# Syntheses and Catalytic Applications of Pincer-Ligated Nickel, Palladium and Copper Complexes

**Thesis**

Submitted to AcSIR for the Award of the Degree of

**DOCTOR OF PHILOSOPHY**

in

**Chemical Sciences**


by

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*under the supervision of*

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**June–2018**

*Dedicated to*

*My Parents and Teachers*

## CSIR – National Chemical Laboratory

# DECLARATION

I hereby declare that the original research work embodied in this thesis entitled, "**Syntheses and Catalytic Applications of Pincer-Ligated Nickel, Palladium and Copper Complexes**" submitted to the Academy of Scientific and Innovative Research (AcSIR) for the award of the degree of the Doctor of Philosophy (Ph.D.) is the outcome of experimental investigations carried out by me under the supervision of Dr. Benudhar Punji, Senior Scientist, CSIR-National Chemical Laboratory, Pune. I affirm that the work incorporated is original, and has not been submitted to any other academy, university or institute for the award of any degree or diploma.

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# THESIS CERTIFICATE

This is to certify that the work incorporated in this Ph.D. thesis entitled **"Syntheses and Catalytic Applications of Pincer-Ligated Nickel, Palladium and Copper Complexes"** submitted by **Mr. Hanumanprasad Pandiri** to the Academy of Scientific and Innovative Research (AcSIR) in fulfillment of the requirements for the award of the degree of **Doctor of Philosophy**, embodies original research work under my supervision. I further certify that this work has not been submitted to any other university or institution in part or full for the award of any degree or diploma. Research material obtained from other sources has been duly acknowledged in the thesis. Any text, illustration, table, etc., used in the thesis from other sources, have been duly cited and acknowledged.

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Place: Pune
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"*Above all, I thank God; the almighty for guiding me in my life.*
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**Hanumanprasad Pandiri**

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# ABBREVIATIONS

| | |
|---|---|
| AgOTf | Silver trifluoromethanesulfonate |
| $AgPF_6$ | Silver hexafluorophosphate |
| $AgSbF_6$ | Silver hexafluoroantimonate |
| bathocuproine | 2,9-Dimethyl-4,7-diphenyl-1,10-phenanthroline |
| bipy | 2,2'-Bipyridine |
| BDMAE | Bis(2-dimethylaminoethyl) ether |
| BINOL | 1,1'-Bi-2-naphthol |
| Cp | Cyclopentadienyl |
| COD | 1,5-cyclooctadiene |
| Cy | Cyclohexyl |
| Davephos | 2-(Dicyclohexylphosphino)-2′-(*N*,*N*-dimethylamino)biphenyl |
| DCE | 1,2-dichloroethane |
| dcype | Dicyclophosphinoethane |
| DFT | Density functional theory |
| DME | Dimethoxy ethane |
| DMA | *N*,*N*-dimethylacetamide |
| DMAP | 4-Dimethylaminopyridine |
| DMF | *N*,*N*-dimethylformamide |
| DMSO | Dimethyl sulfoxide |
| D*t*BEDA | *N*,*N*′-Di-*tert*-butyl ethylenediamine |
| dtbpy | 4,4-Di-*tert*-butyl bipyridine |
| dppf | 1,1'-Bis(diphenylphosphino)ferrocene |
| dppbz | 1,2-Bis(diphenylphosphino)benzene |
| F-SPE | Fluorous-solid phase extraction technique |
| Galvinoxyl | 2,6-Di-*tert*-butyl-α-(3,5-di-*tert*-butyl-4-oxo-2,5-cyclohexadien-1-ylidene)-*p*-tolyloxy |
| HRMS | High resolution mass spectrometry |
| LA | Lewis Acid |
| LiHMDS | Lithium hexamethyldisilazide |
| $Me_2S{\cdot}CuBr$ | Copper(I) bromide dimethyl sulphide |
| MeSCOOH | 2,4,6-trimethylbenzoic acid |

# ABBREVIATIONS

| | |
|---|---|
| Neocuproine | 2,9-dimethyl-1,10-phenanthroline |
| (DME)$NiCl_2$ | Nickel(II) chloride ethylene glycol dimethyl ether |
| (dppp)$NiCl_2$ | Dichloro(1,3-bis(diphenylphosphino)propane)nickel |
| *n*-$Bu_4NBr$ | *n*-Tetrabutyl ammonium bromide |
| NMP | 1-Methyl-2-pyrrolidone |
| OLED | Organic light emitting diodes |
| ORTEP | Oak ridge thermal-ellipsoid plot program |
| OTf | Trifluoromethanesulfonate |
| $Pcyp_3$ | Tricyclo pentyl phosphine |
| $Pd_2(dba)_3$ | Tris(dibenzylideneacetone)dipalladium(0) |
| $Pd(COD)Cl_2$ | Dichloro(1,5 cyclooctadiene)palladium(II) |
| Phen | 1.10-Phenanthroline |
| PIP | 2-Pyridinyl isopropyl |
| Piv | Pivalate |
| $PMe_3$ | Trimethyl phosphine |
| PvPy | Poly(vinylpyridine) |
| Py | Pyridinyl |
| $P(^iPr)_3$ | *Tris*(isopropyl) phosphine |
| $[RhCl(coe)_2]_2$ | Chlorobis(cyclooctenerhodium(I) |
| TADDOL | α,α,α,α-**T**etr**a**aryl-1,3-**d**ioxolane-4,5- **d**imethan**ol**s |
| *t*-AmOH | *tert*-Amylalcohol |
| TBHP | *tert*-Butylhydroperoxide |
| TBAF | tetra-*n*-Butylammonium fluoride |
| TEMPO | (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl |
| TFA | Trifluoroacetic acid |
| TFE | Trifluoroethanol |
| TIPS | Triisopropylsilyl |
| TOF | Turnover frequency |
| TON | Turnover number |

The thesis is divided into five different chapters. Chapter-1 deals with detailed literature survey on the synthetic approaches of pincer-ligated nickel, palladium and copper complexes, and their catalytic applications in the traditional cross-coupling reactions as well as in the direct C–H bond functionalization of arenes and heteroarenes.

Direct C–H bond functionalization of heteroarenes has raised much attention as an alternative to the traditional cross-coupling reaction because such a process bypasses the pre-activation of substrates. In chapter 2, the synthesis of phosphine-free quinolinamide-based pincer palladium complexes and their catalytic activity for the C–H arylation of azoles has been discussed. A variety of quinolinamide-based tridentate ligands were synthesized and metalated with Pd(II)-salts to develop the corresponding pincer Pd-complexes. All the ligands, ($^{R2}$NNN$^{Q}$)–H and palladium complexes, ($^{R2}$NNN$^{Q}$)Pd$^{II}$X were thoroughly characterized by $^{1}$H, $^{13}$C NMR and HRMS. Some of the complexes were structurally characterized by the single crystal X-ray diffraction study. All the pincer palladium complexes were screened and employed for the C–H bond arylation of benzothiazoles with aryl iodides. Preliminary mechanistic studies, such as external additive experiments and filtration experiment were conducted to know the actual role of ($^{R2}$NNN$^{Q}$)Pd$^{II}$ catalyst. Kinetic analysis was performed to understand various steps of the catalytic cycle, and resting state of the catalyst. Finally, a catalytic cycle was proposed for the ($^{R2}$NNN$^{Q}$)Pd-catalyzed arylation of benzothiazoles.

Chapter 3 presents the syntheses of six-membered nickelacycles {$\kappa^{P}$,$\kappa^{C}$,$\kappa^{P}$-(2-$^{i}$Pr$_2$POCH$_2$-C$_6$H$_3$-6-CH$_2$OP$^{i}$Pr$_2$)}NiX, [($^{iPr4}$POCCCOP)NiX], and their catalytic activity in the C–H bond alkylation of benzothiazole. The six-membered pincer nickelacycle, [($^{iPr4}$POCCCOP)NiBr] was synthesized by treating ($^{iPr4}$POCCCOP)–H ligand with (CH$_3$CN)$_2$NiBr$_2$ in the presence of Et$_3$N as a base. Reaction of [($^{iPr4}$POCCCOP)NiBr] complex with AgX (X = OAc, OTf) yielded corresponding acetate/triflate derivatives, [($^{iPr4}$POCCCOP)NiX]. All the complexes [($^{iPr4}$POCCCOP)NiX] were characterized by various analytical techniques. Further, the molecular structure of two complexes [($^{iPr4}$POCCCOP)NiX] (X = Br, OAc) was elucidated by X-ray diffraction analysis. The complex [($^{iPr4}$POCCCOP)NiBr was found to be an efficient catalyst for the alkylation of benzothiazole with alkyl halides containing $\beta$-hydrogen atoms. The catalytic efficiency of ($^{iPr4}$POCCCOP)NiX was found to be superior than the five-membered ($^{iPr4}$PCP)NiX and ($^{iPr4}$POCOP)NiX catalysts.

In chapter 4, the hemilabile {$R_2N$-$CH_2CH_2$-($\mu$-N)-$C_9H_6N$}NiCl pincer complexes were screened and employed for the Sonogashira cross-coupling reaction of phenylacetylene with alkyl iodides. The reaction condition was optimized using phenylacetylene and 1-iodooctane as coupling partner. The complex {$Me_2N$-$CH_2CH_2$-($\mu$-N)-$C_9H_6N$}NiCl as catalyst and CuI as co-catalyst in the presence of $LiO^tBu$ afforded the alkylation products at room temperature. Employing alkyl chloride or bromide as an electrophile, an additive NaI and a temperature of 100 $^oC$ was necessary for the satisfactory coupling of alkyl halides with phenylacetylene. The scope of this alkylation was explored employing diverse alkyl halides and achieved moderate to good yields of alkylated products.

Chapter 5 describes the syntheses and characterization of pincer ($^{Et2}NNN^Q$)Cu(II) complexes and their catalytic activity for the Kumada coupling of alkyl halides. Treatment of ligand ($^{Et2}NNN^Q$)–H with Cu(II)$X_2$ resulted in the formation of complexes ($^{Et2}NNN^Q$)CuX (X = Cl, Br, $OC(O)CH_3$). Surprisingly, the reaction of ($^{Et2}NNN^Q$)–H with Cu(I)X also yielded same complexes ($^{Et2}NNN^Q$)CuX in moderate yield. The formation of Cu(II) complex from Cu(I) precursor may be due to the disproportionation reaction of Cu(I) into Cu(II) and Cu(0). The chloro-derivative ($^{Et2}NNN^Q$)CuCl was treated with AgOTf in acetonitrile to obtain the cationic complex, [($^{Et2}NNN^Q$)Cu($NCCH_3$)]OTf. All the copper complexes were characterized by elemental analysis and the molecular structures of some of them were identified by X-ray diffraction study. The copper complexes were optimized for the Kumada coupling reaction of (3-chloropropyl)benzene with cyclohexylmagnesium chloride, wherein the cationic complex, [($^{Et2}NNN^Q$)$Cu^{II}$($NCCH_3$)]OTf was found to be an efficient catalyst. The scope of this reaction was successfully extended to various alkyl halides as well as benzyl halides.

# Chapter 1

## Introduction

Chapter 1 describes the general classification, nomenclature and properties of various pincer systems. The main focus is on the syntheses of pincer palladium, pincer nickel, pincer copper complexes and their catalytic applications. In this regard, the fundamental properties and synthetic routes of the pincer palladium, nickel and copper complexes are discussed. The utilization of pincer palladium, nickel and copper complexes in various catalytic transformations is documented in detail.

## 1.1 Classification, Nomenclature and Properties of Pincer System

### 1.1.1 Definition and Nomenclature of Pincer System

Development of well-defined ligand system, which can tune and control the properties of a transition metal, is the ultimate aim of inorganic and organometallic chemists. The chemists are always in search of ideal catalyst, which has good stability and high selectivity with a high turnover numbers (TON). These properties can be addressed by the appropriate choice of the ligands. Among various ligand systems known in the literature, the pincer ligands and their complexes have attracted considerable attention because of their high strength, reactivity, and variability. The pincer ligand is the system containing a tridentate chelating organic backbone, which generally has two co-ordinating moieties like amine, phosphine, thioether, carbene, etc., and one anionic moiety like alkyl, aryl, phosphide, silyl, amide or a neutral donor moiety (Figure 1.1).

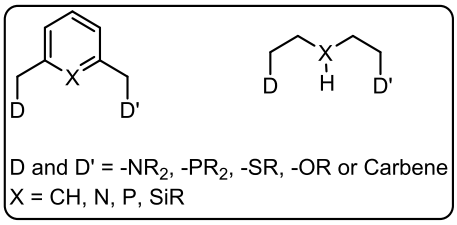



**Figure 1.1** General representations of pincer ligands.

General representation of pincer ligand is shown in Figure 1.1, where D and D' are the co-ordinating groups and X is an anionic or a neutral moiety. Different type of pincer ligand systems are known in the literature. The pincer ligands have been classified into two different types on the basis of co-ordinating atoms: symmetrical and non-symmetrical. If the co-ordinating

atoms D and D' are the same then it is referred to a symmetric pincer ligand, otherwise referred as unsymmetrical.

The pincer complex is the system in which the ligand is coordinated to metal by three donor sites, wherein metal is directly attached with an anionic moiety or a neutral atom and coordinated by two neutral atoms (Figure 1.2).[1] If both neutral species are the same then is called symmetrical pincer complex, if not then denominated as unsymmetrical pincer complex. The pincer backbone influences the properties of pincer metal complexes in the catalytic reactions. As the pincer ligand coordinates to the metal by three sites, it enhances the thermal stability as well as selectivity during catalysis. In the case of pincer complex as three sites are occupied by ligand there will be less number of sites available for the catalysis, which minimizes the formation of unwanted side products resulting from shuffling of ligand during the processes.

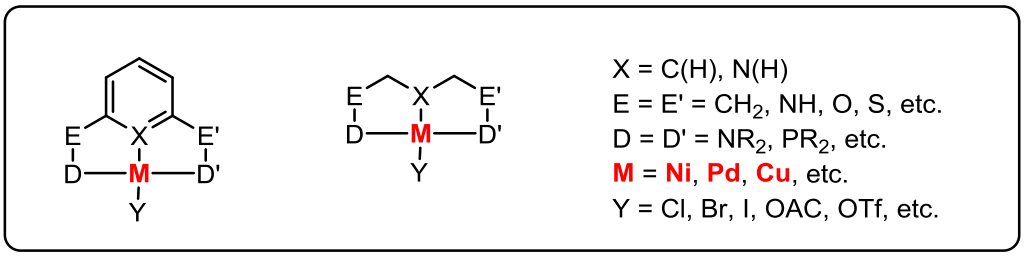



**Figure 1.2** General representations of pincer complexes.

First pincer system was described by Shaw and co-workers in 1976.[2] The complexes were reported with various transition metals such as Ni, Pd, Pt, Rh, Ir and were based on the $PC_{sp2}P$ pincer system as shown in Figure 1.3. These pincer complexes have high potential in the catalytic application, and have the features like thermal stability and ability to sustain unusual oxidation states.

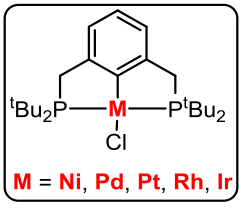



**Figure 1.3** Pincer complexes by Shaw and co-workers.

After the initial achievement by Shaw towards the development of pincer complexes, the chemistry of pincer systems was neglected by the scientific community. Later in 1979, van Koten came up with the NCN-pincer system to continue the pincer chemistry.[3] His group synthesized various pincer complexes of NCN-ligand with Ni, Pd and Pt-transition metals (Figure 1.4: **A**). For the first time, these complexes were structurally characterized and (NCN)Ni(II)-complex was utilized in the Kharasch addition reaction.[4] In addition they have characterized the Ni(III) complex featuring Ni–C linkage and highlighted the importance of NCN-pincer nickel(III) complex for the catalytic activity in Kharasch addition reaction.

In 1982, Fryzuk and co-workers illsutrated an interesting example of the aliphatic "PNP" pincer system which contains soft phosphorus as neutral donor and hard nitrogen as anionic donor.[5] Additionally, the ligand contains two dimethylsilyl moieties at *β*-position to the metal which diminishes the probability of reductive elimination or oxidation of metal. The synthesis and structural characterization of various PNP-pincer complexes of nickel, palladium and platinum (Figure 1.4: **B**) has been well explored by Fryzuk group.

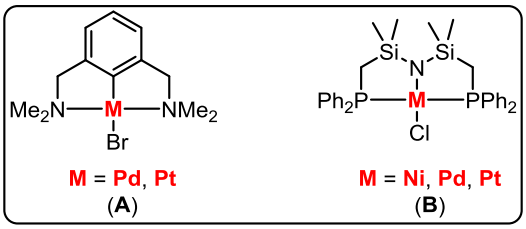



**Figure 1.4** NCN-pincer system (**A**) by van Koten and PNP pincer system (**B**) by Fryzuk.

Following the report of Fryzuk, various research groups across the globe focused towards the development and chemistry of symmetric pincer ligand systems such as NCN,[6,7] POCOP,[8-12] PNCNP,[13] SCS,[14-17] CCC[18-20] (Figure 1.5). Among them the PCP ligand system has been extensively studied compared to other symmetric ligands, which was first introduced by Shaw *et al.*[2] and later explored by Jensen and coworkers.[21] The first (POCOP)Ir and the (PCP)Ir-pincer complexes exhibited excellent reactivity for dehydrogenation of alkanes to olefins.[22-24] Later unsymmetric pincer ligands such as PCN,[25] NCS,[26] and PCS[16] were developed by several research groups (Figure 1.6). The chemistry of unsymmetric ligands is less explored compared to the symmetric pincer ligands.

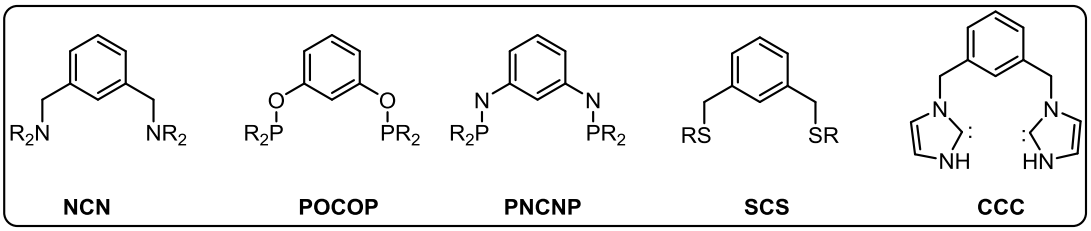



**Figure 1.5** Representative symmetrical pincer ligands.

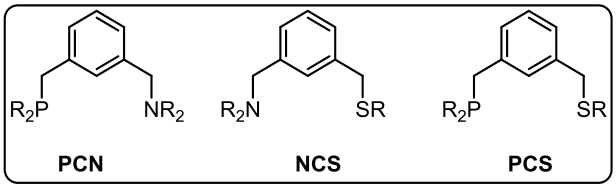



**Figure 1.6** Representative unsymmetrical pincer ligands.

In the case of unsymmetrical ligand system, it is very easy to tune the electronic features of the metal by varying the donor substituents. The hemilabile nature of unsymmetrical pincer ligand, which has control over the other catalytic pathways during catalysis, significantly increases the number of active sites on metal and consequently enhances the rate of reaction. However, the use of hemilabile ligands has drawbacks as it can lead to irreversible dissociation of ligand from the metal that can lead to the decomposition of pincer complexes.[27]

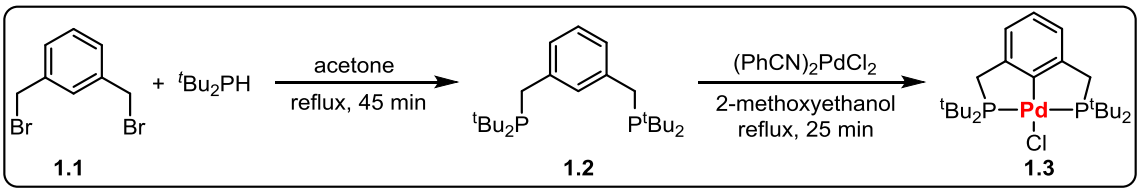
### 1.1.2 Basic Properties of Pincer Complexes

The pincer complexes are known to possess high thermal-stability. The general representation of a pincer complex is shown in Figure 1.2. During catalysis the pincer system usually keeps the metal and ligand together in each catalytic step which generally enhances the catalyst reactivity. In pincer complexes, the sterics and electronics around metal centre can be easily tuned by varying the substituents on ligands which in turn can affect the catalytic activity of these complexes.[28] Till date, several pincer complexes with different ligands around the metal centre are known in the literature which plays a crucial role in the catalysis of various organic transformations.[15,29-42]. The general literature reported methods for the synthesis of palladium pincer complexes has been illustrated in the following section 1.2.

## 1.2 Strategies for the Synthesis of Pincer Palladium Complexes

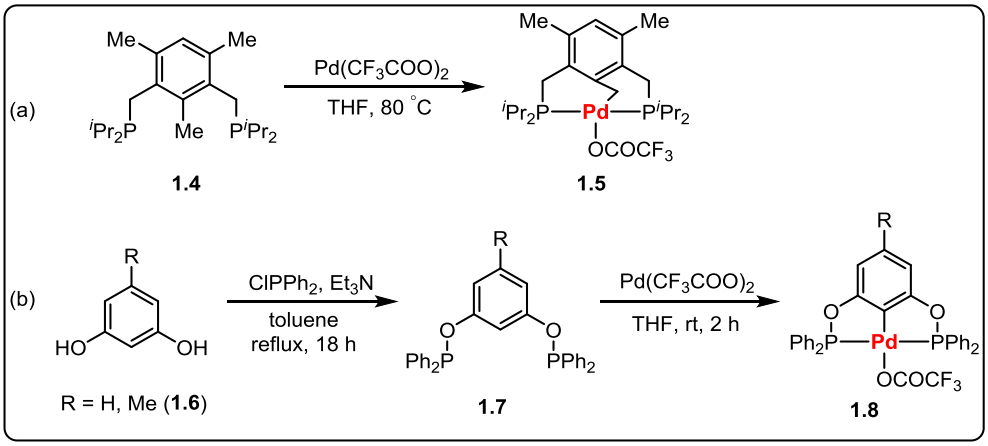
### 1.2.1 C–H Bond Activation Approach

In 1976, Shaw and coworkers reported the synthesis of first pincer complex by using the C–H bond activation strategy.[2] In this approach 1,3-bis(bromomethyl)benzene (**1.1**) on reaction with di-*tert*-butylphosphine in acetone under reflux resulted in the formation of diphosphine ligand $^{t}$Bu4PCP–H (**1.2**) in 97% yield. The ligand **1.2** further on reaction with bis(benzonitrile)palladium(II) chloride in 2-methoxyethanol under reflux resulted the pincer palladium complex ($^{t}$Bu4PCP)PdCl (**1.3**) *via* C–H bond activation (Scheme 1.1).



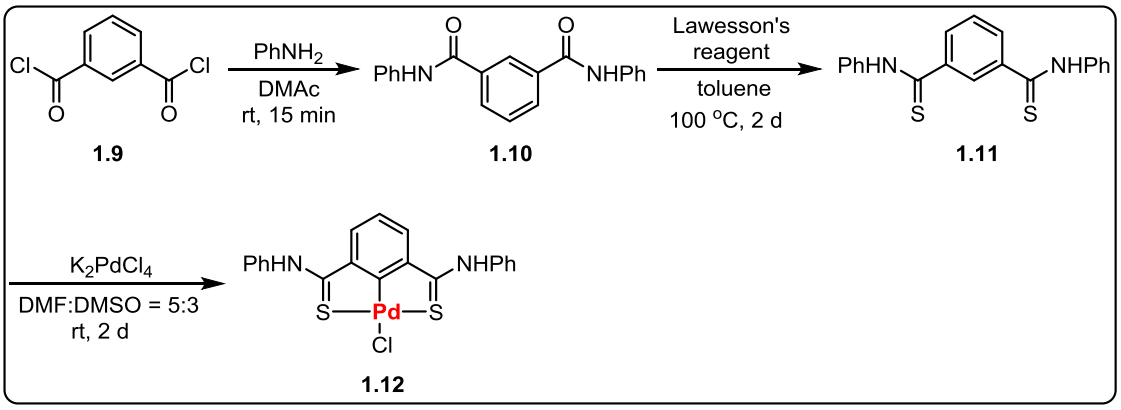

**Scheme 1.1** Synthesis of PCP-Pincer Palladium Complex through C–H Bond Activation.

Milstein and coworkers reported the synthesis of PCP ligand **1.4** and its usage for the synthesis of pincer palladium complex **1.5** *via* the C–H bond activation (Scheme 1.2a).[43] Following this report Bedford *et al.*[44] demonstrated the synthesis of POCOP pincer palladium complex **1.8** from the POCOP–H ligand **1.7** *via* C–H bond activation (Scheme 1.2b).



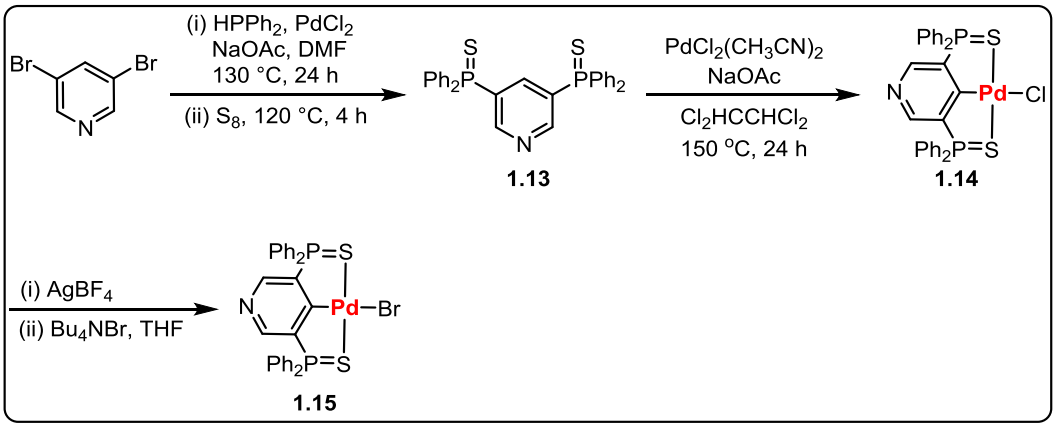

**Scheme 1.2** Synthesis of PCP and POCOP-Pincer Palladium Complexes.

In 2006, James *et al*. reported the synthesis of thioamide-based SCS ligand and the corresponding pincer palladium complex *via* C–H bond activation.[14] In this approach isophthaloyl chloride on reaction with 2 equiv of aniline gave the amide **1.10**, which upon reaction with Lawesson's reagent produced the thioamide-based SCS ligand **1.11**. The SCS ligand on reaction with $K_2PdCl_4$ in DMF/DMSO (5:3) resulted in the formation of pincer palladium complex **1.12** (Scheme 1.3).




**Scheme 1.3** Synthesis of Thioamide-based SCS Pincer Palladium Complex *via* C–H Activation.

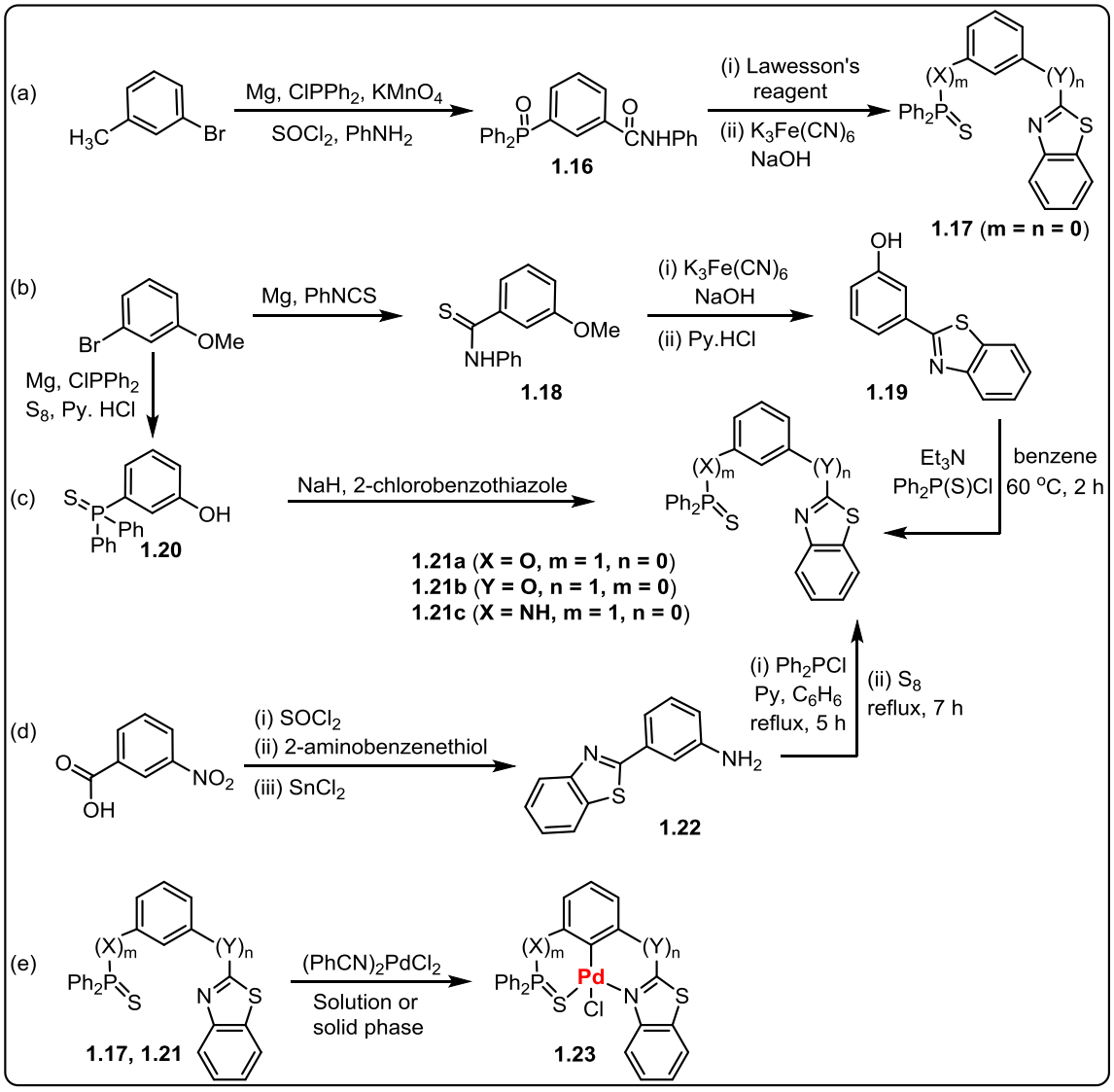
Kanbara and coworkers reported the synthesis of phosphine sulphide-based SCS ligand and corresponding pincer palladium complexes.[15] In this method, 3,5-dibromopyridine was treated with diphenylphosphine in the presence of palladium chloride and sodium acetate which was followed by addition of sulfur to give the corresponding SCS ligand **1.13**. This ligand further on reaction with $(CH_3CN)_2PdCl_2$ in the presence of sodium acetate gave pincer palladium chloride complex **1.14**. This chloride complex upon reaction with $AgBF_4$ and followed by $Bu_4NBr$ produced the corresponding bromide derivative **1.15** (Scheme 1.4).




**Scheme 1.4** Synthesis of Phosphine Sulphide-based SCS Pincer Palladium Complex.

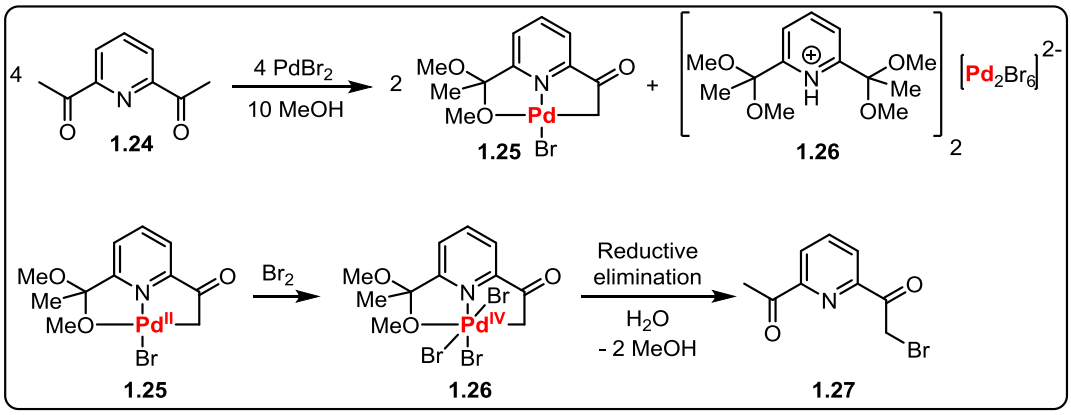
Various SCN ligands and their pincer palladium complexes were synthesized by Odinets *et al*. in solution phase as well as in solid phase (Scheme 1.5).[45] This was the first to report the solid phase synthesis of pincer palladium complexes (Scheme 1.5e).[31] In this approach 3-bromotoluene on reaction with magnesium gave the Grignard reagent, which on reaction with $ClPPh_2$ and oxidation using $KMnO_4$ followed by treatment with $SOCl_2$ and $PhNH_2$ gave the 3-diphenylphosphoryl-*N*-phenylbenzamide (**1.16**). This compound on reaction with Lawesson's reagent produced the 3-diphenylthiophosphoryl-*N*-phenylbenzenecarbothioamide, which was further treated with $K_3Fe(CN)_6$ in the presence of NaOH resulting in the formation of SCN ligand **1.17** (m = n = 0). Similarly, the 3-bromoanisole on reaction with magnesium followed by PhNCS gave 3-methoxy-*N*-phenylbenzenecarbothioamide (**1.18**). The thioamide derivative further on reaction with $K_3Fe(CN)_6$ followed by demethylation gave 3-(1,3-benzothiazol-2-yl)phenol (**1.19**). The phenol was treated with $Ph_2P(S)Cl$ in the presence of $Et_3N$ that produced the corresponding SCN ligand **1.21a** (X = O, m = 1, and n = 0). The 3-bromoanisole on reaction with Mg followed by the reaction with $ClPPh_2$ and sulfur gave 3-(diphenylthiophosphoryl)anisole (**1.20**), which was demethylated to give the corresponding phenol. This phenol derivative on reaction with 2-chlorobenzothiazole in the presence of NaH yielded the corresponding SCN ligand **1.21b** (Y = O, n = 1 and m = 0). The 3-nitrobenzoic acid on reaction with $SOCl_2$/2-aminobenzenethiol followed by the reduction with $SnCl_2$ produced 3-(1,3-benzothiazol-2-yl)aniline (**1.22**). The aniline derivative on reaction with $ClPPh_2$ in the presence of pyridine and sulfur gave the corresponding SCN ligand **1.21c** (X = NH, m = 1 and n

= 0). The SCN ligands (**1.17**, **1.21**) were treated with $(PhCN)_2PdCl_2$ in benzonitrile under reflux to achieve corresponding pincer palladium complexes in good yields. On the other hand, the reaction of SCN ligands with $(PhCN)_2PdCl_2$ in neat at 200 $^oC$ for 15 min also gave the corresponding pincer palladium complexes in solid phase.




**Scheme 1.5** Synthesis of SCN-Pincer Ligands and Palladium Complexes in Solid/Solution Phase.

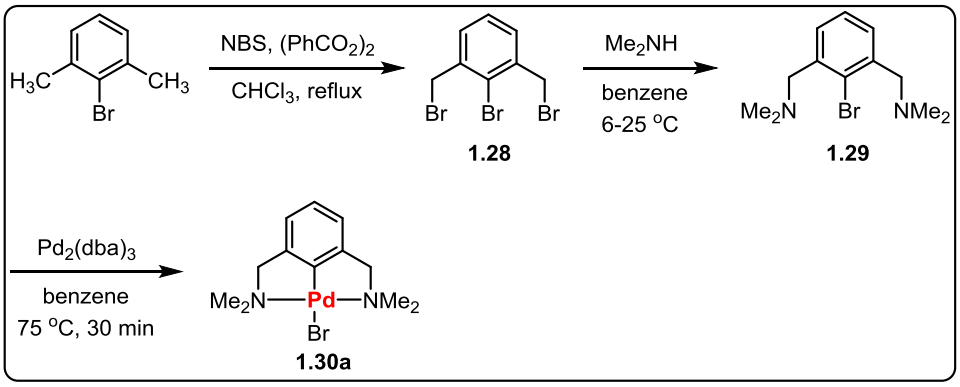
In 2010, Vicente *et al*. for the first time reported the synthesis of pincer palladium(IV) complexes.[39] In this approach 2,6-diacetylpyridine (**1.24**) on reaction with $PdCl_2$ in refluxing methanol resulted in an intermediate **1.25**, which further reaction with excess $Br_2$ produced the ONC-pincer palladium(IV) complex **1.26** (Scheme 1.6). The isolated ONC-pincer palladium(IV) complex was well characterized by X-ray diffraction. The complex **1.26** decomposes into the reductively eliminated product **1.27**.




**Scheme 1.6** Synthesis and Characterization of First Isolated Pincer Palladium(IV) Complex.

### 1.2.2 Oxidative Addition of C–X Bond to Pd(0)

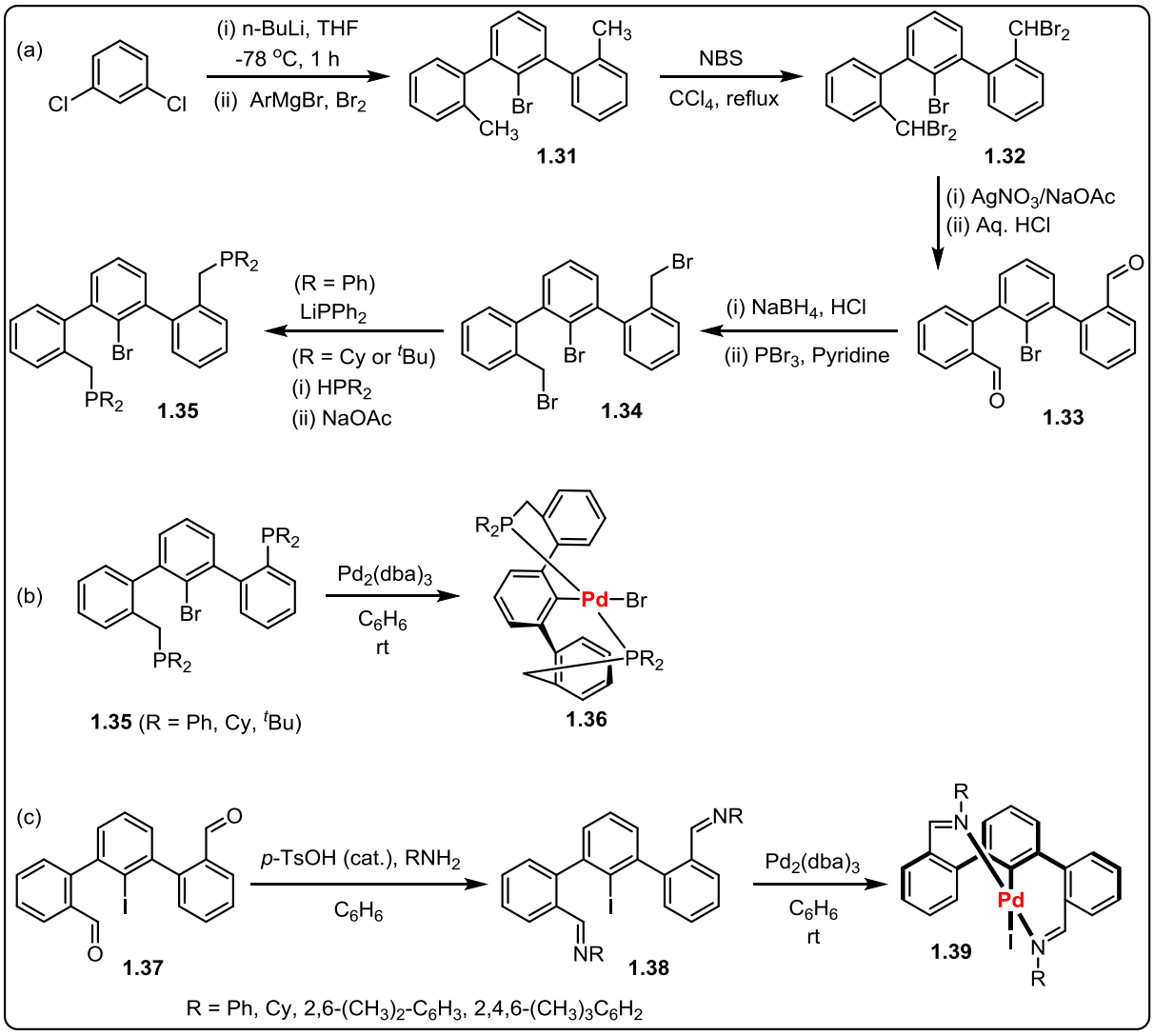
Pincer-based palladium complexes are also synthesized by the oxidative addition of C–X (X = pseudohalide) of ligand to the Pd(0) precursor. In 1992, van Koten and coworkers reported the synthesis of NCN-ligand and the corresponding pincer palladium complex starting with 2-bromo-*m*-xylene (Scheme 1.7).[46] In this method 2-bromo-*m*-xylene on reaction with NBS in the presence of benzoyl peroxide in $CHCl_3$ resulted 2-bromo-1,3-bis(bromomethyl)benzene (**1.28**), which on reaction with dimethylamine produced the corresponding aminated compound **1.29**. The compound **1.29** was treated with $Pd_2(dba)_3$ to afford the corresponding NCN-pincer palladium bromide complex **1.30a** through the oxidative addition of C–Br bond to Pd(0).




**Scheme 1.7** Synthesis of NC(Br)N Ligand and Pincer Palladium Complex *via* Oxidative Addition of C–Br Bond to Pd(0).

Protasiewicz *et al*. reported the syntheses of PCP ligands and the corresponding twisted pincer palladium complexes in 2006 (Scheme 1.8a-b).[35] In 2007, they reported the syntheses of NCN-ligands and their twisted pincer palladium complexes (Scheme 1.8c).[29] Initially, the 1,3-dichlorobenzene was treated with n-BuLi followed by *o*-tolylmagnesium bromide, then brominated to obtain terphenyl bromide derivative **1.31**. The compound **1.31** on reaction with NBS in the presence of benzoyl peroxide gave the corresponding bis(dibromomethyl) derivative **1.32**, which on reaction with $AgNO_3$/NaOAc followed by treatment with aq. HCl produced the dialdehyde derivative **1.33**. The dialdehyde **1.33** was reduced with $NaBH_4$ followed by bromination using $PBr_3$ in the presence of pyridine gave the bis(bromomethyl) derivative **1.34**, which on reaction with $LiPPh_2$ or $HPR_2$ (R = Cy, $^t$Bu) yielded PC(Br)P ligands **1.35**. The ligands **1.35** were treated with $Pd_2(dba)_3$ to afford the corresponding twisted PCP-pincer palladium complexes **1.36** *via* oxidative addition of C–Br bond to Pd(0).

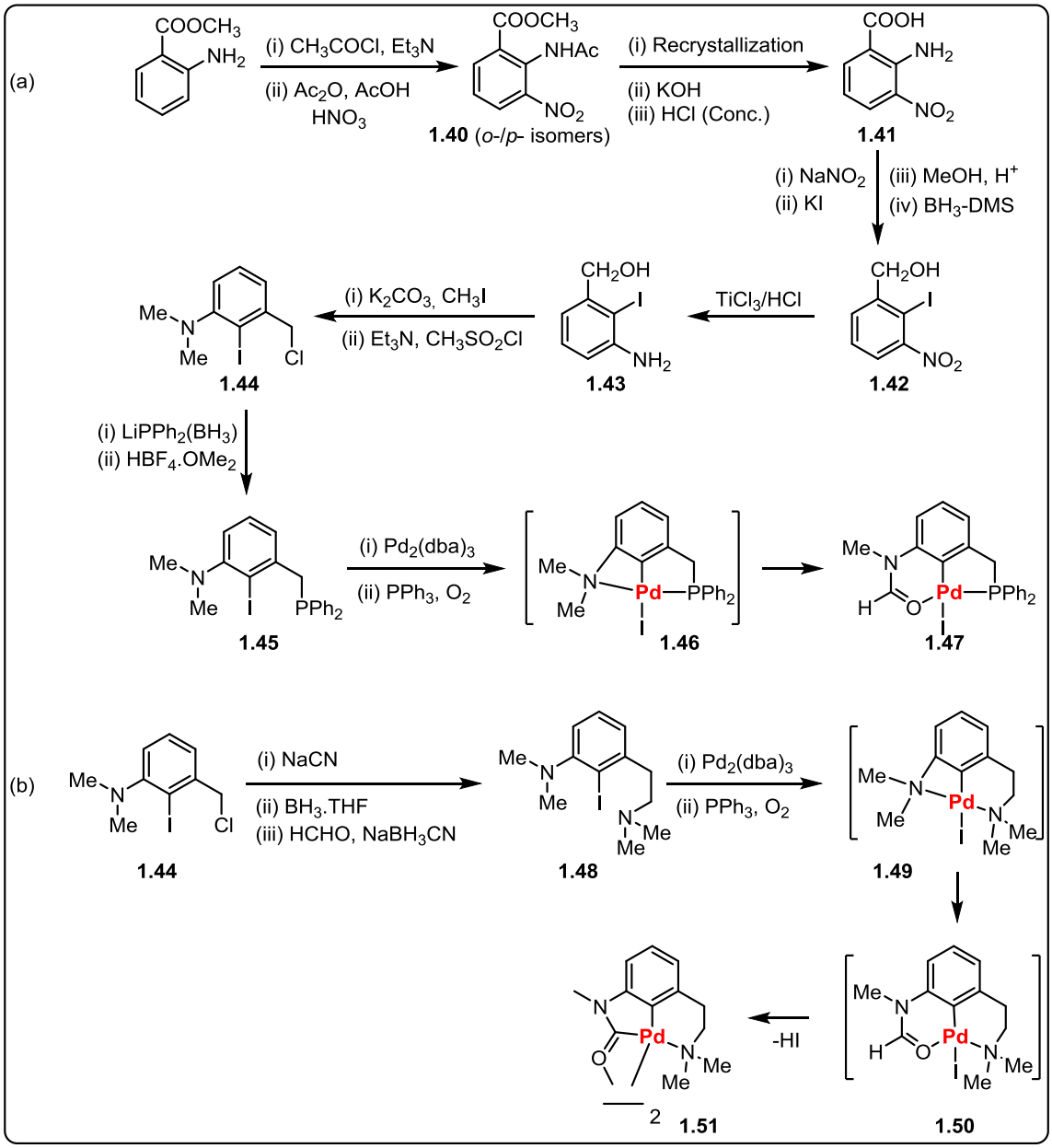
The iodoterphenyl compound **1.37** was treated with alkylamines in the presence of catalytic amount of *p*-TsOH to give the corresponding diimine derivative **1.38**. The diimine on reaction with $Pd_2(dba)_3$ resulted in the formation of twisted NCN-pincer palladium iodide complexes **1.39** in moderate yields.




**Scheme 1.8** Synthesis of PC(Br)P/NC(I)N Ligands and their Twisted Pincer Palladium Complexes *via* Oxidative Addition of C–Br/C–I Bond to Pd(0).

In 2007, Sole *et al*. reported the synthesis of OCP and CCN pincer palladium complexes (Scheme 1.9).[30] Methyl 2-aminobenzoate was treated with acetyl chloride in the presence of $Et_3N$ followed by nitration to form a mixture of 3-nitro and 5-nitro derivatives (**1.40**). The mixture of compounds **1.40** was recrystallized, hydrolyzed in the presence of KOH, and treated with conc. HCl to obtain 2-amino-3-nitrobenzoic acid **1.41**. The acid derivative **1.41** was treated with $NaNO_2$ followed by KI to obtain 2-iodo-3-nitrobenzoic acid, which further on reaction with methanol/$H^+$ followed by $BH_3$-DMS gave 3-nitro-2-iodobenzyl alcohol **1.42**. The nitro derivative

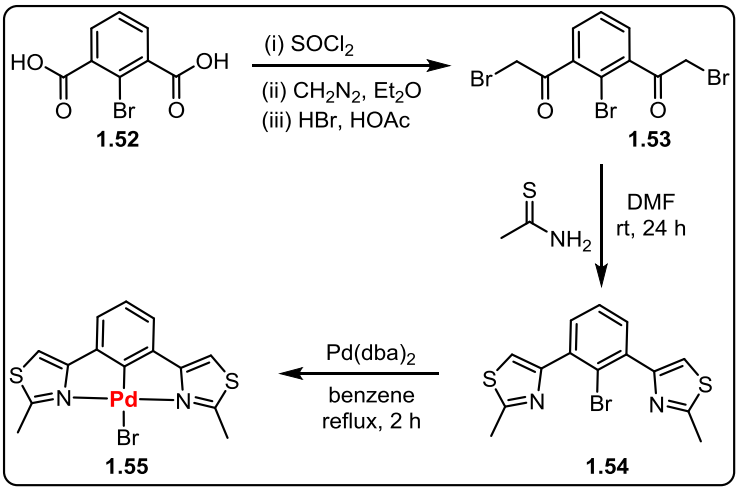
**1.42** was reduced with $TiCl_3$/HCl to get the corresponding amine **1.43**, which on reaction with $CH_3I$ and $CH_3SO_2Cl$ produced 3-(chloromethyl)-2-iodo-*N*,*N*-dimethylaniline **1.44**.




**Scheme 1.9** Syntheses of Monomeric OCP- and Dimeric CCN- Pincer Palladium Complexes *via* Oxidative Addition of C–I Bond to Pd(0)/$sp^3$(C–H) Oxidation.

The chloromethyl derivative **1.44** was treated with $LiPPh_2(BH_3)$ followed by $HBF_4.OMe_2$ to obtain the phosphine derivative **1.45** *via* $SN^2$ reaction. The phosphine derivative **1.45** was treated with $Pd_2(dba)_3$ to give an intermediate (PCN)PdI species **1.46** which was oxidized at *N*-methyl group in the presence of oxygen to form OCP-pincer palladium complex **1.47** (Scheme 1.9a). On the other hand, the reaction of 3-(chloromethyl)-2-iodo-*N*,*N*-dimethylaniline **1.44** with NaCN, $BH_3$.THF and with formalin/$NaBH_3CN$ gave dimethylamine derivative **1.48**. The amine derivative **1.48** on reaction with $Pd_2(dba)_3$ gave the intermediate (NCN)PdI species **1.49**, which was then oxidized at *N*-methyl group in the presence of oxygen to form the corresponding (OCN)PdI intermediate species **1.50**. The intermediate **1.50** on dehydroiodination produced the corresponding dimeric CCN-pincer palladium complex **1.51** (Scheme 1.9b).

Luo, Xiao and their group synthesized bis(thiazole)-based NCN-ligand **1.54** starting from 2-bromoisophthalic acid in two steps, as shown in Scheme 1.10.[47] The NCN-ligand **1.54** was treated with $Pd(dba)_2$ to achieve the corresponding pincer palladium(II) complex **1.55** through the oxidative addition of C–Br bond to Pd(0).

