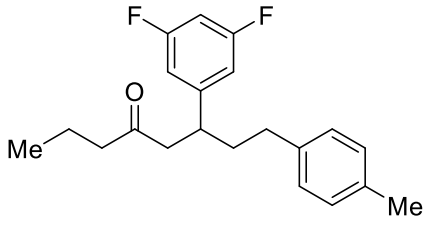
5-(3,5-Difluorophenyl)-7-(4-fluorophenyl)-1-phenylheptan-3-one ***(101)*****:** The title compound **101** as obtained as a yellow oil (120.8 mg, 61% yield) in 6h after purification by silica gel column chromatography (Hex: Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74-1.99 (m, 2H), 2.43 (t, *J*=7.5 Hz, 2H), 2.55-2.75 (m, 4H), 2.86 (t, *J*=7.5 Hz, 2H), 3.16-3.25 (m, 1H), 6.67-6.77 (m, 3H), 6.95-7.08 (m, 4H), 7.14 (d, *J*=9.0 Hz 2H), 7.18-7.32 (m, 3H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 29.7, 32.8, 37.7, 40.4, 45.0, 49.8, 102.2 (t, J_{CF}= 25.1 Hz), 110.5 (dd, J_{CF}= 7.5, 16.5 Hz), 115.3 (d, J_{CF}= 21.0 Hz), 126.3, 128.5 (d, J_{CF}= 18.8 Hz), 129.7 (d, J_{CF}= 8.3 Hz), 137.1 (d, J_{CF}= 3.0 Hz), 140.8, 148.4 (t, J_{CF}= 8.3 Hz), 159.8, 163.2 (dd, J_{CF}= 12.8, 247.5 Hz), 163.0, 207.8 ; ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -116.0, 108.2; **IR (neat):** 2928, 1714, 1594, 1508, 1115 ; **HRMS (ESI):** Calcd for $C_{25}H_{24}F_3O$ $(M+H)^+$ 397.1779, found 397.1785



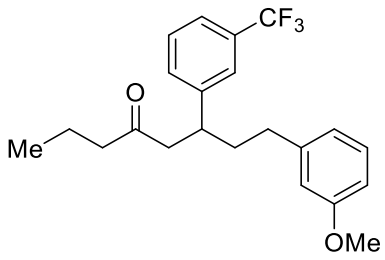
5-(4-Chlorophenyl)-7-(4-methoxyphenyl)-1-phenylheptan-3-one ***(102)*****:** The title compound **102** was obtained as a yellow oil (126.2 mg, 62% yield) in 6h after purification by silica gel column chromatography (Hex: Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.76-1.97 (m, 2H), 2.37 (t, *J*=9.0 Hz, 2H), 2.48-2.63 (m, 2H), 2.68 (d, *J*=9.0 Hz, 2H), 2.79 (t, *J*=9.0 Hz, 2H), 3.11-3.20 (m, 1H), 3.79 (s, 3H), 6.81 (d, *J*=6.0 Hz, 2H), 7.00 (d, *J*=9.0 Hz, 2H), 7.07-7.12 (m, 4H), 7.18-7.29 (m, 5H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 29.6, 32.7, 38.1, 40.2, 45.1, 50.3, 55.4, 113.9, 126.2, 128.4, 128.6, 128.8, 129.1, 129.3, 132.2, 133.8, 141.0, 142.7, 157.9, 208.5 ; **IR (neat):** 2930, 1734, 1511, 1242, 1034 ; **HRMS (ESI):** Calcd for $C_{26}H_{27}ClNaO_2$ $(M+Na)^+$ 429.1597, found 429.1590.



6-(3,5-Difluorophenyl)-8-(p-tolyl) octan-4-one ***(103)*****:** The title compound **103** was obtained as a yellow oil (125.6 mg, 76% yield) in 6h after purification by silica gel column chromatography (Hex: Et_2O = 10:1).

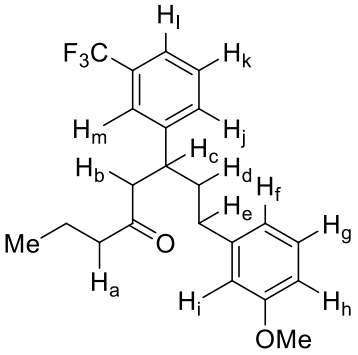
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.84 (t, *J*=7.5 Hz, 3H), 1.46-1.58 (m, 2H), 1.77-1.99 (m, 2H), 2.16- 2.27 (m, 2H), 2.31 (s, 3H), 2.42 (t, *J*=7.5 Hz, 2H), 2.68 (d, *J*=6.0 Hz, 2H), 3.16-3.25 (m, 1H), 6.62-6.78 (m, 3H), 6.99 (d, *J*=9.0 Hz, 2H), 7.08 (d, *J*=6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 13.7, 17.2, 21.1, 33.2, 37.9, 40.6, 45.5, 49.6, 102.0 (t, J_{CF}= 25.5 Hz), 110.6 (dd, J_{CF}= 7.5, 16.5 Hz), 128.3, 129.2, 135.6, 138.5, 148.7 (t, J_{CF}= 7.9 Hz), 163.2 (dd, J_{CF}= 13.1, 246.0 Hz), 209.0 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -108.4 **IR (neat):** 2931, 1712, 1622, 1594, 1115 ; **HRMS (ESI):** Calcd for $C_{21}H_{25}F_2O$ $(M+H)^+$ 331.1873, found 331.1869.



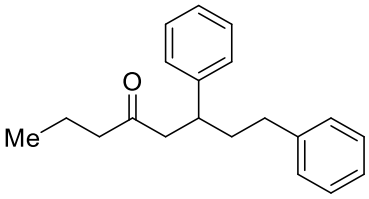
*8-(3-Methoxyphenyl)-6-(3-(trifluoromethyl)phenyl)octan-4-one (**104**)***:** The title compound **104** was obtained as a yellow oil (140.0 mg, 74% yield) in 6h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81(t, *J*=7.5 Hz, 3H), 1.44-1.53 (m, 2H), 1.85-2.07 (m, 2H), 2.14-2.34 (m, 2H), 2.42 (t, *J*=7.5 Hz, 2H), 2.71 (d, *J*=6.0 Hz, 2H), 3.24-3.33 (m, 1H), 3.78 (s, 3H), 6.62-6.74 (m, 3H), 7.18 (t, *J*=7.5 Hz, 1H), 7.40-7.50 (m, 4H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 13.7, 17.2, 33.7, 37.7, 40.6, 45.5, 49.8, 55.2, 111.4, 114.2, 120.8, 123.5(q, J_{CF}= 3.8 Hz), 124.3 (q, J_{CF}= 3.8 Hz), 124.4 (q, J_{CF}= 269.3 Hz), 129.1, 129.5, 130.8 (q, J_{CF}= 31.5 Hz), 131.4, 143.3, 145.4, 159.8, 209.2, ; **^{19}F NMR (282 MHz, $CDCl_3$)**

δ -61.0 ; **IR (neat):** 2935, 1712, 1325, 1120, 1043 ; **HRMS (ESI):** Calcd for $C_{22}H_{26}F_3O_2$ $(M+H)^+$ 379.1885, found 379.1887

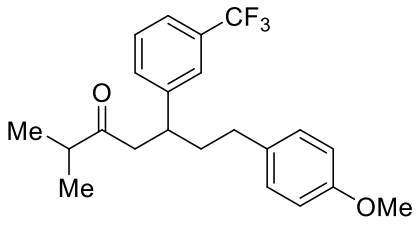


H_b NOE correlations	H_e NOE correlations
H_c 1.4 %	H_c 1.3 %
H_e 0.5 %	H_b 0.6 %
H_a 1.4 %	H_d 1.8 %
H_d 2.0 %	H_i 1.0 %
H_f 1.0 %	



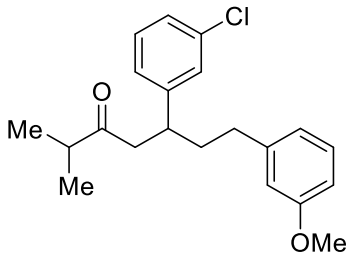
*6, 8-Diphenyloctan-4-one (**105**)***:** The title compound **105** was obtained as a yellow oil (72.8 mg, 52% yield) in 6h after purification by silica gel column chromatography (Hex: DCM = 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (t, *J*=7.5 Hz, 3H), 1.49 (q, *J*=6.0 Hz, 2H), 1.89-2.00 (m, 2H), 2.18-2.27 (m, 2H), 2.46 (t, *J*=9.0 Hz, 2H), 2.64-2.78 (m, 2H), 3.16-3.25 (m, 1H), 7.10 (d, *J*=6.0 Hz, 2H), 7.17-7.35 (m, 8H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 13.8, 17.1, 33.8, 38.1, 41.1, 45.6, 50.3, 125.9, 126.6, 127.8, 128.4, 128.5, 128.7, 142.2, 144.3, 210.0 ; **IR (neat):** 2930, 1710, 1453, 1369, 1123; **HRMS (ESI):** Calcd for $C_{20}H_{25}O$ $(M+H)^+$ 281.1905, found 281.1907.



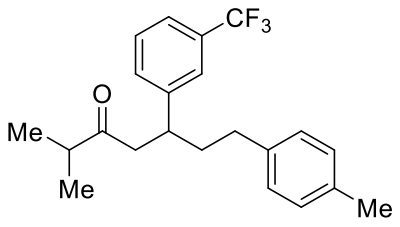
2-Methyl-7-(p-tolyl)-6-(3-(trifluoromethyl)phenyl)heptan-3-one ***(106)*****:** The title compound **106** was obtained as a yellow oil (112.2 mg, 62% yield) in 2h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (d, *J*=6.0 Hz, 3H), 1.01 (d, *J*=6.0 Hz, 3H) 1.81-2.03 (m, 2H), 2.36-2.49 (m, 3H), 2.77 (d, *J*=6.0 Hz, 2H), 3.24-3.33 (m, 1H), 3.78 (s, 3H), 6.81 (d, *J*=9.0 Hz, 2H), 7.00 (d, *J*=9.0 Hz, 2H),7.39-7.49 (m, 4H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 17.8, 18.0, 32.8, 37.9, 40.3, 41.3, 47.5, 55.2, 113.9, 122.5, 123.4 (q, J_{CF}= 3.8 Hz), 124.3 (q, J_{CF}= 270.0 Hz), 124.3 (q, J_{CF}= 3.8 Hz), 126.1, 129.0, 129.3, 130.9 (q, J_{CF}= 31.5 Hz), 131.5, 133.7, 145.7, 157.9, 212.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.0 ; **IR (neat):** 2934, 1709, 1511, 1325, 1120 ; **HRMS (ESI):** Calcd for $C_{22}H_{25}F_3NaO_2$ $(M+Na)^+$ 401.1704, found 401.1691.



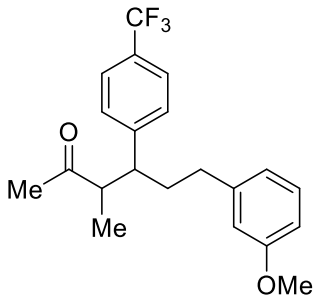
5-(3-Chlorophenyl)-7-(3-methoxyphenyl)-2-methylheptan-3-one ***(107)*****:** The title compound **107** was obtained as a colorless oil (108.4 mg, 63% yield) in 2h after purification by silica gel column chromatography (Hex: Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (d, *J*=6.0 Hz, 3H), 1.02(d, *J*=9.0 Hz, 3H) 1.78-2.02 (m, 2H), 2.39-2.48 (m, 3H), 2.74 (dd, *J*=3.0 Hz, 6.0 Hz, 2H), 3.16-3.25 (m, 1H), 3.78 (s, 3H), 6.63-6.73 (m, 3H), 7.08-7.27 (m, 5H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 17.9, 18.0, 33.8, 37.6, 40.4, 41.5, 47.6, 55.2, 111.3, 114.2, 120.8, 126.2, 126.7, 127.8, 129.4, 129.9, 134.4, 143.5, 146.7, 159.7, 212.8 ; **IR (neat):** 2934, 1708, 1595, 1456, 1259, 1043 ; **HRMS (ESI):** Calcd for $C_{21}H_{26}ClO_2$ $(M+H)^+$ 345.1621, found 345.1631.



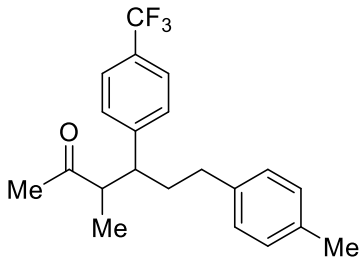
2-Methyl-7-(p-tolyl)-5-(3-(trifluoromethyl)phenyl)heptan-3-one ***(108)*****:** The title compound **108** was obtained as a yellow oil (99.6 mg, 55% yield) in 2h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (d, *J*=6.0 Hz, 3H), 1.05 (d, *J*=6.0 Hz, 3H), 1.89-2.09 (m, 2H), 2.34 (s, 3H), 2.42-2.52 (m, 3H), 2.81 (d, *J*=6.0 Hz, 2H), 3.29-3.39 (m, 1H), 7.01 (d, *J*=6.0 Hz, 2H), 7.11 (d, *J*=9.0 Hz, 2H), 7.43-7.51 (m, 4H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 17.8, 18.0, 21.0, 33.3, 37.9, 40.4, 41.3, 47.6, 123.4 (q, J_{CF}= 3.8 Hz), 124.3 (q, J_{CF}= 270.0 Hz), 124.3 (q, J_{CF}= 3.8 Hz), 128.3, 129.0, , 129.2, 130.8 (q, J_{CF}= 32.3 Hz) , 131.5, 135.4, 138.6, 145.7, 212.6 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.0 ; **IR (neat):** 2970, 1710, 1325, 1121, 1072 ; **HRMS (ESI):** Calcd for $C_{22}H_{25}F_3NaO$ $(M+Na)^+$ 385.1755, found 385.1747.



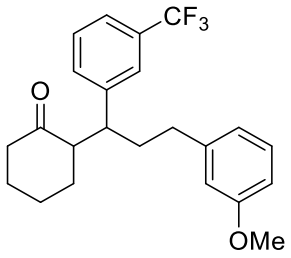
*6-(3-Methoxyphenyl)-3-methyl-4-(4-(trifluoromethyl)phenyl)hexan-2-one (**109**)***:*** The title compound **109** was obtained as a yellow oil (81.9 mg, 45% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80 (d, *J*=6.0 Hz, 0.5×3H), 1.16 (d, *J*=6.0 Hz, 0.5×3H), 1.85 (s, 0.5×3H), 1.86-1.94 (m, 0.5×2H), 2.04-2.09 (m, 0.5×2H), 2.16 (s, 0.5×3H), 2.28-2.35 (m, 2H), 2.74-2.98 (m, 2H), 3.77 (s, 3H), 6.57-6.66 (m, 2H), 6.69-6.74 (m, 1H), 7.12-7.23 (m, 2H), 7.30 (t, *J*=7.5 Hz, 1H), 7.52-7.62 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 14.4, 15.9, 29.3, 29.6, 33.3, 33.4, 33.8, 36.1, 47.3, 47.9, 53.0, 53.1, 55.2, 111.2, 111.3, 114.2, 114.3, 114.8, 120.8, 123.3 (q, J_{CF}= 274.5 Hz), 124.3 (q, J_{CF}= 270.0 Hz), 125.6 (q, J_{CF}= 3.8 Hz), 128.3, 128.7, 128.9, 129.1 (q, J_{CF}= 35.2 Hz), 129.4, 129.5, 143.2, 143.3, 146.5, 147.3, 159.8, 211.5, 212.1; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.9, -60.9 ;**IR (neat):** 2935, 1711, 1325, 1115, 1066 ; **HRMS (ESI):** Calcd for $C_{21}H_{24}F_3O_2$ $(M+H)^+$ 365.1728, found 365.1723.



*3-Methyl-6-(p-tolyl)-4-(4-(trifluoromethyl) phenyl)hexan-2-one (**110**):* The title compound **110** was obtained as a yellow oil (88.8 mg, 51% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

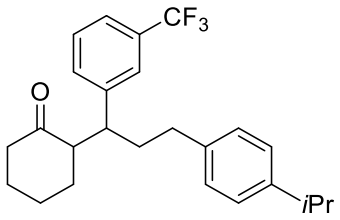
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.80 (d, *J*=6.0 Hz, 0.55×3H), 1.16 (d, *J*=6.0 Hz, 0.45×3H), 1.85 (s, 0.55×3H), 1.86-1.93 (m, 0.55×2H), 2.04-2.14 (m, 0.45×2H), 2.16 (s, 0.45×3H), 2.27-2.37 (m, 5H), 2.74-2.99 (m, 2H), 6.94 (t, *J*=7.5 Hz, 2H), 7.05-7.09 (m, 2H),7.30 (t, *J*=6.0 Hz, 2H) 7.60 (t, *J*=7.5 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 14.4, 15.9, 21.1, 29.3, 29.6, 32.9, 33.2, 33.6, 36.4, 47.3, 47.9, 53.0, 53.1, 124.3 (q, J_{CF}= 272.2 Hz), 124.3 (q, J_{CF}= 272.2 Hz), 125.6 (q, J_{CF}= 3.8 Hz),, 128.3, 128.7, 128.9 (q, J_{CF}= 25.2 Hz),, 129.2, 129.2, 135.5, 135.6, 138.4, 138.6, 146.5, 147.4, 211.6, 212.2 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6, -62.6 ;**IR (neat):** 2926, 1712, 1323, 1161, 1116 ; **HRMS (ESI):** Calcd for $C_{21}H_{23}F_3NaO$ $(M+Na)^+$ 371.1599, found 371.1589.



*2-(3-(3-Methoxyphenyl)-1-(3-(trifluoromethyl)phenyl)propyl)cyclohexan-1-one (**111**)***:*** The title compound **111** was obtained as a colorless oil (123.0 mg, 63% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13-2.17 (m, 9H), 2.32-2.40 (m, 3H), 2.48-2.62 (m, 1H), 3.08-3.16 (m, 0.55×1H), 3.30-3.37 (m, 0.45×1H), 3.77 (s, 0.55×3H), 3.78 (s, 0.45×3H), 6.60-6.73 (m, 3H), 7.13-7.20 (m, 1H), 7.34-7.52 (m, 4H), ; **^{13}C NMR (126 MHz, $CDCl_3$):**

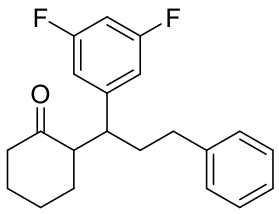
δ 24.5, 25.0, 27.8, 28.7, 29.3, 32.3, 32.6, 33.8, 34.0, 36.1, 42.5, 43.5, 44.4, 55.2, 56.6, 56.8, 111.3, 111.5, 114.0, 114.2, 120.8, 120.9, 123.3 (q, J_{CF}=3.8 Hz), 123.5 (q, J_{CF}=3.8 Hz), , 124.3 (q, J_{CF}=272.2 Hz), 125.3 (q, J_{CF}=3.8 Hz), 125.4 (q, J_{CF}=3.8 Hz), 128.9, 129.1, 129.4, 129.4, 130.8 (q, J_{CF}=31.5 Hz), 130.9 (q, J_{CF}=31.5 Hz), 132.2, 132.2, 143.4, 143.7, 143.7, 144.8, 159.7, 211.3, 212.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.7, -62.; **IR (neat):** 2936, 1706, 1325, 1260, 1119 ; **HRMS (ESI):** Calcd for $C_{23}H_{25}F_3NaO_2$ $(M+Na)^+$ 413.1704, found 413.1687.



2-(3-(4-Isopropylphenyl)-1-(3-(trifluoromethyl) phenyl)propyl)cyclohexan-1-one ***(112)*****:** The title compound **112** was obtained as a yellow oil (112.7 mg, 56% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

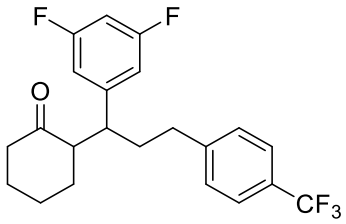
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23-1.26 (m, 6H), 1.54-2.18 (m, 9H), 2.35-2.42 (m, 3H), 2.52-2.64 (m, 1H), 2.84-2.93 (m, 1H), 3.13-3.21 (m, 0.45×1H), 3.33-3.40 (m, 0.55×1H), 7.02 (t, *J*=10.5 Hz, 2H), 7.13 (t, *J*=6.0 Hz, 2H) 7.38-7.53 (m, 4H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.2, 24.4, 25.0, 27.8, 28.6, 29.3, 29.8, 32.5, 33.4, 33.6, 33.8, 36.3, 42.5, 43.6, 44.6, 56.6, 56.8, 122.6, 123.2 (q, J_{CF}= 3.8 Hz), 123.4 (q, J_{CF}= 3.8 Hz), 124.4 (q, J_{CF}= 270.7 Hz), 124.4 (q, J_{CF}= 271.5 Hz), 125.3 (q, J_{CF}= 3.8 Hz), 125.4 (q, J_{CF}= 3.8 Hz), 126.4, 126.5, 126.6, 128.3, 128.4, 128.9, 129.0, 130.5, 130.7 (q, J_{CF}= 31.5 Hz), 130.8 (q, J_{CF}= 32.3 Hz), 130.9, 132.2, 132.3, 139.1, 139.4, 143.7, 144.9, 146.5, 211.3, 212.8 ; **^{19}F NMR (282 MHz,**

$CDCl_3$) δ -61.0, -61.0 ; **IR (neat):** 2957, 1707, 1324, 1120, 1072 ; **HRMS (ESI):** Calcd for $C_{25}H_{29}F_3NaO$ $(M+Na)^+$ 425.2068, found 425.2065.



