Ruthenium Catalyzed Deaminative Coupling Reaction of Amines Via C-N Bond Activation

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RUTHENIUM CATALYZED DEAMINATIVE COUPLING REACTION OF AMINES VIA C-N BOND ACTIVATION

by

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ABSTRACT

RUTHENIUM CATALYZED DEAMINATIVE COUPLING REACTION OF AMINES VIA C-N BOND ACTIVATION

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C–N bond activation via transition-metal catalyst has attracted much attention during the past two decades. This strategy has become one of the most promising way to generate secondary amines, which are very important in a broad spectrum of applications in pharmaceutical industry, synthetic organic chemistry and material science. The secondary amines can be utilized as an important synthetic intermediate for further manipulations. The in-situ formed catalytic system generated from the tetranuclear Ru–H complex with 4-(1,1-dimethylethyl)-1,2-benzenediol ligand was found to be effective for the synthesis of secondary amines from the direct deaminative coupling of amines. The ruthenium catalyst was highly effective for promoting selective coupling of two different primary amines to afford the formation of unsymmetric secondary amines. The treatment of aniline-d_7 with 4-methoxybenzylamine led to the coupling product with significant deuterium incorporation on CH_2 (18% D). The most pronounced carbon isotope effect was observed on the α-carbon isolated from the coupling reaction of 4-methoxybenzylamine. Hammett plot was constructed from measuring the rates of 4-methoxyaniline with a series of para-substituted benzylamines 4-X-$C_6H_4CH_2NH_2$ (X = OMe, Me, H, F, CF_3). ($\rho = -0.8 \pm 0.1$). A plausible mechanistic scheme has been proposed for the coupling reaction on the basis of these results. The catalytic coupling method provides a simple and chemoselective synthesis of secondary amine products without using any reactive reagents or forming wasteful byproducts.

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DEDICATION

To my late father Mr. Dharmadasa Kirinde Arachchi, a key person who installed me with strong and tolerable qualities and my mother, Mrs. Malini Kuruppu Nanayakkara, for unconditional love.

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ABBREVIATIONS

PG – Protecting Group

LG – Leaving Group

RDS – Rate Determining Step

tBuOK – Potassium tert-butoxide

DEMS – Diethoxymethylsilane

DTBM-SEGPHOS – 5,5′-Bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole, [(4*R*)-(4,4′-bi-1,3-benzodioxole)-5,5′-diyl]bis[bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine]

Bn – Benzyl

Ph – Phenyl

Ar – Aryl

AgOTf – Silver trifluoromethanesulfonate

Cp – Cyclopentadienyl

Cp* – 1,2,3,4,5-Pentamethylcyclopentadienyl

TFE – 2,2,2-trifluoroethanol

IMes – 1,3-bis-(2,4,6-trimethylphenyl)imidazole carbene ligand

PPh_3 – Triphenylphosphine

PCy_3 – Tricyclohexylphosphine

Et – Ethyl

R – Alkyl-, Aryl moiety

Nu – Nucleophile

DMF – Dimethylformamide

DPPF – 1,1'-Bis(diphenylphosphino)ferrocene

coe – Cyclooctene

COD – Cyclooctadiene

Me – Methyl

NMR – Nuclear magnetic resonance

s – singlet

d – doublet

t – triplet

q – quartet

m – multiplet

br – broad

ppm – Parts per million

HRMS – High resolution mass spectroscopy

Chapter 1

1.0 Introduction

Synthesis of amines has been received much attention due to their prominent presence in a wide variety of biologically important molecules. Therefore, much attention has been given to the development of efficient synthetic methods to prepare amines as useful intermediates.[1] In particular, secondary amines were identified as an important functionality in many bioactive molecules (**Figure 1.0.1**).[1,2]

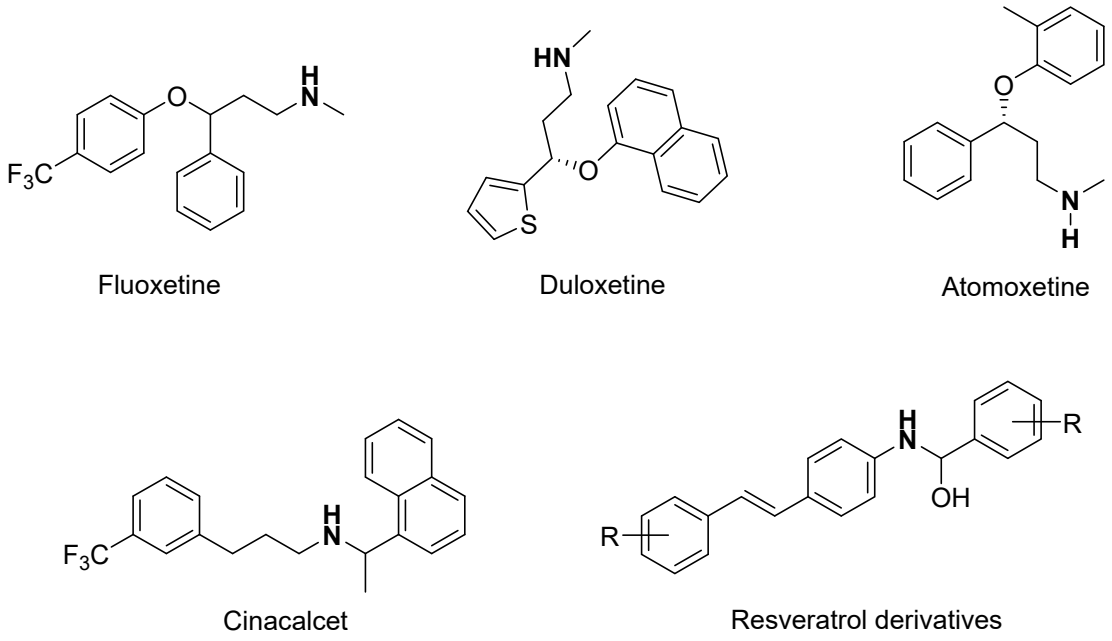


Figure 1.0.1: Selected examples for pharmaceuticals with secondary amine functionality.[2]

Development of efficient synthetic methods for secondary amines that utilize commonly available and abundant precursor molecules is a long-standing goal in chemical research. Secondary amines are important precursors in both pharmaceutical

industry as well as synthetic organic chemistry and material science, where the secondary amines can be utilized as an important synthetic intermediate for further manipulations to synthesize useful compounds. In general, selective and step-efficient one-pot synthesis of secondary amines is highly demanded.[1-3] However, the traditional synthetic methods for secondary amines have been found to have serious drawbacks such as low selectivity, poor yields, harsh reaction conditions, and form copious amount of wasteful and toxic byproducts. **Figure 1.0.2** is a summary of traditional methods used to prepare secondary amines.[1,3]

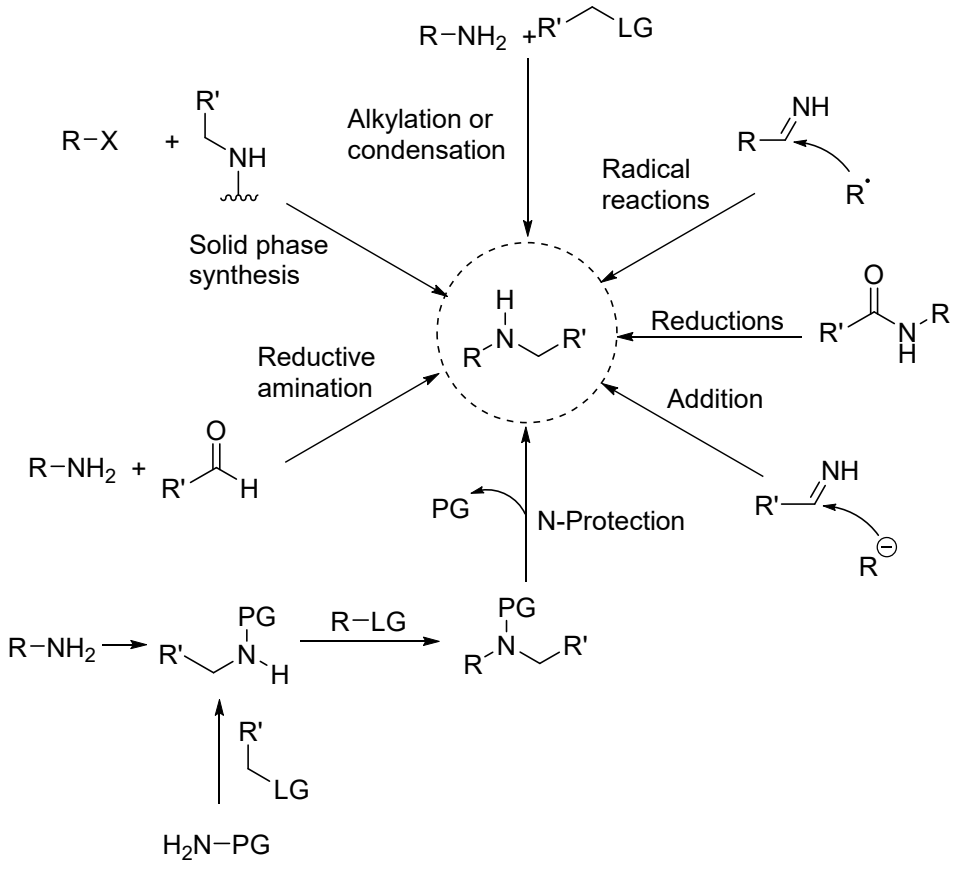


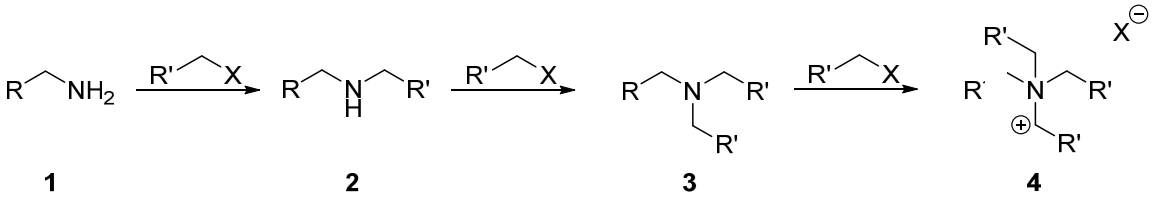
Figure 1.0.2: Traditional methods for the synthesis of secondary amines.

Since the traditional methods have been found to have many drawbacks as discussed above, catalytic C–N bond activation methods have attracted much attention in both medicinal and industrial communities. Transition metal catalyzed C-N activation reactions have emerged as one of the most promising strategies for the synthesis of secondary amines that encompass a broad spectrum of applications. In this chapter, strategies for synthesis of secondary amine products especially with respect to efficient catalytic cleavage of C–N bonds and their applications will be discussed.

1.1 Stoichiometric and Catalytic Methods for N-Alkylation of Primary Amines

1.1.1 N-Alkylation with Alkyl Halides

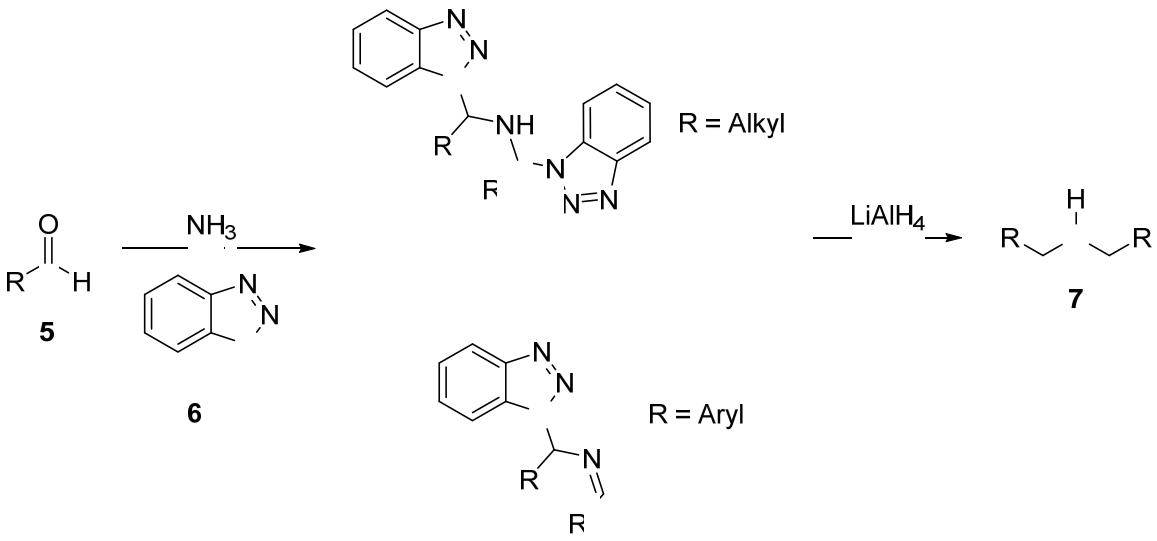
The Hoffmann alkylation method provides straightforward synthesis of secondary amines by treating primary amines **1** with alkyl halides.[1,4] It is generally accepted that the reaction produced a mixture of secondary **2**, tertiary **3** and quaternary ammonium salts **4** (**Scheme 1.1.1.1**:). Since, secondary amines are prepared by treatment of tremendously excess amount of primary amines,[1,5] the method has been recognized as an inefficient process and industrially unfavorable when enantiomerically pure compounds are employed.



Scheme 1.1.1.1: Hoffmann N-Alkylation of aliphatic primary amines with alkyl halides.

1.1.2 Reductive Amination and Alkylation Methods

In the reductive amination reaction of amines and carbonyl compounds, aldehydes or ketones are mixed with a reducing agent (e.g. $NaBH_4$ or H_2/Pd) to generate secondary amines without the formation of imine intermediate or iminium salts. In contrast, the indirect amination reaction involves the formation of intermediate imine products, which is then subjected to reduction in a stepwise fashion. Hitchings and co-workers reported the use of ammonia as the nitrogen source in the reaction with aldehydes **5** and benzotriazoles **6** followed by reduction with $LiAlH_4$ (**Scheme 1.1.2.1**) for the synthesis of symmetrical secondary amines **7**.[6]



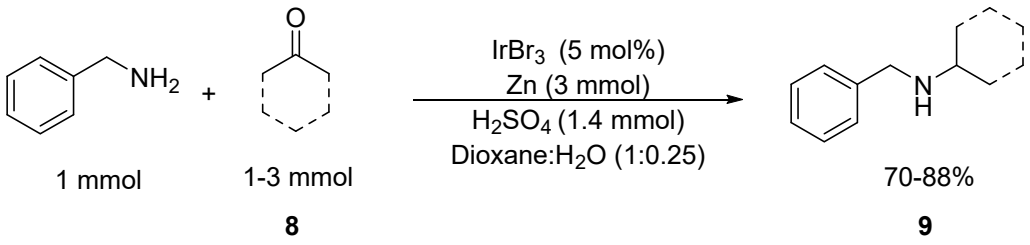
Scheme 1.1.2.1: Ammonia as the nitrogen source for reductive amination of aldehydes.

In the direct reductive amination reaction, the reducing agent must be chosen carefully as there might be a potential for the reduction of carbonyl substrates. $NaBH_3CN$ was the commonly used reducing agent among reducing agents have been reported.[7] However, a large-scale synthesis cannot be performed due to high toxicity of this reagent.

The major drawback of this method is the use of stoichiometric amount of the reducing agent.[1]

1.1.3 Catalytic Reductive Amination of Carbonyl Compounds

Depending on phase of a reducing agent used in a particular reaction, catalytic reductive amination can be classified as heterogeneous catalytic reductive amination (i. e. H_2/Pd) or homogeneous catalytic reductive amination. Bieber and da Silva reported $IrBr_3$ catalyst can be effectively used to generate secondary amines by reductive alkylation of aliphatic ketones with aryl amines in the presence of excess zinc reductant (**Scheme 1.1.3.1**). The reaction scope was found to be effective for a range of aryl and benzyl amines and low molecular weight ketones **8** yielding 70-100% of the products **9**. However, excess of strong acid and ketone substrates were required in most of these cases.[9]

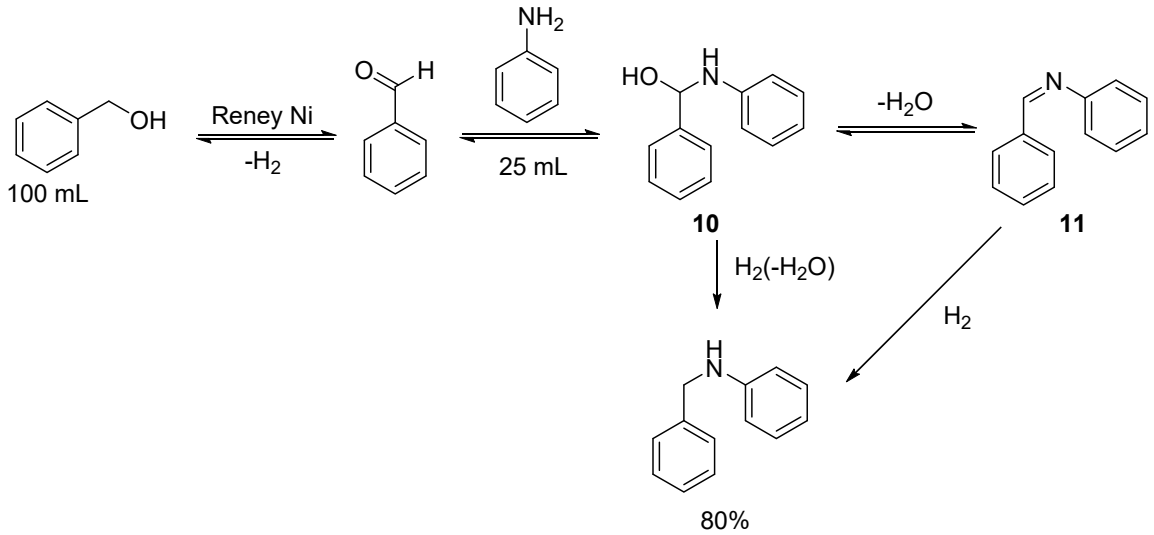


Scheme 1.1.3.1: Ir catalyzed reductive amination of ketones.

1.1.4 N-Alkylation with Alcohols

Direct N-alkylation of amines with alcohols are not possible without transition metal catalysts. The first reaction of N-alkylation of amines with alcohols were reported in 1909 by Sabatier and Mailhe[10] by using ThO_2 catalyst. This was not accepted as a

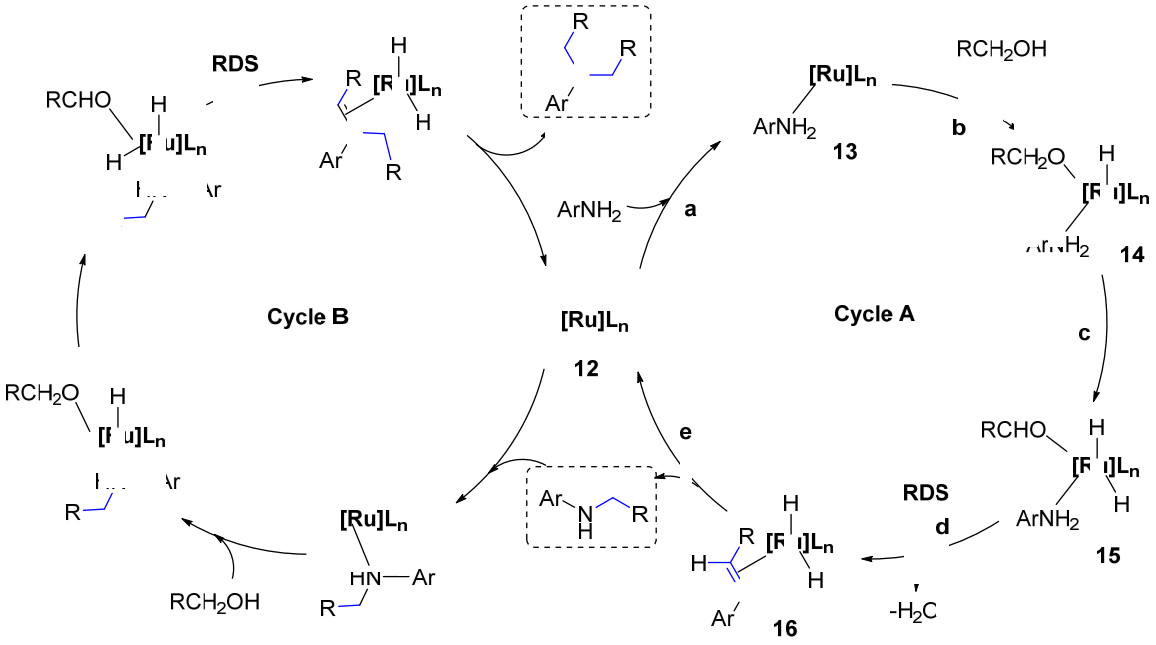
possible transformation to apply as a useful strategy to prepare N-alkylated amines due to inapplicable reaction conditions.[1b] Adkins and Cramer[11] was obtained ethylcyclohexylamine with excellent yield by the hydrogenation of aniline with ethanol by using raney nickel as the catalyst. However, this reaction required high temperature (200 °C) and with limited substrate scope. Later, raney nickel[12], catalyzed transformations of alcohols with amines were observed by a Kohn and Rice in 1955. A mixture of aniline (25 mL) and an excess of a benzyl alcohol (100 mL) were refluxed with raney nickel, to obtain the alkylated product (**Scheme 1.1.4.1**). In this reaction, an alcohol was served as both reactant and solvent. Both the Schiff base **11** and/or the α-hydroxyamines **10** may be hydrogenated to yield the corresponding secondary amine products.



Scheme 1.1.4.1: Mechanistic pathway for the preparation of N-benzylaniline.

In 1984, Ohta[13] and co-workers reported that $RuCl_2(PPh_3)_3$ can be used to generate secondary amines in excellent yields when aminoarenes reacted with an equimolar amount of alcohols. This transformation required 150-180 °C and the tertiary

amines were formed predominantly in the presence of excess alcohol substrate. Mechanistic studies were used to postulate the nucleophilic attack of the aminoarene on aldehyde intermediate as the turnover limiting step of the reaction (**Scheme 1.1.4.2**).



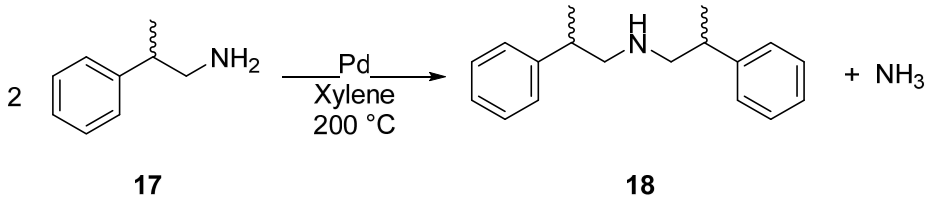
Scheme 1.1.4.2: Proposed mechanism for generation of N-alkylated amines.

The aminoarene coordinates (**a**) to catalytically active species **12**, RuL_n, (L_n = Cl and PPh_3) to generate ruthenium arylamino species **13**. The alcohol adds to **13** to form alkoxide intermediate **14** via path **b**, which then oxidized (**c**) to form aldehyde and amine coordinated ruthenium complex **15**. This type of oxidation reactions has been proposed by several other publications.[14] In 1981, Lappert and Miles were able to isolate the alkylgermanium alkoxohydrido complex[15] for the first time by the oxidative addition of an alcohol with alkylgermanium. Then the aminoarene would be nucleophilically attack (**d**) to the aldehyde by forming Schiff base complex **16**, which was found to be the rate-

determining step. The hydrogenation (**e**) completes the catalytic cycle A by generating N-monoalkylated benzenamine with the regeneration of the active catalyst. Second alkylation will be proceeded by following similar pathway with secondary amine product formed from the cycle A (as depicted in cycle B).

1.1.5 N-Alkylation of Amines with Primary Amines

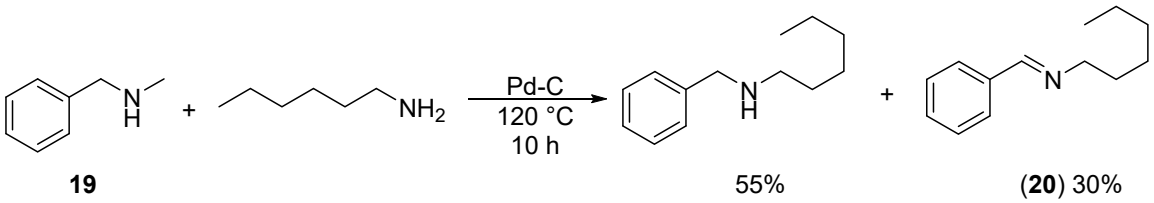
N-Alkylation of amines with primary amines has been rarely achieved without a metal catalyst. There are scattered examples in the literature for the self-condensation of primary amines.[16] In 1925, Rosenmund and Jordan, showed that dibenzyl amine were formed from benzylamine over palladium at 200 °C in boiling xylene or alcohol with the evolution of ammonia. Few years later, in 1931 similar type of reactivity was observed by Kindler with the reaction of β-methylphenylethylamine **17** in boiling xylene or alcohol over 200 °C. The corresponding secondary amine product, di-*β*-phenylethylamine **18** were formed in excellent yields.[17] Nickel catalyst were also found to mediate deaminative alkylation under suitable conditions.[18]



Scheme 1.1.5.1: Deaminative symmetric coupling of primary amine.

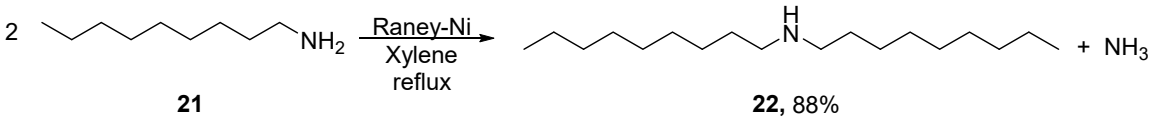
In 1973, Murahashi and co-workers reported a new catalytic process for the synthesis of unsymmetrical secondary or tertiary amines through reductive dehydrogenation by using palladium catalyst. The secondary amine and imine **20**

products were formed from the reaction of secondary amines **19** with primary amines (**Scheme 1.1.5.2**:). Allylamines were reacted to give the imine products in 95% at room temperature, while other transformations required 120-160 °C.



Scheme 1.1.5.2: Formation of secondary amines on palladium black.

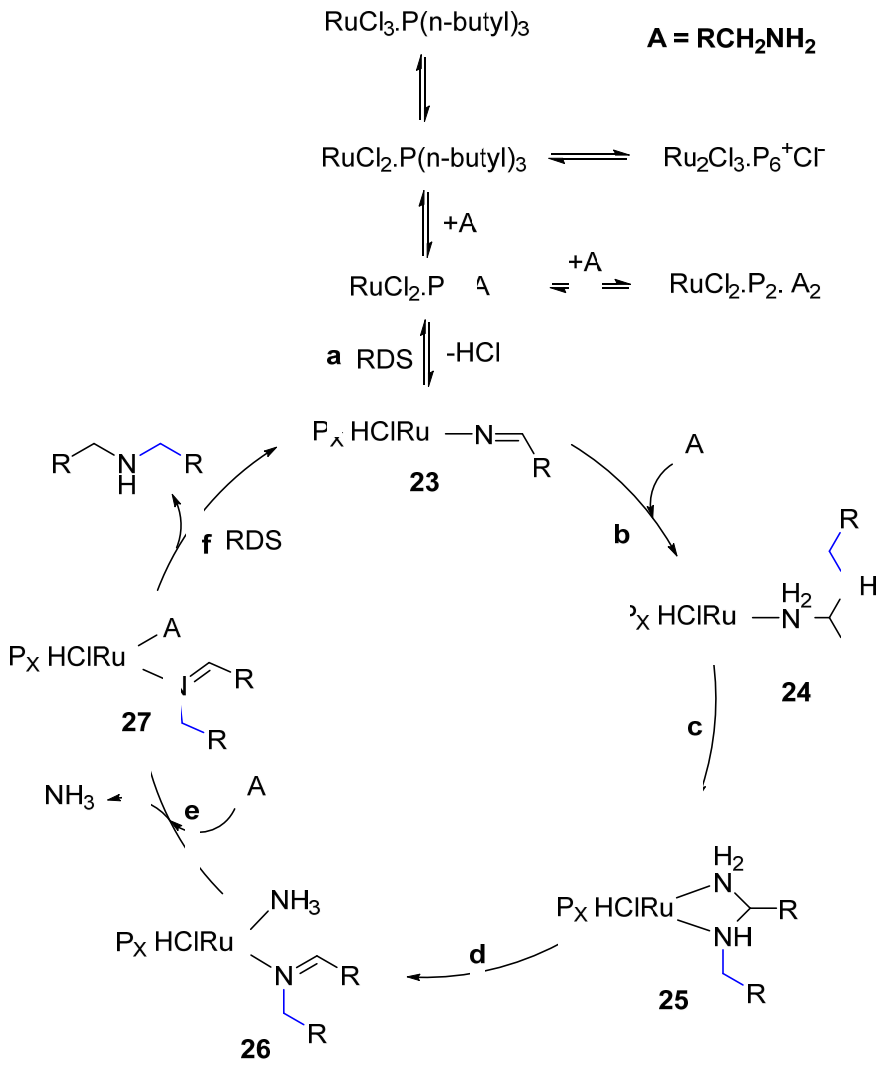
De Angelis and co-workers[16], in 1979 reported the symmetric coupling of the n-nonylamine **21** to form **22** with raney nickel in xylene (**Scheme 1.1.5.3**:). They also observed that the other solvents such as toluene, benzene or cyclohexane were not very suitable for this transformation. However, very few symmetric coupling products have been successfully achieved by amine self-coupling to form secondary amines.



Scheme 1.1.5.3: Deaminative symmetric coupling with Ni catalyst.

In 1983, Garrou and coworkers observed the formation of secondary amines on the $[Ru_2Cl_3(P^nBu_3)_6]Cl$ as the catalyst and proposed a mechanism for the amine coupling reaction.[20] They proposed a decoordination of phosphine ligand during the formation of the active catalyst. Further kinetic studies showed that the hydrogenation of the imine intermediate cannot be the rate determining step for the coupling reaction, as the rate of the hydrogenation step was found to be 200 times faster than the overall reaction rate. It

is noteworthy that this early stage mechanistic studies only relied on the rate of the reactions without any kinetic isotope effect studies.

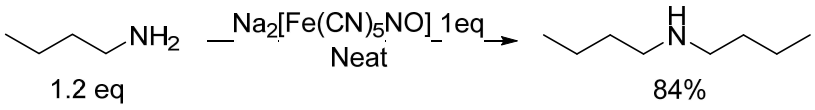


Scheme 1.1.5.4: Proposed mechanism for deaminative coupling by Garrou *et. al.*

Scheme 1.1.5.4 shows the rate determine step of the reaction is the formation of imine followed by dehydrogenation of amine (step **a** and **f**) to form active catalytic species **23**. Then, nucleophilic attack on α-carbon of the imine would generate the mono amine co-ordinated ruthenium di amine species **24** (path **b**) which then undergoes the

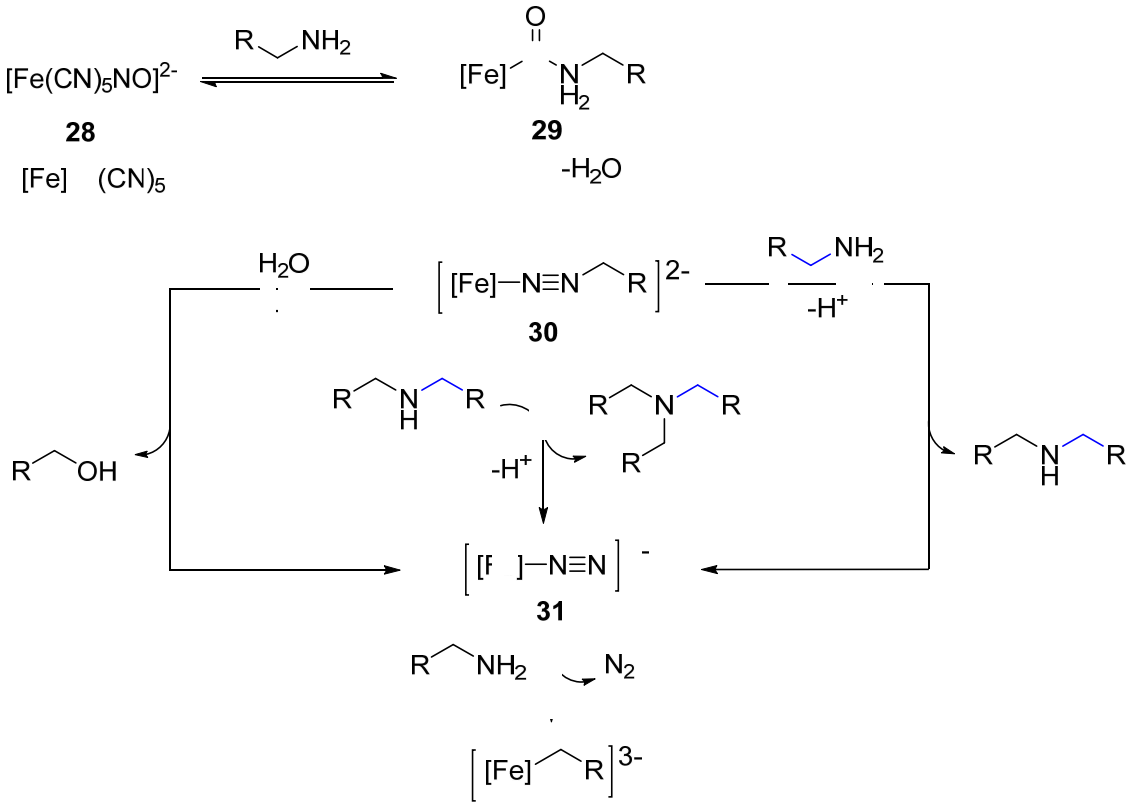
formation of four membered metallocycle **25** by second amine coordination (**c**). Then, C-N activation afforded the intermediate **26** (**d**) and new amine coordination via path **e** form **27** by releasing the ammonia which formed during the C-N bond cleavage step. Hydrogenation of the coordinated imine product **27** by hydrogens, which came from the new amine molecule would produce the active catalytic species with the product.

Watanabe and co-workers[20c] observed similar reactivity pattern for the self amine coupling. Doctorovich and Trhpani[20d] reported secondary amine product (dibutylamine, 84%) formation with pentacyanonitrosylferrate(II) as the stoichiometric reductant (**Scheme 1.1.5.5**).



Scheme 1.1.5.5: Reaction of pentacyanonitrosylferrate(II) with n-butylamine.

Dibenzylamine (30%), pyrrolidine (50%) and N-butylbenzylamine (58%) were also observed under similar conditions. To the best of our knowledge, this was the first reported heteroaliphatic coupling reaction in the literature. However, this reaction did not proceed under catalytic conditions as active catalyst was not regenerated (**Scheme 1.1.5.6**). Nucleophilic attack on NO group of **28** by amine afford the intermediate species **29**, which then undergoes dehydration to form diazonium ion reactive species **30**. Formation of alcohol may be explained by reaction of the coordinated diazonium ion with water, while its reaction with dibutylamine produces tributylamine affording species **31**. Alternatively, the reaction of **30** with an amine will be generated the **31** and symmetric secondary amine product.



Scheme 1.1.5.6: Proposed mechanism for the reaction of n-butylamine with pentacyanonitrosylferrate(II).

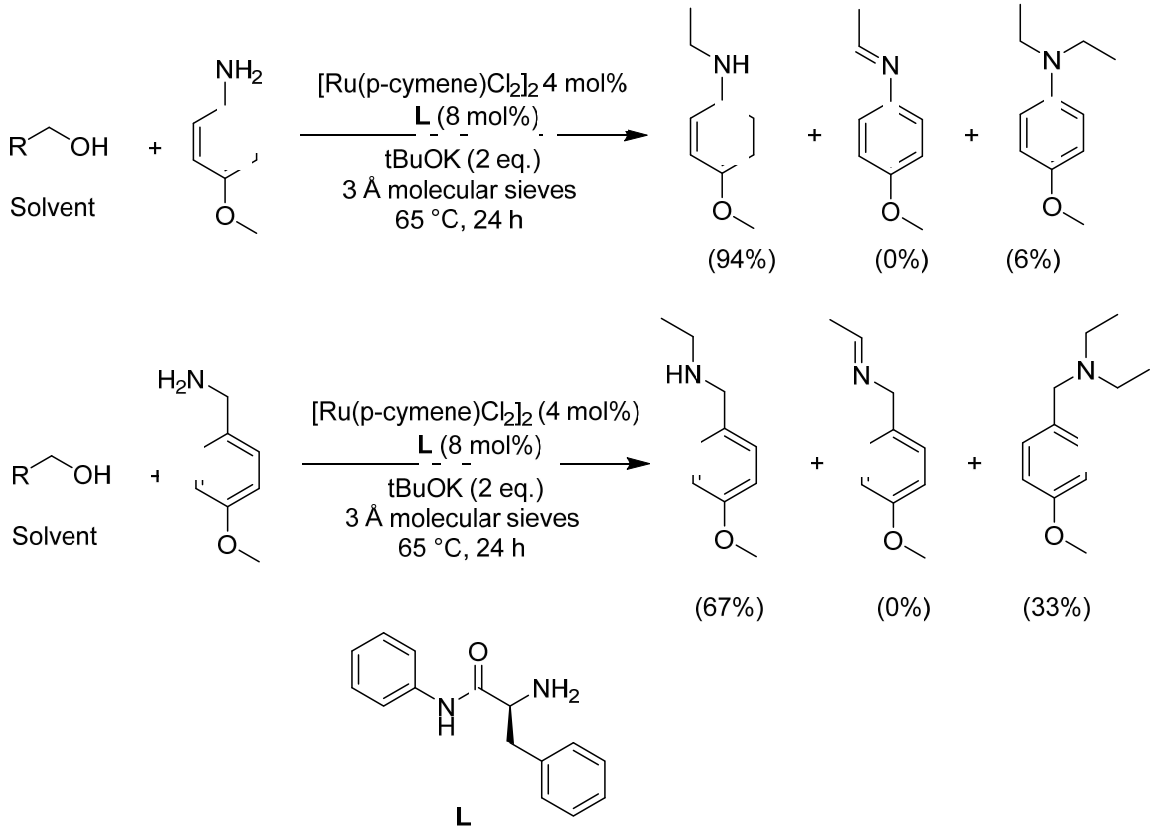
1.2 Recent Developments on Catalytic Methods for N-Alkylation of Primary Amines

The development of a new, general catalytic procedures for the selective formation of aromatic carbon-nitrogen bond is of great significance in wide variety of organic synthesis.[21] Over the years, the synthesis of N-alkylations of amines have received increased interests. In general, the formation of secondary amines with alkyl halides was found to be unsuitable method specially in large scale productions, because it forms toxic byproducts. To overcome cost ineffective methods which generate wasteful byproducts, the development of more environmentally friendly methods is highly sought

which has lower E-factors. As such, much attention has been drawn to develop methods with increasing environmental awareness and integrated in sustainable synthesis. Efficient catalytic methods provide attractive solutions for these problems.[22] This section summarizes the recent progress in this area specifically aimed at catalytic syntheses of secondary amines.

1.2.1 Formation of Secondary Amines from the Reaction of Alcohols

Homogeneous catalytic formation of secondary amine was established with simultaneous introduction of different rhenium[23] and ruthenium[24] catalysts. In recent years, the use of earth abundant metal catalysts for this process attracted considerable attention in the catalysis community. Transition metal catalysts such as iridium[25], ruthenium[26], copper[27], silver[28], iron[29], osmium[30], gold[31], and palladium[32] catalysts have been well studied for the alkylation of amines with alcohols in N-alkylation reaction. In 2014, Moasser and Enyong[26f] reported a ruthenium catalyzed N-alkylation by using a simple amino amide ligand. One-pot alkylation of primary and secondary amines were achieved under different reaction conditions. They demonstrated the alkylation under mild conditions using the alcohol as solvent, where high selectivity was seen at high temperatures in organic solvents (**Scheme 1.2.1.1**).

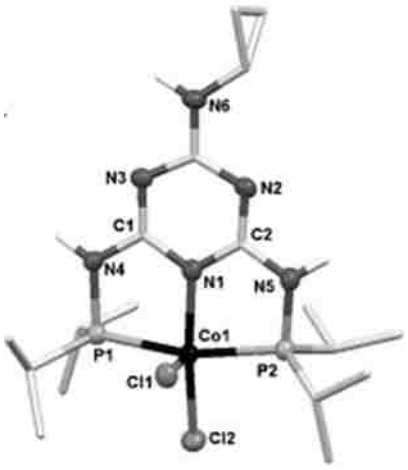


Scheme 1.2.1.1: Ruthenium catalyzed, amino amide ligand enabled secondary amine formation with alcohols.

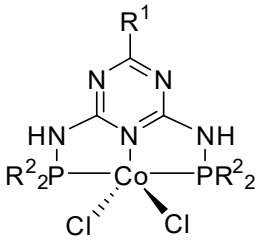
As shown in the **Scheme 1.2.1.1**, arylamines were used to prepare secondary amines selectively. However, the selectivity was obtained only when a large amount of alcohol was used as the solvent for the reaction. Ortho-substituted arylamines remained as an imine product without the hydrogen transfer. Benzyl amines and aliphatic amines were not very selective towards secondary amine formation due to the over alkylation reaction.

In 2015, Kempe and co-workers reported that a novel PNP type cobalt complex **33** (**Figure 1.2.1.1**) successfully catalyzes the selective formation of secondary amines with alcohols[33]. The cobalt catalyst (2 mol%) allows the reaction to be carried out under mild conditions (80 °C), which allow the selective formation of secondary aromatic

amines and the synthesis of unsymmetrical diamines (**Scheme 1.2.1.2**). However, more than stoichiometric amount of base was required to proceed the reaction.



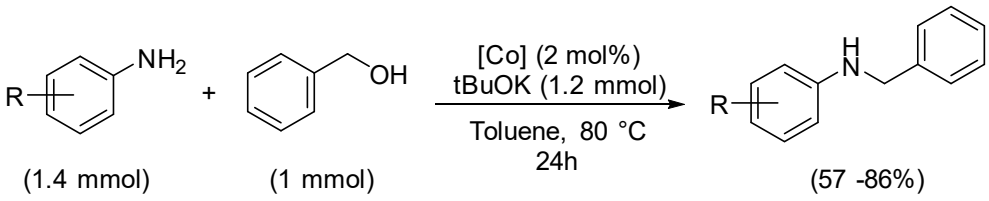
(**32**)



R^1 = H; R^2 = iPr

(**33**)

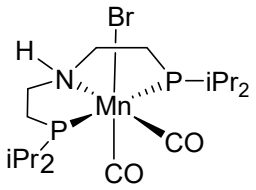
Figure 1.2.1.1: (**32**) X-ray structure of the cobalt complex; (**33**) Active catalyst used to catalyze the secondary amines formation with alcohol and amine.



Scheme 1.2.1.2: PNP type cobalt catalyzed N-alkylation with alcohol.

Very recently, Beller and co-workers reported manganese pincer complexes **34** (**Figure 1.2.1.2**) can be effectively employed the formation of secondary amines.[2a] Substituted anilines are monoalkylated with a variety of alcohols. The reaction tolerated a broad substrate scope including sensitive reducible functional groups such as furfuryl alcohol. Chemo selective monomethylation of primary amines were achieved using

methanol, and the metal catalyst **34** was found to be highly air stable. However, 75% base required for the reaction, and aliphatic and benzyl amines were not stable to form the corresponding secondary amine products.