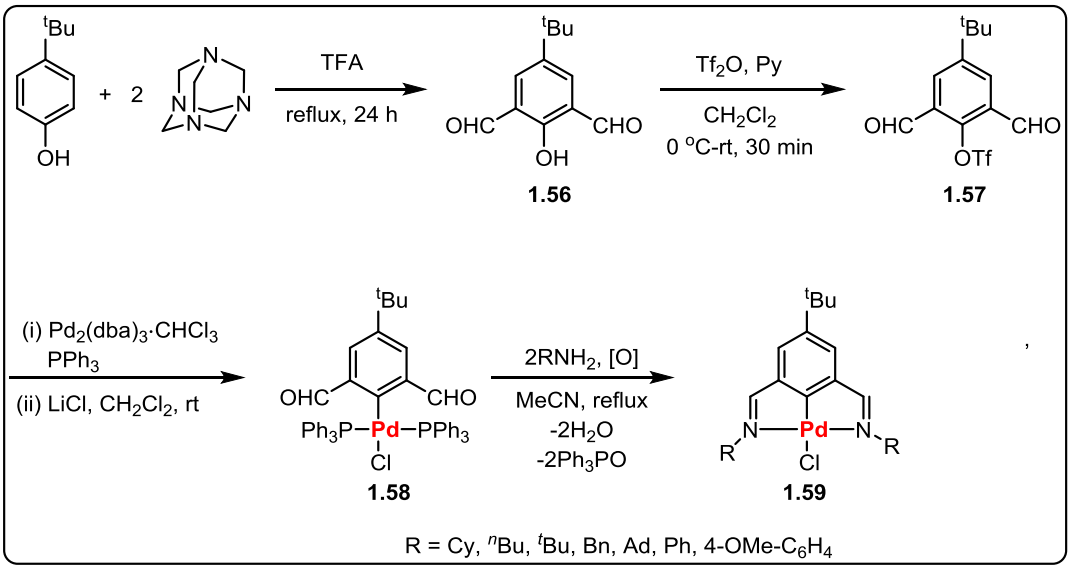



**Scheme 1.10** Synthesis of Bis(thiazole)-based NCN-Pincer Palladium Complexes.

### 1.2.3 Ligand Introduction Route

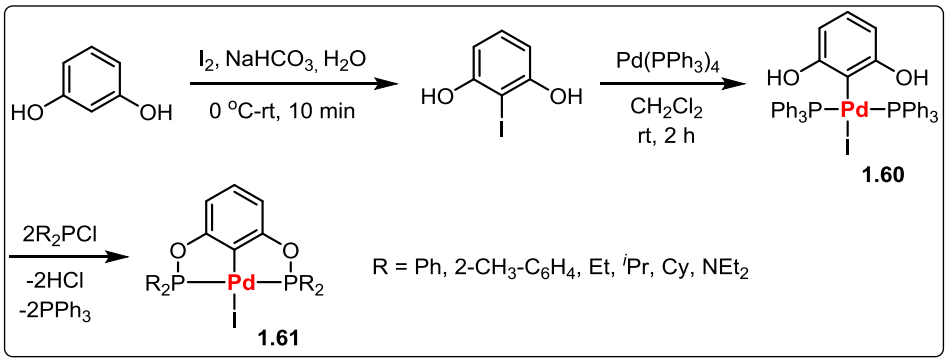
In addition to the synthesis of pincer palladium complexes *via* C–H and C–X activation routes (also called 'metal introduction routes' since the palladium metal was introduced at the last step), the same can also be synthesized by ligand introduction route. The metal introduction

routes give an easy access to the synthesis of pincer palladium complexes; however, sometimes they are sensitive to the sterically hindered substituent on the side arm of the pincer ligands. To overcome this problem, Uozumi and co-workers have demonstrated an interesting method called 'ligand introduction route', in which the palladium metal is introduced at an early stage of the complex synthesis, then the ligand is introduced at the last step.[48-50] In 2005, Uozumi *et al*.[48] reported the synthesis of imine-based NCN-pincer palladium complexes *via* ligand introduction route. In this method, 4-*tert*-butylphenol was treated with 2 equiv of hexamethylenetetramine in anhydrous TFA to form 5-*tert*-butyl-1,3-diformyl-2-hydroxybenzene **1.56**, which on reaction with $(CF_3SO_2)_2O$ gave 4-*tert*-Butyl-2,6-diformylphenyl trifluoromethanesulfonate **1.57** (Scheme 1.11). The compound **1.57** on reaction with $Pd_2(dba)_3{\cdot}CHCl_3$ in the presence of triphenylphosphine afforded palladium(II) chloride complex **1.58** *via* oxidative addition of C–O bond to Pd(0), followed by chloride exchange with LiCl. The introduction of dialkylamine ligands into the palladium complex yielded the corresponding NCN-pincer palladium complexes **1.59** by the elimination of water and triphenylphosphine oxide.



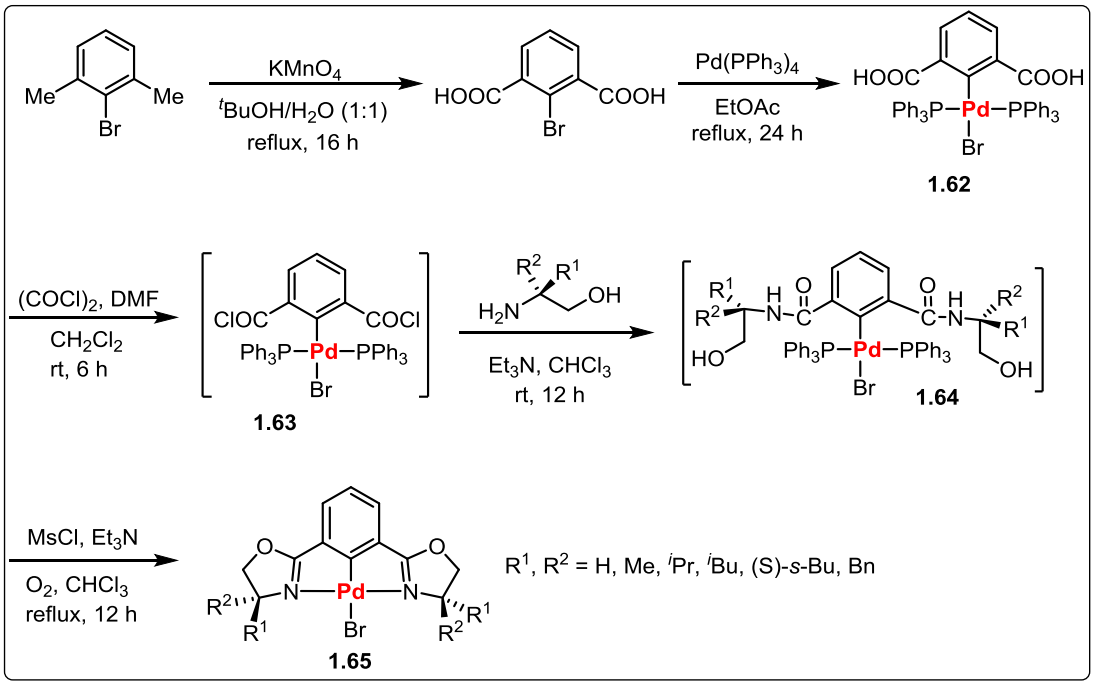

**Scheme 1.11** Syntheses of Imine-based NCN-Pincer Palladium Complexes *via* Ligand Introduction Route.

Same group reported the synthesis of POCOP-pincer palladium complexes starting from resorcinol in three steps (Scheme 1.12).[49] In the first step, resorcinol was treated with $I_2$ in the presence of $NaHCO_3$ in water to give 2-iodoresorcinol which on reaction with $Pd(PPh_3)_4$ gave palladium(II) complex **1.60** *via* oxidative addition of C–I bond to Pd(0). Finally, the introduction of chlorodialkylphosphine ligands into the palladium(II) complex **1.60** resulted in the formation of POCOP-pincer palladium complexes **1.61** in good yields.




**Scheme 1.12** Synthesis of POCOP Pincer Palladium Complexes *via* Ligand Introduction Route.

Further continuation to this, they reported the syntheses of chiral NCN-pincer palladium complexes (Scheme 1.13).[50] The synthesis involved the treatment of 2-bromo-*m*-xylene with 4 equiv of $KMnO_4$ in 1:1 $^t$BuOH/water to obtain 2-bromoisophthalic acid, which on reaction with $Pd(PPh_3)_4$ obtained the Pd(II) complex **1.62**. This palladium complex was reacted with oxalyl chloride, followed by the introduction of chiral amino-alcohol in the presence of $Et_3N$/MsCl to achieve the chiral NCN-pincer palladium complexes **1.65** through the intermediate palladium species **1.63** and **1.64**.



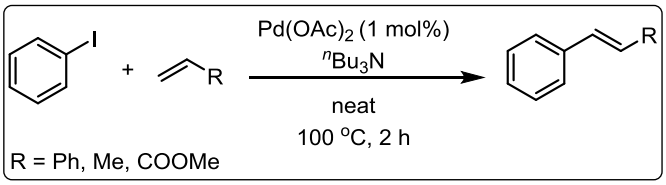

**Scheme 1.13** Synthesis of Chiral NCN-Pincer Palladium Complexes *via* Ligand Introduction Route.

## 1.3 Catalytic Applications of Pincer Palladium Complexes

### 1.3.1 Traditional Cross-Coupling Reactions

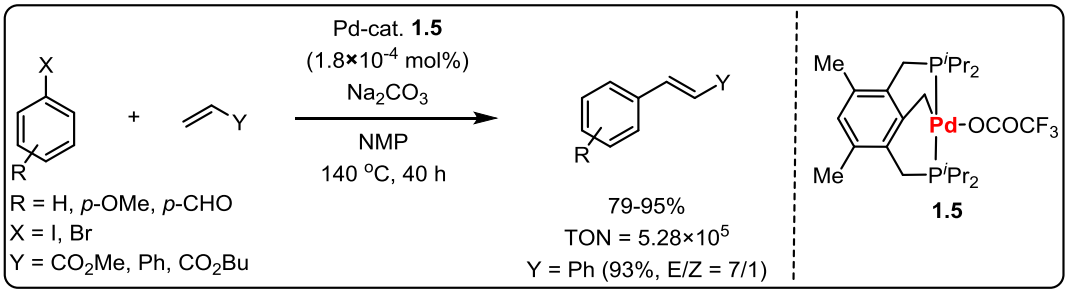
#### 1.3.1.1 Mizoroki-Heck Coupling Reaction

The Mizoroki-Heck reaction is the coupling reaction of an unsaturated halide or triflate with an alkene in the presence of a base and a palladium catalyst to form a substituted alkene.[51] Heck was awarded the 2010 Nobel prize in chemistry which he shared with Negishi and Suzuki, for the discovery and development of this reaction. This reaction was the first example of a C–C bond forming reaction that followed a Pd(0)/Pd(II) catalytic cycle. The Heck reaction is of great importance, as it allows one to do substitution reactions on planar $sp^2$-hybridized carbon atoms. Mizoroki was the first to report the palladium catalyzed coupling reaction of aryl iodides with olefins in 1971,[52] which was later developed by Heck in 1972 (Scheme 1.14).[53] The palladium-catalyzed Mizoroki-Heck reaction is the most efficient route for the vinylation of aryl and vinyl halides or triflates.[18,37,54-59] This C–C bond forming reaction proceeds in the presence of a base.

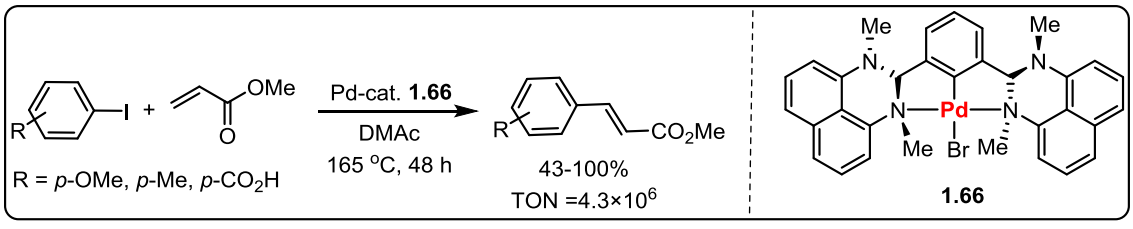



**Scheme 1.14** Palladium-Catalyzed Mizoroki-Heck Coupling Reaction of Aryl Iodide with Olefins.

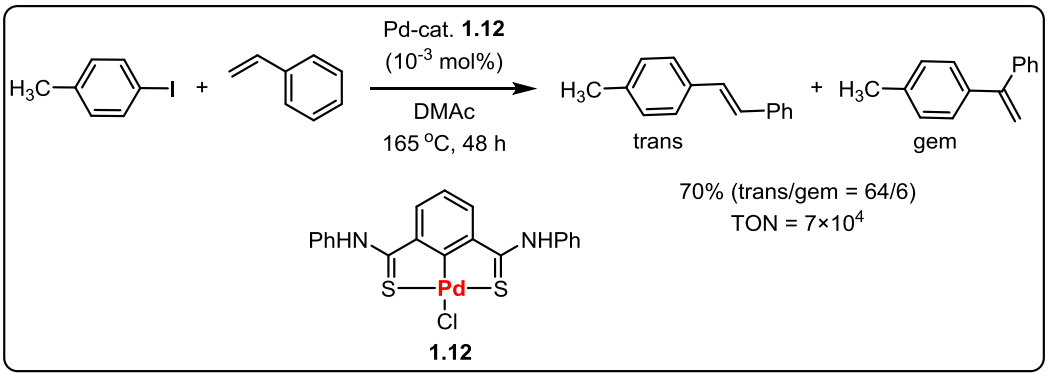
The PCP-pincer palladium complex **1.5** was reported first time for the Heck-coupling by Milstein *et al*. which showed excellent catalytic activity towards reaction of iodobenzene with methyl acrylate to achieve the alkenylated product with TON of $5.28\times10^5$ (Scheme 1.15).[43] In 2003, Chung *et al*. reported the NCN-pincer palladium complex **1.66**,[60] which showed excellent catalytic activity towards Heck-coupling reaction of 4-iodotoluene with methyl acrylate to achieve the corresponding alkenylated product with a maximum TON of $4.3\times10^5$ (Scheme 1.16); whereas the Heck-coupling of 1-bromo-4-nitrobenzene with methyl acrylate gave the alkenylated product in 67% yield with a TON of $6.7\times10^4$. The SCS-pincer palladium complex **1.12** reported by James *et al*. showed good catalytic activity towards Heck-coupling reaction of 4-iodotoluene with styrene to achieve the alkenylated product in TON of $7\times10^4$ (Scheme 1.17).[14]




**Scheme 1.15** PCP-Pincer Palladium-Catalyzed Heck Coupling Reaction.



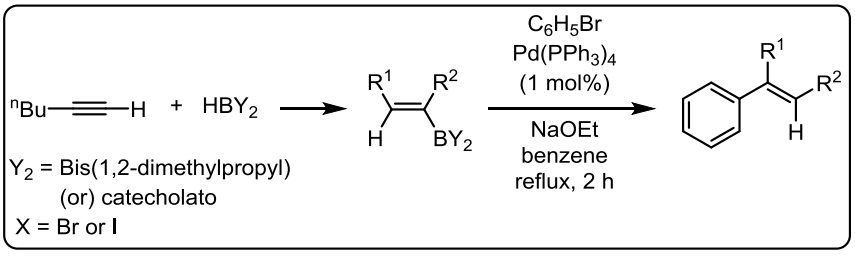

**Scheme 1.16** NCN-Pincer Palladium-Catalyzed Heck Coupling Reaction.




**Scheme 1.17** SCS-Pincer Palladium-Catalyzed Heck Coupling of 4-Iodotoluene with Styrene.

### 1.3.1.2 Suzuki-Miyaura Cross-Coupling Reaction

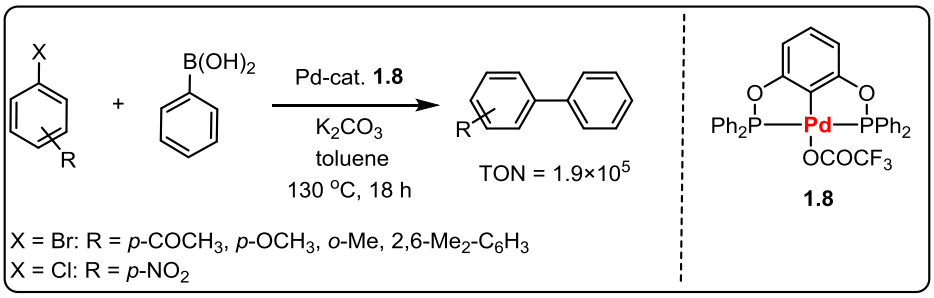
Suzuki-Miyaura coupling is one of the most important C–C bond forming reactions, which is generally the Pd-catalyzed coupling of arylboronic acid with aryl halide under basic condition.[61] In 1979, Suzuki and Miyaura were the first to report the coupling reaction of aryl halides been triggered by the availability of boronic acids (Scheme 1.18).[62] Further, the large scale production of biaryl compounds was achieved by the use of halide or pseudohalide substituents in the Suzuki coupling reaction.[63] This reaction was catalyzed by several literature reported pincer palladium complexes.[26,47,49,55,64-72]



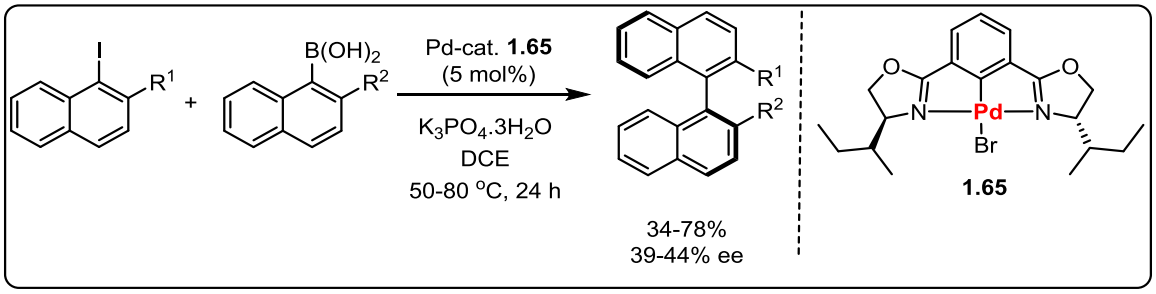

**Scheme 1.18** Suzuki Coupling Reaction of Aryl Halides with Alkenylboranes.

In 2000, Bedford *et al*. synthesized POCOP pincer palladium complexes **1.8**, which showed catalytic application in Suzuki cross-coupling reaction of aryl halides with phenylboronic acid with a maximum TON of $1.9\times10^5$ (Scheme 1.19).[44] Nishiyama and coworkers reported an asymmetric Suzuki-Miyaura coupling reaction catalyzed by chiral bisoxazoline-based NCN-pincer palladium bromide complex **1.65**.[73] In this approach, the

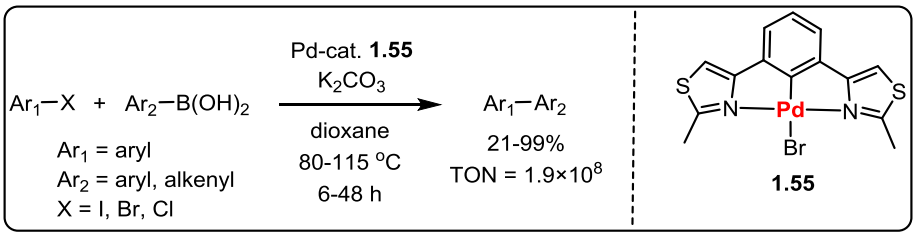
reaction of aryl iodide with aryl boronic acid resulted in the formation of the corresponding arylated product with a maximum yield of 78% in 46% ee for the corresponding (*S*)-isomer (Scheme 1.20). The chiral NCN-pincer palladium chloride [($^{iPr}$phebox)PdCl] catalyst gave a maximum TON of $9\times10^5$ in Suzuki-Miyaura coupling reaction of iodobenzene with phenylboronic acid. Luo and Xiao *et al*. reported Suzuki-Miyaura coupling of aryl halides with arylboronic acids catalyzed by bis(thiazole)-based NCN-pincer palladium complex **1.55** (Scheme 1.21).[47]




**Scheme 1.19** POCOP Pincer Palladium Catalyzed Suzuki Coupling Reaction.



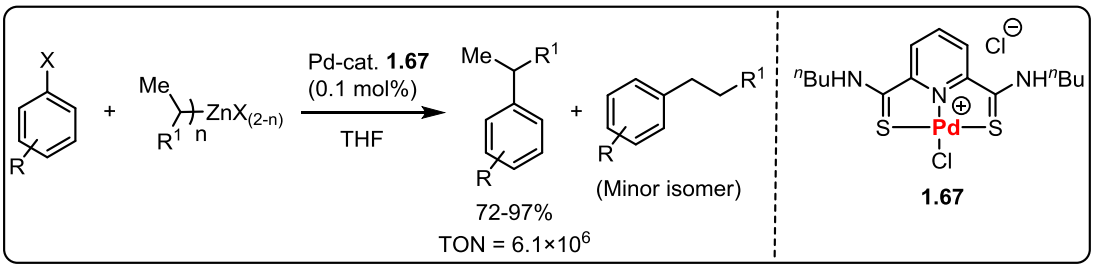

**Scheme 1.20** Chiral NCN-Pincer Palladium Catalyzed Asymmetric Suzuki Coupling Reaction.



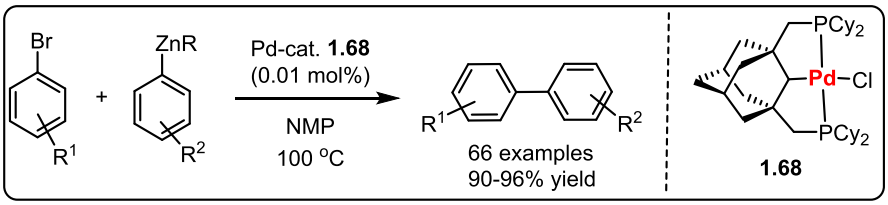

**Scheme 1.21** Bis(thiazole)-based NCN-Pincer Palladium Catalyzed Suzuki-Miyaura Coupling.

### 1.3.1.3 Negishi Coupling Reaction

Cross-coupling of organic halides or triflates with organozinc reagents in the presence of transition-metal catalyst is known as Negishi coupling reaction. Yang *et al.*[74] first attempted the Negishi coupling reaction of ethyl 2-iodobenzoate with cyclohexylzinc chloride by using SNS pincer palladium cationic complex **1.67** (Scheme 1.22). The catalyst is highly efficient with a TON of $6.1\times10^6$. Frech and coworkers[75] developed an adamantane-based PCP pincer palladium complex **1.68** for the Negishi coupling reaction of various electronically substituted aryl bromides with distinct diarylzinc reagents (Scheme 1.23).



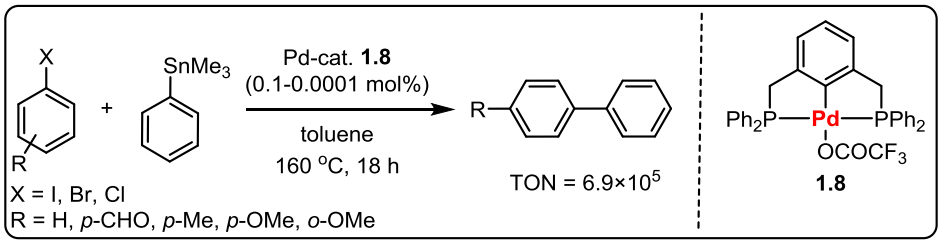

**Scheme 1.22** SNS-Pincer Palladium Catalyzed Negishi Coupling Reaction.




**Scheme 1.23** Negishi Cross-Coupling Reaction Catalyzed by PCP Pincer Palladium Complex.

### 1.3.1.4 Stille Coupling Reaction

Palladium catalyzed cross-coupling reaction of allyl, alkenyl or aryl halides with organotin reagent is known as Stille coupling reaction.[76] Wendt and coworkers described that the PCP pincer complex **1.8** catalyzes the coupling of variously substituted aryl halides with aryl tin (Scheme 1.24).[18] The process is very efficient to produce the coupled product in low catalyst loadings with TON's of $6.9\times10^5$.

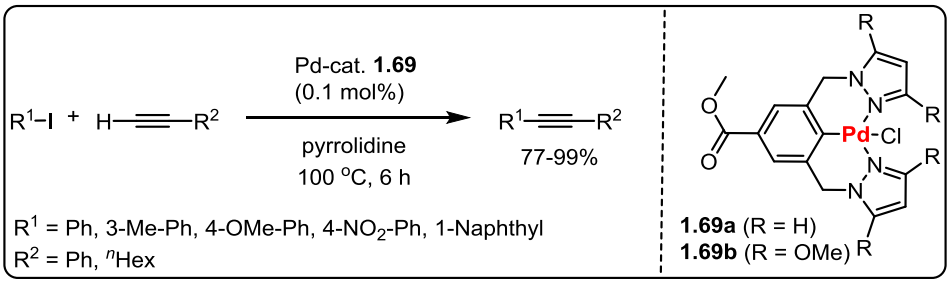



**Scheme 1.24** PCP-Pincer Palladium Catalyzed Stille Coupling Reaction.

### 1.3.1.5 Sonogashira Coupling Reaction

Palladium catalyzed cross coupling reaction of aryl or vinyl halides with alkynes is called Sonagashira coupling reaction. Various pincer palladium complexes were tested in Sonogashira coupling reaction owing to the synthetic importance of the coupled products of alkynes with aryl halides.[55,71,72,77,78] In 2005, San Martin synthesized NCN-pincer palladium complexes containing two pyrazole moieties **1.69** and utilized them in the C–C bond forming reactions such as Heck, Suzuki, and Sonogashira couplings (Scheme 1.25).[55]

In 2008, the same research group synthesized PCN-pincer palladium complex (Figure 1.7: **A**) containing one pyrazole moiety and one phosphinoamine moiety (Figure 1.7) and utilized in the C–C bond forming reactions such as Suzuki, Sonogashira, and Hiyama couplings.[71] Gong and coworkers synthesized imine-phosphinite based PCN-pincer palladium complexes (Figure 1.7: **B**) and revealed their catalytic application in the Suzuki and copper-free Sonogashira cross-coupling reactions.[72] Recently, Singh *et al*. synthesized oxine-based ONS/Se-pincer palladium complexes (Figure 1.7: **C**) and demonstrated their catalytic application in the cross-coupling reaction of variously substituted alkynes with distinct aryl halides.[78]




**Scheme 1.25** NCN-Pincer Palladium Catalyzed Sonogashira Coupling.

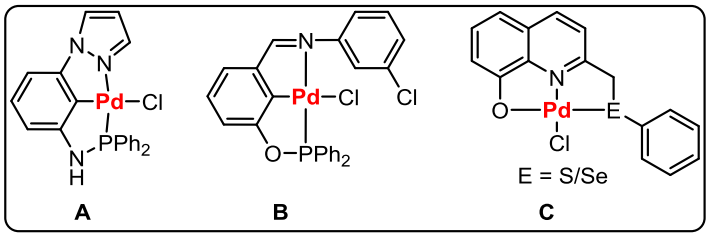
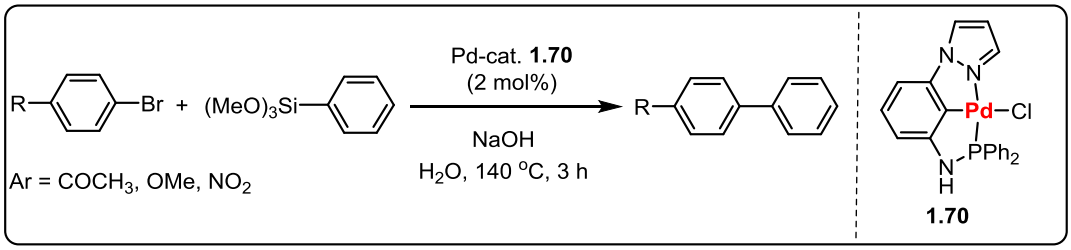



**Figure 1.7** (NCN)PdCl (**A**), (PCN)PdCl (**B**) and (ONS/Se)PdCl (**C**) Catalysts Employed in Sonogashira Coupling**.**

### 1.3.1.6 Hiyama Coupling Reaction

Hiyama coupling reaction is the palladium catalyzed cross-coupling of aryl, alkenyl, alkyl halides or pseudohalides with organosilanes. This reaction can be better understood by employing pincer palladium catalysts. For instance, in 2008 San Martin research group synthesized PCN pincer palladium complex **1.71** and utilized in the C–C bond forming reactions such as Hiyama coupling (Scheme 1.26).[71]

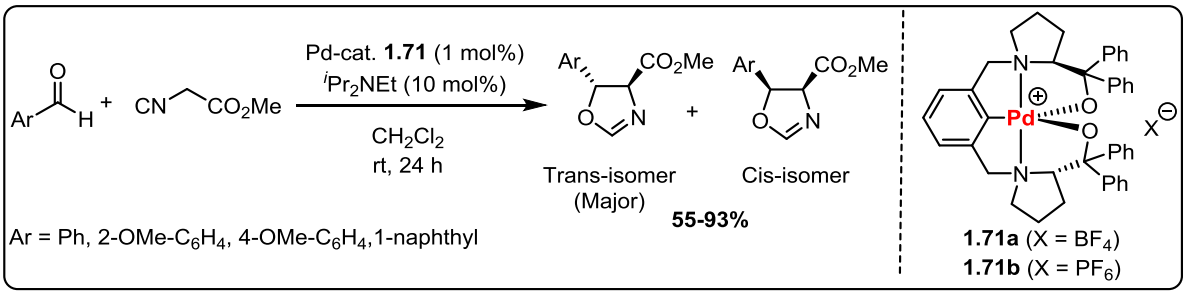



**Scheme 1.26** PCN-Pincer Palladium Complex Catalyzed First Hiyama Coupling.

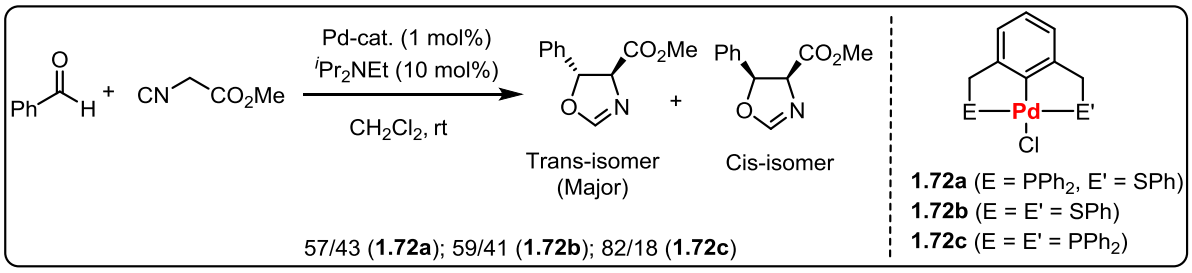
### 1.3.1.7 Aldol Condensation Reaction

The aldol condensation reaction is synthetically important as it involves the carbon-carbon bond formation and generates new stereocentre at the carbon. The high enantioselectivity in aldol reaction has been achieved using chiral pincer palladium complexes.[79,80] There are several precedents for the aldol reaction catalyzed by pincer palladium complexes.[16,42,79-81] Gebbink *et al.*[80] synthesized five-coordinated NCN-pincer palladium cationic complexes **1.71** and tested in the aldol condensation between aromatic aldehydes and methyl α-isocyanoacetate (MIC) in the presence of 10 mol% of $^{i}Pr_2EtN$ at ambient temperature (Scheme 1.27). Similarly, Gebbink and Szabo synthesized symmetrical and unsymmetrical sulfur-containing pincer (PCP, SCS, PCS)

palladium complexes **1.72a-c** and shown their catalytic activity towards aldol condensation between benzaldehyde and MIC (Scheme 1.28).[16]




**Scheme 1.27** Aldol Reaction Catalyzed by Five-Coordinated Chiral NCN-Pincer Palladium Complexes.




**Scheme 1.28** Aldol Reaction Catalyzed by PCP/SCS/PCS-Pincer Palladium Complexes.

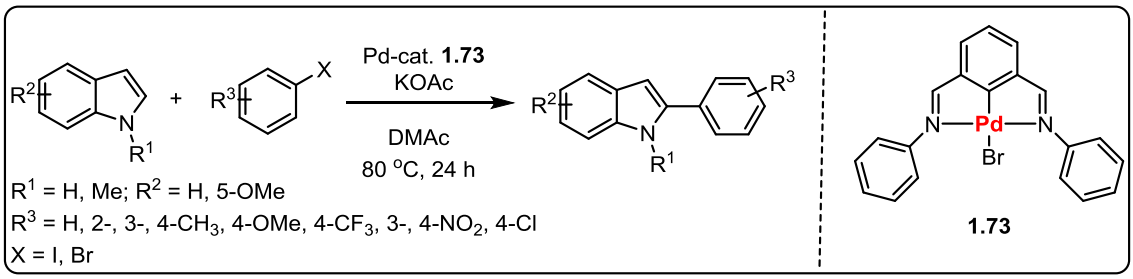
In addition to all the reactions described, the pincer palladium complexes were also employed in allylation of aldehydes and imines,[70,82-86] asymmetric Michael addition,[48,87,88] hydrogenation reactions,[89-91] phenylselenylation,[91] hydrophosphination,[92,93] and decarboxylative cross coupling.[94]

### 1.3.2 C–H Bond Functionalization Reactions

#### 1.3.2.1 C–H Bond Arylation

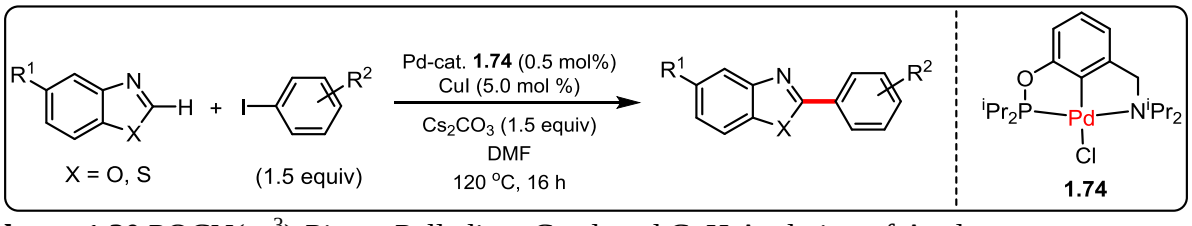
The direct C–H bond activation is more significant than the activation of C–X (X = halide or pseudohalide) bond, as the C–H bond strength is as high as 413 KJ/mol. Especially the C–H bond arylation of heteroarenes such as azoles is important because the arylated azoles are the fundamental unit of many naturally occurring compounds and pharmaceutical products.[95-98]

In 1990, Ohta and coworkers demonstrated the first example of direct C–H bond arylation of various azoles, wherein they observed the selective C-5 arylation of oxazole with chloropyrazine using $Pd(PPh_3)_4$ as catalyst and KOAc as base.[99] In 2014, Cai *et al.*[100] synthesized imine-based pincer palladium complex **1.73** as a precatalyst in the direct C-2 arylation of N-substituted indoles to afford the corresponding 2-arylindoles in moderate to good yields and excellent regio-selectivities (Scheme 1.29). The authors claimed that the NCN-pincer palladium precatalyst decomposes to Pd(0) on heating that catalyzes the actual reaction.

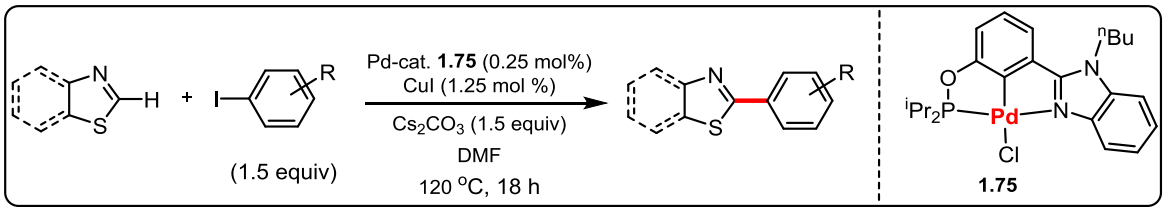



**Scheme 1.29** Direct C-2 Arylation of Indoles Employing NCN-Pincer Palladium Precatalyst.

In 2014, Punji *et al*. synthesized POCN-pincer palladium complex **1.74** and utilized in the catalytic C–H arylation of azoles with aryl iodides in the presence of CuI as co-catalyst (Scheme 1.30).[101,102] The authors isolated the intermediate (POCN)Pd(benzothiazolyl) species and proposed it as an active catalyst during the arylation reaction based on the reactivity studies with aryl iodides. The kinetic studies and Hammett plot experiments gave the preliminary insight into the mechanism of the reaction that the reaction would proceed in Pd(II)-Pd(IV)-Pd(II) catalytic pathway.[103] Recently, Gong and Song *et al*. synthesized POCN($sp^2$)-pincer palladium complexes **1.75** and demonstrated catalytic application in the C–H arylation of azoles (Scheme 1.31),[104] wherein the same hypothesis was made such as the reaction would follow Pd(II)-Pd(IV)-Pd(II) pathway.



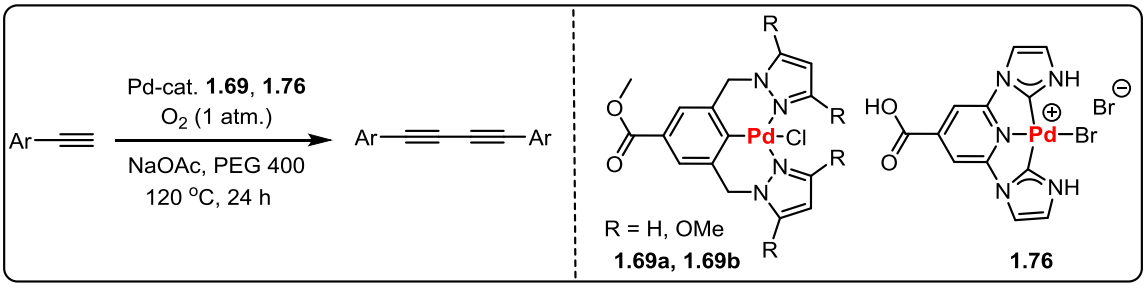

**Scheme 1.30** POCN($sp^3$)-Pincer Palladium Catalyzed C–H Arylation of Azoles.




**Scheme 1.31** POCN($sp^2$)-Pincer Palladium Catalyzed C–H Arylation of Azoles.

### 1.3.2.2 Aerobic Alkyne Homocoupling

San Martin *et al*.[55] demonstrated the NCN and CNC-pincer palladium complexes **1.69** and **1.76**, respectively in the catalytic aerobic copper-free homocoupling of a series of aromatic terminal alkynes (Scheme 1.32).[105] In this reaction, the authors employed very low loading of a catalyst such as $10^{-4}$ mol%, as a result the final products contain metal traces below legal limits for food and drug products. In addition, the reaction was performed in a sustainable medium such as polyethylene glycol (PEG 400), which is environmental friendly technique. The authors proved that the catalysts could be efficiently reused for four cycles.

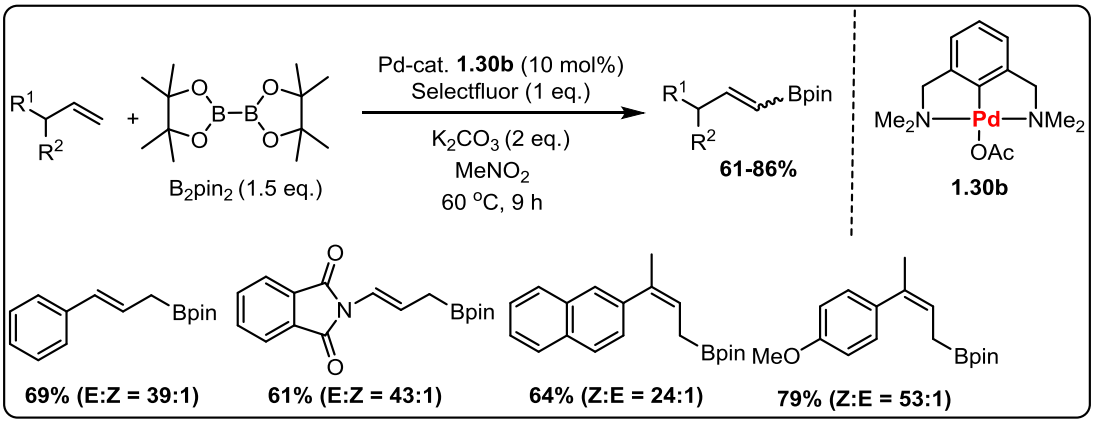



**Scheme 1.32** CNC/NCN-Pincer Palladium Catalyzed Aerobic Homocoupling of Alkenes.

### 1.3.2.3 C–H Bond Borylation

The C–H bond borylation is nothing but the functionalization of C–H bond with a boron-compound catalyzed by a transition-metal to form the C–B bond.[106] Szabo *et al*. synthesized NCN-pincer palladium catalyst **1.30b** and utilized in the C–H bond borylation of alkenes based on oxidative-functionalization and transmetalation followed by olefin insertion into Pd–B bond.[107] Similarly, they have employed the NCN-pincer palladium complex in the allylic C–H bond borylation of alkenes, wherein high regio- and stereoselectivities were achieved with

various linear alkenes (Scheme 1.33).[108] The authors performed preliminary mechanistic studies, which indicate that C–H bond borylation reaction proceeds *via* a Pd(IV) intermediate.

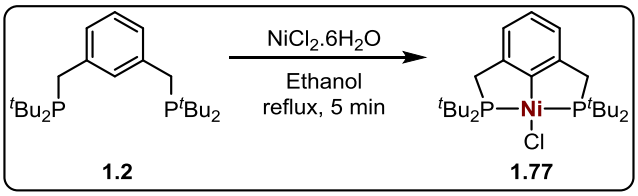



**Scheme 1.33** Allylic C–H Bond Borylation Catalyzed by NCN-Pincer Palladium Complex.

## 1.4 Approaches for the Synthesis of Pincer Nickel Complexes

### 1.4.1 C–H Bond Activation Strategy

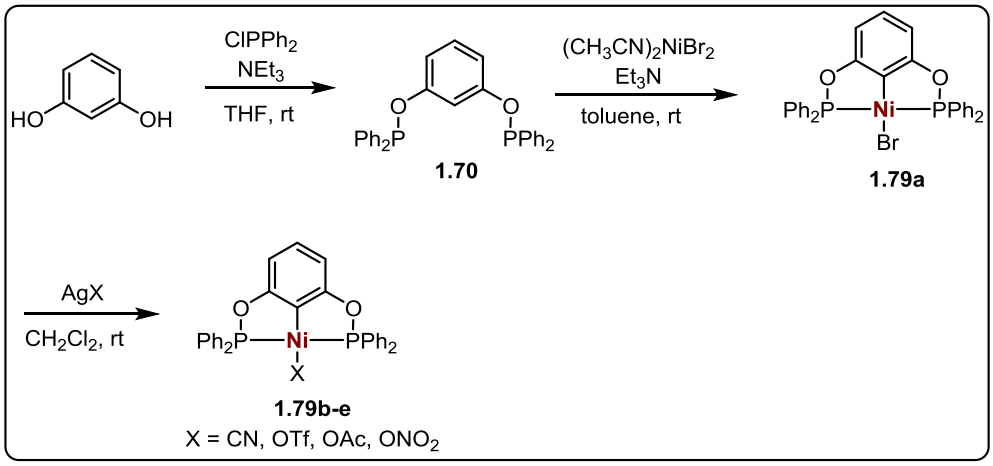
The first pincer complexes synthesized by Shaw and coworkers in 1976 is the best examples that could be considered under the C–H activation approach.[2] The $^{t}$Bu4PCP-ligand **1.2** on reaction with nickel(II) chloride hexahydrate in ethanol under reflux resulted the PCP-pincer nickel complex [($^{t}$Bu4PCP)NiCl] **1.77** *via* C–H bond activation in moderate yield (Scheme 1.34).




**Scheme 1.34** Synthesis of PCP Pincer Nickel Complex through C–H Bond Activation.

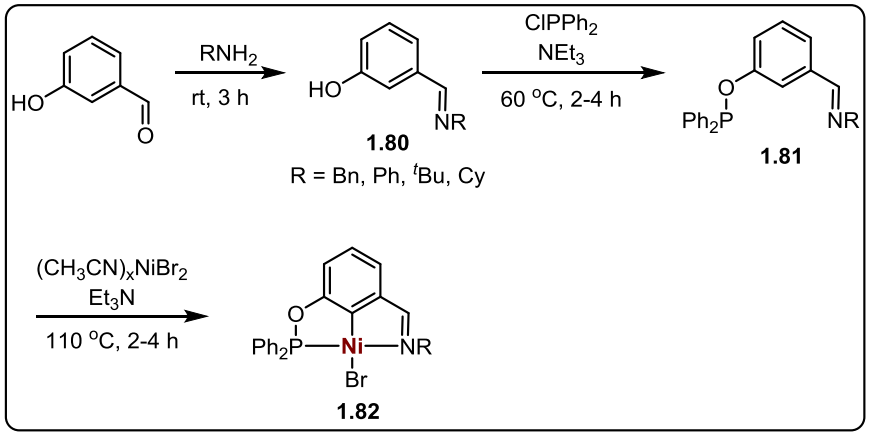
Zargarian *et al*. synthesized the POCOP-ligand and various pincer nickel complexes.[109] The POCOP ligand **1.78** was synthesized from resorcinol by treatment with $ClPPh_2$ in the presence of $Et_3N$ (Scheme 1.35). The POCOP ligand further on reaction with $(CH_3CN)_2NiBr_2$

resulted in the pincer nickel complex **1.79a**, which on reaction with AgX (X = CN, OTf, OAc, $ONO_2$) achieved the corresponding pincer nickel complexes **1.79b-e**.

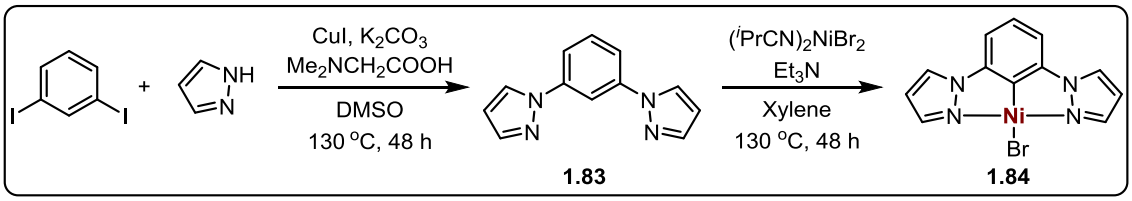



**Scheme 1.35** Synthesis of Bis-Phosphinite POCOP-Pincer Nickel Complexes.

The same research group synthesized imine-phosphinite based POCN-ligands **1.81** by the reaction of 3-hydroxybenzaldehyde with alkylamine and $ClPPh_2$ in the presence of $Et_3N$ (Scheme 1.36).[110] The synthesized POCN-ligands were further reacted with $(CH_3CN)_xNiBr_2$ to obtain the corresponding pincer nickel complexes **1.82**. Similarly, the pyrazole-based NCN-ligand **1.83** was synthesized by the Ullman coupling of pyrazole with 1,3-diiodobenzene.[111] The NCN-ligand **1.83** on reaction with $(^{i}PrCN)_2NiBr_2$ in the presence of $Et_3N$ gave the pincer nickel complex **1.84** through C–H activation (Scheme 1.37).

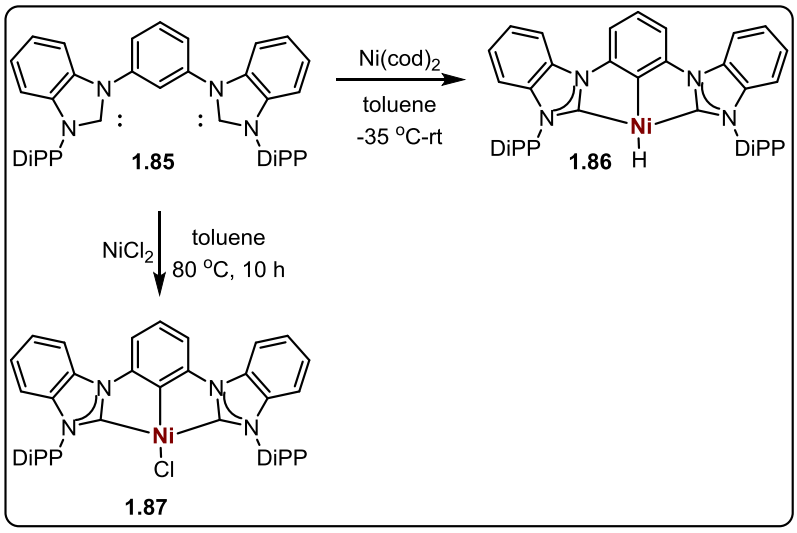



**Scheme 1.36** Synthesis of Imine-Phosphinite based POCN Pincer Nickel Complexes.




**Scheme 1.37** Synthesis of Pyrazole-based NCN-Pincer Nickel Complexes.

In 2015, Fout and coworkers synthesized the NHC-based CCC-pincer nickel hydride complex **1.86** by treating CC(H)C-ligand **1.85** with $Ni(cod)_2$, *via* oxidative addition of C–H bond to Ni(0) (Scheme 1.38); whereas the treatment of the CCC-ligand **1.85** with $NiCl_2$ gave the CCC-pincer nickel chloride complex **1.87** *via* C–H bond activation.[19]

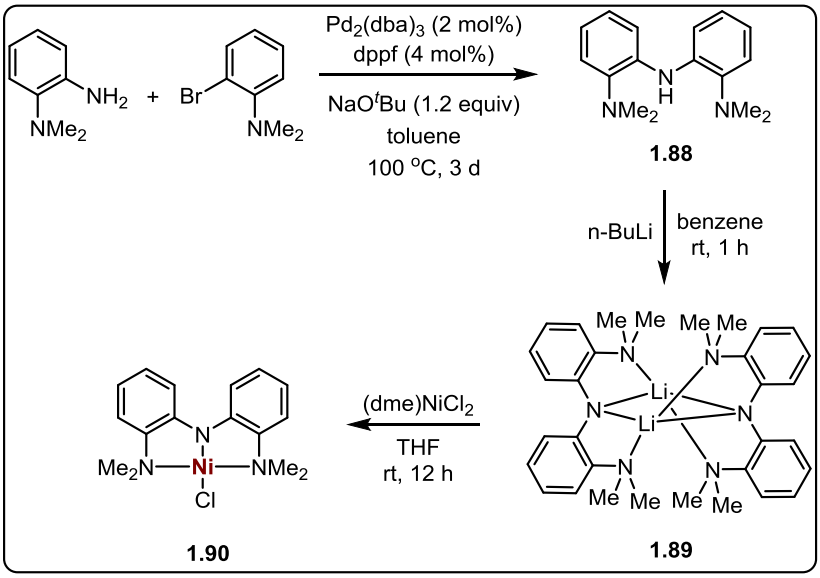



**Scheme 1.38** Syntheses of CCC-Pincer Nickel Chloride and Hydride Complexes *via* C–H Bond Activation.

### 1.4.2 Transmetalation Approach

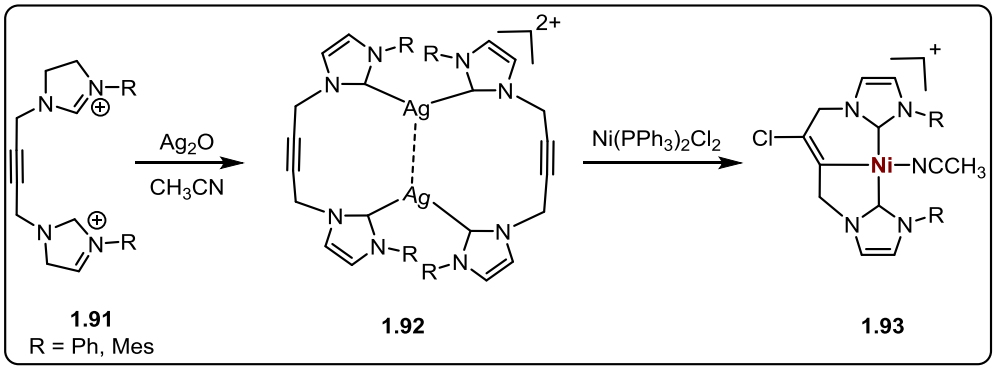
Hu *et al*. synthesized NNN-pincer nickel complex **1.90** and termed it as nickamine.[112] The nickamine was synthesized in three steps starting from 2-bromo-*N*,*N*-dimethylaniline and 2-amino-*N*,*N*-dimethylaniline. The first step involves the Pd(0)/dppf catalyzed C–N coupling reaction. In the second step, the C–N coupled product **1.88** was treated with n-BuLi to obtain a

lithiated NNN-cluster type of compound **1.89**. The final step involves the nickelation of lithiated NNN-cluster *via* transmetalation (Scheme 1.39).