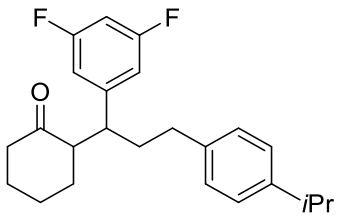
*2-(1-(3,5-Difluorophenyl)-3-phenylpropyl) cyclohexan-1-one (**113**)***:** The title compound **113** was obtained as a yellow oil (101.8 mg, 62% yield) in 14h after purification by silica gel column chromatography (Hex: Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16-2.12 (m, 9H), 2.30-2.55 (m, 4H), 3.01-3.09 (m, 0.5×1H), 3.21-3.29 (m, 0.5×1H), 6.63-6.81 (m, 3H), 7.10 (t, *J*= 9.0 Hz, 2H), 7.16-7.29 (m, 3H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.6, 25.0, 27.8, 28.7, 29.5, 32.5, 32.7, 33.8, 33.9, 36.2, 42.5, 43.6, 44.6, 56.5, 56.6, 101.9 (t, J_{CF}=25.5 Hz), 102.1 (t, J_{CF}= 25.5 Hz), 111.3 (d, J_{CF}= 8.3 Hz), 111.5, 111.6 (d, J_{CF}= 8.3 Hz), 126.0, 128.4, 141.8 (d, J_{CF}=19.5 Hz), 147.0 (t, J_{CF}= 8.3 Hz), 148.2 (t, J_{CF}= 8.3 Hz), 163.2 (dd, J_{CF}= 7.5, 240.0 Hz), 163.3 (dd, J_{CF}= 8.3, 240.0 Hz), 211.1, 212.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -108.8, -108.5; **IR (neat):** 2935, 1735, 1622, 1593, 1449 ; **HRMS (ESI):** Calcd for $C_{21}H_{22}F_2NaO$ $(M+Na)^+$ 351.1536, found 351.1524.



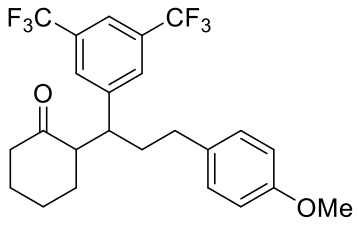
*2-(1-(3,5-Difluorophenyl)-3-(4-(trifluoromethyl) phenyl)propyl)cyclohexan-1-one (**114**)***:** The title compound **114** was obtained as a colorless oil (114.9 mg, 58% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 20:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.12-2.18 (m, 9H), 2.32-2.52 (m, 4H), 2.96-3.04 (m, 0.60×1H), 3.21-3.28 (m, 0.40×1H), 6.67-6.77 (m, 3H), 7.20 (t, *J*= 6.0 Hz, 2H), 7.48-7.52 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.9, 25.1, 27.8, 28.8, 29.3, 31.9, 33.0, 33.7, 33.9, 35.9, 42.5, 42.8, 43.5, 44.7, 56.4, 56.5 , 102.1 (t, J_{CF}=25.1 Hz), 102.3 (t, J_{CF}=25.1 Hz), 111.3 (d, J_{CF}= 24.0 Hz), 124.5 (q, J_{CF}= 269.3 Hz), 122.7, 125.4 (t, J_{CF}=3.8 Hz), 128.3 (q, J_{CF}= 30.8 Hz), 128.8, 145.8, 146.0, 146.8 (t, J_{CF}=8.3 Hz), 147.8 163.2 (dd, J_{CF}= 12.0, 240.0 Hz), 211.0, 212.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -108.5, -108.2, -60.8 ; **IR (neat):** 2936, 1707, 1594, 1322, 1112 ; **HRMS (ESI):** Calcd for $C_{22}H_{21}F_5NaO$ $(M+Na)^+$ 419.1410, found 419.1404.



*2-(1-(3,5-Difluorophenyl)-3-(4-isopropylphenyl)propyl)cyclohexan-1-one (**115**)***:** The title compound **115** was obtained as a colorless oil (80.0 mg, 43% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

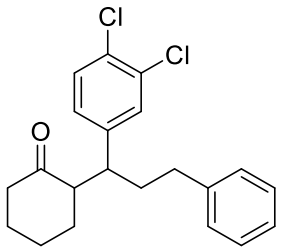
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (d, *J*=6.0 Hz, 6H), 1.54-2.12 (m, 9H), 2.36-2.54 (m, 4H), 2.85-2.90 (m, 1H), 3.04-3.12 (m, 0.58×1H), 3.23-3.30 (m, 0.42×1H), 6.64-6.80 (m, 3H), 7.01-7.15 (m, 4H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.2, 24.6, 25.0, 27.8, 28.7, 29.5, 32.6, 33.4, 33.5, 33.8, 36.3, 42.5, 43.7, 44.7, 56.5, 56.6, 101.8 (t, J_{CF}= 25.5 Hz), 102.0 (t, J_{CF}= 25.5 Hz), 111.3 (d, J_{CF}= 9.0 Hz), 111.4, 111.6 (d, J_{CF}= 9.0 Hz), 126.4, 126.5, 128.3, 146.5, 146.5, 147.1 (t, J_{CF}= 8.3 Hz), 148.3 (t, J_{CF}= 8.3 Hz), 161 (d, J_{CF}= 3.0 Hz), 140.8, 148.4 (t, J_{CF}= 8.3 Hz), 163.1 (dd, J_{CF}= 7.9, 247.5 Hz), 163.3 (dd, J_{CF}= 7.5, 247.5 Hz), 211.1, 212.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -108.8, -108.5 ; **IR (neat):** 2956, 1707, 1622, 1593, 1448 ; **HRMS (ESI):** Calcd for $C_{24}H_{28}F_2NaO$ $(M+Na)^+$ 393.2006, found 393.2009.



*2-(1-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-methoxyphenyl)propyl)cyclohexan-1-one (**116**)* **:** The title compound **116** was obtained as a yellow oil (142.0 mg, 62% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

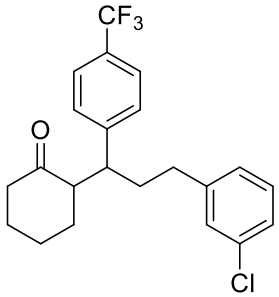
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07-2.17 (m, 9H), 2.32-2.37 (m, 3H), 2.51-2.64 (m, 1H), 3.18-3.27 (m, 0.5×1H), 3.30-3.37 (m, 0.5×1H), 3.77 (s, 3H), 6.77-6.81 (m, 2H), 6.93-6.98 (m, 2H), 7.60 (s, 1H), 7.66 (s, 1H), 7.73 (s, 0.5×1H), 7.75 (s, 0.5×1H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.8, 25.2, 27.8, 28.5, 29.8, 32.4, 32.6, 32.8, 32.9, 36.0, 42.6, 43.7, 44.2, 55.4, 56.1, 56.5, 113.9, 114.0, 120.4 (q, J_{CF}=3.5 Hz), 120.6 (q, J_{CF}=3.8 Hz), 123.5 (q, J_{CF}=270.8 Hz), 123.6 (q, J_{CF}=270.8 Hz),129.0, 129.1, 129.4, 131.6 (q, J_{CF}=33.0 Hz), 131.7 (q, J_{CF}=32.3 Hz), 133.1, 133.4, 145.5, 146.8, 158.0, 210.8, 211.9 ; **^{19}F NMR (282 MHz,**

$CDCl_3$) δ -61.2 ; **IR (neat):** 2928, 1771, 1652, 1540, 1507 ; **HRMS (ESI):** Calcd for $C_{24}H_{24}F_6NaO_2$ $(M+Na)^+$ 481.1578, found 481.1580.



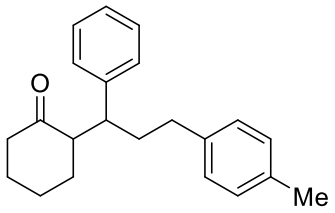
2-(3-(3-Methoxyphenyl)-1-(3-(trifluoromethyl)phenyl)propyl)cyclohexan-1-one ***(117)*****:** The title compound **117** was obtained as a yellow oil (74.1 mg, 41% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.11-2.15 (m, 9H), 2.30-2.56 (m, 4H), 2.99-3.07 (m, 0.43×1H), 3.17-3.24 (m, 0.57×1H), 7.00-7.11 (m, 2H), 7.14-7.20 (m, 1H), 7.23-7.35 (m, 3H), 7.37-7.55 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.5, 25.0, 27.8, 28.6, 29.5, 32.5, 33.8, 36.1, 42.5, 43.1, 43.9, 56.4, 56.6, 126.0, 127.0, 128.2, 128.2, 128.4, 128.9, 130.2, 130.3, 130.4, 130.5, 130.6, 132.4, 132.6, 141.7, 141.9, 143.1, 144.3, 211.2, 212.5 ; **IR (neat):** 2936, 1705, 1470, 1129, 1029 ; **HRMS (ESI):** Calcd for $C_{21}H_{22}Cl_2NaO$ $(M+Na)^+$ 383.0945, found 383.0930.



*2-(3-(3-Chlorophenyl)-1-(4-(trifluoromethyl) phenyl)propyl)cyclohexan-1-one (**118**)***:** The title compound **118** was obtained as a yellow oil (120.4 mg, 61% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.12-2.02 (m, 9H), 2.30-2.44 (m, 3H), 2.49-2.62 (m, 1H), 3.06-3.14 (m, 0.60×1H), 3.28-3.35 (m, 0.40×1H), 6.95 (t, *J*= 7.5 Hz, 1H), 7.04-7.20 (m, 3H), 7.28 (d, *J*= 9.0 Hz, 0.60×2H), 7.34 (d, *J*= 6.0 Hz, 0.40×2H), 7.56-7.60 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 24.7, 25.0, 27.8, 28.7, 29.4, 32.1, 32.8, 33.6, 33.7, 36.0, 42.5, 42.6, 43.6, 44.6, 56.5, 56.7, 124.4 (q, J_{CF}=270.0 Hz), 125.6 (q, J_{CF}=3.8 Hz), 126.2, 126.7, 128.6, 128.9,129.0 (q, J_{CF}=31.5 Hz), 129.1, 129.7, 134.1, 143.9, 144.1, 146.7, 147.8, 211.3, 212.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.8, -60.8 ; **IR (neat**): 2935, 1734, 1323, 1112, 1066 ; **HRMS (ESI):** Calcd for $C_{22}H_{22}ClF_3NaO$ $(M+Na)^+$ 417.1209, found 417.1201.



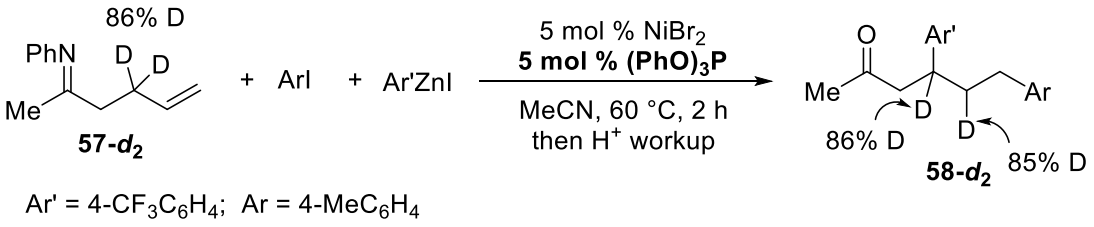
*2-(1-Phenyl-3-(p-tolyl) propyl)cyclohexan-1-one (**119**)***:** The title compound **119** was obtained as a colorless oil (67.4 mg, 44% yield) in 14h after purification by silica gel column chromatography (Hex : Et_2O = 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21-2.13 (m, 9H), 2.27-2.46 (m, 6H), 2.52-2.62 (m, 1H), 3.01-3.09 (m, 0.57×1H), 3.29-3.36 (m, 0.43×1H), 6.98-7.11 (m, 3H), 7.15-7.38 (m, 6H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 21.1, 24.0, 24.7, 27.7, 28.8, 28.9, 32.5, 32.7, 33.3, 33.7,

36.6, 42.2, 42.3, 43.4, 44.6, 56.9, 57.0, 125.7, 126.3, 126.5, 128.3, 128.4, 128.6, 128.7, 129.0, 129.0, 135.1, 135.1, 139.2, 139.5, 142.5, 143.6, 211.8, 213.7 ; **IR (neat):** 2929, 1733, 1705, 1493, 1126; **HRMS (ESI):** Calcd for $C_{22}H_{26}NaO$ $(M+Na)^+$ 329.1881, found 329.1872.

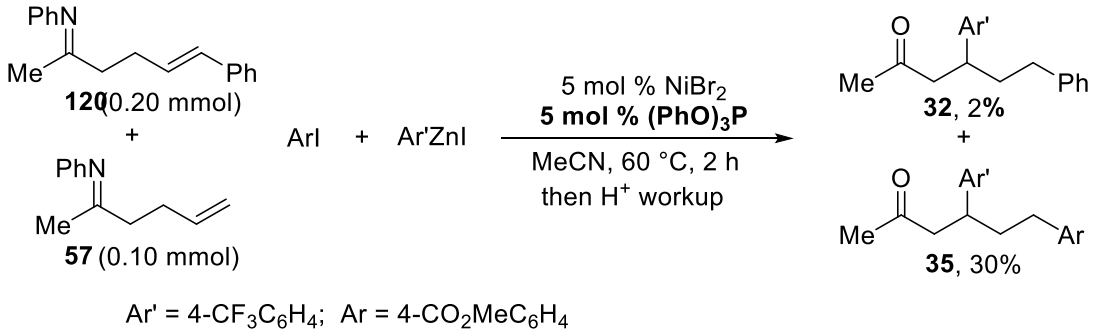
5.2.3. Mechanistic investigation

Deuterium labelling experiment



In a glovebox, stock solution of (4-(trifluoromethyl) phenyl)zinc iodide in THF (0.24 mmol) was taken in a 15 mL sealed tube and the solvent was removed under vacuum. To the residue of aryl zinc iodide, $NiBr_2$ (2.3 mg, 0.01mmol), triphenyl phosphite (3.1 mg, 0.01mmol), 4-iodotoluene (0.3 mmol) and N-phenylhex-5-en-2-imine-4,4-d_2 (0.2 mmol) was added. The mixture was then dissolved in MeCN (1.0 mL). The sealed tube was capped tightly, and placed in an oil-bath preheated to 60 °C with vigorous stirring. After 2h, the reaction mixture was cooled to room temperature, 2 mL of 6N HCl was added and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (3 mL × 4) and the combined ethyl acetate fraction was dried over Na_2SO_4 and the solvent was removed in a rotavapor. The crude was purified by silica gel column chromatography using diethyl ether/hexane (1:10) as an eluent to get the desired product as a colorless liquid (68% yield). The ^1H NMR of the 1,3-diarylated product shows the quantitative migration of one deuterium atom to the □- position of the carbonyl group.

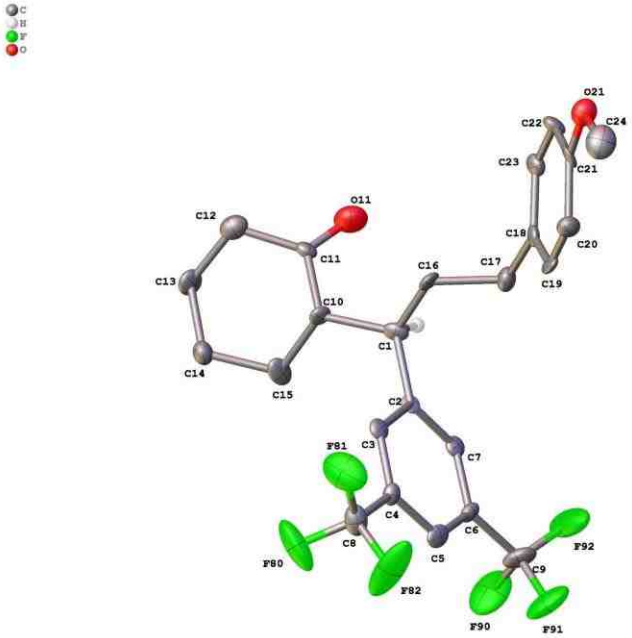
Cross-Over experiment



Ar' = 4-$CF_3C_6H_4$; Ar = 4-$CO_2MeC_6H_4$

In a glovebox, stock solution of (4-(trifluoromethyl) phenyl)zinc iodide in THF (0.12 mmol) was taken in an oven dried 4-dram vial and THF was removed under vacuum. To this residue, $NiBr_2$ (1.2 mg, 0.05 mmol), $(PhO)_3P$ (1.6 mg, 0.05 mmol), Methyl 4-iodobenzoate (0.15 mmol), N,6-diphenylhex-5-en-2-imine (0.2 mmol), N-phenylhex-5-en-2-imine (0.1 mmol) were added. 0.5 ml of MeCN was transferred to the vial and was tightly capped, taken outside the glovebox and placed in a hotplate preheated at 60 °C with well stirring. After reaction was complete, reaction mixture was cooled to room temperature and 50 µl of internal standard (0.2 M stock solution of pyrene in dioxane), 2 ml of ethyl acetate and 1ml of 6N HCl were added. The mixture was well shaken for 2 minutes. Then, 1 ml of the organic layer was taken and filtered through the short pad of silica to get a clear solution which was analyzed in the GC. The product peaks were compared to the retention time of the pure compound. The analysis of the GC peaks of products with pyrene (internal standard) shows the formation of 2% of product **32** and 30% of product **35** in the reaction.

5.2.4. X-ray Crystallographic Data for Compound 61



A colorless plate-like specimen of $C_{24}H_{23}F_6O_2$, approximate dimensions 0.228 mm x 0.157 mm x 0.112 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker APEX II Ultra system equipped with a Double Bounce Multilayer Mirrors monochromator and a MoKα Micro Focus Rotating Anode (λ = 0.71073 Å).

The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a orthorhombic unit cell yielded a total of 10554 reflections to a maximum θ angle of 25.34° (0.83 Å resolution), of which 3994 were independent (average redundancy 2.642, completeness = 99.9%, R_{int} = 15.80%, R_{sig} = 27.01%) and 1802 (45.12%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.5667(13) Å, b = 9.7395(11) Å, c = 23.460(3) Å, volume = 2185.9(5) $Å^3$, are based upon the refinement of the XYZ-centroids of 519 reflections above 20 σ(I) with 4.528° < 2θ <

50.688°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.806. The final anisotropic full-matrix least-squares refinement on F^2 with 284 variables converged at R1 = 8.92%, for the observed data and wR2 = 17.51% for all data. The goodness-of-fit was 0.977. The largest peak in the final difference electron density synthesis was 0.595 e-/Å^3 and the largest hole was -0.304 e-/Å^3 with an RMS deviation of 0.072 e-/Å^3. On the basis of the final model, the calculated density was 1.390 g/cm^3 and F(000), 948 e-.

Table 5.17. Crystal data and structure refinement for compound 116.