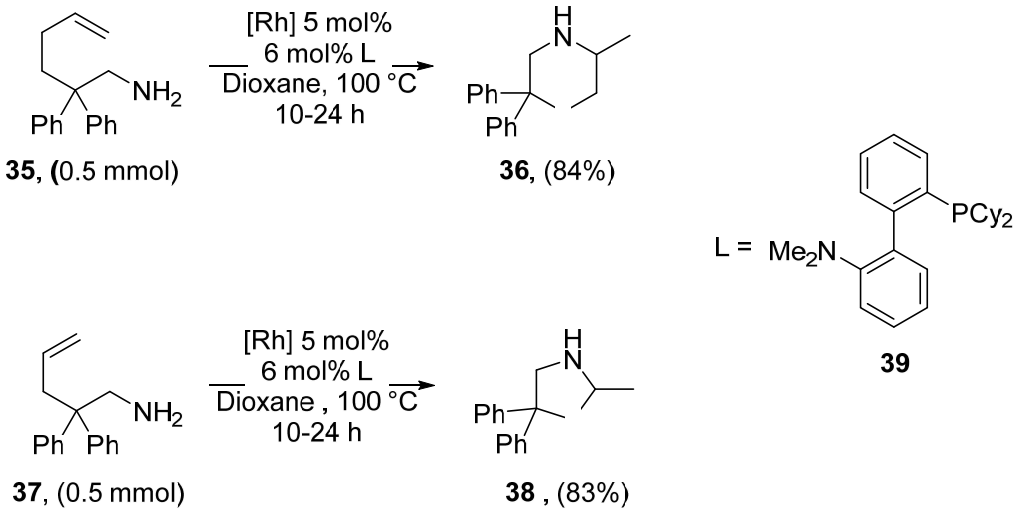
34

Figure 1.2.1.2: Active manganese PNP pincer complex for selective formation of secondary aromatic amines with alcohol.

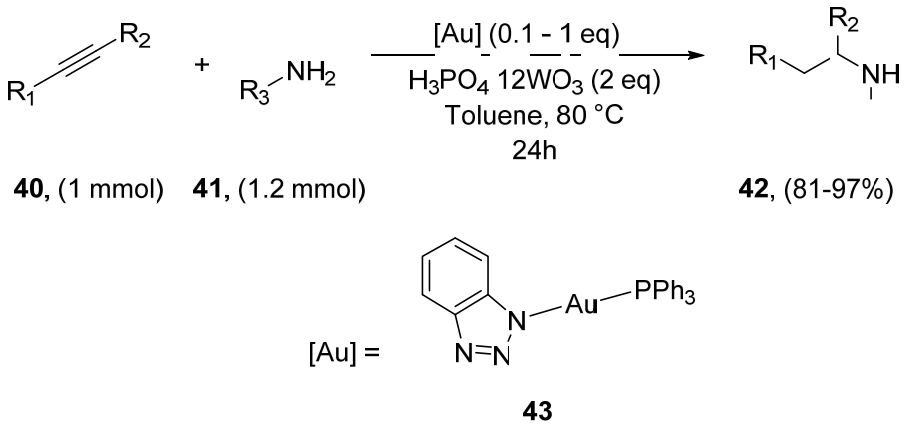
1.2.2 Catalytic Hydroamination of Alkynes and Alkenes

Catalytic heterofunctionalization is an important catalytic protocol that allows the formation of a wide variety of carbon to hetero atom bonds by adding substituents to alkenes or alkynes. Hydroamination is the addition of an N-H bond of an amine across a carbon-carbon double or triple bond of an unsaturated system.[34] The hydroamination is an atom economical and green method if the reactants stoichiometrically formed the products.

In 2008, Liu and Hartwig reported cyclization of aminoalkenes with a rhodium catalyst under mild conditions. (**Scheme 1.2.2.1**).[35] Six-membered cyclic amine **36** was obtained from 1-Amino-2,2-diphenyl-5-hexene **35** and corresponding five-membered cyclic amine **38** was formed from 1-Amino-2,2-diphenyl-4-pentene **37** with the ligand **39** and the catalyst $[Rh(COD_2)]BF_4^-$ in good yields.



Scheme 1.2.2.1: Rhodium catalyzed intramolecular hydroamination of primary aminoalkene to form six- and five-membered cyclic amines.

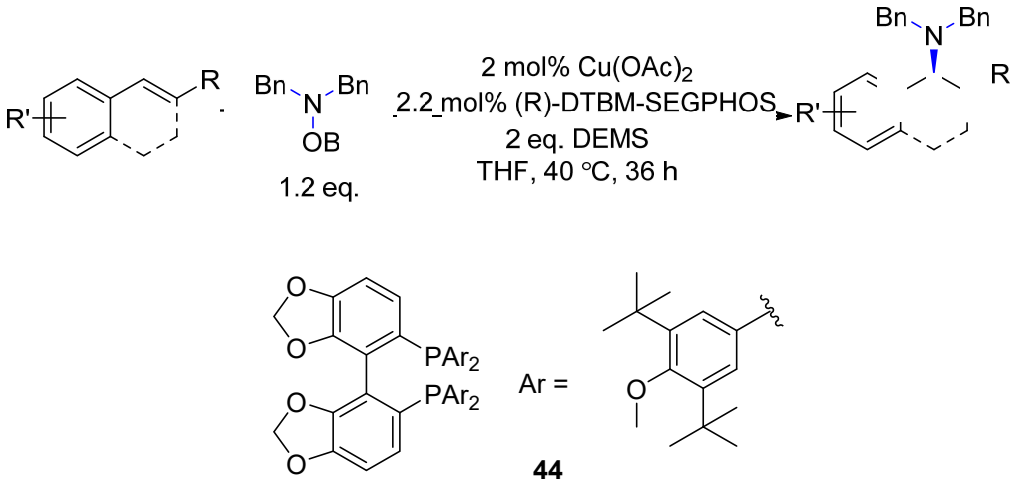


Scheme 1.2.2.2: Gold catalyzed hydroamination with alkyne.

In 2009, Shi and co-workers reported gold catalyzed hydroamination with alkynes **40** and amine **41** to form the secondary amine products **42** in excellent yields (**Scheme 1.2.2.2**).[36] The gold catalyst system **43** has been found to be effective for the challenging transformations, such as intermolecular internal alkyne hydroamination reactions.

Product **42** were yielded by utilizing (**40**; R_1 = Bu, R_2 = H; R_3 = Ph;) 81 % and (**40** R_1 = Ph, R_2 = H; **41** R_3 = p-F-Ph;) 97% with the catalyst **43**. However, the reactions with internal alkynes required a catalyst loading up to 1 mol%. The major disadvantage of this reaction was two equivalents tungstonphosphoric co-catalyst are needed to reduce the hydroaminated product.

In 2013, Buchwald and co-workers reported a highly enantio- and regio-selective (>86-99% ee) copper catalyzed hydroamination reaction of styrene. The reaction required diethoxymethylsilane (DEMS) and esters of hydroxylamines to form enantiosecective tertiary amine products.[37]

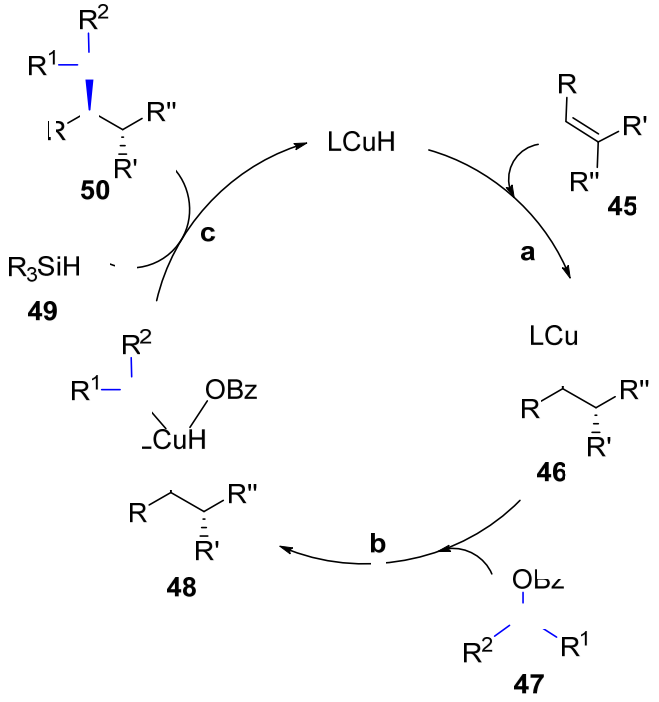


44

Scheme 1.2.2.3: Enantio- and regio-selective hydroamination of styrene derivatives.

A variety of substituted styrenes (with cis-, trans-, and *β,β*- disubstituted styrenes) was found to be suitable for yielding α-branched amines. The reported asymmetric intermolecular hydroamination (step **a),** would proceed by insertion of an alkene **49** into a chiral ligand **44** ((R)-DTBM-SEGPHOS) bounded Cu-H species by forming an

alkylcopper complex **46** (**Scheme**: **1.2.2.4**). Subsequent oxidative addition (step **b**, intermediate species **48**) of an electrophilic hydroxylamine species **47** followed by reductive elimination (step **c**), would form the enatioselective product **50**. Active catalytic species was regenerated by the transmetalation with an external hydride-transfer reagent, in this case DEMS **49**.

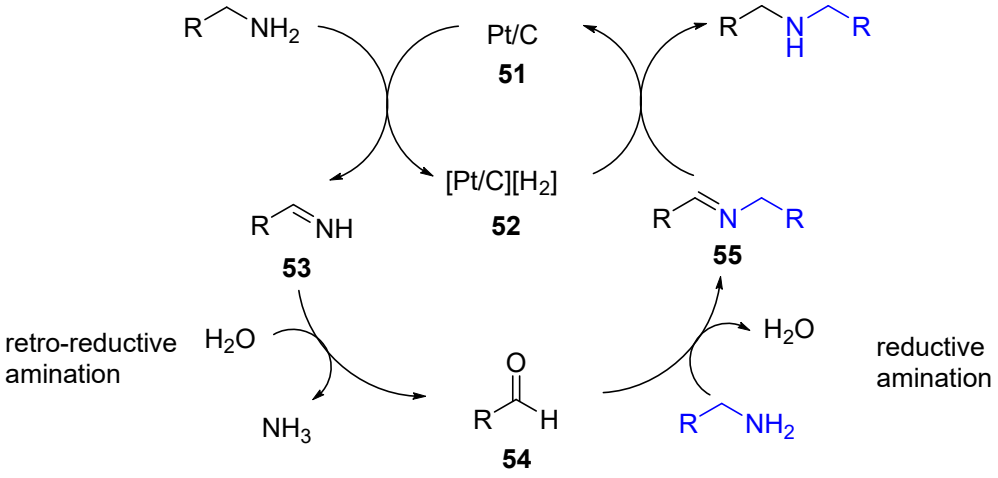


Scheme: **1.2.2.4**: Proposed catalytic cycle for hydroamination of alkenes.

1.2.3 Catalytic Formation of Secondary Amines from the coupling of Amines

Olah and co-workers reported[38] the synthesis of secondary amines from primary amines on Pt/C catalyst. The results were similar as earlier observations by Doctorovich and Trhpani[22d] in 1999, who observed self coupling of amine substrates under microwave irradiation. There is no significant improvement in substrate scope for the reaction

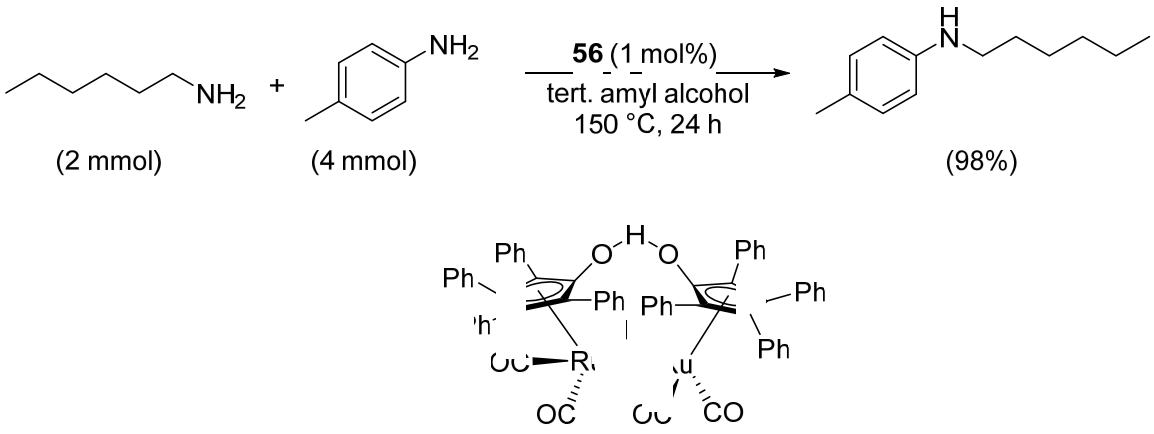
developed. The proposed reaction pathway of Pt/C catalyzed reaction of primary amine to secondary amine in water under microwave irradiation is interesting as both retro-reductive and reductive amination steps were introduced (**Scheme 1.2.3.1**).



Scheme 1.2.3.1: Proposed reaction pathway of Pt/C catalyzed reaction of primary amines.

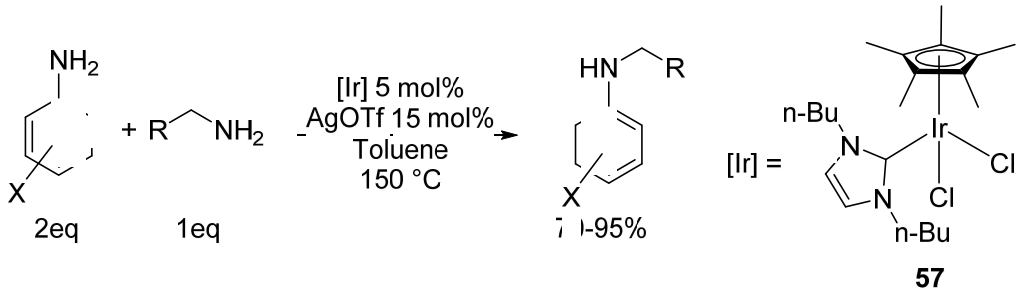
In the beginning of the catalytic cycle, alkylamine would be oxidized to form an imine product **53** by oxidative removal of dihydrogen, which is initially formed in situ in the reaction with **51**. The aldehyde intermediate **54** could be formed by the hydrolysis of imine product in aqueous media by generating ammonia. Then alkylidenealkylamine **55** is formed as the immediate from the reaction of an aldehyde with starting amine. Then the alkylidenealkylamine **55** would be reduced by Pt/C-dihydrogen species **52** to give a secondary amine and regenerate active catalyst **51**. As can be seen in the **Scheme 1.2.3.1**, from primary amine to aldehyde can be identified as *retro-reductive amination* (oxidative deamination) and the product formation can be identified as reductive amination.

Beller and co-workers successfully developed the amine coupling reaction in 2007.[39] They reported selective dealkylation of amines by using Shvo catalyst **56** (**Scheme 1.2.3.2**). This was the first reported arylation of aliphatic amines with anilines that proceeds under transfer hydrogenation conditions.



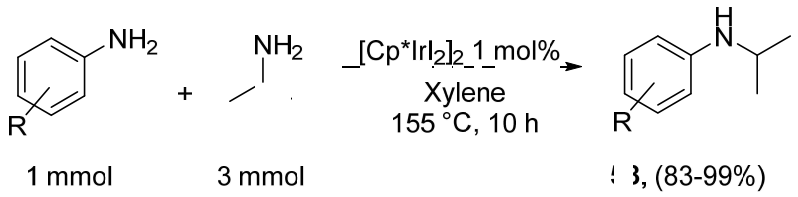
Scheme 1.2.3.2: Amination of aryl compounds by Shvo catalyst **56**.

A variety of functionalized anilines was transformed into secondary amines with n-hexylamine in the presence of Shvo catalyst in excellent yields. Apart from n-hexylamine, few other substrates were transformed to corresponding secondary amines with aniline. In 2008, Peris group demonstrated that Ir catalyst **57** efficiently generate secondary amines from the coupling of aniline and few aliphatic amines (**Scheme 1.2.3.3**).[25a]



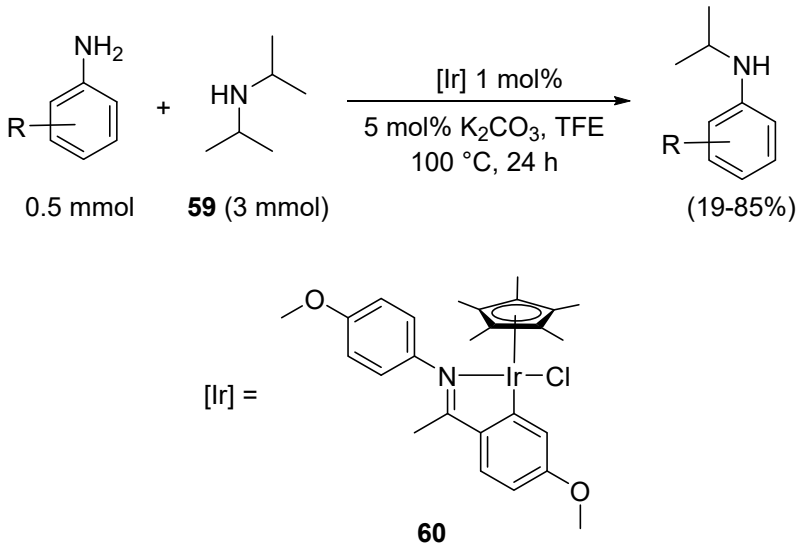
Scheme 1.2.3.3: N-Alkylation of aniline with aliphatic amines by Ir-carbene complex **57**.

In 2009, William's group reported an iridium complex, $[Cp^*IrI_2]_2$ enabled coupling between aryl- or alkyl-amines and N,N-Diisopropylamine to synthesize branched secondary amine derivatives **58** (**Scheme 1.2.3.4**).[40]

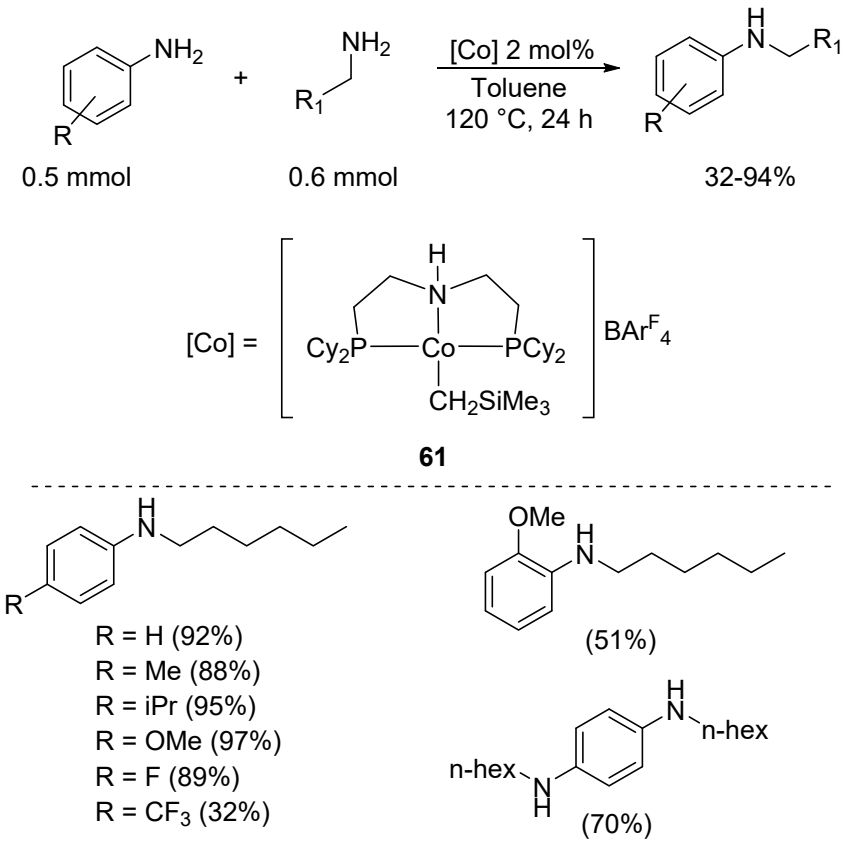


Scheme 1.2.3.4: Conversion of aniline into N-isopropylaniline with Ir catalyst.

However, this study was limited to the synthesis of N-isopropyl substituted aniline derivatives from the alkyl transfer reaction pathway with di-isopropylamine **59**. More recently, Xiao group demonstrated the utilization of a cyclometalated Ir catalyst **60** to achieve the alkylation of anilines with bis-(isopropyl)amine (**Scheme 1.2.3.5**), but the reaction resulted in moderate yields with a very limited scope adding base as an additive.[41]



Scheme 1.2.3.5: Cross-coupling of amines with Ir catalyst.



Scheme 1.2.3.6: Formation of secondary amines with Co-PNP catalyst.

Very recently, Zhang group reported a cobalt-catalyzed selective N-alkylation of amines with aniline substrates to synthesize secondary aromatic amines.[42] The utilization of Co PNP type catalytic system **61** selectively produced secondary amines with n-hexylamine. The reaction tolerated for wide variety of functional groups including complex molecules (**Scheme 1.2.3.5**) with respect to aromatic amine substrate. However, most of them were prepared by using n-hexylamine as the substrate. The cobalt catalyzed monoalkylation of amines achieved via deaminative coupling reaction under "hydrogen-borrowing" pathway (**Figure 1.2.3.1**), which is a generally accepted strategy in catalysis[2a,22,33,39-44].

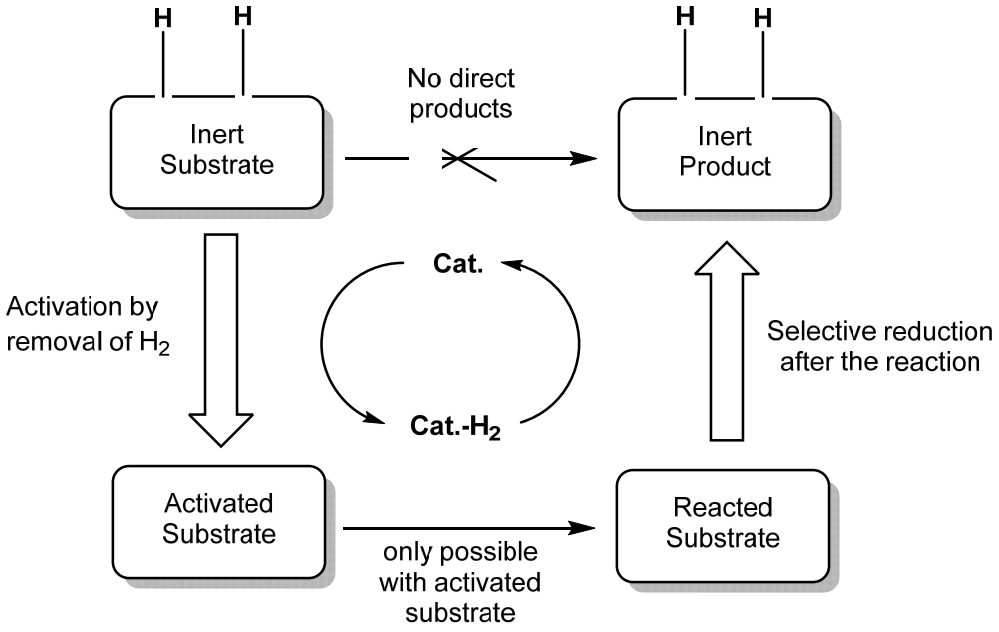


Figure 1.2.3.1: General scheme for "*hydrogen-borrowing*" strategy.

In summary, Transition metal catalysts can activate normally unreactive alcohols or amines by hydrogen abstraction procedure. The inactive alcohol or amine is converted into a carbonyl or imine by abstracting the hydrogen by a catalyst. The more reactive carbonyl or imine intermediate undergoes a condensation reaction or any other type with a nucleophile. Finally, the hydrogen will be returned to the reacted substrate to form the products. The catalytic formation of secondary amines via amine coupling reactions have not been well established. In this context, our goal has been to develop novel environmentally benign, atom economical catalytic methods via C-N bond activation of primary amines to synthesize secondary mines.

1.3 Catalytic C-N Bond Activation Reactions

Transition-metal catalyzed C-N bond activation reaction has been widely explored over the years. This catalytic method is a powerful tool for the synthesis of nitrogen containing molecules, (i. e. amines, amides, amino acids, nitriles) in which the metal bounded carbon and nitrogen species were typically involved in the catalytic cycle.[45] The C-N activation by a transition-metal would also generate either metal bounded carbon, nitrogen or both species (C-M, C-N, C-M-N).[45-47] In principle, the active species formed on the metal center could transferred to another active species to form carbon-carbon or carbon-hetero atom under favorable conditions **(Figure 1.3.1).**

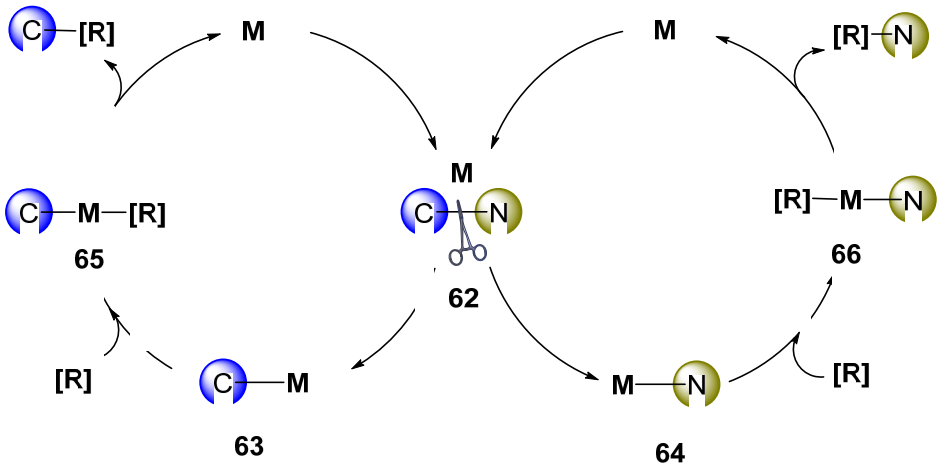
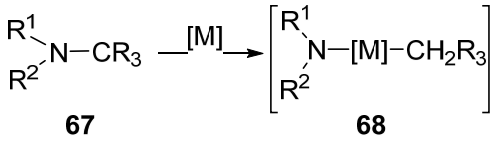


Figure 1.3.1: Schematic representation of C-N bond activation and new bond formation.

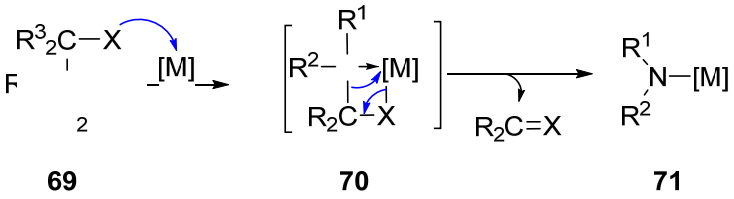
The facile occurrence of the C-N bond metalation step is an important step for successful C-N activation reactions. As can be seen in **Figure 1.3.1** an inert C-N bond **62** was converted into more active metal bounded species **63** and **64** which could form new

activated species **65** and **66** to form new products by reductive elimination. There are three general mechanisms generally accepted as a reasonable explanation for the C-N bond metalation (**Figure 1.3.2**).

a) oxidative addition



b) *β*-N elimination



c) C-H bond cleavage triggered C-N bond activation

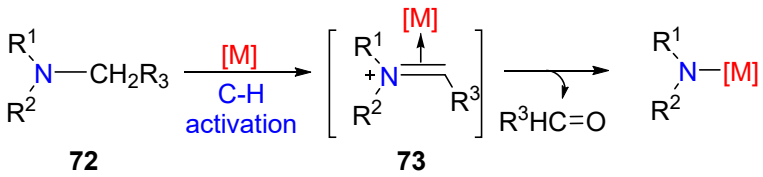


Figure 1.3.2: General mechanisms for C-N bond metalation.

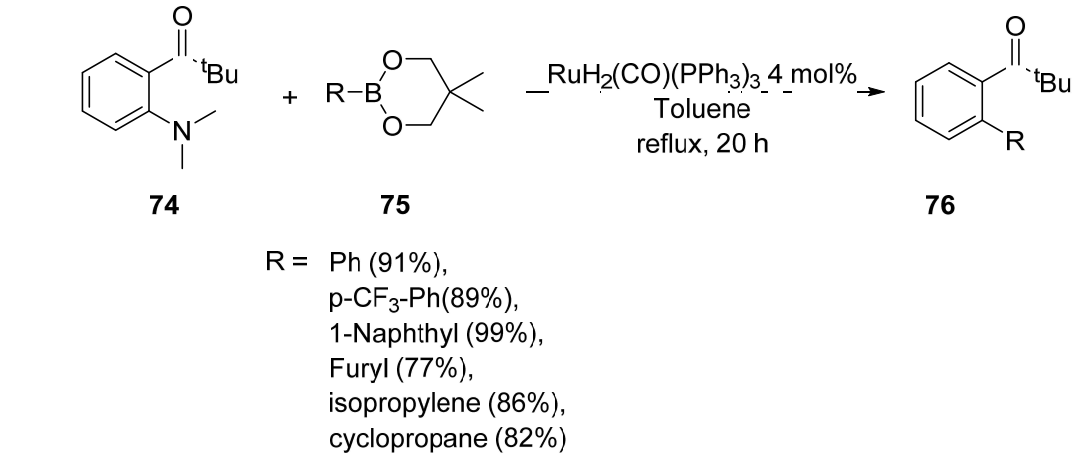
Oxidative addition of C-N bond is the direct way to generate the metal bound active intermediate species **68** from the amine species **67** for further transformations. The *β*-N elimination is possible in the presence of directing atom or functional group (i. e. allyl) **69**, which can be coordinated to metal center to activate the cleavage of C-N bond **70** to form N-metalated moiety **71**. The convenient way for the C-N bond activation is by

C-H bond cleavage triggered C-N bond activation through iminium ion formation **73** (**Figure 1.3.2**: c) from desired amine derivative **72**. This would be facilitated by the hydrogen acceptors on the metal center, such as ligands. Indeed, impressive progress has been achieved in transition-metal catalyzed C-N bond activation reactions throughout past few decades.

1.3.1. Activation of the Arene C(sp^2)-N Bond

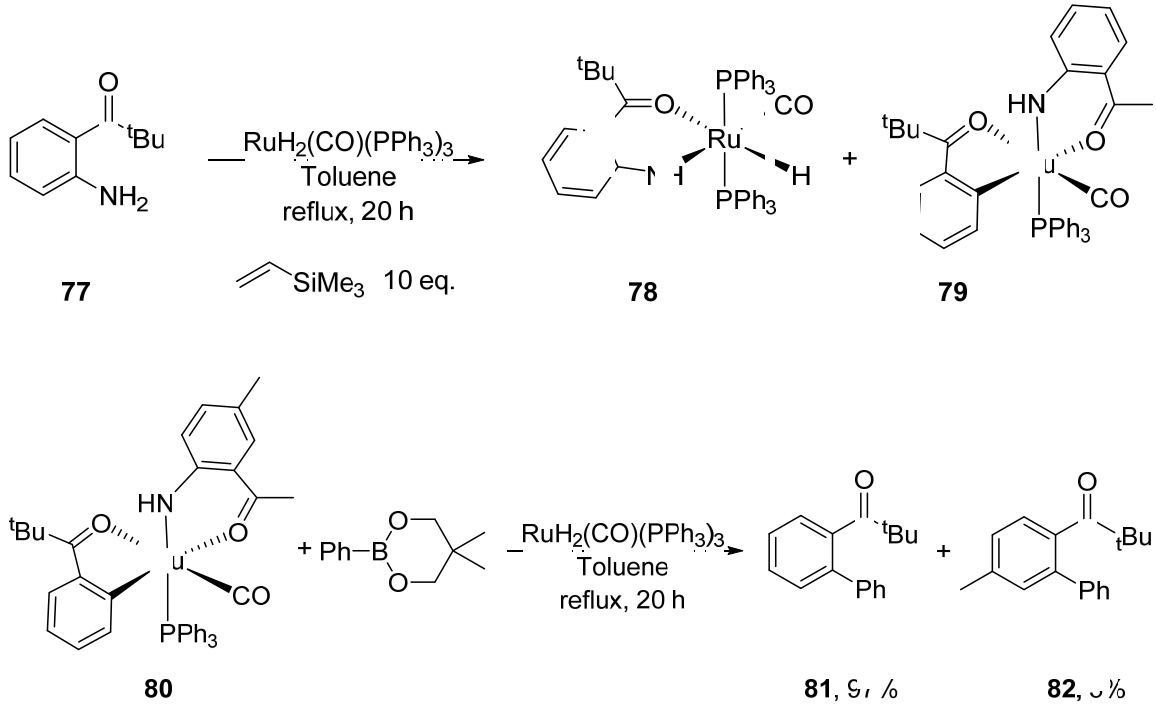
During past twenty years, researchers were keen to establish efficient ways to activate the C(sp^2)-N bond by using transition metal catalysis. These methods would afford biaryls, borylation products and ethylene derivatives, which are fundamental structural motifs in myriads of pharmaceuticals and agrochemicals. MacMillan and co-workers reported the first Suzuki type cross-coupling of aryltrimethylammonium salts. $Ni(COD)_2$ catalyst was used in the presence of IMes as the ligand in dioxane as the solvent at 50 °C.[48]

In 2009, Kakiuchi and co-workers reported the ruthenium-catalyzed C-C coupling reaction of aminoacetophenone with organoboranes via C-N bond activation.[47i] aminoacetophenone C-N bond was activated by relatively electron rich $RuH_2(CO)(PPh_3)_3$ by the assistance of the carbonyl directing group. A wide range of aminoacetophenones (i. e. $-NH_2$, $-NMe_2$, -N(Me)Ac) was shown to be amenable for this reaction. Furthermore, ortho substituted pivalophenones were formed with aryl- and alkyl-boronic acids affording in excellent yields (**Scheme 1.3.1.1**).



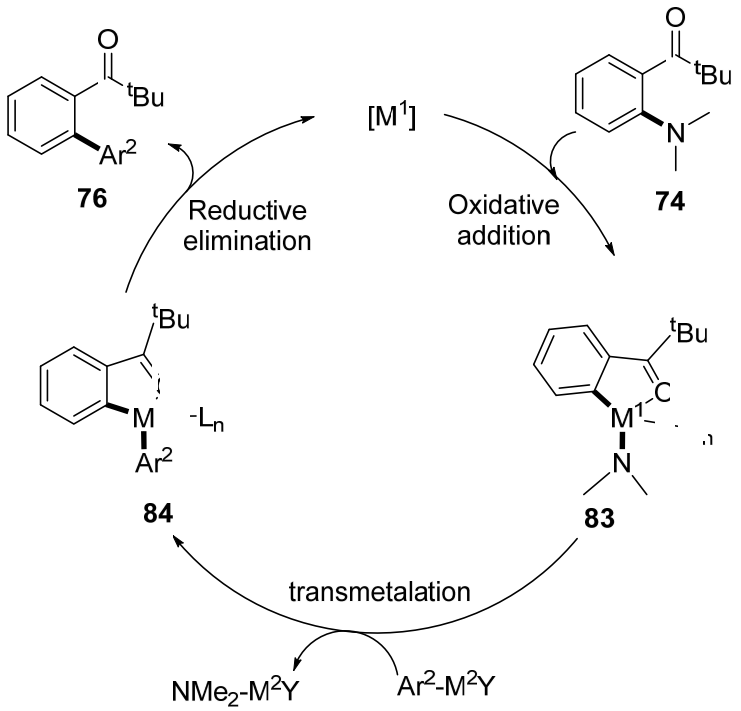
Scheme 1.3.1.1: Ruthenium-catalyzed cross-coupling reaction of aminoacetaphenone with organoborones.

To gain further insight into the mechanism of this reaction, the group has been able to synthesize and investigated the conceivable intermediates, **78**, **79** and **80** formed during the reaction. (**Scheme 1.3.1.2**).[49]



Scheme 1.3.1.2: Generation of ruthenium intermediate species.

Firstly, the arylruthenium complex **79** was obtained in 6% yield with a stoichiometric reaction of $RuH_2(CO)(PPh_3)_3$. Later, compound **79** was improved when 10 equivalents of alkene ($SiMe_3CH=CH_2$) was introduced into the reaction system. Later, unsymmetrical complex **80** was also prepared by following the modified procedure. This was a direct observation of C-N bond cleavage is possible on the ruthenium center. The target coupling product **81** was obtained by conducting the stoichiometric reaction of intermediate **80** under similar reaction conditions, which was yielded expected product in 97% yield. Moreover, the target Suzuki-type coupling was achieved under catalytic conditions.

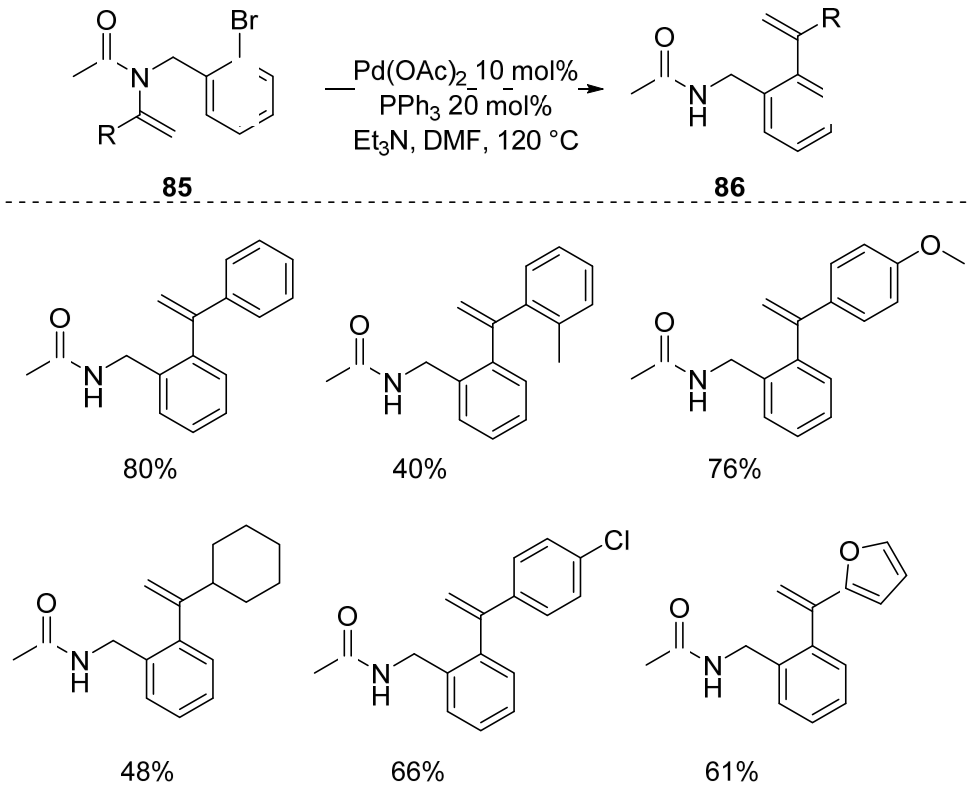


Scheme 1.3.1.3: Proposed mechanism for the Suzuki-type cross coupling.

A reasonable catalytic cycle could be proposed for the formation of new C-C bond by arene Csp^2-N activation (**Scheme 1.3.1.3**). At the beginning C-N bond activation

through oxidative addition of the **74** to the ruthenium complex to form ruthenium amido intermediate **83**. Then the ruthenium amido complex **83** formed, would exchange the alkyl groups by transmetalation with an organoboronate to form intermediate species **84** and finally reductive elimination yields the desired product by regenerating the active catalyst back to the system.

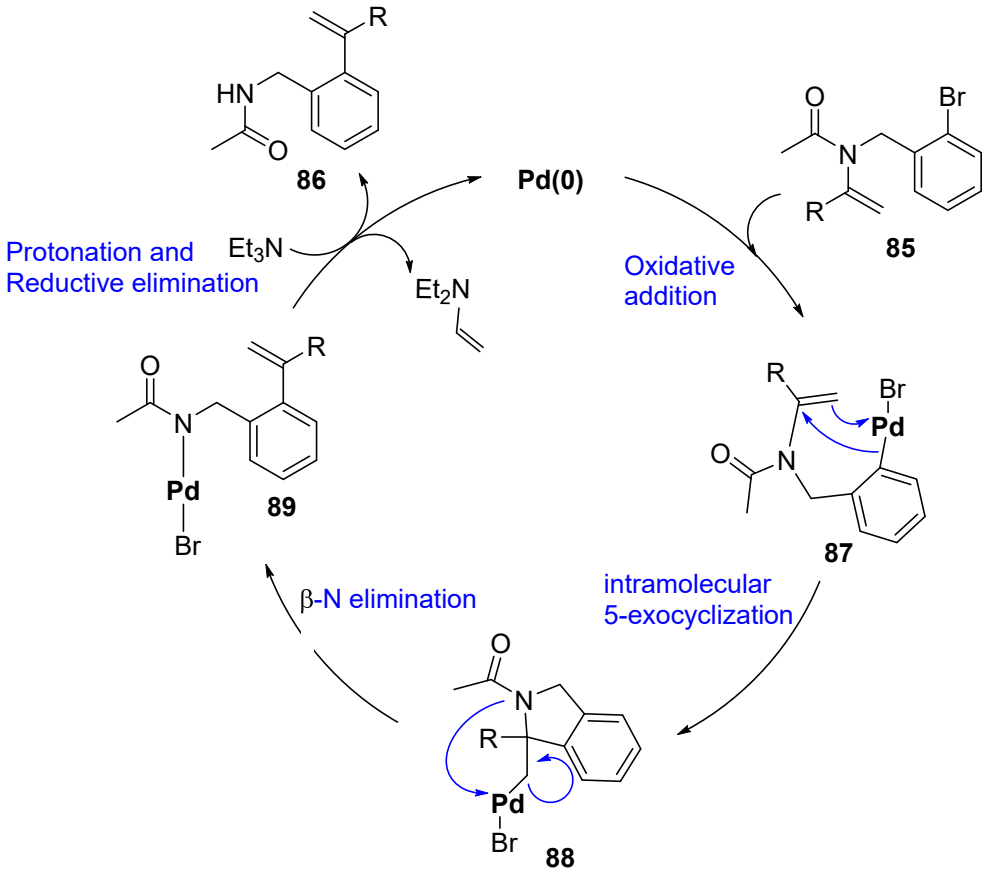
1.3.2. Activation of the Olefinic C(sp^2)-N Bond



Scheme 1.3.2.1: Heck type coupling reaction of N-vinylacetamide derivatives.

Loh and co-workers palladium-catalyzed intramolecular Heck reaction of N-vinylacetamide derivatives were reported in 2015.[50] Intramolecular olefinic C(sp^2)-N

bond cleavage product was obtained in the presence of Et_3N and $Pd(OAc)_2/PPh_3$ as the catalyst in DMF at 120 °C. l,l'-Disubstituted ethylene derivatives were selectively formed, which showed compatibility for both electron-rich and -poor groups on the phenyl ring and tolerated the aliphatic enamine moieties. The reaction was tolerated sterically hindered tert-butyl and cyclohexyl-substituted N-vinylacetamides as well (**Scheme 1.3.2.5**).