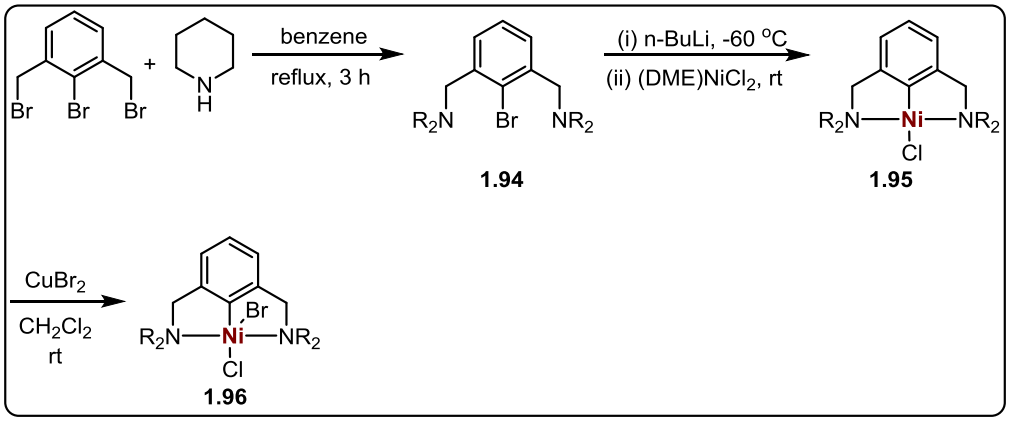

**Scheme 1.39** Synthesis of NNN-Pincer Nickel Complex *via* Transmetalation Approach.

In 2009, Chen and coworkers synthesized the CCC-pincer nickel complexes **1.93** by the transmetalation reactions of the silver complexes **1.92** with $[(PPh_3)_2NiCl_2]$.[20] The complexes **1.92** were obtained by treating the bis(imidazolium) salts **1.91** with $Ag_2O$ (Scheme 1.40). The X-ray diffraction studies showed that the distorted square-planar nickel(II) complexes are supported by anionic terdentate ligands with two imidazolylidenes and one vinyl carbon donor resulting from the chloronickelation of triple bond.



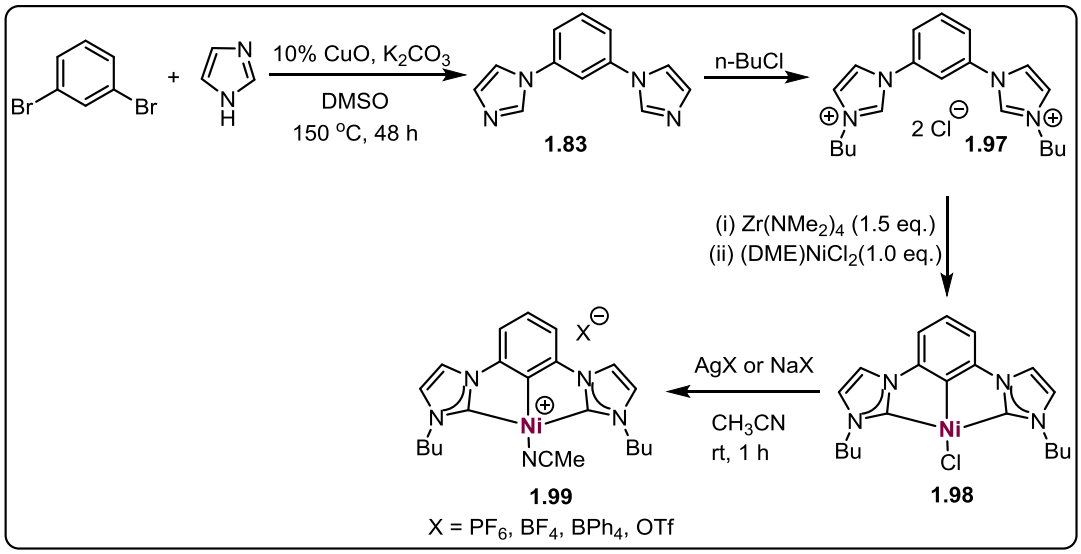

**Scheme 1.40** Synthesis of CCC Pincer Nickel Complexes *via* Transmetalation Approach.

Kozhanov research group developed a mixed halogen NCN-pincer nickel(III) complex **1.96**.[111] In this approach, 2-bromo-1,3-bis(bromomethyl)benzene on reaction with piperidine gave the aminated compound **1.94**, which on lithiation followed by the treatment with (DME)$NiCl_2$ resulted in the formation of NCN-pincer nickel(II) complex **1.95** *via* transmetalation. The oxidation of the pincer nickel(II) complex **1.95** with an excess of $CuBr_2$ produced the corresponding NCN-pincer nickel(III) complex **1.96** (Scheme 1.41). This was the first structurally characterized mixed halogen NCN-pincer nickel(III) complex having square pyramidal geometry, wherein the bromine atom occupies the apical position and the chlorine atom is in the basal plane. The authors recorded the EPR spectrum of the corresponding solution and found that there exists an equilibrium mixture of two structural isomers with bromine or chlorine atoms in the apical position (top of a pyramid).



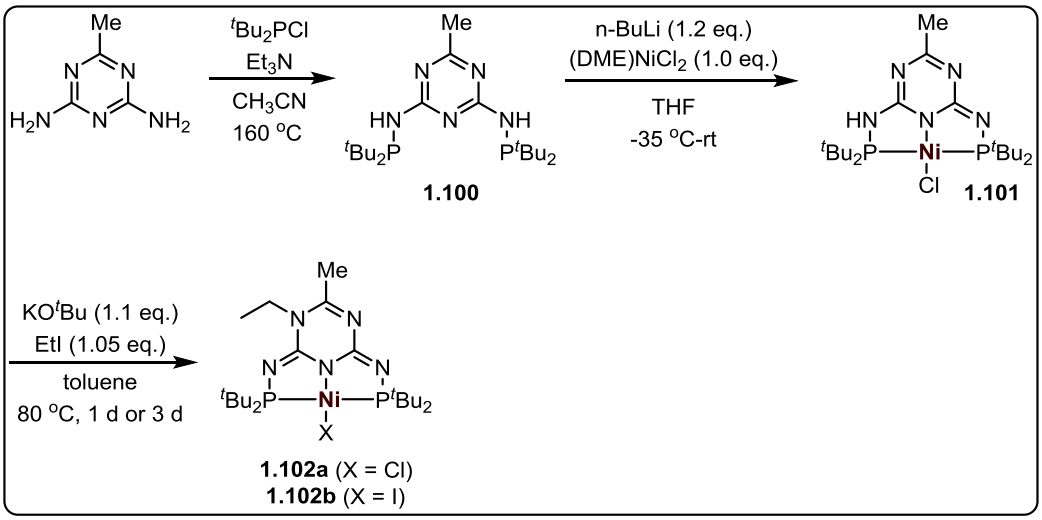

**Scheme 1.41** Synthesis of Mixed Halogen NCN-Nickel(III) Pincer Complexes.

In 2003, Hollis *et al*. synthesized the NHC-based CCC-ligand **1.83** by the C–N bond coupling reaction between 1,3-dibromobenzene and imidazole using CuO and $K_2CO_3$ (Scheme 1.42).[113] Recently the same research group synthesized CCC-pincer nickel(II) complex **1.98** by the treatment of CCC-ligand **1.97** with $Zr(NMe_2)_4$ followed by the reaction with (DME)$NiCl_2$ *via* transmetalation. The reaction of the neutral nickel(II) complex with AgX or NaX produced the cationic complexes **1.99**.[114]




**Scheme 1.42** Synthesis of CCC-Pincer Nickel Complexes.

Recently, Huang research group reported the synthesis of PN$^3$P ligand **1.100** by treating 2,4-diamino-6-methyl-1,3,5-triazine with $^t$Bu$_2$PCl in the presence of Et$_3$N at 160 $^o$C in a sealed reaction vessel (Scheme 1.43).[115] The PN$^3$P ligand **1.100** was then treated with (DME)NiCl$_2$ in the presence of n-BuLi to afford the corresponding PN$^3$P-pincer nickel chloride complex **1.101**. The complex **1.101** further on reaction with EtI in the presence of KO$^t$Bu produced 1-ethyl PN$^3$P-pincer nickel chloride complex **1.102a** in a reaction time of 1 day and the iodo-derivative **1.102b** was achieved in a reaction time of 3 days.



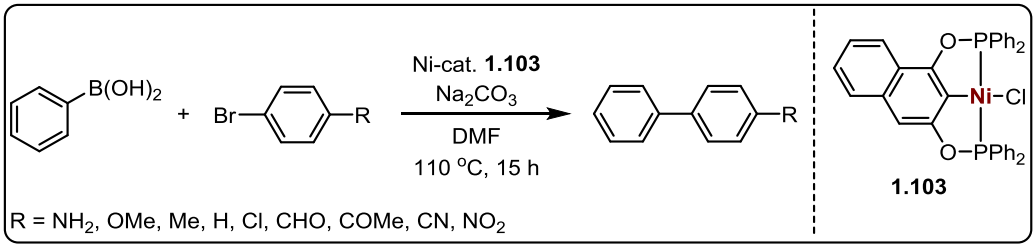

**Scheme 1.43** Synthesis of PN$^3$P-Pincer Nickel Complexes.

## 1.5 Catalytic Applications of Pincer Nickel Complexes

### 1.5.1 Traditional Cross-Coupling Reactions

#### 1.5.1.1 Suzuki-Miyaura Coupling Reaction

Morales-Morales *et al*. synthesized the POCOP-pincer nickel complex **1.103** and employed in the cross-coupling of different *para*-substituted bromobenzenes with phenylboronic acid to obtain the biphenyl derivatives in good yields (Scheme 1.44).[116] Another interesting characteristic of the catalytic system is an easier synthesis from cheap, commercially available starting materials and the use of considerable cheaper and biocompatible Ni(II), thus making this system attractive for its potential application in organic synthesis.




**Scheme 1.44** POCOP-Pincer Nickel Catalyzed Suzuki-Miyaura Coupling Reaction.

In 2017, Chen *et al*. synthesized NHC-based unsymmetrical NCN-pincer mononuclear and dinuclear nickel(II) complexes **1.104** (Figure 1.8) and demonstrated their catalytic application in the Suzuki-Miyaura coupling reaction of aryl iodides and aryl bromides at 110 °C, wherein the aryl chlorides were successfully coupled in the presence of $PPh_3$ as an additive.[117]

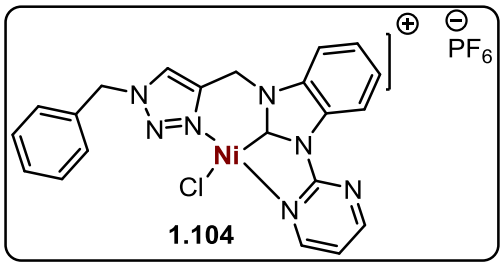
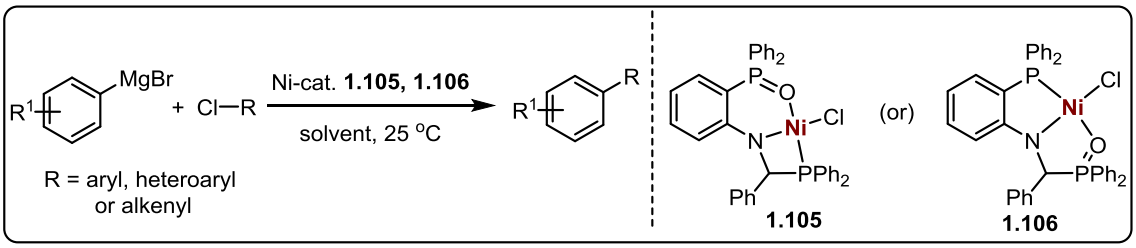



**Figure 1.8** NHC-based unsymmetrical NCN-pincer complex in Suzuki-Miyaura coupling.

### 1.5.1.2 Kumada Coupling Reaction

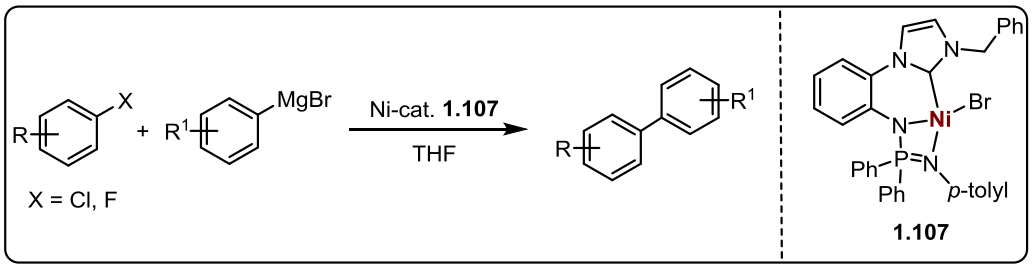
Wang and coworkers synthesized 4/6-fused and 5/5-fused PNO-pincer nickel complexes **1.105** and **1.106**, respectively, which showed application in Kumada coupling reaction of (hetero)aryl/alkenyl chlorides with aryl magnesium bromides (aryl Grignard reagents) (Scheme 1.45).[118] The reactions were conducted at room temperature and tolerated various functional groups on aryl chlorides in the presence of LiCl or $ZnCl_2$ as additives.



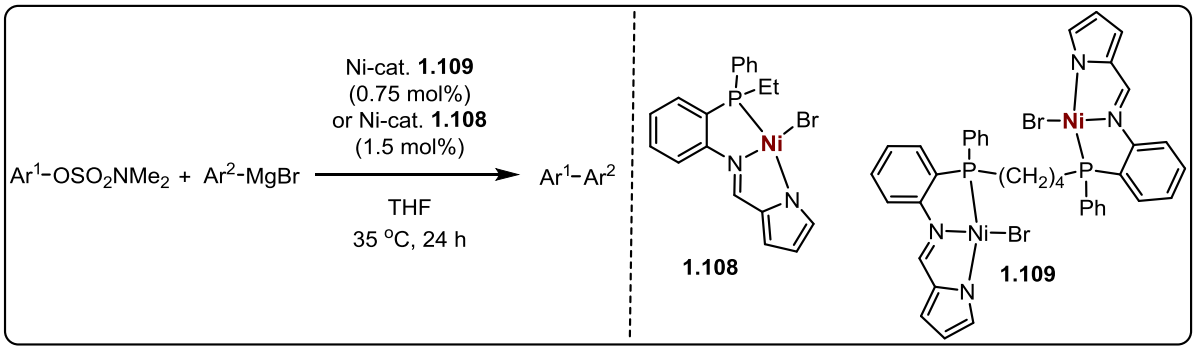

**Scheme 1.45** PNO-Pincer Nickel Catalyzed Kumada Coupling Reaction.

Hu research group utilized the nickamine catalyst **1.90** in Sonogashira coupling reaction of alkyl halides with alkyl Grignard reagents,[119] (hetero)aryl Grignard reagents,[120] and alkynyl Grignard reagents.[121] Good yields were obtained in this cross-coupling, and overcome the inertness of alkyl halides and the decomposition of catalytic intermediates *via* facile *β*-hydride elimination. Although Ni-catalyzed alkyl–alkyl coupling has been reported by a number of research groups, nickamine **1.90** is one of the very few isolated and well-characterized precatalysts known. The resting state of the catalysis is the Ni–alkyl/(hetero)aryl/alkynyl species. Transmetalation occurred before the activation of organic halides in the catalytic cycle. Hence, the mechanism of this catalysis is unique, which can be beneficial in terms of substrate scope and selectivity.[122] In 2013, Wang *et al*. developed the NHC-based CNN-pincer nickel complexes **1.107** and employed in the Kumada coupling of aryl chlorides and fluorides (Scheme 1.46).[123] The CNN-pincer nickel complex catalyzed the cross-coupling of activated, unactivated and deactivated chloroaromatics and fluoroaromatics efficiently with aryl Grignard reagents under mild conditions. In the same year, they developed the PNN-pincer nickel complexes with [4,5]-fused nickelacycles (Figure 1.9: **A**) for the catalytic Kumada coupling of variously substituted aryl chlorides, heteroaryl chlorides, vinyl chlorides and 1,4-dichlorobenzene.[124] In 2014, the

same group synthesized the PNN-pincer nickel complexes with [5,5]-fused nickelacycles (Figure 1.9: **B**) and utilized them in aryl C–Cl and C–F bond activation.[125] These complexes efficiently catalyzed the cross-coupling reaction of distinct aryl fluorides and 2-/3-fluoropyridines with aryl Grignard reagents forming biaryls in good yields. Again in 2014, the group synthesized mono- and dinuclear PNN-pincer nickel complexes **1.108** and **1.109**, respectively, which were demonstrated to be active catalyst for the cross-coupling reaction of aryl sulfamates with aryl Grignard reagents (Scheme 1.47).[126] The reaction was explored with a broad substrate scope, including electron-rich and electron-deficient electrophiles and nucleophiles. The dinuclear complexes showed better catalytic activity than the mononuclear complexes under comparable conditions. This is accredited to cooperative effects in a bimetallic system. Sun *et al*. demonstrated the CNN-pincer nickel complexes with NHC-amine arms (Figure 1.9: **C**) to be the active catalyst for the Kumada coupling of aryl chlorides or aryl dichlorides under mild conditions.[127] Interestingly, activated aryl chlorides with an electron-withdrawing group ($–CF_3$) gave relatively lower yields compared to the unactivated aryl chlorides including p-$MeC_6H_4Cl$ and p-$MeOC_6H_4Cl$. When a sterically hindered Grignard reagent, such as *o*-$MeC_6H_4MgBr$, was used as the nucleophilic species, only lower yields were obtained than those with less hindered reagents *p*-$MeC_6H_4MgBr$ and *p*-$MeOC_6H_4MgBr$.




**Scheme 1.46** NHC-based NCN-Pincer Nickel Catalyzed Kumada Coupling Reaction.




**Scheme 1.47** Mono- and Di-nuclear PNN-Pincer Nickel Catalyzed Kumada Reaction.

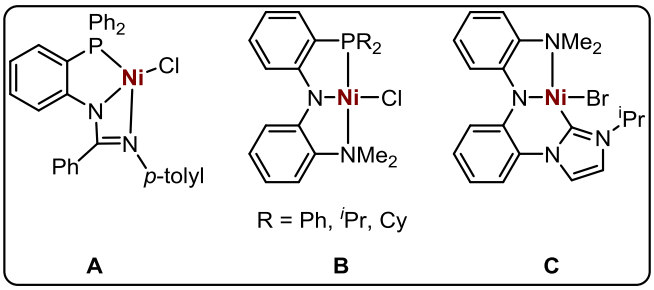


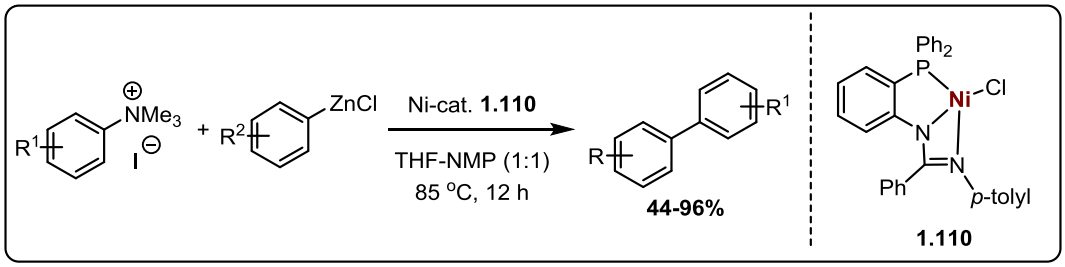

**Figure 1.9** (PNN)Ni complexes with [4,5]-fused, [5,5]-fused nickelacycles (**A**, **B**) and (CNN)Ni complex with NHC-amine arms (**C**) in Kumada coupling reaction.

### 1.5.1.3 Negishi Coupling Reaction

In 2012, Wang and coworkers reported the synthesis of PNN-pincer nickel complex with [4,5]-fused nickelacycles **1.110** and employed in the Negishi coupling reaction of aryltrimethylammonium iodides with (hetero)arylzinc chlorides (Scheme 1.48).[128] This reaction displayed broad substrate scope with low catalyst loading. Further, this reaction proved the potential of PNN-pincer nickel catalyst system for the C–N bond activation of aryltrimethylammonium salts.

The PNN-pincer nickel complexes (Figure 1.8) were also demonstrated to be active catalysts for the coupling of (hetero)aryl chlorides with arylzinc reagents.[125] The zinc reagents used in the reaction include electron-rich and electron-poor substituted phenylzinc chlorides and 2-furylzinc chloride. In most of the cases, the reactions needed low catalyst loadings and showed functional group tolerance including PhC(O), COOEt, $C(O)NEt_2$, CN, $CF_3$ and nitrogen-containing heterocycles. The mono- and dinuclear PNN-pincer nickel complexes **1.108** and

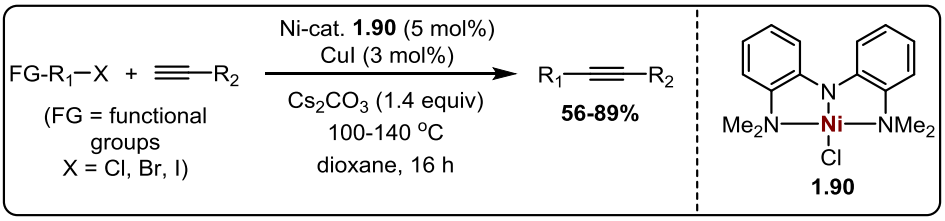
**1.109**, respectively were also used as active catalysts for the cross-coupling reaction of aryl chlorides or aryltrimethylammonium iodides with arylzinc reagents (Scheme 1.48).[126]



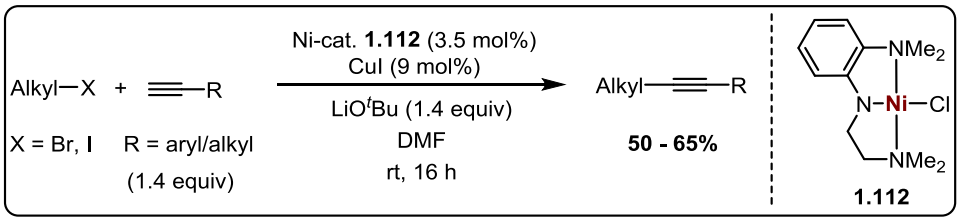

**Scheme 1.48** PNN-Pincer Nickel Complexes with [4,5]-Fused Nickelacycles in Negishi Reaction.

### 1.5.1.4 Sonogashira Coupling Reaction

Hu *et al*. employed the nickamine catalyst **1.90** in Sonogashira coupling reaction of non-activated alkyl halides with terminal alkynes (Scheme 1.49).[122] In 2015, Hu *et al*. synthesized NNN-pincer nickel complex **1.112** in a single step from 2-bromo-*N*,*N*-dimethylaniline and *N*,*N*-dimethylethylenediamine and employed in the Sonogashira coupling reaction, *i.e*. direct coupling of primary alkyl halides with terminal alkynes at room temperature.[129] In this catalysis, broad substrate scope and high functional group tolerance were observed (Scheme 1.50).



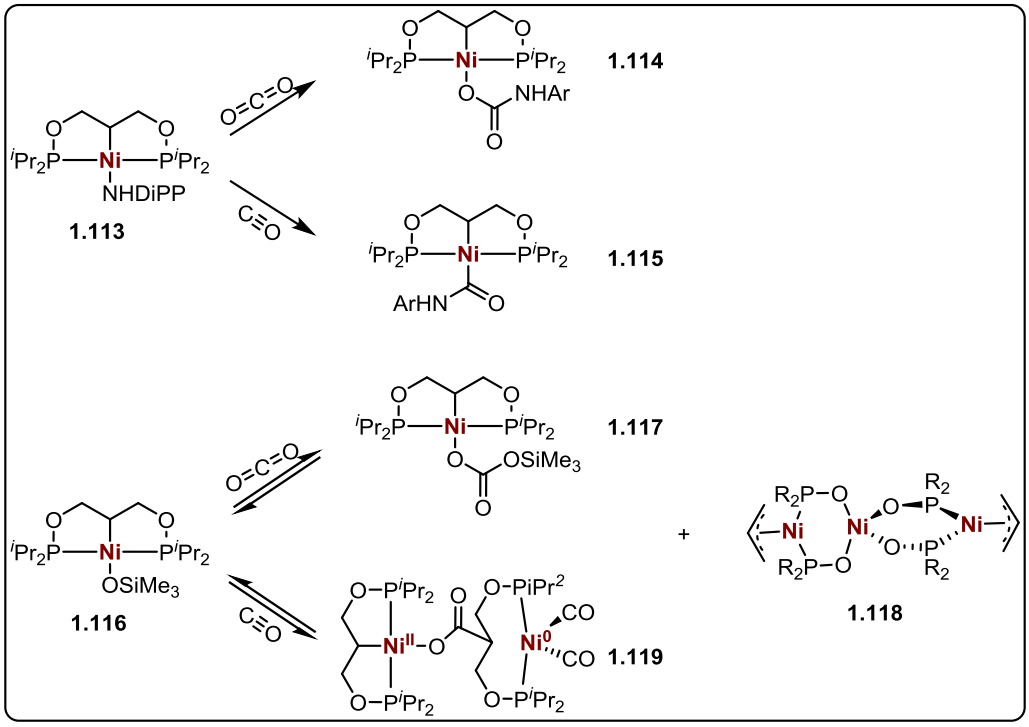

**Scheme 1.49** Nickamine Catalyzed Sonogashira Coupling Reaction.




**Scheme 1.50** NNN-Pincer Nickel Catalyzed Sonogashira Coupling Reaction.

### 1.5.1.5 Small Molecule Activation

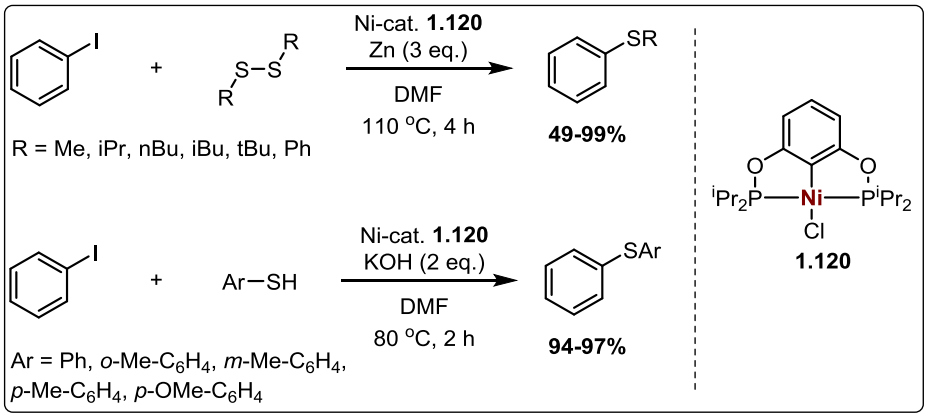
In 2014, Zargarian *et al*. synthesized the $POC_{sp3}OP$–Ni–X (X = $OSiMe_3$, N(DiPP)H) complexes and employed in the activation of small molecules such as $CO_2$, CO, $O_2$, and ArNC.[130] The amido derivative **1.113** on reaction with $CO_2$ and CO resulted in formation of stable carbamate **1.114** and carbamoyl derivatives **1.115**, respectively through their insertion into Ni–N bond. However, the siloxido derivative **1.116** gave kinetically labile insertion products **1.117** that either revert to the starting material (in case of $CO_2$) or react further to give the mixed-valent, dinickel species [$(POC_{sp3}OP)NiOC(O)CH(CH_2OP^iPr_2)_2Ni(CO)_2$] (**1.119**). The zero-valent nickel center is ligated by a new ligand arising from transformation of the $POC_{sp3}OP$ ligand backbone. The authors identified a minor amount of trinickel species [$\{(\eta^3$-allyl)-Ni($\mu^O$,$\kappa^P$-$R_2PO)_2\}_2Ni$] (**1.118**) arising from the complete dismantling of the $POC_{sp3}OP$ ligand (Scheme 1.51).




**Scheme 1.51** Small Molecule Activation by $POC_{sp3}OP$-Pincer Nickel Complex.

### 1.5.1.6 C–S Cross-Coupling Reaction

The cross-coupling of alkyl or aryl halides with thiols or disulfides to form the C–S bond is considered as C–S cross-coupling reaction.[131] In 2006, Morales-Morales and coworkers utilized the POCOP-pincer nickel catalyst **1.120** in the effective thiolation of iodobenzene with alkyl and aryl disulfides in DMF to obtain the C–S coupled products in yields up to 99% (Scheme 1.52).[116] This method employed 3 equiv of Zn for the reduction of Ni(II) to Ni(I) as well as Ni(III) to Ni(II). In 2010, Guan *et al*. reported the direct C–S bond formation from the coupling of iodobenze with thiols employing the pincer nickel-catalyst **1.120** (Scheme 1.52).[132] This improved method used a base KOH instead of Zn-powder to produce the active catalytic species.

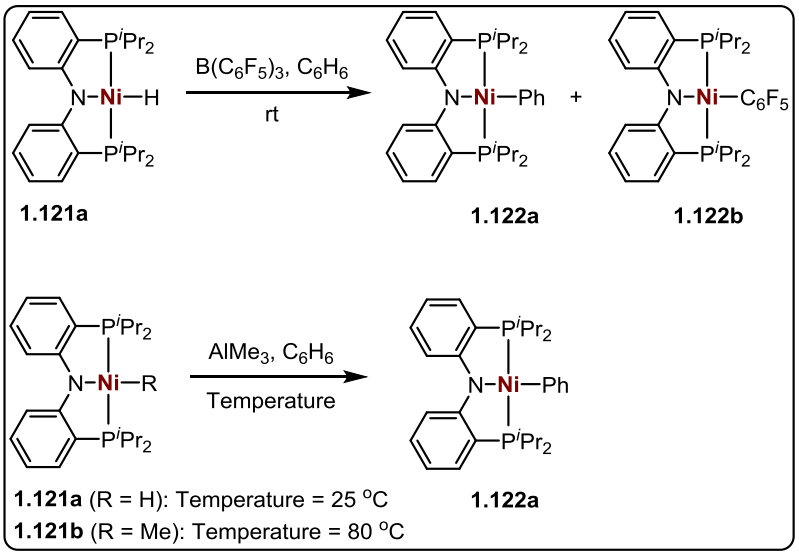



**Scheme 1.52** POCOP-Pincer Nickel Catalyzed C–S Cross-Coupling Reaction.

## 1.5.2 C–H bond Activation Reactions

### 1.5.2.1 Intermolecular C–H Activation

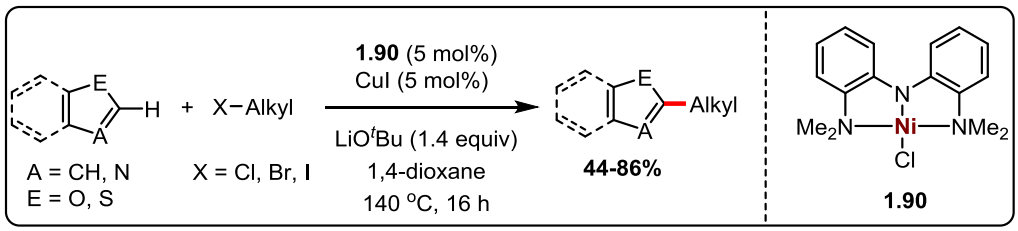
Huang and coworkers demonstrated an efficient intermolecular arene C–H activation mediated by PNP-pincer nickel(II) complexes **1.121** under mild conditions.[133] The authors found the remarkable reactivity of inexpensive Ni(II) as an alternatives of 4d and 5d metals (Scheme 1.53). In this examples, the nickel-hydride complex **1.121a** on reaction with $(C_6F_5)_3B$ in $C_6H_6$ obtained the nickel-phenyl **1.122a** and the nickel-pentafluorophenyl **1.122b** complexes.




**Scheme 1.53** Intermolecular Arene C–H Activation by PNP-Pincer Nickel(II) Complexes.

### 1.5.2.2 C–H Bond Alkylation

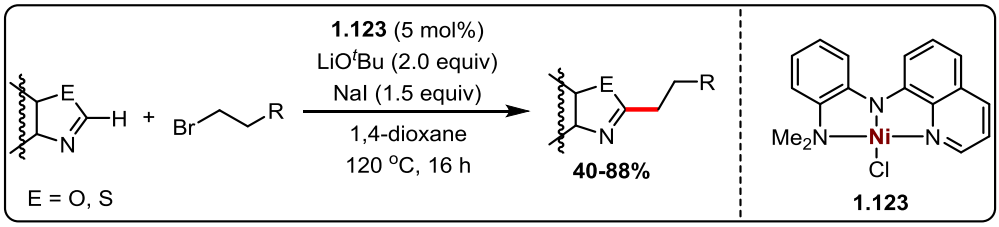
Hu *et al*. employed the nickamine catalyst **1.90** in the C–H bond alkylation of aromatic heterocyclic compounds, where the functionalization took place exclusively at the 2-position of the heterocycles even in presence of more than one reaction site on the heterocycle (Scheme 1.54).[134] In this approach the authors did not observe the formation of any di-alkylated product, which is an advantage in comparison to Friedel-Crafts reactions. Notably, in this method CuI was used as a co-catalyst in addition to nickel catalyst.



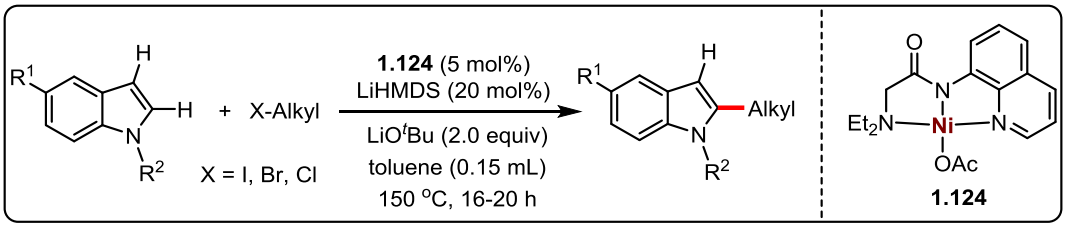

**Scheme 1.54** Nickamine Catalyzed C–H Bond Alkylation of Aromatic Heterocycles.

Similarly, in 2016, Punji *et al*. reported the synthesis of quinoline-based NNN-pincer nickel complex **1.123** and employed in the C–H bond alkylation of azoles with alkyl halides (Scheme 1.55).[135] Importantly, the addition of copper co-catalyst was not necessary in this

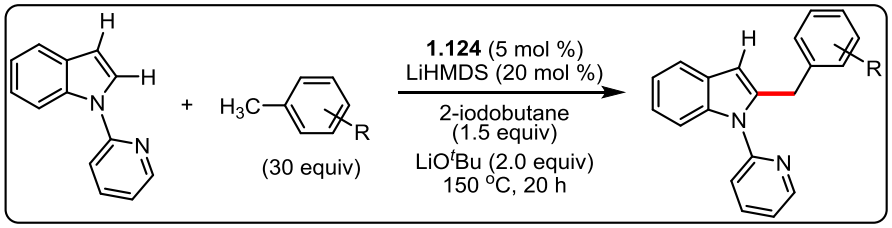
developed method. In the same year, the group reported the synthesis of quinolinamide-based NNN-pincer nickel complex **1.124** and utilized in the C–H bond alkylation of indoles at C-2 position through chelation assistance (Scheme 1.56).[136] This uniquely strategized alkylation proceeded through crucial C−H activation and *via* an alkyl radical intermediate. The reaction by this approach represents a rare example of Ni-catalyzed monodentate chelate-assisted C−H functionalization. In 2017, the group utilized the same catalyst to explore the C($sp^2$)–H/C($sp^3$)–H oxidative coupling of indoles with toluene derivatives (Scheme 1.57).[137] The pincer nickel complex **1.124** was proved to follow the radical pathway during the reaction. The reaction proceeded through a single-electron-transfer (SET) process, wherein both the C− H nickelation of indole and the C−H activation of toluene derivatives have a significant effect on the entire reaction rate.




**Scheme 1.55** Quinoline-based NNN-Pincer Nickel Catalyzed Alkylation of Azoles.



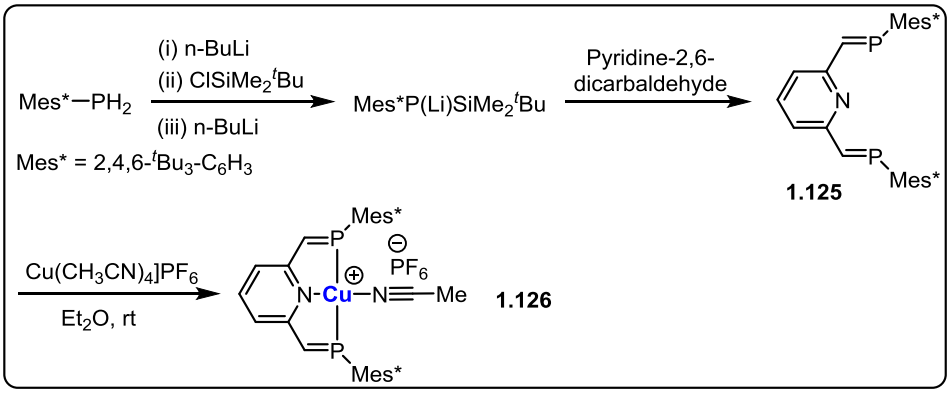

**Scheme 1.56** Quinolinamide-based NNN-Pincer Nickel Catalyzed C-2 Akylation of Indoles.




**Scheme 1.57** NNN-Pincer Nickel Complexes in C($sp^2$)–H/C($sp^3$)–H Oxidative Coupling of Indoles with Toluene Derivatives.

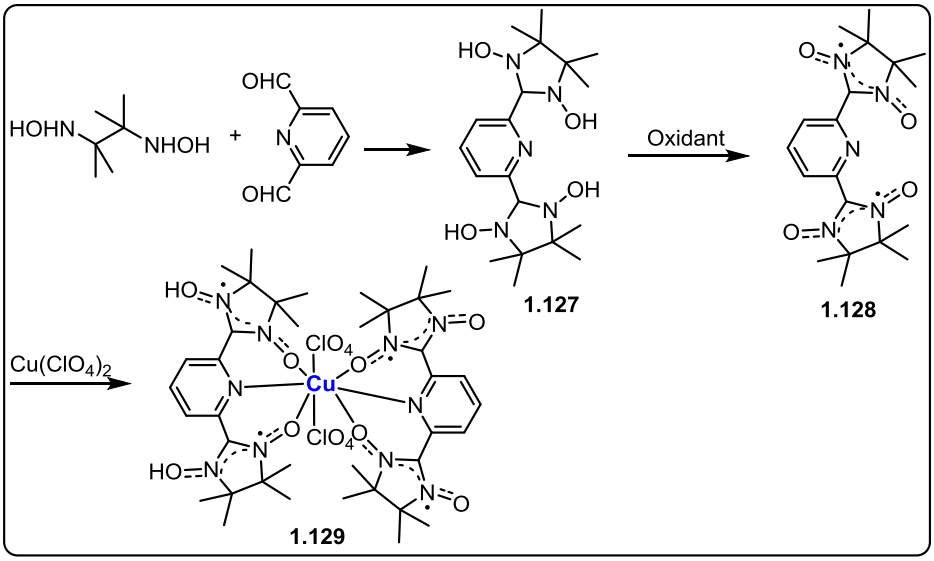
## 1.6 Syntheses of Pincer Copper Complexes

The pincer copper complexes could be synthesized in several ways. Some of the synthetic approaches are discussed in this section. In 1992, Geoffroy and coworkers synthesized the PNP-ligand **1.125** by the reaction of pyridine-2,6- dicarbaldehyde with the lithiated phosphine.[138] Ozawa *et al*. reported the reaction of PNP-ligand **1.125** with $[Cu(CH_3CN)_4]PF_6$ to obtain the corresponding PNP-pincer copper(I) cationic complex **1.126** (Scheme 1.58).[139] Aliphatic chain based PNP-pincer copper complexes were also known in the literature.[140] In 2014, Iluc and coworkers synthesized the olefinic backbone containing PNP-pincer copper complex.[141] In addition to this, Kumar *et al*. reported the synthesis of bis(phosphomide) based PNP-pincer copper complexes.[142]



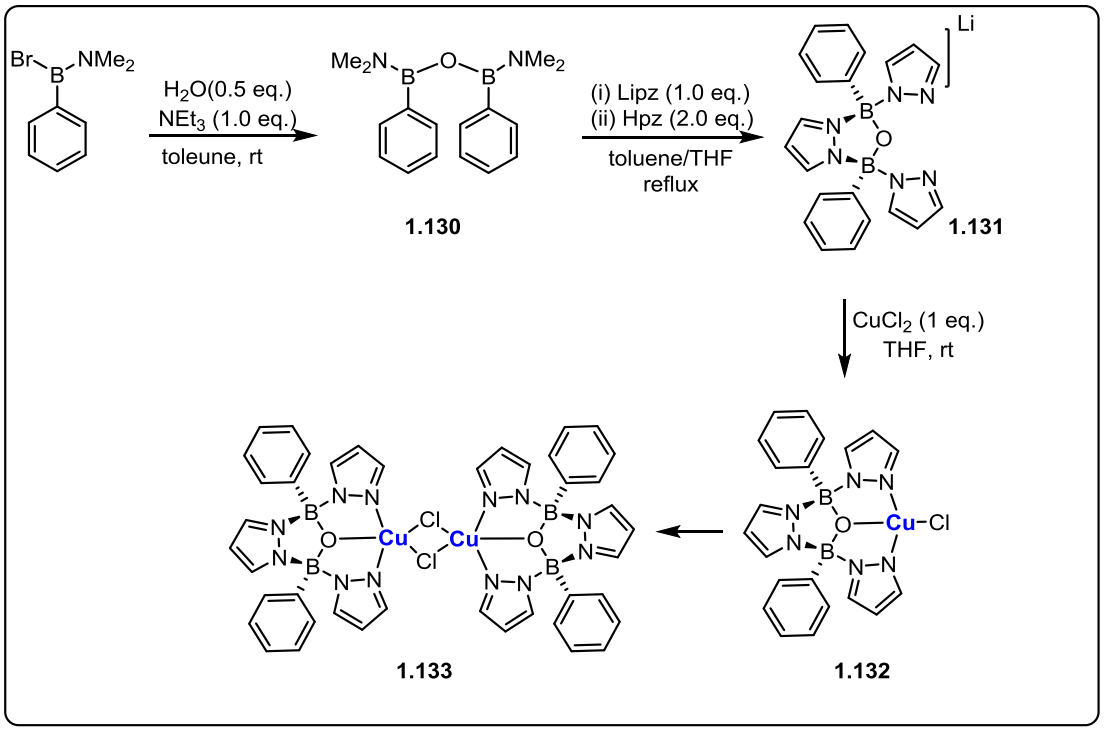

**Scheme 1.58** Synthesis of PNP-Pincer Copper(I) Cationic Complex.

In 1999, Ziessel *et al*. reported the synthesis of ONO-ligand **1.128** starting with pyridine-2,6-dicarbaldehyde in two steps *via* the compound **1.127**, and the corresponding ONO-pincer copper complex **1.129** upon reaction with $Cu(ClO_4)_2$ (Scheme 1.59).[143] In continuation, Klein *et al*. synthesized a variety of ONO-pincer copper complexes.[144]



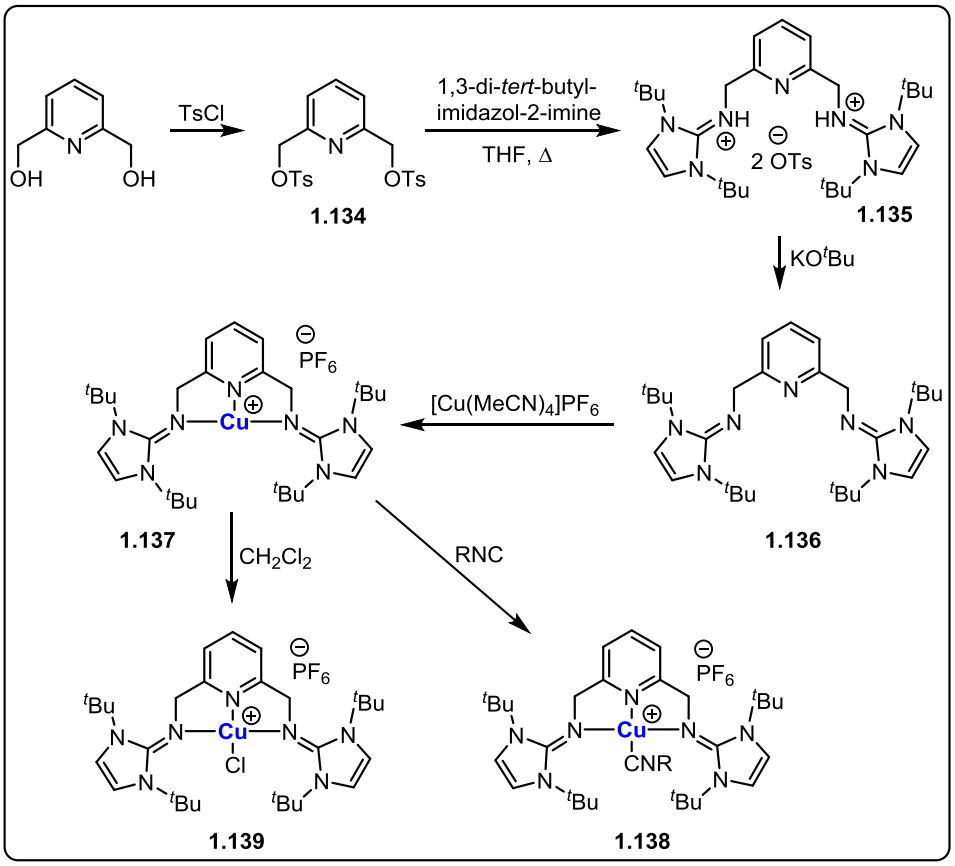

**Scheme 1.59** Synthesis of ONO-Ligand and Pincer Copper(II) Complex.

Wagner research group reported the synthesis of NON-ligand **1.131** starting from 1-bromo-*N*,*N*-dimethyl-1-phenylboranamine in two steps *via* compound **1.130**.[145] The NON-ligand **1.131** further on reaction with $CuCl_2$ resulted in the formation of NON-pincer copper chloride complex **1.132**, which crystallizes as chloro-bridged dimer **1.133** (Scheme 1.60). In extension, NSN-pincer copper complexes were reported by Contel research group and demonstrated in the oxidation of alkenes and as an antimicrobial agent.[146]



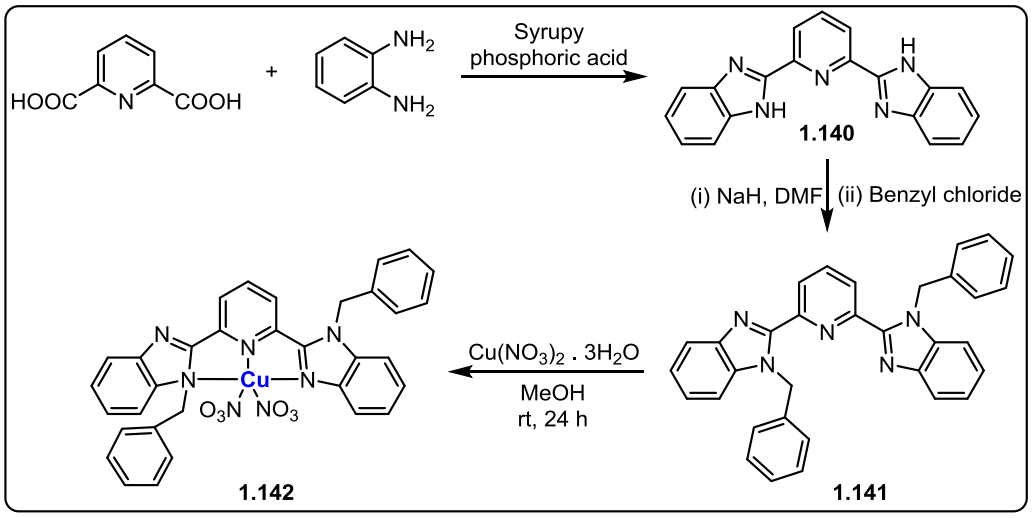

**Scheme 1.60** Synthesis of NON-Pincer Copper(II) Complex *via* Transmetalation.

Tamm *et al.* reported the synthesis of NNN-ligand **1.136** from 2,6-bis(hydroxymethyl)pyridine and 1,3-di-*tert*-butylimidazolin-2-imine (Scheme 1.61).[147] The NNN-ligand **1.136** on reaction with $[Cu(CH_3CN)_4]PF_6$ resulted the NNN-pincer copper(I) cationic complex **1.137** which forms the stable copper(I) isocyanide cationic complex **1.138** whereas in chlorinated solvents like $CHCl_3$ or $CCl_4$, it abstracts chloride by reductive dechlorination of the solvent to form the corresponding copper(II) cationic complex **1.139**.



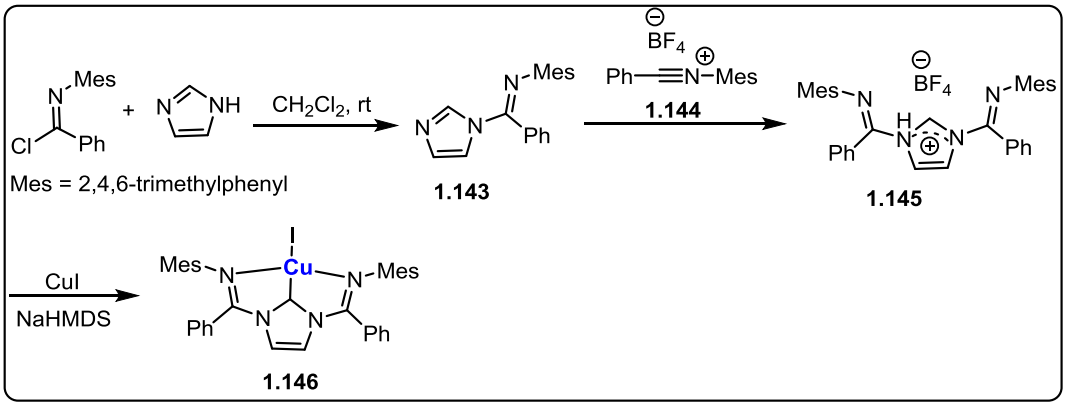

**Scheme 1.61** Synthesis of NNN-Ligand and Pincer Copper(I)/Copper(II) Cationic Complexes.

Chen and coworkers synthesized the benzimidazole-based NNN-ligand **1.141** (Scheme 1.62).[148] In this approach pyridine-2,6-dicarboxylic acid on reaction with 1,2-phenylenediamine resulted in the formation of intermediate compound **1.140**, which on reaction with benzyl chloride in the presence of NaH in DMF produced the ligand **1.141**. The NNN-ligand **1.141** on reaction with $Cu(NO_3)_2$ resulted in the formation of the NNN-pincer copper(II) complex **1.142**.



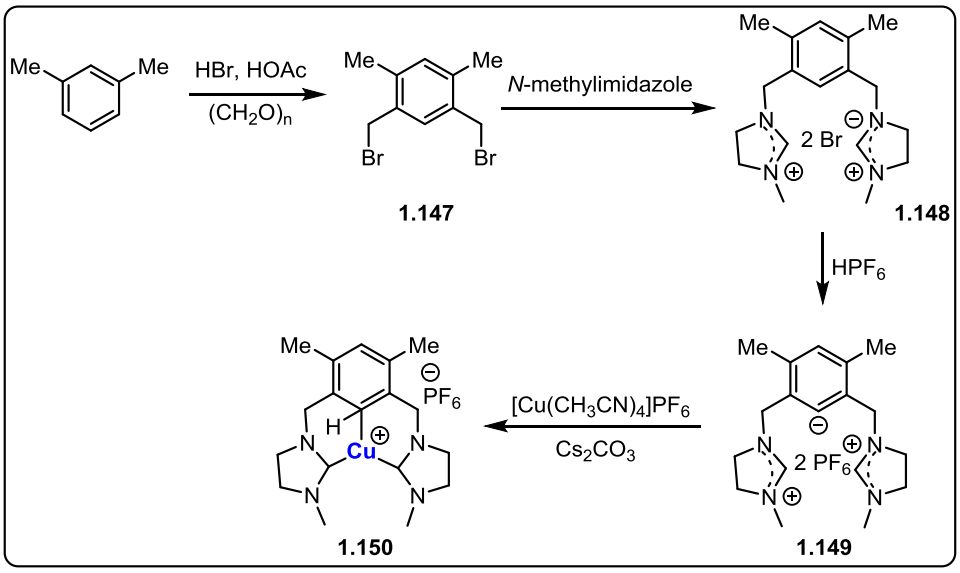

**Scheme 1.62** Synthesis of Benzimidazole-based NNN-Pincer Copper(II) Complex.

In 2010, Lavoie *et al*. synthesized NCN-ligand **1.145** and the corresponding pincer copper complex **1.146** *via* C–H bond activation strategy (Scheme 1.63).[149] The synthesis of NCN-ligand **1.145** started from *N*-mesitylbenzimidoyl chloride in two steps. In this method, *N*-mesitylbenzimidoyl chloride was treated with imidazole to give the *N*-mesityliminobenzyl imidazole **1.143**, which further reaction with reactive nitrilium salt **1.144** (generated *in situ* by the reaction of the *N*-mesitylbenzimidoyl chloride with sodium tetrafluoroborate) produced the imidazolium salt NCN-ligand **1.145**. The imidazolium salt on treatment with CuI in the presence of NaHMDS produced the NCN-pincer copper(I) complex **1.146**, which was the first copper(I) complex with bis(imino) NHC-based NCN-ligand.