Identification code	jsOp212121_a
Empirical formula	$C_{24}H_{23}F_6O_2$
Formula weight	457.42
Temperature/K	99.51
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	9.5667(13)
b/Å	9.7395(11)
c/Å	23.460(3)

α/°	90
β/°	90
γ/°	90
Volume/Å^3	2185.9(5)
Z	4
ρ_{calc}g/cm^3	1.390
μ/mm^{-1}	0.122
F(000)	948.0
Crystal size/mm^3	0.228 × 0.157 × 0.112
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.528 to 50.688
Index ranges	-11 ≤ h ≤ 11, -9 ≤ k ≤ 11, -28 ≤ l ≤ 17
Reflections collected	10554
Independent reflections	3994 [R_{int} = 0.1580, R_{sigma} = 0.2701]
Data/restraints/parameters	3994/0/284
Goodness-of-fit on F^2	0.977

Final R indexes [I>=2σ (I)]	R_1 = 0.0892, wR_2 = 0.1357
Final R indexes [all data]	R_1 = 0.2225, wR_2 = 0.1751
Largest diff. peak/hole / e Å^{-3}	0.59/-0.30
Flack parameter	-1.4(10)

Table 5.18. Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for jsOp212121_a. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
F80	9891(7)	1671(7)	6187(3)	66(2)
F81	10099(6)	2724(6)	5411(3)	57(2)
F82	9041(7)	820(7)	5440(4)	93(3)
F90	3768(7)	1409(7)	6531(3)	66(2)
F91	4132(6)	677(6)	5694(3)	54(2)
F92	2991(6)	2507(6)	5818(4)	75(3)
O11	6465(8)	8980(6)	6587(3)	45(2)

O21	7880(6)	8957(6)	3025(3)	28.8(17)
C1	6628(10)	6349(7)	6116(4)	19(2)
C2	6601(10)	4804(8)	6038(3)	12(2)
C3	7845(10)	4102(8)	5918(3)	16.4(15)
C4	7875(9)	2698(9)	5835(4)	16(2)
C5	6637(10)	1948(9)	5862(4)	20(2)
C6	5400(9)	2615(8)	5979(4)	16(2)
C7	5393(9)	4040(8)	6075(4)	16.4(15)
C8	9213(11)	1980(10)	5723(4)	28(3)
C9	4062(11)	1804(9)	6009(5)	33(3)
C10	7720(9)	6845(8)	6541(4)	18(2)
C11	7518(10)	8322(8)	6710(4)	16(2)
C12	8664(10)	8908(9)	7064(4)	27(3)
C13	8760(10)	8090(8)	7621(4)	27(3)
C14	8873(10)	6545(8)	7506(4)	25(2)
C15	7690(10)	6024(9)	7114(4)	27(3)

C16	6887(9)	7029(8)	5540(4)	19(2)
C17	5688(10)	6922(9)	5116(4)	27(2)
C18	6157(9)	7443(9)	4533(4)	18(2)
C19	6709(9)	6550(9)	4134(4)	26(3)
C20	7271(9)	6988(9)	3621(4)	23(2)
C21	7306(9)	8384(9)	3506(4)	19(2)
C22	6741(9)	9300(8)	3892(4)	19(2)
C23	6197(9)	8827(8)	4399(4)	21(2)
C24	8453(11)	8047(10)	2612(4)	37(3)

Table 5.19. Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for compound 116. The Anisotropic displacement factor exponent takes the form: -

$2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F80	50(4)	111(5)	37(4)	15(4)	-5(4)	45(4)
F81	36(4)	70(4)	66(5)	16(4)	27(4)	17(4)

F82	33(4)	74(5)	173(9)	-93(5)	-7(5)	13(4)
F90	53(5)	90(5)	54(5)	-3(4)	27(4)	-40(4)
F91	39(4)	37(4)	87(6)	-22(4)	20(4)	-22(3)
F92	25(4)	34(4)	165(8)	12(4)	-21(5)	-8(3)
O11	54(6)	26(4)	55(5)	-4(4)	-7(4)	3(4)
O21	30(5)	30(4)	26(4)	-5(3)	0(4)	-1(3)
C1	21(6)	13(5)	23(6)	1(4)	5(5)	7(4)
C2	14(6)	18(5)	4(5)	4(4)	4(4)	-1(4)
C3	22(4)	21(3)	6(3)	2(3)	0(3)	-1(3)
C4	15(6)	20(5)	12(5)	-4(4)	0(5)	0(4)
C5	30(6)	22(5)	7(5)	-6(4)	1(5)	-4(5)
C6	21(6)	16(5)	11(5)	-4(4)	0(4)	-6(5)
C7	22(4)	21(3)	6(3)	2(3)	0(3)	-1(3)
C8	25(7)	36(7)	23(6)	-10(5)	-2(5)	10(5)
C9	39(8)	13(5)	46(8)	-8(6)	7(6)	-3(5)
C10	26(6)	11(5)	17(5)	-7(4)	-2(5)	0(4)

C11	21(6)	13(5)	13(5)	4(4)	1(5)	3(5)
C12	27(7)	23(5)	31(7)	-5(5)	5(5)	0(5)
C13	38(7)	22(5)	21(6)	-12(5)	-6(5)	1(5)
C14	26(6)	24(6)	23(6)	0(4)	-8(5)	2(5)
C15	42(7)	24(5)	15(6)	-10(4)	-6(5)	12(5)
C16	25(6)	11(5)	21(6)	-6(4)	-5(5)	-6(4)
C17	26(7)	24(5)	29(6)	-4(5)	-12(5)	-1(5)
C18	12(6)	23(5)	21(6)	3(5)	-10(5)	-2(5)
C19	18(6)	14(5)	47(8)	3(5)	-19(5)	-7(4)
C20	29(7)	16(5)	23(6)	-3(5)	-3(5)	1(4)
C21	20(6)	22(5)	17(6)	4(5)	-11(5)	8(5)
C22	27(6)	15(5)	16(6)	5(4)	-3(5)	6(5)
C23	15(6)	22(6)	26(6)	3(5)	-6(5)	3(4)
C24	34(7)	50(7)	29(7)	-4(6)	8(6)	-2(6)

Table 5.20. Bond Lengths for compound 116.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
F80	C8	1.302(11)	C5	C6	1.377(11)
F81	C8	1.335(11)	C6	C7	1.406(11)
F82	C8	1.321(11)	C6	C9	1.506(12)
F90	C9	1.313(12)	C10	C11	1.504(11)
F91	C9	1.326(10)	C10	C15	1.564(12)
F92	C9	1.310(11)	C11	C12	1.488(12)
O11	C11	1.229(10)	C12	C13	1.533(12)
O21	C21	1.373(10)	C13	C14	1.533(11)
O21	C24	1.423(10)	C14	C15	1.544(12)
C1	C2	1.517(10)	C16	C17	1.520(12)
C1	C10	1.522(12)	C17	C18	1.527(12)
C1	C16	1.527(12)	C18	C19	1.383(12)
C2	C3	1.401(12)	C18	C23	1.384(11)
C2	C7	1.377(11)	C19	C20	1.384(12)

C3	C4	1.381(11)	C20	C21	1.386(11)
C4	C5	1.393(11)	C21	C22	1.382(11)
C4	C8	1.482(12)	C22	C23	1.377(12)

Table 5.21. Bond Angles for compound 116.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C21	O21	C24	117.4(7)	F92	C9	F90	107.7(9)
C2	C1	C10	114.0(7)	F92	C9	F91	106.3(9)
C2	C1	C16	109.0(7)	F92	C9	C6	112.0(8)
C10	C1	C16	109.3(7)	C1	C10	C15	112.8(7)
C3	C2	C1	119.7(8)	C11	C10	C1	112.9(7)
C7	C2	C1	122.8(8)	C11	C10	C15	105.1(7)
C7	C2	C3	117.5(7)	O11	C11	C10	122.8(9)
C4	C3	C2	122.0(9)	O11	C11	C12	122.3(8)
C3	C4	C5	119.6(9)	C12	C11	C10	114.8(8)
C3	C4	C8	120.7(9)	C11	C12	C13	108.7(8)

C5	C4	C8	119.7(8)	C14	C13	C12	111.4(7)
C6	C5	C4	119.5(8)	C13	C14	C15	112.1(8)
C5	C6	C7	120.1(9)	C14	C15	C10	109.3(8)
C5	C6	C9	119.5(8)	C17	C16	C1	115.2(8)
C7	C6	C9	120.4(8)	C16	C17	C18	109.9(7)
C2	C7	C6	121.3(9)	C19	C18	C17	120.7(8)
F80	C8	F81	105.5(9)	C19	C18	C23	116.5(9)
F80	C8	F82	106.5(8)	C23	C18	C17	122.4(9)
F80	C8	C4	113.1(8)	C18	C19	C20	122.9(8)
F81	C8	C4	112.9(8)	C19	C20	C21	118.8(9)
F82	C8	F81	105.5(9)	O21	C21	C20	124.7(8)
F82	C8	C4	112.6(9)	O21	C21	C22	115.6(8)
F90	C9	F91	106.8(8)	C22	C21	C20	119.7(9)
F90	C9	C6	112.3(9)	C23	C22	C21	119.8(8)
F91	C9	C6	111.4(8)	C22	C23	C18	122.2(9)

Table 5.22. Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for compound 116.

Atom	*x*	*y*	*z*	U(eq)
H1	5687.35	6645.6	6256.15	23
H3	8692.29	4606.11	5892.89	20
H5	6644.81	984.53	5799.22	24
H7	4538.8	4484.78	6167.36	20
H12A	8468.79	9885.69	7147.56	32
H12B	9560.97	8852.41	6854.57	32
H13A	9589.23	8397.45	7838.47	32
H13B	7920.28	8272.95	7855.05	32
H14A	8834.53	6043.79	7872.46	30
H14B	9786.65	6346.58	7325.61	30
H15A	6775.23	6150.32	7303.55	32
H15B	7818.57	5032.79	7036.2	32
H16A	7093.56	8012.85	5603.99	23

H16B	7727.93	6608.83	5366.24	23
H17A	4885.77	7473.9	5252.68	32
H17B	5382.24	5954.05	5084.94	32
H19	6701.06	5594.45	4214.43	31
H20	7627.46	6344.37	3353.92	27
H22	6728.99	10254.22	3808.29	23
H23	5836.6	9471.42	4664.63	25
H24A	8927.58	8579.8	2314.79	56
H24B	7700.71	7504.24	2439.88	56
H24C	9125.57	7431.51	2795.99	56

5.3. Nickel-catalyzed γ, δ-Diarylation of Unactivated Alkene in Ketones

5.3.1. General Information

All the reactions were set up inside a nitrogen-filled glovebox and all the chemicals were handled under nitrogen atmosphere unless stated otherwise. All the glassware including the 4-dram and 1-dram borosilicate (Kimble-Chase) vials, and pressure vessels were properly dried in an oven before use. Bulk solvents were obtained from EMD and

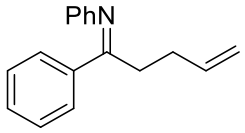
anhydrous solvents (DMF, DMA, DMSO, NMP, dioxane, toluene, MeCN) were obtained from Sigma-Aldrich, and were used directly without further purification. Deuterated solvents were purchased from Sigma-Aldrich. $NiBr_2$ was purchased from Alfa Aesar. $Ni(cod)_2$ was purchased from Strem chemicals. Aryl halides were purchased from Acros, Sigma-Aldrich, Oakwood, TCI-America, Matrix and Alfa-Aesar. ^1H, ^{13}C, and ^{19}F spectra were recorded on a Bruker instrument (500 or 300, 75 or 126, 282 and 121.5 MHz respectively) and internally referenced to the residual solvent signals of $CDCl_3$ for ^1H and ^{13}C NMR at 7.26 ppm, 77.16 ppm and -164.9 ppm respectively, and C_6F_6 at -164.9 ppm for and ^{19}F NMR. The chemical shifts of NMR and the coupling constants (*J*) for ^1H, ^{13}C and ^{19}F NMR reported in δ parts per millions (ppm) and in Hertz, respectively. The following conventions are used for multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublet. High resolution mass of new compounds was recorded at the Mass Spectrometry, University of Texas at Austin. All NMR spectra were collected at the Department of Chemistry and Chemical Biology, University of New Mexico (UNM). Infrared (IR) spectra were recorded on Bruker Alpha-P ATR-IR at UNM and ν_{max} is reported in cm^{-1}.

Note from Acknowledgement: The X-ray crystallographic work (by Timothy J. Boyle) was supported by the Laboratory Directed Research and Development (LDRD) program at Sandia National Laboratories. Sandia National Laboratories is a multi-mission laboratory managed and operated by National Technology and Engineering Solutions of Sandia, LLC., a wholly owned subsidiary of Honeywell International, Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525.

5.3.2. Experimental Section

General Procedure for the Preparation of Ketimines

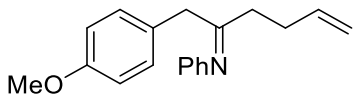
All the ketimines used for the reactions are prepared in accordance with our prior work.[172] 4 Å molecular sieve (1.0 g/mmol) was added to the mixture of ketone (1.0 equiv) and aniline (2.0 equiv) in anhydrous toluene under nitrogen and the mixture was heated at 80 °C for 24h. The reaction mixture was then filtered through the filter paper. The filtrate obtained was concentrated in vacuum. Crude was then purified by distillation under vacuum or flash column chromatography on a silica gel column deactivated by 10% TEA in hexane solution.



1-Phenylpent-4-en-1-one was prepared following general procedure.[173] N,1-diphenylpent-4-en-1-imine was then prepared following general procedure using 1-phenylpent-4-en-1-one and aniline at 80 °C for 24h. The crude was purified by distillation under vacuum at 110 °C (0.3 torr) in which the impurities were distilled out. The remaining reddish liquid was the desired imine (62%).

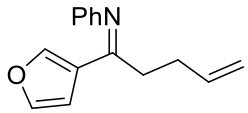
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.24 (q, *J* = 7.8 Hz, 0.84 × 2H), 2.47 (q, *J* = 7.8 Hz, 0.16 × 2H), 2.76 (t, *J* = 7.5 Hz, 0.84 × 2H) 2.90 (t, *J* = 7.5 Hz, 0.16 × 2H), 4.89-5.13 (m, 2H), 5.61-5.74 (m, 0.84×1H), 5.89-6.00 (m, 0.16×1H), 6.65 (d, *J* = 9.0 Hz, 0.16×2H), 6.81 (d, *J* = 9.0 Hz, 0.84×2H), 6.91 (t, *J* = 7.5 Hz, 0.16×1H), 7.09 (t, *J* = 7.5 Hz, 0.84×1H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.46-7.48 (m, 3H), 7.92 (dd, *J* = 3.0, 6.0 Hz, 2H) ; **^{13}C NMR (75**

MHz, $CDCl_3$): δ 29.7, 30.6, 32.1, 40.5, 115.5, 119.2, 120.9, 123.2, 127.7, 127.9, 128.1, 128.6, 129.0, 130.5, 136.9, 138.4, 151.5, 169.1.



1-(4-methoxyphenyl)hex-5-en-2-one was prepared following general procedure.[174] 1-(4-methoxyphenyl)-N-phenylhex-5-en-2-imine was then prepared following general procedure using 1-phenylhex-5-en-2-one and aniline at 80 °C for 24h. The crude was purified by distillation under vacuum at 120 °C (0.3 torr) in which the impurities were distilled out. The remaining reddish liquid was the desired imine (57%).

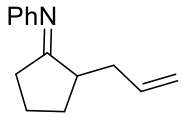
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.17 (s, 0.35× 4H), 2.41 (s, 0.65 × 4H), 3.44 (s, 0.65 × 2H), 3.69 (s, 0.35× 2H), 3.78(s, 0.65× 3H), 3.81 (s, 0.35 × 3H), 4.89-5.07 (m, 2H), 5.55-5.64 (m, 0.35×1H), 5.78-5.91 (m, 0.65×1H), 6.70-6.91 (m, 4H), 6.98-7.07 (m, 2H), 7.26-7.34 (m, 3H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.5, 31.0, 37.2, 38.9, 45.1, 55.4, 114.2, 115.1, 115.6, 119.5, 119.6, 123.2, 128.7, 129.0, 129.1, 130.1, 130.2, 130.5, 137.0, 137.9, 150.9, 151.2, 158.4, 171.9, 173.5.



1-(Furan-3-yl)pent-4-en-1-one was prepared following general procedure.[175] 1-(Furan-3-yl)-N-phenylpent-4-en-1-imine was then prepared following general procedure using 1-phenylhex-5-en-2-one and aniline at 80 °C for 24h. The crude was purified by distillation

under vacuum at 120 °C (0.3 torr) in which the impurities were distilled out. The remaining reddish liquid was the desired imine (64%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13-2.31 (m, 2H), 2.55 (t, *J* = 7.5 Hz, 1H), 2.82 (t, *J* = 7.5 Hz, 0.35× 1H), 2.92 (t, *J* = 7.5 Hz, 0.65× 1H), 4.87-5.14 (m, 2H), 5.60-5.74 (m, 0.65 × 1H), 5.92-6.01 (m, 0.35 × 1H), 6.72-6.89 (m, 2H), 6.79 (s, 0.35 × 1H), 6.89 (s, 0.65 × 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 6.0 Hz, 0.65 × 1H), 7.24 (d, *J* = 6.0 Hz, 0.35 × 1H), 7.29-7.40 (m, 2H), 7.85 (s, 0.65 × 1H), 8.45 (s, 0.35 × 1H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 31.2, 32.6, 34.6, 38.9, 107.8, 109.2, 115.5, 115.7, 119.5, 121.0, 123.3, 126.6, 129.0, 129.1, 129.3, 129.5, 136.9, 137.2, 143.9, 144.0, 150.9, 154.9, 163.0.



2-Allylcyclopentan-1-one was prepared following general procedure.[176] 2-Allyl-N-phenylcyclopentan-1-imine was then prepared following general procedure using 1-phenylhex-5-en-2-one and aniline at 80 °C for 24h. The crude was purified by distillation under vacuum at 80 °C (0.3 torr) in which the impurities were distilled out. The remaining reddish liquid was the desired imine (67%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.44-1.91 (m, 3H), 2.02-2.28 (m, 4H), 2.51-2.74 (m, 2H), 5.03-5.15 (m, 2H), 5.83-5.97 (m, 1H), 6.76 (d, *J* = 9.0 Hz, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 22.7, 30.1, 31.1, 36.7, 46.1, 103.5, 116.2, 119.5, 123.3, 129.0, 136.8, 152.7, 183.5.

General Procedure for the Preparation of Organozinc Reagents[167]

Under nitrogen, anhydrous LiCl (1.0 equiv) and zinc powder (1.5 equiv) were transferred to a Schlenk flask and dried under high vacuum at 150°C to 170°C for 2 h. The mixture was cooled to room temperature and then taken to a glovebox. Anhydrous THF (1ml/mmol) was added and stirred at room temperature. The reaction mixture was stirred for 5 min after the zinc was activated by adding 5 mol % of 1,2 dibromoethane and 3 mol % of TMSCl to the zinc/THF suspension. To this stirred solution was added corresponding aryl iodides (neat) dropwise and the reaction mixture was refluxed for 24 h. The final concentration of the arylzinc reagent was determined by titration with molecular iodine in THF.[168]

General Procedure for Screening Reaction Conditions

In a glovebox, phenylzinc iodide solution in THF (0.15 mmol) was taken in a 1-dram vial and the solvent was removed under vacuum. To the residue, $Ni(cod)_2$ (1.37 mg, 0.005 mmol, 5 mol %), co-catalyst ($AgBF_4$, CuI, $Cu(MeCN)_4BF_4$ or $Cu(MeCN)_4OTf$) (0.015 mmol, 15 mol %), 4-iodobenzotrifluoride (40.8 mg, 0.15 mmol) and N-phenylhex-5-en-2-imine (17.3 mg, 0.10 mmol) were added. The mixture was then dissolved in 0.5 ml of NMP. The vial was capped tightly and placed in a stir-plate at room temperature with vigorous stirring. After 1h, 1 mL of 6 N HCl was added to the reaction mixture and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (1 mL × 3), 50 µL of pyrene (0.010 mmol, 0.20 M stock solution) as an internal standard was added and the solvent was removed in a rotary evaporator. The

residue was dissolved in $CDCl_3$ and NMR spectrum was acquired. The yield was determined by integrating a product peak at 2.9 ppm against the pyrene peak at 8.06 ppm.

General procedure for reaction outside the Glovebox

In a clean and dry 25 ml Schlenk tube, $Ni(cod)_2$ (1.37 mg, 0.005 mmol, 5 mol %), $AgBF_4$ (2.8 mg, 0.015 mmol, 15 mol%), 4-iodobenzotrifluoride (40.8 mg, 0.15 mmol) and N-phenylhex-5-en-2-imine (17.3 mg, 0.10 mmol) were weighed. To this mixture, stock solution of phenylzinc iodide (0.15 mmol) in NMP stored under nitrogen was added. Schlenk tube was then connected to vacuum through Schlenk line and then filled with nitrogen by three cycles of vacuum and nitrogen. Under nitrogen condition, the tube was tightly capped and stirred at room temperature for 1h. After the reaction was complete, 1 mL of 6 N HCl was added to the reaction mixture and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (1 mL × 3), 50 µL of pyrene (0.010 mmol, 0.20 M stock solution) as an internal standard was added and the solvent was removed in a rotary evaporator. The residue was dissolved in $CDCl_3$

and NMR spectrum was acquired. The yield was determined by integrating a product peak at 2.9 ppm against the pyrene peak at 8.06 ppm.