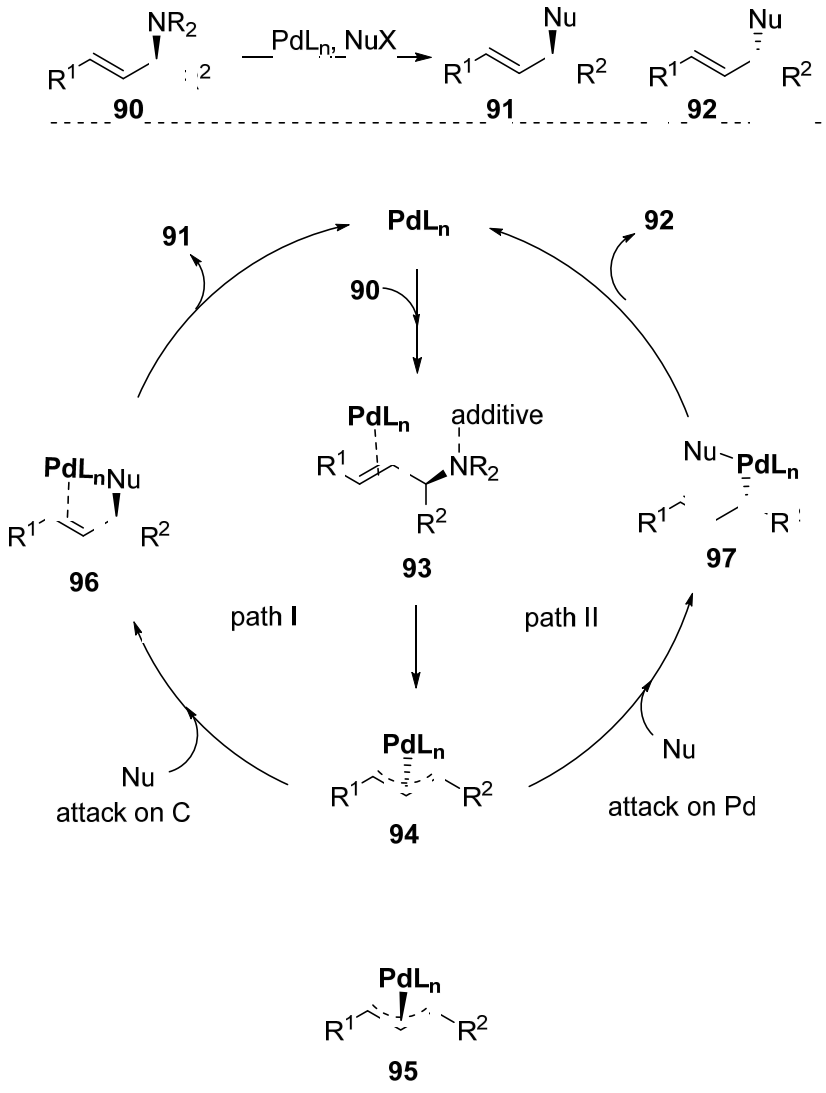
Scheme 1.3.2.2: Proposed mechanism for Heck reaction of N-vinylacetamide derivatives.

The mechanism of Heck reaction can be explained as depicted in **Scheme 1.3.2.2**. Oxidative addition of the C-Br bond to Pd(0) will form the oxidized form of the palladium complex **87**, followed by intramolecular 5-exo-cyclization produce a new five

membered palladium complex **88**. Then the C-N bond activation through *β*-N elimination was occurred to form the intermediate palladium species **89**. Finally, protonation and sequential reductive elimination yielded the desired product utilizing Et_3N as the hydrogen source with the regeneration of active catalytic species.

1.3.3. Activation of the C(sp^3)-N Bond of Amines

1.3.3.1. Activation of the C(sp^3)-N Bond of Allylic Amines



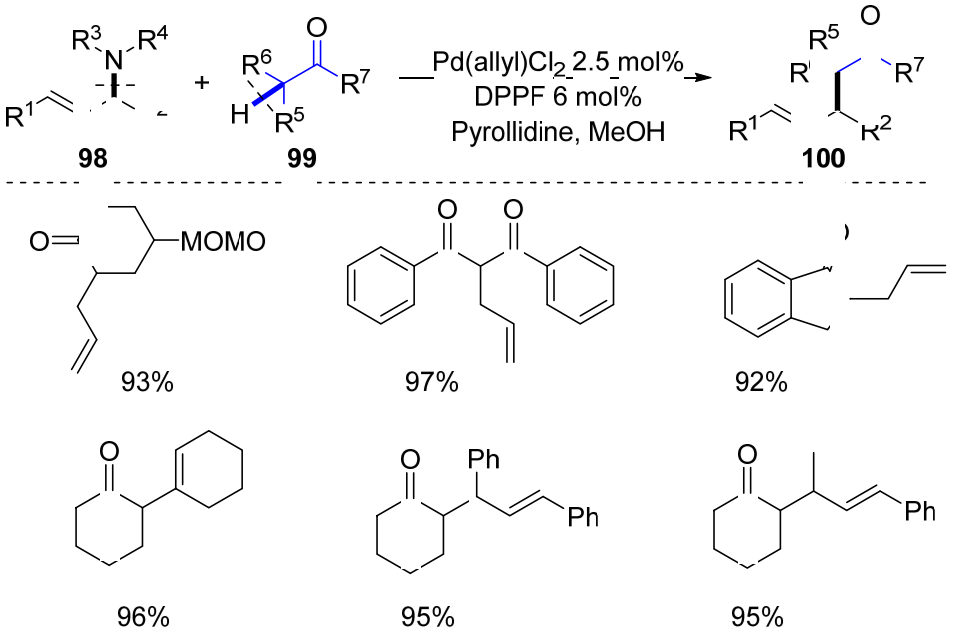
Scheme 1.3.3.1.1: Proposed mechanism for C-N bond activation of allylic amines.

Allylic amines are considered to be a versatile building blocks in synthetic organic chemistry. Oxidative addition to the low-valent metal via C-N bond activation is the key aspect for the chemistry of the allylic amines.

Palladium catalyzed C-N bond activation of allylic amines can be demonstrated as shown in **Scheme 1.3.3.1.1** as a typical pathway to illustrate a C-N bond cleavage mechanism.[45] Firstly, palladium-catalyst coordinates with the allylic substrate through the double bond while the NR_2 group is activated by the Lewis acid by generating palladium coordinated species **93**. Next, oxidative addition through the C-N bond to the Pd(0) provides the π-allyl palladium species **94** or **95**. The binding phase would be dependent on the steric or directing groups present on the used ligands. S_N2 type nucleophilic attack would be expected in the presence of "soft nucleophiles" (pKa of its conjugate acid > 25), on the allylic carbon atom of **94** or **95** gives the complex **96** with the inversion of the configuration with respect to palladium η^2-C bond. Decoordination gives the product **91** with the retention of configuration while regeneration of the low-valent palladium, which is shown in the *Path I*. Alternatively, if the "hard nucleophile" (pKa of its conjugate acid > 425) has been used, the nucleophilic attack would be possible on the palladium center in complex **94** generating **97** (*Path II*). Finally, reductive elimination will be generated the other enantiomer of the product **92**.

In 2011, Tsuji-Trost-type reaction (allylic alkylation) for the carbonyl compounds with allylic amines was developed by Zhang and co-workers which was explained as hydrogen-bond-promoted C-N bond activation.[51] $[Pd(allyl)Cl]_2$ with DPPF (1,1'-Ferrocenediyl-bis(diphenylphosphine)), ligand promoted reaction was proceed efficiently via active enamine intermediates. The enamine intermediate generated from the

condensation of carbonyl compounds with pyrrolidine. Furthermore, excellent enantioselectivities were obtained, when a chiral ferrocene-based phosphinooxazoline was used as a ligand with chiral -allylic substituted ketones. It is noteworthy that C-N bond activation of allylic amines was only possible with the suitable hydrogen donor solvent, in this case methanol (**Scheme 1.3.3.1.1**).

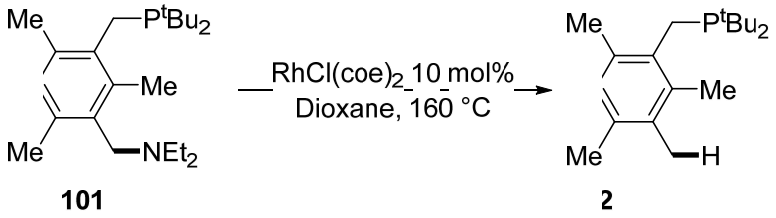


Scheme 1.3.3.1.2: Palladium-catalyzed allylic alkylation of carbonyl compounds.

1.3.3.2. Activation of the C(sp^3)-N Bond of Aliphatic Amines

Milstein and co-workers first reported the rhodium-catalyzed reductive hydro-denitrogenation reaction with tertiary amine **98** as the substrate.[47c] Quantitative product yield was achieved by using $[RhCl(coe)_2]_2$ as a catalyst under the H_2 gas. However, this catalytic reaction was very limited due to pincer-type phosphine-amine substrate. Even

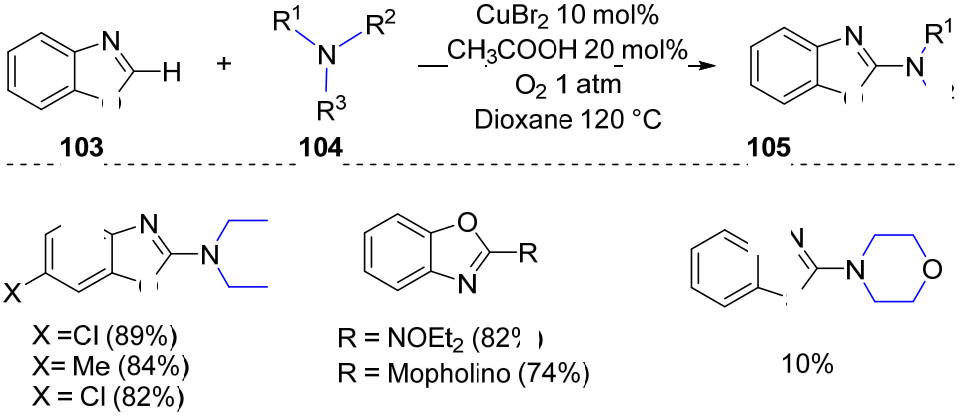
though, the transformation very atom economical, potential application was limited due to a narrow substrate scope. (**Scheme 1.3.3.2.1**).



101 **2**

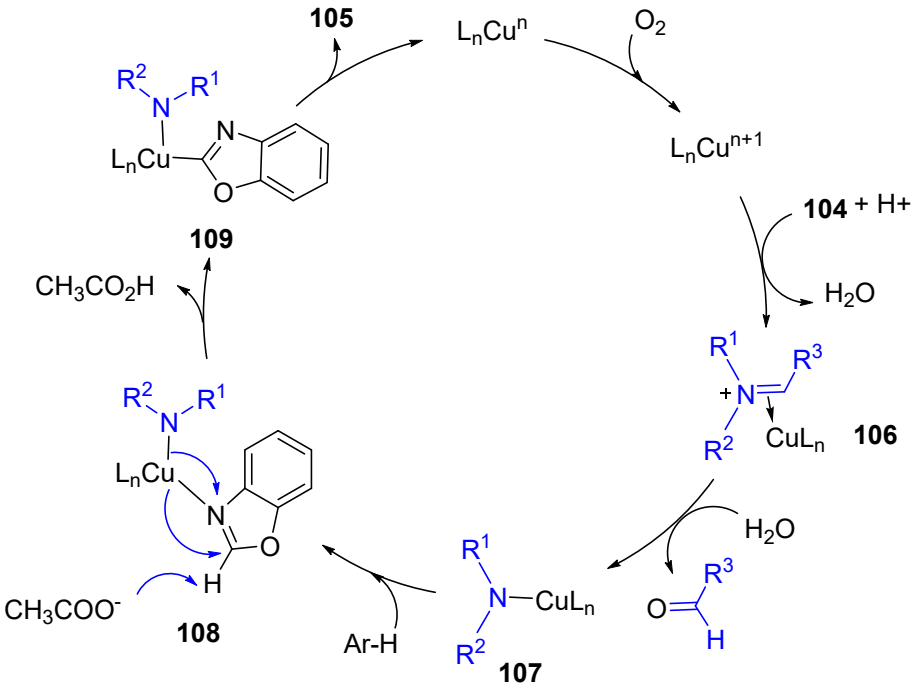
Scheme 1.3.3.2.1: Rhodium-catalyzed hydro-denitrogenation.

In 2011, Huang and co-workers developed a conceptually new strategy for oxidative C-N bond activation triggered via C-H activation.[52] The C-N bond of tertiary amines was found to be cleaved with $CuBr_2$ as a catalyst under O_2. Copper-amide species were identified as the key intermediates for this C-N bond formation reaction. Thus, a new oxidative C-H amination of azoles with tertiary amines was established with a variety of azoles and tertiary amines contains α-H adjacent to the nitrogen atom (**Scheme 1.3.3.2.2**).



Scheme 1.3.3.2.2: Copper-catalyzed oxidative amination of azoles.

Figure 1.3.3.2.3 shows the mechanistic rationale originally proposed by the observation of the mechanistic experiments. Initially, iminium type intermediate **106** will be formed by the activation of the C-H bond of the tertiary amine on the high-valent copper species in the presence of oxygen by elimination of H_2O molecule. Subsequent hydrolysis of iminium type intermediate **106** produces the key copper-amide species **107**, which will be coordinated to azole moiety quickly by forming intermediate **108**. Cleavage of the C-H bond of the azole moiety leads to generate the copper complex **109**, which would undergo reductive elimination to furnish the desired product **105** with the regeneration of the active catalytic species to complete the catalytic cycle.



Scheme 1.3.3.2.3: Proposed mechanism for oxidative amination of azoles.

In summary, transition-metal catalyzed C–N bond activation has prompted many novel methods for synthetic chemistry. It is evident that the new reactions developed over the years via C–N bond cleavage undoubtedly be useful for industrial and pharmaceutical applications. Various late transition-metal catalysts have been explored for novel C-N bond cleavage reactions. The catalytic C-N activation has been emerging as one of the most promising tools in synthetic organic chemistry, but the methods still require careful attention in order to develop industrially applicable coupling reactions.

Chapter 2

Ligand Controlled Synthesis of Symmetrical and Unsymmetrical Secondary Amines from the Ruthenium Catalyzed Deaminative Coupling Reaction of Amines

2.0 Introduction

Carbon-nitrogen (C-N) bond is commonly present in many organic compounds including amino acids and other bioactive molecules. Catalytic C-N bond cleavage reactions are of fundamental importance in a variety of industrial and fine chemical syntheses as well as in biochemical processes.[53] Considerable efforts have been devoted to develop efficient synthetic methods to utilize amines for the synthesis of a complex organic molecules such as pharmaceutical agents, polymer materials, dyes and agrochemicals.[54] Even though many methods has been reported in the recent literature, selective synthesis of secondary amines from the alkylation of primary amines is still challenging due to selectivity of the reaction.[42,43,55] Due to toxicity and high mutagenic properties, alkyl halides have been identified as unsuitable substrates for industrial scale synthesis of N-alkylated amines. Transition-metal-catalyzed monoalkylation reactions of amines with alcohols as alkylating agent could be efficiently employed with ruthenium, iridium, iron and cobalt catalysts.[26,56]

In industrial petrochemical process, heterogeneous Mo catalysts are commonly used for the industrial petroleum hydro-denitrogenation process of hydrocarbon feedstocks. For biochemically significant process, C-H oxidation metalloenzymes such as CytP450 and methane monooxygenase have been well known to mediate biochemical

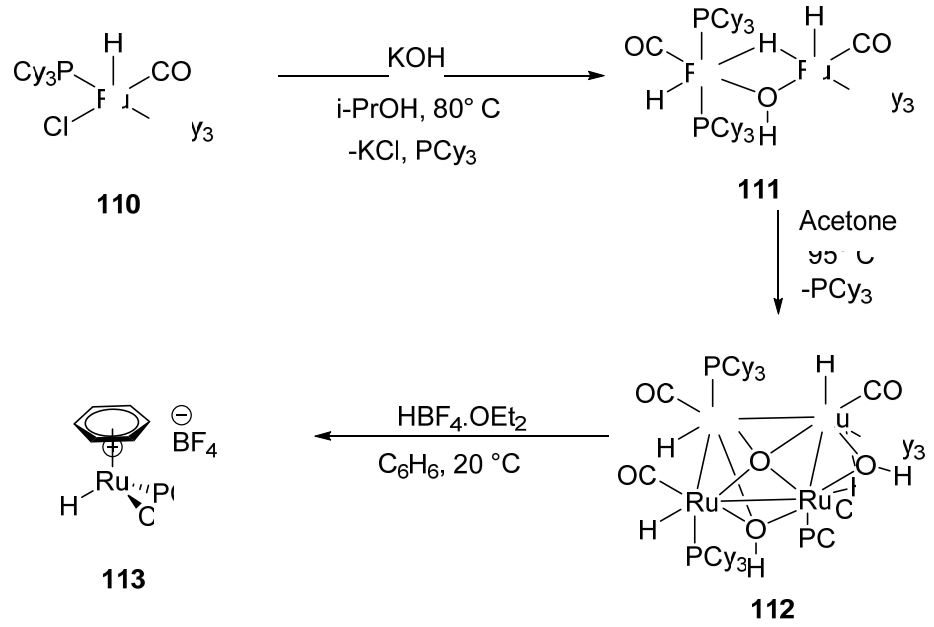
oxidative N-dealkylation of amines, and N-demethylation of an amino group has been shown to be critical step for obesity-related diabetes gene regulation on mRNA.[57] Designing selective catalytic C-N bond cleavage methods has long been an enigmatic problem in homogeneous catalysis directed for the synthesis of complex organic molecules. As an alternative method, transition-metal-catalyzed N-alkylation via C-N bond activation of amines has been shown to be a promising pathway to generate secondary amines. However, earlier efforts showed poor product selectivity and a limited scope for the reaction.[19,58]

While a number of deallylation and aza-Cope type of activated and cyclic C-N bond cleavage reactions have successfully been employed in organic synthesis, selective C–N bond cleavage reactions of simple aliphatic amines have been rarely achieved in part due to their tendency for undergoing energetically more favorable dehydrogenation and oxidation reactions.[59] Although many organic transformations via sp^3 C-N bond cleavage have been widely investigated, the development of simple and practical protocols of selective sp^3 C-N bond cleavage of primary and secondary amines has been proven to be exceedingly difficult in organic synthesis because they are intolerant under strong acidic and basic conditions. Besides the limited examples of precious metal catalyzed amine synthesis, catalytic couplings between amines with more complex molecules have not been explored. In this context, recent advances have focused the development of catalytic methods that are, functional group-tolerant, environmentally benign, and mild reaction conditions. In particular, the challenge is still unsolved for direct formation of C-N bond between amine substrates to form aliphatic and aromatic, secondary amines. Here we describe our effort to design a catalytic system for the

formation of symmetric and unsymmetric secondary amines with a broad substrate scope including complex and bio-active molecules from deaminative coupling reactions of aliphatic and aromatic primary amines, which involve C-N bond activation of primary amine leaving ammonia as the only byproduct.

2.1 Results and discussion

Recently, our research group developed a convenient method for the synthesis for a well-defined cationic ruthenium-hydride complex $[(\eta^6\text{-}C_6H_6)(PCy_3)(CO)RuH]^+BF_4^-$ (**113**) from the protonation reaction of tetranuclear ruthenium complex $\{[(PCy_3)(CO)RuH]_4(\mu\text{-}O)(\mu\text{-}OH)_2\}$ (**112**) with $HBF_4.OEt_2$ (**Figure 2.1.1**). The (**113**) can be obtained by two step synthetic procedures from the ruthenium hydride complex $(PCy_3)_2(CO)RuHCl$ (**110)** (**Scheme 2.1.1**).[60,64] Base hydrolysis reaction of **110** with potassium hydroxide in isopropyl alcohol produced the bimetallic ruthenium complex **111** in (>90%) yield. The complex **111** could be purified by recrystallization techniques (85%) or chromatographic method (90%).[6] The subsequent treatment of **111** with wet acetone at 95 ºC yielded complex **112** in 84 % yield as brown-red powder. Thus, the treatment of **112** (200 mg, 0.12 mmol) with $HBF_4.OEt_2$ (64 μL) in C_6H_6 at room temperature cleanly afforded the cationic ruthenium hydride complex **113**, which was isolated as ivory-colored solid in 90% yield (**Scheme 2.1.1**). The characterization of the ruthenium-hydride complex was performed by NMR spectroscopy and X-ray crystallographic technique. The ruthenium hydride signal of **113** was observed at δ -10.39 (d, J_{PH} = 25.9 Hz) in CD_2Cl_2, and phosphine signal was observed at δ 72.9 ppm by $^{31}P\{^1H\}$ NMR spectroscopy. The molecular structure of the ruthenium hydride **113** showed a three-legged piano-stool geometry, which is capped by a η^6 benzene moiety.



Scheme 2.1.1: Synthesis of cationic ruthenium hydride complex (**113**)**.**

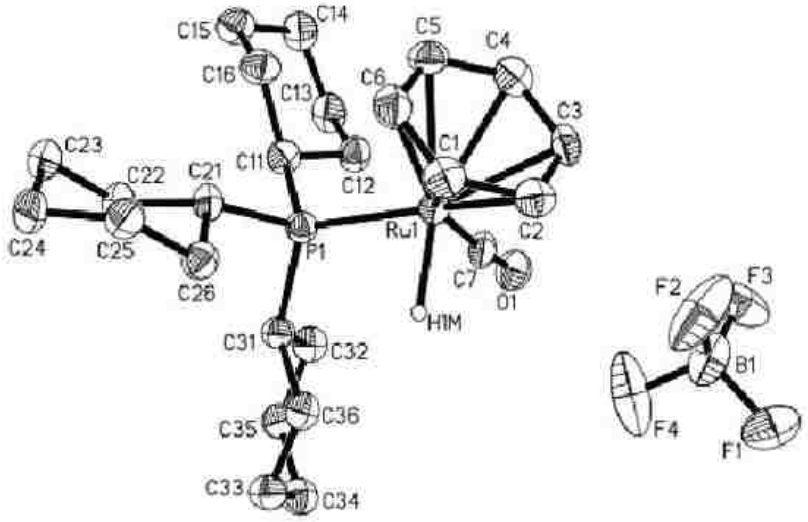


Figure 2.1.1: X-ray crystal structure of cationic ruthenium hydride complex (**113**).

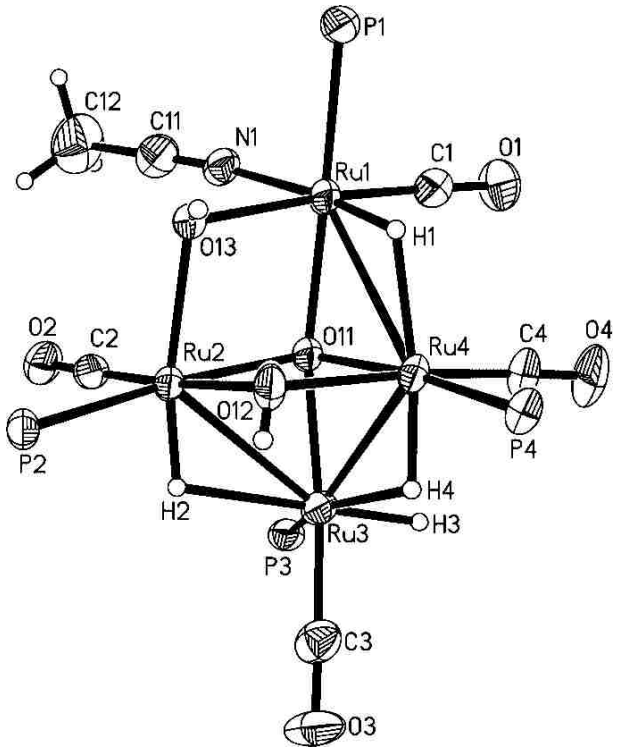
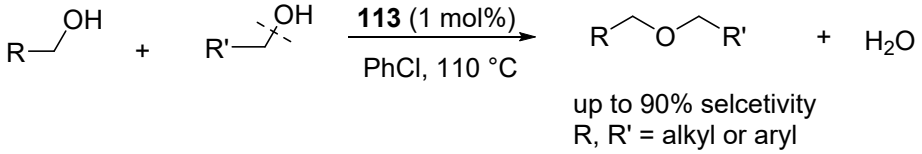


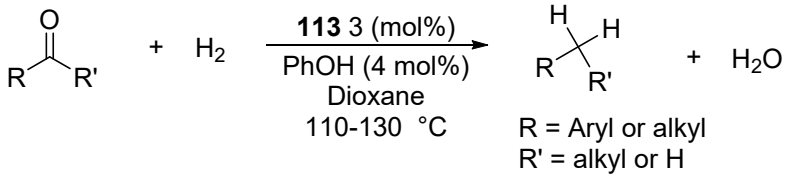
Figure 2.1.2: X-ray crystal structure of **112** drawn with 50% thermal ellipsoids. cyclohexyl groups are omitted for clarity.

In 2014, our group reported selective catalytic synthesis of unsymmetrical ethers from the dehydrative etherification of two different alcohols[61] (**Scheme 2.1.2**). In light of this reaction, our group envisioned the possibility of C-N bond cleavage reaction of primary amines to generate secondary amines. However, repeated initial attempts were failed for this synthetic approach by using catalyst **112/113**.



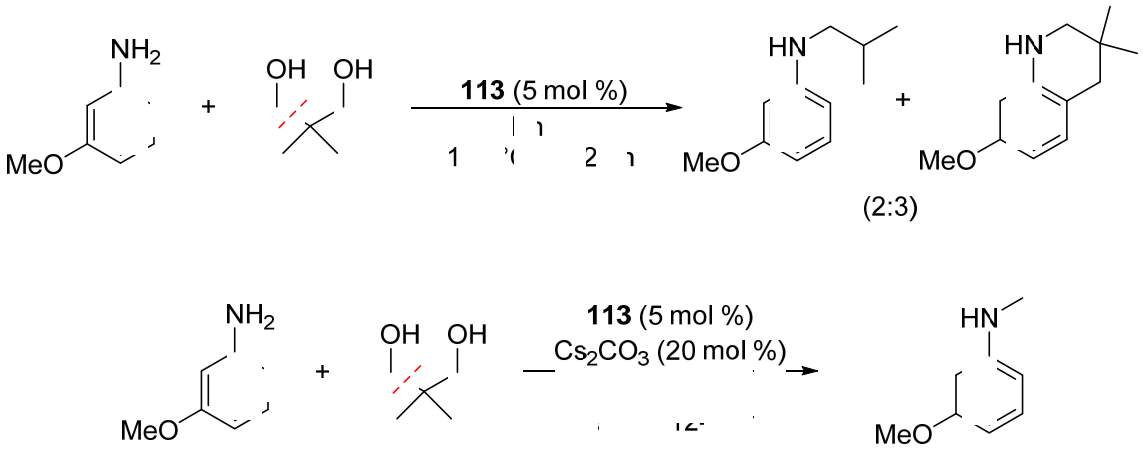
Scheme 2.1.2: Ruthenium catalyzed synthesis of unsymmetrical ethers.

In 2015, we reported that the cationic ruthenium-hydride complex with a phenol ligand exhibited a uniquely high catalytic activity for the hydrogenolysis of carbonyl compounds to yield the corresponding aliphatic products (**Scheme 2.1.3**).[62]



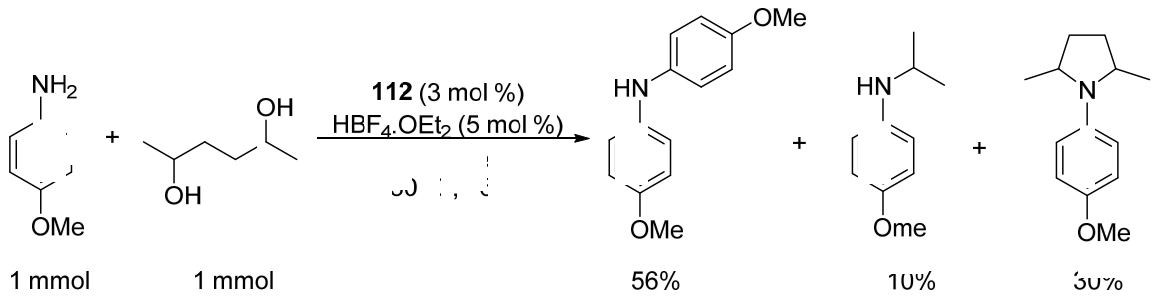
Scheme 2.1.3: Ru-H catalyzed hydrogenolysis of carbonyl compounds.

Our group was very excited about activation of unstrained C-C bond via Ru based catalytic methods. Preliminary result, we recently detected the catalytic dehydrative C-C activation reactions by using 1,2 and 1,3-diols as the substrate and aromatic amines as the trapping agent (**Scheme 2.1.4**).



Scheme 2.1.4: Ru-H catalyzed C-C bond activation of unstrained diols.

In an effort to extend the scope of unstrained C−C activation of diols, we have been exploring the 1,4-diol substrates with 4-methoxyaniline with the catalyst **112** under various conditions. To our delight, we found that the aromatic C-N bond activated product (4-methoxy-N-(4-methoxyphenyl)benzenamine, (56% isolated yield) was formed from the reaction of 4-methoxyaniline, 2,5-hexandiol and $HBF_4.OEt_2$ as an additive in dioxane at 130 °C (**Scheme 2.1.5**). To the best of our knowledge, this was the first catalytic aromatic C-N bond cleavage reaction to generate the aromatic secondary amine products. Further investigations indicated that the diol substrate acted as a ligand to promote the secondary amine product.

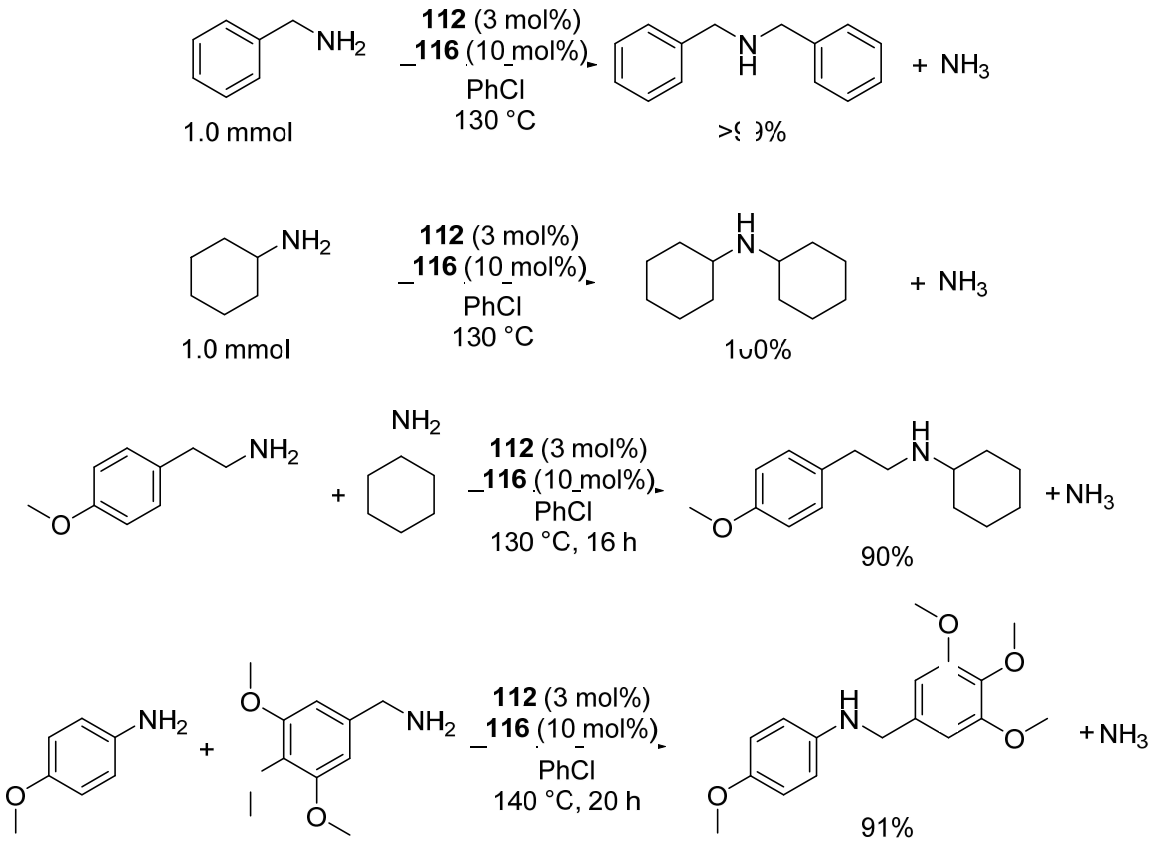


Scheme 2.1.5: Formation of secondary aromatic amine product via Ru catalyzed aryl C-N activation.

These investigations and observations led us to think about the possibility of designing the C-N bond activation reaction by using ligand controlled catalysis. To promote ligand controlled catalysis, we initially screened the effect of phenol and related oxygen and nitrogen ligands on a number of ruthenium catalysts for promoting the C-N cleavage reaction. We also focused on primary amines with a number of mono or multidentate ligands and the ligands containing OH groups to promote for the better activity and selectivity for C-N cleavage reactions. After large number of ligand

screening, we found that benzenediols are the best ligands for promoting the formation of secondary amine products.

Secondary amine products are an important precursor for a variety of pharmaceutical and industrially important intermediates. As will be presented below, the catalytic method employs environmentally friendly and cheaply available primary aliphatic and aromatic amines, and exhibits a broad substrate scope and high chemoselectivity towards the C-N bond cleavage reaction. This reaction does not utilize any reactive agents, such as acids/bases or oxidants, and no wasteful byproducts were not formed. The formation of NH_3 is believed to be the driving force for the reaction. (**Scheme 2.1.6**).

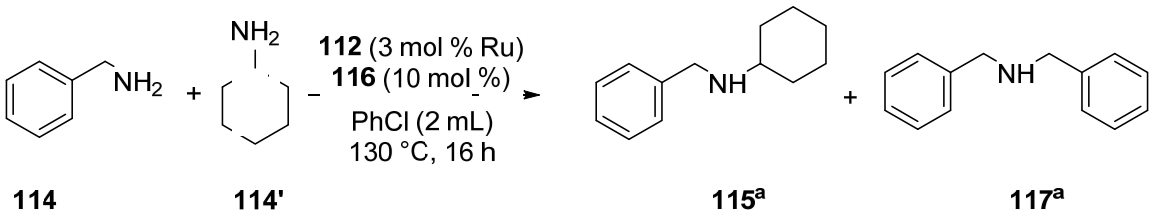


Scheme 2.1.6: Selective synthesis of secondary amines catalyzed by **112**.

2.2 Optimization studies

2.2.1 Catalytic survey

The coupling reaction of benzylamine and cyclohexylamine was used to screen the coupling reaction. Among the screened catalysts, both the tetranuclear Ru-H complex, **112** and the cationic Ru-H, **113** were found to exhibit the most promising activity for the coupling reaction (**Scheme 2.2.1**).



Scheme 2.2.1: Coupling reaction of benzylamine and cyclohexylamine.

Thus, the treatment of benzylamine (0.5 mmol) with cyclohexylamine (0.7 mmol) and 4-(1,1-dimethylethyl)-1,2-benzenediol (**116**) (10 mol%) in the presence of a metal catalyst (3 mol %) in chlorobenzene at 130 ºC was analyzed by GC-MS and NMR after 16 h reaction time by using hexamethylbenzene as an internal standard. The results are summarized in **Table 2.2.1.1**, as analyzed by both GC and NMR spectroscopic methods.

Table 2.2.1.1. Catalyst screening for the reaction of benzylamine with cyclohexylamine.[a]

entry	catalyst	additive	ligand	yield (%)[b]	
				115[a]	**117**[a]
1	$[RuH_2(CO)(PPh_3)_3]$	-	-	0	0
2	$[RuH_2(CO)(PPh_3)_3]$	-	**116**	0	0
3	$[RuH_2(CO)(PPh_3)_3]$	$HBF_4{\cdot}OEt_2$	-	2	0
4	$[RuH_2(CO)(PPh_3)_3]$	$HBF_4{\cdot}OEt_2$	**116**	22	<1
5	RuHCl(*p*-cymene)$_2$	-	-	<1	<1
6	RuHCl(*p*-cymene)$_2$	-	**116**	<1	<1

7	$RuHCl(p\text{-cymene})_2$	$HBF_4{\cdot}OEt_2$	-	2	<2
8	$RuHCl(p\text{-cymene})_2$	$HBF_4{\cdot}OEt_2$	**116**	12	<1
9	$[RuCl_2(PPh_3)_3]$	-	-	4	<1
10	$[RuCl_2(PPh_3)_3]$	-	**116**	5	3
11	$[RuCl_2(PPh_3)_3]$	$HBF_4{\cdot}OEt_2$	-	26	26
12	$[RuCl_2(PPh_3)_3]$	$HBF_4{\cdot}OEt_2$	**116**	20	17
13	$[RuCl_3{\cdot}3H_2O)]$	-	-	<1	<4
14	$[RuCl_3{\cdot}3H_2O)]$	-	**116**	0	31
15	$[RuCl_3{\cdot}3H_2O]]$	$HBF_4{\cdot}OEt_2$	-	4	04
16	$[RuCl_3{\cdot}3H_2O]]$	$HBF_4{\cdot}OEt_2$	**116**	5	20
17	$[Ru(COD)Cl_2]_x$	-	-	<10	6
18	$[Ru(COD)Cl_2]_x$	-	**116**	14	7
19	$[Ru(COD)Cl_2]_x$	$HBF_4{\cdot}OEt_2$	-	1	8
20	$[Ru(COD)Cl_2]_x$	$HBF_4{\cdot}OEt_2$	**116**	0	0
21	$RuHCl(CO)(PCy_3)_2$	-	-	68	20
22	$RuHCl(CO)(PCy_3)_2$	-	**116**	70	15
23	$RuHCl(CO)(PCy_3)_2$	$HBF_4{\cdot}OEt_2$	-	68	25
24	$RuHCl(CO)(PCy_3)_2$	$HBF_4{\cdot}OEt_2$	**116**	62	24
25	**113**	-	-	<5	<1
26	**113**	-	**116**	70	16
27	**112**	-	-	27	7
28	**112**	-	**116**	74	22
29	**112**	$HBF_4{\cdot}OEt_2$	-	13	0
30	**112**	$HBF_4{\cdot}OEt_2$	**116**	65	1

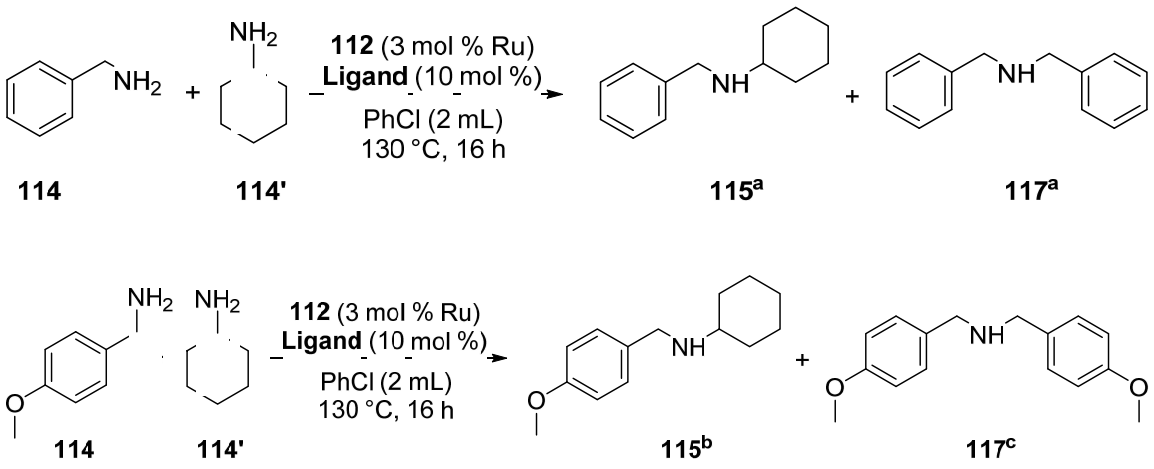
[a]Reaction conditions: catalyst (3 mol % Ru equivalents), ligand **116** (8 mg, 10 mol %), additive (7 mol %), Benzylamine (0.5 mmol), Cyclohexylamine (0.7 mmol), Chlorobenzene (2 mL), 130 °C, 16 h. [b]The product yield of **115**[a] was determined by ^1H NMR using hexamethylbenzene as an internal standard.

Among the surveyed ruthenium catalysts, complex **112** exhibited a uniquely high activity for the deaminative coupling of amines. In the absence of $HBF_4{\cdot}OEt_2$ as an additive, the product was obtained in 74% yield, and conversion for the reaction found to be over 99%. To obtain the best results, we screened a number of Ru catalysts under different conditions, in combination with both additives and ligands. Even though **113** gave 70% yield for the coupling reaction, we decided to use **112** as we observed highest yield and catalyst **112** is the precatalytic species for the catalyst **113**. The **112** is believed

to form the mononuclear Ru-H catalyst after the hydrolysis of the **112** catalyst under mild acidic or basic conditions, as the addition of 10 mol% of ligand **116** (pKa = 9.9, at 25 °C) might be good enough to form an active catalytic species under the optimized reaction conditions. Addition of $HBF_4.OEt_2$ to the catalyst **112** was not effective to increase the selectivity successfully. All the other catalysts were not effective as **112** for this transformation. Therefore, we decided to use **112** with the ligand **116** as the optimized catalytic system for the reaction, which avoids the catalyst **113**, and $HBF_4.OEt_2$.

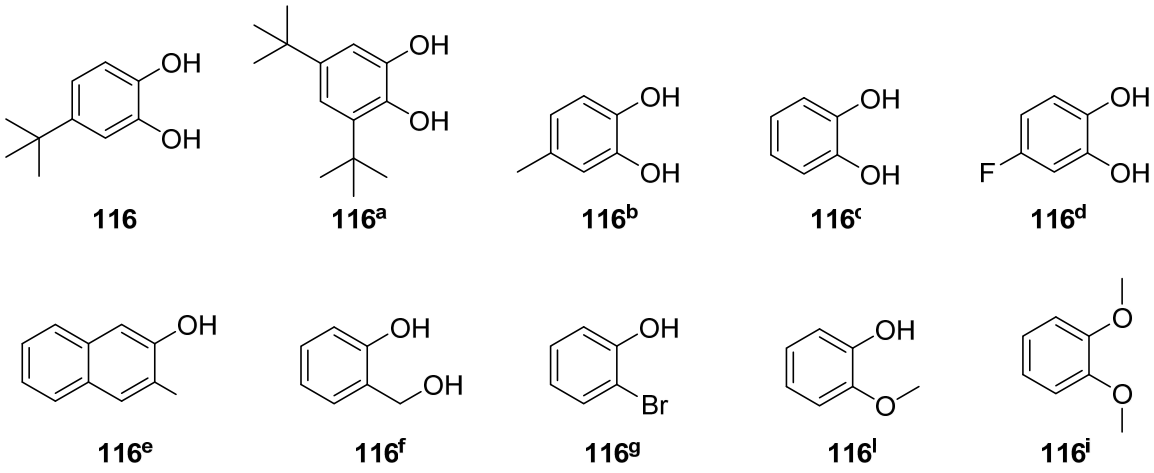
2.2.2 Ligand screening and temperature effects

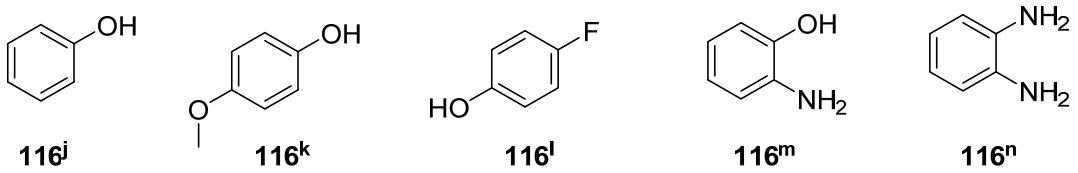
Initially, we surveyed the effect of bidentate ligands with well-defined tetranuclear ruthenium hydride catalyst, **112**, by using primary amines as the substrate to promote the formation of secondary amines. A large number of aliphatic diols, triols, polyols and even simple alcohols were screened under different reaction conditions. However, none of them gave a good product yield and selectivity. Then we decided to screen aromatic ligands including simple phenol derivatives and other common oxygen ligand systems. Catechol derivatives has been shown the highest activity by yielding over 99% product (isolated yield, 95% with high selectivity), selectively for the homo coupling product **117^s**. Therefore, we decided to investigate the best ligand among benzenediols for this noble organic transformation. To find the best ligand among benzenediols and related compounds, we decided to use heterocoupling reaction between benzylamine/4-methoxybenzylamine with cyclohexylamine (**Scheme 2.2.2.1**).