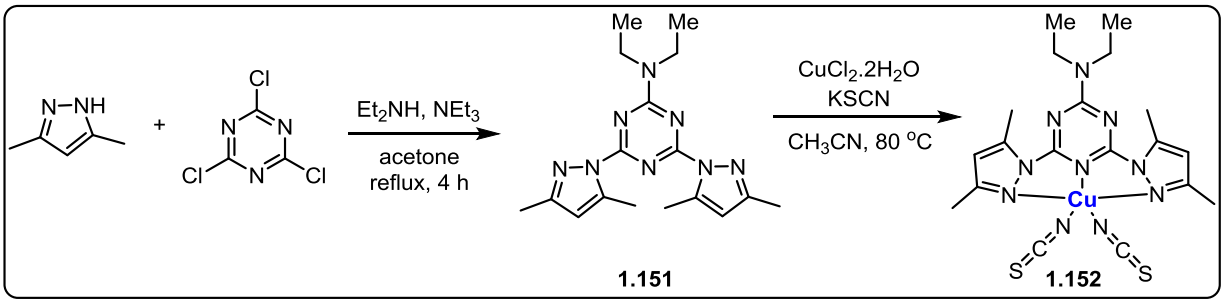

**Scheme 1.63** Synthesis of First Copper(I) Complex with Bis(imino) NHC-based NCN-Ligand.

Braunstein and coworkers reported the synthesis of NHC-based CCC-ligand **1.149** and pincer copper complex **1.150** (Scheme 1.64).[150] In this approach xylene on reaction with paraformaldehyde in the presence of HBr afforded bis(bromomethyl) compound **1.147**, which further on reaction with *N*-methylimidazole, $HPF_6$ gave the imidazolium salt (CCC-ligand **1.149**). The CCC-ligand **1.149** on reaction with $[Cu(CH_3CN)_4]PF_6$ in the presence of $Cs_2CO_3$ yielded Cu(I) cationic complex **1.150** in excellent yield.



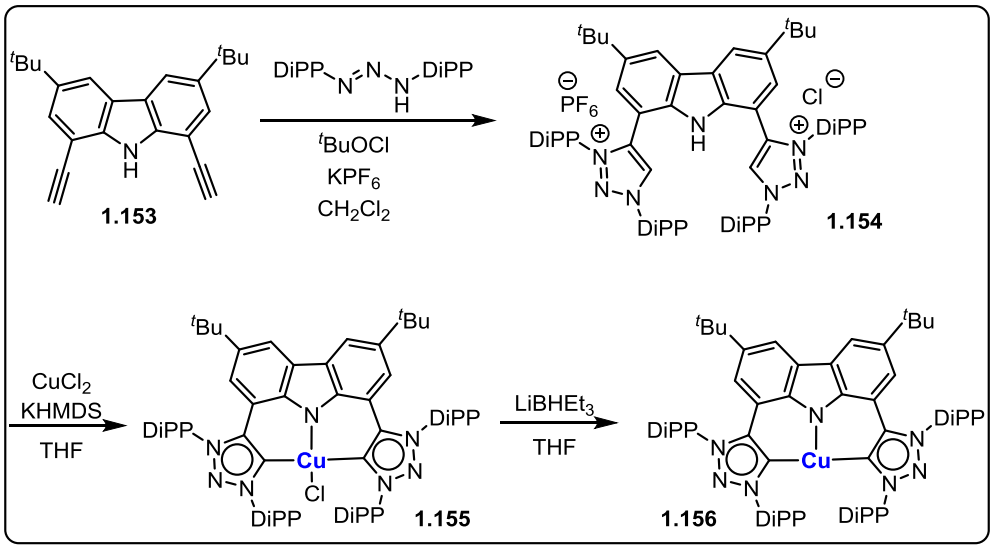

**Scheme 1.64** Synthesis of NHC-based CCC-Pincer Copper(I) Cationic Complex.

In 2013, Xing research group demonstrated the synthesis of 1,3,5-triazine based NNN-pincer copper di-isothiocyanate complex **1.152** (Scheme 1.65).[151] In this approach the ligand used for the synthesis of pincer complex was prepared by the reaction of 3,5-dimethylpyrazole with 2,4,6-trichloro-1,3,5-triazine as reported by the Lu group. After successful synthesis of the ligand **1.151**, the pincer copper complex **1.152** was obtained on reaction with $CuCl_2.2H_2O$ and KSCN in acetonitrile at 80 $^oC$.[152]




**Scheme 1.65** Synthesis of 1,3,5-Triazine based NNN-Pincer Copper(II) Complex.

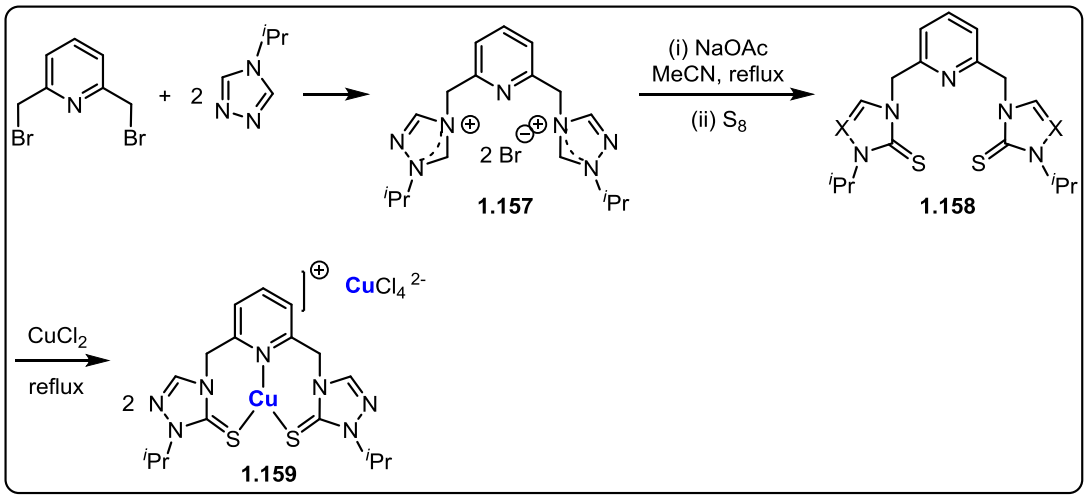
Bezuidenhout *et al*. performed the reaction of 3,6-di-*tert*-butyl-1,8-diethynyl-9*H*-carbazole (**1.153**) with 1,3-bis-(2,6-diisopropylphenyl)triazene in the presence of $^{t}$BuOCl, and $KPF_6$ to obtain the imidazolium salt (CNC ligand **1.154**) which on treatment with $CuCl_2$ in the presence of KHMDS produced CNC-pincer copper(II) complex **1.155** (Scheme 1.66).[153] The complex on reaction with superhydride at -78 $^{o}$C produced the CNC-pincer copper(I) 3-coordinate complex **1.156**. In addition the NHC-based NCN-pincer copper complexes were also reported in the literature.[154,155]



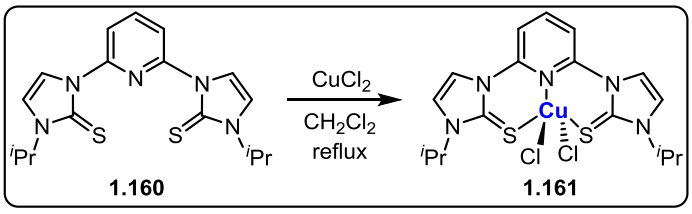

**Scheme 1.66** Synthesis of NHC-based CNC-Pincer Copper(I) Complex.

In 2011, Miecznikowski *et al*. synthesized the bis(thione)-based SNS ligands **1.158** starting from 2,6-bis(bromomethyl)pyridine in two steps.[156] In the first step, 2,6-

bis(bromomethyl)pyridine was treated with 4-isopropyl-1,2,4-triazole derivative to obtain the triazolium salt **1.157**. The second step involves the reaction of triazolium salt **1.157** with NaOAc followed by treatment with $S_8$. The same research group synthesized the SNS-pincer copper(I) cationic complex **1.159** by the reaction of SNS-ligand **1.158** with $CuCl_2$ (Scheme 1.67).[157] In the same year, the research group synthesized five-coordinate copper(II) complex **1.161** bearing a neutral SNS pincer ligand **1.160** and two anionic chloride ligands (Scheme 1.68).[158]

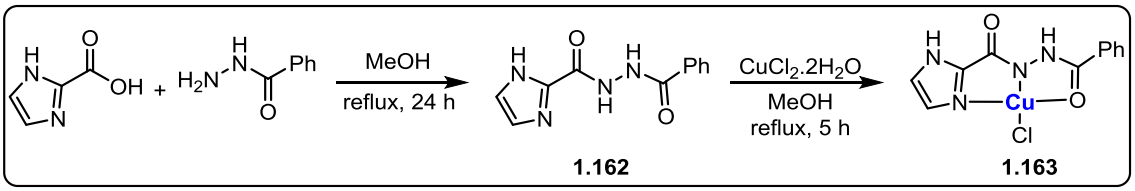



**Scheme 1.67** Synthesis of Bis(thione)-based SNS-Pincer Copper(I) Cationic Complex.



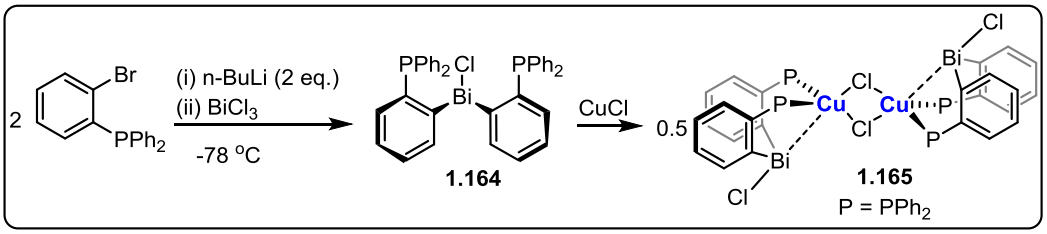

**Scheme 1.68** Synthesis of Bis(thione)-based SNS-Pincer Copper(II) 5-Coordinate Complex.

Dharmaraj research group developed the imidazole-based ONN-ligand **1.162** by the treatment of imidazole-2-carboxylic acid with phenylhydrazide.[159] The ONN-ligand **1.162** further on reaction with $CuCl_2.2H_2O$ gave ONN-pincer copper(II) complex **1.163** (Scheme 1.69).

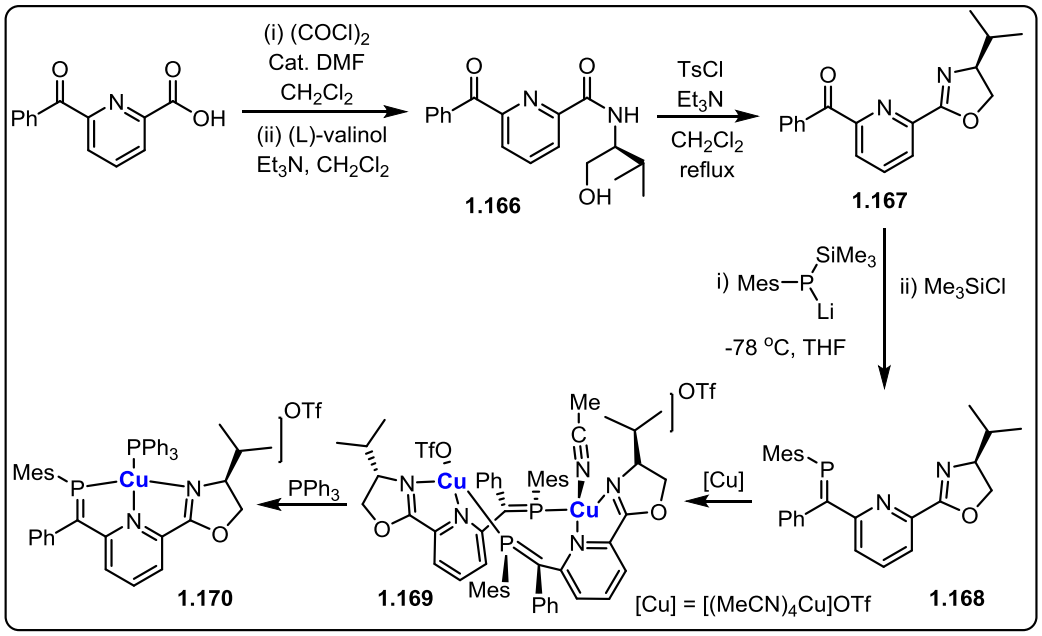



**Scheme 1.69** Synthesis of Imidazole-based ONN-Pincer Copper(II) Complexes.

Limberg *et al*. synthesized the PBiP-ligand **1.164** by the reaction of 1-bromo-2-diphenylphosphinobenzene with n-BuLi, followed by a subsequent salt metathesis reaction with $BiCl_3$.[160] The PBiP-pincer copper(I) dimeric complex **1.165** was synthesized by the reaction of PBiP-ligand **1.164** with CuCl (Scheme 1.70).[161] In 2016, Gates *et al*. synthesized the pyridine-bridged phosphaalkene-oxazoline based PNN-ligand **1.168** starting from 6-benzoylpicolinic acid in three steps *via* compounds **1.166** and **1.167**.[162] The PNN-ligand **1.168** on reaction with $[Cu(CH_3CN)_4]OTf$ gave the di-metallic Cu(I) cationic complex **1.169** which on reaction with 2 equiv of $PPh_3$ achieved the PNN-pincer copper(I) cationic complex **1.170** (Scheme 1.71).[163]

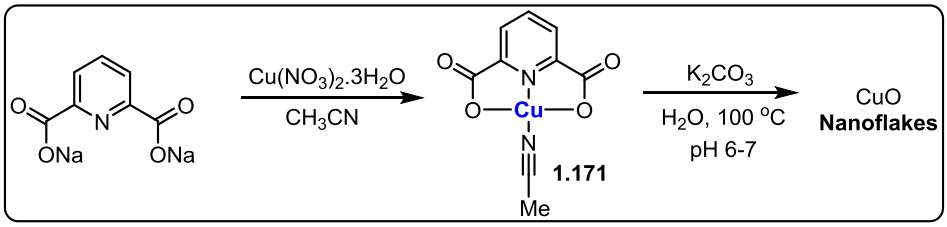



**Scheme 1.70** Synthesis of PBiP-Pincer Copper(I) Dimeric Complex.



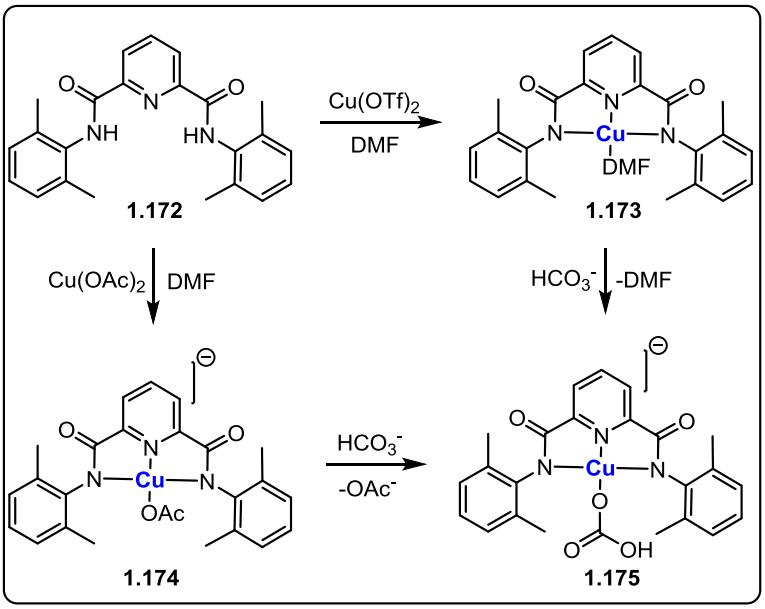

**Scheme 1.71** Synthesis of PNN-Ligand and Pincer Copper(I) Cationic Complex.

Karvembu research group developed the ONO-pincer copper complex **1.171** by the reaction of disodium pyridine-2,6-dicarboxylate with $Cu(NO_3)_2.3H_2O$ in acetonitrile with good yield (Scheme 1.72).[164] The authors synthesized CuO-nanoflakes from the synthesized pincer copper complex **1.171** in the presence of $K_2CO_3$ in water at pH ~ 6-7.



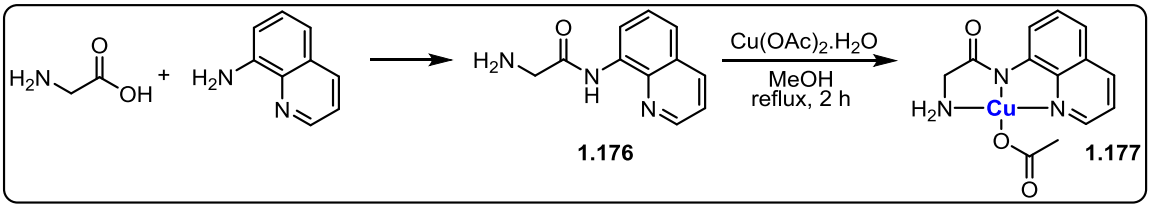

**Scheme 1.72** Synthesis of CuO-Nanoflakes from ONO-Pincer Copper Complex.

Recently, Cao *et al*. reported the synthesis of diamido NNN-pincer copper complexes **1.173** and **1.174** starting from NNN-ligand **1.172** (Scheme 1.73).[165] In this approach the NNN-ligand **1.172** was treated with $CuX_2$ in DMF to obtain the DMF coordinated complex **1.173** (X = OTf), and the acetate complex **1.174** (X = OAc). The reaction of NNN-pincer copper complexes **1.173** and **1.174** with bicarbonate ion produced the bicarbonate complex **1.175**.

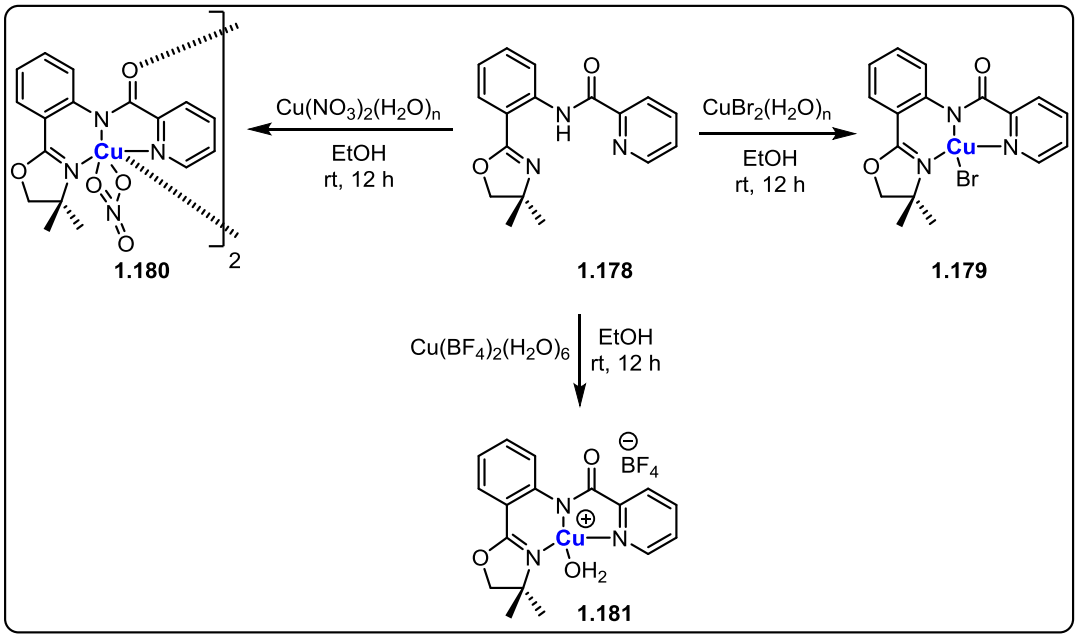



**Scheme 1.73** Synthesis of NNN-Pincer Copper(II) Anionic Complexes.

Shao *et al*. synthesized the quinolinamide-based NNN-pincer copper complex **1.177** by the reaction of NNN-ligand, **1.176** with $Cu(OAc)_2.H_2O$ in methanol under reflux for 2 h (Scheme 1.74).[166,167] Further continuation to this, Gossage *et al*. synthesized various amido NNN-pincer copper complexes **1.179**-**1.181** by the reaction of NNN-ligand **1.178** with $CuX_2(H_2O)_n$ (X = Br, $NO_3$, $BF_4$) in ethanol at room temperature (Scheme 1.75).[168] Many of other NNN-pincer copper pincer complexes were known in the literature.[169-176] Some of them were shown good biological activities.




**Scheme 1.74** Synthesis of Quinolinamide-based NNN-Pincer Copper Complex.

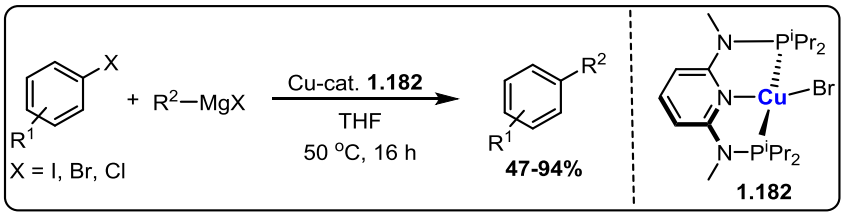



**Scheme 1.75** Synthesis of Amido NNN-Pincer Copper Complexes.

## 1.7 Catalytic Applications of Pincer Copper Complexes

### 1.7.1 Kumada Coupling Reaction

Kirchner *et al*. developed the 2,6-diaminopyridine based PNP-pincer copper(I) complex **1.182** and showed its application in Kumada cross-coupling reaction of aryl halides and alkyl triflates with phenyl- and alkynylmagnesium bromides by employing 1 mol% of the catalyst (Scheme 1.76). [177] The C–C cross-coupled products were obtained in high yields up to 94%.

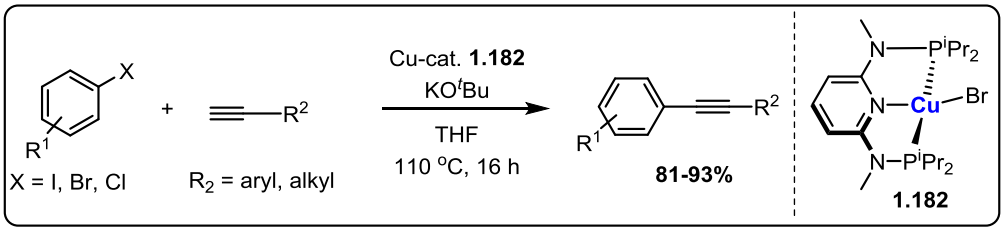



**Scheme 1.76** Utility of PNP-Pincer Copper(I) Complex in Kumada Cross-Coupling Reaction.

### 1.7.2 Sonogashira Coupling Reaction

In 2017, Kirchner *et al*. employed the PNP-pincer copper(I) complex **1.182** in catalytic Sonogashira cross-coupling reaction of (hetero)aryl halides with alkynes (Scheme 1.77).[177] The

catalyst loading was as low as 5 mol% and the C–C cross-coupled products were achieved in excellent yields.




**Scheme 1.77** Employment of PNP-pincer Copper(I) Complex in Catalytic Sonogashira Cross-coupling Reaction.

Recently, Tahsini and coworkers developed a novel protocol for the Sonogashira coupling of aryl iodide and phenylacetylene derivatives employing *N*-heterocyclic carbene based CNC-pincer copper complexes **1.183a-d** (Figure 1.10).[178] The authors performed mechanistic studies, wherein they observed greater coupling yields in the air rather under argon atmosphere. This indicates that there may be a different mechanism than the classical Sonogashira reaction. A high-valent Cu-oxygen adduct might be involved in the mechanism, which was supported by oxygen-reactivity and radical trap experiments. This was the first report of Sonogashira-type cross-coupling reaction under oxidative conditions catalyzed by well-defined copper catalysts, wherein the homocoupling is suppressed to a great extent (< 5%).

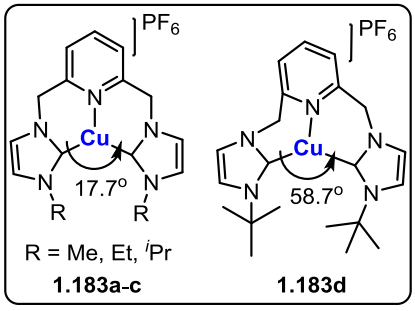
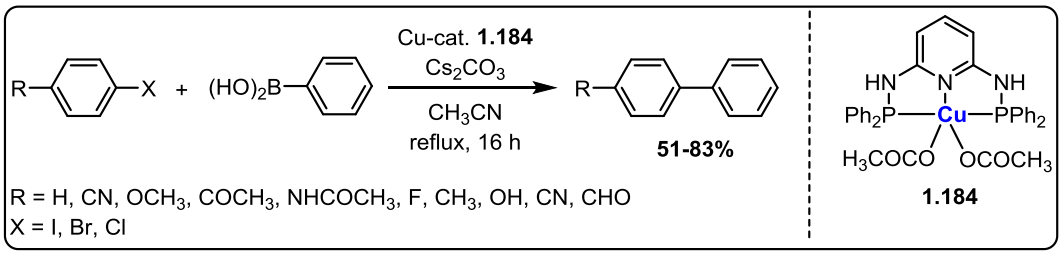



**Figure 1.10** *N*-heterocyclic carbene based CNC-pincer copper(I) complexes in Sonogashira coupling.

### 1.7.3 Suzuki-Miyaura Coupling Reaction

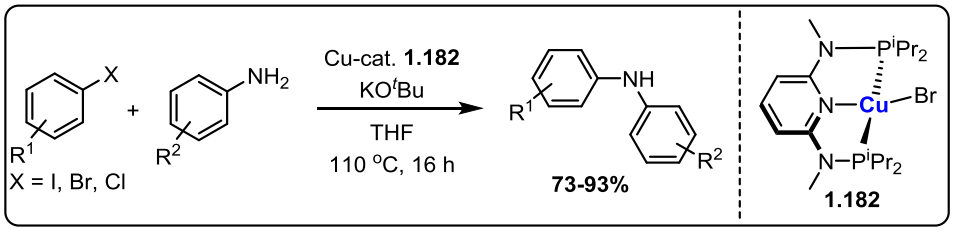
Recently, Kumar *et al*. synthesized a pyridine-based PNP pincer copper(II) complex **1.184** and utilized in catalytic amount in Suzuki cross-coupling reaction of (hetero)aryl halides with phenyl boronic acid in the presence of $Cs_2CO_3$ (Scheme 1.78).[179] The authors claimed that the rate determining oxidative addition step goes *via* a less stable Cu(III) intermediate. They concluded that the synthesized PNP pincer copper complex was a feasible alternative to the more commonly used Pd-catalysts in the cross-coupling reactions.




**Scheme 1.78** Suzuki Cross-Coupling Reaction Catalyzed by PNP-Pincer Copper(II) Complex.

### 1.7.4 C–N Cross-Coupling Reaction

Kirchner *et al*. demonstrated the utility of PNP-pincer copper(I) complex **1.182** in catalytic cross-coupling reaction of (hetero)aryl halides with aromatic amines and indole (Scheme 1.79).[177] The catalyst loading was as low as 3 mol% and the C–N cross-coupled products were achieved in excellent yields.




**Scheme 1.79** PNP-Pincer Copper(I) Catalyzed C–N Cross-Coupling reaction.

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Literature survey demonstrates that there is an immense interest in the chemistry of pincer ligated transition metal complexes because of their unique features. These complexes have shown tremendous applications in diverse catalysis and material chemistry. As summarized in Chapter 1, most of the pincer complexes developed till date involve the use of expensive and toxic phosphorus-based ligand system. The synthesis of phosphorus-based ligand comprises multiple steps and required special techniques. Additionally, the reported pincer transition metal complexes mostly contain five-membered metallacycles. In this regard, there exists a huge scope for the synthesis and development of the pincer ligated transition metal complexes based on inexpensive nitrogen-based ligand system. In addition, the demonstration of pincer-based complexes having six-membered metallacycles could be more interesting. Furthermore, the known pincer complexes are mostly employed in the traditional cross-coupling reactions. Hence, the utilization of developed pincer-ligated transition metal complexes for ubiquitous C–H bond functionalization would be more challenging and interesting. In those directions, one of the major objectives of the present work is to develop the inexpensive and air-stable nitrogen-based pincer ligands, and study their transition metal chemistry with nickel, copper and palladium. The application of synthesized pincer transition metal complexes for diverse catalytic reaction is another aim of this study.

The results obtained from the studies are described in the Chapters 2, 4, and 5. In Chapter 2, the synthesis and characterization of quinolinamide-based NNN-pincer palladium complexes is presented. Additionally, the catalytic efficiency of (NNN)-pincer palladium complexes in the C–H bond arylation of biologically important heteroarenes like benzothiazoles is demonstrated. These (NNN)-pincer palladium catalysts were proved to be robust and recycled for five times with consistent yield of the C–H bond arylation. The controlled studies and the kinetic experiments proved that the pincer-Pd(II) catalyst acts as the active catalytic species with a small decomposition into the Pd(0)-particles.

The synthesis and catalytic activity of six-membered nickellacycle for the C–H bond alkylation is another goal of this thesis. Thus, the third chapter describes the synthesis and application of six-membered POCCCOP-pincer nickel complexes. The $^{i\text{Pr}4}$POCCCOP–H ligand **8** could be synthesized in two steps starting from 1,3-benzenedimethanol. The ($^{i\text{Pr}4}$POCCCOP)NiBr **9** was synthesized by the treatment of the ligand **8** with $(CH_3CN)_2NiBr_2$ in the presence of $Et_3N$. Further the complex **9** was reacted with $AgOCOCH_3$ and $AgOSO_2CF_3$ to

achieve ($^{iPr4}$POCCCOP)Ni(OCOCH$_3$) (**10**) and ($^{iPr4}$POCCCOP)Ni(OSO$_2$CF$_3$) (**11**) complexes in good yields. The synthesized nickel complexes **9**, **10** and **11** were employed in the C–H bond alkylation of benzothiazole. The complex **9** showed better reactivity compared to the five-membered POCOP- and PCP-nickelacycles.

In the fourth chapter, the quinolinamine-based hemilabile NNN-pincer nickel complex that was developed in our lab was utilized for the Sonogashira cross-coupling of phenylacetylene with 1-iodooctane. The optimized reaction condition involves the usage of (NNN)-nickel catalysts and CuI co-catalyst in the presence of Li$O^t$Bu in DMF at room temperature. This catalyst was successfully applied to coupling of various alkyl iodides, bromides and chlorides. All the alkylated phenylacetylenes were identified by GC and GC-MS and the yields were measured by $^1$H NMR technique.

The fifth chapter details the synthesis of quinolinamide-based NNN-pincer copper(II) complexes ($^{Et2}$NNN)CuX (**20**: X = Cl; **21**: X = Br; **22**: X = OCOCH$_3$) by the reaction of ($^{Et2}$NNN)–H with CuX$_2$ in the presence of Et$_3$N. Further the complex **20** upon reaction with AgOSO$_2$CF$_3$ yielded the cationic complex [($^{Et2}$NNN)Cu(CH$_3$CN)]OSO$_2$CF$_3$ (**23**). The synthesized NNN-pincer copper(II) complexes (**20**-**22**) were applied in the catalytic Kumada coupling reaction of (3-chloropropyl)benzene with cyclohexylmagnesium chloride in the presence of LiOMe. The cationic complex **23** was demonstrated to be an efficient catalyst for this coupling reaction. Various alkyl chlorides, bromides and various Grignard reagents were tolerated in this reaction and afforded the alkylated products in moderate to good yields.

# Chapter 2

## Quinolinamide-based Pincer Palladium Complexes: A Robust and Phosphine-free Catalyst System for C–H Arylation of Benzothiazoles

## 2.1 INTRODUCTION

The pincer-ligated palladium complexes have been well precedented in literature for a variety of organic transformations because of their high thermal, air and moisture stability.[1-10] The catalytic applications of pincer-palladium complexes are demonstrated in traditional cross-couplings,[11-28] aldol and Michael reactions,[29-38] allylation of aldehydes and imines,[39-48] borylation and hydrosilylation,[49-54] and many other reactions.[55-63] The advantage with most of these reactions is that they have high TON's as well as broader substrate scope compared to those of similar reactions catalyzed by bidentate- or monodentate-ligated palladium complexes. Moreover, enantioselective synthesis is also achieved by the pincer-ligated palladium complexes.[30,36,38,47,64-68] In contrast, the catalytic application of robust pincer-ligated palladium complexes in more challenging C–H bond functionalization is relatively less explored.[54,69-74]

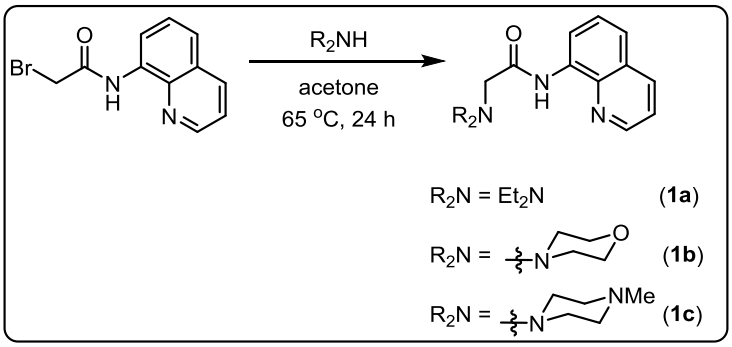
The C–H bond arylation of sulphur-containing electron-rich heterocycles, such as benzothiazoles is very prominent, because many biological and pharmaceutical compounds contain these core moieties.[75-79] The 2-arylated benzothiazole derivatives were obtained by the selective C-2 arylation of benzothiazoles with aryl halides using various transition-metal catalysts, such as Ni,[80-82] Cu,[83-85] Ru,[86] Rh[87-89] or Pd[90-110] with the added ligands. Although these catalysts succeeded in the arylation of benzothiazoles; they need harsh reaction conditions, such as strong and expensive bases, expensive phosphine-based ligands or high loading of catalysts (more than 5 mol%). In addition to this, the actual functioning of the catalyst system was not understood as many of these catalysts were generated *in-situ*. Recently, our group reported well-defined phosphine-amine based pincer palladium systems for the arylation of azoles (including benzothiazoles), with very low loading of catalysts.[111-113] Although the developed catalyst systems are promising and encouraging, there is still a scope for the synthesis of phosphine-free and robust catalyst system. In this chapter, we have discussed the synthesis and catalytic activity of quinolinamide-based NNN-pincer palladium system, ($^{R2}$NNN$^{Q}$)PdX. We hypothesis that the tridentate-nitrogen donor ligand would stabilize the palladium in higher oxidation state during the arylation strategy, which in turn can perform the arylation reaction under mild conditions. Practically, the ($^{R2}$NNN$^{Q}$)PdX system catalyzes the arylation of benzothiazoles with variety of aryl iodides employing very low loading of catalyst (0.5

mol%), and in the presence of a mild base $K_2CO_3$ in DMSO. Further, this catalyst system was demonstrated to be exceptionally robust, which was recycled and reused for five rounds without loss in the catalytic activity.

## 2.2 RESULTS AND DISCUSSION

### 2.2.1 Synthesis and Characterization of ($^{R2}$NNN$^{Q}$)–H Ligands

Recently, $Et_2N$-$CH_2C(O)N(H)C_9H_6N$ ($^{Et2}$NNN$^{Q}$–H; **1a**) ligand and its nickel complexes were synthesized, that were conveniently demonstrated for the alkylation of indoles with diverse alkyl halides.[114] Similar to the synthesis of **1a**, the quinolinyl-amido ligand precursors, $R_2N$-$CH_2C(O)N(H)C_9H_6N$ [$^{R2}$NNN$^{Q}$–H; $R_2$ = -$(CH_2)_2O(CH_2)_2$- (morpholinyl; **1b**) and -$(CH_2)_2NMe(CH_2)_2$- (Me-N-piperazinyl; **1c**)] were efficiently synthesized. Thus, the reaction of 2-bromo-*N*-(quinolin-8-yl)acetamide with the cyclic secondary amines, morpholine and *N*-methyl piperazine afforded the quinolinyl-amido ligands **1b** and **1c**, respectively, in excellent yields (Scheme 2.1). Both the compounds **1b** and **1c** were obtained in analytical pure form as solids, and hence further purification was not necessary. These ligands were characterized by $^1$H and $^{13}$C NMR spectroscopy as well as by the HRMS analysis. Notably, the morpholinyl methylene protons in **1b** resonate as two different sets to give two multiplets (~ 3.89 and ~ 2.69 ppm), whereas those of piperazinyl in **1c** (eight protons) appeared around the same chemical shift as one multiplet (~ 2.67 ppm).

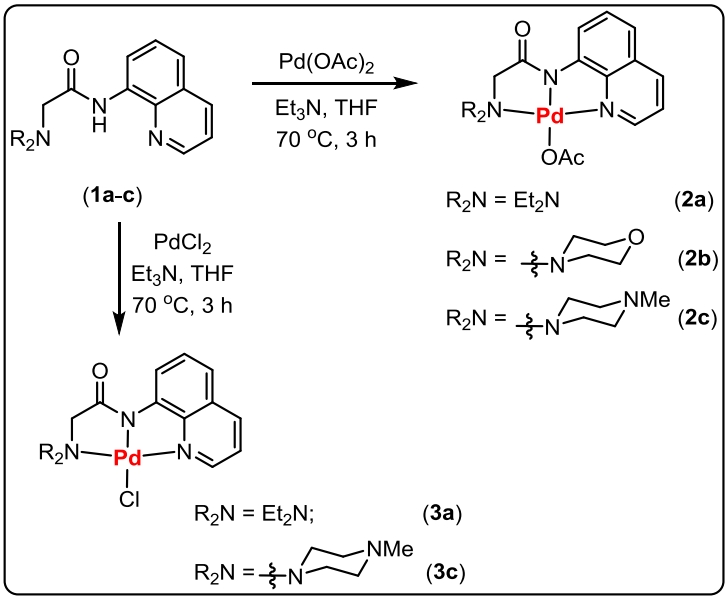



**Scheme 2.1** Synthesis of (8-Quinolinyl)amido-Ligands, ($^{R2}$NNN$^{Q}$)–H.

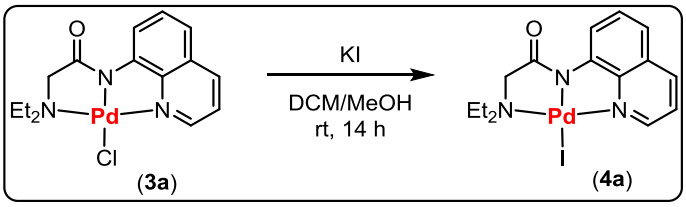
### 2.2.2 Synthesis and Characterization of ($^{R2}$NNN$^{Q}$) Palladium Complexes

The palladation reactions of ligand, $^{Et2}$NNN$^{Q}$–H (**1a**) with $Pd(OAc)_2$ and $PdCl_2$ in the presence of $Et_3N$ in THF under reflux conditions gave {$Et_2N$-$CH_2C(O)$-($\mu$-N)-$C_9H_6N$}Pd(OAc) [($^{Et2}$NNN$^{Q}$)Pd(OAc); **2a**] and {$Et_2N$-$CH_2C(O)$-($\mu$-N)-$C_9H_6N$}PdCl [($^{Et2}$NNN$^{Q}$)PdCl; **3a**], respectively, as yellow crystalline solids in moderate to good yields (Scheme 2.2). In the $^{1}$H NMR spectra of compounds **2a** and **3a**, the disappearance of signal corresponding to the amido-NH proton on ligand backbone indicates the amido-palladium covalent bond formation. Further, the methylene protons on $–NEt_2$ group displayed two sets of multiplets against a single set in **1a**, which suggests the coordination of $–NEt_2$ arm to the Pd-center. Among the two multiplets for methylene protons, one appeared in the down-field region and the other in the up-field region compared to that observed in the free-ligand. The HRMS analyses of both the compounds **2a** and **3a** showed the mass ion peaks corresponding to [**2a**–OAc]$^{+}$ (*m/z* = 362.0493) and [**3a**–Cl]$^{+}$ (*m/z* = 362.0474). These compounds were further characterized by $^{13}$C NMR spectroscopy and elemental analysis. The molecular structures of **2a** and **3a** were determined by single crystal X-ray diffraction study. The pincer palladium complex, ($^{Morp}$NNN$^{Q}$)Pd(OAc) (**2b**) was synthesized in good yield by the reaction of ($^{Morp}$NNN$^{Q}$)–H (**1b**) with $Pd(OAc)_2$ in the presence of $Et_3N$ in THF. However, the attempted synthesis of corresponding chloro-derivative, ($^{Morp}$NNN$^{Q}$)PdCl (**3b**) was sluggish and could not be isolated in pure form. Compound **2b** was obtained as a yellow powder. The $^{1}$H NMR spectrum of **2b** displayed three sets of multiplet for the methylene protons on morpholinyl moiety, in contrast to two sets in free-ligand **1b**. This suggests the coordination of

morpholinyl-arm to the Pd-center. The HRMS analysis of **2b** showed mass peak *m/z* 376.0267 for the ion [**2b**–OAc]$^+$. Pincer complexes, ($^{Pip}$NNN$^{Q}$)Pd(OAc) (**2c**) and ($^{Pip}$NNN$^{Q}$)PdCl (**3c**) were obtained by the treatment of **1c** with $Pd(OAc)_2$ and $PdCl_2$, respectively, in the presence of $Et_3N$ base (Scheme 2.2). Both the compounds **2c** and **3c** were isolated in moderate to good yields as yellow crystalline solids. Notably, the $^1$H NMR spectra of **2c** and **3c** displayed four sets of signals each for the methylene protons on piperazinyl-moiety, which could be due to the diastereotopic methylene protons, generated upon the coordination of piperazinyl arm to the palladium center. All the three complexes **2b**, **2c** and **3c** were further characterized by $^{13}$C NMR spectroscopy, HRMS and elemental analysis. The iodo-derivative, ($^{Et2}$NNN$^{Q}$)PdI (**4a**) was synthesized by the reaction of **3a** with KI in DCM/MeOH (1:1, v:v) at ambient temperature (Scheme 2.3). The complex **4a** was obtained as a brown solid in excellent yield. The $^1$H NMR spectrum of **4a** has a similar splitting pattern to that observed for the complex **3a**. The MALDI-TOF analysis of **4a** showed the mass ion peaks corresponding to [**4a** + H]$^+$ (*m/z* = 489.8192) and [**4a** – I]$^+$ (*m/z* = 361.9155).




**Scheme 2.2** Synthesis of ($^{R2}$NNN$^{Q}$)PdX Complexes.




**Scheme 2.3** Synthesis of ($^{Et2}$NNN$^{Q}$)PdI Complex.

### 2.2.3 Crystal Structure Description

The ORTEP diagrams of complexes **2a** and **3a** are shown in Figures 2.1 and 2.2, respectively. Selected bond lengths and bond angles are given in Table 2.1. In both complexes, ligand **1a** provides a tridentate coordination to the palladium through quinolinyl-*N2*, amido-*N1* and amine-*N3*, and the fourth site is occupied by anionic ligand –OAc (**2a**) or –Cl (**3a**). The coordination geometry around palladium is slightly distorted from the expected square-planar in both **2a** and **3a**. The Pd–N(1) bond lengths in **2a** (1.936(5) Å) and **3a** (1.953(2) Å) are slightly longer than the Pd–N bond length (1.927(5)Å) in a similar amido-complex, {$H_2$N-CH(Me)C(O)-($\mu$-N)-$C_9H_6$N}PdCl;[115] whereas the Pd–N(2) {2.012(5) Å in **2a**, 2.021(1) Å in **3a**} and Pd–N(3) {2.070(5) Å in **2a**, 2.072(2) Å in **3a**} bond lengths are comparable. The Pd–Cl bond length (2.314(1) Å) in **3a** is slightly shorter than the analogous bond length (Pd–Cl = 2.322(1) Å) in the complex {$H_2$N-CH(Me)C(O)-($\mu$-N)-$C_9H_6$N}PdCl. This slight difference in bond length could be due to weaker σ-donor strength of amido-ligand moiety exerted towards palladium in **2a** than the {$H_2$N-CH(Me)C(O)NH-$C_9H_6$N} moiety in {$H_2$N-CH(Me)C(O)-($\mu$-N)-$C_9H_6$N}PdCl. The N(2)–Pd–N(3) bond angles in **2a** (166.8(2)°) and **3a** (166.99(7)°) are comparable with each other and slightly more than that reported for {$H_2$N-CH(Me)C(O)-($\mu$-N)-$C_9H_6$N}PdCl (N(2)-Pd-N(3) = 165.3(2)°). The N(1)–Pd–N(2) and N(1)–Pd–N(3) bond angles in **2a** and **3a** are in the range of 82.35(7)-84.67(7)°. Notably, in the complex **3a**, the N(1)–Pd–N(3) bond angle (84.67(7)°) is significantly larger than the N(1)–Pd–N(2) bond angle (82.35(7)°). The five-membered ring containing Pd, N(1), N(2) is almost planar with the quinolinyl-moiety (Pd(1)-N(2)-C(9)-C(1) = 0.2(7)$^o$), whereas the other five-membered Pd-containing ring is slightly distorted (Pd(1)-N(1)-C(10)-C(11) torsion angle 7.2(7)$^o$) in the complex **2a**. The molecular structure of **4a** was further confirmed by single crystal X-ray diffraction analysis (Figure 2.3). The

coordination geometry around the palladium in **4a** is distorted from the expected square-planar geometry. The Pd–N(1), Pd–N(2) and Pd–N(3) bond lengths (1.967(1), 2.030(1) and 2.079(1) Å, respectively) in **4a** are slightly longer than the corresponding bond lengths (1.953(2), 2.021(1) and 2.072(2) Å) in **3a**, which is due to the larger trans effect and bigger size of iodide than that of chloride. In addition, a slight shortening of the N(1)–Pd–N(2), N(1)–Pd–N(3) and N(2)–Pd–N(3) bond angles (81.77(5), 83.88(5) and 165.64(4)$^{o}$) in **4a** was observed when compared to those in complex **3a**.

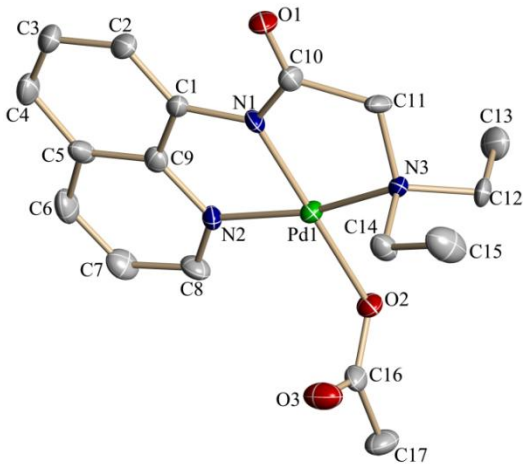



**Figure 2.1** Thermal ellipsoid plot of ($^{Et2}$NNN$^{Q}$)Pd(OAc) (**2a**). All the hydrogen atoms are omitted for clarity.

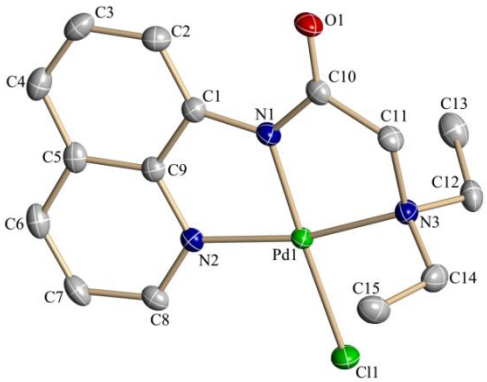



**Figure 2.2** Thermal ellipsoid plot of ($^{Et2}$NNN$^{Q}$)PdCl (**3a**). All the hydrogen atoms are omitted for clarity.

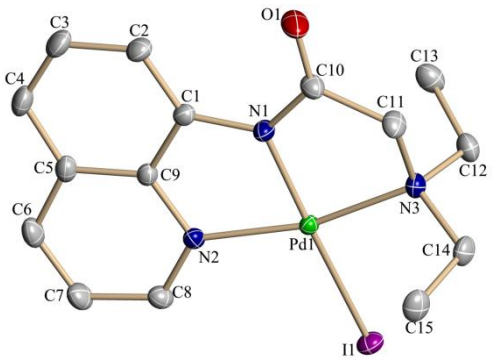



**Figure 2.3** Thermal ellipsoid plot of ($^{Et2}$NNN$^{Q}$)PdI (**4a**). All the hydrogen atoms are omitted for clarity.