General Procedure for 0.5 mmol reactions

In a glovebox, stock solution of arylzinc iodide in THF (0.75 mmol) was taken in a 15 mL sealed tube and the solvent was removed under vacuum. To the residue of arylzinc, $Ni(cod)_2$ (6.9 mg, 0.025 mmol, 5.0 mol %), silver tetrafluoroborate (14.5 mg, 0.075 mmol,

15.0 mol %) or CuI (14.3 mg, 0.075 mmol, 15.0 mol %), aryl iodides (0.75 mmol) and ketimine (0.5 mmol) was added. The mixture was then dissolved in NMP (2.5 mL). The sealed tube was capped tightly and stirred in the stir-plate with vigorous stirring. After 1h, 5 mL of 6 N HCl was added to the reaction mixture and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (3 mL × 4) and the combined ethyl acetate fraction was washed with water (2 ml × 3). The organic layer was then dried over Na_2SO_4 and solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography using diethyl ether/hexanes or dichloromethane/hexanes as eluent.

General procedure for the large-scale reaction

In a glovebox, stock solution of arylzinc iodide in THF (3.0 mmol) was taken in a 48 mL sealed tube and the solvent was removed under vacuum. To the residue of arylzinc, $Ni(cod)_2$ (27.5 mg, 0.1 mmol, 5.0 mol %), silver tetrafluoroborate (58.4 mg, 0.3 mmol, 15.0 mol %), aryl iodides (816 mg, 3.0 mmol) and ketimine (346 mg, 2.0 mmol) was added. The mixture was then dissolved in NMP (10 mL). The sealed tube was capped tightly and stirred in the stir-plate at room temperature with vigorous stirring. After 1h, 10 mL of 6 N HCl was added to the reaction mixture and shaken for about 2 minutes to hydrolyze the imines to ketones. The reaction mixture was then extracted with EtOAc (10 mL × 3) and the combined ethyl acetate fraction was washed with water (5 ml × 3). The ethyl acetate layer was dried over Na_2SO_4 and solvent was removed in a rotary evaporator. The product was purified by silica gel column chromatography (hexanes : ether =10:1).

5.3.3. Mechanistic Investigations

In situ monitoring of reaction progress

Preparation of stock solutions

$Ni(cod)_2$ (0.025 M): Stock solution of $Ni(cod)_2$ was prepared by dissolving 13.7 mg $Ni(cod)_2$ in NMP in a 2.0 mL volumetric flask.

p-FC_6H_4ZnI (0.5 M): 500 µL of the *p*-FC_6H_4ZnI solution (1.0 M) in THF was transferred to the 1.0 ml volumetric flask and THF was removed under vacuum. The remaining residue was then dissolved in NMP to make the volume 1.0 mL.

CuI/*p*-FC_6H_4ZnI (0.05 M/0.5 M): 500 µL of the *p*-FC_6H_4ZnI solution (1.0 M) in THF was transferred to the 1.0 mL volumetric flask and the THF was removed under vacuum. To this volumetric flask, 9.5 mg CuI was weighed. The mixture was then dissolved in NMP to make the volume to 1.0 mL.

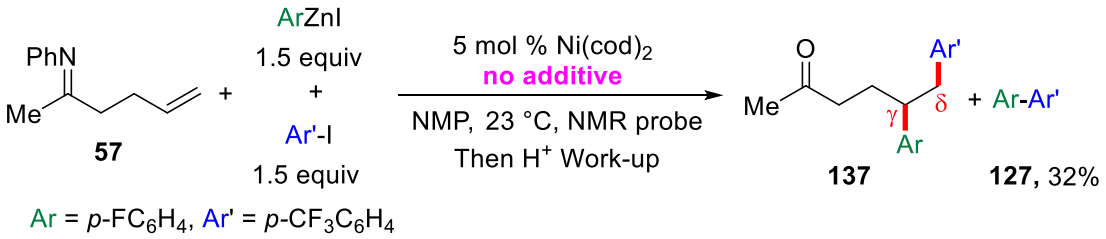
p-$CF_3C_6H_4I$ (0.75 M): 204 mg *p*-$CF_3C_6H_4I$ was weighed in a 1.0 mL volumetric flask and was dissolved in NMP to make the volume to 1.0 mL.

N-Phenylhex-5-en-2-imine (1.0 M): 173.2 mg ketimine was weighed in a 1.0 ml volumetric flask and was dissolved in NMP to make the volume to 1.0 mL.

Benzotrifluoride, Internal standard (0.2 M): 29.2 mg benzotrifluoride was weighed in a 1.0 mL volumetric flask and was dissolved in NMP to make the volume to 1.0 mL.

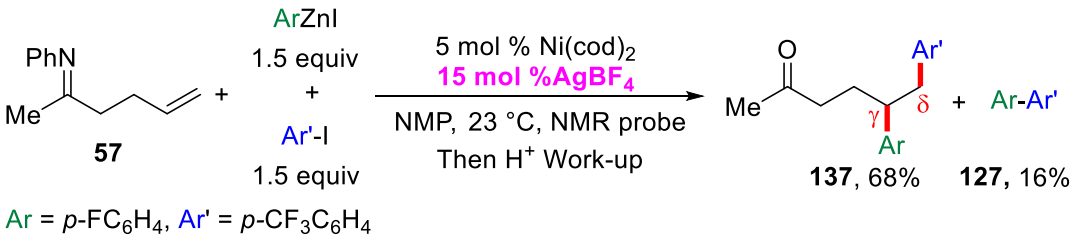
$AgBF_4$ (0.75 M): 29.2 mg $AgBF_4$ was weighed in a 1.0 mL volumetric flask and was dissolved in NMP to make the volume to 1.0 mL.

Reaction of ketimine 57 with *p*-$CF_3C_6H_4I$ and *p*-FC_6H_4ZnI without additives



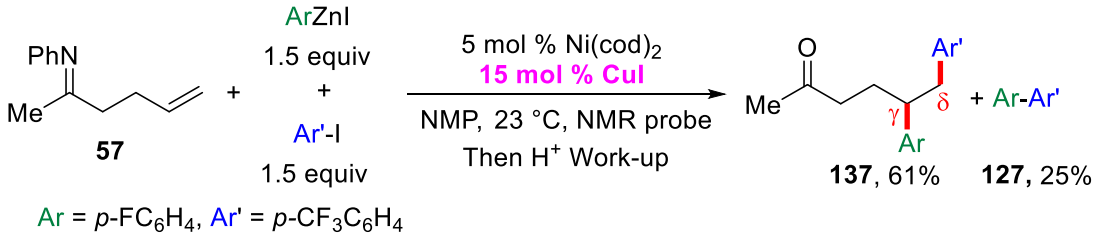
In a glovebox, 300 µl *p*-FC_6H_4ZnI (0.15 mmol), 200 µl *p*-$CF_3C_6H_4I$ (0.15 mmol), 100 µL *N*-Phenylhex-5-en-2-imine (0.1 mmol), 100 µL internal standard and 100 µl NMP were added to screw cap NMR tube from their stock solutions. NMR tube was tightly capped and taken outside the glovebox. ^{19}F-NMR was acquired. 200 µl of $Ni(cod)_2$ (0.005 mmol) was added to the reaction mixture in the NMR tube. The NMR tube was quickly mixed by shaking and ^{19}F-NMR was acquired in an array setup. After the reaction was complete, NMR tube was ejected from NMR probe and immediately quenched with 1 mL of 6N HCl solution. The reaction mixture was then transferred to a vial and extracted with EtOAc (1 mL × 3). EtOAc extract was dried over anhydrous Na_2SO_4. EtOAc was removed and 50 µl freshly prepared pyrene solution (0.2 M in $CDCl_3$) as an internal standard was added to the residue. NMR sample was prepared in $CDCl_3$ and proton NMR spectrum was acquired. The yield was determined by integrating a product peak at 2.9 ppm and direct cross-coupled product at 7.7 ppm against the pyrene peak at 8.06 ppm.

Reaction of ketimine 57 with *p*-$CF_3C_6H_4I$ and *p*-FC_6H_4ZnI in the presence of $AgBF_4$



The procedure for this experiment is same as above but 100 µl $AgBF_4$ solution (0.015 mmol) was added from the stock solution instead of adding 100 µl NMP.

Reaction of ketimine 57 with *p*-$CF_3C_6H_4I$ and *p*-FC_6H_4ZnI in the presence of CuI



The procedure for this experiment is same as above but 300 µl CuI/ *p*-FC_6H_4ZnI solution (0.015 mmol/ 0.15 mmol) was added from the stock solution instead of adding 300 µl *p*-FC_6H_4ZnI.

Table 5.23. Yields of **137** in the experiments with and without co-catalysts at different time intervals

Time (s)	% yield of **137**	% yield of **137**	% yield of **137**

	(no Ag/Cu)	($AgBF_4$)	(CuI)
0.0000	0.0000	0.0000	0.0000
180.00	3.3824	16.032	6.1010
360.00	6.7824	33.635	12.515
540.00	9.6755	49.341	26.920
720.00	12.312	58.225	40.124
900.00	14.766	62.692	49.104
1080.0	16.855	64.550	54.731
1260.0	18.727	65.531	57.909
1440.0	20.475	65.968	59.613
1620.0	22.073	66.347	60.431
1800.0	23.316	67.288	61.010
1980.0	24.539	68.000	61.000
2160.0	25.268		
2340.0	26.255		
2520.0	26.843		
2700.0	27.376		
2880.0	27.920		
3060.0	28.245		

3240.0	28.615
3420.0	28.920
3600.0	29.000

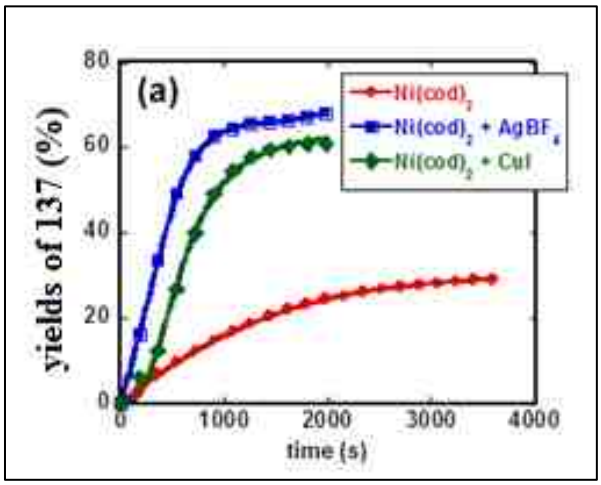


Figure (a): Reaction profiles with and without $AgBF_4$ and CuI. Blue: with $AgBF_4$; green: with CuI; red: without $AgBF_4$ or CuI

Table 5.24. Yields of **137** and **127** in the experiment with and without $AgBF_4$ at different time intervals

Time (s)	% yield of **137** (no $AgBF_4$)	% yield of **137** ($AgBF_4$)	% yield of **127** (no $AgBF_4$)	% yield of **127** ($AgBF_4$)
0.0000	0.0000	0.0000	0.0000	0.0000
180.00	3.3824	16.032	3.4840	3.6478

360.00	6.7824	33.635	7.4840	7.9141
540.00	9.6755	49.341	10.676	11.610
720.00	12.312	58.225	13.585	13.700
900.00	14.766	62.692	16.294	14.751
1080.0	16.855	64.550	18.599	15.188
1260.0	18.727	65.531	20.664	15.419
1440.0	20.475	65.968	22.593	15.522
1620.0	22.073	66.347	24.357	15.611
1800.0	23.316	67.288	25.728	15.832
1980.0	24.539	68.000	27.078	16.000
2160.0	25.268		27.882	
2340.0	26.255		28.971	
2520.0	26.843		29.619	
2700.0	27.376		30.208	
2880.0	27.920		30.809	
3060.0	28.245		31.167	
3240.0	28.615		31.575	
3420.0	28.920		31.911	
3600.0	29.000		32.000	

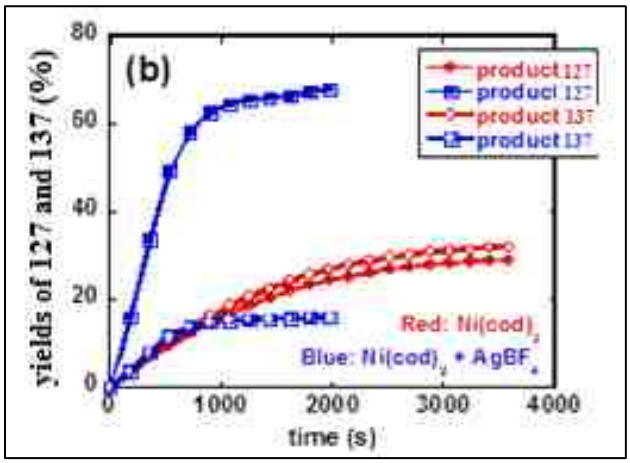


Figure (b). Comparison of reaction rates for the formation of diarylation product **137** and biaryl side product **127** by cross-coupling in the presence and absence of $AgBF_4$. Blue: with $AgBF_4$; red: without $AgBF_4$; hollow square and circle: cross-coupling (**127**); solid square and circle: alkene diarylation (**137**).

Table 5.25. Yields of **137** and **137** in the experiment with and without CuI at different time intervals

Time (s)	% yield of **137** (no CuI)	% yield of **137** (CuI)	% yield of **127** (no CuI)	% yield of **127** (CuI)
0.0000	0.0000	0.0000	0.0000	0.0000
180.00	3.3824	6.1010	3.4840	2.5004
360.00	6.7824	12.515	7.4840	5.1291

540.00	9.6755	26.920	10.676	11.033
720.00	12.312	40.124	13.585	16.444
900.00	14.766	49.104	16.294	20.125
1080.0	16.855	54.731	18.599	22.431
1260.0	18.727	57.909	20.664	23.733
1440.0	20.475	59.613	22.593	24.432
1620.0	22.073	60.431	24.357	24.767
1800.0	23.316	61.010	25.728	25.004
1980.0	24.539	61.000	27.078	25.000
2160.0	25.268		27.882	
2340.0	26.255		28.971	
2520.0	26.843		29.619	
2700.0	27.376		30.208	
2880.0	27.920		30.809	
3060.0	28.245		31.167	
3240.0	28.615		31.575	
3420.0	28.920		31.911	
3600.0	29.000		32.000	

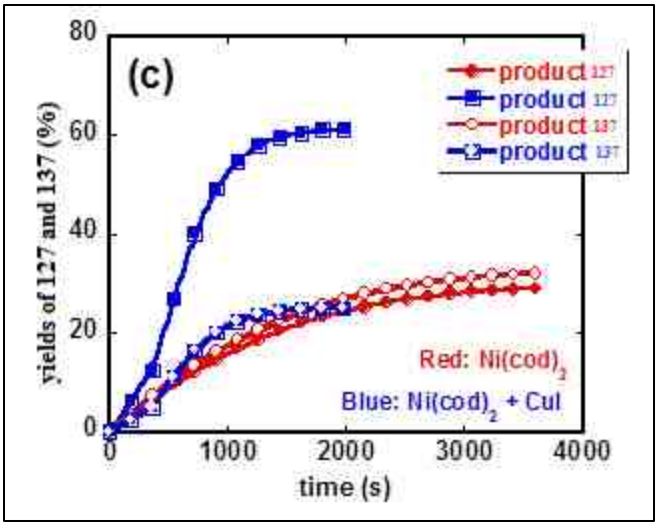
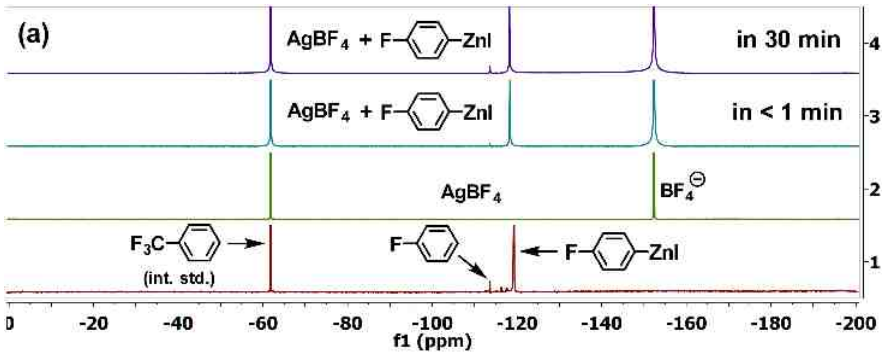


Figure (c): Comparison of reaction rates for the formation of diarylation product **137** and biaryl side product **127** by cross-coupling in the presence and absence of CuI. Blue: with CuI; red: without CuI; hollow square and circle: cross-coupling (**127**); solid square and circle: alkene diarylation (**137**).

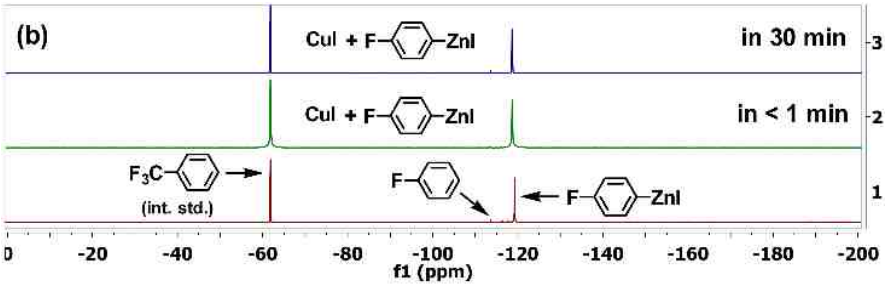
Reactions between *p*-FC_6H_4ZnI and $AgBF_4$

In a glovebox, 50 µl $AgBF_4$ (1.0 M solution in NMP) and 20 µl benzotrifluoride (1.0 M solution in NMP), as an internal standard was taken in a NMR tube with septum screw cap. 830 µl NMP was added and thoroughly mixed. The NMR tube was tightly capped and taken outside the glovebox. ^{19}F-NMR was acquired. NMR sample was then ejected and 100 µl *p*-FC_6H_4ZnI (0.5 M in NMP) was added quickly using nitrogen flushed microliter syringe from the stock solution in the 1-dram vial capped airtightly. The reaction was mixed and immediately injected to the NMR probe and obtain the ^{19}F-NMR spectrum. ^{19}F-NMR spectrum was also obtained after 30 min.

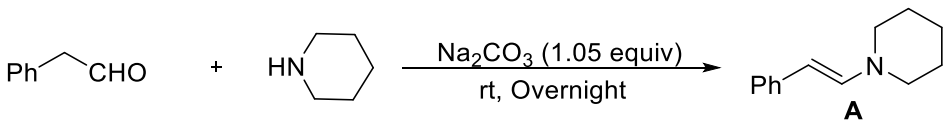


Reactions between *p*-FC_6H_4ZnI and CuI

The procedure for this experiment is same as above but, 9.5 mg CuI was weighed in the vial and transferred to the NMR tube as a suspension in NMP instead of 50 µl $AgBF_4$ solution.

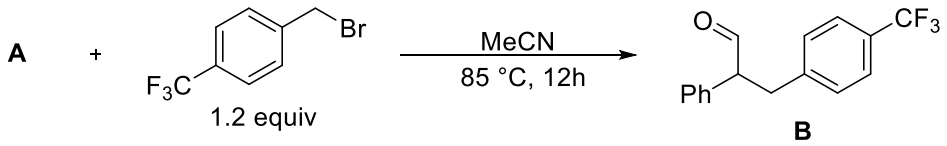


Synthesis of standard Product 129 and conformation of regioselectivity



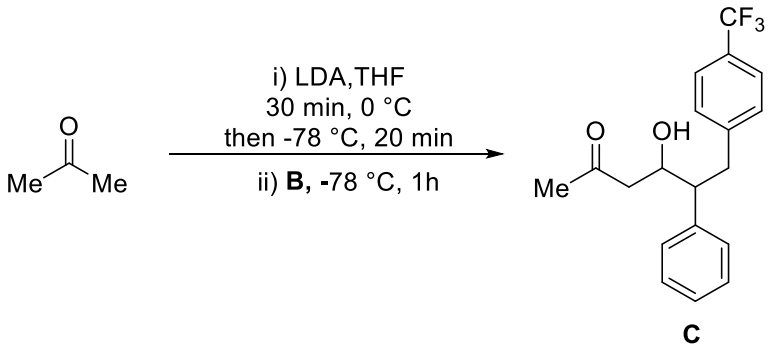
A was synthesized following literature procedure as follows.[177] The mixture of Na_2CO_3 (1.1 g, 10 mmol) and piperidine (7 ml) in a 25 ml R.B flask was cooled in an ice-bath with

stirring for 15 minutes. Phenylacetaldehyde was then added dropwise into the cooled mixture. The reaction was left stirring at room temperature for 8 h. The reaction mixture was filtered and excess piperidine was removed by using rotavapor at higher temperature below the boiling point of piperidine resulting yellow liquid (1.6 g, 85%) which was used in the next step. ^{1}H NMR spectra was consistent with the literature.[177]



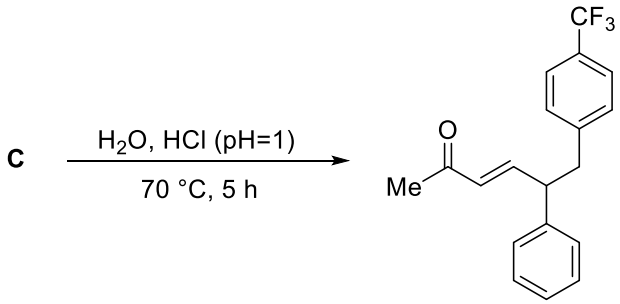
The enamine was used to prepare **B** following literature procedure.[178] In a 100 ml sealed tube, **A** (936 mg, 5 mmol) was dissolved in MeCN (50 ml) together with 1-(bromomethyl)-4-(trifluoromethyl) benzene (1434 mg, 6 mmol) under nitrogen atmosphere. The sealed tube was capped tightly, and the mixture was heated at 85 °C for 12 h. Then it was cooled at room temperature. 10 ml 1M HCl was added to the reaction mixture and stirred for 1 h. The mixture was then extracted with DCM (15 ml × 3). DCM extract was dried over Na_2SO_4, concentrated under vacuum in rotavapor and the crude was purified by column chromatography to get colorless liquid (946 mg, 68%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.01 (dd, *J* = 8.1 Hz, 13.8 Hz, 1H), 3.52 (dd, *J* = 6.3 Hz, 14.1 Hz, 1H), 3.83 (t, *J* = 7.4 Hz, 1H), 7.10-2.16 (m, 4H), 7.28-7.38 (m, 3H), 7.46 (d, *J* = 7.8 Hz, 1H); **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.0.