Scheme 2.2.2.1: Coupling reactions of benzylamine/4-methoxybenzylamine and cyclohexylamine with different ligands (**116**/**116**$^{a-n}$).

The treatment of benzylamine or 4-methoxybenzylamine, **114** (0.5 mmol) and cyclohexylamine **114´** (0.5 mmol) with ligand (10 mol %) in the presence of tetranuclear ruthenium hydride catalyst **112** (3 mol %) in chlorobenzene at 130 ºC was analyzed by GC-MS and NMR techniques after 16-hour reaction time with the hexamethylbenzene as an internal standard. The results are summarized in **Table 2.2.2.1**. The different benzenediol ligands (**116** and **116**$^{a-n}$) and analogous compounds are screened for the reaction as shown in the **Figure 2.2.2.1**.





116[j] **116[k]** **116[l]** **116[m]** **116[n]**

Figure 2.2.2.1: Ligands used for the amine coupling reaction.

Table 2.2.2.1 Ligand screening for the deaminative coupling reaction of benzylamine with cyclohexylamine.[a]

entry	ligand	substrate	catalyst	additive	Temp. (°C)	yield (%)[b]	
						115[a/b]	**117**[a/c]
1	**116**	R = OMe	**112**	$HBF_4{\cdot}OEt_2$	140	71	20
2	-	R = OMe	**112**	$HBF_4{\cdot}OEt_2$	140	23	25
3	**116**	R = OMe	**112**	$HBF_4{\cdot}OEt_2$	120	37	37
4	**116**	R = OMe	**112**	-	140	75	19
5	-	R = OMe	**112**	-	120	0	0
6	-	R = H	**112**	-	120	0	0
7	-	R = H	**112**	-	125	trace	0
8	-	R = H	**112**	-	130	27	7
9	-	R = OMe	**112**	-	120	trace	trace
10	**116**	R = H	**112**	-	140	70	15
11	-	R = H	113	-	130	trace	trace
12	-	R = H	113	-	140	5	trace
13	**116**	R = H	113	-	130	70	16
14	-	R = H	113	-	140	5	trace
15	116[a]	R = H	**112**	$HBF_4{\cdot}OEt_2$	130	65	1
16	**116**	R = H	**112**	-	130	74	22
17	116[b]	R = OMe	**112**	$HBF_4{\cdot}OEt_2$	140	65	28
18	116[c]	R = OMe	**112**	$HBF_4{\cdot}OEt_2$	140	61	26
19	116[c]	R = H	**112**	-	130	68	20
20	116[d]	R = H	**112**	$HBF_4{\cdot}OEt_2$	130	70	10
21	116[d]	R = OMe	**112**	-	130	60	20
22	116[d]	R = H	**112**	-	130	80	15
23	116[e]	R = H	**112**	-	130	63	18
24	116[f]	R = OMe	**112**	$HBF_4{\cdot}OEt_2$	140	62	27
25	116[f]	R = OMe	**112**	-	140	66	15
26	116[f]	R = H	**112**	-	130	60	12
27	116[g]	R = H	**112**	-	130	22	10
28	116[h]	R = H	**112**	-	130	30	15
29	116[i]	R = H	**112**	-	130	trace	trace

30	116[j]	R = H	**112**	-	130	52	16
31	116[k]	R = H	**112**	-	130	40	10
32	116[l]	R = H	**112**	-	130	31	9
33	116[m]	R = H	**112**	-	130	15	10
34	116[n]	R = H	**112**	-	130	27	12
35	-	R = OMe	-	$HBF_4{\cdot}OEt_2$	140	trace	0
36	**116**	R = OMe	-	-	140	trace	0
37	-	R = OMe	-	-	140	trace	0
38	-	R = OMe	-	H_2SO_4	130	0	trace
39	-	R = H	-	H_2SO_4	130	0	trace
40[e]	-	R = H	-	H_2SO_4	130	0	trace

[a]Reaction conditions: catalyst (3 mol % Ru equivalents), additive (7 mol %), benzylamine (0.5 mmol), cyclohexylamine (0.5 mmol), ligand (8 mg, 10 mol %), chlorobenzene (2 mL), 130 °C, 16 h. [b]The product yield of **115[a/b]** was determined by ^{1}H NMR using hexamethylbenzene as an internal standard. [c]Stoichiometric amount of conc. H_2SO_4 was used.

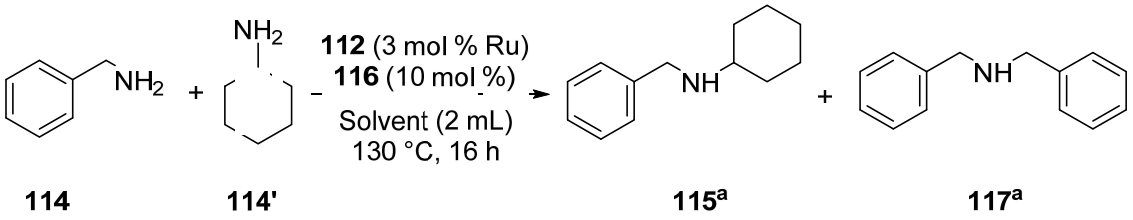
The reaction did not proceed without catalyst, and ligand were found to be mandatory for the selective transformation. The product yield was found to be 23% (**Table 2.2.2.1**, entry 2,) without the ligand even at higher temperature, such as 140 °C with 4-methoxybenzylamine. After addition of the ligand, yield of the product was increased up to 71% (conversion over 95%). Similar results were obtained with benzyl amine as the substrate (**Table 2.2.2.1**, entry 4) which confirmed the importance of the ligand for the reaction. Further investigations were carried out to probe steric and electronic environment on the ligands, to get the selective product. As can be seen in entry 15-26, the product yield was 60-70% with the different benzenediol ligands. This observation suggested that the more sterics or moderate electron donating groups were not very important to improve selectivity towards heterocoupling over homocoupling. In the presence of strong electron withdrawing ligand selectivity was not improved. These observations suggested that there is no significant impact on changing steric or electronic environment on the ligand for the reactivity or selectivity of the screened reaction. It is noteworthy that the entry 22, yield of the product was 80% (over 99% conversion) in the

presence of 4-flurobenzenediol as a ligand. However, the attempts taken to develop the reaction by using 4-flurobenzenediol as a ligand did not work successfully for the other substrates. It has been shown that the **112** ligand promotes the reaction by achieving 74% of the desired product under optimized conditions and found to be effective for the other reactions as well.

The coupling reactions were performed to find optimum temperature with the catalytic system. It has been shown that the C-N activation reactions require the temperatures of 130 °C. Desired product did not form at or below 125 °C, as shown in entry 5-7, (**Table 2.2.2.1**) suggesting that the reaction required at least 130 °C as optimum temperature. Entry 28-34 (**Table 2.2.2.1**) cleary showed that the other relevant phenolic and amine derivatives used were not worked as best as catechol derivatives. However, o-hydroxybenzylalcohol (**122**) gave the 60% of the desired product under optimized conditions, suggested that the reaction could be possible with two hydroxyl groups which are located at close proximities (It is not necessary to have two phenolic groups to support the reaction). Desired product was not obtained with the additives or solvent along. (**Table 2.2.2.1**).

Furthermore, it was found that catalytic and stoichiometric amounts of strong acids such as conc. sulphuric acid, did not give any products. This results clearly demonstrated that the catalytic C-N bond activation is not possible without the ruthenium catalyst and the selectivity and reactivity has been greatly improved by the addition of catechol ligands. Out of those screened benzenediol ligands, ligand **116** was selected as best ligand for the amine coupling reaction.

2.2.3 Solvent and temperature effect study



Scheme 2.2.3.1: Screening for solvent and temperatue by coupling reactions of benzylamine and cyclohexylamine.

Table 2.2.3.1: Solvent effect on the reaction of benzylamine and cyclohexylamine.[a]

Entry	Solvent	Temperature /^{o}C	Yield of **115**^{a} (%)[b]
1	Chlorobenzene	130	74
2	Chlorobenzene	125	<10
3	Dioxane	130	66
4	Dioxane (Anhydrous)	130	68
5	Dioxane (Anhydrous)	120	trace
6	Methanol	130	trace
7	THF	130	30
8	CH_3CN	130	0
9	Toluene	120	0
10	Toluene	120	0
11	Toluene	130	60
12	1,2-DCE	130	40
13	DCM	130	<10

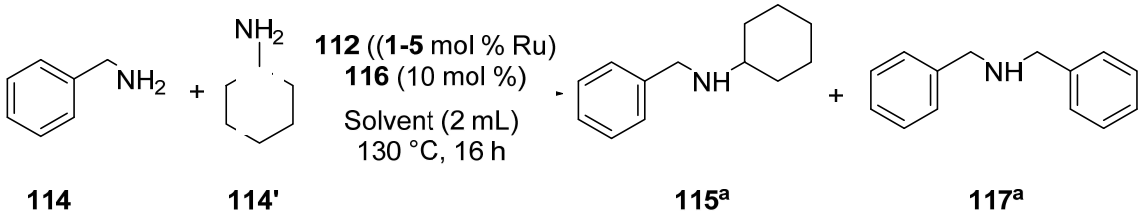
[a]Reaction conditions: catalyst (3 mol % Ru equivalents), benzylamine (0.5 mmol), cyclohexylamine (0.5 mmol), **116** (8 mg, 10 mol %), solvent (2 mL), 16 h. [b]The product yield of **115**^{a} was determined by ^{1}H NMR using hexamethylbenzene as an internal standard.

To establish the best solvent for the reaction, we next conducted the reaction in various solvents by using **112**/**116** for the coupling reaction (**Scheme 2.2.3.1**) of benzylamine with cyclohexylamine (**Table 2.2.3.1**). The treatment of benzylamine (0.5

mmol) and cyclohexylamine (0.5 mmol) with ligand **116** (10 mol%) in the presence of **112** (3 mol %) in different solvents at 130 ºC was analyzed by GC-MS after 16 hour of the reaction time. It was found that the nature of the solvent considerably affects the activity of the coupling reaction. Of the solvents tested, chlorobenzene, toluene and dioxane were found to be effective for the amine coupling reaction. No catalytic activity was observed with acetonitrile as solvent because it strongly coordinates to the ruthenium center and inhibits the catalytic activity. Attempts to decrease the temperature by using the different solvents were not successful (**Table 2.2.3.1**, entry 2,5, 9 and 10). THF also coordinate to Ru center and are less effective for the catalytic reaction observed (**Table 2.2.3.1**, entry 7). Once again, the optimum temperature was confirmed as 130 ºC for the deaminative coupling reaction of amines.

2.2.4 Catalyst loading effect

Table 2.2.4.1 shows the screening results for the coupling reaction under different amounts of catalyst loading. The treatment of benzylamine (0.5 mmol) and cyclohexylamine (0.5 mmol) with **116** (10 mol%) in chlorobenzene at 130 ºC with the **112** was analyzed by GC-MS after 16 hour of the reaction time (**Scheme 2.2.4.1**).



Scheme 2.2.4.1: Effect of catalyst loading on the coupling reactions of benzylamine and cyclohexylamine.

Catalyst loading experimental results illustrated that the 3 mol% (**Table 2.2.4.1**, entry 3) of the catalyst loading is required for the complete conversion. The catalyst loading 1 mol% -1.5 mol% did not produce the product as expected (**Table 2.2.4.1**, entry 1-3), while the application of 5 mol% (**Table 2.2.4.**1, entry 5) did not improve the yield significantly.

Table 2.2.4.1: Effect of catalyst loading on the reaction of benzylamine and cyclohexylamine.[a]

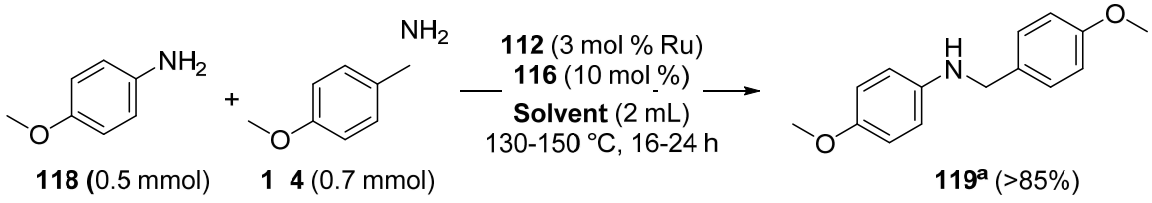
Entry	Catalyst loading /mol%	Yield of **115**[a] (%)[b]
1	1	20
2	1.5	35
3	2	50
4	3	74
5	5	79

[a]Reaction conditions: catalyst (3 mol % Ru equivalents), benzylamine (0.5 mmol), cyclohexylamine (0.5 mmol), ligand (8 mg, 10 mol %), solvent (1 mL), 16 h. [b]The product yield of **115**[a] was determined by ^{1}H NMR using hexamethylbenzene as an internal standard.

2.2.5 Optimization for the coupling reaction of aniline

Having established the optimized conditions for the ruthenium catalyzed N-alkylation of amines with another primary amine substrate, we next investigated substrate scope of aromatic amines. The coupling reaction of aromatic amines with primary amines were not observed under the current optimized conditions. The treatment of 4-methoxyaniline (0.5 mmol) and 4-methoxybenzylamine (0.7 mmol) with ligand **116** (10 mol%) in the presence of **112** (3 mol %) were tested using different solvents, temperatures and time (**Scheme 2.2.5.1**). Products were analyzed by GC-MS with the hexamethylbenzene as an internal standard. The screening results showed that the

aromatic amine coupling reaction with aliphatic amines observed at elevated temperature (140 °C) with a larger reaction time (20 hours).

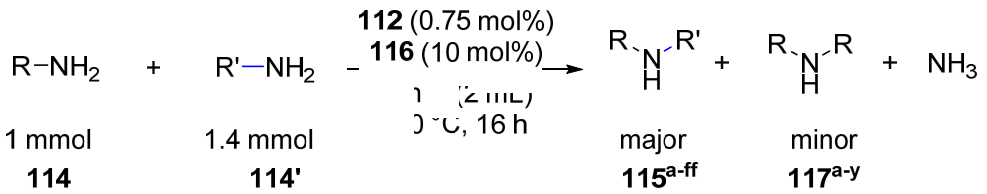


Scheme 2.2.5.1: Coupling reaction of 4-methoxyaniline and 4-methoxybenzylamine.

Finally, we established the optimized conditions for both aliphatic and aromatic amine coupling reaction. Secondary aliphatic amine can be selectively prepared by using primary aliphatic amines with 3 mol % **112** catalytic loading, 10 mol% **116**, 16-hour reaction time at 130 ºC in chlorobenzene. Selective aromatic amine coupling reactions with primary aliphatic amines can be achieved with 3 mol % **112** catalytic loading, 10 mol% **116**, 20-hour reaction time at 140 ºC in chlorobenzene. Having the optimized conditions in hand, we next explored the substrate scope of various aryl and alkyl amines (both primary and secondary) to demonstrate the general applicability of this coupling reaction.

2.3 Reaction Scope

Having determined the optimal reaction conditions, we examined the scope of the transformation with regard to the amine substrate for the coupling reaction. Thus, a variety of amines have been employed for the reaction with other primary amine substrates, and the results are summarized in **Table 2.3.1**.



Scheme 2.3.1: Asymmetric coupling reaction of aliphatic amines.

Unsymmetrical amine products **115$^{a\text{-}ff}$** were selectively formed from the coupling of benzylic amines with a variety of aliphatic amines as well as benzylic amines **114** (**Table 2.4.1**, entry 1-28). In these cases, <20 % of symmetric amine products were formed in crude mixtures, and pure unsymmetric amines were readily isolated by column chromatography on silica. Bioactive molecules, such as tryptamine derivatives and tyramine were tolerated the reaction by giving (**Table 2.3.1**, entry 30-32) excellent yields over 80% and 79% respectively without giving any homocoupling products. Unsubstituted, 4-methoxy-, and 4-fluoro-benzylamine reacted efficiently with cyclohexylamine, producing the corresponding secondary amine products **115^{a}**, **115^{b}** and **115^{c}** in high isolated yields, respectively. The reaction of 4-trifluoromethylbenzylamine resulted in the product **115^{d}** in moderate yield (59%), due to strong electron withdrawing effect of an p-trifluoromethyl group. In addition, β-phenylmethylethylamine also furnished the reaction in moderate isolated yield (63%). Conversion for the reaction for all these cases were over 97%, along with the observation of 15% to 25% homocoupling products.

Table 2.3.1: Deaminative cross coupling reactions of primary amines.[a]

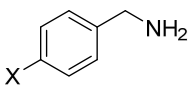
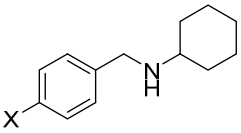
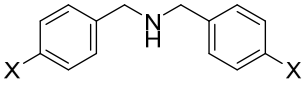
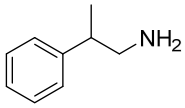
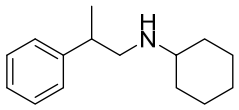
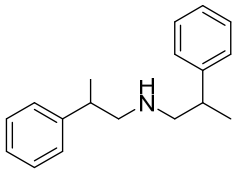
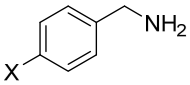
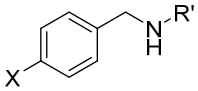
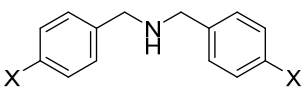
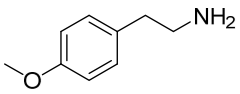
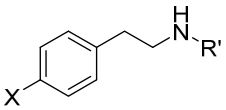
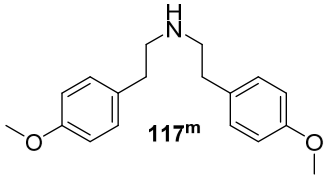
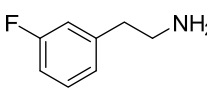
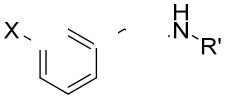
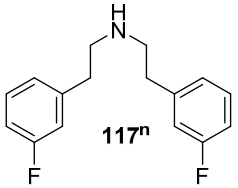
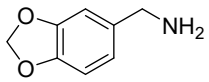
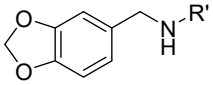
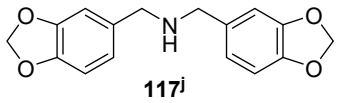
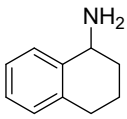
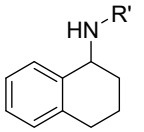
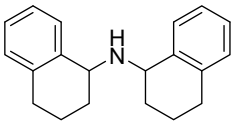
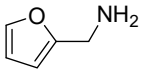
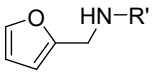
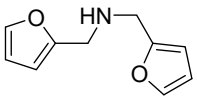
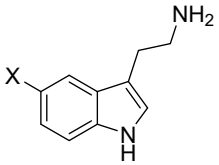
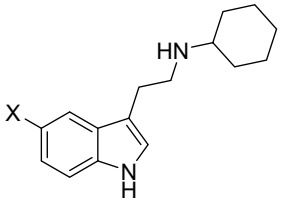
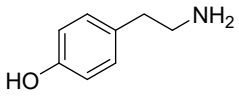
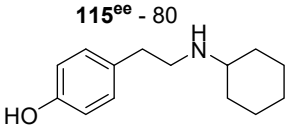
Entry	(R-NH_2) **114**	(R´-NH_2) **114´**	Products and [b]Yield% **115**[(a-ff)]	**117**[(a-y)]
				
1	X = H	R' = Cyclohexyl	**115a** - 74 (**73**)	**117a** - 22
2	X = OMe	R' = Cyclohexyl	**115b** - 80 (**78**)	**117c** - 20
3	X = F	R' = Cyclohexyl	**115c** - 77 (**71**)	**117f** - 18
4	X = CF_3	R' = Cyclohexyl	**115d** - 71 (**59**)	**117g** - 25
				
5		R' = Cyclohexyl	**115e** - 76 (**63**)	**117p** - 17
				
6	X = Cl	R' = $CH_2CH_2C_6H_4$(4-OMe)	**115f** - 71 (**57**)	**117c** - 25
7	X = Ph	R' = n-hexyl	**115g** - 66	**117e** - 18
8	X = Ph	R' = $CH_2C_6H_3$(4-OCH_2O-3)	**115h** - 64 (**56**)	**117e** - 24
9	X = CF_3	R' = n-hexyl	**115i** - 56 (**55**)	**117g** - 24
10	X = F	R' = n-hexyl	**115j** - 66 (**63**)	**117f** - 26
11	X = F	R' = $CH_2C_6H_4$(4-OMe)	**115k** - 74 (**66**)	**117f** - 18
12	X = F	R' = $CH_2CH(Me)C_6H_5$	**115l** - 66 (**58**)	**117f** - 23
13	X = F	R' = $CH_2CH_2C_6H_4$(4-OMe)	**115m** - 56 (**55**)	**117f** - 12
				
14		R' = $CH_2C_6H_5$	**115n** - 74 (**60**)	**117m**
15		R' = n-hexyl	**115o** - 60 (**51**), Timer (**18%**)	
16		R' = Cyclohexyl	**115p** - 90 (**80**)	06
17		R' = 2-indanyl	**115q** - 75 (**54**)	16
18		R' = $CH(Me)C_6H_4$(4-OMe)	**115r** - 65 (**65**)	03
19		R' = $CH(Me)CH_2CH_2C_6H_5$	**115s** - 76 (**73**)	16
20		R' = $CH_2C_6H_4$(4-OMe)	**115t** - 56 (**55**)	17
				
21		R' = 2-indanyl	**115u** - 77 (**76**)	**117n**
22		R' = $CH_2CH(Me)C_6H_5$	**115v** - 60	
23		R' = $CH(Me)C_6H_4$(4-OMe)	**115w** - 60 (**58**)	11

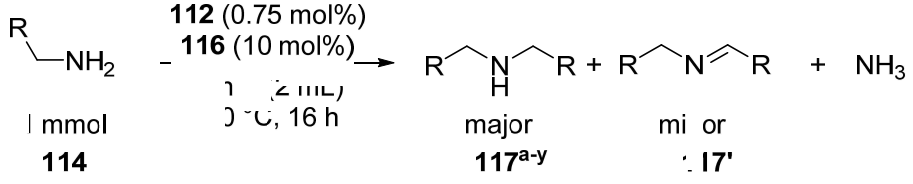
Table 2.3.1: cont……

				 **117^{j}**
24		R' = Cyclohexyl	**115^{x}** - 75 (**59**)	14
25		R' = CH(Me)C_6H_4(4-OMe)	**115^{y}** - 63 (**60**)	04
26		R' = $CH_2CH(Me)C_6H_5$	**115^{z}** - 69 (**56**)	14
				
27		R' = n-hexyl	**115^{aa}** - 75 (**52**)	**117^{y}** - 05
28		R' = $CH_2CH_2C_6H_4$(4-OMe)	**115^{bb}** - 81 (**69**)	00
				
29		R' = Cyclohexyl	**115^{cc}** - 89 (**69**)	**117^{w}** - 06
				
30	X = OMe	R' = Cyclohexyl	**115^{dd}** - 89 (**67**)	00
31	X = H	R' = Cyclohexyl	**115^{ee}** - 80	00
				
32		R' =Cyclohexyl	**115^{ff}** - 83 (**79**)	00

[a]Reaction conditions: amine (1 mmol), amine 2 (1.4 mmol), Ligand **116** (10 mol%), catalyst **112** (3 mol %) in chlorobenzene (2 mL) at 130 ºC. [b]Isolated yields are displayed in parenthesis.

Substrates with an electron-withdrawing group were tested, and interestingly, these substrates having para-substituted electron withdrawing group such as chloro, phenyl, fluro and trifluromethyl **115^{f-m}** (**Table 2.3.1**, entry 6-13) with different types of primary amines were relatively less reactive in giving moderate isolated yields 55-66%. The coupling of phenethyl amines with both benzylic and aliphatic amines also gave the

selective formation of secondary amine products **115^{n-w}** (**Table 2.3.1**, entry 14-23), in very good yields. However, the coupling between n-hexylamines (**Table 2.3.1**, entry 15) typically resulted in a mixture of secondary **115^{o}** (51% isolated yield) and **115$^{o'}$** tertiary amines (18% isolated yield). Piperonylamine bearing 3,4-(methylenedioxy) group as substituents was also suitable substrate, affording **115^{x-z}** (**Table 2.3.1**, entry 24-26) secondary amine product with cyclohexylamine, β-phenylmethylethylamine and 4-methoxy-α-methylbenzenemethanamine in good yields. 1-Aminotetraline selectively formed the secondary amine product **115$^{aa/bb}$** without affording the homocoupling product having good isolated yields (**Table 2.3.1**, entry 27 and 28). The use of furfurylamine with cyclohexylamine also led to asymmetrical sec-amines product **115^{cc}** in 69% isolated yield, while a trimeric product **115$^{cc'}$** (24%) and 6% of homocoupling dimeric product **117^{y}** was observed. The catalytic coupling method exhibits high selectivity toward the formation of unsymmetrical secondary amines without resorting to employing reactive reagents. As observed above, the homocoupling of alkyl amines may occur in some cases, and we were interested in designing the catalytic system to explore the reactions in the presence of only one type of amines. The isolated pure asymmetric amines were fully characterized by ^{1}H and ^{13}C NMR, HRMS and elemental analysis.



Scheme 2.3.2: Symmetric coupling reactions of aliphatic amines.

Table 2.3.2: Scope for symmetric coupling reactions of aliphatic amines.[a]

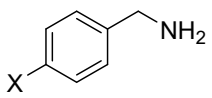
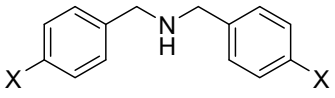
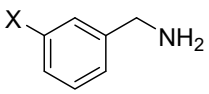
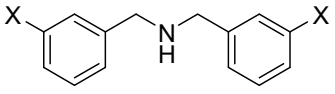
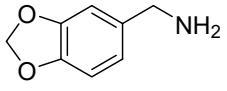
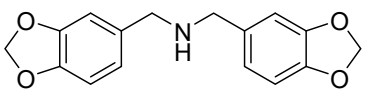
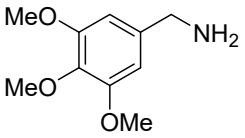
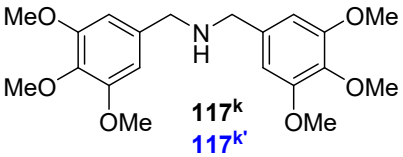
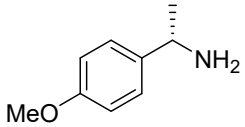
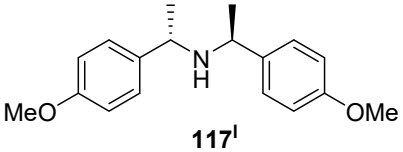
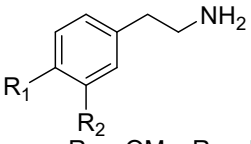
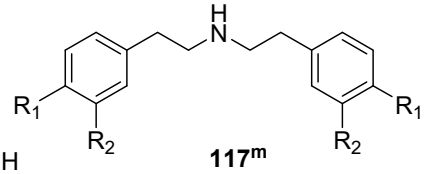
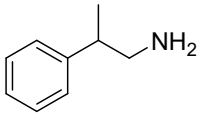
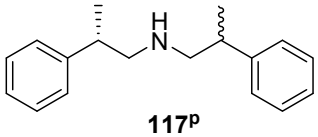
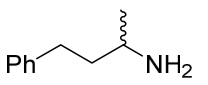
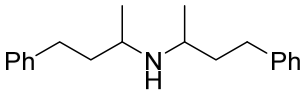
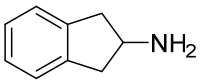
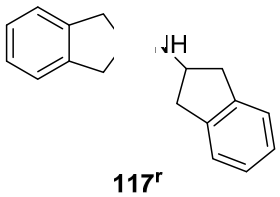
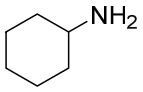
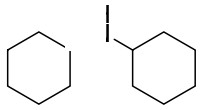
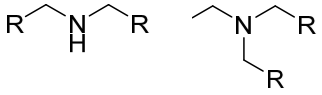
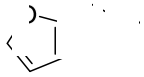
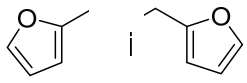
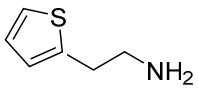
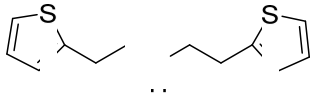
Entry	**114** (Amine)	**117**[a-x] (Products)	Conversion %	[b]Yield
1	 X = H	 **117**[a]	**100**	99 **(89)**
2	X = Me	**117**[b]	**99**	95 **(94)**
3	X = OMe	**117**[c]	**99**	90 **(86)**
4	X = Cl	**117**[d]	**94**	93 **(92)**
5	X = Ph	**117**[e]	**90**	88 **(85)**
6	X = F	**117**[f]	**98**	91 **(91)**
7	X = CF_3	**117**[g]	**95**	84 **(84)**
8	 X = OMe	 **117**[h]	**98**	85 **(84)**
9	X = Cl	**117**[i]	**91**	91 **(89)**
10		 **117**[j] **117**[j']	**92**	80 **(77)** 17
11		 **117**[k] **117**[k']	**97**	65 **(61)** 29
12		 **117**[l]	**82**	75 **(72)** dr = 7:1
13	 R_1 = OMe, R_2 = H	 **117**[m]	**99**	95 **(89)**
14	R_1 = H, R_2 = F	**117**[n]	**98**	90 **(87)**
15	R_1 = H, R_2 = OMe	**117**[o]	**98**	96 **(90)**
16		 **117**[p]	**95**	94 **(93)** dr = 20:23

Table 2.3.2: cont……

17		 **117^{q}**	**95**	95 (**90**)
18		 **117^{r}**	**94**	84 (**73**)
19		 **117^{s}**	**100**	99 (**95**)
20[b]	R = C_5H_{12}	 **117^{t}** **117$^{t'}$**	**99**	43 (**43**) 54 (**54**)
21[b]	R = C_3H_8	**117^{u}** **117$^{u'}$**	**99**	46 (**45**) 53
22[b]	R = $CH_2CH_2CH_2C_6H_5$	**117^{v}** **117$^{v'}$**	**99**	45 (**42**) 55 (**53**)
23		 **117^{w}**	**100**	79 (**80**) 20 (**19**)
24		 **117^{x}**	**96**	90 (**89**)

[a]Reaction conditions: amine (1 mmol), Ligand (10 mol%), catalyst **112** (3 mol %) in chlorobenzene (2 mL) at 130 ºC. [b]Isolated yields are displayed in parenthesis. [c]3,5-ditertiarybutylcatecol (**116^{a}**) used as a ligand.

We next explored the substrate scope for the formation of symmetric secondary amines by using the catalyst **112**/**116** (**Scheme 2.3.2**) with one type of amine (**Table**

2.3.2). To our delight, aliphatic amines and benzylic amines reacted smoothly to afford the secondary amine products **117^{a-j}** (**Table 2.3.2**, entry 1-10) without the formation of tertiary amines or other side products. In case of 3,4,5-trimethoxybenzylamine the product **117^{k}** was isolated in 61% yield, while remaining imine product was formed without transferring hydrogen in the later stage of the catalytic cycle. This might be due to both strong electron donating groups and steric effects of the six methoxy groups on an imine product stabilize the imine product. In general, stereoselectivity of the novel catalytic method did not retained on the products. However, (S)-(−)-4-methoxy-α-methylbenzylamine reacted to form separable diastereomers **117^{l}** in 7:1 ratio. This selectivity could be explained by the transition state of the C-N bond cleavage step, which is believed to be turnover limiting step. Assuming the transition state is having a six membered metallocycle, there are two possible transition states to activate the C-N bond and transfer the hydride on to the benzylic position as shown in **Figure 2.3.1**.

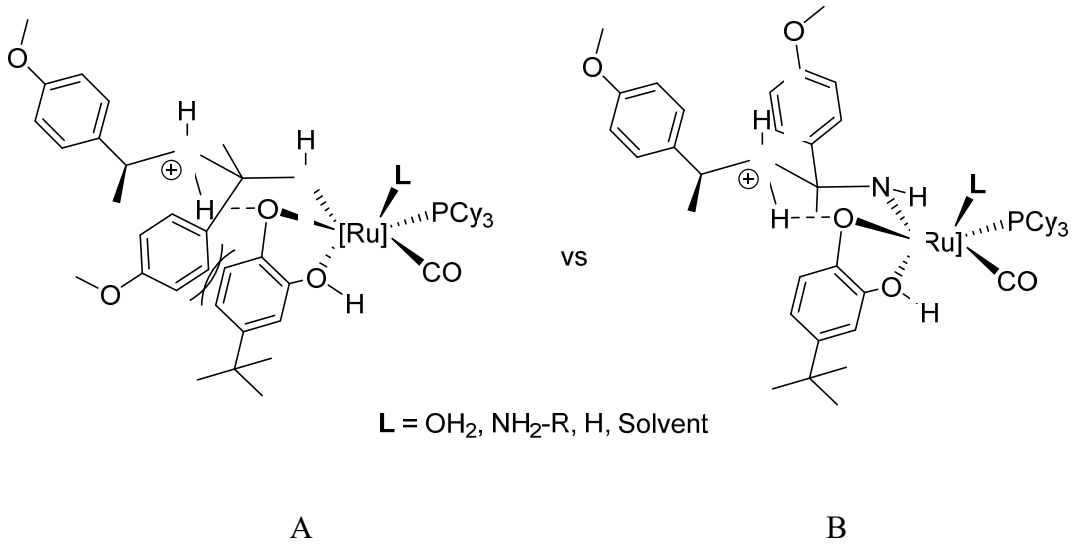
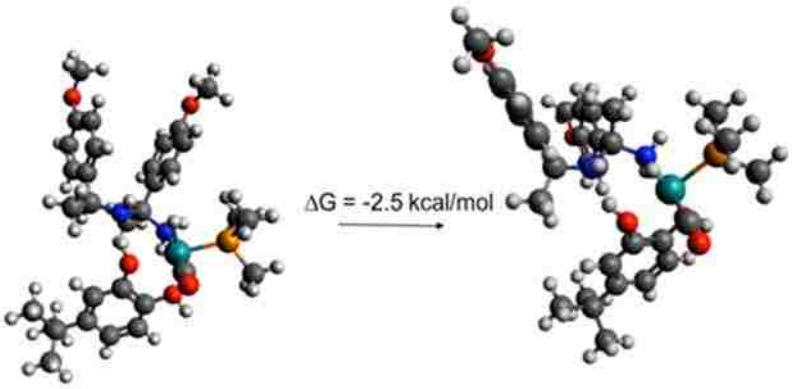


Figure 2.3.1: Proposed transition states of the metal ligand complex during the formation of **117^{l}**.

As can be seen in **Figure 2.3.1: A**, 4-methoxyphenyl group in axial position has much higher steric repulsions, whereas the equatorial orientation which is shown in **Figure 2.3.1: B** would be sterically less favored. This is one possible explanation for the stereoselectivity of the compound **117**^{l}. To get further insights for this explanation DFT calculations was carried out. Geometries were optimized with B3LYP and LANL2DZ basis set for Ru and 6-31G(d) for other atoms. Single-point energies were calculated with M06 and the SDD basis set for Ru and 6-311+G(d,p) for other atoms. The PCM solvation model in chlorobenzene solvent was employed in the single-point energy calculations. All calculations were performed with Gaussian 09 on the Pere cluster at Marquette University. The gas phase energy calculations indicated that the free energy change is favorable for the transition state **B** by 2.5 kcal/mol.

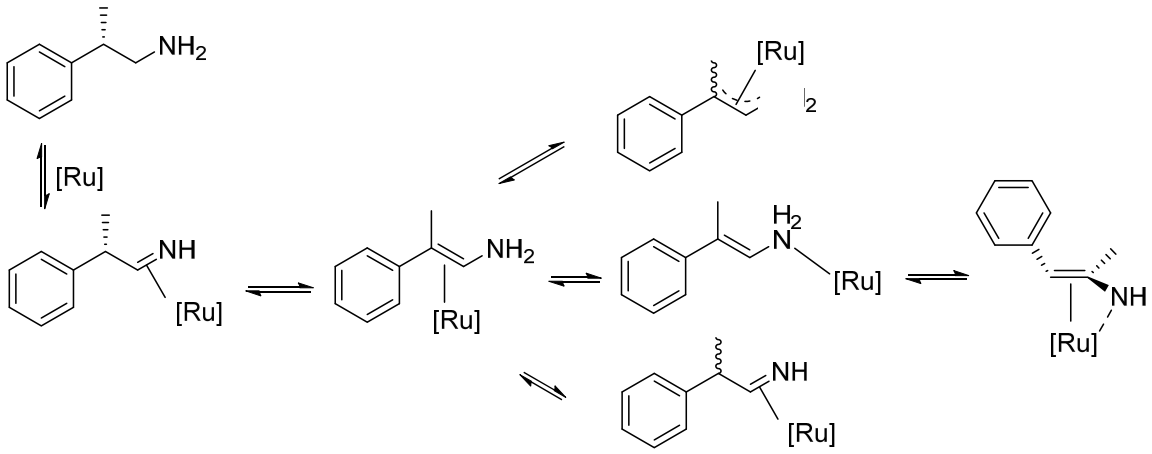


A B

Figure 2.3.2: DFT optimized gas phase transition state of the metal ligand complex (PCy_3 was replaced with PMe_3 for convenience).

On the other hand, (S)-β-methylphenethylamine gave the 20:23 mixture of diastereomers **117**^{p} with 93% as total isolated yield. The diastereomers found to be

difficult to separate by using column chromatographic techniques. The possible reason for this lack of stereoselectivity might be due to the formation of the coordinated enamine complex as shown in **Figure 2.3.3**.



Scheme 2.3.3: Formation of metalalkeneamino complex with ruthenium catalyst.

2-Aminoindane and cyclohexyl amine proceeded smoothly under the same conditions, furnishing the homocoupling products **117^{t}** and **117^{u}** (**Table 2.3.2**, entry 18-19) in excellent yields. (±)-1-Methyl-3-phenylpropylamine yielded 1:1 diastereomeric mixture with 90% isolated yield. Interestingly, for sterically non-demanding aliphatic amines, a mixture of secondary and tertiary amines was formed. Thus, the reaction of 1-hexylmine, 3-phenylpropanamine and fufurylamine resulted in the isolation of tertiary amine products (**Table 2.3.2**, entry 20-23) in 54%, 53% and 19% yields, respectively. The selectivity of secondary amine over tertiary amine was achieved by using 3,5-di-tert-butylcatechol **116^{a}** as the ligand. The catalytic method provides a direct chemoselective formation of secondary amine products.

Table 2.3.3: Scope for the asymmetric coupling reactions of aniline with amines.[a]

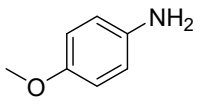
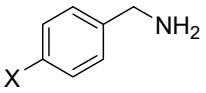
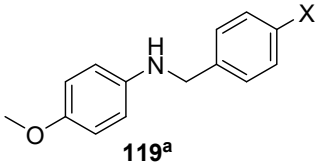
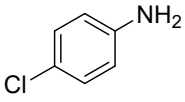
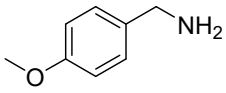
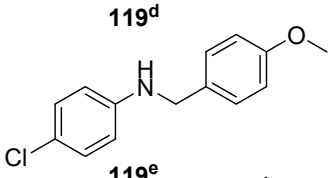
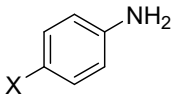
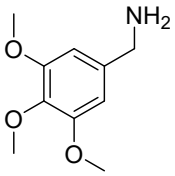
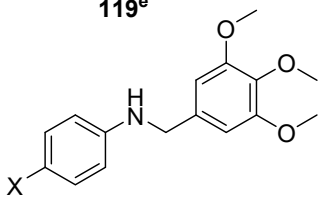
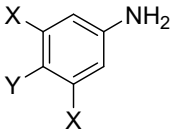
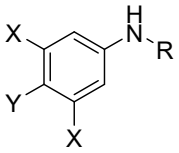
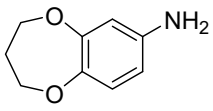
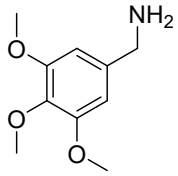
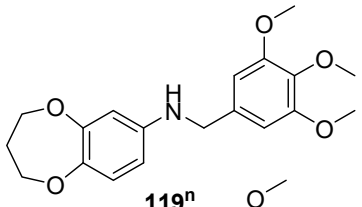
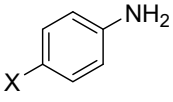
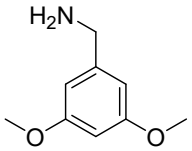
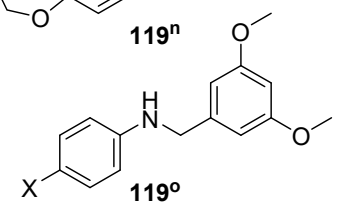
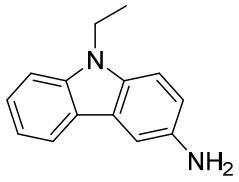
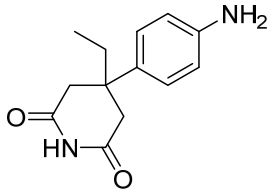
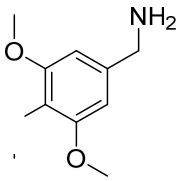
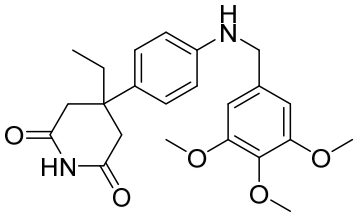
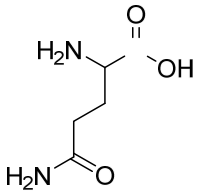
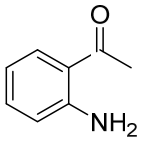
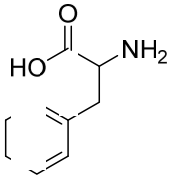
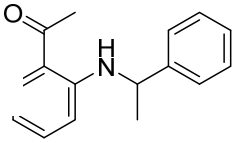
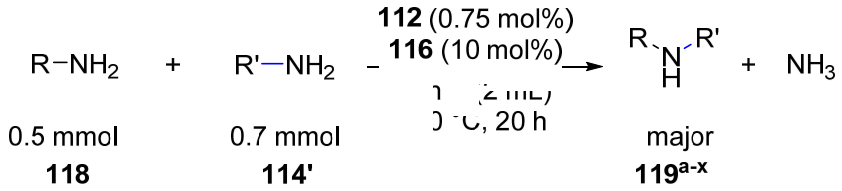
Entry	**118** (R-NH_2)	**114** (R´-NH_2)	**119 (**Product)	[a]Yield %
				
1		X = OMe	**119[a]**	80 **(80)**
2		X = H	**119[b]**	75 **(57)**
3		X = Ph	**119[c]**	86 **(70)**
4		X = F	**119[d]**	65 **(41)**
				
			119[e]	66 **(59)**
5				
			119[f]	98 **(91)**
6	X = OMe		**119[g]**	85 **(71)**
7	X = H		**119[h]**	80 **(72)**
8	X = Cl			
				
9	X = H, Y = OMe	R' = n-hexyl	**119[i]**	65 **(63)**
10	X = H, Y = OMe	R' = $CH_2CH_2CH_2Ph$	**119[j]**	52 **(45)**
11	X = Y= OMe	R' = $CH_2CH_2C_6H_4$-4-OH	**119[k]**	53 **(51)**
12	X = H, Y = OMe	R' = 2-indanyl	**119[l]**	90 **(74)**
13	X = Y = H	R' = $CH_2C_6H_4$-4-OMe	**119[m]**	80 **(71)**
				
14			**119[n]**	89 **(75)**
				
15	X = OMe		**119[o]**	89 **(84)**
16	X = Cl		**119[p]**	62 **(48)**
17	X = CF_3		**119[q]**	40 **(37)**

Table 2.3.3: cont……

18		R' = n-pentyl	**119r**	85 **(70)**
19		R' = Bn	**119s**	45 **(40)**
20			 **11ᵗ**	42 **(40)**
21		R' = $H_2CH_2C_6H_5$	**119u**	80 **(75)**
22		R' = C_6H_4-4-OMe	**119v**	70 **(70)**
23		R' = Bn	**119w**	70 **(66)**
24			 **119x**	35 **(35)**

[a]Reaction conditions: aromatic amine (0.5 mmol), aliphatic/benzylamine (0.7 mmol) Ligand **116** (10 mol%), catalyst **112** (3 mol %) in chlorobenzene (2 mL) at 140 ºC. [b]Isolated yields are displayed in parenthesis.