**Table 2.1** Selected Bond Lengths (Å) and Angles ($^{o}$) for **2a**, **3a** and **4a**

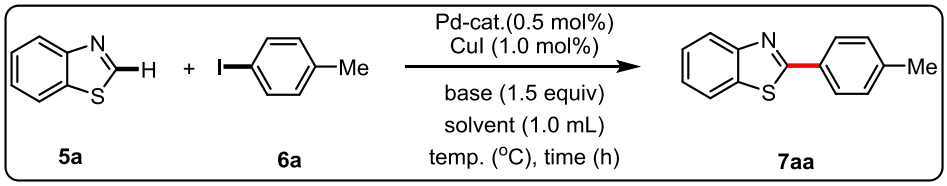
| | **2a** | **3a** | **4a** |
|---|---|---|---|
| Pd(1)–N(1) | 1.936(5) | 1.953(2) | 1.967(1) |
| Pd(1)–N(2) | 2.012(5) | 2.021(1) | 2.030(1) |
| Pd(1)–N(3) | 2.070(5) | 2.072(2) | 2.079(1) |
| Pd(1)–O(2) | 2.055(4) | - | - |
| Pd(1)–Cl(1) | - | 2.314(1) | - |
| Pd(1)–I(1) | - | - | 2.624(1) |
| | | | |
| N(1)–Pd(1)–N(2) | 83.1(2) | 82.35(7) | 81.77(5) |
| N(1)–Pd(1)–N(3) | 83.9(2) | 84.67(7) | 83.88(5) |
| N(2)–Pd(1)–N(3) | 166.8(2) | 166.99(7) | 165.64(4) |
| N(1)–Pd(1)–O(2) | 176.4(2) | - | - |
| N(2)–Pd(1)–O(2) | 94.3(2) | - | - |
| N(1)–Pd(1)–Cl(1) | - | 175.82(5) | - |
| N(2)–Pd(1)–Cl(1) | - | 97.61(5) | - |
| N(3)–Pd(1)–Cl(1) | - | 95.40(5) | - |
| N(1)–Pd(1)–I(1) | - | - | 175.08(3) |
| N(2)–Pd(1)–I(1) | - | - | 97.71(3) |
| N(3)–Pd(1)–I(1) | - | - | 96.55(3) |

### 2.2.4 Catalytic Activity of ($^{R2}$NNN$^{Q}$)PdX for C–H Bond Arylation of Benzothiazoles

#### 2.2.4.1 Optimization of Catalytic Condition

Newly developed phosphine-free pincer palladium complexes were screened, optimized and employed for the direct C–H bond arylation of benzothiazoles with aryl iodides. Initially, all the pincer complexes ($^{R2}$NNN$^{Q}$)PdX (**2a**-**3c**) were screened for the coupling of benzothiazole (**5a**; 0.30 mmol) with 4-iodotoluene (**6a**; 0.45 mmol), employing CuI (1.0 mol%) co-catalyst and $K_3PO_4$ base in DMF at 120 $^{o}$C [standard conditions employed with the ($^{iPr2}$POCN$^{iPr2}$)PdX catalyst] (Table 2.2).[111] Among all the complexes screened, **3a** showed better conversion and afforded the coupled product **7aa** in 76% isolated yield (Table 2, entries 1-5). Interestingly, the arylation reaction also proceeded equally in the polar aprotic DMSO solvent using catalyst **3a** (entry 6). Further, we screened the mild and less expensive bases for the coupling reaction. Surprisingly, the reaction in the presence of $K_2CO_3$ gave excellent yield (86% of **7aa**); however, slightly elevated temperature of 130 $^{o}$C for 24 h was essential (entries 7-9). Other bases like $Na_2CO_3$, NaOAc, KOAc were found to be less effective (entries 10-12). Similarly, the reaction in other polar (NMP, DMA) and non-polar (toluene, 1,4-dioxane) solvents was very poor (entries 13-16). Employment of palladium catalyst **3a** under the standard reaction conditions is essential, without which a small amount of coupled product **7aa** was detected (entry 17). The presence of CuI as co-catalyst was very much necessary to afford good conversion rate. Most likely, the CuI co-catalyst enhances the transmetalation of benzothiazoles to the palladium center.[113] A catalytic reaction of benzothiazole with iodide **6a** employing $PdCl_2$ as catalyst, in the absence of ligand precursor, afforded **7aa** in 46% yield (against 99% GC yield with **3a**). This suggests that a catalyst stabilizing ligand is essential for the better conversion in arylation reaction. After investigating the various reaction parameters, we found that the coupled product 2-(*p*-tolyl)benzothiazole (**7aa**) could be obtained in 86% isolated yield, employing 0.5 mol% of catalyst **3a** and 1.0 mol% of CuI in the presence of $K_2CO_3$ in DMSO (entry 9). Comparable yield of **7aa** has previously been reported with the catalyst $Pd(OAc)_2$, however, a strong base Li$O^{t}$Bu along with more loading of catalyst and co-catalyst $Cu(TFA)_2$ were employed in the described method.[97]

**Table 2.2** Optimization of Reaction Conditions for Arylation of Benzothiazole [a]



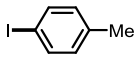
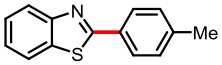
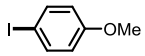
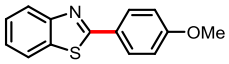
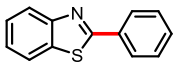
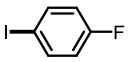
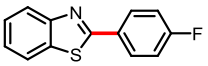
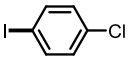
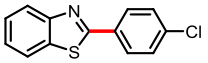
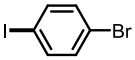
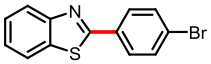
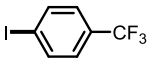
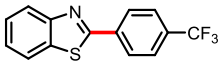
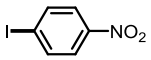
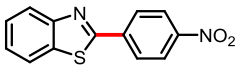
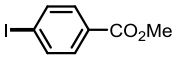
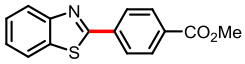
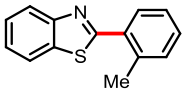
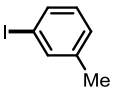
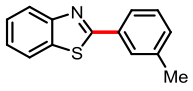
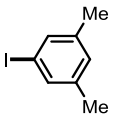
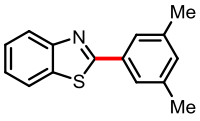
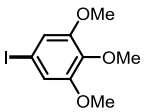
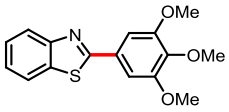
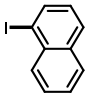
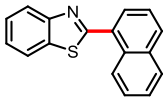
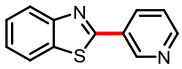

| Entry | Pd-cat. | Base | Solvent | T (°C)/ time (h) | Yield (%) [b] |
|---|---|---|---|---|---|
| 1 | **2a** | $K_3PO_4$ | DMF | 120/16 | 67 |
| 2 | **2b** | $K_3PO_4$ | DMF | 120/16 | 68 |
| 3 | **2c** | $K_3PO_4$ | DMF | 120/16 | 49 |
| 4 | **3a** | $K_3PO_4$ | DMF | 120/16 | 76 |
| 5 | **3c** | $K_3PO_4$ | DMF | 120/16 | 24[c] |
| 6 | **3a** | $K_3PO_4$ | DMSO | 120/16 | 78 |
| 7 | **3a** | $K_2CO_3$ | DMSO | 120/16 | 49[c] |
| 8 | **3a** | $K_2CO_3$ | DMSO | 130/16 | 81 |
| 9 | **3a** | $K_2CO_3$ | DMSO | 130/24 | 86 (99)[c] |
| 10 | **3a** | $Na_2CO_3$ | DMSO | 130/24 | 53[c] |
| 11 | **3a** | NOAc | DMSO | 130/24 | 12[c] |
| 12 | **3a** | KOAc | DMSO | 130/24 | 25[c] |
| 13 | **3a** | $K_2CO_3$ | NMP | 130/24 | 3[c] |
| 14 | **3a** | $K_2CO_3$ | DMA | 130/24 | 27 |
| 15 | **3a** | $K_2CO_3$ | toluene | 130/24 | 2[c] |
| 16 | **3a** | $K_2CO_3$ | 1,4-dioxane | 130/24 | 10[c] |
| 17 | - | $K_2CO_3$ | DMSO | 130/24 | 11[c] |
| 18 | **3a** | $K_2CO_3$ | DMSO | 130/24 | 16[d] |

[a] Conditions: Benzothiazole (0.041 g, 0.30 mmol), 4-iodotoluene (0.098 g, 0.45 mmol), base (0.45 mmol), Pd-cat. (0.0015 mmol), CuI (0.0006 g, 0.003 mmol) and solvent (1.0 mL). [b]Isolated yield. [c] G.C. yield. [d] CuI was not employed.

### 2.2.4.2 Substrate Scope for Arylation of Azoles

The optimized reaction condition was applied to the arylation of benzothiazoles with diversely substituted aryl iodides. As listed in Table 2.3, aryl iodides with different electronic features were coupled with the benzothiazole to yield the desired arylated products in moderate to good yields. In general, with the current catalyst system, the electron-rich aryl iodides were more efficiently reacted than those with electron-deficient ones (Table 2.3, entries 1-9), which is contrary to the Pd(0)-catalyzed coupling reactions, but similar to our previous observations with different catalyst systems.[111-113] Important functional groups, such as, –OMe, –F, –Cl, –Br, $–NO_2$, $–CF_3$, $–CO_2CH_3$ were tolerated on the aryl iodide backbone under the current catalytic conditions, which is very crucial from the synthetic prospective. The *para*-and *meta*-substituted aryl iodides, as well as di- and tri-substituted aryl iodides were coupled with benzothiazole to deliver the desired C-2 arylated benzothiazoles in good yields, though the coupling of sterically demanding *ortho*-substituted aryl iodide resulted in slightly lower yield (entries 10-13). Notably, the heteroaryl iodides, such as pyridinyl and pyrazinyl iodides were reacted with good activity, whereas thiophenyl iodide gave poor yield of the product (entries 15-17). Synthesis of these bis-heterocycles is important, as they can be used as bidentate ligand systems for transition-metal-catalyzed reactions. Methyl- and ethoxy-substituted-benzothiazoles reacted with moderate activity. Unfortunately, the less expensive aryl bromides or chlorides as electrophilic coupling partners reacted sluggishly and gave unsatisfactory yield of the product. Though, many methods are known for the arylation of azoles, the current process involves a phosphine-free catalytic system, which represents a rare example. More particularly, arylation methods of sulphur-containing azoles, such as benzothiazole, are less precedented. In addition, the contrasting reactivity of the electrophiles in the **3a**-catalyzed arylation reaction would be interesting for detailed mechanistic consideration.

**Table 2.3** Scope for the **3a**-Catalyzed Arylation of Benzothiazoles with Aryl Halides [a]

| Entry | Aryl halide (6) | Product (7) | Yield (%)[b] |
|---|---|---|---|
| 1 |  |  | 86 |
| 2 |  |  | 92 |
| 3 |  |  | 89 |
| 4 |  |  | 39 |
| 5 |  |  | 82 |
| 6 |  |  | 59 |
| 7 |  |  | 41 |
| 8 |  |  | 45 |
| 9 |  |  | 55 |
| 10 |  |  | 66 |
| 11 |  |  | 88 |
| 12 |  |  | 88 |
| 13 |  |  | 73 |
| 14 |  |  | 76 |
| 15 |  |  | 64 |

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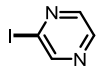
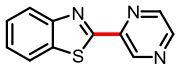
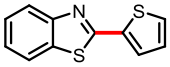
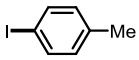
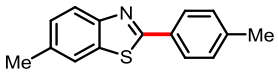
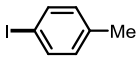
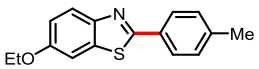
| 16 |  |  | 65 |
| 17 |  |  | 20 |
| 18 |  |  | 64 |
| 19 |  |  | 57 |

[a] Conditions: Substrate **5** (0.3 mmol), Aryl iodide **6** (0.45 mmol), $K_2CO_3$ (0.45 mmol), solvent (1.0 mL). [b] Isolated yields.

### 2.2.5 Catalyst Stability and Recycling Studies for Arylation of Azoles

Since the pincer-based complexes are presumed to be the robust catalysts because of the strong and rigid pincer coordination, we exploited the stability of pincer catalyst **3a**. For examining the air-stability of catalyst, the complex ($^{Et2}$NNN$^{Q}$)PdCl (**3a**, in DMSO-$d_6$) was exposed to air for 5 days. The $^1$H NMR was recorded at regular intervals (1 day, 2 days, 3 days and 5 days) and was analysed, which demonstrates that the complex **3a** largely remains intact. Neither the dissociation of ligand from **3a** nor the decomposition of **3a** was occurred. Further, the catalyst performance was studied by conducting recycling experiments (Figure 2.4). Generally, the catalyst **3a** was inhibited by substrate **5a** and product **7aa**; hence the catalyst recycling experiment was performed by distilling out the product and other volatiles after each experiment/cycle. In a Schlenk tube, the standard catalytic experiment was performed using **5a** (0.5 mmol), **6a** (0.75 mmol), catalyst **3a** (0.0025 mmol), CuI (0.005 mmol), $K_2CO_3$ (0.75 mmol) and DMSO (2.0 mL). After heating the reaction mixture for 24 h (1$^{st}$ cycle), the internal standard *p*-xylene (0.03 mL, 0.243 mmol) was added at ambient temperature and the reaction mixture was subjected to GC analysis, wherein the yield of the coupled product **7aa** was analyzed to be 98% (GC yield w.r.t. standard *p*-xylene). The product and other volatiles were distilled out under high vacuum ($5 \times 10^{-5}$ bar) at 140 $^{o}$C. The reaction vessel was then transferred in to the box and fresh **5a** (0.5 mmol), **6a** (0.75 mmol), $K_2CO_3$ (0.75 mmol) and DMSO (2.0 mL) were added. The reaction was then continued for second cycle, wherein the GC yield of the product **7aa** was analyzed to be 99%. Similarly, in the

3rd, 4th and 5th cycles, the GC yields of the product **7aa** were found to be 98%, 96% and 93%, respectively. At the end of fifth cycle the product **7aa** was isolated and estimated to be 87% yield. These experiments highlighted the exceptional stability and activity of the novel (quinolinyl)amido-palladium catalyst system for the arylation of benzothiazole. This characteristic feature of the catalyst is symbolic for the large scale functionalization of potential biologically relevant compounds.

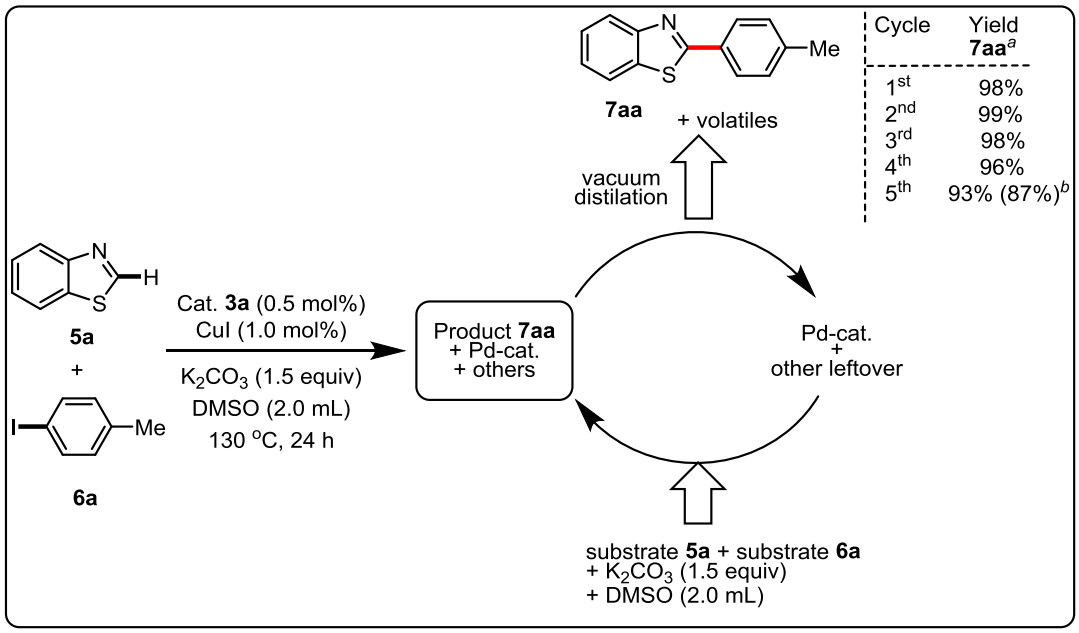



**Figure 2.4** Catalyst recycling experiment. [a]GC yield using *para*-xylene as internal standard. [b]Isolated yield.

### 2.2.6 Mechanistic Studies

#### 2.2.6.1 Resting State Study

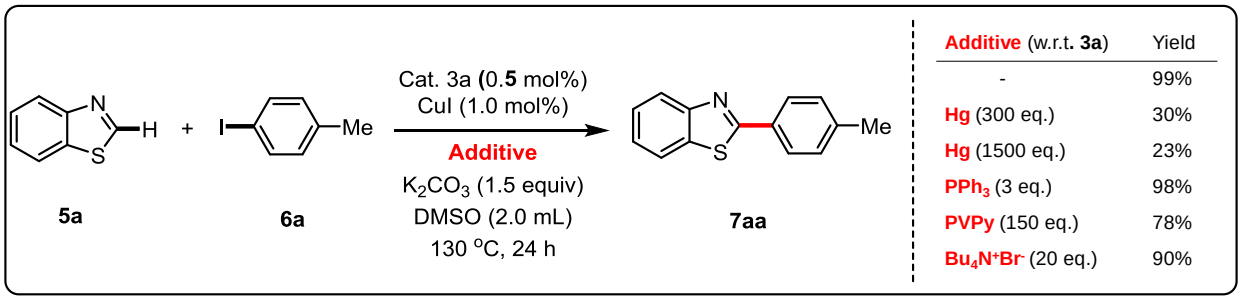
In order to identify the active catalyst species during the arylation, we have performed the catalytic reaction in a J-Young NMR tube using 20 mol% of catalyst ($^{Et2}$NNN$^{Q}$)PdCl (**3a**) in DMSO-$d_6$ and the progress of the reaction was monitored by $^1$H-NMR analysis. Thus, after heating the reaction mixture at 130 °C in a pre-heated oil bath, the major palladium species observed were ($^{Et2}$NNN$^{Q}$)PdCl (**3a**) and ($^{Et2}$NNN$^{Q}$)PdI (**4a**) in 65% and 35% (12 h), 69% and 28% (24 h), and 68% and 28% (48 h), respectively. Further, an independent catalytic reaction employing the complex **4a** afforded the coupled

product **7aa** in 95% yield (GC yield). These findings indicate that either **3a** or **4a** is the resting state of the catalyst during arylation reaction. The complex **4a** might have generated by the halide exchange reaction between **3a** and CuI or KI (KI will produce during the course of catalytic reaction). Further, the catalyst decomposition was negligible even after 24 h (3%) or 48 h (4%) at 130 $^{o}$C. This strongly suggests that the catalyst mostly remains in its molecular form.

### 2.2.6.2 External Additive and Filtration Experiments

Pincer ligated palladium complexes are known for their decomposition into Pd(0) nanoparticles during the coupling reactions, and even a trace of such species can catalyze the reaction and pincer complexes merely serve as the precatalysts.[116-118] To investigate the probable involvement of Pd(0) nanoparticles during **3a**-catalyzed arylation, the standard catalytic reaction was performed in the presence of 300 and 1500 equiv (w.r.t catalyst **3a**) of mercury (Hg),[20] wherein the yield of coupling product **7aa** obtained was 30% and 23%, respectively (Scheme 2.4). The presence of mercury significantly suppressed the arylation suggesting that some Pd(0) particles might have formed, and are responsible for at least some of the observed reactivity. Furthermore, the addition of ligands, such as $PPh_3$ (3.0 equiv w.r.t **3a**), poly(vinyl pyridine) (PVPy; 150 equiv w.r.t **3a**), known for poisoning the Pd(0) nanoparticles,[119-121] afforded the arylated product **7aa** in 98% and 78%, respectively. Though, the arylation reaction remains unaffected in the presence of $PPh_3$, the presence of PVPy lowered the yield of **7aa** to some extent (Scheme 2.4). This result further supports that at least some of the reactivity is promoted by Pd(0) species. However, as the arylation was not completely quenched in the presence of Hg or PVPy, the whole reactivity of the arylation may not have solely emerged from Pd(0) particles. Conversely, these additives could also have some retarding effect on the molecular catalyst, which could disrupt the catalysis.

A filtration experiment was performed after the initial heating (30 min, GC yield 34%) to remove all the heterogeneous particles, and the reaction was subsequently continued after adding fresh $K_2CO_3$. The arylation proceeded convincingly without much decline in the yield of **7aa** (88%; GC yield).




**Scheme 2.4** External Additive Experiments in the Standard Catalytic Reaction.

### 2.2.6.3 Kinetic Experiments

Since the external additive experiments were not conclusive, we performed kinetic experiments to know the progress of the arylation as well as to understand the reactivity of electronically distinct electrophiles. In a standard kinetic experiment, 1.5 mM of **3a**, 3 mM of CuI, benzothiazole (0.3 M), R-$C_6H_4$-I (0.45 M), $K_2CO_3$ (1.5 equiv) and mesitylene (0.03 mL, internal standard) were used, and DMSO was added to make total volume 2.0 mL. All the reactions were performed at 130 $^oC$ and the progress of the arylation was monitored by GC analysis. As shown in Figure 2.5, the formation of arylated product **7aa** followed a linear plot and induction period is absent. This suggests that decomposition of the complex **3a** into a new active catalyst species is unlikely, and **3a** might have directly involved in the catalytic arylation. Further, the initial rates for the arylation of benzothiazole with electronically distinct *para*-substituted aryl iodides (4-R-$C_6H_4$-I) were determined (Figure 2.6). The Hammett plot was drawn from a correlation between the initial rates and $\sigma_p$ values, which resulted in linear fit with a slope of –0.853 (Figure 2.7). The negative slope ($\rho$ value) indicates that a positive charge is produced in the active catalyst species and hence, the electron-donating substituents on the aryl iodide would enhance the rate of arylation reaction. This strongly supports the oxidative addition of aryl iodide to a Pd(II) species rather to a Pd(0) center, because the electron-donating substituent is expected to stabilize the resulting palladium species in higher oxidation state, and in turn would lower the energy of the process. However, as some of the additive experiments were positive for the catalysis by heterogeneous Pd(0) species, we assume that a parallel catalytic reaction by the trace amount of Pd(0) nanoparticles may be operative in addition to the arylation by a molecular Pd(II) species. In order to get more

insight, the isolation and reactivity studies of active palladium intermediate is essential, which is currently under investigation.

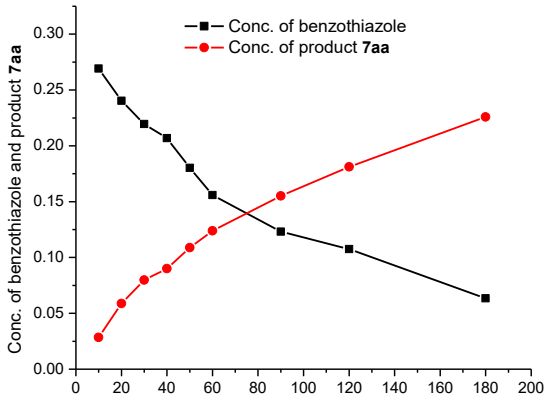



**Figure 2.5** Reaction profile for **3a**-catalyzed arylation of benzothiazole with 4-iodotoluene.

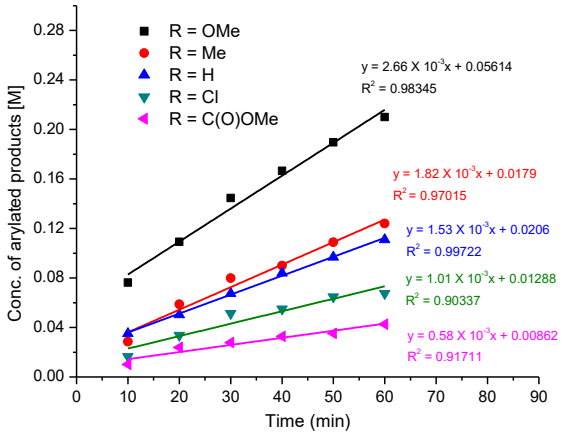



**Figure 2.6** Time-dependent formation of arylated products in the coupling of benzothiazole with various *para*-substituted aryl iodides (4-R-$C_6H_4$-I).

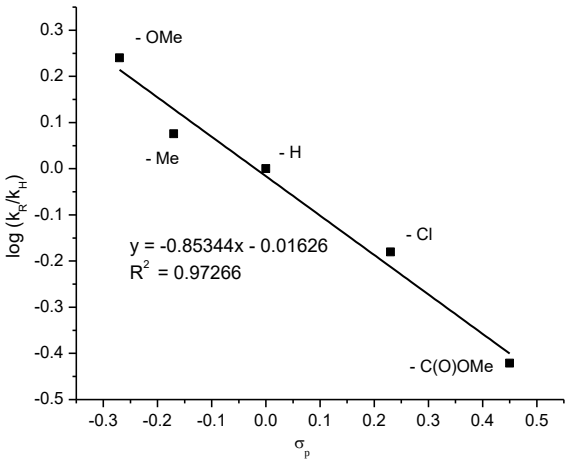



**Figure 2.7** Hammett correlation plot using various aryl iodides (4-R-$C_6H_4$-I).

## 2.3 CONCLUSION

In this chapter, we have shown the synthesis of quinolinylamide-based pincer palladium complexes and disclosed their catalytic application for the C–H bond arylation of benzothiazoles. All the pincer-palladium complexes were fully characterized by NMR spectroscopy, HRMS and elemental analysis. The molecular structures of three complexes were established by single crystal X-ray diffraction study. Complex ($^{Et2}$NNN$^{Q}$)PdCl efficiently catalyzes the arylation of benzothiazoles with substituted aryl iodides. Synthetically important functional groups, such as –OMe, –F, –Cl, –Br, –$NO_2$, –$CF_3$, –$CO_2CH_3$ were tolerated with this catalysis. The (quinolinyl)amido palladium catalyst was demonstrated to be highly robust and was recycled for five rounds with consistent yield of the coupled product. These phosphine-free catalyst systems displayed unique stability and activity for the C–H bond arylation of benzothiazoles. Kinetic analysis has been performed to get preliminary mechanistic insights.

## 2.4 EXPERIMENTAL SECTION

### General Experimental

All manipulations were conducted under an argon atmosphere either in a glove box or using standard Schlenk techniques in pre-dried glass wares. The catalytic reactions were performed in the flame-dried reaction vessels with Teflon screw cap. Solvents were dried over Na/benzophenone or $CaH_2$ and distilled prior to use. Liquid reagents were

flushed with argon prior to use. The 2-bromo-*N*-(quinolin-8-yl)acetamide,[122,123] compound **1a**,[114] and 6-substituted benzothiazoles[124] were synthesized according to previously described procedures. All other chemicals were obtained from commercial sources and were used without further purification. Yields refer to isolated compounds, estimated to be > 95% pure as determined by $^{1}$H-NMR. TLC: TLC Silica gel 60 $F_{254}$. Detection under UV light at 254 nm. Chromatography: Separations were carried out on Spectrochem silica gel (0.120-0.250 mm, 100-200 mesh). High resolution mass spectroscopy (HRMS) mass spectra were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump. M. p.: Büchi 540 capillary melting point apparatus, values are uncorrected. NMR ($^{1}$H and $^{13}$C) spectra were recorded at 200, 400 or 500 MHz ($^{1}$H) and 100 or 125 MHz {$^{13}$C, DEPT (distortionless enhancement by polarization transfer)} on Bruker AV 200, AV 400 and AV 500 spectrometers in $CDCl_3$ solutions, if not then specified; chemical shifts ($\delta$) are given in ppm. The $^{1}$H and $^{13}$C NMR spectra are referenced to residual solvent signals ($CDCl_3$: $\delta$H = 7.26 ppm, $\delta$C = 77.2 ppm).

**GC Method**

Gas Chromatography analyses were performed using a Shimadzu GC-2010 gas chromatograph equipped with a Shimadzu AOC-20s autosampler and a Restek RTX-5 capillary column (30 m × 250 μm). The instrument was set to an injection volume of 1 μL, an inlet split ratio of 10:1, and inlet and detector temperatures of 250 and 320 °C, respectively. UHP-grade argon was used as carrier gas with a flow rate of 30 mL/min. The temperature program used for all the analyses is as follows: 80 °C, 1 min; 30 °C/min to 200 °C, 2 min; 30 °C/min to 260 °C, 3 min; 30 °C/min to 300 °C, 3 min. Response factors for all the required compounds were calculated with respect to standard *para*-xylene or mesitylene from the average of three independent GC runs.

**Synthesis and Characterization of ($^{R2}$NNN$^{Q}$)–H Ligands**

**($^{Morp}$NNN$^{Q}$)–H** (**1b**): A mixture of 2-bromo-*N*-(quinolin-8-yl)acetamide (0.5 g, 1.89 mmol) and morpholine (0.49 g, 5.6 mmol) in acetone (15 mL) was refluxed for 24 h. The reaction mixture was then cooled to ambient temperature and the volatiles were evaporated under vacuum. The crude mixture was quenched with distilled $H_2O$ (20 mL) and the aminated product was extracted with EtOAc (15 mL × 3). The combined organic extract was dried over $Na_2SO_4$.

After filtration and evaporation of the volatiles in *vacuo* pure product of **1b** was obtained as brown solid. Yield = 0.51 g, 99%. M. p. = 122-124 $^{o}$C. $^{1}$H-NMR (200 MHz, $CDCl_3$): $\delta$ = 11.46 (br s, 1H, N–H), 8.85 (dd, *J* = 4.2, 1.6 Hz, 1H, Ar–H), 8.76 (dd, *J* = 5.9, 3.1 Hz, 1H, Ar–H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H, Ar–H), 7.53 (d, *J* = 3.0 Hz, 1H, Ar–H), 7.51 (s, 1H, Ar–H), 7.44 (dd, *J* = 8.3, 4.3 Hz, 1H, Ar–H), 3.92-3.87 (m, 4H, $CH_2$), 3.28 (s, 2H, $CH_2$), 2.71-2.66 (m, 4H, $CH_2$). $^{13}$C-NMR (100 MHz, $CDCl_3$): $\delta$ = 168.9 (CO), 148.7 (CH), 139.1 ($C_q$), 136.3 (CH), 134.4 ($C_q$), 128.2 ($C_q$), 127.4 (CH), 121.9 (CH), 121.7 (CH), 116.7 (CH), 67.4 (2C, $CH_2$), 62.9 ($CH_2$), 53.9 (2C, $CH_2$). HRMS (ESI): *m/z* calcd for $C_{15}H_{17}N_3O_2 + H^+$ $[M + H]^+$ 272.1394, found 272.1391.

**($^{Pip}$NNN$^{Q}$)–H** (**1c**): Procedure similar to the synthesis of **1b** was followed, using 2-bromo-*N*-(quinolin-8-yl)acetamide (0.5 g, 1.89 mmol) and 1-methylpiperazine (0.56 g, 5.6 mmol). The compound **1c** was obtained as brown solid. Yield = 0.52 g, 97%. M. p. = 106-108 $^{o}$C. $^{1}$H-NMR (200 MHz, $CDCl_3$): $\delta$ = 11.45 (br s, 1H, N–H), 8.85 (dd, *J* = 4.3, 1.8 Hz, 1H, Ar–H), 8.77 (dd, *J* = 6.1, 2.8 Hz, 1H, Ar–H), 8.14 (dd, *J* = 8.3, 1.8 Hz, 1H, Ar–H), 7.52 (d, *J* = 3.4 Hz, 1H, Ar–H), 7.50 (s, 1H, Ar–H), 7.44 (dd, *J* = 8.3, 4.3 Hz, 1H, Ar–H), 3.28 (s, 2H, $CH_2$), 2.72-2.62 (m, 8H, $CH_2$), 2.37 (s, 3H, $CH_3$). $^{13}$C-NMR (100 MHz, $CDCl_3$): $\delta$ = 169.3 (CO), 148.6 (CH), 139.2 ($C_q$), 136.3 (CH), 134.5 ($C_q$), 128.2 ($C_q$), 127.5 (CH), 121.8 (CH), 121.7 (CH), 116.7 (CH), 62.5 ($CH_2$), 55.5 (2C, $CH_2$), 53.5 (2C, $CH_2$), 46.2 ($CH_3$). HRMS (ESI): *m/z* calcd for $C_{16}H_{20}N_4O + H^+$ $[M + H]^+$ 285.1710, found 285.1708.

**Synthesis and Characterization of ($^{R2}$NNN$^{Q}$)PdX Complexes**

**($^{Et2}$NNN$^{Q}$)Pd(OAc)** (**2a**): To a Schlenk flask equipped with magnetic stir bar was introduced ligand **1a** (0.167 g, 0.649 mmol) and $Pd(OAc)_2$ (0.146 g, 0.650 mmol). To the resultant reaction mixture, freshly distilled THF (15 mL) and $Et_3N$ (0.12 mL, 0.860 mmol) were added, and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature and the volatiles were evaporated under vacuum. The crude compound was extracted with toluene (10 mL × 2) and the solution was concentrated under vacuum. $Et_2O$ (6.0 mL) was added to precipitate the product, which was then dried under high vacuum to obtain a yellow solid. Yield: 0.16 g, 58%. M. p. = 160 $^{o}$C. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.67 (d, *J* = 7.8 Hz, 1H, Ar–H), 8.26 (d, *J* = 8.3 Hz, 1H, Ar–H), 8.21 (d, *J* = 5.1 Hz, 1H, Ar–H), 7.49 (vt, *J* = 7.7 Hz, 1H, Ar–H), 7.39 (dd, *J* = 7.8, 4.9 Hz, 1H, Ar–H), 7.33 (d, *J* = 8.1 Hz, 1H, Ar–H), 3.69 (s, 2H, $CH_2$), 3.19-

3.11 (m, 2H, $CH_2$), 2.66-2.58 (m, 2H, $CH_2$), 2.10 (s, 3H, $CH_3$), 1.80 (t, *J* = 7.3 Hz, 6H, $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 178.2 (CO), 175.4 (CO), 149.1 (CH), 146.8 ($C_q$), 145.2 ($C_q$), 139.1 (CH), 129.9 ($C_q$), 129.5 (CH), 121.2 (CH), 120.8 (CH), 120.2 (CH), 65.9 ($CH_2$), 57.5 (2C, $CH_2$), 24.1 ($CH_3$), 12.8 (2C, $CH_3$). HRMS (ESI): *m/z* calcd. for $C_{17}H_{21}N_3O_3Pd$ – $OAc^+$ $[M - OAc]^+$ 362.0479, found 362.0493. Anal. Calcd. for $C_{17}H_{21}N_3O_3Pd$: C, 48.41; H, 5.02; N, 9.96. Found: C, 47.98; H, 4.73; N, 9.71.

**($^{Morp}$NNN$^{Q}$)Pd(OAc)** (**2b**): To a Schlenk flask equipped with magnetic stir bar was introduced ligand **1b** (0.05 g, 0.184 mmol) and $Pd(OAc)_2$ (0.041 g, 0.183 mmol). To the resultant reaction mixture, freshly distilled THF (10 mL) and $Et_3N$ (0.032 mL, 0.229 mmol) were added, and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature, filtered through cannula and the volatiles were evaporated under vacuum. The product was then washed with $Et_2O$ (6.0 mL × 3) and dried under high vacuum to obtain a yellow solid compound **2b**. Yield: 0.048 g, 60%. M. p. = 230 $^{o}$C (dec.). $^1$H NMR (500 MHz, $CDCl_3$): *δ* 8.61 (dd, *J* = 7.6, 0.9 Hz, 1H, Ar–H), 8.27 (dd, *J* = 8.2, 1.2 Hz, 1H, Ar–H), 8.15 (dd, *J* = 5.2, 1.5 Hz, 1H, Ar–H), 7.50 (vt, *J* = 7.9 Hz, 1H, Ar–H), 7.40 (dd, *J* = 8.2, 5.2 Hz, 1H, Ar–H), 7.35 (d, *J* = 7.9 Hz, 1H, Ar–H), 4.02 (s, 2H, $CH_2$), 3.94-3.85 (m, 4H, $CH_2$), 3.83-3.79 (m, 2H, $CH_2$), 2.99-2.96 (m, 2H, $CH_2$), 2.17 (s, 3H, $COCH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 178.6 (CO), 172.9 (CO), 148.7 (CH), 146.6 ($C_q$), 145.0 ($C_q$), 139.4 (CH), 129.9 ($C_q$), 129.6 (CH), 121.3 (CH), 121.0 (CH), 120.5 (CH), 69.4 ($CH_2$), 62.4 (2C, $CH_2$), 59.3 (2C, $CH_2$), 24.4 ($CH_3$). HRMS (ESI): *m/z* calcd. for $C_{17}H_{19}N_3O_4Pd$ – $OAc^+$ $[M - OAc]^+$ 376.0272, found 376.0267. Anal. Calcd. for $C_{17}H_{19}N_3O_4Pd$: C, 46.86; H, 4.39; N, 9.64. Found: C, 46.93; H, 4.36; N, 9.68.

**($^{Pip}$NNN$^{Q}$)Pd(OAc)** (**2c**): Procedure similar to the synthesis of **2b** was followed, using **1c** (0.05 g, 0.176 mmol), $Pd(OAc)_2$ (0.04 g, 0.178 mmol) and $Et_3N$ (0.033 mL, 0.237 mmol). The compound **2c** was obtained as a yellow solid. Yield: 0.062 g, 78%. M. p. = 170 $^{o}$C (dec.). $^1$H NMR (500 MHz, $CDCl_3$): *δ* 8.62 (d, *J* = 7.6 Hz, 1H, Ar–H), 8.26 (d, *J* = 8.2 Hz, 1H, Ar–H), 8.16 (d, *J* = 4.3 Hz, 1H, Ar–H), 7.49 (vt, *J* = 7.8 Hz, 1H, Ar–H), 7.39 (dd, *J* = 7.9, 5.5 Hz, 1H, Ar–H), 7.34 (d, *J* = 7.9 Hz, 1H, Ar–H ), 3.94 (s, 2H, $CH_2$), 3.75 (vt, *J* = 10.4 Hz, 2H, $CH_2$), 3.23 (br s, 2H, $CH_2$), 2.62 (br s, 2H, $CH_2$), 2.47 (br s, 2H, $CH_2$), 2.29 (s, 3H, $CH_3$), 2.16 (s, 3H, $CH_3$). $^{13}$C NMR (100 MHz, $CDCl_3$): *δ* 178.5 (CO), 173.6 (CO), 148.9 (CH), 146.7 ($C_q$), 145.0 ($C_q$), 139.3 (CH), 129.9 ($C_q$), 129.6 (CH), 121.2 (CH), 120.9 (CH), 120.4 (CH), 58.7 ($CH_2$), 49.6 (4C, $CH_2$), 46.1 ($CH_3$), 24.5 ($CH_3$). HRMS (ESI): *m/z* calcd. for $C_{18}H_{22}N_4O_3Pd$ –

$OAc^+$ $[M - OAc]^+$ 389.0588, found 389.0576. Anal. Calcd. for $C_{18}H_{22}N_4O_3Pd$: C, 48.17; H, 4.94; N, 12.48. Found: C, 47.84; H, 4.73; N, 11.99.

**($^{Et2}$NNN$^{Q}$)PdCl** (**3a**)**:** To a Schlenk flask equipped with magnetic stir bar was introduced ligand **1a** (0.30 g, 1.166 mmol) and $PdCl_2$ (0.207 g, 1.167 mmol). To the reaction mixture, freshly distilled THF (20 mL) and $Et_3N$ (0.2 mL, 1.434 mmol) was added, and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature and the volatiles were evaporated under vacuum. The crude compound was extracted with toluene (10 mL × 2), concentrated under vacuum and $Et_2O$ (6 mL) was added to obtain crystalline compound of **3a**. Yield: 0.30 g, 65%. M. p. = 165 $^oC$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.93 (d, $J$ = 4.3 Hz, 1H, Ar–H), 8.71 (d, $J$ = 7.9 Hz, 1H, Ar–H), 8.28 (d, $J$ = 8.2 Hz, 1H, Ar–H), 7.52 (vt, $J$ = 7.9 Hz, 1H, Ar–H), 7.42 (dd, $J$ = 8.5, 5.2 Hz, 1H, Ar–H), 7.37 (d, $J$ = 8.2 Hz, 1H, Ar–H), 3.73 (s, 2H, $CH_2$), 3.42-3.35 (m, 2H, $CH_2$), 2.64-2.57 (m, 2H, $CH_2$), 1.82 (t, $J$ = 7.0 Hz, 6H, $CH_3$). $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 175.8 (CO), 150.4 (CH), 147.1 ($C_q$), 145.2 ($C_q$), 139.2 (CH), 130.1 ($C_q$), 129.6 (CH), 121.4 (CH), 120.7 (CH), 120.5 (CH), 66.4 ($CH_2$), 58.8 (2C, $CH_2$), 13.5 ($CH_3$). HRMS (ESI): *m/z* calcd. for $C_{15}H_{18}ClN_3OPd - Cl^+$ $[M - Cl]^+$ 362.0479, found 362.0474. Anal. Calcd for $C_{15}H_{18}ClN_3OPd$: C, 45.24; H, 4.56; N, 10.55. Found: C, 45.21; H, 4.37; N, 10.39.

**($^{Pip}$NNN$^{Q}$)PdCl** (**3c**): Procedure similar to the synthesis of **3a** was followed, using **1c** (0.05 g, 0.176 mmol), $PdCl_2$ (0.032 g, 0.18 mmol), $Et_3N$ (0.032 mL, 0.229 mmol) and THF (10 mL). The compound **3c** was obtained as a yellow crystalline solid. Yield: 0.045 g, 60%. M. p. = 210 $^oC$ (dec). $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.96 (d, $J$ = 4.3 Hz, 1H, Ar–H), 8.64 (d, $J$ = 7.6 Hz, 1H, Ar–H), 8.23 (d, $J$ = 7.9 Hz, 1H, Ar–H), 7.49 (vt, $J$ = 7.9 Hz, 1H, Ar–H), 7.39 (dd, $J$ = 8.2, 5.2 Hz, 1H, Ar–H), 7.34 (d, $J$ = 7.9 Hz, 1H, Ar–H), 4.13 (vt, $J$ = 11.6 Hz, 2H, $CH_2$), 4.00 (s, 2H, $CH_2$), 3.35 (d, $J$ = 11.9 Hz, 2H, $CH_2$), 2.64 (br s, 2H, $CH_2$), 2.43 (br s, 2H, $CH_2$), 2.30 (s, 3H, $CH_3$). $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 174.2 (CO), 150.8 (CH), 147.0 ($C_q$), 144.8 ($C_q$), 139.2 (CH), 130.0 ($C_q$), 129.5 (CH), 121.5 (CH), 120.7 (CH), 120.7 (CH), 59.3 (3C, $CH_2$), 49.4 (2C, $CH_2$), 46.1 ($CH_3$). HRMS (ESI): *m/z* calcd. for $C_{16}H_{19}ClN_4OPd - Cl^+$ $[M - Cl]^+$ 389.0588, found 389.0582. Anal. Calcd for $C_{16}H_{19}ClN_4OPd$: C, 45.19; H, 4.50; N, 13.18. Found: C, 44.87; H, 4.94; N, 12.84.

**($^{Et2}$NNN$^{Q}$)PdI** (**4a**): The mixture of **3a** (0.017 g, 0.043 mmol) and KI (0.011 g, 0.066 mmol) in $CH_2Cl_2$ (5.0 mL)/MeOH (5.0 mL) was stirred at room temperature for 14 h. Then the volatiles were evaporated under vacuum and the compound was extracted with $Et_2O$ (5 mL × 3). Upon evaporation of the solvent, the compound **4a** was obtained as a brown solid. Yield: 0.020 g, 95%. M. p. = 176-178 $^{o}$C (dec.). $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 9.56 (d, $J$ = 4.2 Hz, 1H, Ar–H), 8.78 (d, $J$ = 8.0 Hz, 1H, Ar–H), 8.25 (d, $J$ = 8.0 Hz, 1H, Ar–H), 7.52 (vt, $J$ = 7.8 Hz, 1H, Ar–H), 7.38 (d, $J$ = 8.0 Hz, 1H, Ar–H), 7.33 (dd, $J$ = 8.2, 5.2 Hz, 1H, Ar–H), 3.74 (s, 2H, $CH_2$), 3.64-3.57 (m, 2H, $CH_2$), 2.73-2.67 (m, 2H, $CH_2$), 1.84 (t, $J$ = 7.1 Hz, 6H, $CH_3$). $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 176.9 (CO), 156.4 (CH), 146.9 ($C_q$), 145.6 ($C_q$), 138.9 (CH), 130.4 ($C_q$), 129.6 (CH), 122.2 (CH), 120.8 (CH), 120.7 (CH), 67.1 ($CH_2$), 61.9 (2C, $CH_2$), 14.3 ($CH_3$). MALDI-TOF: *m/z* calcd for $C_{15}H_{18}IN_3OPd + H^+$ $[M + H]^+$ 489.9608, found 489.8192 and $C_{15}H_{18}IN_3OPd - I^+$ $[M - I]^+$ 362.0485, found 361.9155. Anal. Calcd for $C_{15}H_{18}IN_3OPd$: C, 36.79; H, 3.71; N, 8.58. Found: C, 37.39; H, 4.21; N, 7.73.

**Representative Procedure for Arylation of Benzothiazoles**

**2-(*p*-Tolyl)benzo[*d*]thiazole** (**7aa**): To a flame-dried Schlenk tube containing magnetic stir bar were added the catalyst **3a** (0.0015 mmol, 0.5 mol%, 240 µL of 0.0063 M stock solution in toluene) and CuI (0.003 mmol, 1.0 mol%, 60 µL of 0.0525 M stock solution in $CH_3CN$). The Schlenk tube with catalysts mixture was evacuated under vacuum and refilled with argon. Subsequently, 4-iodotoluene (**6a**; 0.098 g, 0.45 mmol), benzothiazole (**5a**; 0.041 g, 0.30 mmol), $K_2CO_3$ (0.062 g, 0.45 mmol) and DMSO (1.0 mL) were added under argon. The resultant reaction mixture was degassed, refilled with argon and was stirred at 130 $^{o}$C in a pre-heated oil bath for 24 h. At ambient temperature, $H_2O$ (10 mL) was added and the reaction mixture was extracted with EtOAc (20 mL x 3). The combined organic layers were dried over $Na_2SO_4$ and the volatiles were evaporated in *vacuo*. The resultant residue was purified by column chromatography on silica gel (petroleum ether/EtOAc: 50/1→ 30/1) to yield **7aa** (0.058 g, 86%) as an off-white solid. The $^{1}$H and $^{13}$C NMR data as well as HRMS of compound **7aa** and other arylated benzothiazoles were in accordance with those reported in the literature.[111-113]

**Procedure for Catalyst Recycling Experiment**

To a flame dried Schlenk tube equipped with magnetic stir bar was introduced the catalyst **3a** (0.001 g, 0.0025 mmol), CuI (0.001g, 0.005 mmol), $K_2CO_3$ (0.104 g, 0.750 mmol), 4-iodotoluene (**6a**; 0.164 g, 0.750 mmol), and benzothiazole (**5a**; 0.071 g, 0.524 mmol). To this reaction mixture, DMSO (2.0 mL) was added and the reaction vessel was heated at 130 $^{o}$C in a preheated oil bath for 24 h. At ambient temperature, the reaction vessel was transferred to glove box and *para*-xylene (0.030 mL, 0.243 mmol, internal standard) was added into it. The solution was shaken well and an aliquot of the sample was withdrawn and subjected to the GC analysis. The yield of the arylated product **7aa** was determined to be 98% by the GC analysis w.r.t. the internal standard *para*-xylene. The product **7aa** and other volatiles were distilled out under high vacuum ($5 \times 10^{-5}$ bar) at 140 $^{o}$C. The GC analysis of the remaining residue confirms the absence of both the starting compounds as well as product **7aa** in the reaction vessel. The reaction vessel was further charged with fresh $K_2CO_3$ (0.104 g, 0.750 mmol), **6a** (0.164 g, 0.750 mmol) and **5a** (0.070 g, 0.516 mmol), and DMSO (2.0 mL) inside the glove box (cat. **3a** and CuI were not added). The resultant reaction mixture was then stirred at 130 $^{o}$C in a preheated oil bath for the second cycle. Following the steps mentioned above, the yield of the arylated product **7aa** was determined to be 99% by GC analysis for the second cycle. This recycling experiment was continued for further three cycles and the yields of the product **7aa** were analyzed to be 98%, 96% and 93% for the third, fourth and fifth cycles, respectively. At the end of 5$^{th}$ cycle, the product was isolated by column chromatography, wherein the yield of coupled product **7aa** was 87%.

**Procedure for NMR tube Experiment**

A mixture of **3a** (0.015 g, 0.038 mmol), CuI (0.014 g, 0.075 mmol), $K_2CO_3$ (0.026 g, 0.188 mmol), benzothiazole (0.026 g, 0.192 mmol) and 4-iodotoluene (0.041 g, 0.188 mmol) was taken in a J. Young NMR tube, and DMSO-$d_6$ (0.5 mL) was added into it. The J. Young NMR tube with the reaction mixture was heated in a pre-heated oil-bath at 130 $^{o}$C. At regular intervals, the J. Young NMR tube was taken out from the oil bath and reaction progress was monitored by $^{1}$H NMR analysis. The major palladium species observed were ($^{Et2}$NNN$^{Q}$)PdCl/I (**3a**/**4a**) in 65/35% (12 h), 69/28% (24 h), and 68/28%

(48 h), respectively. The yields (%) were calculated w.r.t the external standard mesitylene (in toluene-$d_8$) in a sealed capillary.

**Procedure for External Additive (Hg, $PPh_3$, PVPy) Experiments**

Additive experiments were performed following the procedure similar to the representative procedure for arylation of benzothiazoles, additionally employing Hg (0.09 g, 0.45 mmol; 0.45 g, 2.24 mmol) or $PPh_3$ (0.0012 g, 0.0045 mmol) or PVPy (0.024 g, 0.225 mmol). After stirring the reaction mixtures at 130 $^oC$ for 24 h, the reactions were quenched with $H_2O$ (5.0 mL) at ambient temperature, and EtOAc (5 mL) and *para*-xylene (0.030 mL, 0.243 mmol; internal standard) were added. An aliquot of the reaction mixture was subjected to GC analysis. The GC yield of the coupled product **7aa** obtained was 30% (0.45 mmol Hg), 23% (2.24 mmol Hg), 98% (0.0045 mmol $PPh_3$) and 78% (0.225 mmol PVPy).

**Procedure for Kinetic Experiment**

To a flame dried Schlenk tube was introduced catalyst **3a** (0.0012 g, 0.003 mmol), CuI (0.0011 g, 0.006 mmol), $K_2CO_3$ (0.124 g, 0.9 mmol), benzothiazole **5a** (0.081 g, 0.6 mmol) and 4-iodootoluene (0.196 g, 0.9 mmol) or [4-iodoanisole (0.211 g, 0.9 mmol); iodobenzene (0.0184 g, 0.9 mmol); 4-chloro-iodobenzene (0.215 g, 0.9 mmol); methy-4-iodobenzoate (0.236 g, 0.9 mmol)] and required amount of DMSO to make total volume 2.0 mL. To the reaction mixture, mesitylene (0.030 mL, 0.2156 mmol) was added as an internal standard. The reaction mixture was then stirred at 130 $^oC$ in a pre-heated oil bath. At regular intervals, the reaction vessel was cooled to ambient temperature and an aliquot of sample was withdrawn under argon and subjected to GC analysis. The concentration of the product **7aa** obtained in each sample was determined with respect to the internal standard mesitylene. The data was collected till 60 min. The final data was obtained by averaging the results of two independent experiments. The initial rate for the coupling reactions are shown in Figure 6. The Hammett plot was drawn from the correlation between the initial rates and Hammett substituent constants, *i.e* log ($k_R/k_H$) *vs.* $\sigma_p$, and obtained a slope of -0.85344, *i.e.* Hammett reaction constant ($\rho$) < 0 (Figure 7).

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# Chapter 3

## Six-Membered Pincer Nickelacycles and their Application in Alkylation of Benzothiazole

## 3.1 INTRODUCTION

Pincer-based transition-metal complexes have attracted considerable attention because of their applications in diverse catalytic transformations and advanced materials.[1-5] The tridentate coplanar coordination of the pincer ligands to the transition metals largely provides strong metal-ligand bonds and robust structures, which contribute to the thermal, air and moisture stability of the pincer complexes.[6] The pincer nickel complexes based on bis(phosphine) [1,3-$(R_2PCH_2)_2$ $C_6H_4$; (PCP)–H] and bis(amine) [1,3-$(R_2NCH_2)_2C_6H_4$; (NCN)–H] ligands were among the early reports demonstrated by Shaw[7] and van Koten,[8,9] respectively. Particularly, the PCP[10-16]- and NCN[17-21]-type pincer nickel complexes have been most extensively studied, which led to the discoveries of diverse applications. In the last two decades, a number of new pincer nickel complexes based on electronically distinct ligand systems, such as POCOP,[22-33] POCN,[34-40] PNP,[41-51] NNN,[52-59] $PC_{sp3}P$,[60-62] $POC_{sp3}OP$[14,23,63,64] were developed (Figure 3.1). In this context, the groups of Guan and Zargarian have reported the reactivity and catalytic activity of (POCOP)NiX in a wide range of reactions.[25,65-69] Similarly, the unsymmetrical hybrid (POCN)NiX complexes have shown excellent activity for certain reactions compared to their symmetrical counterparts.[39,40] In all the reported pincer nickel complexes, the ligating properties of the pincer ligand system were systematically tuned by changing the substituents on $PR_2$ and $NR_2$ (R = alkyl, aryl), and by changing the $PR_2$-linker. These developments have underscored the importance of ligand tuning that has a direct impact on the reactivities of pincer nickel complexes. Notably, all the described pincer-nickels (nickelacycles) constitute two five-membered rings (Figure 3.1). Unfortunately, the impact of nickelacycle ring size on the reactivity and catalytic activity has rarely been examined on a pincer nickel complex.[70-74] This could be partially due to the difficulties in synthesizing higher ring size (six- or seven-membered) or lower ring size pincer nickel complexes, because of the low stability of such nickelacycles. Nevertheless, Jensen demonstrated the six-membered ring palladacycle as an excellent catalyst for the Heck coupling reaction compared to the five-membered palladacycle counterpart.[75] Encouraged by the Jensen observation, and as a part of our activity on the development of pincer-based nickel complexes for the C–H bond functionalization,[58,76-78] in this chapter, we have described the synthesis and structural characterization of six-membered nickelacycles $\{\kappa^P,\kappa^C,\kappa^P$-(2-$^i$Pr$_2$POCH$_2$-C$_6$H$_3$-6-CH$_2$OP$^i$Pr$_2$)$\}$NiX, [($^{i\text{Pr4}}$POCCCOP)NiX], and demonstrate their catalytic activity for the alkylation of benzothiazole. Interestingly, various

structural parameters of this phosphinite-based (POCCCOP)NiX complexes are distinct from both the phosphine-based (PCP)NiX and phosphinite-based (POCOP)NiX system, though they are much akin to the (PCP)NiX complex. The (POCCCOP)NiX complex acts as an active catalyst for the alkylation of benzothiazole with alkyl halides bearing *β*-hydrogen atoms.