C

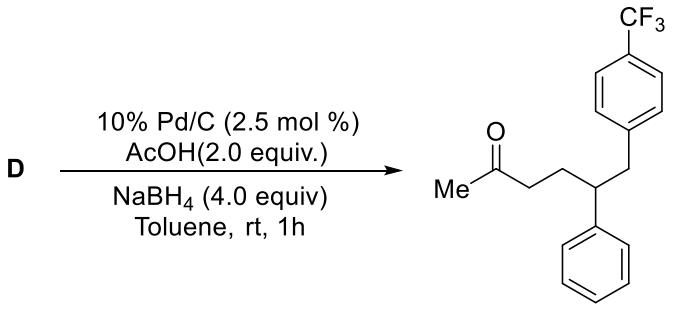
C was prepared following literature procedure using **B**.[179] LDA was prepared by adding *n*BuLi (1.56 ml, 2.5 mmol) in Diisoproyl amine (0.38 ml, 2.5 mmol) solution in THF (5 mL) at 0 °C and stirred the mixture for 30 minutes. The solution was cooled to -78 °C and to this solution, acetone (0.18 ml, 2.5 mmol) was added dropwise and was stirred for 20 minutes. The enolate solution formed was then treated with **B** and the mixture was stirred for 1h at -78 °C. Then, solvent was removed by rotavapor and the remaining was dissolved in ether and was treated with 0.5 ml conc. HCl. The mixture was then extracted with ether (5ml × 3). The ether extract was dried over Na_2SO_4. Solvent was removed, and the crude (681 mg, 81%) was used for the next step without further purification.



D

D was prepared following literature procedure.[180] The equal volume of water with β-Ketol **C** (672 mg, 2.0 mmol) was added to the substrate and the resulting emulsion was treated with conc. HCl to pH 1. The mixture was then stirred vigorously at 70 °C for 5 h. The

reaction mixture was extracted with diethyl ether (10 ml × 3) and the extract was washed with water (10 ml), saturated $NaHCO_3$ (10 ml). The ether layer was then dried over Na_2SO_4 and concentrated in vacuum to get **D** (503 mg, 79%) which was used in the next step without further purification.



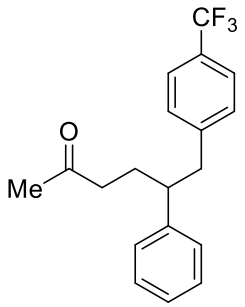
126

11 was prepared by reducing **D** following literature procedure.[181] In a 25 ml R.B flask, 10% Pd/C (40.5 mg, 0.0375 mmol), **D** (477 mg, 1.5 mmol) and toluene (7 ml) were added and the mixture was stirred at room temperature. To the reaction mixture, acetic acid (0.16 ml, 3 mmol) was added in one portion. Powder of $NaBH_4$ (225 mg, 6 mmol) was also added in one portion and the reaction mixture was left stirring at room temperature for 1h. The mixture was quenched with 0.1 M of HCl until the hydrogen gas evolution stops. The reaction mixture was treated with $NaHCO_3$ to make the solution basic. Then, the mixture was extracted with diethyl ether (5 ml × 3). The ether layer was dried over Na_2SO_4 and purified by column chromatography to get the desired product **126** as a colorless oil in (360.4 mg, 75%) yield.

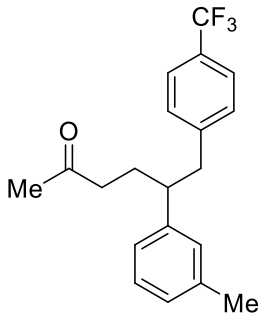
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.86-1.92 (m, 1H), 2.00 (s, 3H), 2.01-2.07 (m,1H), 2.24-2.28 (m, 2H), 2.80-2.85 (m, 1H), 2.92-3.00 (m, 2H), 7.08 (d, *J* = 5.0 Hz, 2H), 7.12 (d, *J* = 5.0 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.45 (d, *J* = 5.0 Hz, 2H) ;

^{13}C NMR (126 MHz, $CDCl_3$): δ 29.4, 30.1, 41.6, 43.8, 47.2, 124.4 (q, J_{CF} = 270.9 Hz), 125.1 (q, J_{CF} = 3.8 Hz), 126.8, 127.8, 128.3 (q, J_{CF} = 31.5 Hz), 128.7, 129.5, 143.3, 144.5, 208.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.9 ; **IR (neat):** 3028, 1713, 1321, 1159, 1107, 1065 ; **HRMS (ESI):** Calcd for $C_{19}H_{19}F_3NaO$ $(M+Na)^+$ 343.1286 found 343.1289.

5.3.4. Characterization Data for New Compounds

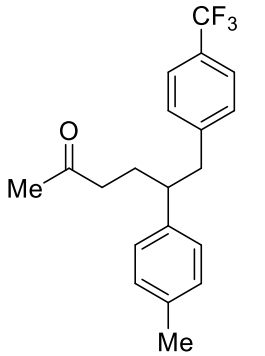


*5-(3-Chlorophenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**126**):*The title compound **126** was obtained as a colorless oil (121.7 mg, 76% in 0.5 mmol scale) and (461.3 mg, 72% in 2.0 mmol scale) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.41 (hexanes : ether = 3:2). This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (117 mg, 73%). The characterization data is consistent with the independently synthesized compound above.



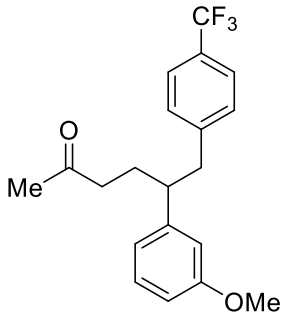
*5-(m-Tolyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**129**)* : The title compound **129** was obtained as a yellow oil (110.3 mg, 66% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.38 (hexanes : ether = 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78-1.91 (m, 1H), 1.94-2.05 (m, 1H), 2.00 (s, 3H), 2.25 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 2.72- 2.82 (m, 1H), 2.94 (d, *J* = 6.0 Hz, 2H), 6.86- 6.88 (m, 2H), 7.02 (d, *J* = 9.0 Hz, 1H), 7.14 (t, *J* = 6.0 Hz, 3H), 7.45 (d, *J* = 6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 21.6, 29.3, 30.1, 41.7, 43.8, 47.1, 124.5 (q, J_{CF} = 270.0 Hz), 124.8, 125.1 (q, J_{CF} = 3.8 Hz), 127.5, 128.5, 129.1 (q, J_{CF} = 30.0 Hz), 129.5, 138.2, 143.4, 144.6, 208.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.7 ; **IR (neat):** 2926, 1714, 1321, 1159, 1108, 1065 ; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO$ $(M+Na)^+$ 357.1442, found 357.1450.



*5-(p-Tolyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**130**)*: The title compound **130** was obtained as a yellow oil (101.9 mg, 61% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f =0.42 (hexanes : ether = 1:1).

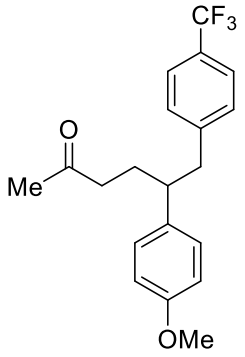
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.81-1.89 (m, 1H), 1.95-2.05 (m, 1H), 2.00 (s, 3H), 2.24 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 2.75- 2.82 (m, 1H), 2.93 (d, *J* = 9.0 Hz, 2H), 6.95 (d, *J* = 6.0 Hz, 2H), 7.06-7.13 (m, 4H), 7.44 (d, *J* = 6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 21.2, 29.5, 30.1, 41.7, 43.9, 46.7, 124.5 (q, J_{CF} = 273.8 Hz), 125.2 (q, J_{CF} = 3.8 Hz), 127.8, 128.8 (q, J_{CF} = 39.0 Hz), 129.4, 129.5, 136.3, 140.3, 144.6, 208.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.3 ; **IR (neat):** 2923, 1714, 1495, 1323, 1120, 1066 ; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO$ $(M+Na)^+$ 357.1442, found 357.1442.



*5-(3-Methoxyphenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**131**)*: The title compound **131** was obtained as a colorless oil (105.1 mg, 60% yield) after purification by silica gel column chromatography(hexanes : ether = 10:1). R_f = 0.55 (hexanes : ether 1:1).

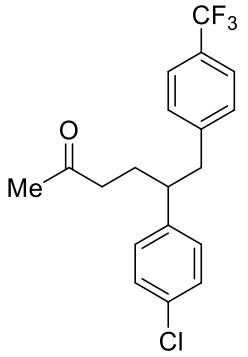
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.82-1.88 (m, 1H), 1.97-2.03 (m, 1H), 2.00 (s, 3H), 2.26 (t, *J* = 7.5 Hz, 2H), 2.76-2.81 (m, 1H), 2.93 (dd, *J* = 5.0 Hz, 10.0 Hz, 2H), 3.76 (s, 3H), 6.59 (s, 1H), 6.66 (d, *J* = 10.0 Hz, 1H), 6.74 (dd, *J* = 5.0 Hz, 10.0 Hz, 1H), 7.12 (d, *J* = 10.0 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 10.0 Hz, 2H); **^{13}C NMR (75 MHz,**

$CDCl_3$): δ 29.3, 30.1, 41.6, 43.8, 47.2, 55.3, 111.7, 113.8, 120.2, 124.5 (q, J_{CF} = 272.2 Hz), 125.2 (q, J_{CF} = 3.8 Hz), 128.4 (q, J_{CF} = 31.5 Hz), 129.5, 129.7, 144.4, 145.1, 159.9, 208.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.1 ; **IR (neat):** 2938, 1713, 1321, 1257, 1108, 1065 ; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO_2$ $(M+Na)^+$ 373.1391, found 373.1400.



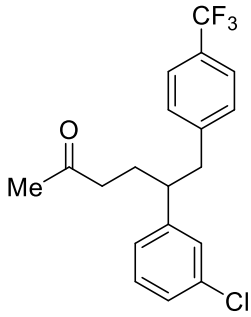
5-(4-Methoxyphenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one ***(132)***: The title compound **132** was obtained as a yellow oil (98.1 mg, 56% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.56 (hexanes : ether 1:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.78-1.86 (m, 1H), 1.96-2.04 (m,1H), 2.00 (s, 3H), 2.22-2.26 (m, 2H), 2.74-2.79 (m, 1H), 2.86-2.96 (m, 2H), 3.78 (s, 3H), 6.80 (d, *J* = 10.0 Hz, 2H), 6.96 (d, *J* = 10.0 Hz, 2H), 7.09 (d, *J* = 10.0 Hz, 2H), 7.43 (d, *J* = 10.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 29.6, 30.1, 41.7, 44.0, 46.4, 55.3, 114.0, 124.5 (q, J_{CF} = 272.2 Hz), 125.1 (q, J_{CF} = 3.8 Hz), 128.3 (q, J_{CF} = 32.8 Hz), 128.7, 129.5, 135.2, 144.6, 158.3, 208.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.1 ; **IR (neat):** 2933, 1713, 1611, 1510, 1322, 1245 ; **HRMS (ESI):** Calcd for $C_{20}H_{21}F_3NaO_2$ $(M+Na)^+$ 373.1391, found 373.1402.



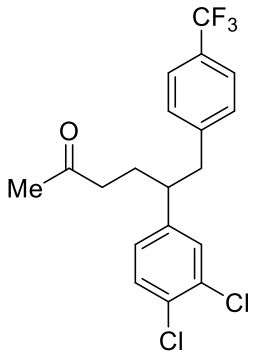
*5-(4-Chlorophenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**133**)*: The title compound **133** was obtained as a yellow oil (131.2 mg, 74% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.42 (hexanes : ether = 7:3). This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (122.4 mg, 69%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.79-1.88 (m, 1H), 1.99-2.06 (m, 1H), 2.01 (s, 3H), 2.22-2.26 (m, 2H), 2.80- 2.89 (m, 2H), 2.94-2.98 (m, 1H), 6.98 (d, *J* = 10.0 Hz, 2H), 7.08 (d, *J* = 10.0 Hz, 2H), 7.23 (d, *J* = 10.0 Hz, 2H), 7.44 (d, *J* = 10.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 29.4, 30.2, 41.5, 43.8, 46.6, 124.4 (q, J_{CF} = 272.2 Hz), 125.3 (q, J_{CF} = 3.8 Hz), 128.5 (q, J_{CF} = 29.0 Hz), 128.9, 129.2, 129.5, 132.5, 141.8, 144.0, 208.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.3 ; **IR (neat):** 2931, 1714, 1322, 1160, 1118, 1065 ; **HRMS (ESI):** Calcd for $C_{19}H_{18}ClF_3NaO$ $(M+Na)^+$ 377.0896, found 377.0886.



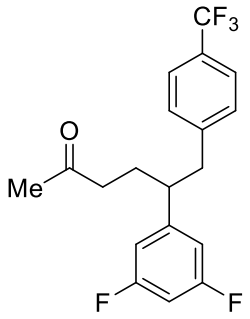
*5-(3-Chlorophenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**134**)*: The title compound **134** was obtained as a yellow oil (120.6 mg, 68% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.39 (hexanes : ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.76-1.89 (m, 1H), 1.96-2.08 (m,1H), 2.02 (s, 3H), 2.25 (t, *J* = 7.5 Hz, 2H), 2.78-2.86 (m, 1H), 2.90-3.00 (m, 2H), 6.92 (t, *J* = 3.0 Hz, 1H), 7.08 (d, *J* = 6.0 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 2H), 7.18-7.19 (m, 2H), 7.46 (d, *J* = 9.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 29.3, 30.1, 41.4, 43.6, 47.0, 124.3 (q, J_{CF} = 259.5 Hz), 125.3 (q, J_{CF} = 3.8 Hz), 126.2, 127.1, 127.8, 128.6 (q, J_{CF} = 32.3 Hz), 129.5, 130.0, 134.6, 143.9, 145.6, 208.2 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.2 ; **IR (neat):** 2929, 1713, 1322, 1160, 1109, 1065; **HRMS (ESI):** Calcd for $C_{19}H_{18}ClF_3NaO$ $(M+Na)^+$ 377.0896, found 377.0897.



*5-(3,4-Dichlorophenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**135**)*: The title compound **135** was obtained as a yellow oil (118.7 mg, 61% yield) after purification by silica gel column chromatography (hexanes : ether = 8:1). R_f = 0.39 (hexanes : ether = 7:3).

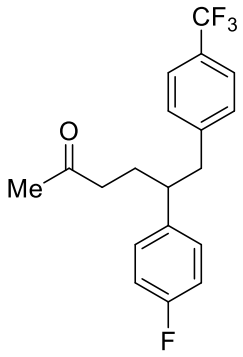
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.77-1.84 (m, 1H), 2.0-2.06 (m, 1H), 2.03 (s, 3H), 2.25 (t, *J* = 7.5 Hz, 2H), 2.81-2.98 (m, 3H), 6.88 (dd, *J* = 10.0 Hz, 5.0 Hz, 1H), 7.10 (d, *J* = 10.0 Hz, 2H), 7.16 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 29.2, 30.1, 41.3, 43.5, 46.4, 124.3 (q, J_{CF} = 272.2 Hz), 125.4 (q, J_{CF} = 3.8 Hz), 127.3, 128.7 (q, J_{CF} = 31.5 Hz), 129.4, 129.6, 130.7, 130.7, 132.8, 143.6, 143.8, 208.0 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.2 ; **IR (neat):** 2932, 1714, 1321, 1160, 1107, 1065 ; **HRMS (ESI):** Calcd for $C_{19}H_{17}Cl_2F_3NaO$ $(M+Na)^+$ 411.0506, found 411.0502.



5-(3,5-Difluorophenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one ***(136)***: The title compound **136** was obtained as a colorless oil (126.5 mg, 71% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.35 (hexanes : ether = 7:3).

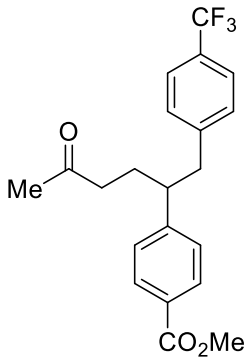
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74-1.86 (m, 1H), 1.97-2.08 (m,1H), 2.03 (s, 3H), 2.26 (t, *J* = 7.5 Hz, 2H), 2.83-2.97 (m, 3H), 6.57-6.68 (m, 3H), 7.12 (d, *J* = 9.0 Hz, 2H), 7.46 (d, *J* = 6.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 29.3, 30.1, 41.2, 43.4, 47.0, 102.3 (t, J_{CF} = 24.8 Hz), 110.6 (dd, J_{CF} = 7.5, 16.5 Hz), 124.3 (q, J_{CF} = 270.8), 125.4 (q, J_{CF} =

3.8 Hz), 128.8 (q, J_{CF} = 32.3 Hz), 129.4, 143.5, 147.7, 163.3 (dd, J_{CF} = 12.8, 247.5 Hz), 208.0 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -109.5, -62.4 ; **IR (neat):** 2927, 1713, 1493, 1323, 1120, 1068 ; **HRMS (ESI):** Calcd for $C_{19}H_{17}F_5NaO$ $(M+Na)^+$ 379.1097, found 379.1099.



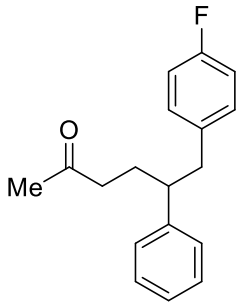
*5-(4-Fluorophenyl)-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**137**)*: The title compound **137** was obtained as a colorless oil (110.0 mg, 65% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.39 (hexanes : ether = 7:3). This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (96.4 mg, 57%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79-1.90 (m, 1H), 1.99-2.10 (m, 1H), 2.01 (s, 3H), 2.22-2.27 (m, 2H), 2.78-3.00 (m, 3H), 6.92-7.02 (m, 4H), 7.08 (d, *J* = 9.0 Hz, 2H), 7.44 (d, *J* = 9.0 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):** 29.6, 30.1, 41.5, 43.9, 46.5, 115.5 (d, J_{CF} = 21.0 Hz), 124.4 (J_{CF} = 267.0 Hz), 125.2 (q, J_{CF} = 3.0 Hz), 128.5 (q, J_{CF} = 33.0 Hz), 129.1, (d, J_{CF} = 7.5 Hz), 129.5, 138.9, 144.2 161.7 (d, J_{CF} = 243.0 Hz), 208.4 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -115.03, -61.1 ; **IR (neat):** 2930, 1714, 1508, 1322, 1158, 1109 ; **HRMS (ESI):** Calcd for $C_{19}H_{18}F_4NaO$ $(M+Na)^+$ 361.1191, found 361.1198.