Scheme 2.3.4: Amino coupling reaction of aniline derivatives and bio-active molecules (R = alkyl, aryl; R′ = alkyl).

To further illustrate synthetic versatility of the catalytic coupling method, we next explored the coupling reaction of aniline derivatives with primary amine substrates of biological relevance (**Table 2.3.3**). The coupling of 4-methoxyaniline with para-substituted benzylic amines led to the selective formation of unsymmetrical amine products (**Table 2.3.3**, entry 1-4) without a significant amount of symmetric amine products. The compounds with electron donating group facilitated the reaction by having excellent yields. Similarly, the reaction of para-substituted anilines with 3,4,5-trimethoxybenzylamine afforded the coupling products (**Table 2.3.3**, entry 6-8) in high yields. The structure of **119^{f}** was determined by X-ray crystallography.

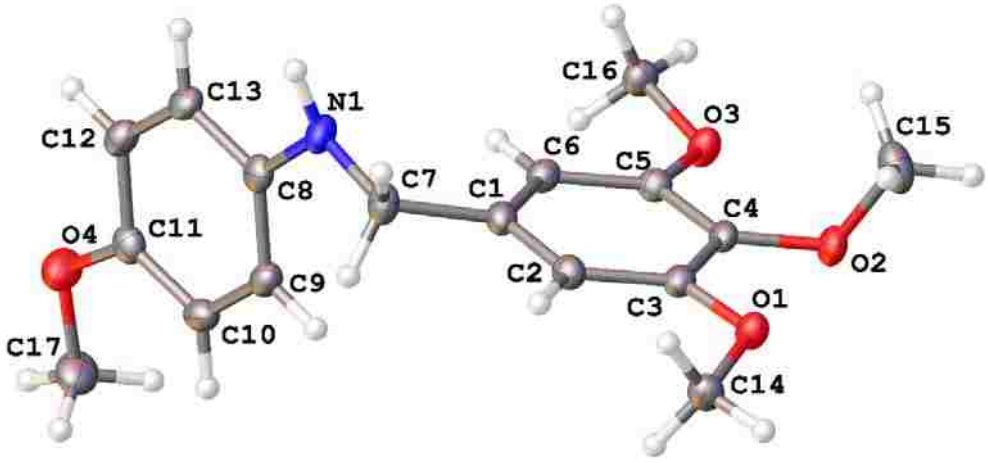
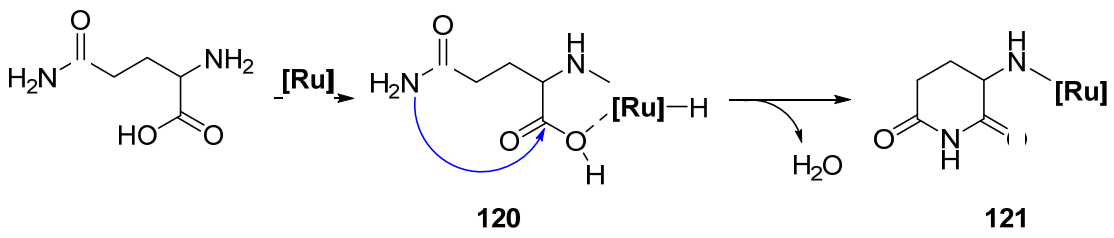


Figure 2.3.3: X-ray crystal structure of **119^{f}** (3,4,5-Trimethoxy-N-(4-methoxyphenyl)benzenemethanamine).

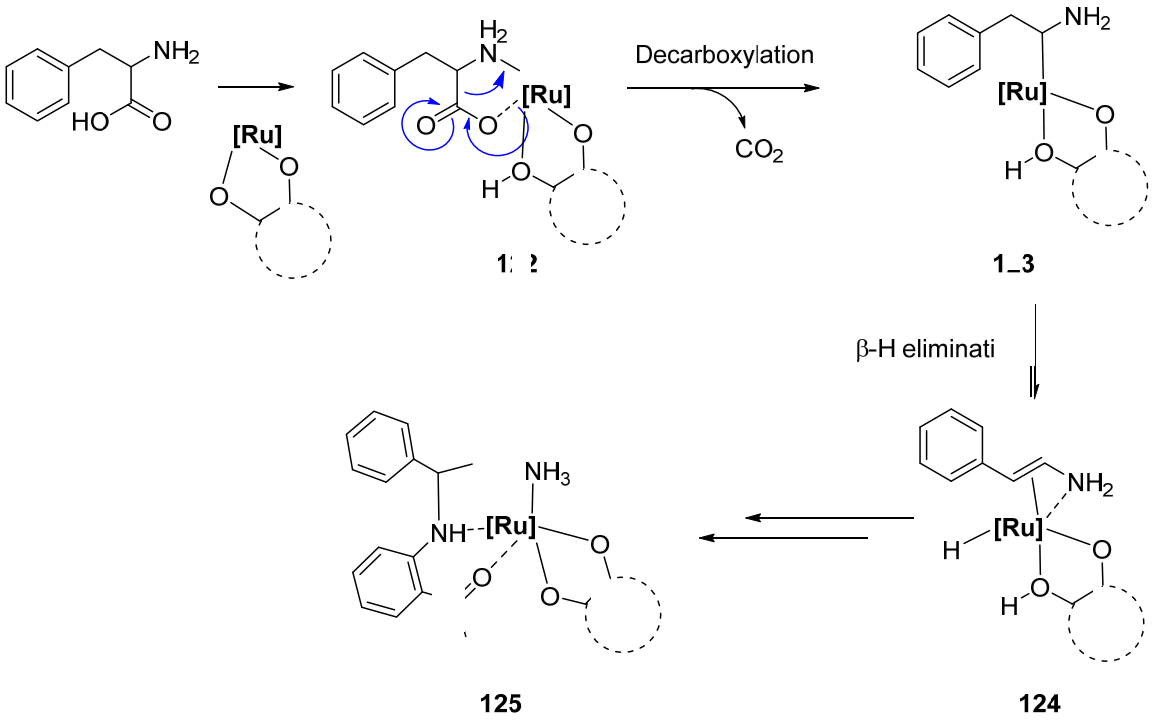
As observed in these cases, the homocoupling aromatic amines were not observed. To our delight, aromatic amines with electron donating group with alkyl amines and phenylalkylamines were reacted to form the secondary amine products in moderate to high yields. Substrates with ortho electron-donating methoxy group was

relatively ineffective. Anilines bearing cyclic moieties such as 3,4-dihydro-2H-1,5-benzodioxepin-7-amine (**Table 2.3.3**, entry 14) were suitable substrates, affording **119^{n}** in excellent yield. Aniline derivatives with strong electron-withdrawing trifluoromethyl group was found to be a sluggish substrate for this reaction, and the product **119^{q}** (**Table 2.3.3**, entry 17) was isolated in 40% yield. Interestingly, 3-amino-9-ethylcarbazole (a bioactive molecule) was afforded the reaction with n-hexylamine having very good isolated yield (70%), whereas benzylamine gave moderate yield (40%). The treatment of 3,4,5-trimethoxyaniline with (R)-(+)-aminoglutethimide (a bioactive molecule) led to the optically active coupling product **119^{t}**, without any detectable racemization. In addition, amino acid derivatives were tested under the standard conditions, and decarboxylative, deaminative secondary amine products were obtained in excellent yields. However, L-glutamine found to be specific substrate for this catalytic method. L-glutamine was reacted with primary amines, such as 3-phenylpropylamine, 4-methoxybenzylamine and benzylamine to provide the cyclized imido products **119^{u}**, **119^{v}** and **119^{w}** in 75%, 70% and 66% isolated yields respectively. Ruthenium coordinated glutamine **120** proceeds to form ruthenium 2-amino-glutarimide intermediate species **121** by dehydrative *six-exo-trig cyclization* which is leading to form the amine coupling product **119$^{u\text{-}w}$** (**Scheme 2.3.5**).



Scheme 2.3.5: Formation of intermediate, 2-amino-glutarimide species.

Encouraged by the results above showing a broad range of amines suitable for the ruthenium-catalyzed deaminative coupling reaction, we investigated the possibility of 2-aminoacetaphenone with amino acid (L-phenylalanine). Surprisingly, reaction tolerated the carbonyl group by giving, 1-[2-[(1-phenylpropyl)amino]phenyl]-1-ethanone product with reasonable yield. Ruthenium catalyst has been reported for initial stage decarboxylation of amino acids.[60e] Ruthenium coordinated phenylalanine species **122** would be afforded the product **123** by decarboxylative alkylation pathway. The product **124** will be formed by β-H elimination of the intermediate species **123**. The intermediate **124** might be leaded to afford the product **119^{x}** by several possible pathways via the intermediate species **125** (**Scheme 2.3.6**).



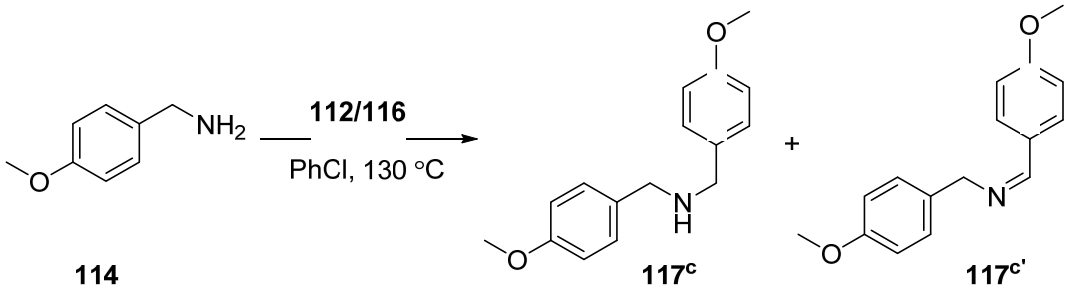
Scheme 2.3.6: Proposed reaction pathway for the formation of product **119^{x}**.

It is worth to say that, the major product of this reaction was characterized by NMR techniques and found to be quinoline derivative. This finding opens new area to discover the possibility of developing a new catalytic system for the formation of quinoline and quinazoline derivatives, is currently ongoing project. Our experiments further confirmed the reaction of primary amine with secondary amine gave the mixture of alkyl exchanged secondary and tertiary amine products with decent yields. However, selectivity must be improved for this transformation by changing the catalytic system.

Finally, aniline, aliphatic amine units and highly functionalized amines proved to be suitable substrates for the coupling reaction with **112**/**116** catalytic system, affording secondary and tertiary amine products with decent to excellent yields without forming any toxic or wasteful byproducts.

2.4 Mechanistic Studies

The following kinetic experiments were performed to gain mechanistic insights into catalytic C-N bond cleavage step. The formation of symmetric coupling reaction of 4-methoxybenzylamine was monitored under the optimized conditions (**Scheme 2.4.1**).



Scheme 2.4.1: Symmetric coupling reaction of 4-methoxybenzylamine.

2.4.1 Reaction profile

Complex **112** (0.75 mol %) and **116** (10 mol %) were dissolved with chlorobenzene, and 4-methoxybenzylamine (2 mmol) was added to the reaction tube. The tube was kept in an oil bath maintained at 130 °C. The tube was taken out from the oil bath at 20 min time intervals and small amount of homogenized mixture was analyzed by ^{1}H NMR. The product concentration was measured by monitoring the appearance of the product signals on ^{1}H NMR, which was normalized against the internal standard peak (hexamethylbenzene). The plot of relative concentration vs time was constructed, which is shown in **Figure 2.4.1**.

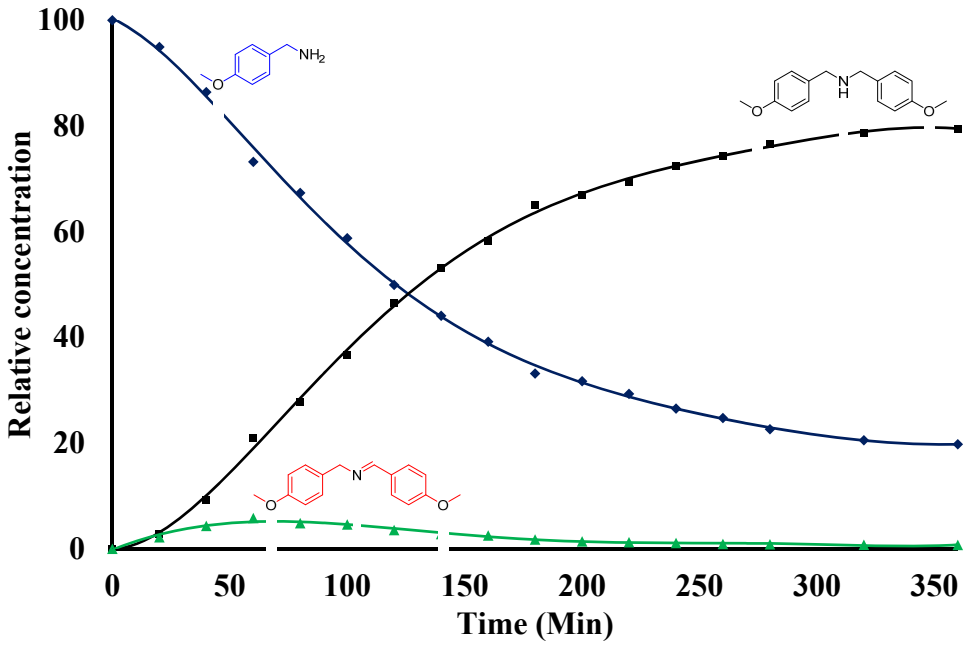


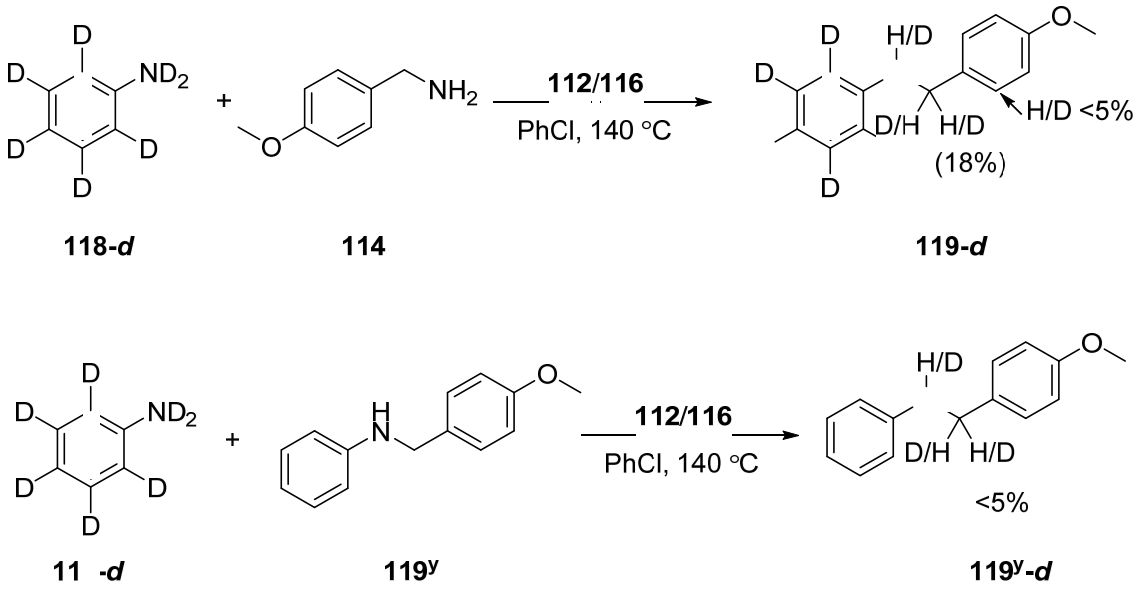
Figure 2.4.1.1: Reaction profile for the coupling of 4-methoxyaniline with benzylamine catalyzed by **112**/**116** in chlorobenzene.

As expected, the formation of bis(4-methoxybenzyl)amine (**117^{c}**) was observed at the expense of the benzylamine substrate. Initially, the formation of imine product PhCH=NCH$_2$Ph (**117$^{c'}$**) was observed along with **117^{c}**, which then disappeared gradually

within 200 min. This observation suggested that the catalytic species remove the H from the amine to form the activated form of the substrate **114**. This result provides an evidence for the *hydrogen borrowing* mechanism.

2.4.2 H/D exchange experiment

To examine H/D exchange pattern of benzylamine, the reaction of aniline-d_7 (0.5 mmol, 99% D) with 4-methoxybenzylamine (0.7 mmol) in chlorobenzene (1 mL) in the presence of **112** (3 mol %), was performed under optimized conditions, and the purified products were analyzed by both ^{1}H and ^{2}H NMR. A trace amount of deuterium incorporation (<5%) was observed at the *ortho* position to the benzylic methelene (**Scheme 2.4.2.1**).



Scheme 2.4.2.1: H/D exchange pattern of benzylamine with Aniline-d_7.

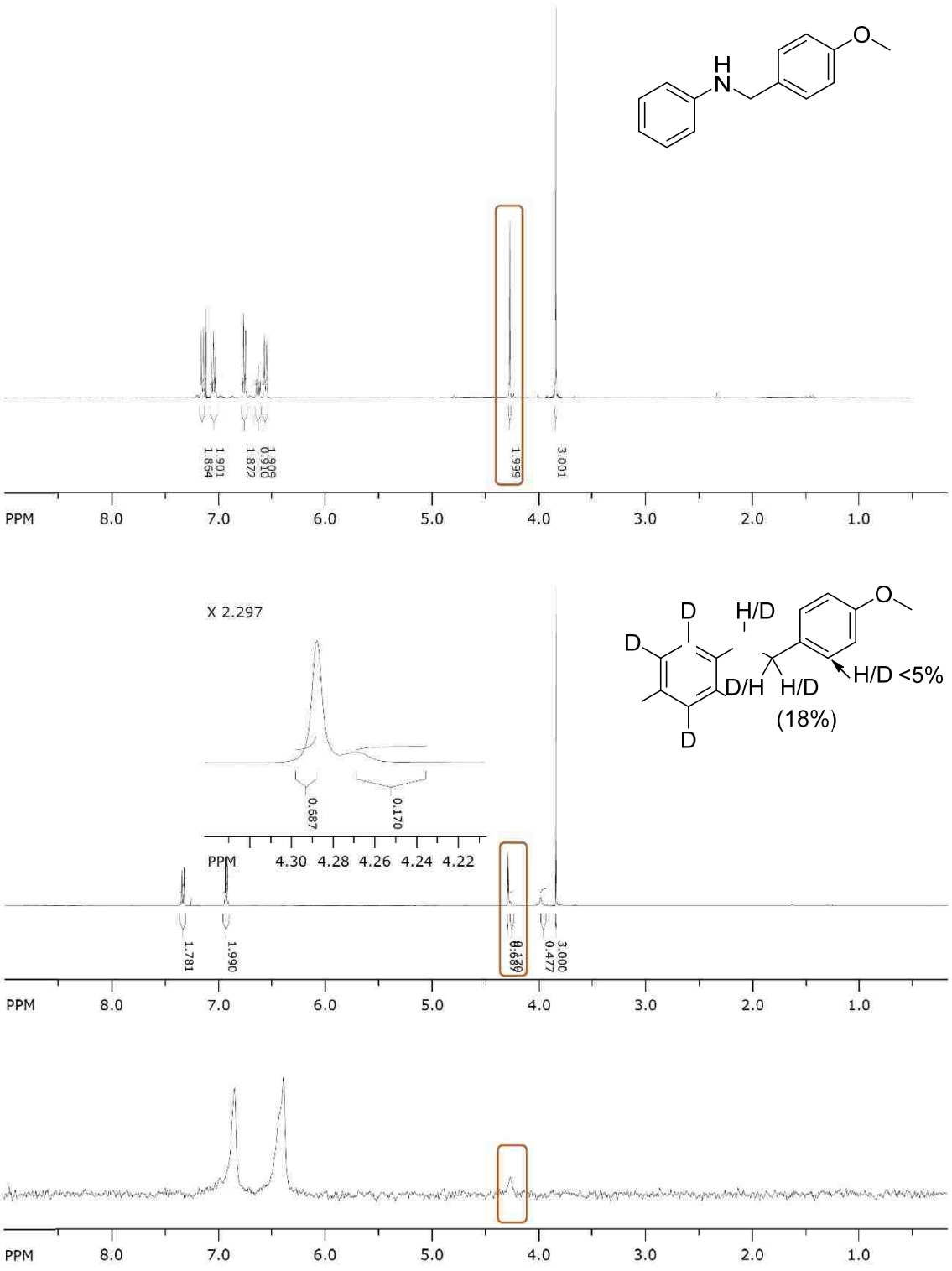
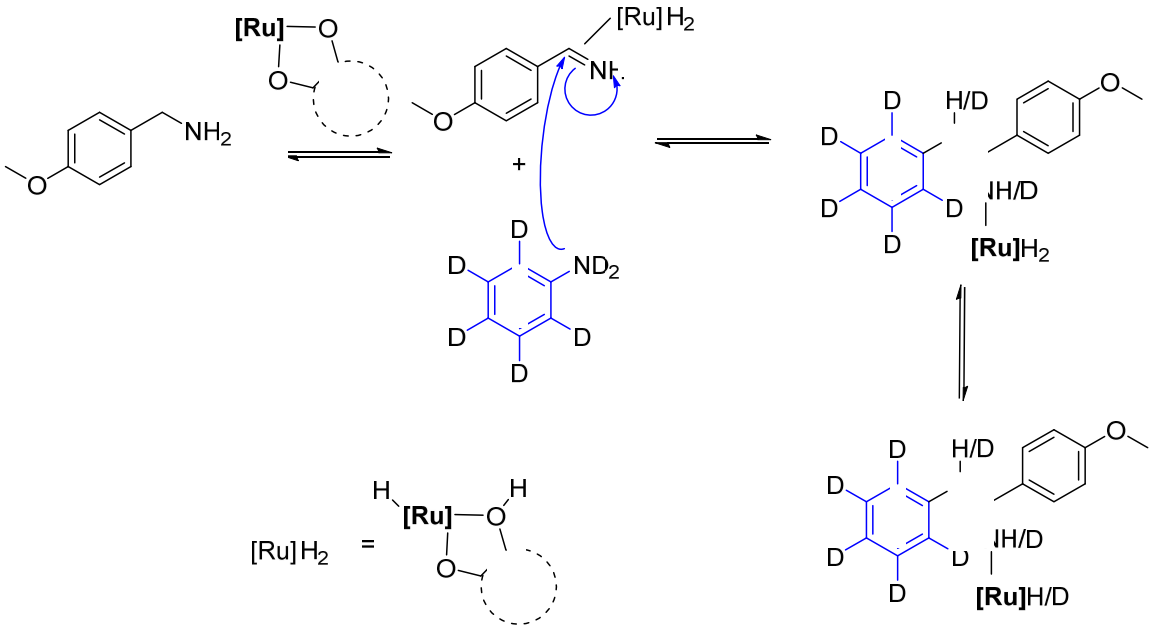


Figure 2.4.2.1: ^{1}H and ^{2}H NMR spectra of the product **119**^{y} and **119**-*d* isolated from the reaction of aniline-d_7 with 4-methoxybenzylamine.

Control experiment was conducted with the pure product **119^{y},** (107 mg, 0.5 mmol) with aniline-d_7 **118-*d*** (50 mg, 0.5 mmol) with the **112** (7 mg, 0.75 mol %) and **116** (8 mg, 10 mol %) dissolved in chlorobenzene (1 mL). A trace amount (<5%) of deuterium incorporation at benzylic position was observed without detectable deuterium exchange in aniline group, suggesting the aniline might be strongly bonded to the active catalytic center or active catalytic species will not be generated without primary aliphatic amines.

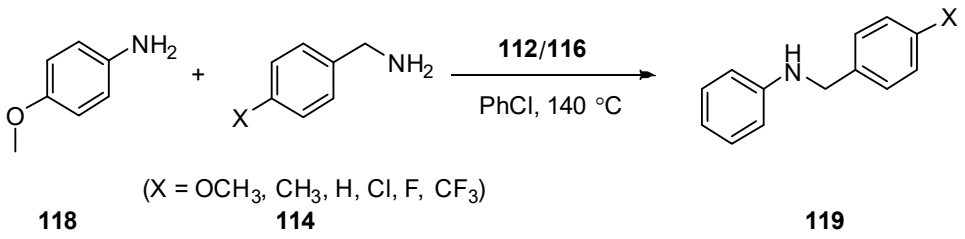


Scheme 2.4.2.2: Possible mechanistic rationale for the observed H/D exchange pattern.

The results indicate that the ortho-metalation was significantly involved during the coupling reaction. No observable H/D exchange was on the deuterated aniline, suggesting that the aniline compound is not directly coordinated to the ruthenium center.

Possibly the aromatic amine acted as a nucleophile at the latter part of the catalytic cycle. Interestingly, significant amount (18%) of deuterium exchange was observed at the benzylic position of the product. This clearly indicated that the formation of imine as an intermediate and hydrogen transfer takes place at the latter stage the catalytic cycle. One possible explanation for the mechanism of the reaction is via the formation of imine product which is a well-known transformation for Ru catalysts.[60] Since the observed data are consistent with this argument, we propose that the amine activation and formation of an imine is a possible step for the reaction. (**Scheme 2.4.2.2**).

2.4.3 Hammett Study



Scheme 2.4.3.1: Hammett study of *para*-substituted benzylamine substrates, *p*-X-$C_6H_5CH_2NH_2$ (X = OCH_3, CH_3, H, Cl, F, CF_3).

Hammett studies of *para*-substituted benzylamine substrates were performed to determine the electronic effects of benzylamine substrates on the C-N bond cleavage step (**Scheme 2.4.3.1**). Para-substituted benzylamines, *p*-X-$C_6H_5CH_2NH_2$ (X = OCH_3, CH_3, H, Cl, F, CF_3) (0.25 mmol), ligand (10 mol%) and the ruthenium hydride complex **112** (3 mol %) were dissolved in chlorobenzene (2 mL) in six separate 25 mL Schlenk tubes. ^{1}H NMR analysis were performed to find the k_{obs} from a first-order plot of -*ln*([*p*-X-$C_6H_5CH_2NH_2]_t$/*p*-X-$C_6H_5CH_2NH_2]_0$) vs. time. The Hammett plot of log(k_X/k_H) vs. σ_p is

shown in **Figure 2.4.3.1**.

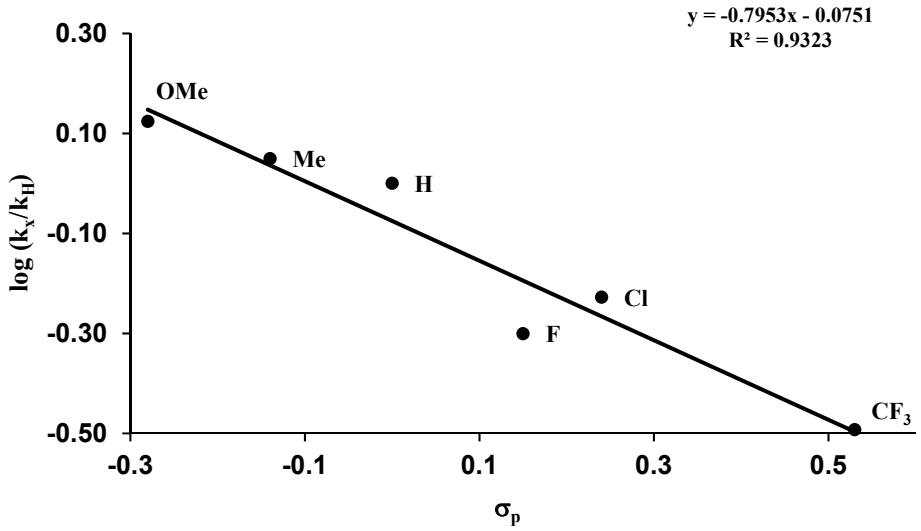
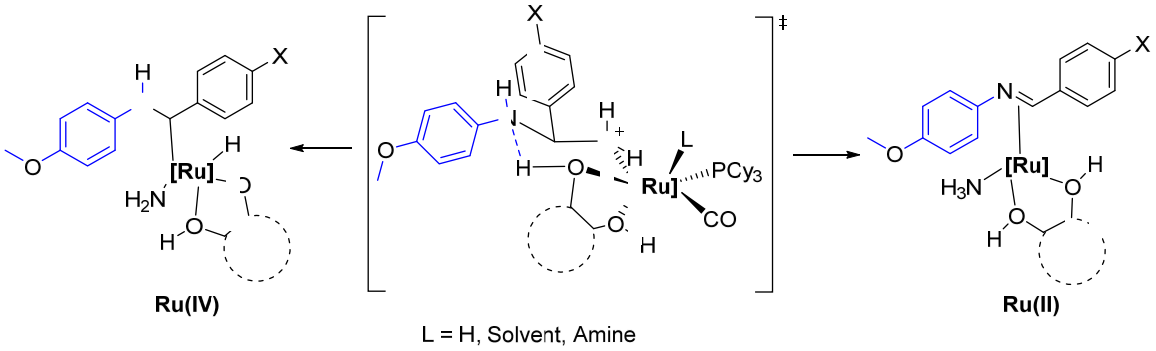


Figure 2.4.3.1: Hammett Plot of *p*-X-$C_6H_5CH_2NH_2$ (X = OCH_3, CH_3, H, Cl, F, CF_3) with *p*-$C_6H_5NH_2$.

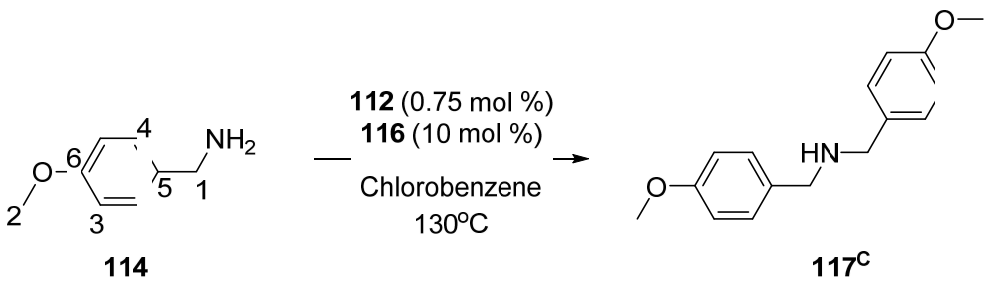


Scheme 2.4.3.2: Possible reaction pathways to illustrate the cationic character on the transition state.

It was found that the benzylamines having electron donating groups accelerated the rate of the reaction. The Hammett correlation of *para*-substituted benzylamine

substrates (*p*-X-$C_6H_4CH_2NH_2$ (X = OCH_3, CH_3, H, Cl, F, CF_3) found to be ρ = -0.8±0.1. The negative value of **ρ** indicates considerable cationic character in the transition state on the C-N cleavage step. After the formation of the imine product, there might be an equilibrium with ruthenium complex to transfer proton and activation of C-N bond. As shown in the **Scheme 2.4.3.2**, transition state of the complex has a positive character. This consistent with the observed results from the Hammett experiment. *Hydrogen bonding* with nitrogen attached to aniline moiety would create favorable bonding interactions to activate the C-N bond via neutral ruthenium or ruthenium(II) path ways to afford the products. These pathways shown to be consistent with the well establish hydrogen borrowing methodology.[3,9]

2.4.4 Carbon isotope effect study



Scheme 2.4.4.1: Homocoupling experiment for KIE study.

^{13}C KIE experiment was performed to determine the turnover limiting step of the catalytic reaction. Therefore, we performed Singleton's NMR technique[63] to measure the $^{12}C/^{13}C$ kinetic isotope effect (KIE) for the homocoupling experiment with 4-methoxybenzylamine, in order to establish the rate determining step of the reaction. **112**

(0.75 mol%) and **116** (10 mol %) were dissolved in chlorobenzene (2 mL). The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. Then, 4-methoxybenzylamine (2 mmol), and chlorobenzene (2 mL) were added to the reaction tube. It was stirred in an oil bath at 130 °C for 16 h. The tubes were cooled to room temperature and filtered through a small silica column (CH_2Cl_2), the conversion was determined by GC (86%, 89% and 88% conversion). Similarly, low conversion (15%, 13% and 12%) experiment was performed by adding catalyst (0.75 mol%), **116** (10 mol %) and 4-methoxybenzylamine (5 mmol) were dissolved in chlorobenzene (5 mL). After the tube was sealed, it was brought out of the box, and was stirred in an oil bath at 130 °C for 2h. Products were separated by a column chromatography on silica gel (hexanes/EtOAc) for $^{13}C\{1H\}$ NMR analysis. The ^{13}C NMR analysis of the product of N,N-Bis(4-methoxybenzyl)amine was performed by following Singleton's ^{13}C NMR method[15]. The NMR sample was prepared identically by dissolving N,N-bis(4-methoxybenzyl)amine (200 mg) in $CDCl_3$ (0.5 mL) in a 5 mm high precision NMR tube. The $^{13}C\{1H\}$ NMR spectra were recorded with H-decoupling and 45 degree pulses. A 60 s delay between pulses was imposed to minimize T1 variations (d1 = 120 s, at = 5.0 s, np = 245098, nt = 512, dm = 'nny'). KIE was calculated by following the original Singleton procedure, found to be 1.02 at the benzylic position (**Figure 2.4.4.1**). This indicate that the C-N bond cleavage has been occurred at slowest step as the significant amount of C-N bond cleaved from the ^{12}C isotope during the lower conversion. The results are consistent with C-N bond cleavage step as turnover limiting step of the reaction. This result is also consistent with the previously discussed mechanistic data.

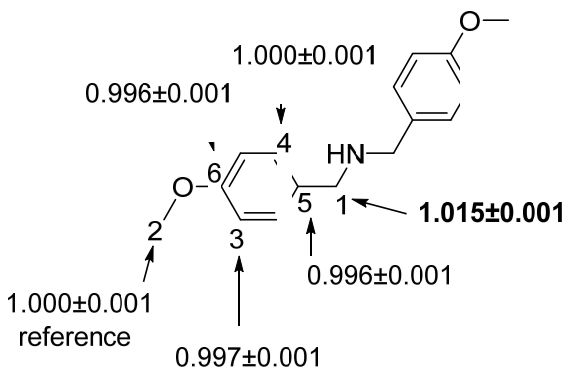


Figure 2.4.4.1: Observed kinetic isotope effect on the symmetric coupling product **117**[c]; (Reference = C2).

2.4.5 Efforts to detect catalytic intermediate species

To search for active catalytic intermediates for the reaction, we performed NMR experiments and x-ray crystallographic preparations with the tetrameric ruthenium hydride complex. Thus far, we have not been successful on the preparation of single crystals for the active catalytic species. However, in 2015 our group demonstrated that the phenol ligands with the ruthenium hydride catalyst can be used to promote the hydrogenolysis reaction of ketones.[14]

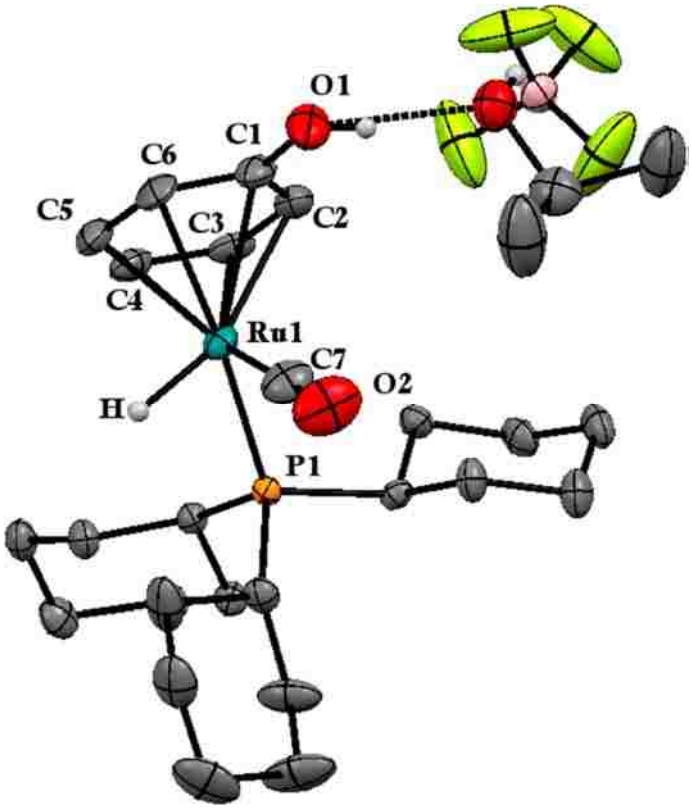
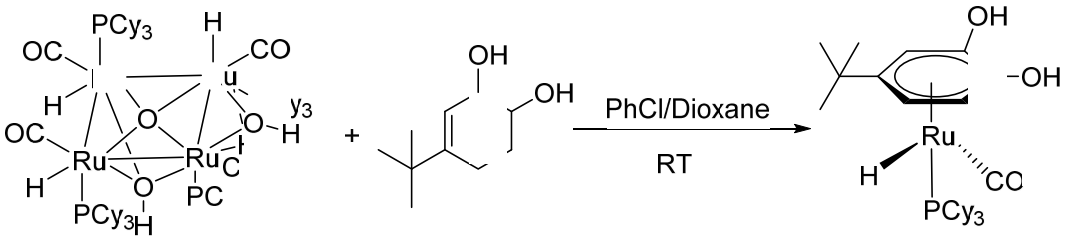


Figure 2.4.5.1: Molecular structure of $[(C_6H_5OH)(PCy_3)(CO)RuH]^+BF_4^-$ cocrystallized with a 2-propanol molecule.

Figure 2.4.5.1 represents that the phenol ligand bonded to the Ru center by replacing the benzene ligand. Reaction of cationic Ru-H complex with catechol ligand expected to be formed η^6 coordinated ruthenium catechol complex by replacing the benzene ligand. Similarly, we are assuming that the neutral Ru-H catechol complex would be formed after addition of catechol ligand to the tetranuclear ruthenium hydride catalyst following slow hydrolysis reaction (**Scheme 2.4.5.1**). Hydrolysis of reddish brown tetranuclear ruthenium hydride complex is well established in the presence of acidic or basic conditions, by producing di or mono nuclear complexes[60].



112

Scheme 2.4.5.1: Formation of neutral ruthenium catechol complexes.

However, the complex shown in **Scheme 2.4.5.1**, might not be the active catalytic species for the amino coupling reaction. The following experiment was performed to get the information on active catalytic species. In a sealed NMR tube **112** (17 mg) and **116** (3 mg) were dissolved in 1 mL of chlobenzene-d_5. The resultant mixture was homogenized and ^{1}H and ^{31}P NMR spectra were recorded at room temperature. Then, 4-methoxybenzylamine (4 mg) was added and ^{1}H and ^{31}P NMR spectra were recorded before and after heating at the 85 °C in an oil bath. NMR studies has been clearly shown that the hydride signals[18] δ -18.64 (dt, J_{HP} = 13.2, 4.8 Hz), -15.28 (d, J_{HP} = 34.5 Hz), -15.01 (d, J_{HP} = -16.8 Hz), and -14.55 (d, J_{HP} = 20.1 Hz), disappeared with the prolong heating of the reaction mixture with the substrate at 85 °C, about 6 hours (**Figure 2.4.5.2**). This result clearly indicated that the active catalytic species does not have a ruthenium hydride species.

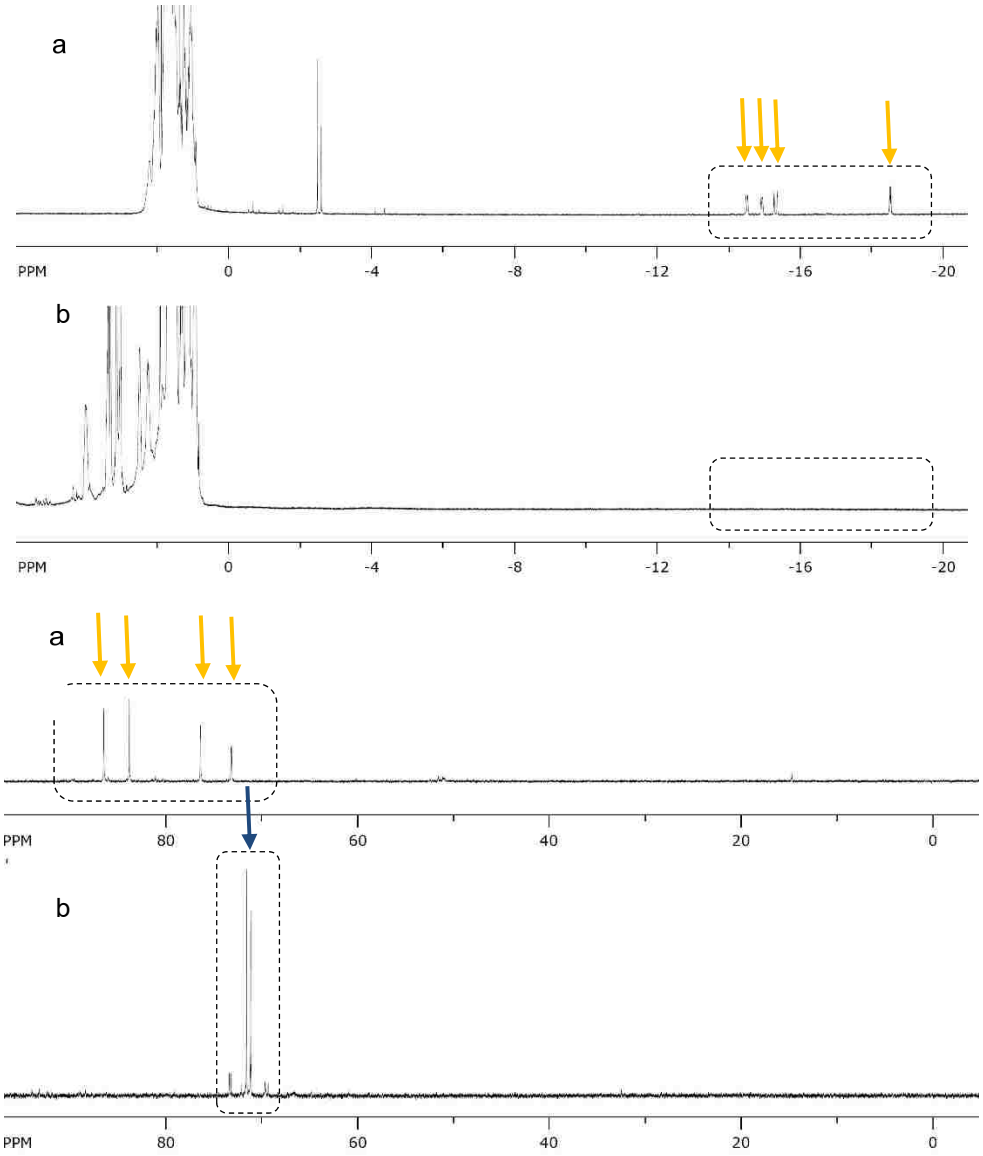
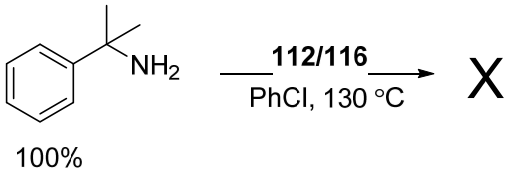


Figure 2.4.5.2: a. ^{1}H and ^{31}P NMR spectra of the **112** (17mg) b. ^{1}H and ^{31}P NMR spectra of the **112** (17mg), **116** (3 mg) and 4-methoxybenzylamine heated at 85 °C, 6 hours.