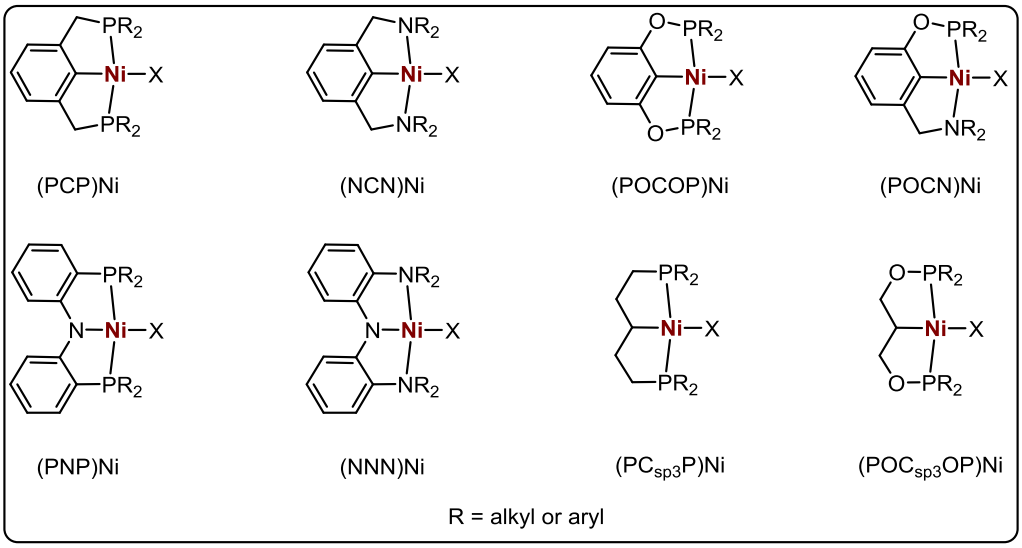


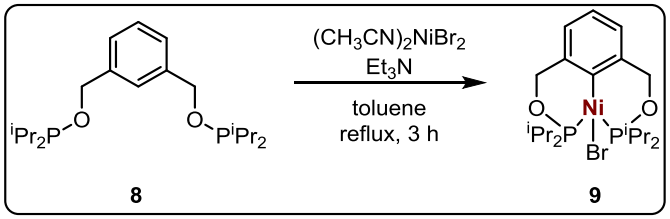

**Figure 3.1** Representative pincer nickel complexes.

## 3.2 RESULTS AND DISCUSSION

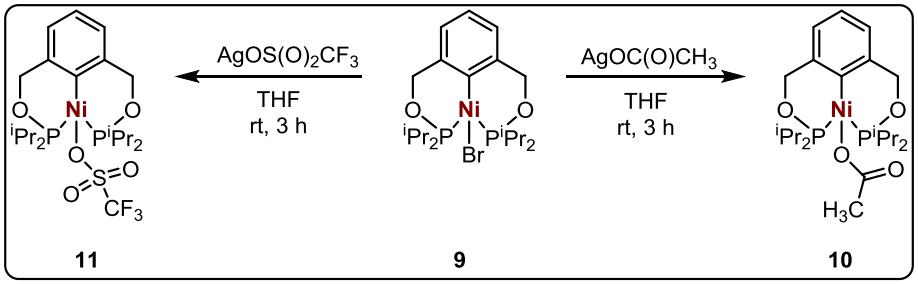
### 3.2.1 Synthesis and Characterization of ($^{iPr4}$POCCCOP) Nickel Complexes

The 1,3-$^{i}Pr_2POCH_2$-$C_6H_4$-$CH_2OP^{i}Pr_2$ [($^{i}Pr_4$-POCCCOP)−H, (**8**)] ligand was prepared by following the literature procedure.[75] Treatment of the pro-pincer ligand **8** with $(CH_3CN)_2NiBr_2$ in the presence of triethylamine afforded the pincer complex, {$\kappa^P,\kappa^C,\kappa^P$-(2-$^{i}Pr_2POCH_2$ -$C_6H_3$-6-$CH_2OP^{i}Pr_2$)}NiBr, [($^{i}Pr_4$-POCCCOP)NiBr] (**9**) *via* C(2)–H bond activation on the ligand, ($^{i}Pr_4$-POCCCOP)–H (Scheme 3.1). The complex **9** was obtained as a brownish yellow solid. The $^{31}$P NMR spectrum of complex **9** shows a single resonance at 141.6 ppm, which is *ca.* 14 ppm, upfield shifted than the free ligand. In the $^{1}$H NMR spectrum of **9**, the –$CH_2$ protons show two broad singlets against a single set for all the four protons in free-ligand **8**. Similarly, the four methylene (–$CH_2$) protons displayed two broad singlets. The twenty four protons on eight methyl (–$CH_3$) groups displayed three sets of signals contrary to a single set in the ligand **8**. The HRMS analysis of complex **9** shows a molecular mass peak *m/z* 507.1698, which corresponds to the [**9**+H]$^+$ ion. The molecular structure of complex **9** was further confirmed by the single crystal X-

ray diffraction study. The acetate and triflate derivatives of the nickel complex were synthesized by the reaction of complex **9** with AgOAc and AgOTf, respectively in quantitative yields. Hence, the treatment of **9** with AgOAc and AgOTf in THF afforded the complexes $\{\kappa^P,\kappa^C,\kappa^P$-(2-$^i$Pr$_2$POCH$_2$-C$_6$H$_3$-6-CH$_2$OP$^i$Pr$_2$)}Ni(OCOCH$_3$), [($^i$Pr$_4$-POCCCOP)Ni(OAc)] (**10**) and $\{\kappa^P,\kappa^C,\kappa^P$-(2-$^i$Pr$_2$POCH$_2$-C$_6$H$_3$-6-CH$_2$OP$^i$Pr$_2$)}Ni(OSO$_2$CF$_3$), [($^i$Pr$_4$-POCCCOP)Ni(OTf)] (**11**) as a brown crystalline solid and a brown-powder, respectively (Scheme 3.2). The complexes **10** and **11** show the single peaks at 136.5 and 133.6 ppm, respectively in the $^{31}$P NMR spectrum. The $^1$H NMR data of complexes **10** and **11** are almost identical to that of **9**, except the methyl protons on acetate (–OC(O)CH$_3$) displaying a singlet at 1.71 ppm in case of complex **10**. There was a signal at –80.3 ppm in the $^{19}$F NMR, which confirms that the triflate (-OSO$_2$CF$_3$) moiety attached to the nickel center in complex **11**. The mass spectrum of the complex **10** displayed peaks at *m/z* 487.0840 and 427.1461 for the ions [**10** + H]$^+$ and [**10**–OAc]$^+$, respectively. The X-ray analysis further establishes the structure of compound **10**. The mass spectra of the complex **11** displayed peaks at *m/z* 577.3794 and 427.1870 for the ions [**11** + H]$^+$ and [**11**–OTf]$^+$, respectively.




**Scheme 3.1** Synthesis of [($^{iPr4}$POCCCOP)NiBr] Complex.




**Scheme 3.2** Synthesis of [($^{iPr4}$POCCCOP)NiX] Derivatives.

### 3.2.2 Crystal Structure Description

The ORTEP diagrams of complexes **9** and **10** are shown in Figures 3.2 and 3.3, respectively. Selected bond lengths and bond angles are given in Table 3.1. The coordination geometry around the nickel center in both the complexes **9** and **10** is square planar. Both the Ni–P bond distances (2.1951(6) Å) in **9** are exactly same and slightly longer than the corresponding bond distance in (2, 6-($^{i}$Pr$_2$PCH$_2$)$_2$C$_6$H$_3$)NiBr (2.1645(6) Å)[61] and (2, 6-($^{i}$Pr$_2$PO)$_2$C$_6$H$_3$)NiBr (*ca.* 2.142-2.153 Å).[79] The Ni–C bond distance follows the same trend, being slightly longer in **9** (1.934(3) Å) than the PCP- (*ca.* 1.918 Å) and POCOP-analogue (*ca.* 1.885 Å). The Ni–Br bond distance in **2** (2.3416(6) Å) is comparable with that of PCP-analogue (*ca.* 2.344 Å),[61] whereas it is slightly longer than that observed in POCOP-analogue (*ca.* 2.323 Å).[79] This can be attributed to the similar σ-donor strength of the ligands (POCCCOP) and PCP towards nickel in the respective nickel complexes. The nickel center in complex **9** forms a perfect square plane with the *cis* angles *ca.* 89.2 and 90.7° and the *trans* angles *ca.* 178.5 and 180.0°. The P–Ni–P bite angle of the POCCCOP ligand in complex **9** (178.51(3)°) is significantly larger than that in PCP-analogue (*ca.* 170.6°) and POCOP-analogue (*ca.* 164.9°). Similarly, the C–Ni–P bond angle in **9** (89.254(17)°) is larger than the corresponding bond angles in PCP-analogue (*ca.* 85.3°) and POCOP-analogue (*ca.* 82.3, 82.7°). The comparison of all the bond lengths and bond angles of **9** with (PCP)NiBr and (POCOP)NiBr shows that the structural features of complex **9** are closer to the (PCP)NiBr than with the (POCOP)NiBr complex. This could be due to the electronic density provided by the (POCCCOP)-moiety towards nickel in (POCCCOP)NiX is similar to that provided by (PCP)-moiety towards nickel in the complex (PCP)NiBr. The presence of methylene (–CH$_2$) group in the six-membered nickelacycle (POCCCOP)NiX might have a crucial role for these changes. The Ni–P and Ni–C bond lengths in complex **10** are comparable to that observed in complex **9**. However, the P–Ni–P bite angle in **10** (170.59(3)°) is significantly shorter than the corresponding bond angle in **9**. Both the six-membered nickelacycles containing Ni, P, O and C exist in a boat-like conformation, and they are anti to each other (Figure 3.4). This is the first solid-state structure for a six-membered pincer nickelacycle complex.

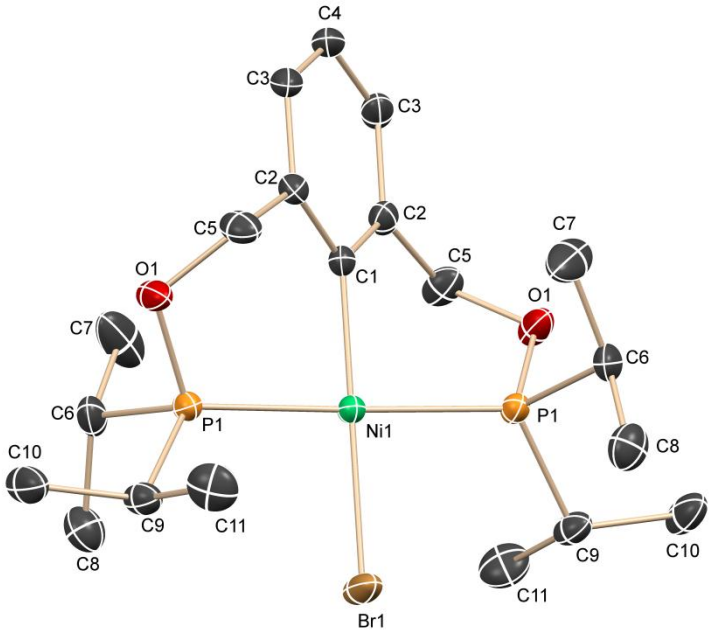



**Figure 3.2** Thermal ellipsoid plot of [($^{iPr4}$POCCCOP)NiBr] (**9**). All the hydrogen atoms are omitted for clarity.

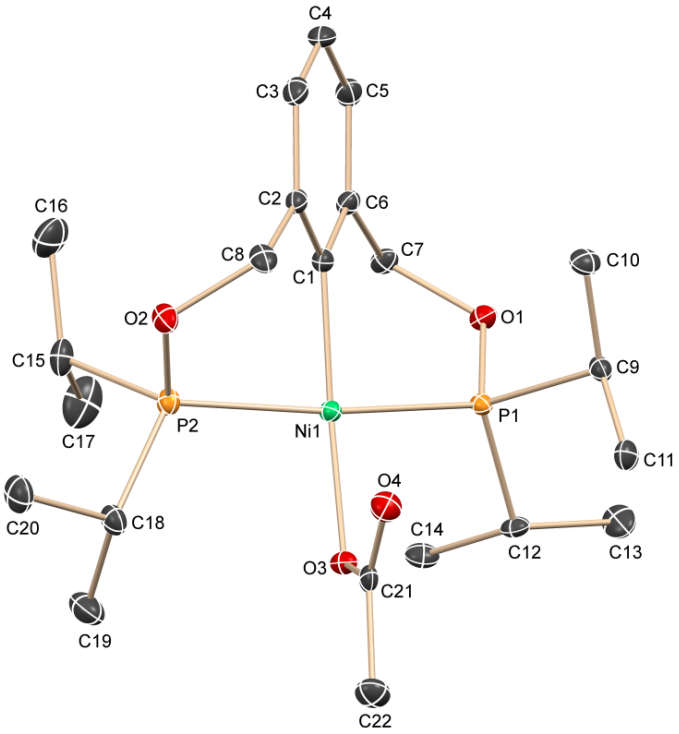



**Figure 3.3** Thermal ellipsoid plot of [($^{iPr4}$POCCCOP)Ni(OAc)] (**10**). All the hydrogen atoms are omitted for clarity.

**Table 3.1** Selected Bond Lengths (Å) and Bond Angles (°) of Compounds **9** and **10**.

| | Bond Lengths (Å) | | | Bond Angles (°) | |
|---|---|---|---|---|---|
| | **9** | **10** | | **9** | **10** |
| Ni(1)–C(1) | 1.934(3) | 1.910(3) | C(1)–Ni(1)–O(3) | – | 173.99(9) |
| Ni(1)–O(3) | – | 1.9445(17) | C(1)– Ni(1)–P(1) | 89.254(17) | 88.33(8) |
| Ni(1)–P(1) | 2.1950(6) | 2.1774(7) | C(1)–Ni(1)–P(2) | 89.254(17) | 85.69(8) |
| Ni(1)–P(2) | 2.1950(6) | 2.1955(7) | C(1)–Ni(1)–P(2) | 180.0 | – |
| Ni(1)–Br(1) | 2.3416(6) | – | P(1)–Ni(1)–Br(1) | – | 92.23(5) |
| | | | P(2)–Ni(1)–O(3) | – | 94.48(5) |
| | | | P(1)–Ni(1)–Br(1) | 90.746(17) | – |
| | | | P(2)–Ni(1)–Br(1) | 90.746(17) | – |
| | | | P(1)–Ni(1)–P(2) | 178.51(3) | 170.59(3) |

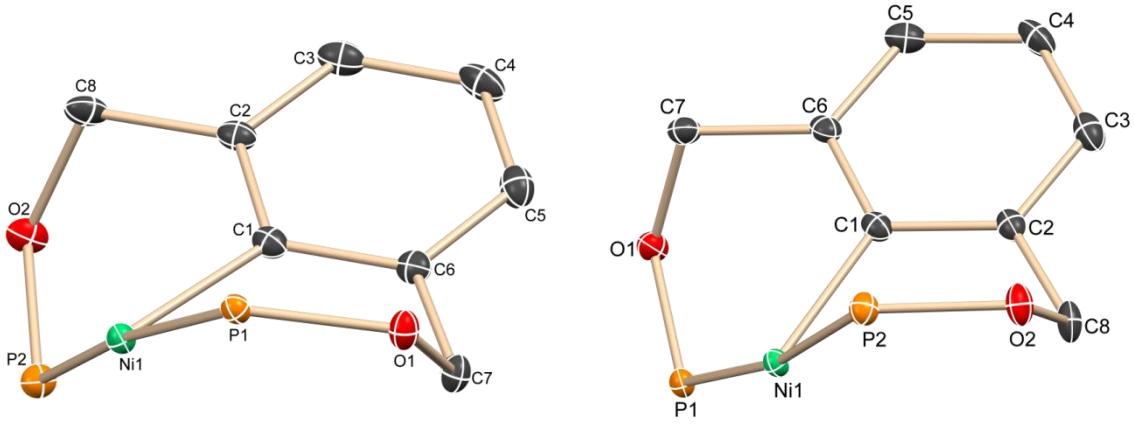


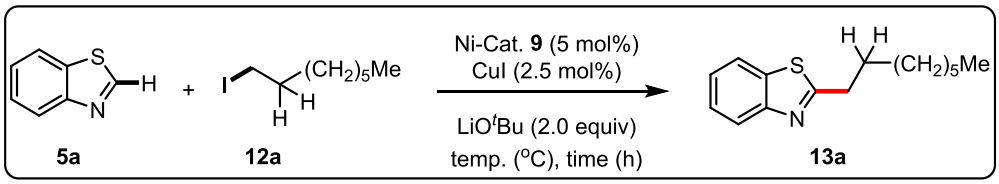

**Figure 3.4** Thermal ellipsoid plot of [($^{iPr4}$POCCCOP)NiBr] (**9**) showing two different nickelacycle cores.

### 3.2.3 Catalytic Activity of [($^{iPr4}$POCCCOP)NiBr] for C–H Bond Alkylation of Benzothiazole

#### 3.2.3.1 Optimization of Catalytic Condition

The C–H bond functionalization of sulphur containing azoles, such as benzothiazole, is very crucial as they are ubiquitous building blocks of several pharmaceutical and biologically active compounds.[80-83] Particularly, the alkylation of benzothiazole with alkyl halides containing $\beta$–hydrogens is a very important and challenging reaction, due to the undesired $\beta$–elimination from these electrophiles at the active metal center after the oxidative addition of the same.[84-86] In this regard, the newly developed six-membered nickelacycle (*i*Pr$_4$-POCCCOP)NiBr (**9**) was screened and employed for the alkylation of benzothiazole (**5a**) with alkyl halides (**12**) to obtain the alkylated products (**13**). The optimization was carried out using 1-iodooctane (**12a**) as the alkylating reagent employing 5 mol% of the nickel complex **9** as catalyst and 5 mol% of CuI as co-catalyst (Table 3.2). The alkylation of benzothiazole with 1-iodooctane was performed by using $Li_2CO_3$ as the base in 1,4-dioxane at 120 $^oC$ for 16 h. But there was not observed the formation of any coupled product (entry 1). The change of the base to $K_2CO_3$ also didn't result the formation of coupled product **13a** (entry 2). Then the phosphate base, *i.e.* $K_3PO_4$ was used to get the product in 6%, confirmed by G.C (entry 3). The use of a strong base, *i.e.* Li$O^t$Bu resulted the product **13a** in 46%, where if the time was extended to 24 h, the product was formed in 61% (entries 4 and 5). The decrease of temperature to 100 $^oC$ increased the yield of **13a** to 81% (entry 6). The increase in the loading of CuI to 10 mol% decreased the yield of **13a** to 56%, whereas the decrease in CuI to 2.5 mol% increased the yield of **13a** to 91% (G.C.), which was isolated in 82% (entries 9 and 10). The use of further strong base, i.e. Na$O^t$Bu gave the product in lower yields (entries 7 and 8). On the other hand, the use of other solvents (toluene, *o*-xylene, THF, DMF, DMSO, diglyme) resulted the product **13a** in unsatisfactory yileds (entries 11-16). After screening various reaction parameters, such as base, solvent, temperature and time, we found that the coupled product 2-(*n*-octyl)benzothiazole (**13a**) could be obtained in 91% isolated yield, employing 5 mol% of catalyst **9** and 2.5 mol% of CuI in the presence of Li$O^t$Bu in 1,4-dioxane (entry 10).

**Table 3.2** Optimization of Reaction Conditions for Alkylation of Benzothiazole.[a]



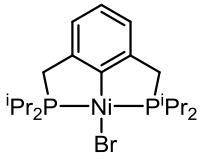
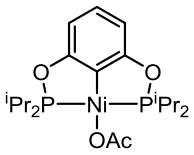
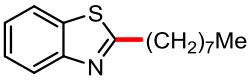
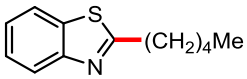
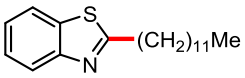
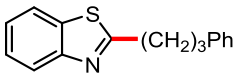

| Entry | Base | Solvent | Temp. (°C) | Time (h) | Yield (%) [b] |
|---|---|---|---|---|---|
| 1 | $Li_2CO_3$ | 1,4-dioxane | 120 | 16 | - |
| 2 | $K_2CO_3$ | 1,4-dioxane | 120 | 16 | - |
| 3 | $K_3PO_4$ | 1,4-dioxane | 120 | 16 | 6 |
| 4 | LiO$^t$Bu | 1,4-dioxane | 120 | 16 | 46 |
| 5 | LiO$^t$Bu | 1,4-dioxane | 120 | 24 | 61 |
| 6 | LiO$^t$Bu | 1,4-dioxane | 100 | 24 | 81 |
| 7 | NaO$^t$Bu | 1,4-dioxane | 100 | 24 | 30 |
| 8 | NaO$^t$Bu | Toluene | 100 | 24 | 22 |
| 9 [c] | LiO$^t$Bu | 1,4-dioxane | 100 | 24 | 56 |
| 10 [d] | LiO$^t$Bu | 1,4-dioxane | 100 | 24 | 91 (82) [e] |
| 11 | LiO$^t$Bu | Toluene | 100 | 24 | 10 |
| 12 | LiO$^t$Bu | *o*-xylene | 100 | 24 | 11 |
| 13 | LiO$^t$Bu | THF | 100 | 24 | 39 |
| 14 | LiO$^t$Bu | DMF | 100 | 24 | 13 |
| 15 | LiO$^t$Bu | DMSO | 130 | 24 | 16 |
| 16 | LiO$^t$Bu | Diglyme | 100 | 24 | - |

[a] Conditions: Benzothiazole (0.027 g, 0.2 mmol), 1-Iodooctane (0.096 g, 0.4 mmol), **9** (0.005 g, 0.01 mmol), CuI (0.002 g, 0.01 mmol), LiO$^t$Bu (0.032 g, 0.4 mmol), 1,4-dioxane (1.0 mL). [b] G. C. Yield of **13a** with respect to an internal standard, n-dodecane. [c] 10.0 mol% of CuI was used. [d] 2.5 mol% of CuI was used. [e] Isolated Yield.

### 3.2.3.2 Substrate Scope for Alkylation of Benzothiazole

Notably, the alkylation reaction of benzothiazole with various alkyl halides afforded better yields while employing six-membered nickelacycle ($^{iPr4}$POCCCOP)NiBr (**9**) as a catalyst than with either ($^{iPr4}$PCP)NiBr or ($^{iPr4}$POCOP)Ni(OAc) catalysts (Table 3.3). As the length of alkyl chain in the substrate **12** increases, then the coupling is less effective (**12a**, **12b** and **12c**). In the case of the bromide coupling partner (**12d**), the coupling is the least effective due to the less electrophilic site compared to that in iodide coupling partners (**12a-c**). However, the catalyst **9** is slightly inferior to earlier reported catalyst system $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-$C_6H_4$-*o*-$NMe_2$}NiCl [($^{Q}$NNN$^{Me2}$)NiCl, **15**] for the same reaction.[58,87,88] This catalyst system requires further study to establish the actual activation path.

**Table 3.3** Alkylation of Benzothiazole with Alkyl Halides Using Various [Ni] Catalysts.[a]

| Alkyl halides (12) | Products (13) | Yield (%) of products with various [Ni]-catalysts | | |
|---|---|---|---|---|
| | |  |  |  |
| | | **(9)** | **($^{iPr4}$PCP)NiBr** | **($^{iPr4}$POCOP)Ni(OAc)** |
| $Me(CH_2)_7$–I **(12a)** |  **(13a)** | 91 | 53 | 42 |
| $Me(CH_2)_4$–I **(12b)** |  **(13b)** | 94 | 72 | 56 |
| $Me(CH_2)_{11}$–I **(12c)** |  **(13c)** | 61 | 32 | 7 |
| $Ph(CH_2)_3$–Br **(12q)** |  **(13d)** | 23 | 6 | 2 |

[a] Reaction conditions: Benzothiazole (0.027 g, 0.2 mmol), alkyl halide (0.4 mmol), [Ni]-catalyst (0.01 mmol, 5.0 mol%), CuI (0.001 g, 0.005 mmol, 2.5 mol%), Li$O^t$Bu (0.032 g, 0.4 mmol), 1,4-dioxane (1.0 mL), 100 $^o$C, 24 h. Yields were determined using *n*-dodecane as an internal standard.

## 3.3 CONCLUSION

In this chapter, we have demonstrated the synthesis of two six-membered pincer nickelacycle complexes and their catalytic application in the alkylation of benzothiazole. Both the six-membered pincer nickelacycles, [($^{iPr4}$POCCCOP)NiX; (X = Br, OAc, OTf)] were synthesized in good yields and structurally characterized. The electronic features of these bis(phosphinite)-nickelacycles are very similar to the bis(phosphine), ($^{iPr4}$PCP)Ni rather than the bis(phosphinite), ($^{iPr4}$POCOP)Ni complex. The complex, ($^{iPr4}$POCCCOP)NiBr catalyzed the alkylation of benzothiazole with alkyl iodides. The C–H alkylation by the six-membered nickelacycle ($^{iPr4}$POCCCOP)NiBr is superior to the five-membered nickel complexes, ($^{iPr4}$PCP)NiBr and ($^{iPr4}$POCOP)Ni(OAc). Further utilization of these sixmembered pincer nickelacycles, ($^{iPr4}$POCCCOP)NiX in other C–H functionalization reactions is currently underway in our laboratory.

## 3.4 EXPERIMENTAL SECTION

### Synthesis and Characterization of ($^{iPr4}$POCCCOP)NiX Complexes

**($^{iPr4}$POCCCOP)NiBr** (**9**): To the mixture of bisphosphinite, 1,3-$C_6H_4(CH_2OP^iPr_2)_2$ (0.272g, 0.734 mmol) and $(CH_3CN)_2NiBr_2$(0.221 g, 0.735 mmol) in a Schlenk flask were added toluene (15 mL) and $Et_3N$ (0.133 mL, 0.954 mmol). The resulted brown reaction mixture was stirred at 110 $^oC$ for 3 h. At ambient temperature, the volatiles were evaporated under vacuum and the product was extracted with pentane (20 mL × 3). Slow evaporation of the pentane solution at room temperature afforded the brownish yellow crystalline compound of ($^{iPr4}$POCCCOP)NiBr (**9**). Yield: 0.230 g, 62%. M.p.: 145◦C (dec). $^1$H NMR (500 MHz, $CDCl_3$):$\delta$ 6.95–6.84 (m, 3H, Ar–H), 5.10 (br s, 2H, $CH_2$), 4.86 (br s, 2H, $CH_2$), 3.04 (br s, 2H, CH), 1.91 (br s, 2H, CH), 1.50 (br s, 6H, $CH_3$), 1.21 (br s, 12H, $CH_3$), 0.41 (br s, 6H, CH3). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 144.4 (t, $J_{P–C}$ = 26.7Hz, $C_q$), 142.8 (t, $J_{P–C}$ = 6.2Hz, 2C, $C_q$), 126.9 (2C, CH), 124.3 (CH), 78.9 (2C, $CH_2$), 27.5 (4C, CH), 18.1 (6C, $CH_3$), 15.9 (2C, $CH_3$). $^{31}$P{$^1$H} NMR (202 MHz, $CDCl_3$): $\delta$ 141.6 (s). HRMS (ESI): *m/z* calcd. for $[C_{20}H_{35}O_2P_2BrNi+H]^+$ $[M+H]^+$ 507.0722 and 509.0701; found 507.1698 and 509.1648; $[C_{20}H_{35}O_2P_2BrNi - Br]^+$ $[M - Br]^+$ 427.1460, found 427.1462. Anal. Calcd. For $C_{20}H_{35}O_2P_2BrNi$: C, 47.28; H, 6.94%. Found: C, 46.93; H, 6.77%.

**($^{iPr4}$POCCCOP)Ni(OAc)** (**10**): To the solution of ($^{i}$Pr$_4$-POCCCOP)NiBr (**9**; 0.05 g, 0.098 mmol) in THF (10 mL) was added AgOAc (0.0197 g, 0.118 mmol). The reaction mixture in Schlenk flask was covered with aluminium foil, and was stirred at room temperature for 3 h. The reaction mixture was filtered through cannula filtration to remove the insoluble materials, and the filtrate was concentrated under vacuum to obtain nickel complex ($^{iPr4}$POCCCOP)Ni(OAc) (**10**) as brown crystalline solid. Yield: 0.032 g, 67%. $^{1}$H NMR (500 MHz, THF-$d_8$): $\delta$ 6.88–6.76 (br s, 3H, Ar–H), 5.53–5.32 (m, 2H, $CH_2$), 4.94–4.77 (m, 2H, $CH_2$), 2.22 (br s, 2H, CH), 1.86 (br s, 2H, CH), 1.71 (s, 3H, $OCH_3$), 1.42 (d, $J$ = 5.7Hz, 6H, $CH_3$), 1.22–1.10 (m, 12H, $CH_3$), 0.40 (d, $J$ = 5.7Hz, 6H, $CH_3$). $^{13}$C{$^{1}$H} NMR (125 MHz, THF-$d_8$): $\delta$ 176.5 ($C_q$, $COCH_3$ ), 144.4 (t, $J_{P–C}$ = 6.2Hz, 2C, $C_q$), 142.9 (t, $J_{P–C}$ = 29.1Hz, $C_q$), 126.9 (2C, CH), 124.3 (CH), 79.0 (2C, $CH_2$), 28.2 (t, $J_{P–C}$ = 13.4Hz, 2C, CH), 27.3 (t, $J_{P–C}$ = 9.5Hz, 2C, CH), 24.3 ($CH_3$), 18.0 (6C, $CH_3$), 16.2 (2C, $CH_3$). $^{31}$P{1H} NMR (202 MHz, THF-$d_8$): $\delta$ 136.5 (s). HRMS (ESI): *m/z* calcd. for $[C_{22}H_{38}O_4P_2Ni+H]^+$ $[M+H]^+$ 487.1672, found 487.0840; $[C_{22}H_{38}O_4P_2Ni–OAc]^+$ $[M–OAc]^+$ 427.1460, found 427.1461. This compound is highly moisture and thermal sensitive; hence, a satisfactory elemental analysis was not obtained.

**($^{iPr4}$POCCCOP)Ni(OTf)** (**11**): To the solution of ($^{iPr4}$POCCCOP)NiBr (**9**; 0.02 g, 0.039 mmol) in THF (10 mL) was added AgOTf (0.011 g, 0.043 mmol). The reaction mixture in Schlenk flask was covered with aluminium foil, and was stirred at room temperature for 3 h. The reaction mixture was filtered through cannula filtration to remove the insoluble materials, and the filtrate was concentrated under vacuum to obtain nickel complex ($^{i}$Pr$_4$-POCCCOP)Ni(OTf) (**11**) as brown powder. Yield: 0.015 g, 65%. $^{1}$H NMR (500 MHz, $C_6D_6$): $\delta$ 6.64 (t, $J$ = 7.1 Hz, 1H, Ar–H), 6.48 (d, $J$ = 7.3 Hz, 2H, Ar–H), 5.37 (d, $J$ = 10.7 Hz, 2H, $CH_2$), 4.63-4.50 (m, 2H, $CH_2$), 3.04-2.93 (m, 2H, CH), 1.82-1.71 (m, 2H, CH), 1.42 (q, $J$ = 7.3, 6.9 Hz, 6H, $CH_3$), 1.09-1.01 (m, 12H, $CH_3$), 0.22 (q, $J$ = 6.9, 6.7 Hz, 6H, $CH_3$). $^{31}$P{$^{1}$H} NMR (202 MHz, $C_6D_6$): $\delta$ 133.7. $^{19}$F{$^{1}$H} NMR (376 MHz, THF-$d_8$): $\delta$ -80.3., $^{13}$C{$^{1}$H} NMR (125 MHz, $C_6D_6$): $\delta$ 142.9 (t, $J_{P–C}$ = 6.2 Hz, 2C, $C_q$), 134.7 (t, $J_{P–C}$ = 29.1 Hz, $C_q$), 128.4 ($CF_3$), 127.0 (2C, CH), 125.1 (CH), 78.5 ($CH_2$), 27.1 (2C, CH), 26.7 (t, $J$ = 13.4 Hz, 2C, CH), 18.4 (2C, $CH_3$), 17.7 (2C, $CH_3$), 17.2 (2C, $CH_3$), 16.0 (2C, $CH_3$). HRMS (ESI): *m/z* calcd. for $[C_{21}H_{35}O_5F_3NiP_2S+H]^+$ $[M+H]^+$ 577.1059, found 577.3794; $[C_{21}H_{35}O_5F_3NiP_2S–OTf]^+$ $[M–OTf]^+$ 427.1460, found 427.1870. This compound is also highly moisture and thermal sensitive; hence, a satisfactory elemental analysis was not obtained.

**Representative Procedure for Alkylation of Benzothiazole**

**2-(*n*-Octyl)benzo[*d*]thiazole** (**13a**): To a flame dried screw cap tube equipped with magnetic stirrer bar was introduced catalyst 2 (0.006 g, 0.01 mmol, 5.0 mol%), CuI (0.001 g, 0.005 mmol, 2.5 mol%), Li$O^t$Bu (0.032 g, 0.4 mmol), benzothiazole (**5a**; 0.027 g, 0.2 mmol) and 1-iodooctane (**12a**; 0.096 g, 0.4 mmol) inside the glove box. To the above reaction mixture, 1,4-dioxane (1.0 mL) was added under an argon atmosphere, and the resultant reaction mixture was stirred at 100 $^oC$ in a preheated oil bath for 24 h. At ambient temperature, the reaction mixture was quenched with distilled water (5 mL) and neutralized with 2 N HCl (0.5 mL). The crude product was then extracted with ethyl acetate (10 mL × 3) and the organic extract was dried over $Na_2SO_4$. Then, *n*-dodecane (0.025 mL, internal standard) was added and the mixture was stirred vigorously. An aliquot of the sample was withdrawn to a GC vial and subjected to the GC analysis. The yield of the coupled product **13a** was found to be 91% (*Note*: The authenticity of all the coupled products was verified by comparing them with the isolated products).[58]

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# Chapter 4

## Quinolinamine-based Pincer Nickel Complexes for Sonogashira Cross-Coupling of Phenylacetylene with Alkyl Halides

## 4.1 INTRODUCTION

Pincer-ligated nickel complexes have been widely explored in diverse catalytic organic transformations due to their stability under heat, moisture and air.[1-7] Among the various reactions, the pincer-nickel complexes are commonly explored as catalysts for traditional C–C cross-couplings,[8-18] direct C–H functionalizations,[19-23] Kharasch addition,[24-26] olefin isomerisation,[27] small molecule activation,[28] hydrosilylation of alkenes,[29-31] carbonyl compounds,[32,33] hydroboration,[34,35] and many other[36,37] reactions. Most of these reactions were resulted with high turnover numbers and broad substrates scope than the similar reactions with a bidentate- or monodentate-ligated nickel catalyst. Further, the pincer-ligated nickel complexes were also demonstrated in enantioselective synthesis.[37-39] The Sonogashira cross coupling is one of the prominent cross-coupling reactions where an alkyne is coupled with alkyl or aryl halides.[40] Many transition-metal catalysts based on Pd,[41-49] Mn,[50] Fe,[51] Co,[40,52] Ni,[53-55] and Cu[56,57] were employed in the Sonogashira cross-coupling reaction. But very few Pincer-ligated complexes are known to catalyze Sonogashira cross-coupling, for example by (pincer)Pd,[58-62] (pincer)Ni,[10,12,63] and (pincer)Cu complexes.[64,65]

Recently, Hu developed ($NN_2$)NiCl and ($NNN^{Me2}$)NiCl catalyst systems that were efficiently employed in the Sonogashira cross-coupling. Unfortunately, the synthesis of these catalysts involve multiple steps and uses expensive $Pd_2(dba)_3$ precursor. Thus, these catalysts limit the scope for a large scale synthesis. In this chapter, we discuss the use of ($^{Q}NNN^{Me2}$)NiCl catalyst that was easily synthesized in two steps with inexpensive precursors. The quinolinylamino-pincer nickel system, ($^{R2}NNN^{Q}$)NiCl [$\kappa^N,\kappa^N,\kappa^N$-{$R_2NCH_2CH_2$-($\mu$-N)-$C_9H_6N$}NiCl] ($R_2N$ = $Me_2N$, pyrrolidinyl) was developed with the assumption that the tridentate-nitrogen donor ligand would stabilize the nickel-centre in higher oxidation states during the alkylation process, which in turn can perform the alkylation reaction under mild conditions (Figure 4.1). In fact, the ($^{Q}NNN^{Me2}$)NiCl catalyst system catalyzes the alkylation of phenylacetylene with distinct alkyl halides employing low catalyst loading in the presence of Li$O^t$Bu as a base. A variety of alkyl halides were efficiently coupled with phenylacetylene and afforded the desired products in good yields.

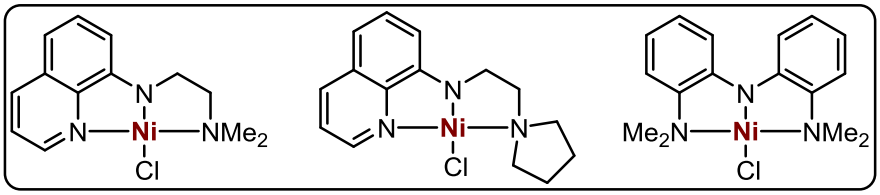



**Figure 4.1** Qunolinamine-based NNN-pincer nickel complexes for Sonogashira cross-coupling.

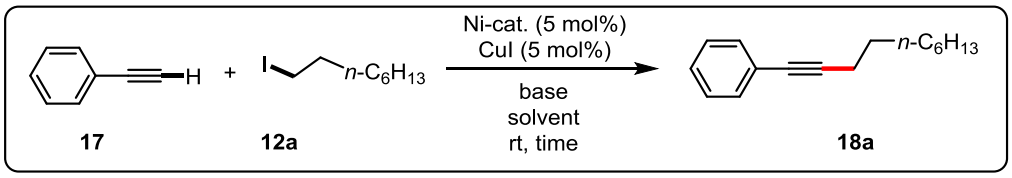
## 4.2 RESULTS AND DISCUSSION

### 4.2.1 Catalytic Activity of ($^{Q}$NNN$^{R2}$)NiCl Complexes for Sonogashira Cross-Coupling

Newly developed pincer nickel complexes in our group were screened, optimized and employed for Sonogashira coupling of phenylacetylene with alkyl halides. Initially, all the pincer complexes $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-$CH_2CH_2$-$NR_2$}NiCl [($^{Q}$NNN$^{R2}$)NiCl {$R_2N$ = $Me_2N$, **14a**; $C_4H_8N$, **14b**}], $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-$C_6H_4$-*o*-$NMe_2$}NiCl [($^{Q}$NNN$^{Me2}$)NiCl, **15**] were screened for the coupling of phenylacetylene (**17**; 0.30 mmol) with 1-iodooctane (**12a**; 0.20 mmol), employing CuI (5.0 mol%) co-catalyst and Li$O^t$Bu base in DMF at room temperature (standard conditions employed with the hemilabile $\kappa^N,\kappa^N,\kappa^N$-[{$C_6H_4$-*o*-$NMe_2$-($\mu$-N)-$CH_2CH_2$-$NMe_2$}NiCl] [(NNN$^{Me2}$)NiCl] catalyst).[12] Among all the complexes screened, the complex **14a** showed better conversion and afforded the coupled product **18a** in 58% isolated yield (Table 4.1, entries 1-4). The reaction in polar aprotic solvents such as DMSO, DMAc, NMP and diglyme proceeded slowly using catalyst **14a** (entries 5-8). Further, the mild and less expensive bases were screened for the coupling reaction, but the conversion of substrate **17** into product **18a** was not up to the mark (entries 9-11). Surprisingly, the reaction in the presence of a strong base Na$O^t$Bu didn't give a better conversion (entry 12). The absence of CuI co-catalyst in the reaction resulted in the formation of trace product (entry 13). Further, the increasing amount of base and decreasing the reaction time did not improve the yield of **18a**, though the reaction was completed during that time (entries 14-18). Interestingly, the decrease in the amount of solvent from 1 mL to 0.3 mL gave the product **18a** in a maximum of 63% isolated yield (entry 19). Employment of nickel catalyst **14a** under this reaction condition was essential, without which small amount of coupled product was detected (entry 21). The presence of CuI as co-catalyst was very much essential to afford good conversion rate. Most likely, the CuI co-catalyst enhances the transmetalation of phenylacetylene to the nickel center.[12] After investigating various reaction parameters, we found that the coupled product 1-octyl-2-phenylacetylene (**18a**) could be obtained in 63% isolated

yield, employing 5 mol% of catalyst **14a** and 5.0 mol% of CuI in the presence of LiO$^t$Bu in DMF at room temperature for 2 h (entry 19).

**Table 4.1** Optimization of Reaction Conditions for ($^{R2}$NNN$^{Q}$)Ni-catalyzed Sonogashira Cross-Coupling of Phenylacetylene with 1-Iodooctane.[a]




| Entry[a] | Ni-cat. | Base (equiv) | Solvent | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | **14a** | LiO$^t$Bu (1.5) | DMF | 16 | 58[c] |
| 2 | **14b** | LiO$^t$Bu (1.5) | DMF | 16 | 21 |
| 3 | **15** | LiO$^t$Bu (1.5) | DMF | 16 | 10 |
| 4 | **16** | LiO$^t$Bu (1.5) | DMF | 16 | 16 |
| 5 | **14a** | LiO$^t$Bu (1.5) | DMSO | 16 | 20 |
| 6 | **14a** | LiO$^t$Bu (1.5) | DMAc | 16 | 15 |
| 7 | **14a** | LiO$^t$Bu (1.5) | NMP | 16 | 3 |
| 8 | **14a** | LiO$^t$Bu (1.5) | Diglyme | 16 | - |
| 9 | **14a** | $K_2CO_3$ (1.5) | DMF | 16 | 15 |
| 10 | **14a** | $Cs_2CO_3$ (1.5) | DMF | 16 | 42 |
| 11 | **14a** | $K_3PO_4$ (1.5) | DMF | 16 | 16 |
| 12 | **14a** | NaO$^t$Bu (1.5) | DMF | 16 | 32 |
| 13 | **14a** | LiO$^t$Bu (1.5) | DMF | 16 | 8[d] |
| 14 | **14a** | LiO$^t$Bu (2.5) | DMF | 8 | 55[c] |
| 15 | **14a** | LiO$^t$Bu (2.5) | DMF | 6 | 50 |
| 16 | **14a** | LiO$^t$Bu (2.5) | DMF | 4 | 53 |
| 17 | **14a** | LiO$^t$Bu (2.5) | DMF | 2 | 54 |
| 18 | **14a** | LiO$^t$Bu (2.5) | DMF | 1 | 45 |

| | | | | | |
|---|---|---|---|---|---|
| 19 | **14a** | LiO$^t$Bu (2.5) | DMF | 2 | 63[c,e] |
| 20 | **14a** | LiO$^t$Bu (1.3) | DMF | 6 | 23 |
| 21 | **14a** | LiO$^t$Bu (2.5) | DMF | 2 | 5[e,f] |

[a]Conditions: 1-Iodooctane (0.048 g, 0.20 mmol), phenylacetylene (0.031 g, 0.30 mmol), base 0.3-0.5 mmol), Ni-cat. (0.01 mmol), CuI (0.002 g, 0.01 mmol) and solvent (1.0 mL). [b]G.C. yield. [c]Isolated yield. [d]CuI was not employed. [e]0.3 mL of DMF was added. [f]Without Ni-cat.

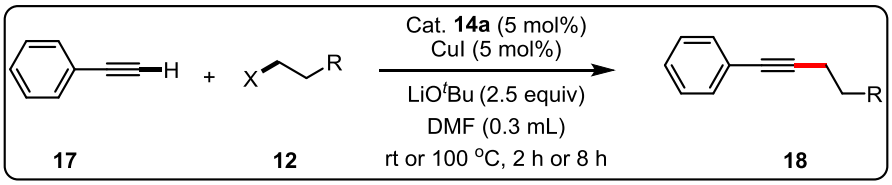
*Note*: Catalyst **16** is the quinolinamine-based phosphine complex, $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-$C_6H_4$-*o*-$PPh_2$}NiCl [($^Q$NNP$^{Ph2}$)NiCl].

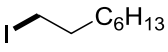
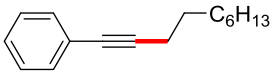
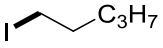
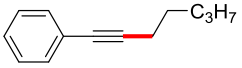
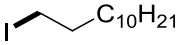
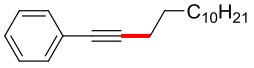
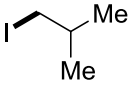
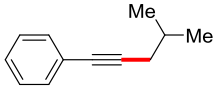
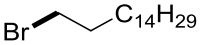
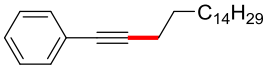
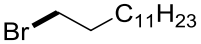
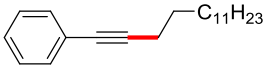
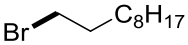
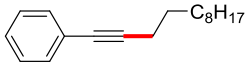
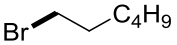
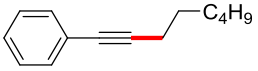
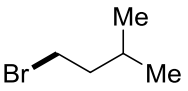
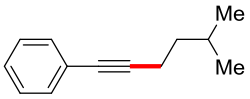
### 4.2.2 Substrate Scope for Alkyl Halides in the 14a-Catalyzed Sonogashira Cross-Coupling

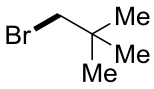
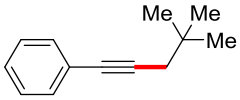
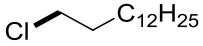
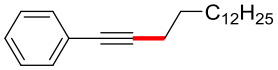
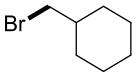
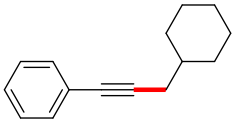
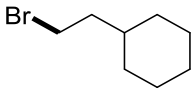
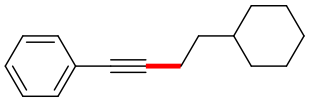
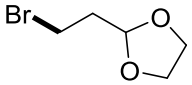
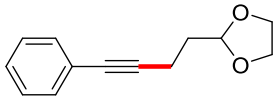
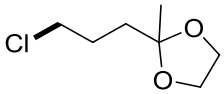
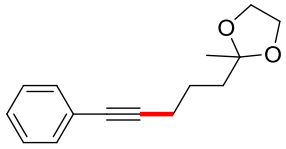
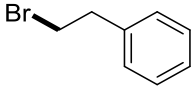
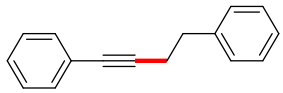
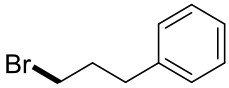
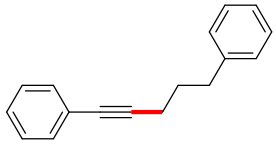
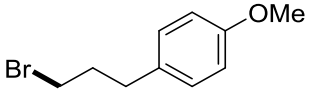
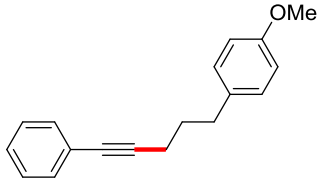
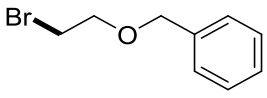
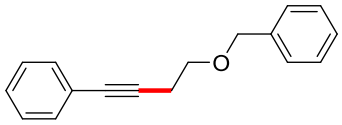
With the optimized reaction condition in hand, the Sonogashira cross-coupling of phenylacetylene (**17**) with various alkyl halides **12a-y** was performed (Table 4.2). Alkyl iodides with distinct alkyl chains **12a-d** were coupled with the phenylacetylene (**17**) to give the desired alkylated products **18a-d** in moderate to good yields (entries 1-4). Alkyl bromides with different alkyl chains **12e-h** were successfully coupled with the substrate **17** to obtain the alkylated products **18e-h** in moderate yields. Alkyl bromides with branching at $\beta$- and $\gamma$-position reacted smoothly to give the products **18i-j** in good yields. The alkyl chloride **12k** was employed for coupling with **17** to yield the corresponding alkylated product **18k** in 43% yield. Generally, alkyl iodides were more reactive than alkyl bromides, which in turn are more reactive than the alkyl chlorides (entries 1-11). The alkyl bromides bearing cyclohexyl ring **12l**, **12m** were also successfully employed for coupling with **17** to produce the alkylated products **18l**, **18m** in good yields (entries 12, 13). The alkyl halides bearing dioxolane ring **12n**, **12o** were also employed for cross-coupling with **17** to yield the expected coupled products **18n**, **18o** (entries 14, 15). The alkyl halides carrying aromatic phenyl ring **12p-r** were efficiently coupled with **17** to achieve the corresponding alkylated products **18p-r** (entries 16-18). The alkyl bromide, bearing ether functional group as well as phenyl ring **12s**, undergone the coupling with **17** to yield the product **18s** (entry 19). Finally, the dihalo alkanes **12t-y** were coupled with **17** to achieve the coupling at more electrophilic site and yield the regioselective products **18t-y**. The tolerance of selectively one halide functionality in the reaction is very important as they can be used for further coupling. Notably, a cyano group tolerated efficiently under the catalytic conditions (entry 23). The

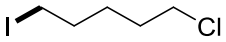
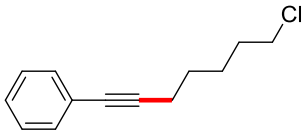
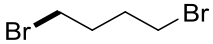
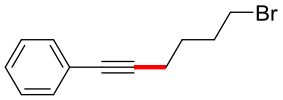
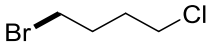
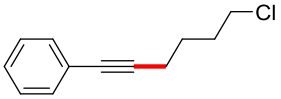
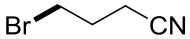
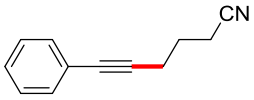
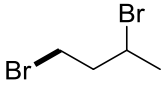
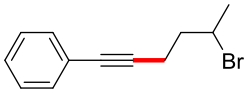
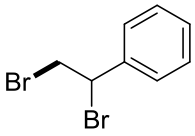
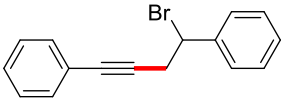
primary bromide is reacted efficiently in the presence of secondary bromide center. Considering the tolerance of sensitive functional group and high chemoselectivity, this methodology will make a huge impact for the other coupling reactions.

**Table 4.2** Scope for the 14a-Catalyzed Alkylation of Phenylacetylene with Alkyl Halides.[a]




| Entry | Alkyl halide (12) | Product (18) | Yield (%)[b] |
|---|---|---|---|
| 1 |  (**12a**) |  (**18a**) | 65(63) |
| 2 |  (**12b**) |  (**18b**) | 74 |
| 3 |  (**12c**) |  (**18c**) | 59 |
| 4 |  (**12d**) |  (**18d**) | 78 |
| 5 |  (**12e**) |  (**18e**) | 49 |
| 6 |  (**12f**) |  (**18f**) | 50 |
| 7 |  (**12g**) |  (**18g**) | 54 |
| 8 |  (**12h**) |  (**18h**) | 80 |
| 9 |  (**12i**) |  (**18i**) | 70 |

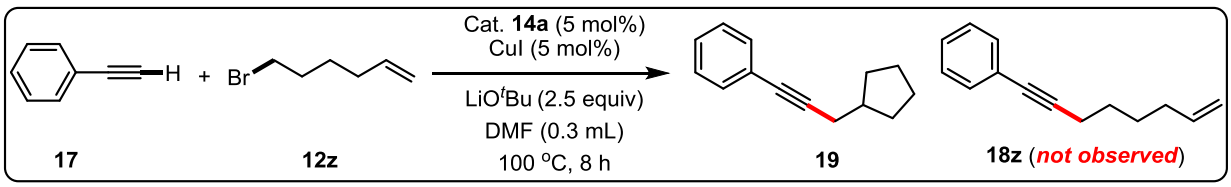
| | | | | |
|---|---|---|---|---|
| 10 |  | **(12j)** |  | **(18j)** | 66 |
| 11 |  | **(12k)** |  | **(18k)** | 43 |
| 12 |  | **(12l)** |  | **(18l)** | 80 |
| 13 |  | **(12m)** |  | **(18m)** | 73 |
| 14 |  | **(12n)** |  | **(18n)** | 71 |
| 15 |  | **(12o)** |  | **(18o)** | 64 |
| 16 |  | **(12p)** |  | **(18p)** | 67 |
| 17 |  | **(12q)** |  | **(18q)** | 66 |
| 18 |  | **(12r)** |  | **(18r)** | 72 |
| 19 |  | **(12s)** |  | **(18s)** | 57 |

| | | | | |
|---|---|---|---|---|
| 20 |  | **(12t)** |  | **(18t)** | 71 |
| 21 |  | **(12u)** |  | **(18u)** | 70 |
| 22 |  | **(12v)** |  | **(18v)** | 76 |
| 23 |  | **(12w)** |  | **(18w)** | 81 |
| 24 |  | **(12x)** |  | **(18x)** | 68 |
| 25 |  | **(12y)** |  | **(18y)** | 79 |

[a] Conditions: Phenylacetylene (**17**, 0.3 mmol), alkyl halide (**12**, 0.2 mmol), LiO$^t$Bu (0.5 mmol), DMF (0.3 mL). [b] G.C. yields. Isolated yields are given in parenthesis.