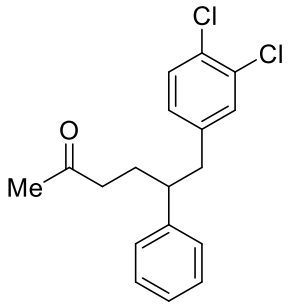
*Methyl 4-(5-oxo-1-(4-(trifluoromethyl)phenyl)hexan-2-yl)benzoate (**138**)*: The title compound **138** was obtained as a yellow oil (92.7 mg, 49% yield) after purification by silica gel column chromatography (hexanes : ether = 5:1). R_f = 0.43 (hexanes : ether = 1:1)

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84-1.94 (m, 1H), 1.99 (s, 3H), 1.99-2.11 (m, 1H), 2.20-2.26 (m, 2H), 2.87-3.01 (m, 3H), 3.88 (s, 3H), 7.07 (d, *J* = 6.0 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 7.42 (d, *J* = 9.0 Hz, 2H), 7.93 (d, *J* = 9.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.3, 30.1, 41.3, 43.5, 47.2, 52.1, 124.3 (q, J_{CF} = 270.0 Hz), 125.2 (q, J_{CF} = 4.5 Hz), 127.9, 128.5 (q, J_{CF} = 32.3 Hz), 128.8, 129.4, 130.0, 143.8, 148.8, 167.0, 208.2; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.0 ; **IR (neat):** 2950, 1714, 1322, 1277, 1102, 1065 ; **HRMS (ESI):** Calcd for $C_{21}H_{21}F_3NaO_3$ $(M+Na)^+$ 401.1340, found 401.1348.



*6-(4-Fluorophenyl)-5-phenylhexan-2-one (**139**)*: The title compound **139** was obtained as a colorless oil (71.6 mg, 53% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.42 (hexanes : ether = 1:1).

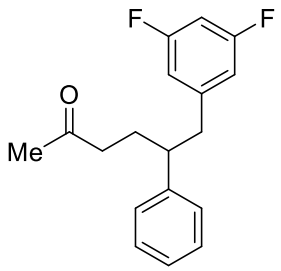
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.82-1.88 (m, 1H), 1.98-2.05 (m, 1H), 1.99 (s, 3H), 2.22-2.26 (m, 2H), 2.72- 2.78 (m, 1H), 2.82-2.90 (m, 2H), 6.86 (t, *J* = 7.5 Hz, 2H), 6.93-6.96 (m, 2H), 7.06 (d, *J* = 5.0 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 29.3, 30.1, 41.8, 43.2, 47.6, 114.9 (d, J_{CF} = 21.4 Hz), 126.6, 127.9, 128.6, 130.5, 130.6, 143.8, 161.4 (d, J_{CF} = 243.2 Hz), 208.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -117.5 ; **IR (neat):** 2924, 1712, 1508, 1416, 1218, 1124 ; **HRMS (ESI):** Calcd for $C_{18}H_{19}FNaO$ $(M+Na)^+$ 293.1318, found 293.1320.



*6-(3,4-Dichlorophenyl)-5-phenylhexan-2-one (**140**)*: The title compound **140** was obtained as a yellow oil (107.6 mg, 67% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.30 (hexanes : ether = 7:3).

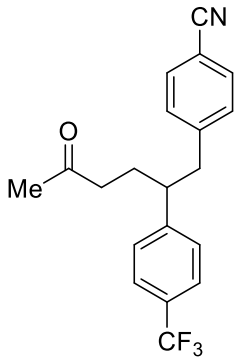
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78-1.92 (m, 1H), 1.95-2.08 (m, 1H), 2.00 (s, 3H), 2.22-2.27 (m, 2H), 2.73- 2.88 (m, 3H), 6.79 (dd, *J* = 3.0 Hz, 9.0 Hz, 1H), 7.03-7.06 (m, 2H), 7.09 (d, *J* = 3.0 Hz, 1H), 7.19-7.28 (m, 4H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.3, 30.1,

41.6, 43.1, 47.1, 126.8, 127.8, 128.6, 128.7, 129.9, 130.0, 131.0, 132.0, 140.6, 143.1, 208.6 ; **IR (neat):** 2927, 1712, 1493, 1395, 1131, 1029 ; **HRMS (ESI):** Calcd for $C_{18}H_{19}Cl_2O$ $(M+H)^+$ 321.0813, found 321.0808.



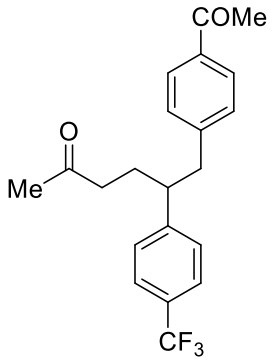
*6-(3,5-Difluorophenyl)-5-phenylhexan-2-one (**141**)*: The title compound **141** was obtained as a colorless oil (93.7 mg, 65% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.40 (hexanes : ether = 1:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.81-1.91 (m, 1H), 1.97-2.07 (m, 1H), 2.00 (s, 3H), 2.22-2.27 (m, 2H), 2.75-2.91 (m, 3H), 6.50-6.61 (m, 3H), 7.06 (d, *J* = 9.0 Hz, 2H), 7.17-7.30 (m, 3H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 29.4, 30.1, 41.6, 43.8, 47.0, 101.6 (d, J_{CF} = 31.5 Hz), 111.9 (dd, J_{CF} = 7.1 Hz, 16.5 Hz), 126.9, 127.8, 128.7, 143.1, 144.3 (t, J_{CF} = 9.0 Hz), 162.9 (dd, J_{CF} = 12.8 Hz, 246.0 Hz), 208.6 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -110.9 ; **IR (neat):** 2930, 1713, 1593, 1452, 1321,1114; **HRMS (ESI):** Calcd for $C_{18}H_{18}F_2NaO$ $(M+Na)^+$ 311.1223, found 311.1227.



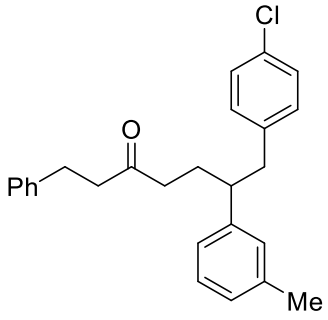
*4-(5-Oxo-2-(4-(trifluoromethyl)phenyl)hexyl)benzonitrile (**142**)*: The title compound **142** was obtained as a yellow oil (96.7 mg, 56% yield) after purification by silica gel column chromatography (hexanes : ether = 4:1). R_f = 0.38 (hexanes : ether = 1:1). This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (103.6 mg, 60%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.83-1.92 (m, 1H), 2.02 (s, 3H), 2.03-2.12 (m, 1H), 2.22-2.27 (m, 2H), 2.86-3.06 (m, 3H), 7.08 (d, *J* = 9.0 Hz, 2H), 7.15 (d, *J* = 9.0 Hz, 2H), 7.46-7.53 (m, 4H),; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.3, 30.2, 41.2, 43.8, 46.9, 110.3, 119.0, 124.3 (q, J_{CF} = 272.2 Hz), 125.7 (q, J_{CF} = 3.8 Hz), 128.1, 129.3 (q, J_{CF} = 32.8 Hz), 129.9, 132.2, 145.3, 147.2, 208.1; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.7 ; **IR (neat):** 2927, 2227, 1713, 1617, 1322, 1109 ; **HRMS (ESI):** Calcd for $C_{20}H_{18}F_3NNaO$ $(M+Na)^+$ 368.1238, found 368.1247.



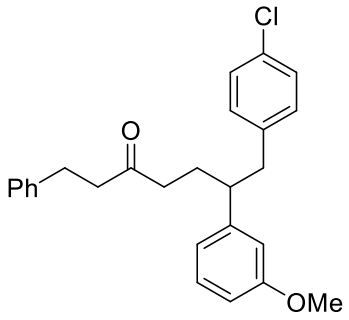
*6-(4-Acetylphenyl)-5-(4-(trifluoromethyl)phenyl)hexan-2-one (**143**)*: The title compound **143** was obtained as a yellow oil (94.2 mg, 52% yield) after purification by silica gel column chromatography (hexanes : ether = 5:1). R_f = 0.56 (hexanes : ether = 1:4) This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (105.1 mg, 58%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.86-1.94 (m, 1H), 2.01 (s, 3H), 2.03-2.09 (m, 1H), 2.21-2.27 (m, 2H), 2.54 (s, 3H), 2.90-3.02 (m, 3H), 7.08 (d, *J* = 9.0 Hz, 2H), 7.17 (d, *J* = 9.0 Hz, 2H), 7.51 (d, *J* = 9.0 Hz, 2H) 7.79 (d, *J* = 9.0 Hz, 2H),; **^{13}C NMR (75 MHz, $CDCl_3$):** 26.7, 29.3, 30.1, 41.4, 43.7, 47.0, 124.3 (q, J_{CF} = 272.2 Hz), 125.6 (q, J_{CF} = 3.8 Hz), 128.2, 128.5, 129.1 (q, J_{CF} = 32.8 Hz), 129.5, 135.4, 145.4, 147.7, 197.9, 208.2 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.4 ; **IR (neat):** 2931, 1715, 1681, 1325, 1162, 1069 ; **HRMS (ESI):** Calcd for $C_{21}H_{22}F_3NaO_2$ $(M+Na)^+$ 363.1572 found 363.1562.



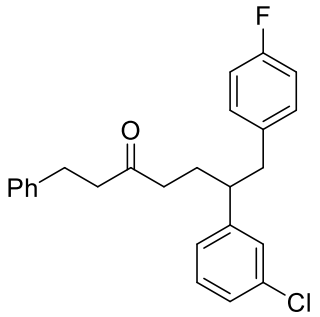
*7-(4-Chlorophenyl)-1-phenyl-6-(m-tolyl)heptan-3-one (**144**)*: The title compound **144** was obtained as a colorless oil (127.1 mg, 65 % yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.63 (hexanes : ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.76-1.87 (m, 1H), 1.94- 2.00 (m, 1H), 2.18 (t, *J* = 7.5 Hz, 2H), 2.30 (s, 3H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.66-2.74 (m, 1H), 2.77-2.89 (m, 4H), 6.83 (d, *J* = 6.0 Hz, 2H), 6.94 (d, *J* = 9.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 1H), 7.09-7.20 (m, 6H), 7.22-7.28 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 21.6, 29.2, 29.8, 41.0, 43.3, 44.4, 47.2, 124.9, 126.2, 127.4, 128.3, 128.4, 128.5, 128.6, 130.6, 131.7, 138.1, 138.9, 141.2, 143.6, 209.9 ; **IR (neat):** 2923, 1711, 1490, 1370, 1091, 1014 ; **HRMS (ESI):** Calcd for $C_{26}H_{27}ClNaO$ $(M+Na)^+$ 413.1648, found 413.1658.



*7-(4-Chlorophenyl)-6-(3-methoxyphenyl)-1-phenylheptan-3-one (**145**)*: The title compound **145** was obtained as a white solid (136.3 mg, 67% yield after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.60 (hexanes : ether = 1:1). This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (144.5 mg, 71%).

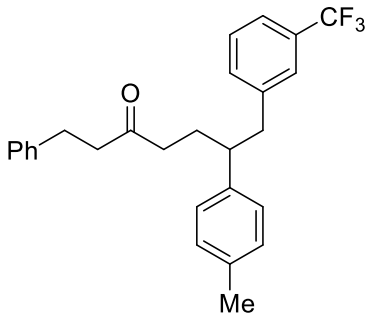
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.76-1.89 (m, 1H), 1.94- 2.07 (m, 1H), 2.22 (t, *J* = 7.5 Hz, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 2.70-2.77 (m, 1H), 2.79-2.86 (m, 4H), 3.78 (s, 3H), 6.59 (s, 1H), 6.64 (d, *J* = 6.0 Hz, 1H), 6.74 (dd *J* = 3.0 Hz, 9.0 Hz, 1H**)**, 6.95 (d, *J* = 9.0 Hz, 2H), 7.11-7.29 (m, 8H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.3, 29.8, 40.9, 43.3, 44.4, 47.4, 55.2, 111.6, 113.8, 120.3, 126.2, 128.3, 128.4, 128.6, 129.6, 130.5, 131.8, 138.7, 141.2, 145.3, 159.8, 209.8 ; **IR (neat):** 2972, 1712, 1579, 1152, 1042, 1012 ; **HRMS (ESI):** Calcd for $C_{26}H_{27}ClNaO_2$ $(M+Na)^+$ 429.1597, found 429.1604.



*6-(3-Chlorophenyl)-7-(4-fluorophenyl)-1-phenylheptan-3-one (**146**)*: The title compound **146** was obtained as a colorless oil (120.4 mg, 61% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.69 (hexanes : ether = 7:3).

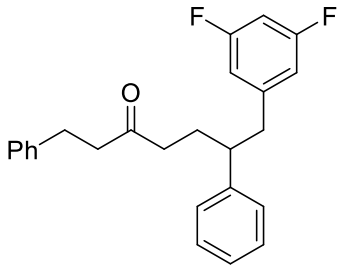
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.79-1.86 (m, 1H), 1.99- 2.07 (m, 1H), 2.21 (t, *J* = 10.0 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.73-2.76 (m, 1H), 2.79-2.89 (m, 4H), 6.90 (t, *J = 7.5* Hz, 3H), 6.94-6.97 (m, 2H), 7.06 (s, 1H), 7.14 (d, *J* = 10.0 Hz, 2H), 7.18-7.21 (m, 3H), 7.26- 7.29 (m, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.1, 29.8, 40.8, 43.0, 44.4, 47.3, 115.1 (d, J_{CF} = 21.4 Hz), 126.2, 126.2, 126.9, 127.9, 128.4, 128.6, 129.9, 130.5(d, J_{CF} = 7.6 Hz), 134.4, 135.4 (d, J_{CF} = 3.8 Hz), 141.1, 146.0, 161.5 (d, J_{CF} = 243.2 Hz), 209.6 ; **^{19}F NMR**

(282 MHz, $CDCl_3$) δ -117.2 ; **IR (neat):** 2926, 1711, 1508, 1219, 1079, 1015 ; **HRMS (ESI):** Calcd for $C_{25}H_{24}ClFNaO$ $(M+Na)^+$ 417.1397, found 417.1413.



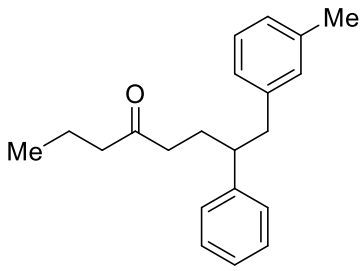
*1-Phenyl-6-(p-tolyl)-7-(3-(trifluoromethyl)phenyl)heptan-3-one (**147**)*: The title compound **147** was obtained as a colorless oil (152.8 mg, 72% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.42 (hexanes : ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78-1.91 (m, 1H), 1.94- 2.05 (m, 1H), 2.21 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 2.71-2.85 (m, 3H), 2.91 (dd, *J* = 3.0 Hz, 9.0 Hz, 2H), 6.91 (d, *J* = 6.0 Hz, 2H), 7.05-7.32 (m, 10H), 7.40 (d, *J* = 9.0 Hz, 1H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 21.1, 29.3, 29.8, 41.0, 43.9, 44.4, 46.8, 122.9 (q, J_{CF} = 3.8 Hz), 124.1 (q, J_{CF} = 273.4 Hz), 126.0 (q, J_{CF} = 3.8 Hz), 126.2, 127.7, 128.4, 128.6, 129.3, 130.4 (q, J_{CF} = 32.8 Hz), 132.6, 136.3, 140.1, 141.2, 141.3, 209.9 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6 ; **IR (neat):** 2926, 1714, 1372, 1162, 1123, 1073 ; **HRMS (ESI):** Calcd for $C_{27}H_{27}F_3NaO$ $(M+Na)^+$ 447.1912, found 447.1924.



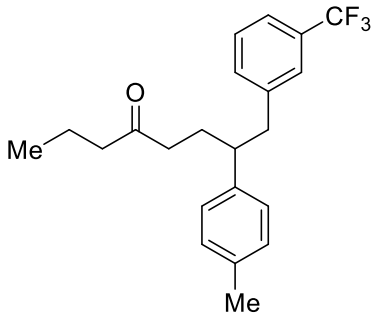
*7-(3,5-Difluorophenyl)-1,6-diphenylheptan-3-one (**148**)*: The title compound **148** was obtained as a yellow oil (105.9 mg, 56% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.56 (hexanes : ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.83-1.94 (m, 1H), 1.99- 2.09 (m, 1H), 2.23 (t, *J* = 7.5 Hz, 2H), 2.59 (t, *J* = 7.5 Hz, 2H), 2.76-2.94 (m, 5H), 6.53-6.61 (m, 3H), 7.06 (d, *J* = 9.0 Hz, 2H), 7.15 (d, *J* = 9.0 Hz, 2H), 7.18-7.32 (m, 6H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.4, 29.8, 40.8, 43.7, 44.4, 47.0, 101.6 (t, J_{CF} = 25.5 Hz), 111.9 (dd, J_{CF} = 7.5 Hz, 16.5 Hz), 126.2, 126.9, 127.8, 128.4, 128.6, 128.7, 141.2, 143.1, 144.25 (t, J_{CF} = 9.4 Hz) , 162.8 (dd, J_{CF} = 13.1 Hz, 246.8 Hz), 209.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -110.9 ; **IR (neat):** 2927, 1711, 1593, 1452, 1139, 1029 ; **HRMS (ESI):** Calcd for $C_{25}H_{24}F_2NaO$ $(M+Na)^+$ 401.1693, found 401.1701.



*7-Phenyl-8-(m-tolyl)octan-4-one (**149**)*: The title compound **149** was obtained as a colorless oil (70.6 mg, 48 % yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.70 (hexanes : ether = 7:3).

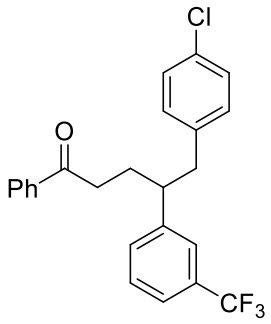
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.83 (t, *J* = 7.5 Hz, 3H), 1.47-1.51 (m, 2H), 1.81-1.88 (m, 1H), 1.97- 2.06 (m, 1H), 2.17-2.22 (m, 4H), 2.28 (s, 3H), 2.77-2.90 (m, 3H), 6.84 (d, *J* = 10.0 Hz, 2H), 6.87 (s, 1H), 7.08-7.12 (m, 3H), 7.18-7.21 (m, 1H), 7.25-7.29 (m, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 13.9, 17.3, 21.5, 29.2, 40.9, 44.1, 44.8, 47.5, 126.3, 126.5, 126.8, 127.9, 128.1, 128.5, 130.1, 137.7, 140.4, 144.4, 211.2 ; **IR (neat):** 2927, 1710, 1605, 1452, 1409, 1124 ; **HRMS (ESI):** Calcd for $C_{21}H_{26}NaO$ $(M+Na)^+$ 317.1881, found 317.1879.



*7-(p-Tolyl)-8-(3-(trifluoromethyl)phenyl)octan-4-one (**150**)*: The title compound **150** was obtained as a colorless oil (117.8 mg, 65% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.50 (hexanes : ether = 4:1).

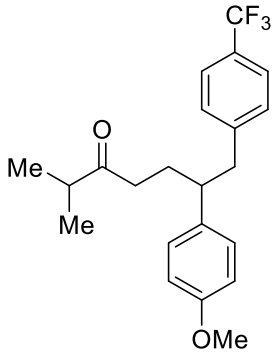
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.83 (t, *J* = 7.5 Hz, 3H), 1.46-1.53 (m, 2H), 1.82-1.88 (m, 1H), 1.96- 2.03 (m, 1H), 2.21 (t, *J* = 7.5 Hz, 3H), 2.31 (s, 3H), 2.75-2.79 (m, 1H), 2.87-2.96 (m, 2H), 6.93 (d, *J* = 10.0 Hz, 2H), 7.07 (d, *J* = 4.5 Hz, 2H), 7.17 (d, *J* = 4.5 Hz, 1H),

7.22-7.30 (m, 2H), 7.39 (d, J = 5.0 Hz, 1H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 13.8, 17.3, 21.1, 29.3, 40.8, 44.0, 44.9, 46.9, 122.9 (q, J_{CF} = 3.8 Hz), 124.3 (q, J_{CF} = 273.4 Hz), 125.9 (q, J_{CF} = 3.8 Hz), 127.7, 128.6, 129.3, 130.4 (q, J_{CF} = 31.5 Hz) ,132.6, 136.2, 140.2, 141.4, 211.1 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6 ; **IR (neat):** 2926, 1711, 1327, 1200, 1120, 1072 ; **HRMS (ESI):** Calcd for $C_{22}H_{25}F_3NaO$ $(M+Na)^+$ 385.1755, found 385.1757.