2.5 Proposed Mechanism

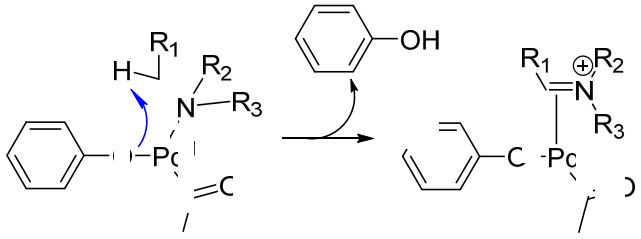
Even though detailed reaction mechanism remains unclear, we present a plausible mechanistic scheme for the coupling reaction on the basis of these results (**Scheme 2.5.3**). We propose that the cationic Ru-imine species **127** is initially generated from the

dehydrogenation of amine substrate. In supporting evidence for the Ru-imine species **127**, we have been able to detect the formation of **117c´** (an imine product) from the crude reaction mixture. The cumylamine (**Scheme 2.5.1**) substrate, which does not have a α-H was not proceeded to form the desired coupling product.



Scheme 2.5.1: Homocoupling reaction with cumylamine.

Earlier literature clearly indicated that the presence of α-H is mandatory to proceed the reaction. The observed H/D exchange pattern on both the coupling product and the recovered phenol substrate is consistent with a facile *ortho*-C–H activation step[66]. In support of this notion, Jia group reported that the alkoxide attack on the α-CH_2 position of the tertiary amine, generate an iminium-type intermediate via facile *ortho*-C–H activation (**Scheme 2.5.2**).[66b] As discussed in chapter 1, there are three general mechanisms, (Oxidative addition, β-N elimination and C-H bond cleavage) for transition metal mediated C–N bond metalation which can be used to rationalize the mechanism of the reaction.[45b]



Scheme 2.5.2: C-H bond cleavage triggered C-N bond activation path way.

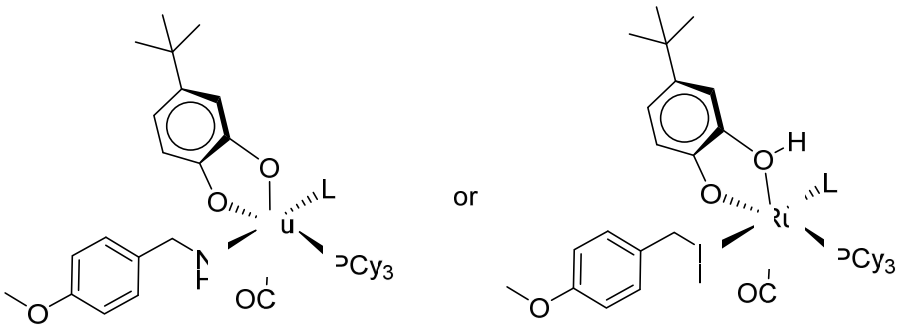
The deuterium labeling pattern was examined from the reaction of aniline-d_7 with 4-methoxybenzylamine. A significant amount of deuterium was incorporated to the CH_2 position of **123** (18% D), but no deuterium incorporation was observed on the arene positions. The observed deuterium exchange suggests that the H/D ammonia-to-aniline-d_7 might have transferred to the imine byproduct during the course of reaction. Control experiment H/D exchange aniline-d_7 with the product **119** was conducted, and the results shows that the H/D in cooperation on the CH_2 position of **119** (<5% D). This result is consistent with the C-N bond activation via formation of the imine product. Furthermore, dehydrogenation of alcohol, formation of indole products with diol substrates by dehydrogenation are known for the tetrameric ruthenium catalyst.[64] Recently we observed the formation of quinoline and quinazoline derivatives by dehydrogenation of amine substrates, where the formation of imine product was detected by both NMR and GC-MS analysis of crude mixtures. These results are consistent with the proposed mechanistic rationale via the imine formation.

The significant carbon isotope effect on the CH_2 carbon for the product is consistent with the C–N bond cleavage as the turnover-limiting step of the coupling reaction. In support of this notion, Singleton and co-workers showed that the observation of most pronounced carbon isotope effect has been a definitive evidence for establishing the rate-limiting step for both C–C and C–O bond forming reactions.[63] The C–N bond cleavage step has also been commonly considered as the turnover limiting step for catalytic coupling reactions of nitrogen compounds.[45b, 47]

The Hammett plot was constructed from measuring the rate of the coupling of 4-methoxyaniline with a series of para-substituted benzylamines 4-X-$C_6H_4CH_2NH_2$ (X =

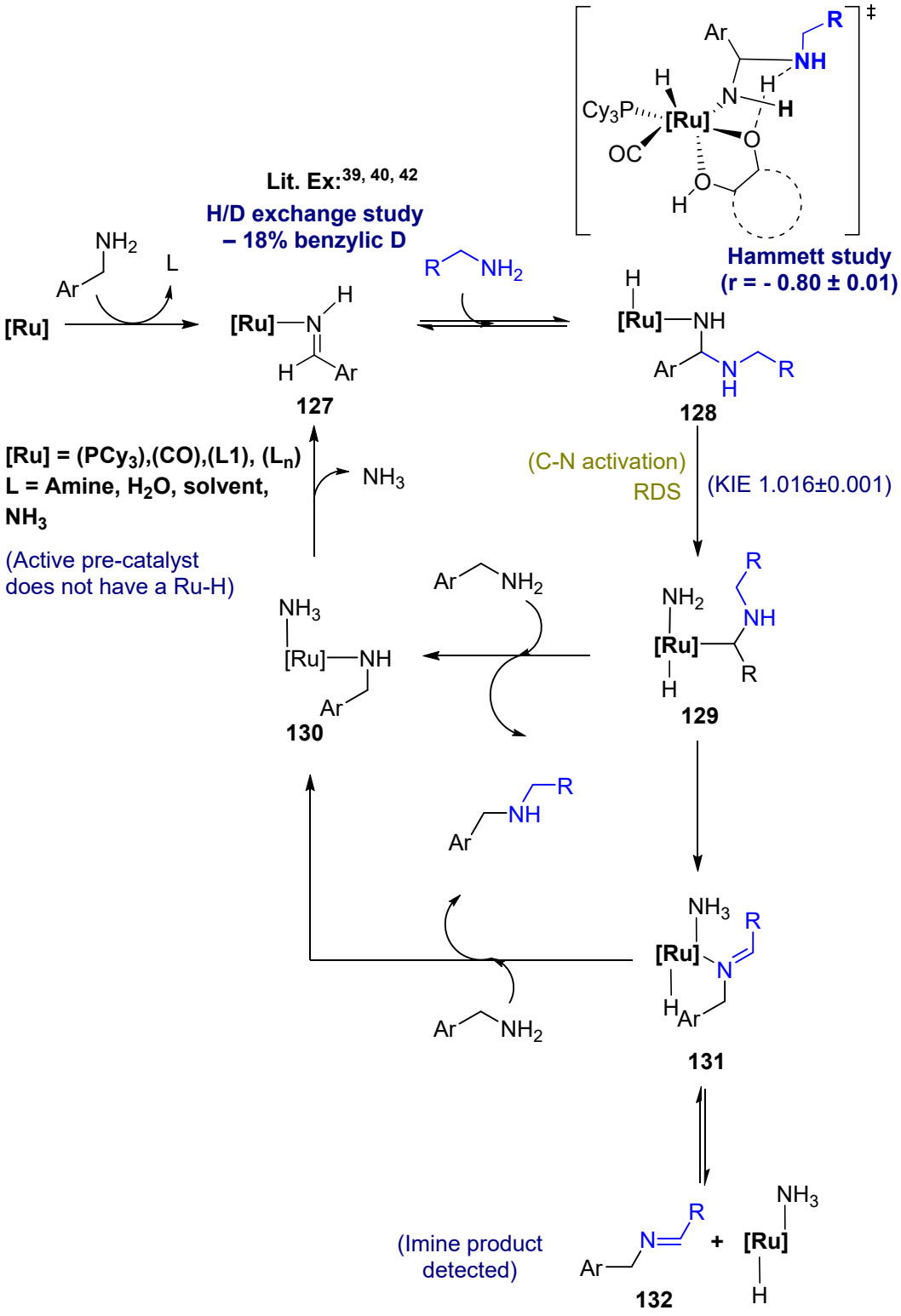
OMe, Me, H, F, CF_3) in the presence of **116** in toluene-d_8. The Hammett plot of $\log(k_X/k_H)$ vs σ_p showed a linear correlation pattern. A negative linear slope ($\rho = -0.79 \pm 0.1$) is indicative of the formation of cationic character on the turnover limiting step. The observation of a strong promotional effect by the electron releasing group on benzylamine is consistent with a nucleophilic displacement of the coordinated amine via an electrophilic ruthenium−imine species.

NMR studies were performed in an effort to detect catalytically relevant species New phosphine peak at δ 71.5 and 71.1 ppm by $^{31}P\{^1H\}$ NMR were observed after heating the compound **114** with **112**/**116** at 85 °C for six hours. Disappearance of Ru−H signals of tetranuclear ruthenium complex which indicate the formation of new ruthenium complex with the ligand and 4-methoxybenzylamine. We tentatively assign the new set of peaks to an arene-coordinated Ru-catechol complex **126**, in light of the previously observed arene exchange reactions.[12c,13] (**Figure 2.5.1**).



126

Figure 2.5.1: Proposed active catalytic intermediate species, (octahedral, 18 electrons, Ru(II), L = solvent, RCH_2NH_2, H_2O).



Scheme 2.5.3: Proposed mechanism for deaminative coupling of amines to form secondary amines.

The proposed mechanistic pathway begins with, coordination of the benzyl amine to the ruthenium ligand complex followed by α-H activation lead to form the active catalytic species **127**. Then S_N2 type nucleophilic attack on to the α-C by another molecule of amine would form a ruthenium bound diamine species **128**. The complex **128** then proceeds to activate the C-N bond through oxidative addition to form an intermediate species **129**. Co-ordination of another amine molecule would produce the secondary amine product and intermediate species **130**. Active catalytic species **127** will be regenerate by liberating ammonia molecule by β-H elimiation. Alternatively, β-H elimination would form the ruthenium co-ordinated imin intere intermediate species **131** which can equilibrate with **132** imine product. **131** would proceeds to form the desired secondary amine product by co-ordination with another amine affording an intermediate species **130**.

2.6 Conclusion

In conclusion, we have successfully developed a novel catalytic deaminative coupling method of primary amines to generate secondary amines. The catalytic method employs environmentally friendly and cheaply available amine substrates and exhibits a broad substrate scope and high chemo selectivity. We are currently exploring the detailed mechanism for these reactions. As an extension of the project we found several other important C-C and C-N bond forming reactions result from C-N bond activation.

2.7 Future Plans

Now that, we have been able to demonstrate the ligand controlled catalysis for deaminative coupling reactions of amines, we plan to investigate the following new set of coupling reactions.

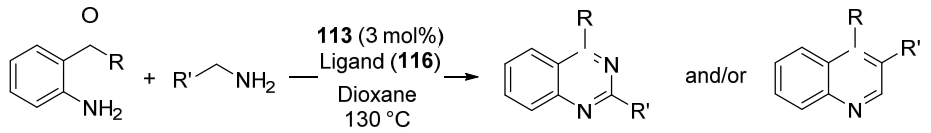
Goal # 1: To establish the detailed mechanism, we plan to identify ruthenium intermediate by spectroscopic techniques. Both spectroscopic and experimental evidences will be taken to establish the possible catalytically active species for the coupling reaction.

Goal #2: We will seek to probe other supportive ligands such as catechol and its derivatives, to promote catalytically more active and selective species for other coupling reactions.

Generation I catalyst Generation II catalst

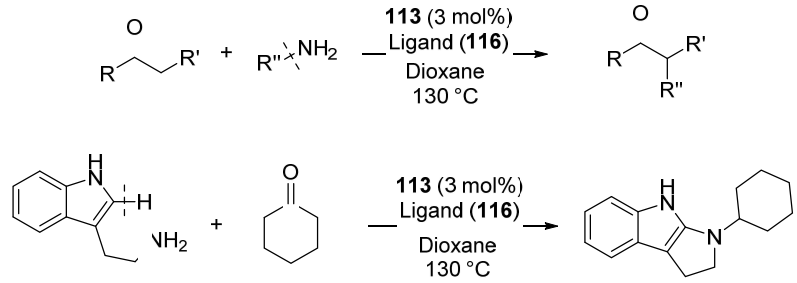
Figure 2.7.1: Different ruthenium hydride catalyst.

Goal #3: We will use the ligand controlled catalysis to design new coupling reactions. We recently observed a new dehydrative cyclization reaction to produce quinazoline and quinoline derivatives of amino ketones with amines. We will complete the investigation on the scope of the reaction.



Scheme 2.7.1: Ruthenium hydride catalyzed synthesis of quinazoline.

We provisionally found a novel C-C bond forming reaction by deaminative and decarboxylative reaction of amino acids with ketones.[62] Recently, we found the deaminative C-C bond formation reaction of primary amines with ketones. Since the C-N activation under this catalytic method was very successful, we tried to incorporate the method for the C-H activation reactions. Surprisingly intramolecular cyclization reaction was observed by aromatic C-H activation with primary amines and ketones. We will investigate the scope and selectivity of the novel cyclization reactions.



Scheme 2.7.2: Ruthenium hydride catalyzed selective *α-alkylation* and *aromatic C-H activation* reactions.

Chapter 3

Experimental Section

3.0 General Information.

All operations were carried out in a nitrogen-filled glove box or by using standard high vacuum and Schlenk techniques unless otherwise noted. All the solvents used were freshly distilled over appropriate drying reagents. Chlorobenzene was distilled from purple solutions of sodium and benzophenone, and hexanes was dried over calcium hydride prior to use. All organic substrates were received from commercial sources and were used without further purification. The ^{1}H, ^{2}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Varian 400 MHz FT-NMR spectrometer, and the data are reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constant(s) in Hz; integration. Mass spectra were recorded from Agilent 6850 GC-MS spectrometer by using a HP-5 (5% phenylmethylpolysiloxane) column (30 m, 0.32 mm, 0.25 μm). High resolution mass spectra were obtained at the Mass Spectrometry/ICP Lab, Department of Chemistry and Biochemistry, University of Wisconsin-Milwaukee, Milwaukee, WI. Elemental analyses were performed at the Midwest Microlab, Indianapolis, IN.

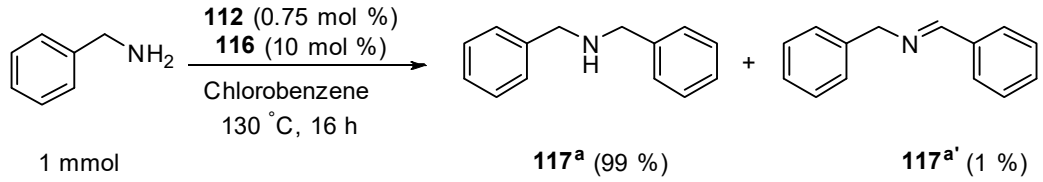
3.1 General Procedure for the Catalytic Synthesis of Secondary Amines.

In a glove box, complex **112** (13 mg, 0.75 mol %) and 4-(1,1-dimethylethyl)-1,2-benzenediol (**116**), (16 mg, 10 mol %) were dissolved in chlorobenzene (1 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. In an alternative procedure, the complex **113** (17 mg, 3 mol %) and **116** (16 mg, 10 mol %) were dissolved in anhydrous 1,4-dioxane (1 mL). Two amine substrates (1.0 mmol and 1.4 mmol) in chlorobenzene (1 mL) were added to the reaction tube. After the tube was sealed, it was brought out of the glove box, and was stirred in an oil bath maintained at 130-140 °C for 16-20 h. The reaction tube was taken out of the oil bath, and was cooled to room temperature. After the tube was open to air, the solution was filtered through a short silica gel column by eluting with CH_2Cl_2 (10 mL), and the filtrate was analyzed by GC-MS. Analytically pure product was isolated by a simple column chromatography on silica gel (280-400 mesh, hexanes/EtOAc or hexanes/EtOAc/methanol). Yields were calculated on the basis of limited amine substrate with isolated desired product.

3.1.1 Symmetric Coupling Reactions of Aliphatic Amines.

In a glove box, complex **112** (13 mg, 0.75 mol %) and **116** (16 mg, 10 mol %) were dissolved in chlorobenzene (1 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 min until the solution turned to a reddish green color. Then, benzylamine (107 mg, 1.0

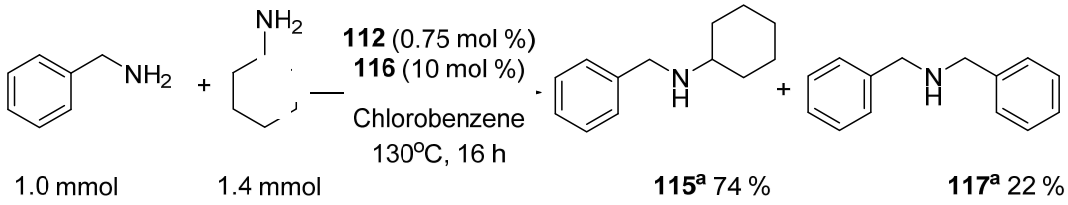
mmol), and chlorobenzene (1 mL) were added to the reaction mixture in a tube. After the Schlenk tube was sealed, it was brought out of the glove box, and was stirred in an oil bath maintained at 130 °C for 16 h. The reaction tube was taken out of the oil bath, and let it to cool to room temperature. Crude mixture was filtered through a short silica gel column by eluting with CH_2Cl_2 (10 mL), and the filtrate was analyzed by GC-MS. Analytically pure product was isolated by a simple column chromatography on silica gel (280-400 mesh, *n*-hexane/EtOAc).



Scheme 3.1.1.1: Symmetric coupling reactions of aliphatic amines.

3.1.2. Asymmetric Coupling Reactions of Aliphatic Amines.

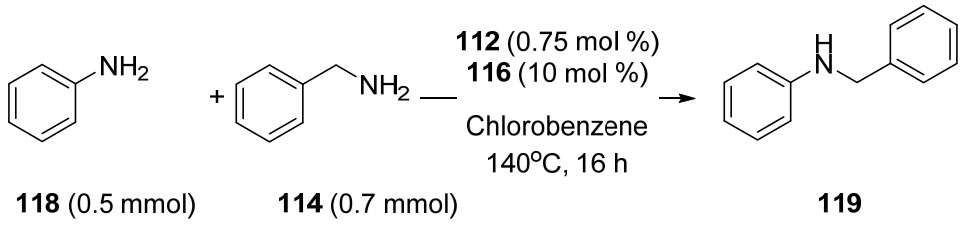
In a glove box, complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) were dissolved in chlorobenzene (1 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. An amine substrate which is less reactive (1.0 mmol), amine substrate which is more reactive (1.4 mmol), and chlorobenzene (1 mL) were added to the reaction tube. The tube was brought out of the glove box, and was stirred in an oil bath maintained at 130 °C for 16 h. The reaction tube was taken out of the oil bath, and let it to cooled to room temperature. Resultant solution was filtered through a short silica gel column by eluting with CH_2Cl_2 (10 mL), and the filtrate was analyzed by GC-MS. Analytically pure product was isolated by a simple column chromatography on silica gel (280-400 mesh, *n*-hexane/EtOAc/methanol).



Scheme 3.1.2.1: Symmetric coupling reactions of aliphatic amines.

3.1.3. Asymmetric Coupling Reactions of Aromatic Amines.

In a glove box, complex **112** (7 mg, 0.75 mol %) and **116** (8 mg, 10 mol %) were dissolved in chlorobenzene (1 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 min until the solution turned to a reddish green color. Aniline (47 mg, 0.5 mmol), Benzyl amine (75 mg, 0.7 mmol) and chlorobenzene (1 mL) were added to the reaction tube. After the tube was sealed, it was brought out of the glove box, and was stirred in an oil bath maintained at 140 °C for 20 h. The reaction tube was taken out of the oil bath, and was cooled to room temperature. Analytically pure product was isolated by a simple column chromatography on silica gel (280-400 mesh, *n*-hexane/EtOAc or *n*-hexane/EtOAc/methanol).



Scheme 3.1.3.1: Asymmetric coupling reactions of aromatic amines.

3.2 Synthesis of Ru Catalysts

The tetrametallic complex **112** was synthesized in two steps from the ruthenium-hydride complex $(PCy_3)_2(CO)RuHCl$ (**110**). Thus, the reaction of **110** with KOH in 2-propanol produced the bimetallic complex **111**, which was isolated in 85% yield after recrystallization in hexanes.

3.3 Synthesis of $[(\eta^6\text{-}C_6H_6)RuH(CO)(PCy_3)]^+BF_4^-$ (113).

In a glove box, complex **112** (200 mg, 0.12 mmol) was dissolved in benzene (10 mL) in a 25 mL Schlenk tube equipped with a Teflon screw-cap stopcock and a magnetic stirring bar. The tube was brought out of the box, and $HBF_4 \cdot OEt_2$ (64 μL, 0.48 mmol) was added via syringe under N_2 stream. The color of the solution was changed from dark red to pale yellow immediately. After stirring for 1 h at room temperature, the solvent was removed under vacuum, and the residue was crashed by adding hexanes (20 mL). Filtering the resulting solid through a fritted funnel and recrystallization from CH_2Cl_2/hexanes yielded the product as a pale-yellow powder (262 mg, 95% yield). Single crystals of **113** suitable for X-ray crystallography were obtained from a slow evaporation of benzene and hexanes solution.

For **113**: ^1H NMR (CD_2Cl_2, 400 MHz) δ 6.53 (s, C_6H_6), 2.0-1.2 (m, PCy_3), -10.39 (d, J_{PH} = 25.9 Hz, Ru-H); $^{13}C\{1H\}$ NMR (CD_2Cl_2, 100 MHz), δ 196.4 (d, J_{CP} = 19.3 Hz, CO), 100.0 (C_6H_6), 38.4, 38.2, 30.2, 29.9, 27.4, 27.3 and 26.2 (PCy_3); $^{31}P\{1H\}$ NMR (CD_2Cl_2,

162 MHz) δ 72.9 (PCy_3); IR (KBr) *v*CO = 1991 cm^{-1}; Anal. Calcd for **xx** $C_{25}H_{40}BF_4OPRu$: C, 52.18; H, 7.01. Found: C, 51.73; H, 6.91.[60]

3.4 Reaction profile.

In a glove box, complex **112** (28 mg, 0.75 mol %) and **116** (32 mg, 10 mol %) were dissolved chlorobenzene in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. Then, 4-methoxybenzylamine (274 mg, 2 mmol), were added to the reaction tube and homogenized the solution. The tube was brought out of the glove box, and was kept in an oil bath maintained at 130 °C. The tube was taken out from the oil bath at 20 min time intervals and small amount of homogenized mixture was taken out in the glove box and the sample was analyzed by ^{1}H NMR. The product concentration was measured by monitoring the appearance of the product signals on ^{1}H NMR, which was normalized against the internal standard peak (hexamethylbenzene). The plot of relative concentration vs time is shown in **Figure 2.4.1.1**. In an alternative procedure benzylamine (34 mg, 0.25 mmol) and catalyst **113** (3 mg, 0.75 mol %)/**116** (4 mg, 10 mol %) were dissolved in toluene-d_8 (0.5 mL) in a J-Young NMR tube equipped with a Teflon screw cap stopcock. The reaction tube was heated in an oil bath at 130 °C at 20 min time intervals, and the progress was monitored by ^{1}H NMR.

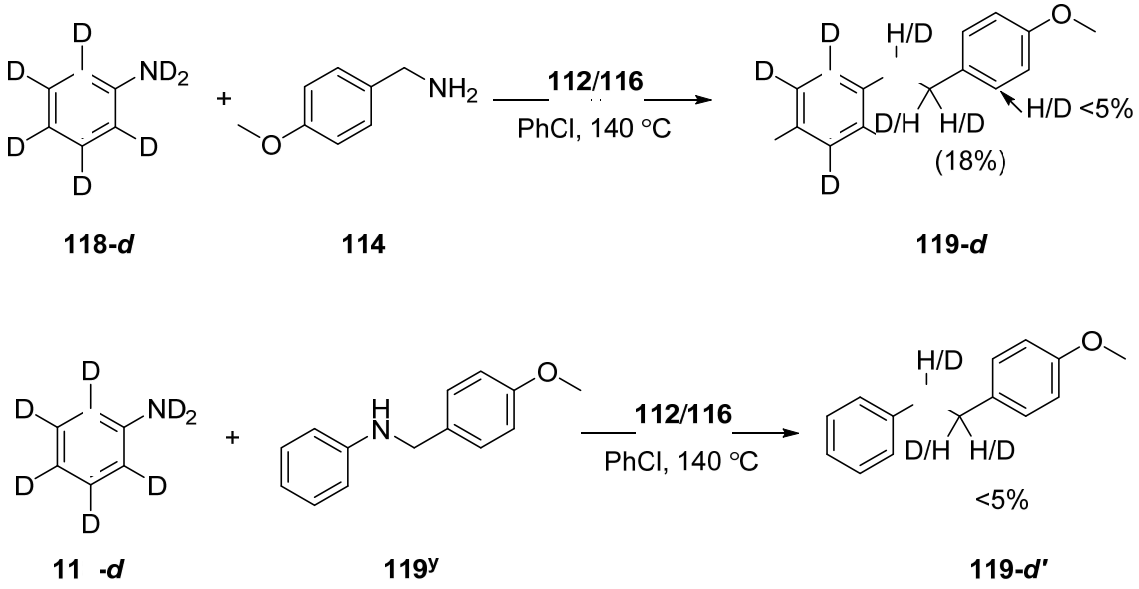
3.5 Detection of Active Catalytic Intermediate Species

In a glove box, complex **112** (0.017 mg, 10 μmol) and **116** (0.004 mg, 25 μmol) were dissolved in chlorobenzene-*d*5 (0.5 mL) in a J young tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. After the tube was sealed, it was brought out of the glove box, and kept in an oil bath maintained at 85 °C. The ^{1}H and ^{31}P NMR spectra of the products were obtained. After that 4-methoxybenzylamine (0.014 mg, 100 μmol) was added into the tube. After the tube was sealed it was heated in an oil bath maintained at 85 °C for further six hours and ^{1}H and ^{31}P NMR spectra of the products were obtained. Similar experiment was conducted with the **113** catalyst.

3.6 Deuterium Labeling Study.

In a glove box, complex **112** (7 mg, 0.75 mol %) and **116** (8 mg, 10 mol %) were dissolved in chlorobenzene (1 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. Aniline-d_7 (50 mg, 0.5 mmol) and 4-methoxybenzylamine (78 mg) in chlorobenzene (1 mL) were added to the reaction tube. After the tube was sealed, it was brought out of the glove box, and was stirred in an oil bath maintained at 140 °C for 20 h. Analytically pure product was isolated by a simple column chromatography on silica gel (280-400 mesh, *n*-hexanes/EtOAc). The ^{1}H and ^{2}H NMR spectra of the product **119-*d*** are recorded (**Scheme 3.6.1**). Control experiment was coduted with the pure product **119^{y},** (107 mg,

0.5 mmol) with Aniline-d_7 (50 mg, 0.5 mmol) with the catalyst (7 mg, 0.75 mol %) and **116** (8 mg, 10 mol %) which were dissolved in chlorobenzene (1 mL). Trace (<5%) amount of deuterium incooparation at benzylic position was observed without detectable deuterium exchange in aniline group (**Scheme 3.6.1**)



Scheme 3.6.1: H/D exchange pattern of benzyl amine with aniline -d_7.

3.7 Hammett Study.

In a glove box, complex **112** (20 mg, 0.75 mol %) and **116** (24 mg, 10 mol %) were dissolved in toluene-d_8 (1.5 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. Then, 4-methoxyaniline (185 mg, 1.5 mmol), were added to the reaction tube and homogenized the solution, it was equally divided into 6 parts and *p*-X-$C_6H_4CH_2NH_2$ (0.3 mmol) were (X = OMe, Me, H, F, Cl, CF_3) put into the divided portions separately. After that mixture was homogenized and transferred into J young NMR tube equipped

with a Teflon screw cap stopcock. The tubes were brought out of the glove box, and was kept in an oil bath maintained at 140 °C. Each tube was taken out from the oil bath at 30 min time intervals and it was analyzed by ^{1}H NMR after cooled in ice-water bath. The reaction rate was measured by monitoring the appearance of the product signals on ^{1}H NMR, which was normalized against the internal standard peak. The k_{obs} was determined from a first-order plot of -*ln*([*p*-X-$C_6H_5CH_2NH_2$]$_t$/*p*-X-$C_6H_5CH_2NH_2$]$_0$) vs time. The Hammett plot of log(k_X/k_H) vs σ_p is shown in **Figure 3.7.1**:

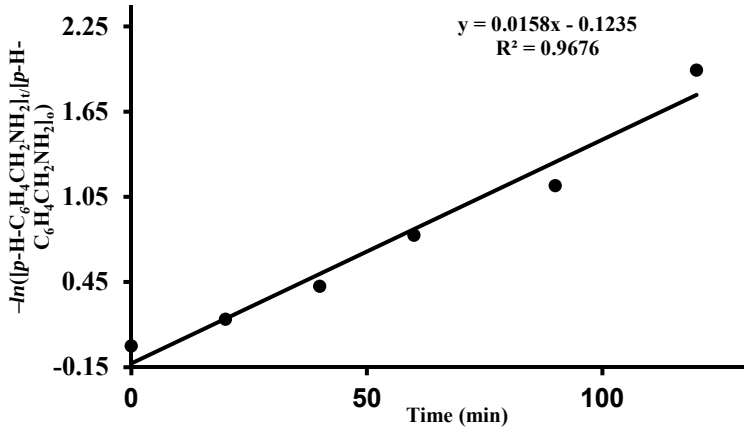


Figure 3.7.1: First order plot of –*ln*([*p*-H-$C_6H_4CH_2NH_2$]$_t$/[*p*-H-$C_6H_4CH_2NH_2$]$_o$) vs. time.

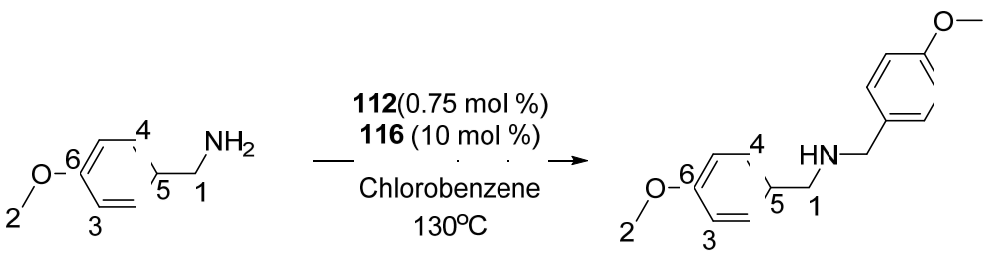
3.8 Carbon Isotope Effect Study.

In a glove box, **112** (28 mg, 0.75 mol%) and **116** (32 mg, 10 mol %) were dissolved in chlorobenzene (2 mL) in a 25 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. The resulting mixture was stirred for 5 to 10 minutes until the solution turned to a reddish green color. Then, 4-methoxybenzylamine (274 mg, 2 mmol), and chlorobenzene (2 mL) were added to the reaction tube. After the tube was sealed, those were brought out of the box, and was stirred in an oil bath at 130 °C for 16 h. The tubes were cooled to

room temperature and filtered through a small silica column (CH_2Cl_2), the conversion was determined by GC (86%, 89% and 88% conversion). Similarly, low conversion (15%, 13% and 12%) experiment was performed by adding **112** (52 mg, 0.75 mol%) and **116** (80 mg, 10 mol %) were dissolved in chlorobenzene (5 mL) in a 100 mL Schlenk tube equipped with a Teflon screw cap stopcock and a magnetic stirring bar. Then, 4-methoxybenzylamine (685 mg, 5 mmol), and chlorobenzene (5 mL) were added to the reaction tube. After the tube was sealed, it was brought out of the box, and was stirred in an oil bath at 130 °C for 2h. Products were separated by a column chromatography on silica gel (hexanes/EtOAc) for $^{13}C\{1H\}$ NMR analysis. The ^{13}C NMR analysis of the product of N,N-Bis(4-methoxybenzyl)amine was performed by following Singleton's ^{13}C NMR method.[63] The NMR sample was prepared identically by dissolving N,N-Bis(4-methoxybenzyl)amine (200 mg) in $CDCl_3$ (0.5 mL) in a 5 mm high precision NMR tube. The $^{13}C\{1H\}$ NMR spectra were recorded with H-decoupling and 45 degree pulses. A 60 s delay between pulses was imposed to minimize T1 variations (d1 = 120 s, at = 5.0 s, np = 245098, nt = 512, dm = 'nny'). The data obtained were summarized in **Table 3.8.1**.

Table 3.8.1: Average ^{13}C Integration of the Product **119** Obtained from 4-Methoxybenzylamine at High Conversion (Virgin, R_0; 88% conversion), at Low Conversion (R; avg 13% conversion) and the Calculated ^{13}C KIE using **112/116**. (C2 = reference)

Carbon #	High Conversion (R_0)	Low Conversion (R)	R_0/R	KIE
1	**1.0844**	**1.0681**	**1.0152**	**1.0152**
2	1.0000	1.0000	1.0000	1.0000
3	1.9800	1.9862	0.9969	0.9969
4	2.0735	2.0742	0.9997	0.9997
5	1.2465	1.2510	0.9964	0.9964
6	1.2338	1.2520	0.9854	0.9854



Scheme 3.8.1: Carbon isotope effect on product **117**[c].

3.9 X-Ray Crystallographic Determination of 119[f]

Colorless single crystals of **119**[f] were grown in dichloromethane/*n*-hexane at room temperature. A suitable crystal with the dimension of 0.4341 × 0.0928 × 0.0487 mm^3 was selected and mounted on an Oxford SuperNova, Dual, Cu at zero, Atlas diffractometer. The crystal was kept at 100.0(3) K during data collection. Using Olex2[67], the structure was solved with the olex2.solve[68] structure solution program using Charge Flipping and refined with the XL[69] refinement package using Least Squares minimization. The molecular structure of **119**[f] is shown in Figure **3.9.1**.

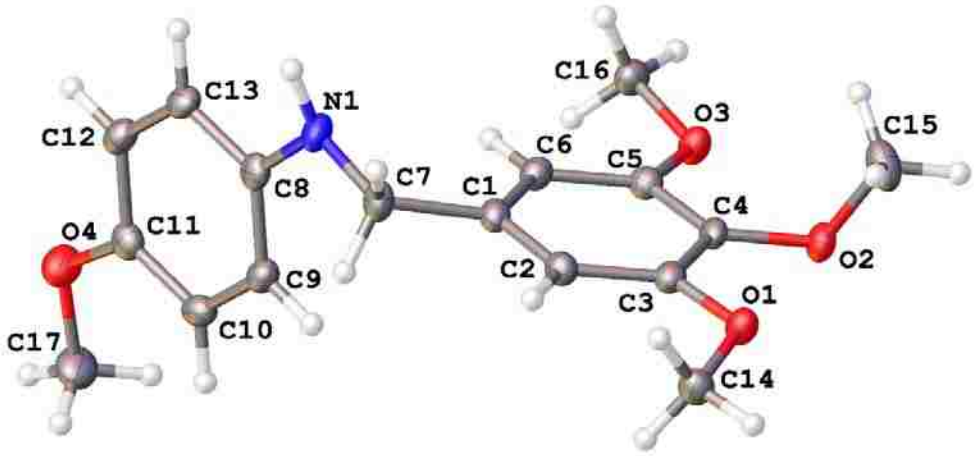


Figure 3.9.1: Molecular Structure of **119**[f].

3.9.1 Structure description

The central bond NH-CH_2 is twisted by 94.4º. The secondary amino group has a non-planar configuration with N-H bond making an angle of 17.1º with the CNC plane (0º for an ideal planar-trigonal coordination, 54.7º for a tetrahedral one – including LP). All Methoxy groups are coplanar to (conjugated with) the adjacent benzene rings, except OMe group O2-C15, which is rotated out of conjugation by 80.9º because of apparent sterical hindrances from its ortho-positioned counterparts.

3.9.2 Crystal packing

The molecules form translational chains along y axis through intermolecular H-bonds N-H…O. The crystal structure overall is chiral.

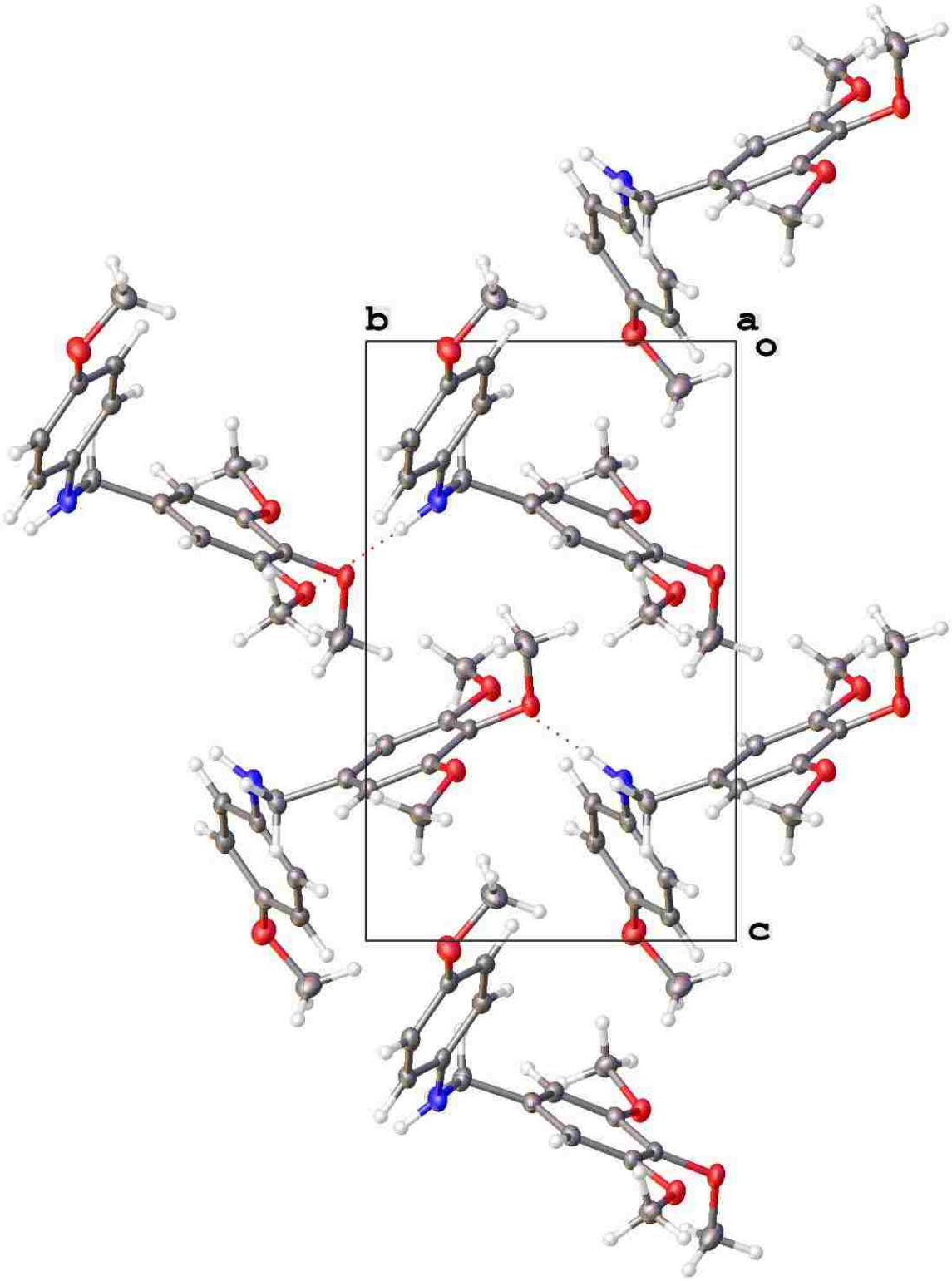
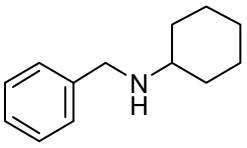


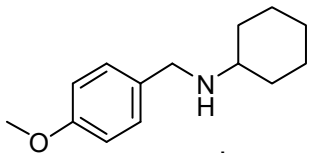
Figure 3.9.2.1: Crystal packing of **119**[f].