### 4.2.3 Investigation of Reaction Mechanism

An experiment was performed to investigate whether the reaction goes *via* radical path way (Scheme 4.1). For this purpose, phenylacetylene was treated with 6-bromo-1-hexene (**12z**). In this reaction, the expected product **18z** was not obtained; instead the radical at the electrophilic carbon was cyclized to the double bond lying on the end of the chain **12z**. As a result, the reaction produced the cyclic product **19** in good yield. In addition, the catalytic reaction was completely quenched in the presence of a radical inhibitor TEMPO. These experiments indicate that the reaction most likely proceed *via* a radical manifold.




**Scheme 4.1** Radical Clock Experiment.

Based on the preliminary mechanistic experiments and literature precedents,[20,21] a probable mechanism for the reaction was proposed (Figure 4.2). Initially, LiO$^t$Bu could abstract a proton from phenyl acetylene and undergo cupration with CuI to give the phenylacetylenecopper species **A**, which would undergo transmetalation with the nickel catalyst **14a** to obtain ($^{Q}$NNN$^{Me2}$)Ni(phenylacetylene) species **B**. The nickel(II) species **B** would react with alkyl halide to generate the Ni(III)-intermediate **C** and the alkyl radical . The nickel(III) intermediate **C** and the alkyl radical could combine each other to generate the nickel(IV) species **D**, which would then undergo reductive elimination to deliver the product **18** and regenerate the catalyst **14a**.

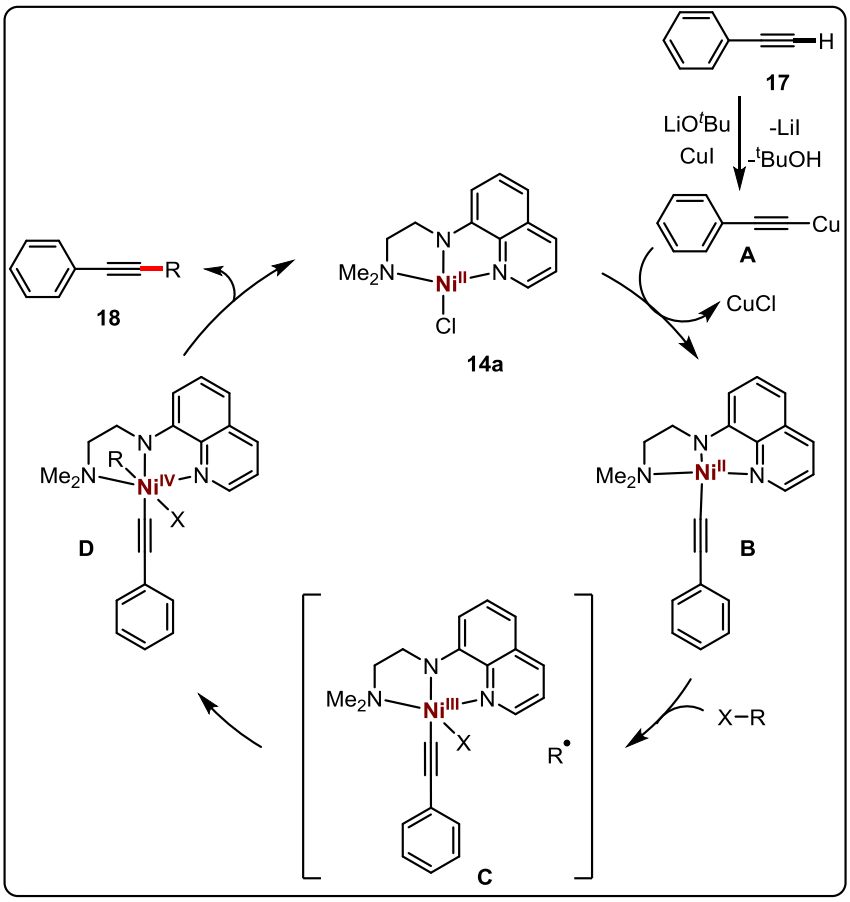



**Figure 4.2** Proposed mechanism for **14a**-catalyzed Sonogashira cross-coupling of phenylacetylene with alkyl halides.

## 4.3 CONCLUSION

In this chapter, we have discussed the application of quinolinamine-based NNN-pincer nickel complexes (**14a**, **14b**, **15** and **16**) in the Sonogashira cross-coupling of phenylacetylene with various alkyl halides. The catalyst **14a** shows excellent functional group tolerance and high chemoselectivity. The reaction was explored by employing a variety of starting precursors and in all the cases the corresponding coupling products are obtained in good to excellent yields. The current transformation was successfully achieved by using starting precursors that contain cyano and bromo functionality giving the desired coupling products. Preliminary mechanistic study suggests that the reaction follow a radical pathway.

## 4.4 EXPERIMENTAL SECTION

### Representative Procedure for Arylation of Benzothiazoles

**1-Octyl-2-phenylacetylene** (**18a**): To a flame-dried Schlenk tube containing magnetic stir bar were added the catalyst **14a** (0.003 g, 0.010 mmol) and CuI (0.002 g, 0.010 mmol). The Schlenk tube with catalysts mixture was evacuated under vacuum and refilled with argon. Subsequently, phenylacetylene (**17**; 0.031 g, 0.3 mmol), 1-iodooctane (**12a**; 0.048 g, 0.2 mmol), Li$O^t$Bu (0.040 g, 0.5 mmol) and DMF (0.3 mL) were added under argon. The resultant reaction mixture was degassed, refilled with argon and was stirred at room temperature for 2 h. The reaction mixture was quenched with the saturated aqueous $NH_4Cl$ solution (10 mL) and the reaction mixture was extracted with $CH_2Cl_2$ (20 mL x 3). The combined organic layers were dried over $Na_2SO_4$ and the volatiles were evaporated in *vacuo*. The resultant residue was purified by column chromatography on silica gel (petroleum ether) to yield **18a** (0.027 g, 63%) as a colourless liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.49-7.33 (m, 2H, Ar–H), 7.32-7.14 (m, 3H, Ar–H), 2.40 (t, $J$ = 7.0 Hz, 2H), 1.71-1.52 (m, 3H), 1.50-1.39 (m, 2H), 1.37-1.26 (m, 7H), 0.99-0.77 (m, 3H).

The $^1$H and $^{13}$C NMR data as well as HRMS of the alkylated products **18a-y** are in accordance with those reported in the literature.[67-81]

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# Chapter 5

## Synthesis and Characterization of Pincer-based Copper(II) Complexes: Application in Kumada Coupling of Alkyl Halides

## 5.1 INTRODUCTION

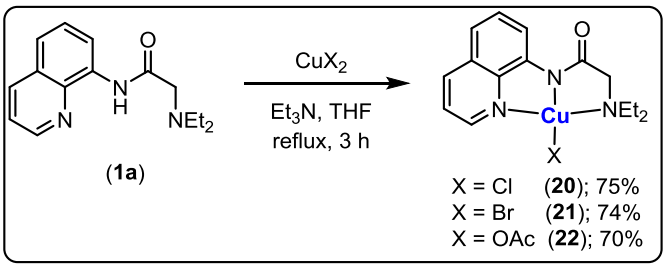
Pincer-ligated transition metal complexes have found tremendous application in catalysis as well as in material chemistry.[1] Particularly, high thermal stability and rigid structure of pincer complexes make them extensively useful in diverse organic transformations, because the tight coplanar coordination keeps the pincer and metal together in a catalytic cycle, wherein the steric and electronic factors on ligands are effectively transferred to the metal centre.[1,2] Pincer complexes of noble metals, such as Pd, Rh and Ir are extensively studied and employed as catalysts in important chemical reactions.[3-20] Recently, pincer complex based on earth-abundant and inexpensive 3d metals has give special attention because of the economical viability and unique feature of these transition metals. In that regards, complexes of Mn,[21-38] Fe,[39-46] Co,[47-55] Ni,[56-63] and Cu[64-80] are developed and effectively employed in numerous applications. Among them, the pincer copper complexes were used in biological applications like anti-oxidants, luminescence, medicine and antibacterial activity.[69,79,81-96] In addition, the pincer complexes are explored in several catalytic cross-couplings as well as in direct C–H bond functionalizations.[67,97-122]

The Kumada coupling is one of the most important cross-coupling reactions, useful in achieving C–C coupled products by the reaction of the Grignard reagent with an organic halide.[123] The Kumada coupling is well precedented by early transition-metal salts, such as Fe,[124-132] Co,[133,134] Ni[135,136] and Cu[137-140]. Moreover, the pincer complexes of Mn,[141] Fe,[142] Ni[117,121,143-150] and Cu[110] are also employed in the Kumada coupling reaction. Liu and co-workers demonstrated the Kumada coupling of non-activated secondary alkyl tosylates and mesitylates employing CuI/TMEDA or CuI/dppm catalyst system.[138,139] Recently, Kirchner utilized a well-defined phosphazine-based PNP-pincer copper complex in the Kumada coupling of aryl triflates and bromides with aryl Grignard reagents.[110] Although the developed copper catalyst systems are promising and encouraging, there is still scope for the development of defined pincer complexes based on *N*-ligand that can be utilized for the Kumada coupling of more challenging and readily available alkyl chlorides. In this chapter, I have discussed the synthesis and characterization of a series of quinolinyl-based NNN-pincer copper complexes $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-$C(O)CH_2NEt_2$}CuX [($^{Q}NNN^{Et2}$)CuX (**21-24**). The well-defined phosphine-free copper complexes were efficiently demonstrated for the Kumada coupling of alkyl chlorides with alkyl magnesium chloride.

## 5.2 RESULTS AND DISCUSSION

### 5.2.1 Synthesis of ($^{Q}$NNN$^{Et2}$)-Ligated Copper(II) Complexes

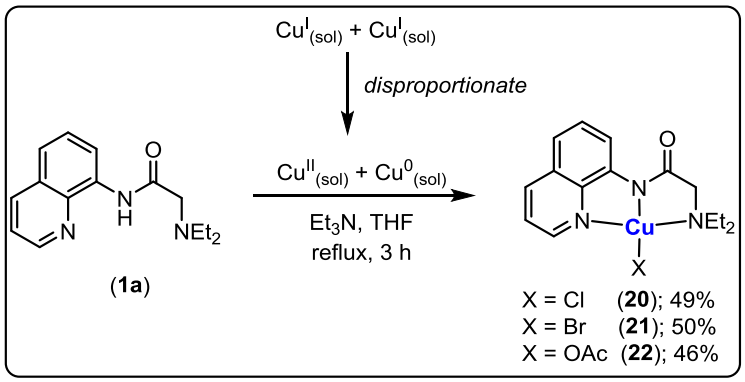
Recently, $C_9H_6N$-NHC(O)$CH_2NEt_2$ [($^{Q}$NNN$^{Et2}$)–H; **1a**] ligand and pincer nickel complexes [($^{Q}$NNN$^{Et2}$)NiX; **1.124**] were developed in our group, wherein pincer nickel complexes were found to be very efficient catalyst for the C–H bond alkylation, arylation and benzylation of indoles.[115,116] In this chapter, the reactivity of ligand **1a** with various copper precursors was explored. Thus, the metallation of ligand, $^{Q}$NNN$^{Et2}$–H (**1a**) with $CuCl_2$, $CuBr_2$ and $Cu(OAc)_2$ in the presence of $Et_3N$ in THF under reflux condition afforded copper(II) complexes $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-C(O)$CH_2NEt_2$}CuCl [($^{Q}$NNN$^{Et2}$)CuCl; **20**], $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-C(O)$CH_2NEt_2$}CuBr [($^{Q}$NNN$^{Et2}$)CuBr; **21**] and $\kappa^N,\kappa^N,\kappa^N$-{$C_9H_6N$-($\mu$-N)-C(O)$CH_2NEt_2$Cu(OAc)} [($^{Q}$NNN$^{Et2}$)Cu(OAc); **22**], respectively, in good yields (Scheme 5.1). The resulted complexes are paramagnetic in nature and hence could not be characterized by $^{1}$H and $^{13}$C NMR analyses. However, all three complexes were characterized by elemental analysis and HRMS. The HRMS of **20** shows peak at *m/z* 319.0734 and 355.0500 corresponding to [**20** – Cl]$^+$ and [**20** + H]$^+$, respectively. Similarly, the complexes **21** and **22** show peaks at 319.0735, 396.9861, 319.0745 and 379.0307 for [**21** – Br]$^+$, [**21** – H]$^+$, [**22** – OAc]$^+$ and [**22** + H]$^+$, respectively. The molecular structures of complexes **20**, **21** and **22** were further confirmed by single crystal X-ray diffraction studies.




**Scheme 5.1** Synthesis of Pincer Complexes ($^{Q}$NNN$^{Et2}$)CuX.

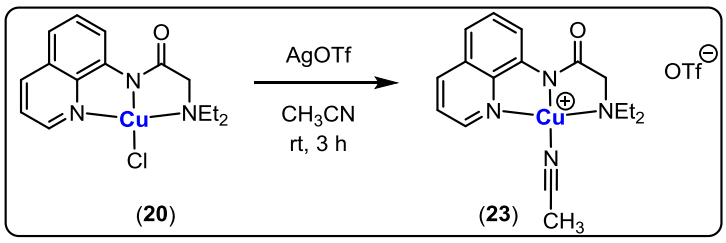
Further, the synthesis of copper(I) complexes of ($^{Q}$NNN$^{Et2}$)–H (**1a**) employing different Cu(I) precursors were planned. However, upon treatment of ligand **1a** with CuCl, CuBr and Cu(OAc) in the presence of $Et_3N$ in THF under reflux condition, the copper(II) complexes **20**, **21** and **22** were obtained in 49%, 50% and 46% yields, respectively. Notably the yields of the complexes **20**, **21** and **22** by the reaction of the ligand **1a** with Cu(I) salts are about 50%. This

may be due to the fact that Cu(I) salts in solution undergo disproportionation into Cu(II) and Cu(0) species. The resulting Cu(II) species would react with the ligand **1a** to produce the corresponding pincer copper(II) complexes in less than 50% yields (Scheme 5.2). Similar disproportionate reaction of copper is well established by various groups.[151-156] Molecular compositions as well as the molecular structures of complexes **20**-**22**, synthesized *via* this approach, are verified that well correlates with the complexes synthesized by employing Cu(II) precursors.




**Scheme 5.2** Reaction of Ligand ($^{Q}$NNN$^{Et2}$)–H with Cu(I)X to Produce ($^{Q}$NNN$^{Et2}$)Cu(II)X.

The reaction of complex ($^{Q}$NNN$^{Et2}$)CuCl (**20**) with AgOTf in acetonitrile at room temperature resulted in the formation of cationic complex, [($^{Q}$NNN$^{Et2}$)Cu($CH_3CN$)](OTf) (**23**) in 80% yield (Scheme 5.3). The complex **23** was characterized by elemental analysis as well as by MALDI-TOF-MS analysis. The MALDI-TOF analysis of the complex **23** showed the *m/z* values 508.8325 and 318.9736 that correspond to $[M]^+$ and $[M - (CH_3CN+OTf)]^+$, respectively. The cationic complex **23** was found to be very robust compared to complexes **20**-**22** as it decomposes above 230 $^{o}$C.




**Scheme 5.3** Synthesis of Cationic Complex [($^{Q}$NNN$^{Et2}$)Cu(MeCN)]OTf (**23**).

### 5.2.2 Crystal Structure Description of ($^{Q}$NNN$^{Et2}$)CuX Complexes

The ORTEP diagrams of complexes **20**, **21** and **22** are shown in Figures 5.1, 5.2 and 5.3, respectively. Selected bond lengths and bond angles are given in Table 5.1. In all three complexes, ligand **1a** provides a tridentate coordination to the copper through quinolinyl-*N*3, amido-*N*2 and amine-*N*1, and the fourth site is occupied by anionic ligand –Cl (**20**) or –Br (**21**) or –OAc (**22**). The coordination geometry around copper is slightly distorted from the expected square planar in all three complexes **20**, **21** and **22**. The Cu–N(2) bond lengths in **20** (1.9086(10) Å) and **21** (1.9097(12) Å) are slightly shorter than a similar Cu–N bond length (1.936(4) Å) in amido-complex, {$C_9H_6N$-($\mu$-N)-C(O)$CH_2$-$NH_2$}Cu($OCOCH_3$);[157] whereas the Cu–N(1) bond lengths (2.0690(10) Å in **20** and 2.0691(12) Å in **21**) and Cu–N(3) bond lengths (2.0093(10) Å in **20** and 2.0128(12) Å in **21**) are comparable with the corresponding bond lengths in {$C_9H_6N$-($\mu$-N)-C(O)$CH_2$-$NH_2$}Cu($OCOCH_3$). The N(1)–Cu–N(3) bond angles in **20** (166.80(4) Å) and **21** (166.84(5)$^{o}$) are comparable to each other, and significantly larger than that reported for {$C_9H_6N$-($\mu$-N)-C(O)$CH_2NH_2$}Cu($OCOCH_3$) (159.7(2)°). The N(1)–Cu–N(2), N(2)–Cu–N(3) bond angles in **20** and **21** are 84.55(4), 82.57(4)$^{o}$ and 84.57(5), 82.60(5)°, respectively. The five-membered ring containing Cu, N(2), N(3) is almost planar with the quinolinyl-moiety (Cu(1)-N(2)-C(3)-C(11) = -5.17(13) for **20** and 6.02(15) for **21**), whereas other five-membered Cu-containing ring is highly distorted (Cu(1)-N(1)-C(1)-C(2) torsion angle 15.80(11) for **20** and -15.99(13) for **21**).

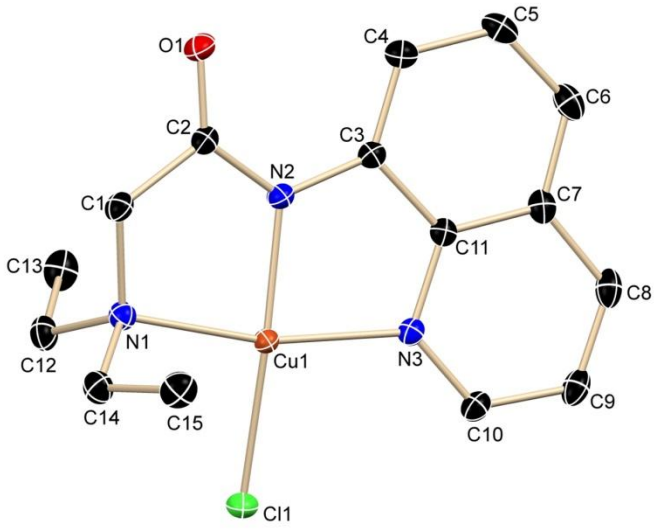



**Figure 5.1** Thermal ellipsoid plot of ($^{Q}$NNN$^{Et2}$)CuCl (**20**). All the hydrogen-atoms are omitted for clarity.

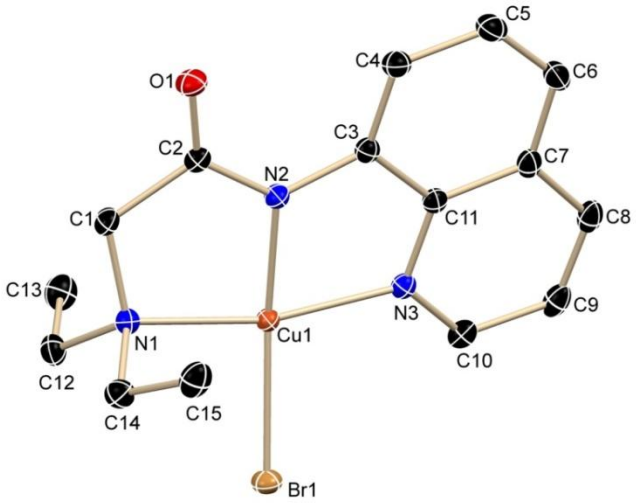



**Figure 5.2** Thermal ellipsoid plot of ($^{Q}$NNN$^{Et2}$)CuBr (**21**). All the hydrogen-atoms are omitted for clarity.

The complex **22** crystallizes in two different patterns: (i) in one, a molecule of $H_2O$ bridges between two copper complexes **22** (Figure 5.3), wherein the geometry around Cu(II)-center is distorted square planar and (ii) in other, complex **22** exists as a polymeric form (Figure 5.4), where the geometry around Cu(II)-centre is square-pyramidal. Complex **22**.$(H_2O)_{0.5}$ was most likely obtained by the presence of ubiquitous water in the solvent used for recrystallization. Particularly, this complex was formed from the crystallization process of the reaction of ligand **1a** with $Cu(OAc)_2$. However, the polymeric form of **22** was obtained when the mother liquor was completely dried. This complex was often recrystalized from the reaction of **1a** with Cu(OAc). In the complex **22**.$(H_2O)_{0.5}$, two molecules of ($^{Q}$NNN$^{Et2}$)Cu(OAc) are held together by hydrogen bonding between the bonded oxygen atom of acetate in **22** with water in a [Cu]–AcO$^{\cdots}$H–O–H$^{\cdots}$OAc–[Cu] mode, wherein AcO–H distance is 2.055 Å and AcO–H–O bond angle in 177.56$^{o}$ (Figure 5.3). In the polymeric structure of complex **22**, the ligand carbonyl oxygen of one ($^{Q}$NNN$^{Et2}$)Cu(OAc) makes a bond with the Cu-centre of another ($^{Q}$NNN$^{Et2}$)Cu(OAc), resulting in the formation of a catemeric structure, wherein Cu(1)–O(3) bond distance is 2.488 Å and O(3)–Cu(1)–C(2) bond angle is 134.47° (Figure 5.4). The Cu–N(2) bond lengths in **22**.$(H_2O)_{0.5}$ (1.9109(14) Å**)** and (**22**)$_n$ (1.926(2) Å) are slightly shorter than the similar Cu–N bond length (1.936(4) Å) in amido-complex, {$C_9H_6N$-($\mu$-N)-C(O)$CH_2$-$NH_2$}Cu($OCOCH_3$);[157] whereas the Cu–N(1) bond lengths in **22**.$(H_2O)_{0.5}$ (2.0633(13) Å) and (**22**)$_n$ (2.083(2) Å) as well as Cu–N(3) bond lengths in **22**.$(H_2O)_{0.5}$ (2.0107 Å) and (**22**)$_n$ (2.035(2) Å) are comparable. The Cu–O(1)

bond length (1.9618(11) Å) in **22**.$(H_2O)_{0.5}$ is slightly longer than the Cu–O(1) bond length (1.9302(19) Å) in $(\mathbf{22})_n$, which could be due to the involvement of oxygen atom O(1) of former complex in hydrogen bonding with water molecule. The N(1)–Cu–N(3) bond angles in **22**.$(H_2O)_{0.5}$ (162.42(6)°) and $(\mathbf{22})_n$ (1618(9)°) are comparable to each other and significantly larger than that reported for $\{C_9H_6N\text{-}(\mu\text{-}N)\text{-}C(O)CH_2\text{-}NH_2\}Cu(OCOCH_3)$ (159.7(2)°).[157] The N(1)–Cu–N(2), N(2)–Cu–N(3) bond angles in **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$ are 83.99(6), 82.51(6)$^o$ and 82.89(9), 81.50(9)°, respectively.

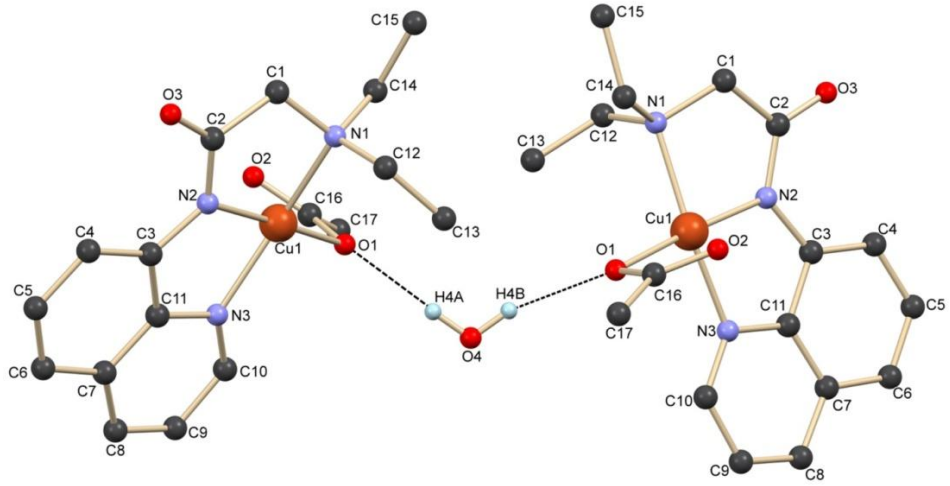



**Figure 5.3** Thermal ellipsoid plot of $(^{Q}NNN^{Et2})Cu(OAc).(H_2O)_{0.5}$ [**22**.$(H_2O)_{0.5}$]. All the hydrogen-atoms are omitted for clarity except on water molecule.

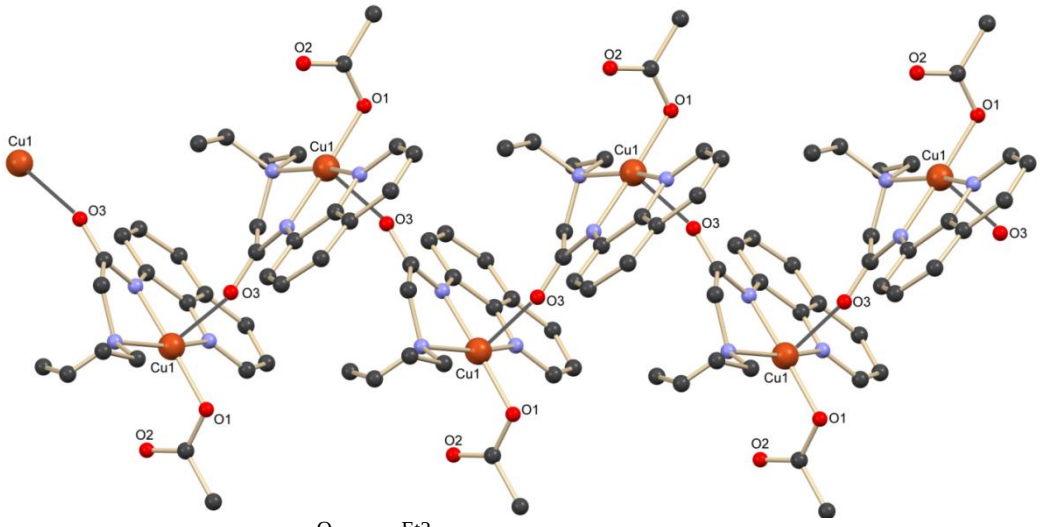



**Figure 5.4** Complete model of $[(^{Q}NNN^{Et2})Cu(OAc)]_n$ $[(\mathbf{22})_n]$. All the hydrogen-atoms are omitted for clarity.

**Table 5.1** Selected Bond Lengths (Å) and Angles (◦) for **20**, **21**, **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$

| | **20** | **21** | **22**.$(H_2O)_{0.5}$ | $(\mathbf{22})_n$ |
|---|---|---|---|---|
| **Bond Lengths** | | | | |
| Cu(1)–N(1) | 2.0690(10) | 2.0691(12) | 2.0633(13) | 2.083(2) |
| Cu(1)–N(2) | 1.9086(10) | 1.9097(12) | 1.9109(14) | 1.926(2) |
| Cu(1)–N(3) | 2.0093(10) | 2.0128(12) | 2.0107(13) | 2.035(2) |
| Cu(1)–O(1) | - | - | 1.9618(11) | 1.9302(19) |
| Cu(1)–Br(1) | - | 2.3523(2) | - | - |
| Cu(1)–Cl(1) | 2.2105(3) | - | - | - |
| **Bond Angles** | | | | |
| N(1)–Cu(1)–N(2) | 84.55(4) | 84.57(5) | 83.99(6) | 82.89(9) |
| N(1)–Cu(1)–N(3) | 166.80(4) | 166.84(5) | 162.42(6) | 1618(9) |
| N(2)–Cu(1)–N(3) | 82.57(4) | 82.60(5) | 82.51(6) | 81.50(9) |
| N(1)–Cu(1)–O(1) | - | - | 99.01(5) | 99.12(9) |
| N(2)–Cu(1)–O(1) | - | - | 175.85(5) | 17249(9) |
| N(3)–Cu(1)-O(1) | - | - | 95.08(5) | 95.89(9) |
| N(1)–Cu(1)–Br(1) | - | 95.90(3) | - | - |
| N(2)–Cu(1)–Br(1) | - | 171.48(4) | - | - |
| N(3)–Cu(1)–Br(1) | - | 97.23(3) | - | - |
| N(1)–Cu(1)–Cl(1) | 9264(3) | - | - | - |
| N(2)–Cu(1)–Cl(1) | 172.07(3) | - | - | - |
| N(3)–Cu(1)–Cl(1) | 97.42(3) | - | - | - |

### 5.2.3 X-ray Photoelectron Spectroscopy Studies for Complexes 22.$(H_2O)_{0.5}$ and $(22)_n$

The crystals **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$ were separated and characterized by XPS to determine the oxidation state of copper in both complexes. XPS analysis has been carried out using Thermo Scientific instrument with Al Kα monochromator source and obtained results were shown in Figure 5.5. The Cu 2p spectrum for both the complexes **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$ shows two main intense spin orbit splitting peaks $2p_{3/2}$ (933.5 eV) and $2p_{1/2}$ (953.4 eV). Along with the main peaks, two broad satellite peaks (**s**) at 942.2 and 962.2 eV were also observed. These satellite peaks normally appear in Cu(II) complexes due to charge transfer from the ligand ($O^{2-}$) to Cu(II)

centre. Hence, both the complexes have copper centre in +2 oxidation state. The obtained binding energies are in accordance with that reported for similar Cu(II) complexes.[158]

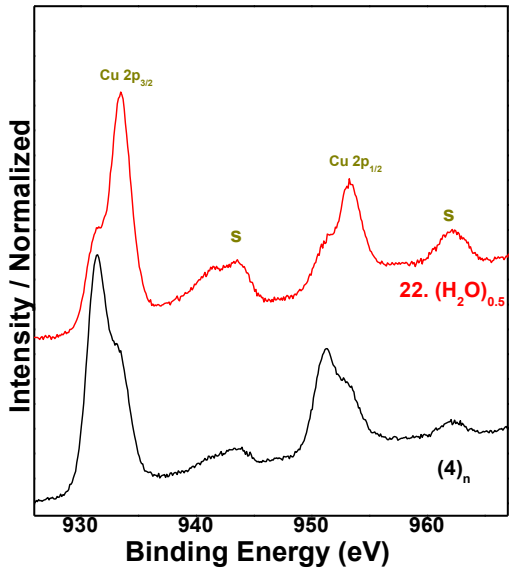



**Figure 5.5** The X-ray photoelectron spectra of Cu 2p of the complexes **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$ with normalized intensities.

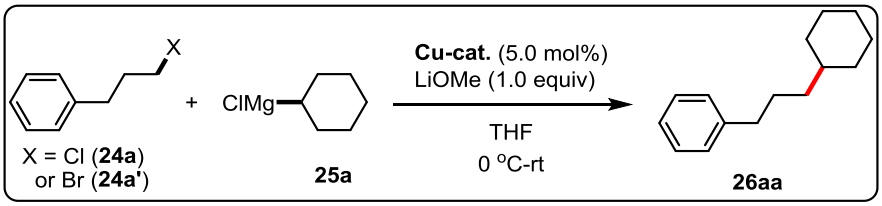
### 5.2.4 Catalytic Activity of ($^{Q}$NNN$^{Et2}$)CuX Complexes for Kumada Coupling Reaction

#### 5.2.4.1 Optimization of Catalytic Condition

The newly developed neutral pincer copper complexes ($^{Q}$NNN$^{Et2}$)CuX (**20**-**22**) along with cationic complex, [($^{Q}$NNN$^{Et2}$)Cu($CH_3CN$)](OTf) (**23**) were screened and employed for the Kumada coupling of alkyl halides with cyclohexylmagnesium chloride (Table 5.2). Initially, the complex **20** was employed for Kumada coupling of (3-bromopropyl)benzene (0.20 mmol) with cyclohexylmagnesium chloride (0.40 mmol) using a mild base LiOMe at 0 $^{o}$C, a reaction condition previously reported by Liu for similar reaction.[139] The desired coupled product **26aa** was obtained in 15% using the catalyst **20** (entry 1). By employing catalyst **21** and **22**, the NMR yield of the product **26aa** was 20% and 18%, respectively (entries 2,3). Notably, the use of cataionic complex **23** as catalyst afforded **26aa** in 57% isolated yield (entry 4). Reducing the amount of CyMgCl led to the decreasing yield of product (entry 5). Next, we moved to check the feasibility of coupling of (3-chloropropyl)benzene (**24a**), wherein 45% of product **26aa** was isolated (entry 6). Interestingly, in this reaction complete conversion of substrate to product was

noticed, though the isolated yield is low. Thus, increasing the amount of CyMgCl to 3.0 equiv and reducing the reaction time to 8 h, the coupled product **26aa** was isolated in 63% (entry 8). Further, lowering the reaction time to 6 h did improve the reaction and resulted with the 38% formation of **26aa** (entry 9).

**Table 5.2** Optimization of Reaction Conditions for the ($^{Q}$NNN$^{Et2}$)CuX-catalyzed Kumada Coupling.[a]




| Entry | Cu-cat. | X | 7a (equiv) | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | **20** | Br | 2 | 24 | 15 |
| 2 | **21** | Br | 2 | 24 | 20 |
| 3 | **22** | Br | 2 | 24 | 18 |
| 4 | **23** | Br | 2 | 24 | 67 (57)[c] |
| 5 | **23** | Br | 1.5 | 24 | 61 |
| 6 | **23** | Cl | 2 | 24 | 58 (45)[c] |
| 7 | **23** | Cl | 2 | 16 | 42 |
| **8** | **23** | **Cl** | **3** | **8** | **70 (63)[c]** |
| 9 | **23** | Cl | 3 | 6 | 38 |

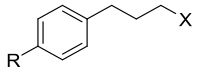
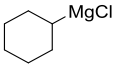
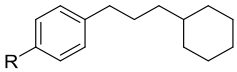
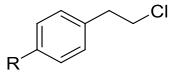
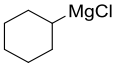
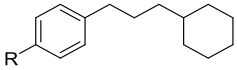
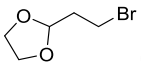
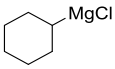
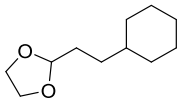
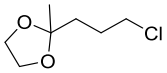
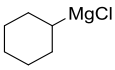
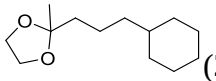
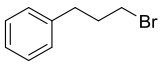
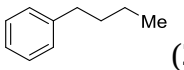
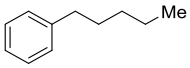
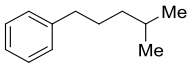
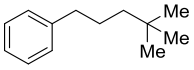
[a]Conditions: (3-halopropyl)benzene (0.2 mmol), cyclohexylmagnesium chloride (0.22-0.6 mmol), LiOMe (0.2 mmol), THF (1.0 mL). [b]Yields determined by $^{1}$H NMR. [c]Isolated yield is given in parentheses.

### 5.2.4.2 Substrate Scope for Kumada Coupling Reaction

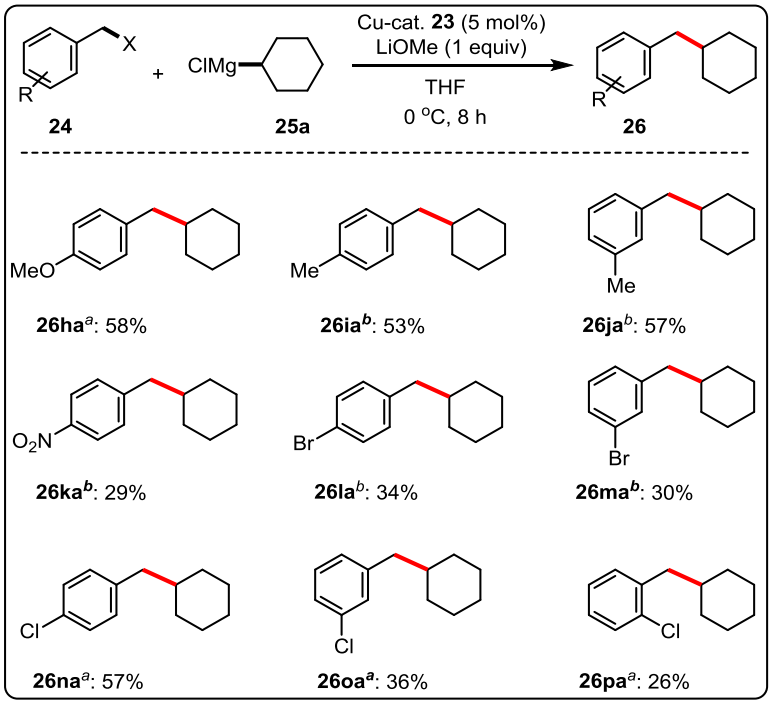
With the optimized reaction conditions in hand, the scope for various alkyl halides as well as alkyl Grignard reagents was explored (Table 5.3). In the case of alkyl halides, the cyclohexylmagnesium chloride (**25a**) was used as a coupling partner (entries 1-7). Substrate **24b** with an electron-donating OMe substituent at *para*-position and X = Br, gave the C–C coupled

product **26ba** in excellent yield (entry 2). The substrates with two methylene groups on the aryl ring with the *para*-substituents H, Cl, OMe (**24c-e**) gave the products **26ca-ea** in good yields (entries 3-5). For the coupling of alkyl halide **24d** with the Grignard reagent **25a**, an inseparable mixture of the product **26da** and the by-product bicyclohexyl was obtained in 87% yield (**26da**:bicyclohexyl = 70:30, accounting for the 61% of **26da**). With the dioxolane ring containing substrates **24f** and **24g**, the coupling products **26fa** and **26ga** were achieved in good to moderate yields (entries 6, 7). In the case of Grignard reagent scope, the bromo-substrate **24a'** was used as an electrophile (entries 8-11). The nucleophilic Grignard reagents such as methylmagnesium chloride (**25b**), ethylmagnesium chloride (**25c**), *i*-propylmagnesium chloride (**25d**) and *t*-butylmagnesium chloride (**25e**) were coupled with the substrate **24a'**, giving rise to excellent yields of the products **26ab-ae**. If the chloro-substrate **24a** was used as an electrophile, for the coupling with **25b**, most of the substrate **24a** left unreacted. However, dehalogenated product such as $Ph(CH_2)_3–H$ was obtained along with the unreacted substrate **24a** in the case of the Grignard reagents **25c-e**. Apart from all these alkyl halides, benzyl halides **24h-p** were also coupled with cyclohexylmagnesium chloride (**25a**) to deliver the coupled products **26ha-pa** in moderate to low yields employing the catalyst **23** (Scheme 5.4), wherein all the yields of the coupled products were determined by $^1H$ NMR using $CH_2Br_2$ as an internal standard. The coupling of the benzyl halides with electron-donating substituents such as OMe, Me with **25a** gave the coupling products **26ha-ja** in moderate yields, whereas, the coupling of the benzyl halides with electron-withdrawing substituents such as $NO_2$, Br and Cl with **25a** gave the coupling products **26ka-ma**, **26oa**, **26pa** in low yields. Interestingly, the benzyl halide with the electron-withdrawing chlorine atom at *para*-postion gave the moderate yield of the product **26na**.

**Table 5.3** Scope for the Kumada Coupling of Alkyl Halides Catalyzed by **23**[a]

| Entry | Alkyl halide (**24**) | Grignard reagent (**25**) | Product (**26**) | Yield (%)[b] |
|---|---|---|---|---|
| 1 |  R = H, X = Cl (**24a**) |  (**25a**) |  R = H (**26aa**) | 63(65) |
| 2 | R = OMe, X = Br (**24b**) | | R = OMe (**26ba**) | 92(95) |
| 3 |  R = H (**24c**) |  (**25a**) |  R = H (**26ca**) | 76 (80) |
| 4 | R = Cl (**24d**) | | R = Cl (**26da**) | 87 |
| 5 | R = OMe (**24e**) | | R = OMe (**24ea**) | 82 |
| 6 |  (**24f**) |  (**25a**) |  (**26fa**) | 82 (85) |
| 7 |  (**24g**) |  (**25a**) |  (**26ga**) | 56 (62) |
| 8 |  (**24a'**) | MeMgCl (**25b**) |  (**26ab**) | 93 |
| 9 | **24a'** | EtMgCl (**25c**) |  (**26ac**) | 92 |
| 10 | **24a'** | $^{i}$PrMgCl (**25d**) |  (**26ad**) | 90 |
| 11 | **24a'** | $^{t}$BuMgCl (**25e**) |  (**26ae**) | 90 |

[a]Conditions: Alkyl halide (0.2 mmol, X = Cl), cyclohexylmagnesium chloride (0.6 mmol), LiOMe (0.2 mmol), THF (1 mL), 0 $^{o}$C, 8 h. [b]Isolated yields. Yields determined by $^{1}$H NMR are given in parenthesis.




**Scheme 5.4** Kumada Coupling of Benzyl Halides with Cyclohexylmagnesium Chloride Employing **23** as Catalyst. [a] X = Cl. [b] X = Br. The yields were determined by $^1$H NMR using $CH_2Br_2$ as an internal standard.

## 5.3 CONCLUSION

In this chapter, we have demonstrated the synthesis of quinolinyl-amide based pincer copper complexes ($^{Q}$NNN$^{Et2}$)CuX (**20**-**23**) from both the copper (II) and copper (I) precursors. All the complexes were characterized by elemental analysis and HRMS. Molecular structures of complexes **20**, **21** and **22** were elucidated by single crystal X-ray diffraction studies. Complex **22** crystallizes in dimeric form with bridge $H_2O$ [**22**.$(H_2O)_{0.5}$] as well as in catemeric form $(\mathbf{22})_n$. XPS analysis of **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$ obtained from the Cu(II) and Cu(I) precursors highlights that the copper is present in +2 oxidation state. The cationic copper complex **23** is found to be an active catalyst for the Kumada coupling of alkyl chlorides with alkyl Grignard reagents.

## 5.4 EXPERIMENTAL SECTION

### Synthesis of ($^{Q}$NNN$^{Et2}$)-Ligated Copper Complexes

**($^{Q}$NNN$^{Et2}$)CuCl** (**20**): To an oven dried Schlenk flask were introduced ligand ($^{Q}$NNN$^{Et2}$)-H (0.10 g, 0.389 mmol) and $CuCl_2$ (0.052 g, 0.389 mmol), and THF (10 mL) was added in to it. To the resultant reaction mixture, $Et_3N$ (0.071 mL, 0.506 mmol) was added and the reaction mixture was stirred at 70 $^{o}$C for 3 h in a preheated oil bath. The reaction was cooled to room temperature and all the volatiles were evaporated. Product was then extracted with toluene (10 mL × 2), concentrated under vacuum and added $Et_2O$ (3 mL) to obtain crystalline compound **20**. Yield: 0.104 g, 75%. M. p. = 127 $^{o}$C. Anal. Calcd for $C_{15}H_{18}ON_3ClCu$: C, 50.70; H, 201; N, 11.83. Found: C, 50.35; H, 4.79; N, 11.38. HRMS (ESI): *m/z* Calcd for $C_{15}H_{18}ON_3ClCu+H^+$ $[M+H]^+$ 355.0507, found 355.0500 and $C_{15}H_{18}ON_3ClCu–Cl^+$ $[M–Cl]^+$ 319.0740, found 319.0734.

*Note:* By employing CuCl as a metal precursor instead of $CuCl_2$, compound **20** was obtained in 0.067 g, 49%.

**($^{Q}$NNN$^{Et2}$)CuBr** (**21**): This compound was synthesized following the procedure similar to the synthesis of complex **20**, using ($^{Q}$NNN $^{Et2}$)-H (0.1 g, 0.389 mmol), $CuBr_2$ (0.087 g, 0.389 mmol) and $Et_3N$ (0.506 mmol, 0.071 mL). The crude product was recrystallized in toluene/$Et_2O$ to obtain a crystalline compound **21**. Yield: 0.115 g, 74%. M. p. = 124 $^{o}$C (dec). Anal. Calcd for $C_{15}H_{18}ON_3BrCu$: C, 45.07; H, 4.54; N, 10.51. Found: C, 44.48; H, 4.28; N, 10.19. HRMS (ESI): *m/z* Calcd for $C_{15}H_{18}ON_3BrCu–H^+$ $[M–H]^+$ 396.9846, found 396.9861; and $C_{15}H_{18}ON_3BrCu–Br^+$ $[M–Br]^+$ 319.0740, found 319.0735.

*Note:* By employing CuBr as a metal precursor instead of $CuBr_2$, compound **21** was obtained in 0.078 g, 50%.

**($^{Q}$NNN$^{Et2}$)Cu(OAc).($H_2O$)$_{0.5}$ [22.($H_2O$)$_{0.5}$]:** This compound was synthesized following the procedure similar to the synthesis of complex **20**, using ($^{Q}$NNN $^{Et2}$)-H (0.1 g, 0.389 mmol), $Cu(OAc)_2$ (0.071 g, 0.389 mmol) and $Et_3N$ (0.506 mmol, 0.071 mL). The crude product was recrystallized in toluene/$Et_2O$ to obtain a crystalline compound **22**.($H_2O$)$_{0.5}$. M. p. = 131 $^{o}$C (dec). Anal. Calcd for $C_{17}H_{21}O_3N_3Cu.(H_2O)_{0.5}$: C, 52.64; H, 262; N, 10.83. Found: C, 52.57; H, 251; N, 10.96. HRMS (ESI): *m/z* Calcd for $C_{17}H_{22}O_{3.5}N_3Cu–(H_2O)_{0.5}+H^+$ $[M–(H_2O)_{0.5}+H]^+$ 379.0952, found 379.0307 and $[C_{17}H_{22}O_{3.5}N_3Cu–\{OAc+(H_2O)_{0.5}\}]^+$ $[M–\{OAc+(H_2O)_{0.5}\}]^+$ 319.0740, found 319.0745.

*Note*: By employing Cu(OAc) as a metal precursor instead of $Cu(OAc)_2$, compound **22** was obtained in 0.068 g, 46%.

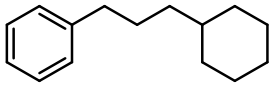
**[($^{Q}$NNN$^{Et2}$)Cu(MeCN)]OTf (23):** To an oven dried Schlenk flask the complex **20** (0.05 g, 0.141 mmol) and AgOTf (0.036 g, 0.141 mmol) were introduced and acetonitrile (10 mL) was added in to it. The reaction mixture was stirred at room temperature for 3 h. The resultant mixture was filtered through cannula and mother liquor was concentrated under vacuum and added $Et_2O$ (3 mL) to obtain a blue-green compound **23**. Yield: 0.057 g, 79%. M. p. = 230 $^{o}$C (dec). Anal. Calcd for $C_{18}H_{21}O_4N_4F_3SCu$: C, 42.39; H, 4.15; N, 10.99; S, 6.29. Found: C, 40.97; H, 4.22; N, 10.29; S, 6.29. MALDI-TOF: *m/z* Calcd for $[C_{18}H_{21}O_4N_4F_3SCu]^+$ $[M]^+$ 509.0532, found 508.8325 and $[C_{18}H_{21}O_4N_4F_3SCu–(CH_3CN+OTf)]^+$ $[M–(CH_3CN+OTf)]^+$ 319.0740, found 318.9736.

**Representative Procedure for Kumada Coupling**

**(3-Cyclohexylpropyl)benzene** (**26aa**): To a flame-dried Schlenk tube containing magnetic stir bar were added the catalyst **23** (0.005 g, 0.01 mmol) and LiOMe (0.008 g, 0.2 mmol). The Schlenk tube with mixture was then evacuated and refilled with argon. Subsequently, (3-chloropropyl)benzene (**24a**, 0.031 g, 0.2 mmol) and THF (1.0 mL) were added and degassed the reaction mixture. Finally, cyclohexylmagnesium chloride (**25a**, 0.3 mL, 2 M in $Et_2O$, 0.6 mmol) was added at 0 $^{o}$C under argon. The resultant reaction mixture was then stirred to continue at 0 $^{o}$C for 8 h. At ambient temperature, saturated aqueous ammonium chloride solution (10 mL) was added and the reaction mixture was extracted with $CH_2Cl_2$ (20 mL x 3). The combined organic layers were dried over $Na_2SO_4$ and the solvent was evaporated in *vacuo*. The resulting residue was purified by column chromatography on silica gel (petroleum ether) to yield **26aa** (0.0255 g, 63%) as a colorless liquid.

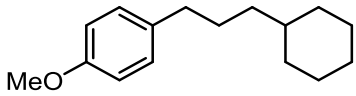
**Characterization Data of the Products 26aa-ga and 26ab-ae**

**(3-Cyclohexylpropyl)benzene** (**26aa)**



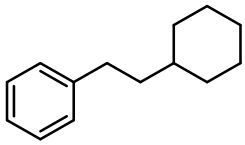
The compound **26aa** was obtained as a colorless liquid. Yield: 0.0255 g, 63%. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.35-7.27 (m, 2H, Ar–H), 7.26-7.15 (m, 3H, Ar–H), 2.61 (t, $J$ = 7.63 Hz, 2H), 1.86-1.60 (m, 7H), 1.32-1.12 (m, 6H), 0.96-0.81 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 143.2 ($C_q$), 128.6 (2C, CH), 128.4 (2C, CH), 122.6 (CH), 37.8 (CH), 37.4 ($CH_2$), 36.5 ($CH_2$), 33.6 (2C, $CH_2$), 29.0 ($CH_2$), 26.9 ($CH_2$), 26.6 (2C, $CH_2$). The NMR spectral data is in accordance with the reported data.[138]

**1-(3-Cyclohexylpropyl)-4-methoxybenzene** (**26ba**)




The compound **26ba** was obtained as a colorless liquid. Yield: 0.042 g, 90%. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.10 (d, $J$ = 7.9 Hz, 2H, Ar–H), 6.83 (d, $J$ = 8.5 Hz, 2H, Ar–H), 3.79 (s, 3H), 2.53 (t, $J$ = 7.9 Hz, 2H), 1.75-1.55 (m, 7H), 1.31-1.10 (m, 6H), 0.97-0.80 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 157.7 ($C_q$), 132.2 ($C_q$), 129.4 (2C, CH), 113.8 (2C, CH), 52.3 ($CH_3$), 37.8 (CH), 37.3 ($CH_2$), 324 ($CH_2$), 33.6 (2C, $CH_2$), 29.2 ($CH_2$), 26.9 ($CH_2$), 26.6 (2C, $CH_2$). The NMR spectral data is in accordance with the reported data.[159]

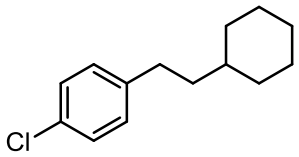
**(3-Cyclohexylethyl)benzene** (**26ca**)



The compound **26ca** was obtained as a colorless liquid. Yield: 0.029 g, 76%. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.34-7.22 (m, 2H, Ar–H), 7.21-7.11 (m, 3H, Ar–H), 2.66-2.56 (m, 2H), 1.89-1.59 (m, 6H), 1.58-1.44 (m, 2H), 1.40-1.11 (m, 5H), 1.03-0.81 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 143.4 ($C_q$), 128.5 (2C, CH), 128.4 (2C, CH), 122.6 (CH), 39.6 ($CH_2$), 37.5

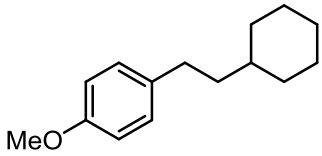
(CH), 33.5 (2C, $CH_2$), 33.5 ($CH_2$), 26.9 ($CH_2$), 26.5 (2C, $CH_2$). The NMR spectral data is in accordance with the reported data.[160]

**1-Chloro-4-(2-cyclohexylethyl)benzene** (**26da**)



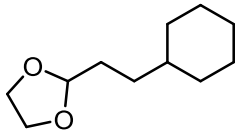

The compound **26da** was obtained as a light yellow liquid. Yield: 0.039 g, 87% (**26da**:bicyclohexyl = 70:30, inseparable mixture). $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.25-7.21 (m, 2H, Ar–H), 7.13-7.08 (m, 2H, Ar–H), 2.61-2.53 (m, 2H), 1.50-1.43 (m, 2H), 1.29-1.15 (m, 7H), 1.00-0.87 (m, 4H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 141.8 ($C_q$), 131.3 ($C_q$), 129.9 (2C, CH), 128.5 (2C, CH), 43.6 (CH), 39.5 ($CH_2$), 33.5 (2C, $CH_2$), 32.8 ($CH_2$), 30.3 ($CH_2$), 26.5 (2C, $CH_2$). HRMS (ESI): *m/z* Calcd for $C_{14}H_{19}Cl$ $[M]^+$ 222.1170, found 222.1181.