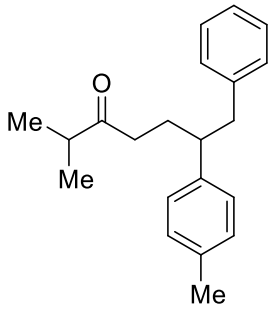
*5-(4-Chlorophenyl)-1-phenyl-4-(3-(trifluoromethyl)phenyl)pentan-1-one (**151**)*: The title compound **151** was obtained as a yellow oil (116.7 mg, 56% yield) after purification by silica gel column chromatography (hexanes : ether = 8:1). R_f = 0.40 (hexanes : ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01-2.11 (m, 1H), 2.19- 2.30 (m, 1H), 2.74-3.05 (m, 5H), 6.92 (d, J = 9.0 Hz, 2H), 7.16 (d, J = 9.0 Hz, 2H), 7.24-7.27 (m, 1H), 7.34-7.52 (m, 6H), 7.79 (d, J = 6.0 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** 29.8, 36.4, 43.3, 47.4, 123.7 (q, J_{CF} = 3.8 Hz), 124.3 (q, J_{CF} = 270.0 Hz) 124.5 (q, J_{CF} = 2.3 Hz), 128.0, 128.5, 128.7, 129.1, 130.5, 130.9 (q, J_{CF} = 32.3 Hz), 131.5 132.1, 133.2, 136.9, 138.1, 144.8, 199.8 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -63.2 ; **IR (neat):** 2927, 1715, 1683, 1325, 1161, 1120 ; **HRMS (ESI):** Calcd for $C_{24}H_{20}ClF_3NaO$ $(M+Na)^+$ 439.1052, found 439.1062.



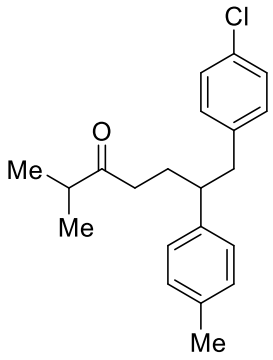
*6-(4-Methoxyphenyl)-2-methyl-7-(4-(trifluoromethyl)phenyl)heptan-3-one (**152**)*: The title compound **152** was obtained as a colorless oil (121 mg, 64% yield) after purification by silica gel column chromatography (hexanes : dichloromethane = 4:1). R_f = 0.56 (hexanes : ether = 7:3). This product was also isolated using 15 mol % CuI instead of $AgBF_4$ (115.4 mg, 61%).

^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (dd, *J* = 3.0 Hz, 6.0 Hz, 6H), 1.76-1.87 (m, 1H), 1.97-2.07 (m, 1H), 2.23-2.29 (m, 2H), 2.37-2.47 (m, 1H), 2.75- 2.98 (m, 3H), 3.78 (s, 3H), 6.80 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 7.09 (d, *J* = 9.0 Hz, 2H), 7.43 (d, *J* = 9.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 18.3, 18.5, 29.6, 38.3, 41.0, 44.2, 46.3, 55.3, 114.0, 124.5 (q, J_{CF} = 272.2 Hz), 125.1 (q, J_{CF} = 3.8 Hz), 128.3 (q, J_{CF} = 32.8 Hz), 128.8, 129.5, 135.3, 144.6, 158.3, 214.7 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.5 ; **IR (neat):** 2934, 1708, 1511, 1322, 1246, 1117 ;**HRMS (ESI):** Calcd for $C_{22}H_{26}F_3O_2$ $(M+H)^+$ 379.1885, found 379.1876.



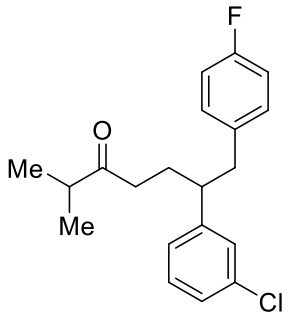
*2-Methyl-7-phenyl-6-(p-tolyl)heptan-3-one (**153**)*: The title compound was **153** obtained as a colorless oil (100.1 mg, 68% yield) after purification by silica gel column chromatography (hexanes : dichloromethane = 4:1). R_f = 0.73 (hexanes : ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): 0.97 (dd, *J* = 4.5 Hz, 9.0 Hz, 6H), 1.80-1.88 (m, 1H), 1.96-2.06 (m, 1H), 2.22-2.28 (m, 2H), 2.31 (s, 3H), 2.39-2.44 (m, 1H), 2.75- 2.91 (m, 3H), 6.99 (d, *J* = 9.0 Hz, 2H), 7.06 (t, *J* = 9.0 Hz, 3H), 7.13-7.23 (m, 4H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 18.2, 18.4, 21.2, 29.3, 38.5, 40.8, 44.3, 47.0, 125.9, 127.7, 128.2, 129.2, 129.3, 135.8, 140.6, 141.2, 214.8 ; **IR (neat):** 2967, 1708, 1513, 1465, 1382, 1364 ; **HRMS (ESI):** Calcd for $C_{21}H_{27}O$ $(M+Na)^+$ 295.2062, found 295.2061.



*7-(4-Chlorophenyl)-2-methyl-6-(p-tolyl)heptan-3-one (**154*** : The title compound **154** was obtained as a yellow oil (116.7 mg, 71% yield) after purification by silica gel column chromatography (hexanes : dichloromethane = 4:1). R_f = 0.45 (hexanes : ether = 7:3).

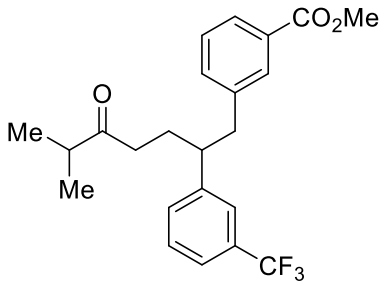
^{1}H NMR (300 MHz, $CDCl_3$): 0.96 (dd, *J* = 3.0 Hz, 6.0 Hz, 6H), 1.75-1.85 (m, 1H), 1.93-2.02 (m, 1H), 2.20-2.30 (m, 2H), 2.30 (s, 3H), 2.36-2.46 (m, 1H), 2.70- 2.77 (m, 2H), 2.80-2.84 (m, 2H), 6.92 (d, *J* = 6.0 Hz, 3H), 7.05 (d, *J* = 6.0 Hz, 2H), 7.14 (dd, *J* = 3.0 Hz, 9.0 Hz, 2H) 7.26 (d, *J* = 3.0 Hz, 1H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 18.3, 18.5, 21.2, 29.4, 38.4, 40.9, 43.6, 46.9, 127.7, 128.3, 129.3, 130.6, 131.7, 136.0, 139.0, 140.6, 214.7 ; **IR (neat):** 2925, 1708, 1513, 1490, 1091, 1015 ; **HRMS (ESI):** Calcd for $C_{21}H_{26}ClO$ $(M+H)^+$ 329.1672, found 329.1667.



*6-(3-Chlorophenyl)-7-(4-fluorophenyl)-2-methylheptan-3-one (**155**)*: The title compound **155** was obtained as a colorless oil (109.8 mg, 66% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.50 (hexanes : ether = 7:3).

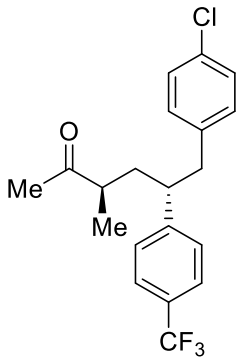
^{1}H NMR (300 MHz, $CDCl_3$): 0.98 (dd, *J* = 3.0 Hz, 6.0 Hz, 6H), 1.74-1.86 (m, 1H), 1.97-2.08 (m, 1H), 2.23-2.28 (m, 2H), 2.39-2.48 (m, 1H), 2.76-2.89 (m, 3H), 6.87-6.94 (m, 5H), 7.05 (s, 1H), 7.16-7.18 (m, 2H); **^{13}C NMR (126 MHz, $CDCl_3$):** δ 18.2, 18.4, 29.1, 38.1,

40.9, 43.1, 47.3, 115.1 (d, J_{CF} = 21.4 Hz), 126.2, 126.8, 127.9, 129.8, 130.5 (d, J_{CF} = 7.6 Hz), 134.4, 135.5 (d, J_{CF} = 3.8 Hz), 146.1, 161.5 (d, J_{CF} = 244.4 Hz), 214.4 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -115.7 ; **IR (neat):** 2969, 1707, 1508, 1219, 1157, 1079 ; **HRMS (ESI):** Calcd for $C_{20}H_{22}ClFNaO$ $(M+Na)^+$ 355.1241, found 355.1252.



*Methyl 3-(6-methyl-5-oxo-2-(3-(trifluoromethyl)phenyl)heptyl)benzoate (**156**)*: The title compound **156** was obtained as a colorless oil (130.1 mg, 64% yield) after purification by silica gel column chromatography (hexanes : ether = 4:1). R_f = 0.35 (hexanes : ether = 7:3).

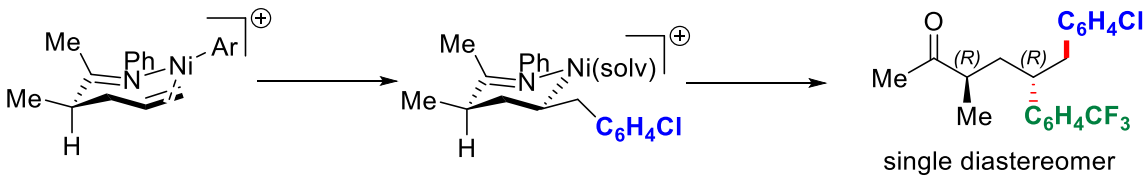
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (d, *J* = 6.0 Hz, 6H) 1.84-1.93 (m, 1H), 2.00-2.11 (m, 1H), 2.22-2.29 (m, 2H), 2.37-2.46 (m, 1H), 2.87-3.00 (m, 3H), 3.86 (s, 3H), 7.12 (d, *J* = 6.0 Hz, 1H), 7.21-7.28 (m, 3H), 7.36 (d, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 1H), 7.69 (s, 1H), 7.81 (d, *J* = 9.0 1Hz) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 18.2, 18.4, 29.0, 38.0, 40.9, 43.7, 47.1, 52.1, 124.2 (q, J_{CF} = 270.8 Hz), 123.5 (q, J_{CF} = 4.5 Hz), 124.6 (q, J_{CF} = 3.8 Hz), 127.6, 128.4, 129.1, 130.2, 130.8 (q, J_{CF} = 31.5 Hz), 131.3, 133.8, 140.0, 144.7, 167.2, 214.1 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.6 ; **IR (neat):** 2969, 1715, 1446, 1324, 1280, 1120 ; **HRMS (ESI):** Calcd for $C_{23}H_{25}F_3NaO_3$ $(M+Na)^+$ 429.1653, found 429.1664.

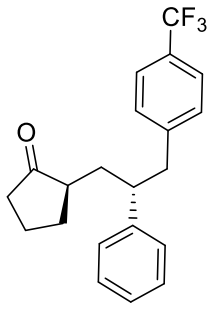


(±)-(R,R)-6-(4-Chlorophenyl)-3-methyl-5-(4-(trifluoromethyl)phenyl)hexan-2-one ***(157)***: The title compound **157** was obtained as a colorless oil (94 mg, 51% yield) after purification by silica gel column chromatography (hexanes : dichloromethane = 4:1). R_f = 0.63 (hexanes : ether = 1:1). Single diastereomer was observed by GC of the crude reaction mixture and by ^{1}H and ^{13}C NMR of the isolated product.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (d, *J* = 6.0 Hz, 3H), 1.58-1.63 (m, 1H), 1.97 (s, 3H), 2.09-2.28 (m, 2H), 2.75-2.92 (m, 3H), 6.87 (d, *J* = 9.0 Hz, 2H), 7.13 (d, *J* = 9.0 Hz, 4H), 7.51 (d, *J* = 9.0 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 18.2, 28.6, 38.8, 43.4, 44.8, 45.8, 124.3 (q, J_{CF} = 272.2 Hz), 125.6 (q, J_{CF} = 3.8 Hz), 128,2, 128.5, 129.0 (q, J_{CF} = 32.8 Hz), 130.4, 132.0, 137.9, 148.1, 212.3 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.32 ; **IR (neat):** 2932, 1711, 1322, 1161, 1116, 1065 ; **HRMS (ESI):** Calcd for $C_{20}H_{20}ClF_3NaO$ $(M+Na)^+$ 391.1052, found 391.1052.

Model for predicting the diastereoselectivity

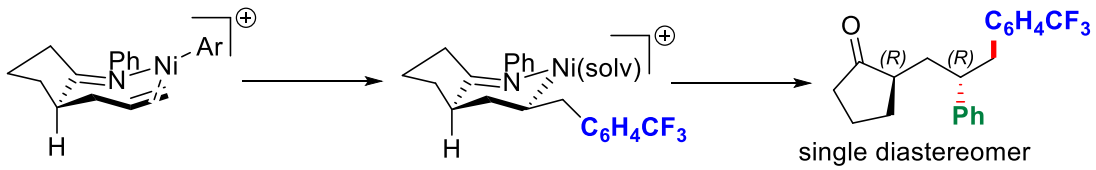


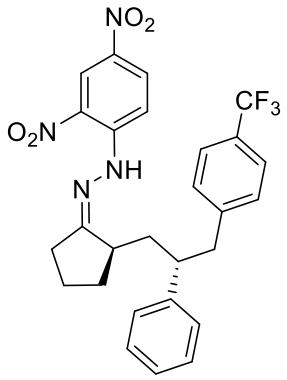


*(±)-(R,R)-2-(2-Phenyl-3-(4-(trifluoromethyl)phenyl)propyl)cyclopentan-1-one (**158**)*: The title compound **158** was obtained as a colorless oil (72.7 mg, 42% yield) after purification by silica gel column chromatography (hexanes : dichloromethane = 4:1). R_f = 0.34 (hexanes : ether = 7:3). Single diastereomer was observed by GC of the crude reaction mixture and by ^{1}H and ^{13}C NMR of the isolated product.

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29-1.50 (m, 2H), 1.55-1.76 (m, 2H), 1.88-2.31 (m, 5H), 2.84-2.97 (m, 3H), 7.09-7.14 (m, 4H), 7.21 (d, *J* = 6.0 Hz, 1H), 7.26 (t, *J* = 3.0 Hz, 2H), 7.44 (d, *J* = 6.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 20.7, 29.6, 35.6, 38.1, 44.5, 46.0, 47.2, 124.4 (q, J_{CF} = 272.2 Hz), 125.2 (q, J_{CF} = 3.8 Hz), 126.9, 127.8, 128.4 (q, J_{CF} = 32.8 Hz),128.8, 129.5, 142.9, 144.5, 221.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.8 ; **IR (neat):** 2969, 1721, 1467, 1405, 1127, 1107 ; **HRMS (ESI):** Calcd for $C_{21}H_{22}F_3O$ $(M+H)^+$ 347.1623, found 347.1612.

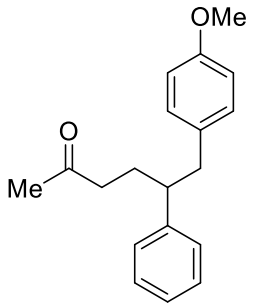
Model for predicting the diastereoselectivity





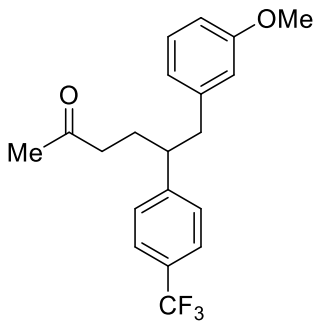
(±)-(R,R)-1-(2,4-Dinitrophenyl)-2-(2-(2-phenyl-3-(4-trifluoromethyl)phenyl)propyl)cyclopentyli-dene)hydrazine ***(158-DNP)***: The title compound **158-DNP** was prepared following literature procedure using 0.2 mmol and obtained as a yellow solid (80 mg, 76% yield) after purification by recrystallization in ethanol.[182]

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.22-1.40 (m, 1H), 1.58-1.70 (m, 2H), 1.95-2.15 (m, 2H), 2.26-2.55 (m, 4H), 2.96-3.03 (m, 3H), 7.13-7.26 (m, 5H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.46 (d, *J* = 9.0 Hz, 2H), 7.94 (d, *J* = 9.0 Hz, 1H), 8.32 (dd, *J* = 3.0, 12.0 Hz, 1H), 9.10 (d, *J* = 3.0 Hz, 1H), 10.76 (s, 1H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 22.7, 28.5, 31.4, 37.9, 43.0, 44.5, 46.0, 116.4, 123.7, 124.4 (q, J_{CF} = 270.9 Hz), 125.2 (q, J_{CF} = 3.8 Hz), 126.9, 127.8, 128.4 (q, J_{CF} = 32.8 Hz), 128.8, 128.9, 129.5, 130.0, 137.6, 143.2, 144.5, 145.2, 170.1 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.8.



*6-(4-Methoxyphenyl)-5-phenylhexan-2-one (**159**)*: The title compound **159** was obtained as a colorless oil (67.8 mg, 48% yield) after purification by silica gel column chromatography (hexanes : ether = 10:1). R_f = 0.43 (hexanes : ether = 2:1).

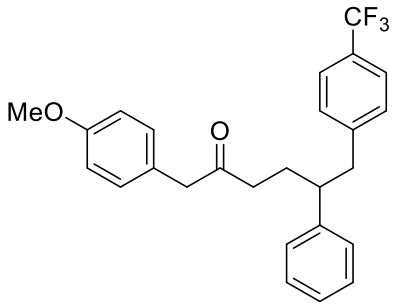
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.77-1.90 (m, 1H), 1.95-2.06 (m, 1H), 2.01 (s, 3H), 2.20-2.26 (m, 2H), 2.71-2.85 (m, 3H), 3.76 (s, 3H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 7.09 (d, *J* = 6.0 Hz, 2H), 7.19 (t, *J* = 9.0 Hz, 1H) 7.27 (t, *J* = 7.5 Hz, 2H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 29.3, 30.0, 41.9, 43.1, 47.6, 55.3, 113.6, 126.5, 127.9, 128.5, 130.1, 132.4, 144.3, 157.9, 208.9 ; **HRMS (ESI):** Calcd for $C_{19}H_{23}O_2$ $(M+H)^+$ 283.1698, found 283.1670.



*6-(3-Methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)hexan-2-one (**160**)*: The title compound **160** was obtained as a colorless oil (91.1 mg, 52% yield) after purification by

silica gel column chromatography (hexanes : ether = 10:1) R_f = 0.46 (hexanes : ether = 2:1).

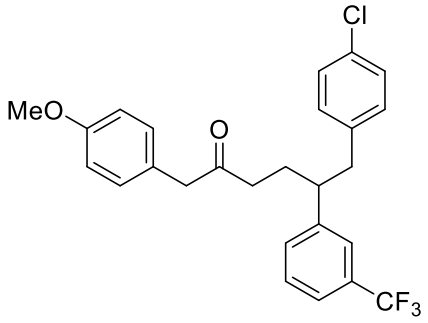
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.84-1.93 (m, 1H), 2.01 (s, 3H), 2.03-2.07 (m, 1H), 2.20-2.27 (m, 2H), 2.83-2.96 (m, 3H), 3.70 (s, 3H), 6.51 (s, 1H), 6.61(d, *J* = 6.0 Hz, 1H), 6.69 (dd, *J* = 3.0, 7.5 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 9.0 Hz, 2H) 7.52 (d, *J* = 6.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** 29.2, 30.1, 41.6, 43.8, 47.2, 55.2, 111.7, 114.8, 121.6, 124.4 (J_{CF} = 272.2 Hz), 125.5 (q, J_{CF} = 3.8 Hz), 128.2, 128.9 (q, J_{CF} = 32.8 Hz), 129.3, (d, J_{CF} = 7.5 Hz), 141.2, 148.4, 159.6, 208.4 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -60.9 ; **HRMS (ESI):** Calcd for $C_{20}H_{22}F_3O_2$ $(M+H)^+$ 351.1572, found 351.1571.



*1-(4-Methoxyphenyl)-5-phenyl-6-(4-(trifluoromethyl)phenyl)hexan-2-one (**161**)*: The title compound **161** was obtained as a yellow oil (115.1 mg, 54% yield) after purification by silica gel column chromatography (hexanes : ether = 8:1). R_f = 0.34 (Hexanes : Ether = 7:3).

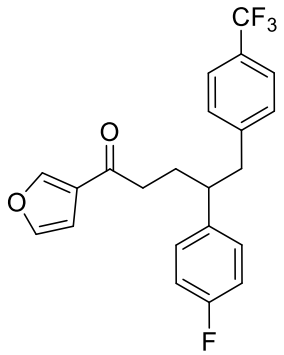
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.79-1.89 (m, 1H), 1.96- 2.06 (m, 1H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.75-2.83 (m, 1H), 2.91 (d, *J* = 9.0 Hz, 2H), 3.46 (s, 2H), 3.78 (m, 3H), 6.82 (d, *J* = 9.0 Hz, 2H), 7.00 (d, *J* = 9.0 Hz, 4H), 7.07 (d, *J* = 9.0 Hz, 2H), 7.18-7.28 (m, 3H), 7.42

(d, J = 6.0 Hz, 2H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 29.5, 39.7, 43.7, 46.9, 49.3, 55.3, 114.2, 124.4 (q, J_{CF} = 272.2 Hz), 125.1 (q, J_{CF} = 3.8 Hz), 126.2, 126.7, 127.8, 128.3 (q, J_{CF} = 32.8 Hz), 128.6, 129.5, 130.4, 143.3, 144.4, 158.7, 208.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -62.3 ; **HRMS (ESI):** Calcd for $C_{26}H_{26}F_3O_2$ $(M+H)^+$ 427.1885, found 427.1899.