3.10 Characterization of Organic Products



115[a]

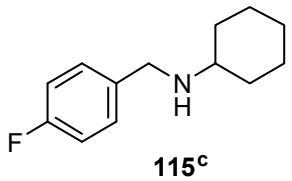
Table 2.3.1, compound 115[a]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), benzylamine (107 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[a]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 138 mg, 73%. Data for **115[a]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 4H), 7.28–7.20 (m, 1H), 3.81 (s, 2H), 2.49 (tt, *J* = 10.3, 3.7 Hz, 1H), 1.96–1.88 (m, 2H), 1.78–1.70 (m, 2H), 1.65–1.58 (m, 1H), 1.32–1.07 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 140.8, 128.3, 128.0, 126.7, 56.1, 51.0, 33.5, 26.1, 25.0 ppm; GC-MS for $C_{13}H_{19}N$, m/z = 189 (M^+).[70]



115[b]

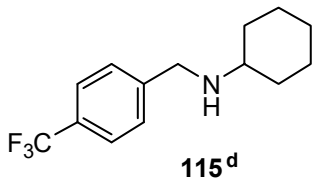
Table 2.3.1, compound 115[b]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzylamine (137 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[b]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 172 mg, 78%. Data for **115[b]**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.25–7.21 (m, 2H), 6.88–6.83 (m, 2H), 3.79 (s, 3H), 3.74 (s, 2H), 2.47 (tt, *J* = 10.4, 3.7

Hz, 1H), 1.96–1.86 (m, 2H), 1.77–1.68 (m, 2H), 1.65–1.56 (m, 1H), 1.31 (br s, 1H), 1.30–1.05 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.4, 133.0, 129.2, 113.7, 56.0, 55.2, 50.4, 33.5, 26.1, 25.0 ppm; GC-MS for $C_{14}H_{21}NO$, m/z = 219 (M^+).^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[71]



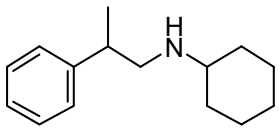
115^{c}

Table 2.3.1, compound 115^{c}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-fluorobenzylamine (125 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{c}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 147 mg, 71%. Data for **115^{c}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.23 (m, 2H), 7.02–6.95 (m, 2H), 3.76 (s, 2H), 2.45 (tt, J = 10.3, 3.8 Hz, 1H), 1.94–1.85 (m, 2H), 1.77–1.68 (m, 2H), 1.64–1.56 (m, 1H), 1.37 (br s, 1H), 1.32–1.04 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.7 (d, J_{CF} = 244.2 Hz), 136.6 (d, J_{CF} = 3.1 Hz), 129.5 (d, J_{CF} = 7.9 Hz), 115.1 (d, J_{CF} = 21.2 Hz), 56.1, 50.2, 33.5, 26.1, 24.9 ppm; GC-MS for $C_{13}H_{18}FN$, m/z = 207 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[72]



115^{d}

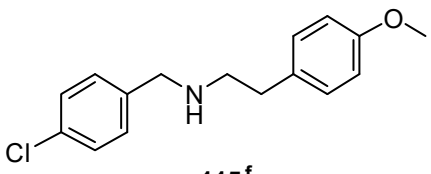
Table 2.3.1, compound 10[d]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 150.75 mol %), **116** (16 mg, 10 mol %), 4-trifluromethylbenzylamine (175 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[d]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 152 mg, 59%. Data for **115[d]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.53 (m, 2H), 7.45–7.41 (m, 2H), 3.86 (s, 2H), 2.46 (tt, J = 10.3, 3.5 Hz, 1H), 1.95–1.86 (m, 2H), 1.77–1.69 (m, 2H), 1.64–1.56 (m, 1H), 1.30–1.05 (m, 5H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.1, 129.0 (q, J_{CF} = 32.2 Hz), 128.2, 125.2 (q, J_{CF} = 3.8 Hz), 124.3 (q, J_{CF} = 271.9 Hz), 56.2, 50.4, 33.5, 26.0, 24.9 ppm; GC-MS for $C_{14}H_{18}F_3N$, m/z = 257 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[73, 74]



115[e]

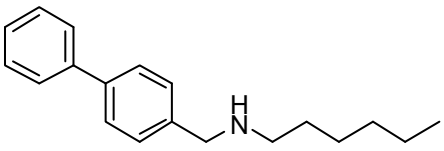
Table 2.3.1, compound 115[e]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), β-methylphenethylamine (135 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[e]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 136 mg, 63%. Data for **115[e]**: ^{1}HNMR (400 MHz, $CDCl_3$) 7.35–7.27 (m, 2H), 7.25–7.28 (m, 3H), 2.93 (sext, J = 7.0 Hz, 1H), 2.86–2.74 (m, 2H), 2.37 (tt, J = 10.6, 3.6 Hz, 1H), 1.89–1.62 (m, 5H), 1.62–1.54 (m, 1H), 1.26 (d, J = 6.9 Hz, 3H), 1.24–0.95 (m, 5H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.4, 128.5, 127.1, 126.3, 56.7,

54.0, 40.0, 33.3, 33.3, 26.1, 25.0, 20.3 ppm; GC-MS for $C_{15}H_{23}N$, m/z = 217 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{15}H_{23}N$, ($[M+H]^+$): 218.1903. Found: 218.1916.



115^f

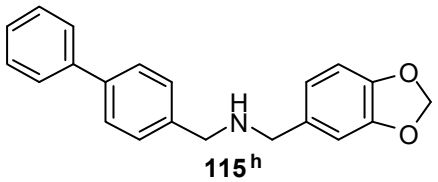
Table 2.3.1, compound 115^f. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-chlorobenzylamine (141 mg, 1.0 mmol) and 4-methoxybenzeneethanamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^f** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 158 mg, 57%. Data for **115^f**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 2H), 7.24–7.19 (m, 2H), 7.15–7.09 (m, 2H), 6.87–6.82 (m, 2H), 3.79 (s, 3H), 3.76 (s, 2H), 2.87–2.82 (m, 2H), 2.80–2.74 (m, 2H), 1.73 (br s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 138.6, 132.5, 131.7, 129.5, 129.3, 128.4, 113.8, 55.1, 53.0, 50.5, 35.2 ppm; GC-MS for $C_{16}H_{18}ClNO$, m/z = 275 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{18}ClNO$, ($[M+H]^+$): 276.1094. Found: 276.1090.



115^g

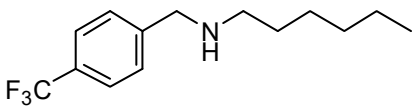
Table 2.3.1, compound 115^g. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-pheylbenzylamine (183 mg, 1.0 mmol) and *n*-hexylamine (141 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^g** was

isolated by a column chromatography on silica gel (*n*-hexanes/ethyl acetate = 100:1 to 10:1). Isolated yield: 179 mg, 66%. Data for **115^{g}**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.61 – 7.54 (m, 4H), 7.46 – 7.37 (m, 4H), 7.36 – 7.31 (m, 1H), 3.83 (s, 2H), 2.66 (t, *J* = 7.3 Hz, 2H), 1.58 – 1.50 (m, 2H), 1.36 – 1.26 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H), ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.0, 139.8, 139.6, 128.7, 128.5, 128.4, 127.1, 127.0, 53.7, 49.6, 31.8, 30.1, 27.0, 22.6, 14.1 ppm; GC-MS for $C_{19}H_{25}N$, m/z = 267.



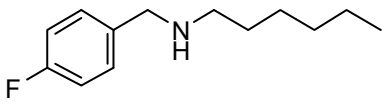
115^{h}

Table 2.3.1, compound 115^{h}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-pheylbenzylamine (183 mg, 1.0 mmol) and 1,3-benzodioxol-5-ylmethylamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{h}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 178 mg, 56%. Data for **115^{h}**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.62–7.55 (m, 4H), 7.47–7.39 (m, 4H), 7.37–7.32 (m, 1H), 6.90–6.88 (m, 1H), 6.82–6.76 (m, 2H), 5.95 (s, 2H), 3.84 (s, 2H), 3.75 (s, 2H), 1.67 (br s, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 147.7, 146.5, 140.9, 139.9, 139.3, 134.2, 128.7, 128.6, 127.1, 127.1, 127.0, 121.2, 108.7, 108.0, 100.9, 52.9, 52.6 ppm; GC-MS for $C_{21}H_{19}NO_2$, m/z = 317 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{21}H_{19}NO_2$ ($[M+H]^+$): 318.1489, Found: 318.1486.



115^{i}

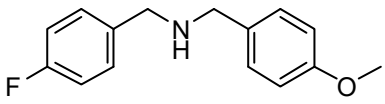
Table 2.3.1, compound 115^{i}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-trifluromethylbenzylamine (175 mg, 1.0 mmol) and *n*-hexylamine (141 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{i}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 142 mg, 55%. Data for **115^{i}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 3.84 (s, 2H), 2.61 (t, J = 7.21 Hz, 2H), 1.58 (br s, 1H), 1.55–1.46 (m, 2H), 1.37–1.22 (m, 6H), 0.91–0.84 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.6, 129.1 (q, J_{CF} = 32.3 Hz), 128.3, 125.3 (q, J_{CF} = 3.8 Hz), 124.2 (q, J_{CF} = 272.0 Hz), 53.5, 49.5, 31.7, 30.0, 27.0, 22.6, 14.0; GC-MS for $C_{14}H_{20}F_3N$, m/z = 259 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{14}H_{20}F_3N$ ($[M+H]^+$): 260.1621, Found: 260.1627.



115^{j}

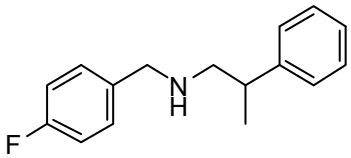
Table 2.3.1, compound 115^{j}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-flurobenzylamine (125 mg, 1.0 mmol) and *n*-hexylamine (141 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{j}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 132 mg, 63%. Data for **115^{j}**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m,

2H), 7.02–6.95 (m, 2H), 3.74 (s, 2H), 2.59 (t, J = 7.3, 2H), 1.53–1.44 (m, 2H), 1.35–1.21 (m, 6H), 0.90–0.84 (br m, 3H, peaks overlapped); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J_{CF} = 244.6 Hz), 136.2 (d, J_{CF} = 3.1 Hz), 129.6 (d, J_{CF} = 7.9 Hz), 115.0 (d, J_{CF} = 21.2 Hz), 53.3, 49.4, 31.7, 30.0, 27.0, 22.6, 14.0 ppm; GC-MS for $C_{13}H_{20}FN$, m/z = 209 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{13}H_{20}FN$ ($[M+H]^+$): 210.1653, Found: 210.1654.



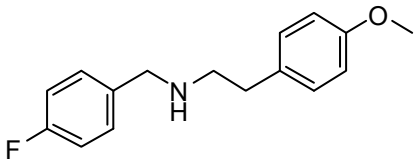
115^{k}

Table 2.3.1, compound 115^{k}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-flurobenzylamine (125 mg, 1.0 mmol) and 4-methoxybenzylamine (192 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{k}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 162 mg, 66%. Data for **115^{k}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.29 (m, 2H), 7.27 (d, J = 8.3 Hz, 2H), 7.06–6.99 (m, 2H), 6.90 (d, J = 8.3 Hz, 2H), 3.81 (s, 3H), 3.76 (s, 2H), 3.74 (s, 2H), 1.78 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J_{CF} = 244.6 Hz), 158.5, 135.9 (d, J_{CF} = 3.1 Hz), 132.1, 129.6 (d, J_{CF} = 7.9 Hz), 129.2, 115.0 (d, J_{CF} = 21.2 Hz), 113.7, 55.1, 52.4, 52.1; GC-MS for $C_{15}H_{16}FNO$, m/z = 245 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[75]



115^{l}

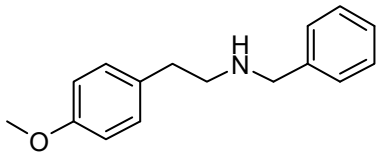
Table 2.3.1, compound 115^{l}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-flurobenzylamine (125 mg, 1.0 mmol) and β-methylphenethylamine (189 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{l}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 141 mg, 58%. Data for **115^{l}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.30 (m, 2H), 7.26–7.19 (m, 5H), 7.03–6.96 (m, 2H), 3.74 (ABq, J = 13.5 Hz, 2H), 2.99 (qt, J = 7.1, 7.0 Hz, 1H), 2.84–2.77 (m, 2H), 1.55 (br s, 1H), 1.28 (d, J = 7.0 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.7 (d, J = 244.2 Hz), 145.1, 135.8 (d, J = 3.1 Hz), 129.4 (d, J = 7.9 Hz), 128.5, 127.1, 126.3, 115.0 (d, J_{CF} = 21.2 Hz), 56.1, 52.9, 39.9, 20.0 ppm; GC-MS for $C_{16}H_{18}FN$, m/z = 243 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{18}FN$ ($[M+H]^+$): 244.1496, Found: 244.1500.



115^{m}

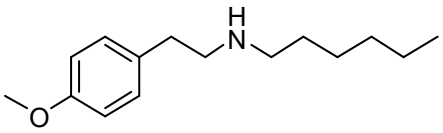
Table 2.3.1, compound 115^{m}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-flurobenzylamine (125 mg, 1.0 mmol) and 4-methoxybenzeneethanamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{m}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc

= 100:1 to 10:1). Isolated yield: 142 mg, 55%. Data for **115^{m}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.21 (m, 2H), 7.15–7.10 (m, 2H), 7.03–6.96 (m, 2H), 6.87–6.82 (m, 2H), 3.79 (s, 3H), 3.76 (s, 2H), 2.88–2.83 (m, 2H), 2.80–2.74 (m, 2H), 1.69 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J_{CF} = 244.6 Hz), 157.9, 135.8 (d, J_{CF} = 3.1 Hz), 131.8, 129.5, 129.5 (d, J_{CF} = 7.9 Hz), 115.0 (d, J_{CF} = 21.2 Hz), 113.8, 55.1, 53.0, 50.6, 35.2 ppm; GC-MS for $C_{16}H_{18}FNO$, m/z = 259 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{18}FNO$ ($[M+H]^+$): 260.1445, Found: 260.1439.



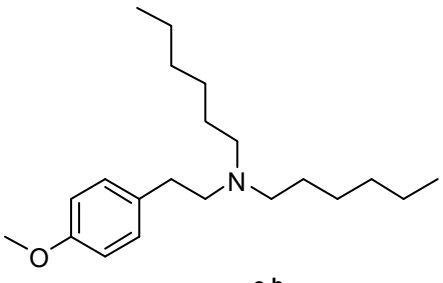
115^{n}

Table 2.3.1, compound 115^{n}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and benzylamine (150 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{n}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 169 mg, 70%. Data for **115^{n}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.23 (m, 5H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.3 Hz, 2H), 3.82 (s, 2H), 3.80 (s, 3H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.80 (t, *J* = 6.9 Hz, 2H), 1.66 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 140.1, 131.9, 129.5, 128.3, 128.0, 126.8, 113.8, 55.1, 53.8, 50.6, 35.3 ppm; GC-MS for $C_{16}H_{19}NO$, m/z = 241 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[76]



115$^{o\text{-}a}$

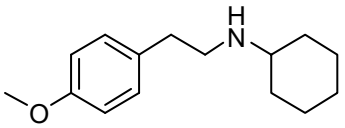
Table 2.3.1, compound 115$^{o\text{-}a}$. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and *n*-hexylamine (141 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115$^{o\text{-}a}$** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 119 mg, 51%. Data for **115$^{o\text{-}a}$**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14–7.10 (m, 2H), 6.86–6.81 (m, 2H), 3.78 (s, 3H), 2.86–2.81 (m, 2H), 2.78–2.72 (m, 2H), 2.62–2.57 (m, 2H), 1.68 (br s, 1H), 1.50–1.41 (m, 2H), 1.33–1.23 (m, 6H), 0.89–0.84 (m, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 132.0, 129.6, 113.8, 55.2, 51.4, 49.9, 35.3, 31.7, 29.9, 27.0, 22.6, 14.0 ppm; GC-MS for $C_{15}H_{25}NO$, m/z = 235 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{15}H_{25}NO$ ($[M+H]^+$): 236.2009. Found 236.2005:



115$^{o\text{-}b}$

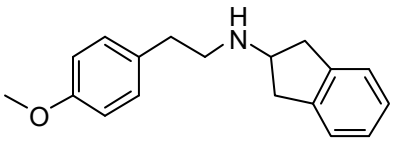
Table 2.3.1, compound 115$^{o\text{-}b}$. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and *n*-hexylamine (141 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115$^{o\text{-}b}$** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1

to 10:1). Isolated yield: 57 mg, 18%. Data for **115$^{o\text{-}b}$**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.3 Hz, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 3.78 (s, 3H), 2.78–2.63 (m, 4H), 2.52 (t, *J* = 7.5 Hz, 4H), 1.54–1.40 (m, 4H), 1.35–1.22 (m, 12H), 0.96–0.82 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.8, 132.5, 129.6, 113.8, 56.1, 55.2, 53.9, 32.2, 31.8, 27.2, 26.6, 22.6, 14.1 ppm; GC-MS for $C_{21}H_{37}NO$, m/z = 319 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{21}H_{37}NO$ ($[M+H]^+$): 320.2948. Found: 320.2943.



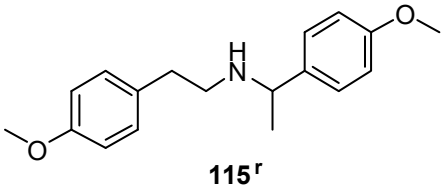
115^{p}

Table 2.3.1, compound 120^{p}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{p}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 187mg, 80%. Data for **115^{p}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13–7.08 (m, 2H), 6.83–6.79 (m, 2H), 3.75 (s, 3H), 2.86–2.81 (m, 2H), 2.74–2.68 (m, 2H), 2.39 (tt, *J* = 10.6, 3.8 Hz, 1H), 1.88–1.78 (m, 2H), 1.74–1.64 (m, 2H), 1.62–1.54 (m, 1H), 1.48 (br s, 1H), 1.29–0.95 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.8, 132.0, 129.4, 113.7, 56.6, 55.0, 48.3, 35.5, 33.4, 26.0, 24.9 ppm; GC-MS for $C_{15}H_{23}NO$, m/z = 233 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{15}H_{23}NO$ ($[M+H]^+$): 234.1852. Found: 234.1854.



115[q]

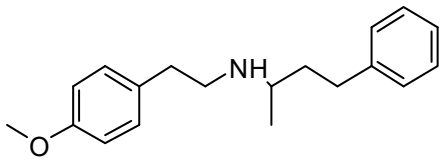
Table 2.3.1, compound 115[q]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and 2-aminoindane (186 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[q]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 144 mg, 54%. Data for **115[q]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.12 (m, 6H), 6.89–6.83 (m, 2H), 3.80 (s, 3H), 3.65 (quintet, J = 7.0 Hz, 1H), 3.17 (dd, J = 7.2 Hz, 2H), 2.96–2.90 (m, 2H), 2.82–2.70 (m, 4H), 1.67 (br s, 1H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.0, 141.6, 131.9, 129.5, 126.3, 124.6, 113.9, 59.5, 55.2, 49.7, 39.9, 35.5 ppm; GC-MS for $C_{18}H_{21}NO$, m/z = 267 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{18}H_{21}NO$ ($[M+H]^+$): 268.1696, Found: 268.1699.



115[r]

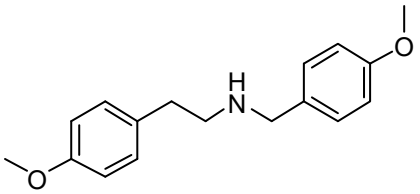
Table 2.3.1, compound 115[r]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and (R)-(+)-1-(4-methoxyphenyl)ethylamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[r]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 186 mg, 65%. Data for **115[r]**: ^{1}H NMR

(400 MHz, $CDCl_3$) δ 7.21–7.15 (m, 2H), 7.10–7.05 (m, 2H), 6.87–6.79 (m, 4H), 3.79 (s, 3H), 3.78 (s, 3H), 3.73 (q, *J* = 6.6 Hz, 1H), 2.79–2.60 (m, 4H), 1.86 (br s, 1H), 1.32 (d, *J* = 6.6, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.3, 157.8, 137.4, 131.9, 129.4, 127.4, 113.7, 113.6, 57.4, 55.0, 48.9, 35.2, 24.1 ppm; GC-MS for $C_{18}H_{23}NO_2$, m/z = 285 (M^+); HRMS (IT-TOF/ESI) Calcd for ($[M+H]^+$): 286.1802, Found: 286.1798.



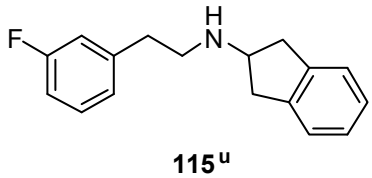
115ˢ

Table 2.3.1, compound 115ˢ. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and (±)-3-phenyl-1-propanamine (189 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115ˢ** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 228 mg, 73%. Data for **115ˢ**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 2H), 7.21–7.11 (m, 5H), 6.88–6.83 (m, 2H), 3.79 (s, 3H), 2.94–2.84 (m, 1H), 2.82–2.70 (m, 3H), 2.70–2.52 (m, 3H), 1.82–1.72 (m, 1H), 1.66–1.56 (m, 1H), 1.54 (br s, 1H), 1.10 (d, *J* = 6.3 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 142.2, 132.0, 129.6, 128.3, 128.2, 125.6, 113.8, 55.2, 52.4, 48.5, 38.5, 35.5, 32.2, 20.2 ppm; GC-MS for $C_{19}H_{25}NO$, m/z = 283 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{19}H_{25}NO$ ($[M+H]^+$): 284.2009, Found: 284.2010.



115^{t}

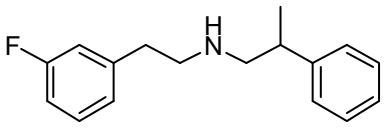
Table 2.3.1, compound 115^{t}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) and 4-methoxybenzylamine (192 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{t}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 149 mg, 55%. Data for **115^{t}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.3 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 6.90–6.82 (m, 4H), 3.80 (s, 3H), 3.79 (s, 3H), 3.75 (s, 2H), 2.87 (t, *J* = 7.1 Hz, 2H), 2.78 (t, *J* = 6.9 Hz, 2H), 1.71 (br s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.5, 157.9, 132.3, 131.9, 129.5, 129.2, 113.7, 113.6, 55.1, 55.1, 53.2, 50.6, 35.2 ppm; GC-MS for $C_{17}H_{21}NO_2$, m/z = 271 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[76]



115^{u}

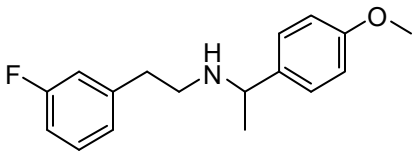
Table 2.3.1, compound 115^{u}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 2-(3-fluorophenyl)ethylamine (139 mg, 1.0 mmol) and 2-aminoindane (186 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{u}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc =

100:1 to 10:1). Isolated yield: 193 mg, 76%. Data for **115[u]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3–7.24 (m, 1H), 7.24–7.12 (m, 4H), 7.06–7.00 (m, 1H), 6.99–6.89 (m, 2H), 3.67 (quintet, J = 6.9 Hz, 1H), 3.18 (dd, J = 15.5, 7.2 Hz, 2H), 3.01–2.92 (m, 2H), 2.89–2.81 (m, 2H), 2.75 (dd, J = 15.5, 6.6 Hz, 2H), 1.63 (br s, 1H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.8 (d, J_{CF} = 245.5 Hz), 142.5 (d, J_{CF} = 7.2 Hz), 141.5, 129.8 (d, J_{CF} = 8.3 Hz), 126.4, 124.6, 124.3 (d, J_{CF} = 2.7 Hz), 115.4 (d, J_{CF} = 20.8 Hz), 113.0 (d, J_{CF} = 21.0 Hz) ppm; GC-MS for $C_{17}H_{18}FN$, m/z = 255 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{17}H_{18}FN$ ($[M+H]^+$): 256.1496, Found: 256.1501.



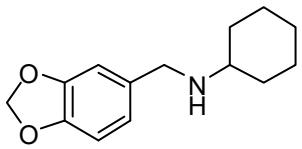
115[v]

Table 2.3.1, compound 120[v]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 2-(3-Fluorophenyl)ethylamine (139 mg, 1.0 mmol) and (R)-(+)-β-Methylphenethylamine (189 mg, 1.4 mmol) was stirred at 130 °C for 16 h. Yield: 60% (Determined by GC-MS, hexamethylbenzene as an internal standard.)



115[w]

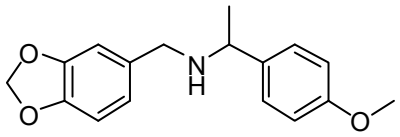
Table 2.3.1, compound 115^{w}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 2-(3-fluorophenyl)ethylamine (139 mg, 1.0 mmol) and (R)-(+)-1-(4-methoxyphenyl)ethylamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **120^{w}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 157 mg, 58%. Data for **115^{w}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.16 (m, 3H), 6.98–6.80 (m, 5H), 3.80 (s, H), 3.73 (q, J = 6.6 Hz, 1H), 2.83–2.63 (m, 4H), 1.60 (br s, 1H), 1.32 (d, J = 6.6 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.8 (d, J_{CF} = 245.4 Hz), 158.5, 142.6 (d, J_{CF} = 7.2 Hz), 137.3, 129.74 (d, J_{CF} = 8.3 Hz), 127.5, 124.3 (d, J_{CF} = 2.7 Hz), 115.4 (d, J_{CF} = 20.9 Hz), 113.7, 112.9 (d, J_{CF} = 21.0 Hz), 57.5, 55.2, 48.5, 36.07 (d, J_{CF} = 1.7 Hz), 24.2 ppm; GC-MS for $C_{17}H_{20}FNO$, m/z = 273 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{17}H_{20}FNO$ ($[M+H]^+$): 274.1602, Found: 274.1604.



115^{x}

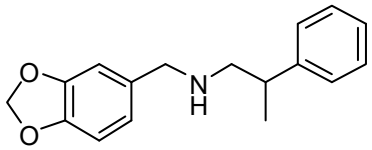
Table 2.3.1, compound 115^{x}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 1-(1,3-benzodioxol-5-yl)methanamine (151 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{x}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 139 mg, 59%. Data for **115^{x}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83–6.81 (m, 1H), 6.75–6.73 (m, 2H), 5.92 (s, 2H), 3.70 (s, 2H),

2.45 (tt, J = 10.4, 3.8 Hz, 1H), 1.95–1.84 (m, 2H), 1.77–1.67 (m, 2H), 1.64–1.54 (m, 1H), 1.30–1.04 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 147.6, 146.3, 134.8, 121.1, 108.6, 108.0, 100.8, 55.9, 50.7, 33.4, 26.1, 24.9 ppm; GC-MS for $C_{14}H_{19}NO_2$, m/z = 233 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[77]



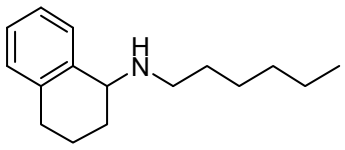
115^{y}

Table 2.3.1, compound 115^{y}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 1-(1,3-benzodioxol-5-yl)methanamine (151 mg, 1.0 mmol) and (R)-(+)-1-(4-methoxyphenyl)ethylamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{y}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 171 mg, 60%. Data for **115^{y}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 2H), 6.93–6.86 (m, 2H), 6.82–6.78 (m, 1H), 6.77–6.67 (m, 2H), 5.93 (s, 2H), 3.82 (s, 3H), 3.76 (q, J = 6.6 Hz, 1H), 3.52 (q, J = 13.2 Hz, 2H), 1.70 (br s, 1H), 1.34 (d, J = 6.6 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.5, 147.6, 146.3, 137.4, 134.5, 127.7, 121.1, 113.8, 108.7, 108.0, 100.8, 56.5, 55.2, 51.3, 24.4 ppm; GC-MS for $C_{17}H_{19}NO_3$, m/z = 285 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{17}H_{19}NO_3$ ($[M+H]^+$): 286.1438, Found: 286.1427.



115^{z}

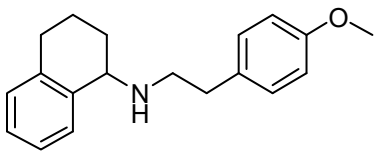
Table 2.3.1, compound 120[z]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 1-(1,3-benzodioxol-5-yl)methanamine (151 mg, 1.0 mmol) and (±)-1-(4-methoxyphenyl)ethylamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[z]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 152 mg, 56%. Data for **115[z]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 2H), 7.24–7.18 (m, 3H), 6.76–6.70 (m, 2H), 6.70–6.65 (m, 1H), 5.93 (s, 2H), 3.66 (dd, *J* = 33.3, 6.9 Hz, 2H), 2.96 (sextet, *J* = 7.1 Hz, 1H), 2.77 (d, *J* = 7.3 Hz, 2H), 1.66 (br s, 1H), 1.26 (d, *J* = 6.9 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 147.6, 146.4, 145.2, 134.1, 128.5, 127.2, 126.4, 121.1, 108.6, 108.0, 100.8, 56.0, 53.5, 39.9, 20.1 ppm; GC-MS for $C_{17}H_{19}NO_2$, m/z = 269 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{17}H_{19}NO_2$ ($[M+H]^+$): 270.1489, Found: 270.1463.



115[aa]

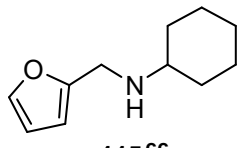
Table 2.3.1, compound 115[aa]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 1,2,3,4-tetrahydro-1-naphthalenamine (147 mg, 1.0 mmol) n-hexylamine (141 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[aa]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 105 mg, 46%. Data for **115[aa]**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.37–7.30 (m, 1H), 7.21–7.05 (m, 3H), 3.77 (t, *J* = 4.8 Hz, 1H), 2.87–2.61 (m, 1H), 2.03–1.91 (m, 1H), 1.91–1.81 (m, 2H), 1.78–1.68 (m, 1H), 1.56–1.46 (m, 2H), 1.41–1.19 (m, 7H), 0.94–0.85 (m, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 139.3, 137.3,

129.0, 128.7, 126.5, 125.6, 55.4, 47.3, 31.8, 30.4, 29.3, 28.2, 27.1, 22.6, 18.9, 14.1 ppm; GC-MS for $C_{16}H_{25}N$, m/z = 231 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{25}N$ ($[M+H]^+$): 232.2060, Found: 232.2053.



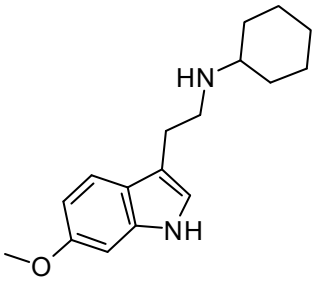
115^{bb}

Table 2.3.1, compound 115^{bb}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 1,2,3,4-tetrahydro-1-naphthalenamine (147 mg, 1.0 mmol) and 4-methoxybenzeneethanamine (211 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115^{bb}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 177 mg, 63%. Data for **115^{bb}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.23 (m, 1H), 7.21–7.13 (m, 4H), 7.12–7.07 (m, 1H), 6.90–6.85 (m, 2H), 3.82 (s, 3H), 3.81 (t, *J* = 4.7 Hz, 1H), 3.05–2.89 (m, 2H), 2.87–2.69 (m, 4H), 2.01–1.86 (m, 3H), 1.80–1.70 (m, 1H), 1.63 (br s, 1H) ppm; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 139.0, 137.3, 132.1, 129.6, 129.0, 128.5, 126.5, 125.6, 113.7, 55.3, 55.2, 48.6, 35.7, 29.3, 28.2, 19.0 ppm; GC-MS for $C_{19}H_{23}NO$, m/z = 281 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{19}H_{23}NO$ ($[M+H]^+$): 282.1852, Found: 282.1843.



115^{cc}

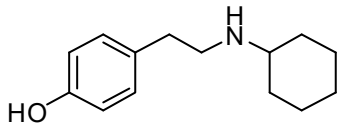
Table 2.3.1, compound 115[cc]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 2-(2-aminoethyl)furan (111 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[cc]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 124 mg, 69%. Data for **115[cc]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.28 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.14–6.12 (m, 1H), 3.78 (s, 2H), 2.42 (tt, *J* = 10.4, 3.8, Hz, 1H), 1.90–1.81 (m, 2H), 1.74–1.66 (m, 2H), 1.63–1.46 (m, 2H), 1.28–1.02 (m, 5H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.2, 141.5, 110.0, 106.4, 55.7, 43.2, 33.2, 26.0, 24.9 ppm; GC-MS for $C_{11}H_{17}NO$, m/z = 179 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[78]



115[dd]

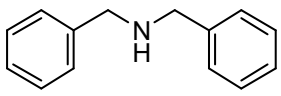
Table 2.3.1, compound 120[dd]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), 5-methoxytryptamine (190 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[dd]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 182 mg, 67%. Data for **115[dd]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.26–7.20 (m, 1H), 7.08–7.05 (m, 1H), 7.02–6.99 (m, 1H), 6.85 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.86 (s, 3H), 3.07–2.90 (m, 4H), 2.45 (tt, *J* = 10.5, 3.7 Hz, 1H), 1.91–1.78

(m, 3H), 1.75–1.65 (m, 2H), 1.64–1.55 (m, 1H), 1.29–0.99 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 153.8, 131.5, 127.8, 122.8, 113.6, 112.1, 111.8, 100.6, 56.8, 55.9, 46.8, 33.5, 26.1, 25.9, 25.0 ppm; GC-MS for $C_{17}H_{24}N_2O$, m/z = 272 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{17}H_{24}N_2O$ ($[M+H]^+$): 273.1961, Found: 273.1960.



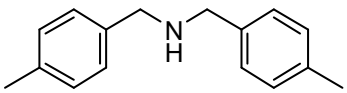
115[ff]

Table 2.3.1, compound 115[ff]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %), tyramine (136 mg, 1.0 mmol) and cyclohexylamine (139 mg, 1.4 mmol) was stirred at 130 °C for 16 h. The product **115[ff]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 124 mg, 69%. Data for **115[ff]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, J = 8.3 Hz, 2H), 6.72 (d, J = 8.3 Hz, 2H), 4.71 (br s, 1H), 2.93 (t, J = 6.9 Hz, 2H), 2.75 (t, J = 6.9 Hz, 2H), 2.47 (tt, J = 10.6, 3.6 Hz, 1H), 1.92–1.85 (m, 2H), 1.75–1.66 (m, 2H), 1.64–1.55 (m, 1H), 1.31–1.03 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 155.5, 130.0, 129.7, 115.9, 56.9, 47.6, 34.7, 32.9, 25.9, 25.0 ppm; GC-MS for $C_{14}H_{21}NO$, m/z = 219 (M^+); Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65. Found: C, 76.78; H, 9.35; HRMS (IT-TOF/ESI) Calcd for $C_{14}H_{21}NO$ ($[M+H]^+$): 220.1696, Found: 220.1698.



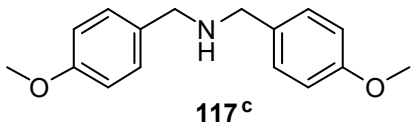
117[a]

Table 2.3.2, compound 117[a]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and benzylamine (107 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117[a]** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 88 mg, 89%. Data for **117[a]**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.42–7.24 (m, 10H), 3.84 (s, 4H), 2.08 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 140.0, 128.4, 128.1, 126.9, 53.0 ppm; GC-MS for $C_{14}H_{15}N$, m/z = 197 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[79]



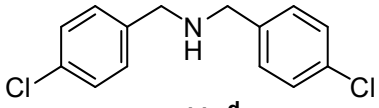
117[b]

Table 2.3.2, compound 117[b]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 4-methylbenzylamine (121 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117[b]** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 100:1 to 10:1). Isolated yield: 106 mg, 94%. Data for **117[b]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 7.9 Hz, 4H), 7.18 (d, J = 7.9 Hz, 4H), 3.80 (s, 4H), 2.38 (s, 6H), 1.70 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 137.2, 136.4, 129.0, 128.1, 52.7, 21.1 ppm; GC-MS for $C_{16}H_{19}N$, m/z = 225 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[79,80]



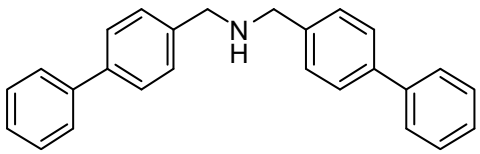
117 c

Table 2.3.2, compound 117c. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol **116** (16 mg, 10 mol %) and 4-methoxylbenzylamine (137 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117c** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 111 mg, 86%. Data for **117c** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 4H), 6.91–6.86 (m, 4H), 3.81 (s, 6H), 3.74 (s, 4H), 1.76 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.5, 132.4, 129.2, 113.6, 55.1, 52.3 ppm; GC-MS for $C_{16}H_{19}NO_2$, m/z = 257 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[79,80]



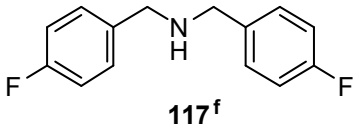
117 d

Table 2.3.2, compound 117d. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 4-chlorobenzylamine (141 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117d** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 122 mg, 92%. Data for **117d** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.28 (m, 4H), 3.76 (s, 4H), 1.64 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 138.5, 132.6, 129.4, 128.5, 52.2 ppm; GC-MS for $C_{14}H_{13}Cl_2N$, m/z = 265 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[80,81]



117[e]

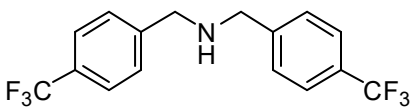
Table 2.3.2, compound 117[e]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 4-phenylbenzylamine (183 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117[e]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 148 mg, 85%. Data for **117[e]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 8.4 Hz, 8H), 7.49–7.42 (m, 8H), 7.34 (t, J = 7.6 Hz, 2H), 3.90 (s, 4H), 1.65 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 140.9, 139.9, 139.4, 128.7, 128.6, 127.1, 127.0, 52.8 ppm (one carbon signal overlapped); GC-MS for $C_{26}H_{23}N$, m/z = 349 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[82]



117[f]

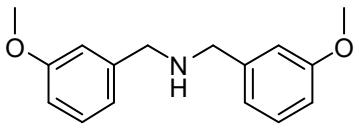
Table 2.3.2, compound 117[f]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 4-phenylbenzylamine (125 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117[f]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 106 mg, 91%. Data for **117[f]** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 4H), 7.07–6.99 (m, 4H), 3.78 (s, 4H), 1.67 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.8 (d, J_{CF} = 244.5 Hz), 135.8 (d, J_{CF} = 3.1 Hz), 129.6 (d, J_{CF} = 8.0 Hz), 115.1 (d, J_{CF} = 21.3 Hz), 52.3 ppm;

GC-MS for $C_{14}H_{13}F_2N$, m/z = 233 (M^+). ^1H and ^{13}C NMR spectral data were in good agreement with the literature values.[81]



117^g

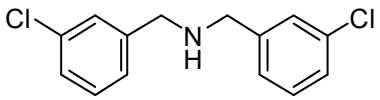
Table 2.3.2, compound 117^g. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 4-(trifluoromethyl)benzenemethanamine (175 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^g** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 140 mg, 84%. Data for **117^g** ^1H NMR (400 MHz, $CDCl_3$) δ 7.64–7.57 (m, 4H), 7.51–7.46 (m, 4H), 3.88 (s, 4H), 1.75 (br s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 144.1, 129.4 (q, J_{CF} = 32.4 Hz), 128.3, 125.3 (q, J_{CF} = 3.8 Hz), 124.2 (q, J_{CF} = 271.8 Hz), 52.6 ppm; GC-MS for $C_{16}H_{13}F_6N$, m/z = 333 (M^+). ^1H and ^{13}C NMR spectral data were in good agreement with the literature values.[81,83]



117^h

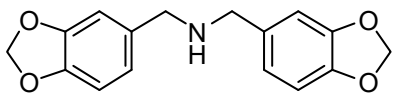
Table 2.3.2, compound 117^h. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3-methoxylbenzylamine (137 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^h** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 108 mg, 84%. Data for **117^h** ^1H NMR (400 MHz, $CDCl_3$) δ 7.29–7.22 (m, 2H), 6.97-6.91 (m, 4H),

6.84–6.78 (m, 2H), 3.82 (s, 6H), 3.80 (s, 4H), 1.71 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.6, 141.9, 129.3, 120.4, 113.5, 112.4, 55.1, 53.0 ppm; GC-MS for $C_{16}H_{19}NO_2$, m/z = 257 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[79]



117^{i}

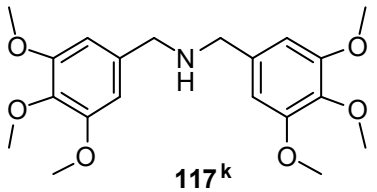
Table 2.3.2, compound 4i. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3-chlorobenzylamine (141 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^{i}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 118 mg, 89%. Data for **117^{i}** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.34 (m, 2H), 7.29–7.19 (m, 6H), 3.77 (s, 4H), 1.65 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.1, 134.2, 129.6, 128.1, 127.2, 126.2, 52.5 ppm; GC-MS for $C_{14}H_{13}Cl_2N$, m/z = 265 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[84]



117^{j}

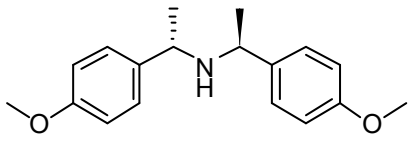
Table 2.3.2, compound 117^{j}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 1-(1,3-benzodioxol-5-yl)methanamine (151 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^{j}** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 110 mg, 77%. Data for **117^{j}** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 2H), 6.77–6.75 (m, 4H), 5.94

(s, 4H), 3.69 (s, 4H), 1.59 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 147.7, 146.5, 134.3, 121.2, 108.7, 108.0, 100.9, 52.7 ppm; GC-MS for $C_{16}H_{15}NO_4$, m/z = 285 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{15}NO_4$ ($[M+H]^+$): 286.1074, Found: 286.1070.



117k

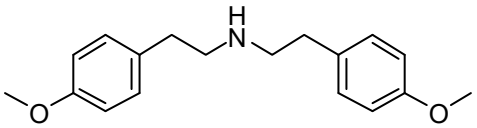
Table 2.3.2, compound 117k. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3,4,5-trimethoxylbenzylamine (197 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117k** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 115 mg, 61%. Data for **117k** ^{1}H NMR (400 MHz, $CDCl_3$) 6.56 (s, 4H), 3.84 (s, 12H), 3.81 (s, 6H), 3.74 (s, 4H), 1.80 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 153.1, 136.6, 135.8, 104.7, 60.7, 55.9, 53.3 ppm; GC-MS for $C_{20}H_{27}NO_6$, m/z = 377 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{15}NO_4$ ($[M+H]^+$): 378.1911, Found: 378.1892.



117l

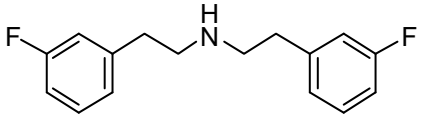
Table 2.3.2, compound 4l. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and (R)-(+)-1-(4-methoxyphenyl)ethylamine (151 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117l** was isolated by a column chromatography on silica gel (*n*-hexanes/EtOAc = 100:1 to 10:1). Isolated yield: 107 mg,

75%, 7:1 mixture of diastereomers. Data for **117l** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.6 Hz, 4H), 6.89–6.84 (m, 4H), 3.82 (s, 6H, 3.45 (q, *J* = 6.7 Hz, 2H), 1.54 (br s, 1H), 1.25 (d, *J* = 1.2 Hz, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.4, 137.7, 127.6, 113.7, 55.2, 54.2, 24.9 ppm; GC-MS for $C_{18}H_{23}NO_2$, m/z = 285 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[85]



117m

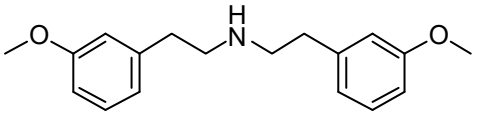
Table 2.3.2, compound 117m. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 4-methoxybenzeneethanamine (151 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117m** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 127 mg, 89%. Data for **117m** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10–7.05 (m, 4H), 6.84–6.79 (m, 4H), 3.79 (s, 6H), 2.88–2.82 (m, 4H), 2.76–2.70 (m, 4H), 1.56 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 157.9, 131.9, 129.5, 113.8, 55.2, 51.2, 35.3 ppm; GC-MS for $C_{18}H_{23}NO_2$, m/z = 285 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{18}H_{23}NO_2$ ($[M+H]^+$): 286.1802, Found: 286.1800.