*6-(4-Chlorophenyl)-1-(4-methoxyphenyl)-5-(3-(trifluoromethyl)phenyl)hexan-2-one (**162**)*: The title compound **162** was obtained as a yellow oil (140.5 mg, 61% yield) after purification by silica gel column chromatography (hexanes : ether = 8:1). R_f = 0.35 (Hexanes : Ether = 7:3).

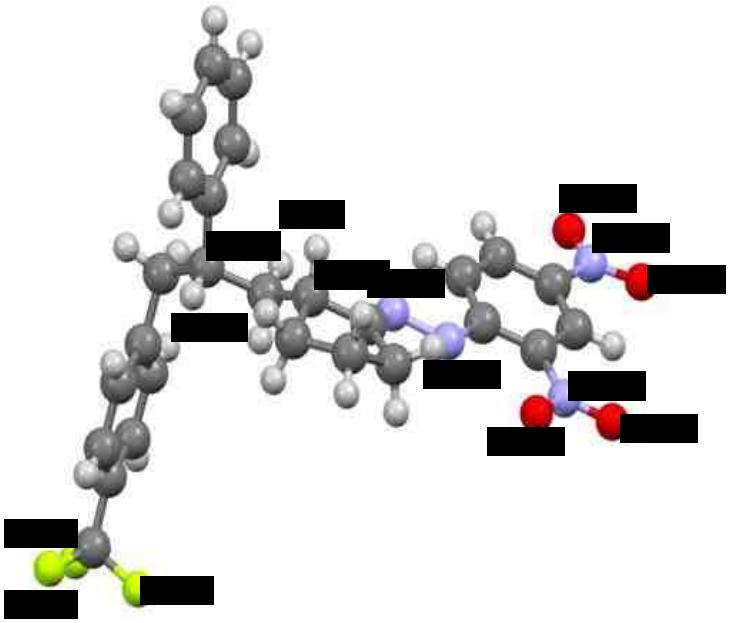
^{1}H NMR (300 MHz, $CDCl_3$): δ 1.78-1.88 (m, 1H), 2.01- 2.08 (m, 1H), 2.24-2.29 (m, 2H), 2.76-2.92 (m, 3H), 3.49 (s, 2H), 3.80 (s, 3H), 6.80-6.85 (m, 3H), 7.01 (dd, J = 3.0, 9.0 Hz, 2H), 7.13 (d, J = 6.0 Hz, 2H), 7.27-7.37 (m, 4H), 7.46 (d, J = 9.0 Hz, 1H) ; **^{13}C NMR (126 MHz, $CDCl_3$):** δ 29.1, 39.4, 43.1, 46.9, 49.4, 55.4, 114.3, 120.1, 123.6 (q, J_{CF} = 3.8 Hz), 124.0 (q, J_{CF} = 252.0 Hz), 124.4 (q, J_{CF} = 3.8 Hz), 126.1, 129.1, 130.4, 130.7 (q, J_{CF} = 24.8 Hz), 130.9, 131.4, 138.6, 144.6, 158.8, 208.5 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -61.0.



4-(4-Fluorophenyl)-1-(furan-3-yl)-5-(4-(trifluoromethyl)phenyl)pentan-1-one (***163***): The title compound **163** was obtained as a yellow oil (109.3 mg, 56% yield) after purification by silica gel column chromatography (hexanes : ether = 3:1). R_f = 0.42 (Hexanes : Ether = 7:3).

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93-2.03 (m, 1H), 2.14- 2.25 (m, 1H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.88-3.02 (m, 3H), 6.67 (d, *J* = 3.0 Hz, 1H) 6.95-7.03 (m, 4H), 7.09 (d, *J* = 9.0 Hz, 2H), 7.38 (t, *J* = 3.0 Hz, 1H), 7.44 (d, *J* = 9.0 Hz, 2H), 7.79 (s,1H) ; **^{13}C NMR (75 MHz, $CDCl_3$):** δ 30.1, 38.1, 44.0, 46.5, 108.6, 115.5(d, J_{CF} = 21.0 Hz), 124.4 (q, J_{CF} = 270.0 Hz), 125.4 (q, J_{CF} = 3.8 Hz), 127.7, 128.5 (q, J_{CF} = 33.0 Hz), 129.3 (d, J_{CF} = 8.3 Hz), 129.5, 138.9, 144.1, 144.3, 147.1, 161.7 (d, J_{CF} = 243.0 Hz), 194.6 ; **^{19}F NMR (282 MHz, $CDCl_3$)** δ -114.6, -60.8 ; **HRMS (ESI):** Calcd for $C_{22}H_{19}F_4O_2$ $(M+H)^+$ 391.1321, found 391.1309.

5.3.5. X-ray Crystallographic Data for Compound 158-DNP



A specimen of $C_{27}H_{24}F_3N_4O_4$, approximate dimensions 0.194 mm x 0.240 mm x 0.570 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The integration of the data using a monoclinic unit cell yielded a total of 35109 reflections to a maximum θ angle of 25.51° (0.83 Å resolution), of which 4549 were independent (average redundancy 7.718, completeness = 100.0%, R_{int} = 17.11%, R_{sig} = 14.59%) and 1940 (42.65%) were greater than $2\sigma(F^2)$. The final cell constants of a = 15.571(3) Å, b = 9.728(2) Å, c = 16.373(4) Å, β = 100.123(8)°, volume = 2441.5(9) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9390 and 0.9780.

The final anisotropic full-matrix least-squares refinement on F^2 with 343 variables

converged at R1 = 6.97%, for the observed data and wR2 = 21.88% for all data. The goodness-of-fit was 0.941. The largest peak in the final difference electron density synthesis was 0.548 $e^-/Å^3$ and the largest hole was -0.298 $e^-/Å^3$ with an RMS deviation of 0.077 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.430 g/cm^3 and F(000), 1092 e^-.

Table 5.26. Sample and crystal data for Compound 158-DNP.

Identification code	Giri 1001
Chemical formula	$C_{27}H_{24}F_3N_4O_4$
Formula weight	525.50 g/mol
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal size	0.194 x 0.240 x 0.570 mm
Crystal system	monoclinic
Space group	P 1 21/n 1
Unit cell dimensions	a = 15.571(3) Å α = 90°
	b = 9.728(2) Å β = 100.123(8)°

	c = 16.373(4) Å γ = 90°
Volume	2441.5(9) $Å^3$
Z	4
Density (calculated)	1.430 g/cm^3
Absorption coefficient	0.113 mm^{-1}
F(000)	1092

Table 5.27. Data collection and structure refinement for Compound 158-DNP

Theta range for data collection	1.67 to 25.51°
Index ranges	-18<=h<=18, -11<=k<=11, -19<=l<=16
Reflections collected	35109
Independent reflections	4549 [R(int) = 0.1711]
Max. and min. transmission	0.9780 and 0.9390
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2013 (Sheldrick, 2013)

Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	4549 / 0 / 343
Goodness-of-fit on F^2	0.941
Final R indices	1940 data; R1 = 0.0697, wR2 = 0.1630 $I>2\sigma(I)$
	all data R1 = 0.1836, wR2 = 0.2188
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.1016P)^2]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	0.548 and -0.298 eÅ^{-3}
R.M.S. deviation from mean	0.077 eÅ^{-3}

Table 5.28. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for Compound 158-DNP.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C11	0.0127(3)	0.1420(4)	0.1128(3)	0.0371(12)

	x/a	y/b	z/c	U(eq)
C12	0.0929(3)	0.1347(5)	0.1645(3)	0.0409(12)
C13	0.1267(3)	0.0085(5)	0.1964(3)	0.0444(13)
C14	0.0787(3)	0.8895(4)	0.1780(3)	0.0378(12)
C141	0.1109(3)	0.7555(5)	0.2149(3)	0.0495(13)
F141	0.19711(19)	0.7443(3)	0.22950(18)	0.0655(9)
F142	0.0871(2)	0.7349(3)	0.2897(2)	0.0729(10)
F143	0.0803(2)	0.6472(3)	0.16776(19)	0.0762(11)
C15	0.9978(3)	0.8967(5)	0.1270(3)	0.0415(12)
C16	0.9656(3)	0.0205(4)	0.0941(3)	0.0401(12)
C21	0.8407(3)	0.4222(4)	0.0414(3)	0.0363(11)
C111	0.9760(3)	0.2760(4)	0.0771(3)	0.0418(12)
C121	0.8870(3)	0.3126(4)	0.0990(3)	0.0349(11)
C131	0.8956(3)	0.3494(4)	0.1906(3)	0.0381(12)
C22	0.7687(3)	0.3908(5)	0.9827(3)	0.0533(14)

	x/a	y/b	z/c	U(eq)
C23	0.7269(3)	0.4898(6)	0.9287(3)	0.0579(15)
C24	0.7568(3)	0.6226(5)	0.9346(3)	0.0512(14)
C25	0.8278(3)	0.6560(5)	0.9911(3)	0.0432(12)
C26	0.8706(3)	0.5572(4)	0.0449(3)	0.0408(12)
C31	0.8087(3)	0.3707(4)	0.2194(3)	0.0341(11)
C32	0.7467(3)	0.2468(4)	0.2067(3)	0.0398(12)
C33	0.6828(3)	0.2715(5)	0.2653(3)	0.0387(12)
C34	0.7401(3)	0.3357(4)	0.3426(3)	0.0408(12)
C35	0.8134(3)	0.4029(4)	0.3095(3)	0.0321(11)
C41	0.9130(3)	0.6017(4)	0.4759(3)	0.0343(11)
C42	0.9073(3)	0.6292(4)	0.5593(3)	0.0362(11)
N421	0.8480(3)	0.5541(4)	0.6033(3)	0.0437(10)
O421	0.7984(2)	0.4683(3)	0.5648(2)	0.0562(10)
O422	0.8494(2)	0.5788(4)	0.6770(2)	0.0593(10)

	x/a	y/b	z/c	U(eq)
C43	0.9555(3)	0.7341(4)	0.6034(3)	0.0368(11)
C44	0.0126(3)	0.8079(4)	0.5664(3)	0.0377(12)
N441	0.0634(3)	0.9169(4)	0.6139(3)	0.0467(11)
O441	0.1216(2)	0.9699(4)	0.5841(2)	0.0632(11)
O442	0.0460(3)	0.9469(3)	0.6817(2)	0.0659(11)
C45	0.0217(3)	0.7829(4)	0.4849(3)	0.0394(12)
C46	0.9730(3)	0.6825(4)	0.4406(3)	0.0390(12)
N461	0.8642(2)	0.5021(3)	0.4315(2)	0.0371(10)
N462	0.8726(2)	0.4812(3)	0.3485(2)	0.0348(9)

Table 5.29. Bond lengths (Å) for Compound 158-DNP

C11-C12	1.382(6)	C11-C16	1.396(6)
C11-C111	1.500(6)	C12-C13	1.400(6)
C13-C14	1.383(6)	C14-C15	1.385(6)

C14-C141	1.486(6)	C141-F141	1.325(5)
C141-F143	1.343(5)	C141-F142	1.356(6)
C15-C16	1.378(6)	C21-C22	1.378(6)
C21-C26	1.391(6)	C21-C121	1.519(6)
C111-C121	1.533(6)	C121-C131	1.525(6)
C131-C31	1.523(6)	C22-C23	1.389(6)
C23-C24	1.371(7)	C24-C25	1.351(6)
C25-C26	1.392(6)	C31-C35	1.497(6)
C31-C32	1.535(6)	C32-C33	1.517(6)
C33-C34	1.546(6)	C34-C35	1.498(6)
C35-N462	1.276(5)	C41-N461	1.361(5)
C41-C42	1.409(6)	C41-C46	1.420(6)
C42-C43	1.391(6)	C42-N421	1.462(6)
N421-O422	1.226(4)	N421-O421	1.233(5)
C43-C44	1.364(6)	C44-C45	1.389(6)

C44-N441	1.463(6)	N441-O441	1.216(5)
N441-O442	1.223(5)	C45-C46	1.364(6)
N461-N462	1.404(5)		

Table 5.30. Bond angles (°) for Compound 158-DNP.

C12-C11-C16	118.3(4)	C12-C11-C111	121.6(4)
C16-C11-C111	120.1(4)	C11-C12-C13	120.9(4)
C14-C13-C12	120.0(4)	C13-C14-C15	119.2(4)
C13-C14-C141	121.0(4)	C15-C14-C141	119.7(4)
F141-C141-F143	106.6(4)	F141-C141-F142	104.7(4)
F143-C141-F142	106.0(4)	F141-C141-C14	113.9(4)
F143-C141-C14	113.2(4)	F142-C141-C14	111.7(4)
C16-C15-C14	120.6(4)	C15-C16-C11	120.9(4)
C22-C21-C26	117.6(4)	C22-C21-C121	121.1(4)

C26-C21-C121	121.3(4)	C11-C111-C121	114.1(4)
C21-C121-C131	113.3(4)	C21-C121-C111	111.6(4)
C131-C121-C111	110.9(3)	C31-C131-C121	114.0(3)
C21-C22-C23	121.5(5)	C24-C23-C22	119.5(5)
C25-C24-C23	120.1(5)	C24-C25-C26	120.7(5)
C21-C26-C25	120.5(4)	C35-C31-C131	116.2(4)
C35-C31-C32	102.6(4)	C131-C31-C32	115.1(3)
C33-C32-C31	104.9(3)	C32-C33-C34	103.6(3)
C35-C34-C33	104.2(4)	N462-C35-C31	121.6(4)
N462-C35-C34	127.5(4)	C31-C35-C34	111.0(4)
N461-C41-C42	121.9(4)	N461-C41-C46	121.5(4)
C42-C41-C46	116.6(4)	C43-C42-C41	121.4(4)
C43-C42-N421	116.1(4)	C41-C42-N421	122.4(4)
O422-N421-O421	122.5(4)	O422-N421-C42	118.9(4)

O421-N421-C42	118.6(4)	C44-C43-C42	119.4(4)
C43-C44-C45	121.3(4)	C43-C44-N441	118.7(4)
C45-C44-N441	120.1(4)	O441-N441-O442	124.2(4)
O441-N441-C44	117.7(4)	O442-N441-C44	118.0(5)
C46-C45-C44	119.7(5)	C45-C46-C41	121.6(4)
C41-N461-N462	118.8(4)	C35-N462-N461	112.9(4)

Table 5.31. Anisotropic atomic displacement parameters (Å^2) for Compound 158-DNP.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	**U_{22}**	**U_{33}**	**U_{23}**	**U_{13}**	**U_{12}**
C11	0.039(3)	0.036(3)	0.038(3)	-0.005(2)	0.012(2)	0.002(2)
C12	0.041(3)	0.040(3)	0.042(3)	0.000(2)	0.007(2)	-0.004(2)
C13	0.040(3)	0.049(3)	0.042(3)	-0.003(2)	0.000(2)	-0.001(2)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C14	0.039(3)	0.035(3)	0.038(3)	0.003(2)	0.004(2)	0.000(2)
C141	0.048(3)	0.046(3)	0.053(4)	0.003(3)	0.004(3)	0.002(3)
F141	0.054(2)	0.0543(19)	0.085(2)	0.0118(16)	0.0031(17)	0.0132(15)
F142	0.087(2)	0.068(2)	0.067(2)	0.0249(17)	0.0227(18)	0.0113(18)
F143	0.089(2)	0.0390(18)	0.088(2)	-0.0020(17)	-0.020(2)	0.0042(17)
C15	0.043(3)	0.035(3)	0.046(3)	-0.007(2)	0.004(2)	-0.004(2)
C16	0.043(3)	0.036(3)	0.041(3)	-0.003(2)	0.008(2)	0.005(2)
C21	0.033(3)	0.034(3)	0.044(3)	-0.004(2)	0.013(2)	0.000(2)
C111	0.044(3)	0.038(3)	0.044(3)	-0.002(2)	0.010(2)	-0.001(2)
C121	0.033(3)	0.030(3)	0.042(3)	0.000(2)	0.009(2)	-0.002(2)
C131	0.043(3)	0.030(2)	0.042(3)	0.003(2)	0.008(2)	0.001(2)
C22	0.058(3)	0.045(3)	0.054(3)	0.001(3)	0.001(3)	-0.010(3)
C23	0.056(4)	0.063(4)	0.049(3)	0.009(3)	-0.005(3)	-0.010(3)
C24	0.051(3)	0.053(3)	0.052(3)	0.013(3)	0.014(3)	0.005(3)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C25	0.050(3)	0.032(3)	0.049(3)	0.002(2)	0.015(3)	0.002(2)
C26	0.044(3)	0.033(3)	0.044(3)	-0.004(2)	0.004(2)	-0.003(2)
C31	0.038(3)	0.025(2)	0.040(3)	0.000(2)	0.010(2)	0.002(2)
C32	0.044(3)	0.036(3)	0.039(3)	-0.003(2)	0.008(2)	0.001(2)
C33	0.036(3)	0.034(3)	0.047(3)	-0.001(2)	0.009(2)	-0.004(2)
C34	0.044(3)	0.035(3)	0.045(3)	-0.001(2)	0.011(2)	0.000(2)
C35	0.036(3)	0.022(2)	0.039(3)	-0.001(2)	0.007(2)	0.003(2)
C41	0.035(3)	0.033(3)	0.034(3)	0.005(2)	0.002(2)	0.009(2)
C42	0.039(3)	0.035(3)	0.036(3)	0.006(2)	0.011(2)	0.005(2)
N421	0.051(3)	0.043(3)	0.037(3)	-0.001(2)	0.011(2)	0.004(2)
O421	0.066(2)	0.052(2)	0.052(2)	0.0075(18)	0.0126(19)	0.0209(19)
O422	0.076(3)	0.061(2)	0.045(2)	0.0061(18)	0.022(2)	-0.010(2)
C43	0.039(3)	0.037(3)	0.032(3)	0.001(2)	0.001(2)	0.009(2)
C44	0.037(3)	0.034(3)	0.038(3)	-0.004(2)	-0.003(2)	0.004(2)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N441	0.057(3)	0.035(2)	0.045(3)	-0.001(2)	0.001(2)	-0.003(2)
O441	0.064(3)	0.057(2)	0.070(3)	0.0184(19)	0.017(2)	-0.020(2)
O442	0.101(3)	0.048(2)	0.049(2)	0.0130(18)	0.015(2)	-0.018(2)
C45	0.040(3)	0.032(3)	0.045(3)	0.004(2)	0.005(2)	-0.001(2)
C46	0.042(3)	0.040(3)	0.034(3)	0.000(2)	0.003(2)	0.004(2)
N461	0.042(2)	0.031(2)	0.035(2)	0.0015(17)	0.0016(19)	0.0057(17)
N462	0.039(2)	0.030(2)	0.036(2)	0.0008(17)	0.0076(19)	0.0013(18)

Table 5.32. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for Compound 158-DNP

	x/a	y/b	z/c	U(eq)
H12	1.1256	0.2164	0.1785	0.049
H13	1.1826	0.0047	0.2307	0.053
H15	0.9641	-0.1845	0.1147	0.05
H16	0.9106	0.0233	0.0582	0.048

	x/a	y/b	z/c	U(eq)
H11A	0.9703	0.2722	0.0160	0.05
H11B	1.0178	0.3503	0.0974	0.05
H121	0.8503	0.2278	0.0899	0.042
H13A	0.9280	0.2751	0.2241	0.046
H13B	0.9305	0.4347	0.2013	0.046
H22	0.7471	0.2992	-0.0210	0.064
H23	0.6780	0.4656	-0.1121	0.069
H24	0.7274	0.6912	-0.1011	0.061
H25	0.8487	0.7479	-0.0058	0.052
H26	0.9206	0.5821	0.0842	0.049
H31	0.7785	0.4491	0.1869	0.041
H32A	0.7158	0.2421	0.1485	0.048
H32B	0.7791	0.1600	0.2206	0.048
H33A	0.6563	0.1842	0.2795	0.046

	x/a	y/b	z/c	U(eq)
H33B	0.6359	0.3354	0.2406	0.046
H34A	0.7066	0.4043	0.3690	0.049
H34B	0.7623	0.2641	0.3839	0.049
H43	0.9487	0.7541	0.6586	0.044
H45	1.0616	0.8355	0.4600	0.047
H46	0.9794	0.6662	0.3848	0.047

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