117n

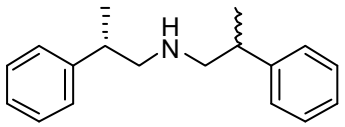
Table 2.3.2, compound 117n. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3-fluorobenzeneethanamine (139 mg, 1.0

mmol) was stirred at 130 °C for 16 h. The product **117ⁿ** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 114 mg, 87%. Data for **117ⁿ** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.18 (m, 2H), 6.98–6.83 (m, 6H), 2.93–2.86 (m, 4H), 2.82–2.76 (m, 4H), 1.68 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.9 (d, J_{CF} = 245.7 Hz), 142.3 (d, J_{CF} = 7.1 Hz), 129.9 (d, J_{CF} = 8.3 Hz), 124.3 (d, J_{CF} = 2.8 Hz), 115.4 (d, J_{CF} = 20.9 Hz), 113.1 (d, J_{CF} = 21.0 Hz), 50.6, 35.9 (d, J_{CF} = 1.4 Hz) ppm; GC-MS for $C_{16}H_{17}F_2N$, m/z = 261 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{15}NO_4$ ($[M+H]^+$): 262.1402, Found: 262.1389.



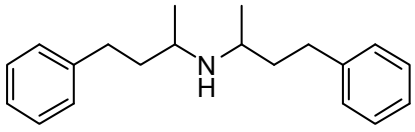
117ᵒ

Table 2.3.2, compound 117ᵒ. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3-methoxybenzeneethanamine (139 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117ᵒ** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 100:1 to 10:1). Isolated yield: 128 mg, 90%. Data for **117ᵒ** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.16 (m, 2H), 6.80–6.71 (m, 6H), 3.79 (s, 6H), 2.91 (t, J = 7.2 Hz, 4H), 2.79 (t, J = 7.2 Hz, 4H), 1.91 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 159.6, 141.4, 129.4, 121.0, 114.3, 111.5, 55.1, 50.9, 36.2 ppm; GC-MS for $C_{18}H_{23}NO_2$, m/z = 285 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{18}H_{23}NO_2$ ($[M+H]^+$): 286.1802, Found: 286.1798.



117ᵖ

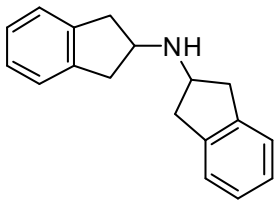
Table 2.3.2, compound 117ᵖ. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and (R)-(+)-β-methylphenethylamine (135 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117ᵖ** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 100:1 to 10:1). Isolated yield: 118 mg, 93%, 2:7 mixture of diastereomers. Data for **117ᵖ** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.21 (m, 4H), 7.19–7.14 (m, 2H), 7.13–7.07 (m, 4H), 2.94–2.84 (m, 2H), 2.84–2.66 (m, 4H), 1.49 (br s, 1H), 1.21–1.17 (d, J = 8.9 Hz, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 145.1, 128.5, 127.0, 126.2, 56.7, 39.5, 19.8 ppm; GC-MS for $C_{18}H_{23}N$, m/z = 253 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[86]



117ᵠ

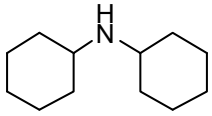
Table 2.3.2, compound 117ᵠ. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and α-methylbenzenepropanamine (149 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117ᵠ** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 126 mg, 90%, 1:1 mixture of diastereomers. Data for **117ᵖ** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–6.97 (m, 10H), 2.85–2.74 (m, 2H), 2.73–2.58 (m, 4H), 1.84–1.70 (m, 2H), 1.69–1.57 (m, 1H), 1.15–1.04 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.4, 142.4, 128.3,

128.3,128.2, 125.6, 49.4, 49.2, 39.3, 38.8, 32.4, 32.2, 21.1, 20.7 ppm; GC-MS for $C_{20}H_{27}N$, m/z = 281 (M^+). ^1H and ^{13}C NMR spectral data were in good agreement with the literature values.[87]



117^r

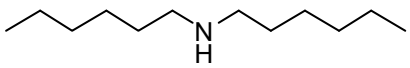
Table 2.3.2, compound 117^r. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 2-indanamine (133 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^r** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 91 mg, 73%. Data for **117^r** ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 4H), 7.24–7.18 (m, 4H), 3.83 (quintet, J = 7.2 Hz, 2H), 3.26 (dd, J = 15.4, 7.2 Hz, 4H), 2.85 (dd, J = 15.4, 7.2 Hz, 4H), 1.77 (br s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 141.5, 126.3, 124.5, 58.1, 40.2 ppm; GC-MS for $C_{18}H_{19}N$, m/z = 249 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{18}H_{19}N$ ($[M+H]^+$): 250.1590, Found: 250.1598.



117^s

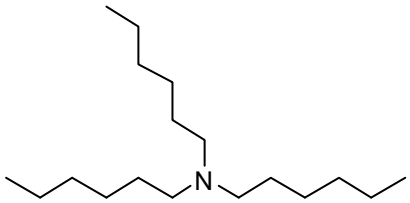
Table 2.3.2, compound 117^s. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and cyclohexylamine (99 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^s** was isolated by a column chromatography on

silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 86 mg, 95%. Data for **117^{s}** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (tt, *J* = 10.6, 3.7 Hz, 2H), 1.82–1.74 (m, 4H), 1.68–1.59 (m, 4H), 1.57–1.49 (m, 2H), 1.24–0.88 (m, 10H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 52.8, 34.1, 26.0, 25.1 ppm; GC-MS for $C_{12}H_{23}N$, m/z = 181 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[88, 89]



117^{t}

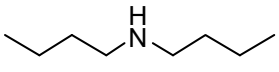
Table 2.3.2, compound 117^{t}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and *n*-hexylamine (101 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^{t}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 40 mg, 43%. Data for **117^{t}** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (t, *J* = 7.4, 4H), 2.24 (br s, 1H), 1.54–1.44 (m, 4H), 1.35–1.19 (m, 12H), 0.90–0.82 (m, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 50.0, 31.7, 29.8, 27.1, 22.6, 14.0 ppm; GC-MS for $C_{12}H_{27}N$, m/z = 185 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[89, 90]



117$^{t'}$

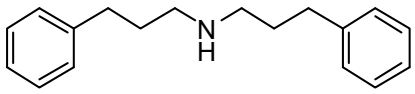
Table 2.3.2, compound 117$^{t'}$. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and *n*-hexylamine (101 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117$^{t'}$** was isolated by a column chromatography

on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 48 mg, 54%. Data for **117$^{t'}$** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45–2.34 (m, 6H), 1.47–1.36 (m, 6H), 1.35–1.19 (m, 18H), 0.92–0.83 (m, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 54.1, 31.8, 27.3, 26.8, 22.7, 14.1 ppm; GC-MS for $C_{18}H_{39}N$, m/z = 269(M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[89]



117^u

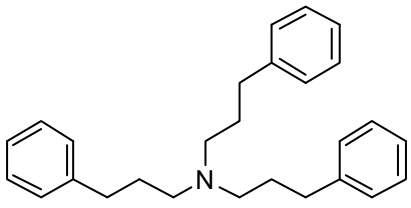
Table 2.3.2, compound 117^u. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and *n*-butylamine (73 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^u** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 30 mg, 45%. Data for **117^u** ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (t, *J* = 7.2 Hz, 4H), 1.37–1.25 (m, 4H), 1.24–1.11 (m, 4H), 0.86 (br s, 1H), 0.75 (t, *J* = 7.3 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 49.6, 32.1, 20.2, 13.7 ppm; GC-MS for $C_8H_{19}N$, m/z = 129 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[80]



117^v

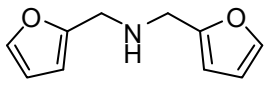
Table 2.3.2, compound 117^v. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3-phenyl-1-propanamine (135 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^v** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 48 mg,

42%. Data for **117**^{v} ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.25 (m, 4H), 7.32–7.15 (m, 6H), 2.65 (t, *J* = 7.4 Hz, 8H), 1.84 (quintet, *J* = 7.5 Hz, 4H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.0, 128.3, 128.3, 125.8, 49.4, 33.6, 31.5 ppm; GC-MS for $C_{18}H_{23}N$, m/z = 253 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[91]



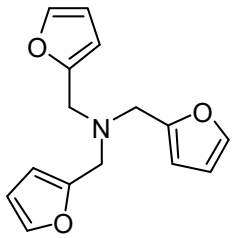
117$^{v'}$

Table 2.3.2, compound 117$^{v'}$. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 3-phenyl-1-propanamine (135 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117**$^{v'}$ was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 66 mg, 53%. Data for **117**$^{v'}$ ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.26 (m, 6H), 7.23–7.15 (m, 9H), 2.62 (t, *J* = 7.8 Hz, 6H), 2.50 (t, *J* = 7.5 Hz, 6H), 1.77 (t, *J* = 7.6 Hz, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.1, 128.3, 128.3, 125.7, 53.3, 33.6, 28.4 ppm; GC-MS for $C_{28}H_{33}N$, m/z = 371 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[87]



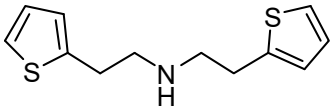
117^{w}

Table 2.3.2, compound 117^{w}. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and Furfurylamine (97 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117^{w}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 71 mg, 80%. Data for **117^{w}** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.31 (m, 2H), 6.34–6.27 (m, 2H), 6.22–6.13 (m, 2H), 3.78 (s, 4H), 1.89 (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 153.3, 141.9, 110.1, 107.2, 44.9 ppm; GC-MS for $C_{10}H_{11}NO_2$, m/z = 177 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[92]



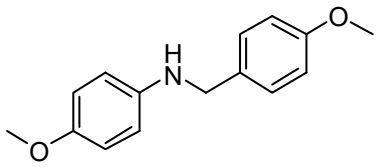
117$^{w'}$

Table 2.3.2, compound 117$^{w'}$. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and Furfurylamine (97 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117$^{w'}$** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 100:1 to 10:1). Isolated yield: 17 mg, 19%. Data for **117$^{w'}$** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 1.8 Hz, 3H), 6.33 (dd, J = 3.1, 1.8 Hz, 3H), 6.26 (d, J = 3.1 Hz, 3H), 3.67 (s, 6H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 151.9, 142.2, 110.0, 109.0, 49.1 ppm; GC-MS for $C_{15}H_{15}NO_3$, m/z = 257 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{15}NO_4$ ($[M+H]^+$): 258.1125, Found: 258.1116.



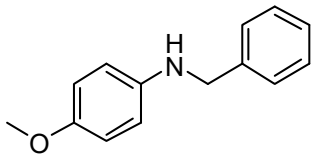
117[x]

Table 2.3.2, compound 117[x]. A chlorobenzene (2.0 mL) solution of complex **112** (13 mg, 0.75 mol %), **116** (16 mg, 10 mol %) and 2-thiopheneethanamine (127 mg, 1.0 mmol) was stirred at 130 °C for 16 h. The product **117[x]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 10:1). Isolated yield: 108 mg, 89%. Data for **117[x]** ^{1}H NMR (400 MHz, $CDCl_3$) δ (m, 2H), (m, 2H), (m, 2H), (s, 4H), (br s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 142.2, 126.8, 125.0, 123.5, 50.7, 30.2 ppm; GC-MS for $C_{10}H_{11}NO_2$, m/z = 237 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{15}NO_4$ ($[M+H]^+$): 238.0719, Found: 238.0716.



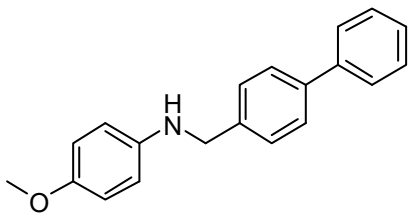
119[a]

Table 2.3.3, compound 119[a]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 4-methoxybenzylamine (96 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[a]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 97 mg, 80%. Data for **119[a]** ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 6.91–6.86 (m, 2H), 6.81–6.76 (m, 2H), 6.66–6.60 (m, 2H), 4.22 (s, 2H), 3.81 (s, 3H), 3.75 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.8, 152.2, 142.2, 131.4, 128.9, 114.8, 114.3, 113.9, 55.8, 55.2, 48.8 ppm; GC-MS for $C_{15}H_{17}NO_2$ m/z = 243 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[75, 93]



119[b]

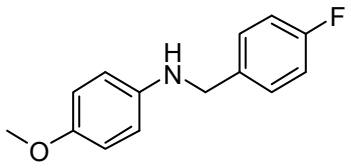
Table 2.3.3, compound 119[b]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and benzylamine (75 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[b]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 61 mg, 57%. Data for **119[b]** ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.46–7.29 (m, 5H), 6.87–6.81 (m, 2H), 6.69–6.63 (m, 2H), 4.33 (s, 2H), 3.79 (s, 3H), ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 152.1, 142.2, 139.5, 128.5, 127.5, 127.1, 114.8, 114.1, 55.7, 49.1 ppm; GC-MS for $C_{14}H_{15}NO$, m/z = 213 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[94,95]



119[c]

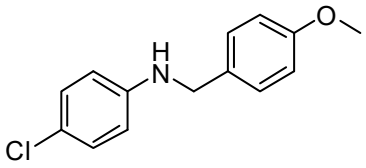
Table 2.3.3, compound 119[c]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 4-phenylbenzylamine (128 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[c]** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 150:1 to 40:1). Isolated yield: 101 mg, 70%. Data for **119[c]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.55 (m, 4H), 7.47–7.42 (m, 4H), 7.35 (tt, *J* = 7.3, 1.3, Hz, 1H), 6.82–6.77 (m, 2H), 6.69–

6.65 (m, 2H), 4.34 (s, 2H), 3.75 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 152.5, 141.7, 140.8, 140.2, 138.3, 128.7, 128.1, 127.3, 127.2, 127.0, 114.9, 114.6, 55.8, 49.2 ppm; GC-MS for $C_{20}H_{19}NO$ m/z = 289 (M^+). ^1H and ^{13}C NMR spectral data were in good agreement with the literature values.[96]



119[d]

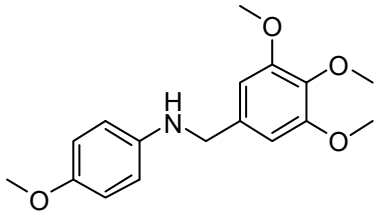
Table 2.3.3, compound 119[d]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 4-fluorobenzylamine (88 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[d]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 47 mg, 41%. Data for **119[d]**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.30 (m, 2H), 7.07–6.99 (m, 2H), 6.83–6.76 (m, 2H), 6.66–6.59 (m, 2H), 4.26 (s, 2H), 4.09 (br s, 1H), 3.75 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0 (d, J_{CF} = 245.1 Hz), 152.4, 141.7, 135.0 (d, J_{CF} = 3.1 Hz), 129.1 (d, J_{CF} = 8.0 Hz), 115.3 (d, J_{CF} = 21.4 Hz), 114.8, 114.4, 55.7, 48.6 ppm; GC-MS for $C_{14}H_{14}FNO$ m/z = 231 (M^+). ^1H and ^{13}C NMR spectral data were in good agreement with the literature values.[97, 98]



119[e]

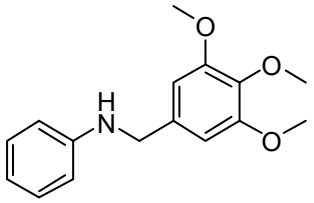
Table 2.3.3, compound 119[e]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-chloroaniline (64 mg, 0.5 mmol) and 4-

methoxybenzylamine (96 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{e}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 73 mg, 59%. Data for **119^{e}**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.30–7.25 (m, 2H), 7.14–7.09 (m, 2H), 6.92–6.87 (m, 2H), 6.59–6.53 (m, 2H), 4.23 (s, 2H), 4.15 (br s, 1H), 3.81 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.9, 146.5, 130.7, 129.0, 128.7, 122.1, 114.0, 114.0, 55.3, 47.9 ppm; GC-MS for $C_{14}H_{14}ClNO$, m/z = 247 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[99]



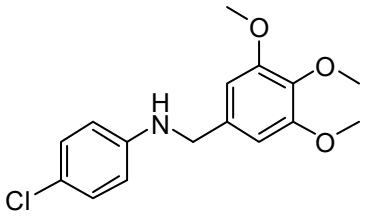
119^{f}

Table 2.3.3, compound 119^{f}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 3,4,5-trimethoxybenzylamine (138 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{f}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 138 mg, 91%. Data for **119^{f}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81–6.76 (m, 2H), 6.65–6.60 (m, 4H), 4.21 (s, 2H), 3.84 (s, 9H), 3.74 (s, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.3, 152.3, 142.1, 136.9, 135.3, 114.8, 114.3, 104.3, 60.8, 56.0, 55.7, 49.7 ppm; GC-MS for $C_{17}H_{21}NO_4$, m/z = 303 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[X-ray,100-102]



119[g]

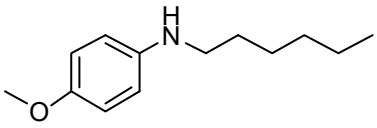
Table 2.3.3, compound 119[g]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), aniline (47 mg, 0.5 mmol) and 3,4,5-trimethoxybenzylamine (138 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[g]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 97 mg, 71%. Data for **119[g]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.17 (m, 2H), 6.75 (tt, *J* = 7.3, 1.1 Hz, 1H), 6.69–6.65 (m, 2H), 6.63 (s, 2H), 4.27 (s, 2H), 4.13 (br s, 1H), 3.86 (s, 3H), 3.85 (s, 6H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.3, 148.0, 136.8, 135.1, 129.1, 117.6, 112.8, 104.2, 60.7, 55.9, 48.7 ppm; GC-MS for $C_{16}H_{19}NO_3$, m/z = 273 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[103, 104]



119[h]

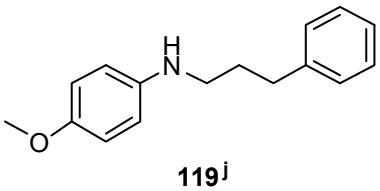
Table 2.3.3, compound 119[h]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-chloroaniline (64 mg, 0.5 mmol) and 3,4,5-trimethoxybenzylamine (138 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[h]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 111 mg, 72%. Data for **119[h]**: ^{1}HNMR (400 MHz, $CDCl_3$) δ 7.14–

7.10 (m, 2H), 6.58 (s, 2H), 6.58–6.54 (m, 2H), 4.23 (s, 2H), 3.84 (s, 3H), 3.84 (s, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 153.4, 146.4, 137.0, 134.5, 129.0, 122.3, 114.0, 104.1, 60.8, 56.0, 48.8 ppm; GC-MS for $C_{16}H_{18}ClNO_3$, m/z = 307 (M^+). Anal. Calcd for $C_{16}H_{18}ClNO_3$: C, 62.44; H, 5.90. Found: C, 62.88; H, 6.05.



119^{i}

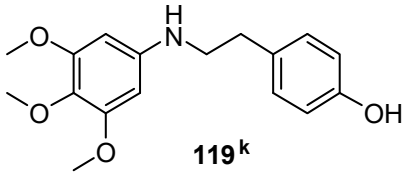
Table 2.3.3, compound 119^{i}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 1-hexanamine (40 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{i}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 65 mg, 63%. Data for **119^{i}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82–6.77 (m, 2H), 6.63–6.58 (m, 2H), 3.75 (s, 3H), 3.39 (br s, 1H), 3.06 (t, *J* = 7.2 Hz, 2H), 1.61 (quintet, *J* = 7.4 Hz, 2H), 1.44–1.26 (m, 6H), 0.91 (t, *J* = 6.9 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 152.1, 142.5, 114.8, 114.2, 55.8, 45.2, 31.6, 29.5, 26.8, 22.6, 14.0 ppm; GC-MS for $C_{13}H_{21}NO$, m/z = 207 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[92]



119^{j}

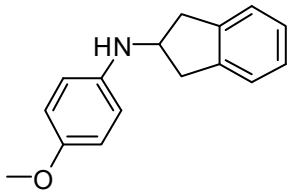
Table 2.3.3, compound 119^{j}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 3-phenyl-

1-propanamine (95 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{j}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 54 mg, 45%. Data for **119^{j}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.29 (m, 2H), 7.25–7.18 (m, 3H), 6.80 (d, *J* = 8.9 Hz, 2H), 6.60 (d, *J* = 8.9 Hz, 2H), 3.76 (s, 3H), 3.13 (t, *J* = 7.1 Hz, 2H), 2.75 (t, *J* = 7.6 Hz, 2H), 1.96 (quintet, *J* = 7.4 Hz, 2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.2, 142.2, 141.7, 128.4, 128.4, 125.9, 114.8, 114.3, 55.8, 44.6, 33.4, 31.0 ppm; GC-MS for $C_{16}H_{19}NO$, m/z = 241 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[104, 105]



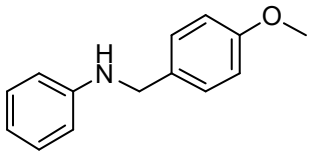
119^{k}

Table 2.3.3, compound 119^{k}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 3,4,5-trimethoxyaniline (62 mg, 0.5 mmol) and 2-(4-hydroxyphenyl)ethanamine (96 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{k}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 77 mg, 51%. Data for **119^{k}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09–7.05 (m, 2H), 6.81–6.77 (m, 2H), 5.90 (s, 2H), 3.81 (s, 6H), 3.77 (s, 3H), 3.33 (t, *J* = 7.1 Hz, 2H), 2.86 (t, *J* = 7.1 Hz, 2H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 154.4, 153.9, 144.1, 130.7, 130.5, 129.8, 115.5, 91.1, 61.1, 55.9, 46.2, 34.4 ppm; GC-MS for $C_{17}H_{21}NO_4$, m/z = 303 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{17}H_{21}NO_4$ ($[M+H]^+$): 304.1543, Found: 304.1507.



119^{l}

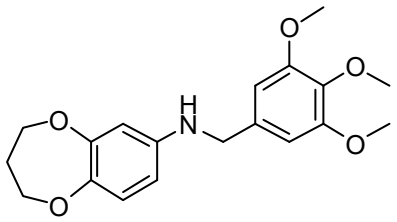
Table 2.3.3, compound 119^{l}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 3,4,5-trimethoxyaniline (62 mg, 0.5 mmol) and 2-aminoindan (93 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{l}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 88 mg, 74%. Data for **119^{l}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.17 (m, 4H), 6.86–6.80 (m, 2H), 6.67–6.62 (m, 2H), 4.33 (tt, *J* = 6.8, 4.4 Hz,1H), 3.79 (s, 3H), 3.37 (dd, *J* = 16.0, 6.8 Hz, 2H), 2.90 (dd, *J* = 16.0, 4.4 Hz, 2H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 152.2, 141.4, 141.4, 126.5, 124.9, 114.9, 114.9, 55.7, 54.9, 40.1 ppm; GC-MS for $C_{16}H_{17}NO$, m/z = 239 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{17}NO$ ($[M+H]^+$): 240.1383, Found: 240.1377.



119^{m}

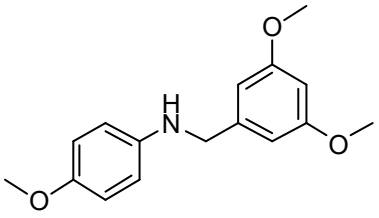
Table 2.3.3, compound 119^{m}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), aniline (47 mg, 0.5 mmol) and 4-methoxybenzylamine (96 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{m}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 76 mg, 71%. Data for **119^{m}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.6 Hz, 2H), 7.22–7.16 (m, 2H), 6.88 (dd, *J* = 8.6 Hz, 2H), 6.77–6.72 (m, 1H),

6.70–6.65 (m, 2H), 4.26 (s, 2H), 3.80 (s, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 158.9, 129.2, 129.0, 128.9, 118.0, 118.0, 114.0, 113.3, 55.3, 48.1 ppm; GC-MS for $C_{14}H_{15}NO$, m/z = 213 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[106,107]



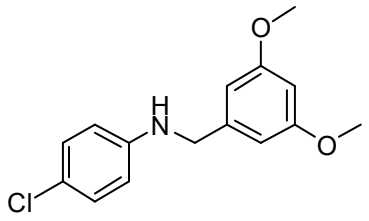
119^{n}

Table 2.3.3, compound 119^{n}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 3,4-dihydro-2H-1,5-benzodioxepin-7-amine (83 mg, 0.5 mmol) and 3,4,5-trimethoxybenzylamine (138 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{n}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 129 mg, 75%. Data for **119^{n}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (d, *J* = 8.6 Hz, 1H), 6.59 (s, 2H), 6.38–6.34 (m, 1H), 6.31–6.26 (m, 1H), 4.19 (s, 2H), 4.15 (t, *J* = 5.4 Hz, 2H), 4.09 (t, *J* = 5.5 Hz, 2H), 3.84 (s, 6H), 3.83 (s, 3H), 2.14 (quintet, *J* = 5.5 Hz, 2H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 153.3, 152.1, 143.9, 143.6, 137.0, 134.4, 122.2, 108.7, 106.5, 104.5, 70.9, 70.8, 60.8, 56.1, 49.8, 32.4 ppm; GC-MS for $C_{19}H_{23}NO_5$, m/z = 345 (M^+); Anal. Calcd for $C_{19}H_{23}NO_5$: C, 66.07; H, 6.71. Found: C, 66.57; H, 6.73.



119°

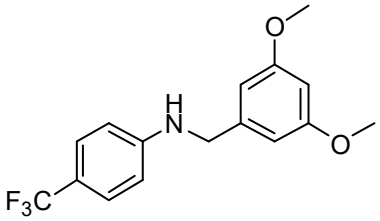
Table 2.3.3, compound 119°. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-methoxyaniline (62 mg, 0.5 mmol) and 3,5-dimethoxybenzylamine (117 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119°** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to 40:1). Isolated yield: 115 mg, 84%. Data for **119°** δ ^{1}H NMR (400 MHz, $CDCl_3$) 6.82–6.77 (m, 2H), 6.64–6.59 (m, 2H), 6.57 (d, *J* = 2.3 Hz, 2H), 6.40 (t, *J* = 2.3 Hz, 1H), 4.23 (s, 2H), 3.79 (s, 6H), 3.76 (s, 3H), ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 160.9, 152.0, 142.3, 142.2, 114.7, 114.0, 105.2, 98.9, 55.6, 55.2, 49.2 ppm; GC-MS for $C_{16}H_{19}NO_3$, m/z = 273 (M^+). ^{1}H and ^{13}C NMR spectral data were in good agreement with the literature values.[108]



119ᵖ

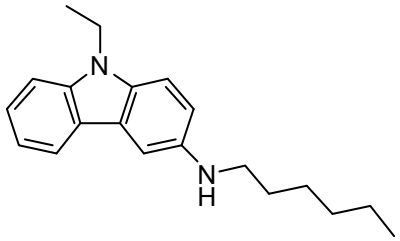
Table 2.3.3, compound 119ᵖ. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-chloroaniline (62 mg, 0.5 mmol) and 3,5-dimethoxybenzylamine (117 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119ᵖ** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 150:1 to

40:1). Isolated yield: 66 mg, 48%. Data for **119p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13–7.08 (m, 2H), 6.58–6.53 (m, 2H), 6.52–6.49 (m, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 4.24 (s, 2H), 3.78 (s, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.1, 146.3, 141.3, 129.0, 122.3, 114.1, 105.2, 99.1, 55.3, 48.6 ppm; GC-MS for $C_{15}H_{16}ClNO_2$, m/z = 277 (M^+). HRMS (IT-TOF/ESI) Calcd for $C_{15}H_{16}ClNO_2$ ($[M+H]^+$): 278.0942, Found: 278.0928.



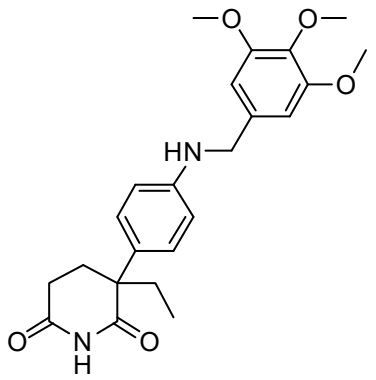
11q

Table 2.3.3, compound 119q. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 4-trifluoromethylaniline (81 mg, 0.5 mmol) and 3,5-dimethoxybenzylamine (117 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119q** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 150:1 to 40:1). Isolated yield: 58 mg, 37%. Data for **119q**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.6 Hz, 2H), 6.63 (d, *J* = 8.6 Hz, 2H), 6.51 (d, *J* = 6.5 Hz, 2H) 6.39 (t, *J* = 2.3 Hz, 1H), 4.55 (br s, 1H), 4.30 (s, 2H), 3.78 (s, 6H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.1, 150.3, 140.9, 126.6 (q, J_{CF} = 3.8 Hz), 124.9 (q, J_{CF} = 270.6 Hz), 119.2 (q, J_{CF} = 32.6 Hz), 112.1 105.2, 99.1, 55.3, 48.0 ppm; GC-MS for $C_{16}H_{16}F_3NO_2$, m/z = 311 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{16}F_3NO_2$ ($[M+H]^+$): 312.1206, Found: 312.1207.



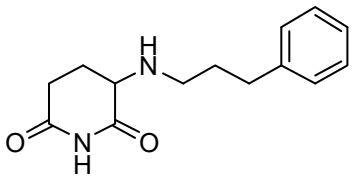
119^{r}

Table 2.3.3, compound 119^{r}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 3-Amino-9-ethylcarbazole (105 mg, 0.5 mmol) and 1-hexamine (71 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{r}** was isolated by a column chromatography on silica gel (*n*-hexane/ethyl acetate = 150:1 to 40:1). Isolated yield: 103 mg, 70%. Data for **119^{r}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.04 (m, 1H), 7.48–7.42 (m, 1H), 7.40–7.34 (m, 2H), 7.26 (d, *J* = 7.3 Hz, 1H), 7.19 (dd, *J* = 7.3, 1.2 Hz, 1H), 6.91 (dd, *J* = 8.6, 2.3 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 3.40 (br s, 1H), 3.25 (t, *J* = 7.2 Hz, 2H), 1.72 (quintet, *J* = 7.4 Hz, 2H), 1.55–1.45 (m, *2*H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.41–1.33 (m, 4H), 1.12–0.92 (m, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 141.9, 140.2, 133.9, 125.2, 123.6, 122.6, 120.3, 117.8, 114.6, 109.0, 108.3, 103.3, 45.7, 37.4, 31.7, 29.7, 27.0, 22.6, 14.0, 13.8 ppm; GC-MS for $C_{20}H_{26}N_2$, m/z = 294 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{20}H_{26}N_2$ ($[M+H]^+$): 295.2169, Found: 295.2167.



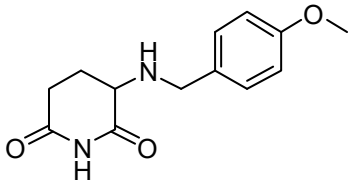
119[t]

Table 2.3.3, compound 119[t]. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), (±)-aminoglutethimide (116 mg, 0.5 mmol) and 3,4,5-trimethoxybenzylamine (138 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119[t]** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 100:1 to 5:1). Isolated yield: 82 mg, 40%. Data for **119[t]**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (br s, 1H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 6.59 (s, 2H), 4.24 (s, 2H), 3.83 (s, 9H), 2.62–2.52 (m, 1H), 2.44 (dd, *J* = 13.2, 4.9 Hz, 1H), 2.31 (ddd, *J* = 14.2, 4.8, 2.7 Hz, 1H), 2.16 (dd, *J* = 13.8, 4.8 Hz, 1H), 1.99 (sextet, *J* = 7.4 Hz, 1H), 1.87 (sextet, *J* = 7.4 Hz, 1H), 0.85 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 175.5, 172.5, 153.4, 147.0, 137.1, 134.5, 127.1, 113.4, 113.4, 104.4, 60.8, 56.1, 50.2, 48.9, 32.9, 29.3, 26.9, 9.0 ppm; GC-MS for $C_{23}H_{28}N_2O_5$, m/z = 412 (M^+);



119[u]

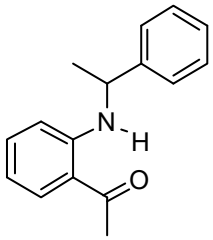
Table 2.3.3, compound 119^{u}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), glutamine (73 mg, 0.5 mmol) and 3-phenyl-1-propanamine (95 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{u}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 50:1 to 1:1). Isolated yield: 92 mg, 75%. Data for **119^{u}** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.23 (m, 2H), 7.22–7.12 (m, 3H), 6.73 (br s, 1H), 4.08 (dd, *J* = 9.0, 4.8 Hz, 1H), 3.28 (dd, *J* = 8.9, 4.8 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 2.50–2.37 (m, 1H), 2.37–2.19 (m, 2H), 2.16–2.05 (m, 1H), 1.84 (quintet, *J* = 7.4 Hz, 2H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 179.5, 172.1, 141.4, 128.4, 128.3, 126.0, 57.1, 39.3, 33.2, 30.8, 29.4, 25.7 ppm; GC-MS for $C_{14}H_{18}N_2O_2$, m/z = 246 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{14}H_{18}N_2O_2$ ($[M+H]^+$): 247.1441, Found: 247.1408.



119^{v}

Table 2.3.3, compound 119^{v}. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), glutamine (73 mg, 0.5 mmol) and (96 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^{v}** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 50:1 to 1:1). Isolated yield: 87 mg, 70%. Data for **119^{v}**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.5 Hz, 2H), 6.92 (br s, 1H), 6.83 (d, *J* = 8.5 Hz, 2H), 4.40–4.29 (m, 2H), 4.13 (dd, *J* = 9.0, 4.7 Hz, 1H), 3.77 (s, 3H), 2.53–2.41 (m, 1H), 2.34–2.20 (m, 2H), 2.20–2.09 (m, 1H), 1.87 (br s, 1H) ppm;

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 179.5, 172.2, 158.8, 130.1, 128.9, 113.8, 57.0, 55.1, 42.7, 29.2, 25.5 ppm; GC-MS for $C_{13}H_{16}N_2O_3$, m/z = 248 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{13}H_{16}N_2O_3$ ($[M+H]^+$): 249.1234, Found: 249.1202.



119^x

Table 2.3.3, compound 119^x. A chlorobenzene (2.0 mL) solution of complex **112** (7 mg, 0.75 mol %), **116** (8 mg, 10 mol %), 1-(2-aminophenyl)ethanone (68 mg, 0.5 mmol) and (±)-phenylalanine (116 mg, 0.7 mmol) was stirred at 140 °C for 20 h. The product **119^x** was isolated by a column chromatography on silica gel (*n*-hexane/EtOAc = 50:1 to 1:1). Isolated yield: 42 mg, 35%. Data for **119^x**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (br d, J = 5.1 Hz, 1H), 7.78–7.73 (m, 1H), 7.37–7.28 (m, 4H), 7.27–7.16 (m, 2H), 6.59–6.52 (m, 1H), 6.47 (d, J = 8.6 Hz, 1H), 4.60 (quintet, J = 6.6 Hz, 1H), 2.63 (s, 3H), (d, J = 6.8 Hz, 3H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 201.1, 150.0, 144.8, 134.8, 132.6, 128.7, 126.9, 125.7, 117.6, 114.2, 113.1, 52.6, 28.0, 25.0 ppm; GC-MS for $C_{16}H_{17}NO$, m/z = 239 (M^+); HRMS (IT-TOF/ESI) Calcd for $C_{16}H_{17}NO$ ($[M+H]^+$): 240.1383, Found: 240.1373.

3.11 X-Ray Crystallographic data for 119^{f}

Table 3.11.1: Crystal data and structure refinement for **119^{f}**.

Empirical formula	$C_{17}H_{21}NO_4$
Formula weight	303.35
Temperature/K	100.0(3)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	8.5915(2)
b/Å	7.48777(15)
c/Å	12.7605(4)
α/°	90.00
β/°	108.580(3)
γ/°	90.00
Volume/Å^3	778.12(3)
Z	2
ρ_{calc}g/cm^3	1.295
μ/mm^{-1}	0.753
F(000)	324.0
Crystal size/mm^3	0.4341 × 0.0928 × 0.0487
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.3 to 148.3
Index ranges	$-10 \leq h \leq 10$, $-9 \leq k \leq 9$, $-15 \leq l \leq 15$
Reflections collected	8045
Independent reflections	2988 [R_{int} = 0.0272, R_{sigma} = 0.0294]
Data/restraints/parameters	2988/1/208
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0294, wR_2 = 0.0711
Final R indexes [all data]	R_1 = 0.0321, wR_2 = 0.0732
Largest diff. peak/hole / e Å^{-3}	0.15/-0.15
Flack parameter	-0.13(14)

Table 3.11.2: Bond lengths for **119[f]**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O1	C3	1.373(16)	C1	C7	1.523(2)
O1	C14	1.432(18)	C2	C3	1.392(2)
O2	C4	1.380(17)	C3	C4	1.399(2)
O2	C15	1.430(2)	C4	C5	1.395(19)
O3	C5	1.375(17)	C5	C6	1.401(2)
O3	C16	1.434(17)	C8	C9	1.397(2)
O4	C11	1.377(17)	C8	C13	1.403(2)
O4	C17	1.420(2)	C9	C10	1.398(2)
N1	C7	1.447(2)	C10	C11	1.389(2)
N1	C8	1.393(19)	C11	C12	1.393(2)
C1	C2	1.391(2)	C12	C13	1.382(2)
C1	C6	1.389(2)			

Table 3.11.3: Bond angles for **119[f]**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C3	O1	C14	115.69(11)	O3	C5	C4	115.30(12)
C4	O2	C15	112.35(12)	O3	C5	C6	124.12(12)
C5	O3	C16	116.68(11)	C4	C5	C6	120.58(13)
C11	O4	C17	116.63(12)	C1	C6	C5	119.42(13)
C8	N1	C7	122.91(13)	N1	C7	C1	115.01(13)
C2	C1	C7	117.15(13)	N1	C8	C9	123.22(13)
C6	C1	C2	120.45(14)	N1	C8	C13	118.92(14)
C6	C1	C7	122.33(13)	C9	C8	C13	117.85(13)
C1	C2	C3	119.98(13)	C8	C9	C10	120.92(13)
O1	C3	C2	124.13(13)	C11	C10	C9	120.27(14)
O1	C3	C4	115.61(12)	O4	C11	C10	125.51(14)
C2	C3	C4	120.25(13)	O4	C11	C12	115.22(13)
O2	C4	C3	120.65(12)	C10	C11	C12	119.27(13)
O2	C4	C5	120.05(13)	C13	C12	C11	120.38(13)
C5	C4	C3	119.27(12)	C12	C13	C8	121.30(14)

Table 3.11.4: Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for **119f**. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
O1	-1255.5(12)	2572.4(13)	2839.7(9)	21.2(2)
O2	1353.7(13)	546.1(13)	3928.8(9)	21.9(2)
O3	4424.8(12)	1631.3(14)	4209.7(9)	22.4(2)
O4	8250.9(13)	7758.2(15)	145.7(10)	29.0(3)
N1	3989.6(16)	8065.1(16)	2650.9(11)	23.7(3)
C1	2123.4(18)	5522.2(19)	2706.7(12)	19.9(3)
C2	530.4(18)	4918(2)	2535.9(13)	20.0(3)
C3	268.3(17)	3263.4(18)	2948.3(12)	18.7(3)
C4	1602.0(18)	2197.1(18)	3527.9(12)	18.0(3)
C5	3192.9(17)	2794.3(19)	3667.8(12)	19.3(3)
C6	3460.2(18)	4461.2(19)	3257.3(13)	19.8(3)
C7	2320.5(18)	7405(2)	2316.5(14)	23.5(3)
C8	4991.9(17)	7933.1(18)	1984.9(13)	20.1(3)
C9	4608.8(18)	6869.7(19)	1036.7(13)	21.6(3)
C10	5661.1(18)	6780.9(19)	398.6(13)	21.5(3)
C11	7115.8(17)	7749(2)	702.4(13)	21.1(3)
C12	7518.4(18)	8798.2(19)	1653.1(13)	22.2(3)
C13	6477.7(18)	8882.0(19)	2284.3(13)	21.5(3)
C14	-2616.4(18)	3507(2)	2094.9(13)	23.6(3)
C15	1002(2)	673(2)	4948.7(15)	33.0(4)
C16	6069.0(17)	2316(2)	4536.5(13)	22.8(3)
C17	7981(2)	6536(2)	-745.8(15)	34.6(4)

Table 3.11.5: Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for **119f**. 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	19.0(5)	17.7(5)	25.1(6)	2.7(4)	4.5(4)	0.0(4)
O2	25.1(5)	14.2(5)	27.0(6)	2.8(4)	9.3(4)	-0.6(4)
O3	19.0(5)	17.3(5)	28.4(6)	3.3(4)	4.1(4)	-0.3(4)
O4	32.4(6)	26.9(6)	32.2(6)	-4.7(5)	16.6(5)	-2.7(5)
N1	28.9(7)	16.9(6)	27.9(7)	-1.9(5)	12.9(6)	-5.5(5)
C1	25.9(7)	16.0(7)	19.1(8)	-0.3(5)	9.2(6)	-1.2(6)
C2	23.1(7)	16.9(7)	19.6(8)	1.2(6)	6.3(6)	2.4(5)

C3	21.9(7)	16.3(7)	18.8(7)	-1.9(5)	7.8(6)	-1.1(5)
C4	24.7(7)	12.2(6)	17.7(7)	-0.6(5)	7.5(6)	-1.3(5)
C5	21.4(7)	16.5(6)	19.5(7)	-0.5(6)	6.0(5)	2.5(6)
C6	21.0(7)	18.0(7)	21.1(8)	-2.0(6)	7.5(6)	-1.5(6)
C7	26.3(7)	17.5(7)	28.4(8)	3.8(6)	11.1(6)	0.3(6)
C8	23.4(7)	13.2(6)	23.3(8)	4.1(6)	6.8(6)	3.1(5)
C9	22.9(7)	17.2(7)	22.3(8)	1.2(6)	3.7(6)	-1.7(6)
C10	26.8(7)	16.9(7)	17.9(7)	0.1(6)	2.8(6)	2.2(6)
C11	24.5(7)	16.5(6)	22.6(8)	3.9(6)	7.8(6)	4.9(6)
C12	21.2(7)	16.7(7)	26.4(8)	0.2(6)	4.1(6)	-1.0(6)
C13	26.4(7)	14.3(6)	22.2(8)	-2.2(6)	5.6(6)	-0.7(6)
C14	21.2(7)	24.2(8)	23.0(8)	2.9(6)	3.6(6)	0.1(6)
C15	44.0(9)	26.4(8)	35.1(10)	10.5(7)	21.6(8)	7.7(7)
C16	20.2(7)	23.6(7)	24.0(8)	0.2(6)	6.3(6)	-2.5(6)
C17	47.4(10)	32.5(9)	30.4(10)	-5.4(7)	21.7(8)	-4.1(8)

Table 3.11.6: Hydrogen Bonds for **119[f]**.

D	**H**	**A**	**d(D-H)/Å**	**d(H-A)/Å**	**d(D-A)/Å**	**D-H-A/°**
N1	H1	O3[1]	0.93(2)	2.35(2)	3.2792(17)	173.7(16)

1+X,1+Y,+Z

Table 3.11.7: Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for **119^f**.

Atom	***x***	***y***	***z***	**U(eq)**
H1	4200(20)	9050(30)	3125(16)	26(5)
H2	-378	5634	2138	24
H6	4546	4863	3355	24
H7A	1875	7432	1499	28
H7B	1649	8229	2603	28
H9	3619	6198	823	26
H10	5380	6056	-246	26
H12	8514	9460	1869	27
H13	6774	9596	2933	26
H14A	-2695	4701	2388	35
H14B	-3632	2845	2016	35
H14C	-2454	3612	1371	35
H15A	1909	1282	5500	49
H15B	869	-529	5213	49
H15C	-14	1353	4833	49
H16A	6828	1410	4969	34
H16B	6137	3391	4987	34
H16C	6366	2614	3877	34
H17A	7911	5321	-480	52
H17B	8894	6609	-1049	52
H17C	6952	6836	-1324	52

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