**1-(2-Cyclohexylethyl)-4-methoxybenzene** (**26ea**)



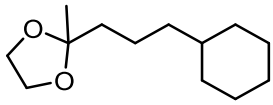

The compound **26ea** was obtained as a colorless liquid. Yield: 0.036 g, 82%. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.09 (d, $J$ = 8.0 Hz, 2H, Ar–H), 6.82 (d, $J$ = 7.6 Hz, 2H, Ar–H), 3.79 (s, 3H), 2.55 (t, $J$ = 8.0 Hz, 2H), 1.84-1.60 (m, 6H), 1.46 (q, $J$ = 7.1 Hz, 2H), 1.02 - 0.78 (m, 5H). $^{13}$C{$^1$H} NMR (125 MHz, $CDCl_3$): $\delta$ 157.7 ($C_q$), 132.4 ($C_q$), 129.4 (2C, CH), 113.9 (2C, CH), 52.3 ($CH_3$), 39.8 ($CH_2$), 37.4 (CH), 33.5 (2C, $CH_2$), 32.5 ($CH_2$), 26.9 ($CH_2$), 26.5 (2C, $CH_2$).
The NMR spectral data is in accordance with the reported data.[160]

**2-(2-Cyclohexylethyl)-1, 3-dioxolane** (**26fa**)



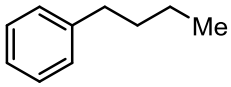
The compound **26fa** was obtained as a colorless liquid. Yield: 0.032 g, 82%. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.48 (t, $J$ = 4.9 Hz, 1H), 4.10 (dd, $J$ = 11.0, 4.9 Hz, 2H), 3.82-3.71 (m, 2H), 2.14-2.01 (m, 1H), 1.72-1.65 (m, 4H), 1.39-1.26 (m, 4H), 1.22-1.08 (m, 4H), 0.92-0.84 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 103.0 (CH), 67.11 (2C, $CH_2$), 37.7 (CH), 33.4 (2C, $CH_2$), 32.9 ($CH_2$), 31.7 ($CH_2$), 26.8 ($CH_2$), 26.5 (2C, $CH_2$). The NMR spectral data is in accordance with the reported data.[161]

**2-(3-Cyclohexylpropyl)-2-methyl-1,3-dioxolane** (**26ga**)



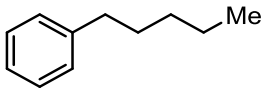
The compound **26ga** was obtained as a colorless liquid. Yield: 0.025 g, 58%. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 4.01-3.83 (m, 4H), 1.74-1.64 (m, 5H), 1.61 (d, $J$ = 6.1 Hz, 2H), 1.44-1.33 (m, 4H), 1.31 (s, 3H), 1.23-1.13 (m, 6H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 110.4 ($C_q$), 64.8 (2C, $CH_2$), 39.7 ($CH_2$), 37.8 (CH), 37.8 ($CH_2$), 33.6 (2C, $CH_2$), 26.9 ($CH_2$), 26.6 (2C, $CH_2$), 23.9 ($CH_3$), 21.6 ($CH_2$). HRMS (ESI): *m/z* Calcd for $C_{13}H_{25}O_2$ $[M+H]^+$ 213.1849, found 213.1845.

***n*-Butylbenzene** (**26ab**)



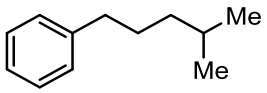

The compound **26ab** was obtained as a colorless liquid. Yield: 0.025 g, 93%. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.31-7.24 (m, 2H), 7.22-7.14 (m, 3H), 2.61 (t, $J$ = 7.8 Hz, 2H), 1.64-1.56 (m, 2H), 1.40-1.32 (m, 2H), 0.93 (t, $J$ = 7.2 Hz, 3H). $^{13}$C{$^{1}$H} NMR (125 MHz, $CDCl_3$): $\delta$ 143.1 ($C_q$), 128.6 (2C, CH), 128.4 (2C, CH), 122.6 (CH), 35.9 ($CH_2$), 33.9 ($CH_2$), 22.6 ($CH_2$), 14.1 ($CH_3$). The NMR spectral data is in accordance with the reported data.[162]

***n*-Pentylbenzene** (**26ac**)



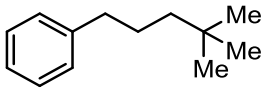

The compound **26ac** was obtained as a colorless liquid. Yield: 0.027 g, 92%. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.30-7.24 (m, 2H), 7.22-7.13 (m, 3H), 2.60 (t, $J$ = 7.8 Hz, 2H), 1.62 (quin, $J$ = 7.3 Hz, 2H), 1.35-1.30 (m, 4H), 0.89 (t, $J$ = 6.5 Hz, 3H). $^{13}$C{$^{1}$H} NMR (125 MHz, $CDCl_3$): $\delta$ 143.2 ($C_q$), 128.6 (2C, CH), 128.4 (2C, CH), 125.7 (CH), 36.2 ($CH_2$), 31.7 ($CH_2$), 31.4 ($CH_2$), 22.7 ($CH_2$), 14.2 ($CH_3$). The NMR spectral data is in accordance with the reported data.[163]

**(4-Methylpentyl)benzene** (**26ad**)




The compound **26ad** was obtained as a colorless liquid. Yield: 0.029 g, 90%. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.52-6.94 (m, 5H, Ar–H), 2.58 (t, $J$ = 7.9 Hz, 2H), 1.66-1.52 (m, 3H), 1.27-1.19 (m, 2H), 0.87 (d, $J$ = 6.8 Hz, 6H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$): $\delta$ 143.2 ($C_q$), 128.6 (2C, CH), 128.4 (2C, CH), 125.8 (CH), 38.9 ($CH_2$), 36.4 ($CH_2$), 29.6 ($CH_2$), 28.1 (CH), 22.8 (2C, $CH_3$). The NMR spectral data is in accordance with the reported data.[137]

**(4,4-Dimethylpentyl)benzene** (**26ae**)




The compound **26ae** was obtained as a colorless liquid. Yield: 0.032 g, 90%. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.32-7.26 (m, 2H, Ar–H), 7.23-7.16 (m, 3H, Ar–H), 2.59 (t, $J$ = 7.8 Hz, 2H), 1.64-1.56 (m, 2H), 1.28-1.22 (m, 2H), 0.88 (s, 9H). $^{13}$C{$^{1}$H} NMR (125 MHz, $CDCl_3$): $\delta$ 143.2 ($C_q$), 128.6 (2C, CH), 128.4 (2C, CH), 125.8 (CH), 44.1 ($CH_2$), 37.1 ($CH_2$), 30.5 ($C_q$), 29.6 (3C, $CH_3$), 26.9 ($CH_2$). The NMR spectral data is in accordance with the reported data.[139]

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## Kinetics Data for 3a-Catalyzed Arylation of Benzothiazole

Kinetics Data for the Arylation of Benzothiazole with 4-Iodotoluene.

| Time (min) | Conc. of Benzothiazole [M] | Conc. of 7aa [M] |
|---|---|---|
| 10 | 0.2691 | 0.0285 |
| 20 | 0.2403 | 0.0588 |
| 30 | 0.2196 | 0.0798 |
| 40 | 0.2068 | 0.0900 |
| 50 | 0.1803 | 0.1089 |
| 60 | 0.1559 | 0.1239 |
| 90 | 0.1232 | 0.1551 |
| 120 | 0.1076 | 0.1812 |
| 180 | 0.0634 | 0.2259 |

Conditions: Benzothiazole (0.3 M), 4-Iodotoluene (0.45 M), $K_2CO_3$ (1.5 equiv), **3a** (0.0015 M), CuI (0.003 M), mesitylene (internal standard, 0.1077 M)., DMSO (required amount to make total volume 2.0 mL).

Concentration of Various Arylation Products of Benzothiazole with 4-R-$C_6H_4$-I.

| Time (min) | Conc. of various arylated products of benzothiazole [M] | | | | |
|---|---|---|---|---|---|
| | R = OMe | R = Me | R = H | R = Cl | R = C(O)OMe |
| 10 | 0.0762 | 0.0285 | 0.0351 | 0.0165 | 0.0102 |
| 20 | 0.1092 | 0.0588 | 0.0504 | 0.0336 | 0.0238 |
| 30 | 0.1446 | 0.0798 | 0.0675 | 0.0513 | 0.0278 |
| 40 | 0.1665 | 0.0900 | 0.0840 | 0.0549 | 0.0328 |
| 50 | 0.1896 | 0.1089 | 0.0969 | 0.0648 | 0.0352 |
| 60 | 0.2100 | 0.1239 | 0.1110 | 0.0675 | 0.0426 |

Conditions: Benzothiazole (0.3 M), 4-iodoarene (0.45 M), $K_2CO_3$ (1.5 equiv), **3a** (0.0015 M), CuI (0.003 M), mesitylene (internal standard, 0.1077 M)., DMSO (required amount to make total volume 2.0 mL).

Values of $k_R$, $k_R/k_H$, $\log(k_R/k_H)$ and Hammett Substituent Constant ($\sigma_p$).

| | R = OMe | R = Me | R = H | R = Cl | R = C(O)OMe |
|---|---|---|---|---|---|
| $k_R$ | 2.66 | 1.82 | 1.53 | 1.01 | 0.58 |
| $k_R/k_H$ | 1.74 | 1.19 | 1.00 | 0.66 | 0.38 |
| $\log (k_R/k_H)$ | 0.24 | 0.08 | 0.00 | -0.18 | -0.42 |
| $\sigma_p$ | -0.27 | -0.17 | 0.00 | 0.23 | 0.45 |

$k_R$ = slope of corresponding plots of conc. of product *vs* time. $\sigma_p$ values are *para* substituent constants determined by Hammett.

## X-ray Structure Determination

X-ray intensity data measurements of all complexes were carried out on a Bruker SMART APEX II CCD diffractometer with graphite-monochromatized ($MoK_{\alpha}$= 0.71073 Å) radiation range 90(2) - 297 (2) K. The X-ray generator was operated at 50 kV and 30 mA. A preliminary set of cell constants and an orientation matrix were calculated from three sets of 12 frames (total 36 frames). Data were collected with $\omega$ scan width of 0.5° at eight different settings of $\varphi$ and $2\theta$ with a frame time of 10 sec keeping the sample-to-detector distance fixed at 5.00 cm for both compounds. The X-ray data collection was monitored by the APEX2 program (Bruker, 2006).[1] All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2006). SHELX-97 was used for structure solution and full matrix least-squares refinement on $F^2$.[2] Hydrogen atoms were placed in geometrically idealized position and constrained to ride on their parent atoms.

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Crystal data and structure refinement for the complexes **2a**, **3a** and **4a**

| | **2a** | **3a** | **4a** |
|---|---|---|---|
| Empirical formula | $C_{17}H_{23}N_3O_4Pd$ | $C_{15}H_{18}ClN_3OPd$ | $C_{15}H_{18}IN_3OPd$ |
| Formula weight | 439.78 | 398.17 | 489.62 |
| Temperature, K | 200(2) | 150(2) | 100(2) |
| Cryst. Syst. | Monoclinic | Monoclinic | Monoclinic |
| Space group | P2(1)/c | C2/c | P2(1)/c |
| *a* (Å) | 10.8321(4) | 14.7945(6) | 10.5522(12) |
| *b* (Å) | 23.7645(8) | 13.1480(5) | 11.3163(18) |
| *c* (Å) | 6.9558(2) | 16.0956(7) | 13.8002(13) |
| α ($^o$) | 90 | 90 | 90 |
| *β* ($^o$) | 103.107(2) | 102.202(2) | 13.8002(13) |
| γ ($^o$) | 90 | 90 | 90 |
| V (Å$^3$) | 1743.91(10) | 3060.2(2) | 1597.0(3) |
| Z | 4 | 8 | 4 |
| $\rho_{cald.}$ Mg/m$^3$ | 1.675 | 1.728 | 2.036 |
| $\varepsilon$ (mm$^{-1}$) | 1.091 | 1.389 | 3.097 |
| *F* (000) | 896 | 1600 | 944 |
| Crystal size (mm) | 0.46 x 0.31 x 0.21 | 0.46 x 0.40 x 0.32 | 0.22 x 0.19 x 0.11 |
| *θ* (min, max) (°) | 1.714, 24.996 | 2.093, 24.995 | 2.685, 33.498 |
| R(int) | 0.0411 | 0.0179 | 0.0511 |
| Independent reflections | 3049 | 2696 | 6134 |
| Completeness to θ (%) | 96.5 | 97.5 | 99.8 |
| Max. and min. transmission | 0.8033, 0.6342 | 0.6649, 0.5675 | 0.727, 0.549 |
| Data / restraints / parameters | 3049 / 0 / 237 | 2696 / 0 / 192 | 6134 / 0 / 193 |
| GOF on F$^2$ | 1.300 | 1.101 | 1.190 |
| R1, wR2 ($I>2\sigma(I)$) | 0.0621, 0.1062 | 0.0181, 0.0420 | 0.0195, 0.0379 |
| R1, wR2 (all data) | 0.0742, 0.1099 | 0.0187, 0.0423 | 0.0253, 0.0392 |

Crystal Data and Structure Refinement for Complexes **9** and **10**

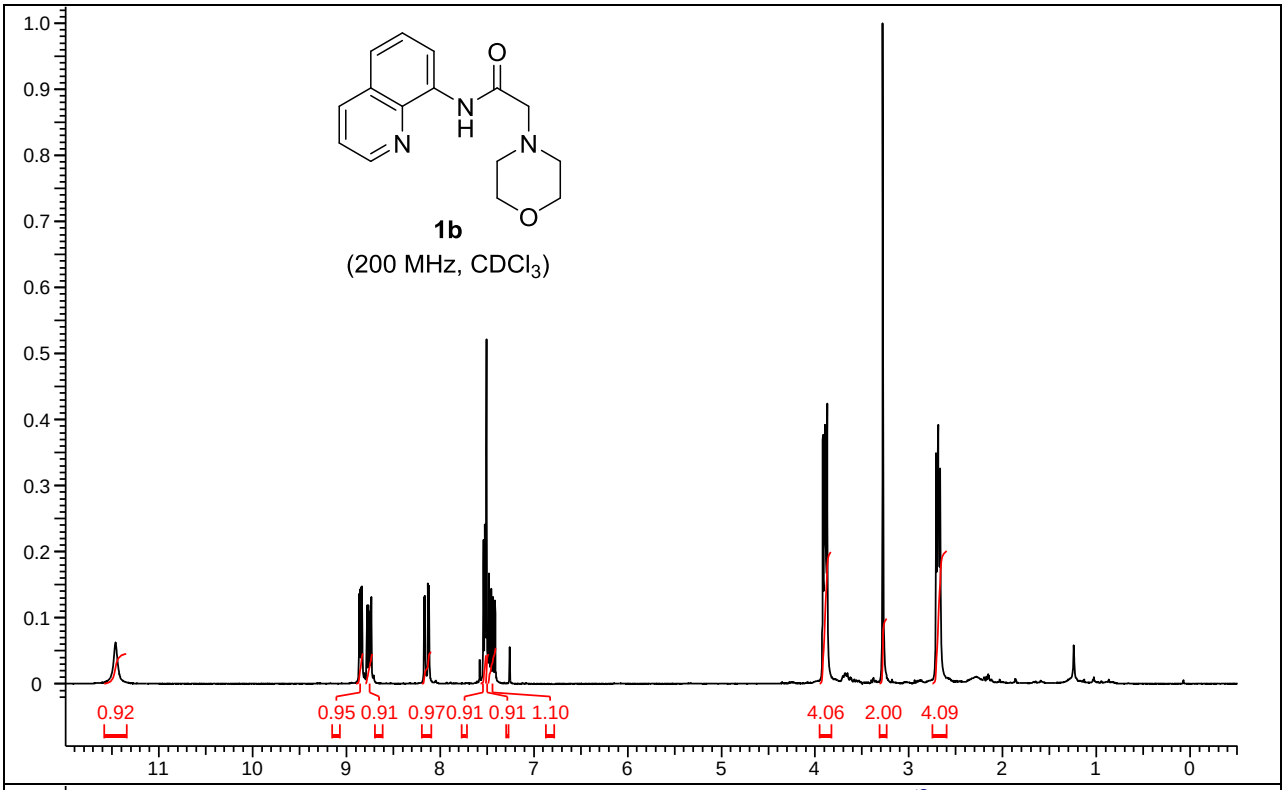
| | **9** | **10** |
|---|---|---|
| Empirical formula | $C_{20}H_{35}BrNiO_2P_2$ | $C_{22}H_{38}NiO_4P_2$ |
| Formula weight | 508.04 | 487.17 |
| Temperature, K | 296(2) | 100(2) |
| Cryst. Syst. | Monoclinic | Triclinic |
| Space group | C2/c | P-1 |
| *a* (Å) | 7.8480(6) | 7.3969(2) |
| *b* (Å) | 26.140(2) | 11.2664(3) |
| *c* (Å) | 11.5713(9) | 14.8162(4) |
| $\alpha$ (°) | 90 | 93.368(2) |
| $\beta$ (°) | 91.517(4) | 96.251(2) |
| $\gamma$ (°) | 90 | 96.745(2) |
| V (Å3) | 2373.0(3) | 1215.69(6) |
| Z | 4 | 2 |
| $\rho_{cald.}$ Mg/m3 | 1.422 | 1.331 |
| $\varepsilon$ (mm-1) | 2.648 | 0.954 |
| *F* (000) | 1056 | 520 |
| Crystal size ($mm^3$) | 0.39 x 0.33 x 0.24 | 0.32 x 0.21 x 0.15 |
| $\theta$ (min, max) (°) | 2.711, 25.000 | 2.211, 24.998 |
| R(int) | 0.0552 | 0.0281 |
| Independent reflections | 2096 | 4216 |
| Completeness to θ (%) | 99.9 | 98.5 |
| Max. and min. transmission | 0.569, 0.425 | 0.870, 0.750 |
| Data / restraints / parameters | 2096 / 0 / 124 | 4216 / 0 / 271 |
| GOF on F2 | 1.054 | 1.071 |
| R1, wR2 ($I>2\sigma(I)$) | 0.0306, 0.0785 | 0.0377, 0.0745 |
| R1, wR2 (all data) | 0.0336, 0.080 | 0.0458, 0.0774 |

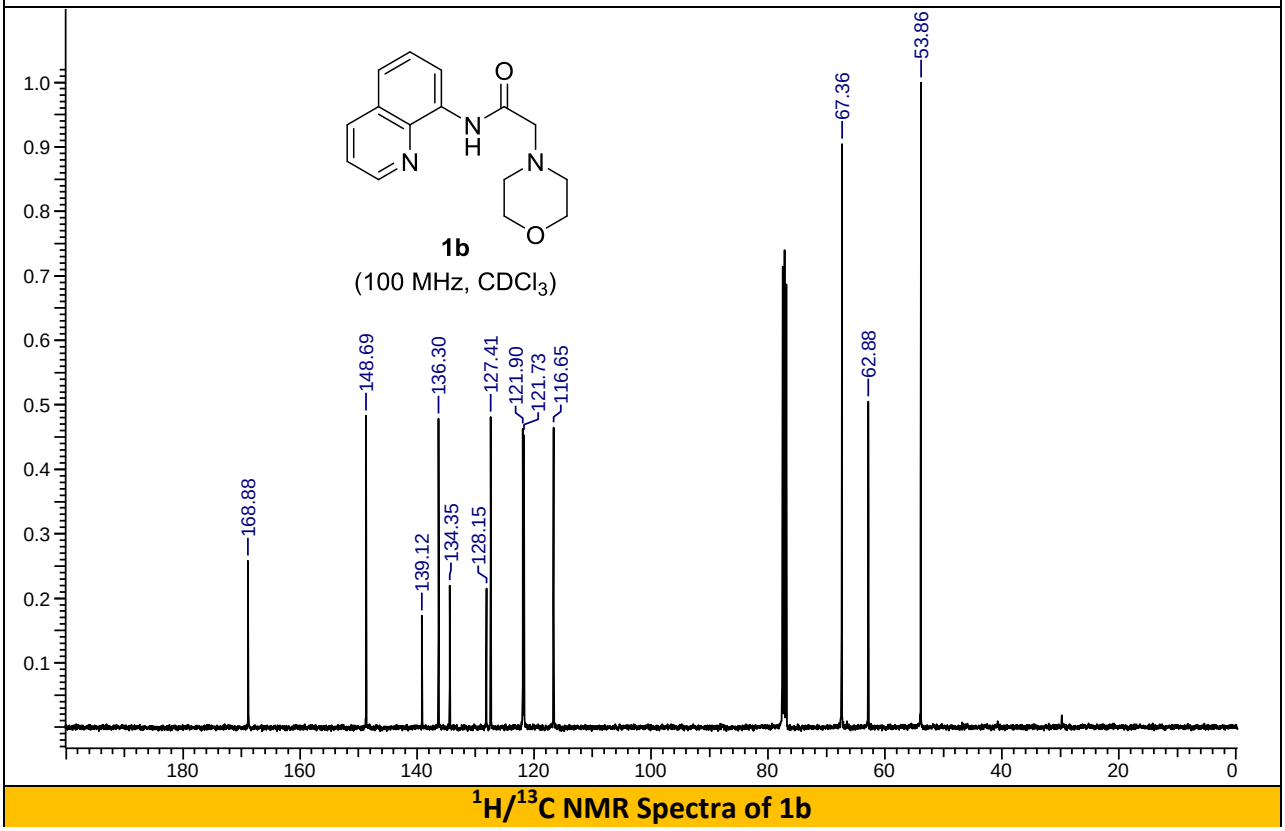
Crystal Data and Structure Refinement for Complexes **20** and **21**

| | **20** | **21** |
|---|---|---|
| Empirical formula | $C_{15}H_{18}ClCuN_3O$ | $C_{15}H_{18}BrCuN_3O$ |
| Formula weight | 355.31 | 399.77 |
| Temperature, K | 100(2) K | 100(2) K |
| Cryst. Syst. | Monoclinic | Monoclinic |
| Space group | C2/c | C2/c |
| *a* (Å) | 14.5925(6) | 14.8335(5) |
| *b* (Å) | 13.2202(6) | 13.3212(4) |
| *c* (Å) | 16.1405(6) | 16.1662(5) |
| α ($^o$) | 90 | 90 |
| β ($^o$) | 101.955(2) | 101.8220(10) |
| γ ($^o$) | 90 | 90 |
| V (Å$^3$) | 3046.2(2) | 3126.68(17) |
| Z | 8 | 8 |
| $\rho_{cald.}$ Mg/m$^3$ | 1.549 | 1.699 |
| $\varepsilon$ (mm$^{-1}$) | 1.611 | 3.954 |
| *F* (000) | 1464 | 1608 |
| Crystal size (mm$^3$) | 0.314x0.276x0.081 | 0.22x0.08x0.04 |
| $\theta$ (min, max) (°) | 2.304, 30.515 | 2.574, 30.503 |
| R(int) | 0.0230 | 0.0260 |
| Independent reflections | 4633 | 4765 |
| Completeness to θ (%) | 99.9 | 99.9 |
| Max. and min. transmission | 0.881, 0.632 | 0.858, 0.477 |
| Data/restraints/parameters | 4633/0/192 | 4765/0/192 |
| GOF on F$^2$ | 1.043 | 1.058 |
| R1, wR2 ($I>2\sigma(I)$) | 0.0228, 0.0582 | 0.0209, 0.0510 |
| R1, wR2 (all data) | 0.0259, 0.0598 | 0.0252, 0.0527 |

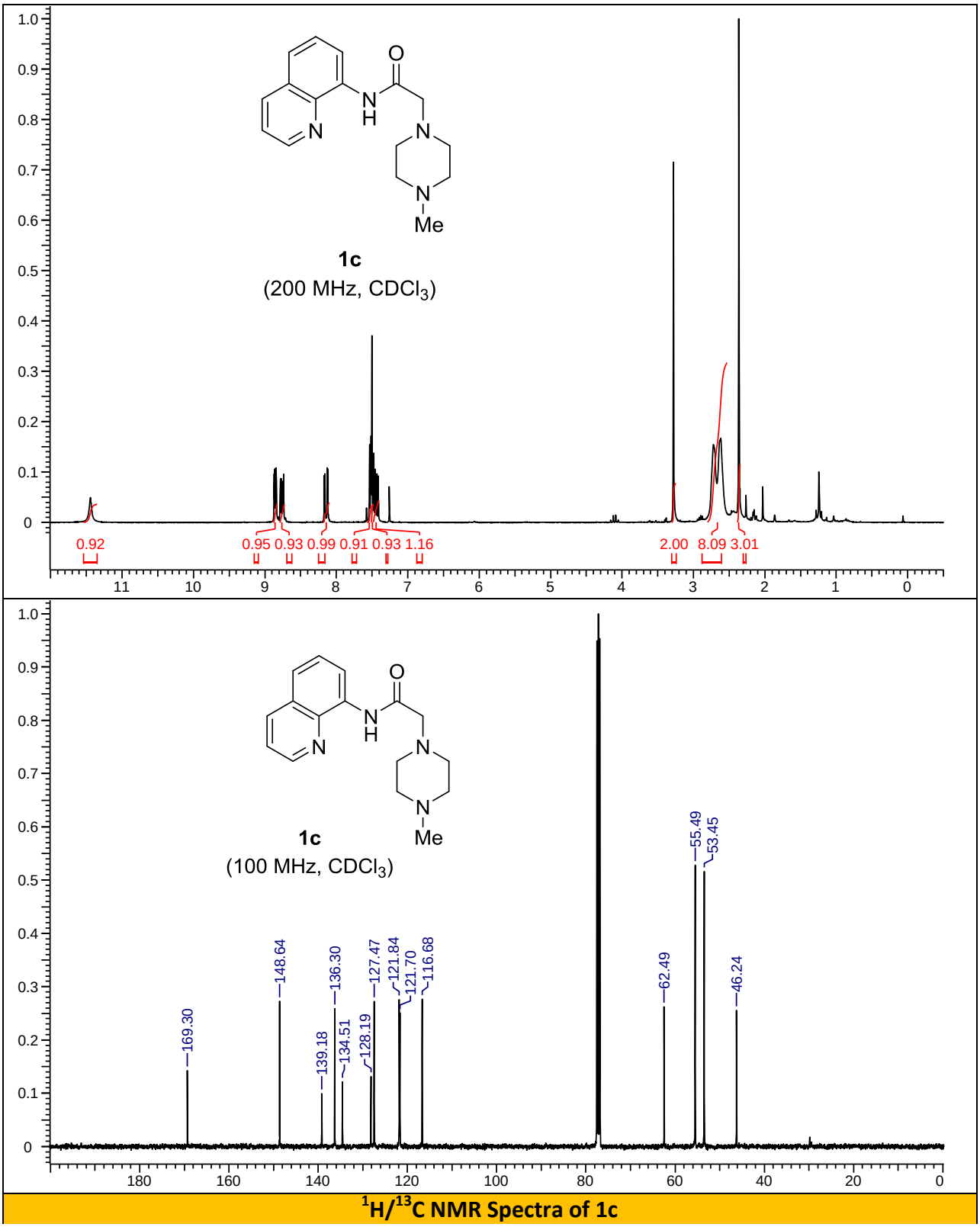
Crystal Data and Structure Refinement for Complexes **22**.$(H_2O)_{0.5}$ and $(\mathbf{22})_n$

| | **22**.$(H_2O)_{0.5}$ | $(\mathbf{22})_n$ |
|---|---|---|
| Empirical formula | $C_{17}H_{22}CuN_3O_{3.5}$ | $C_{17}H_{21}CuN_3O_3$ |
| Formula weight | 387.91 | 378.92 |
| Temperature, K | 150(2) | 297(2) K |
| Cryst. Syst. | Monoclinic | Monoclinic |
| Space group | C2/c | $P2_1/n$ |
| *a* (Å) | 11.7397(4) | 13.750(3) |
| *b* (Å) | 13.8992(5) | 7.8669(17) |
| *c* (Å) | 21.0927(8) | 16.223(4) |
| α ($^o$) | 90 | 90 |
| β ($^o$) | 90.547(2) | 98.271(10) |
| γ ($^o$) | 90 | 90 |
| V (Å$^3$) | 3441.6(2) | 1736.6(7) |
| Z | 8 | 2 |
| $\rho_{cald.}$ Mg/m$^3$ | 1.497 | 1.449 |
| $\varepsilon$ (mm$^{-1}$) | 1.293 | 1.277 |
| *F* (000) | 1616 | 788 |
| Crystal size (mm$^3$) | 0.43x0.31x0.21 | 0.42x0.32x0.22 |
| $\theta$ (min, max) (°) | 1.931, 27.992 | 1.817, 28.660 |
| R(int) | 0.0214 | 0.0592 |
| Independent reflections | 4129 | 4256 |
| Completeness to θ (%) | 99.9 | 98.6 |
| Max. and min. transmission | 0.773, 0.606 | 0.766, 0.616 |
| Data/restraints/parameters | 4129/0/228 | 4256/0/220 |
| GOF on F$^2$ | 1.070 | 1.050 |
| R1, wR2 ($I>2\sigma(I)$) | 0.0287, 0.0708 | 0.0470, 0.1163 |
| R1, wR2 (all data) | 0.0326, 0.0725 | 0.0633, 0.1253 |

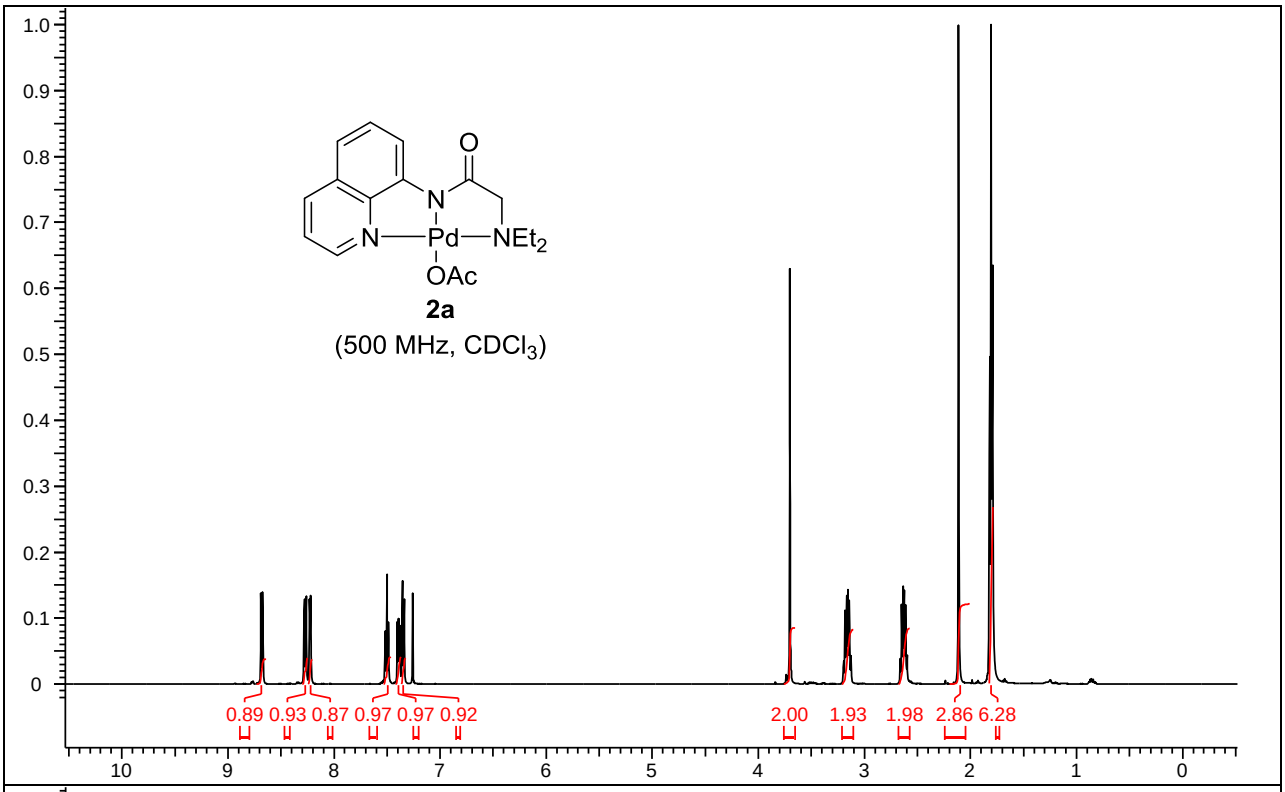


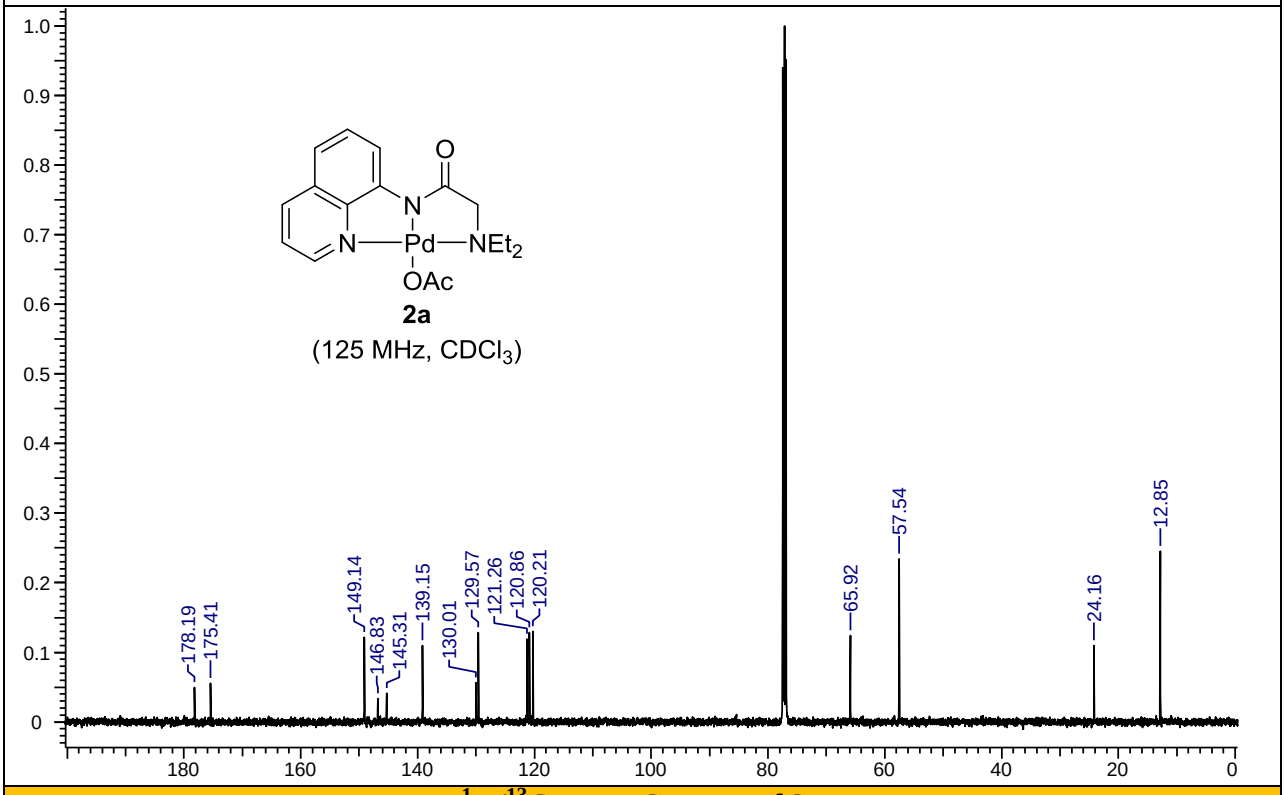




$^{1}H/^{13}C$ NMR Spectra of 1b

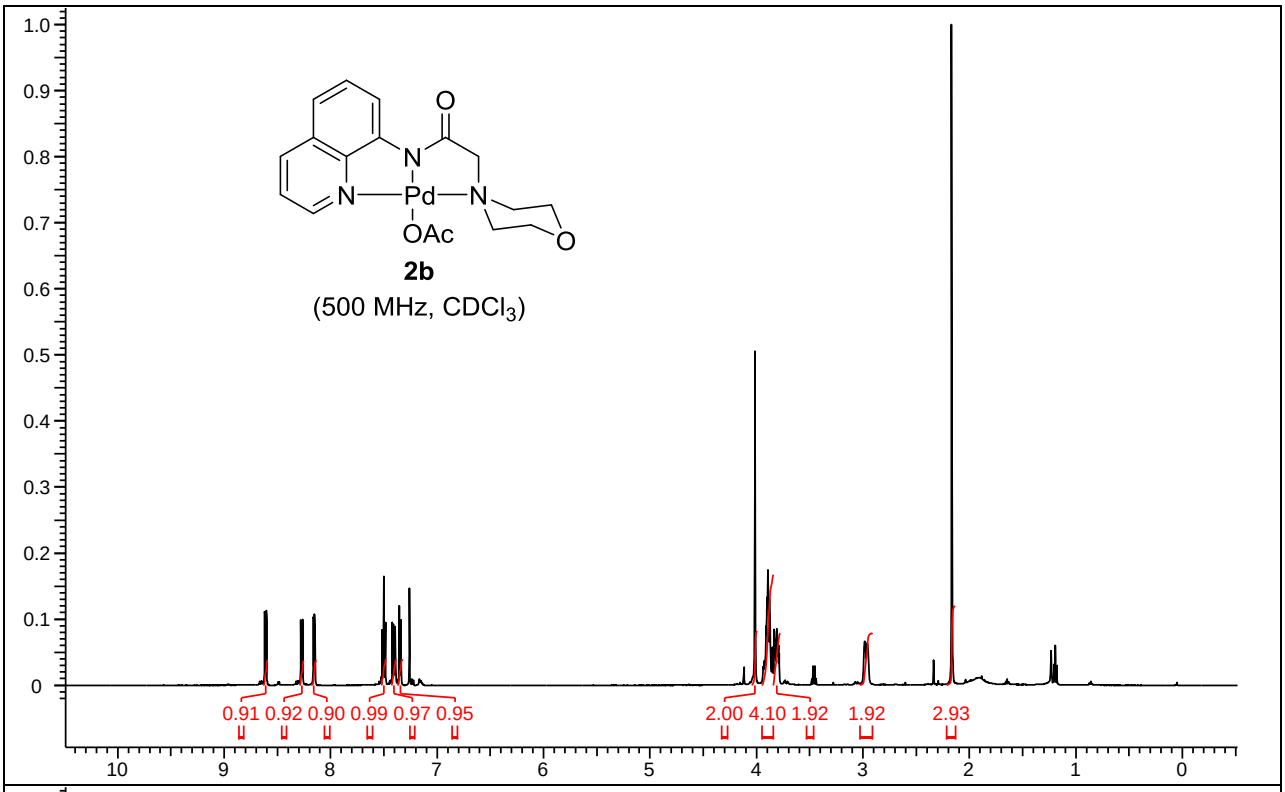


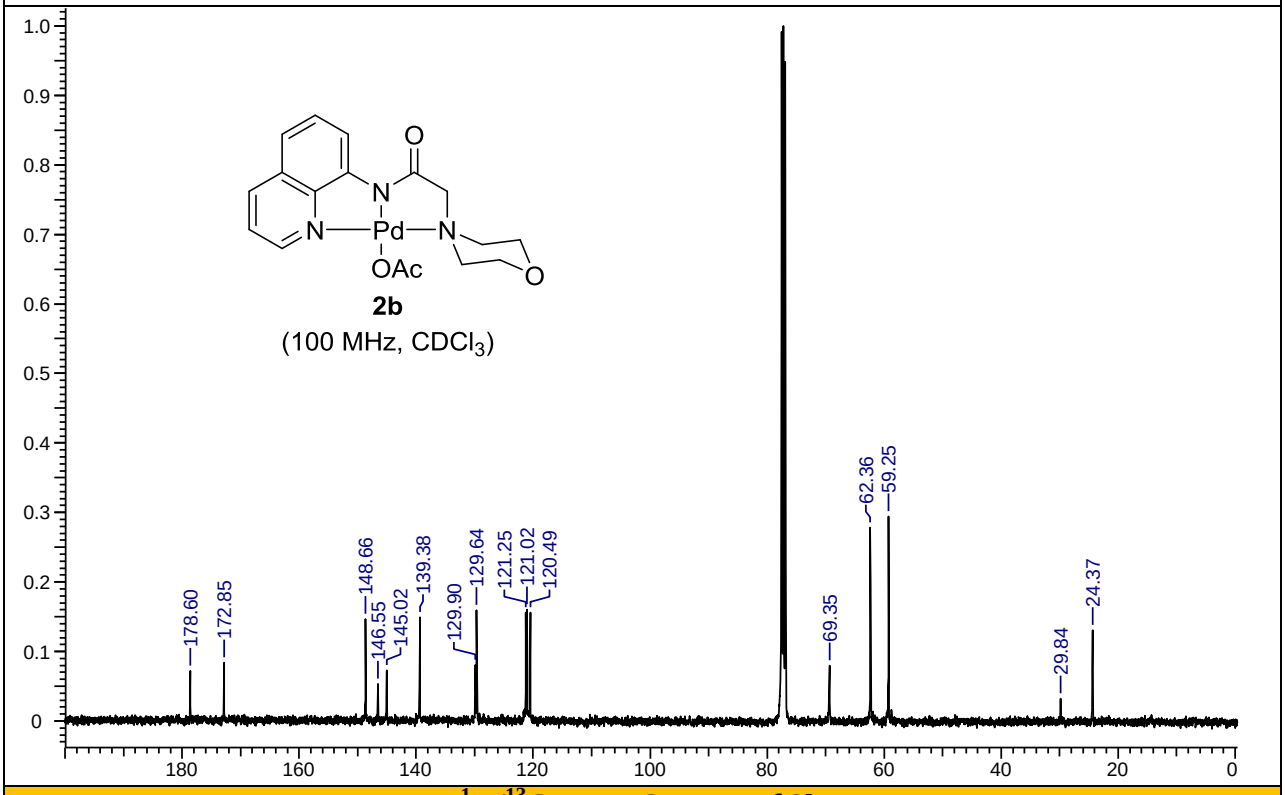

$^{1}H/^{13}C$ NMR Spectra of 1c



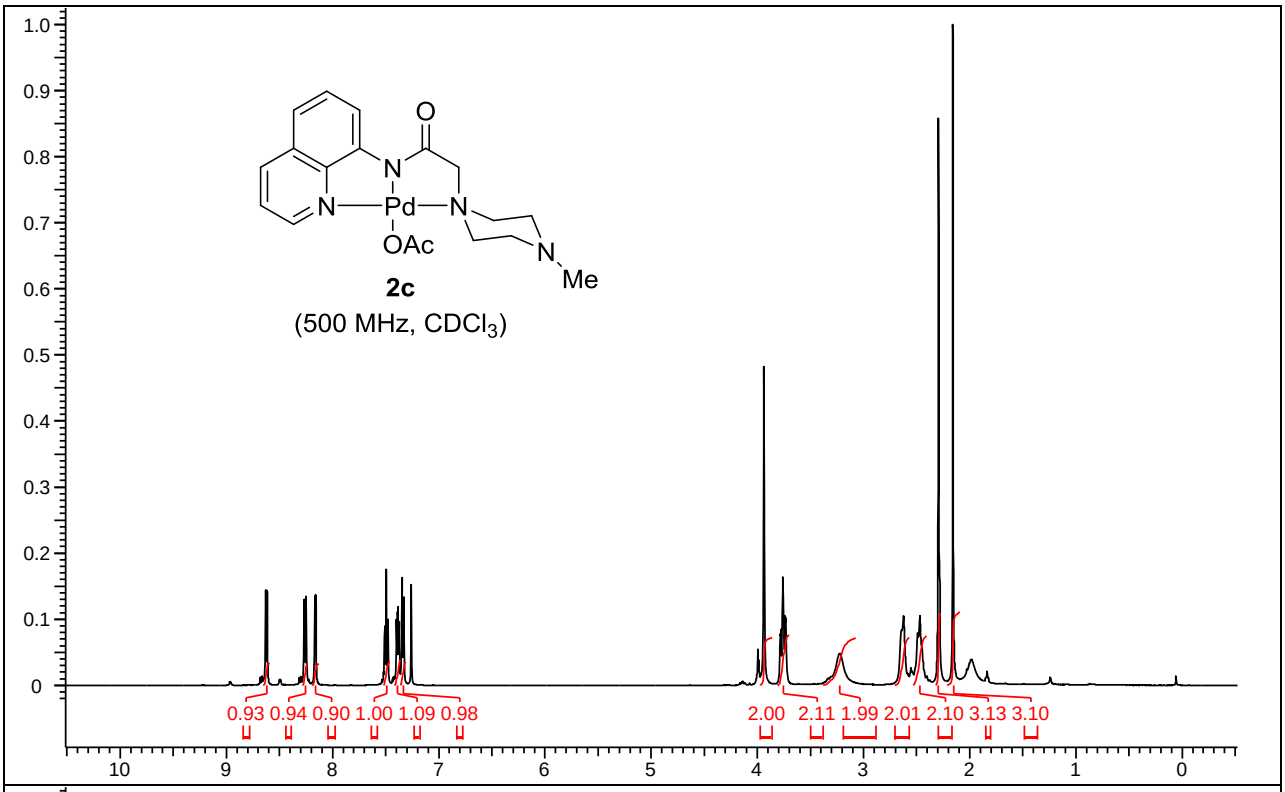



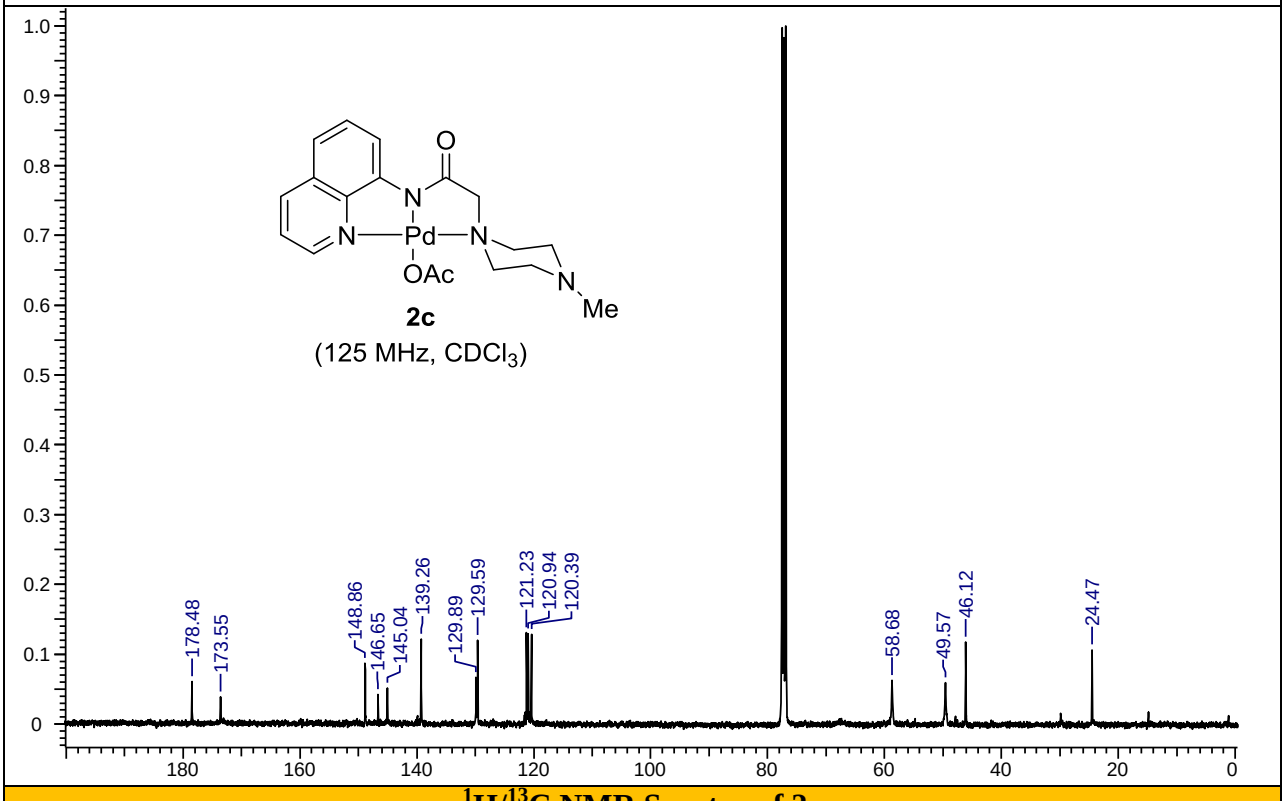

**$^{1}H/^{13}C$ NMR Spectra of 2a**



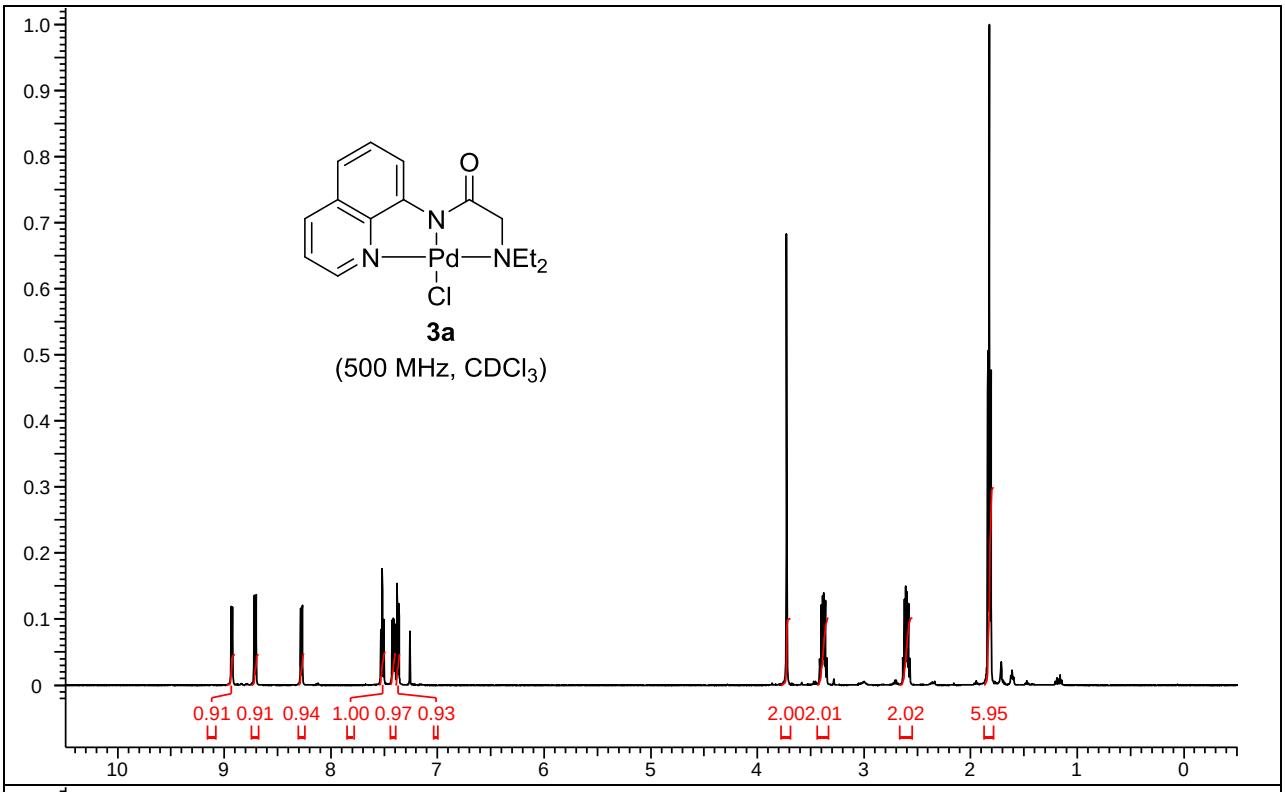



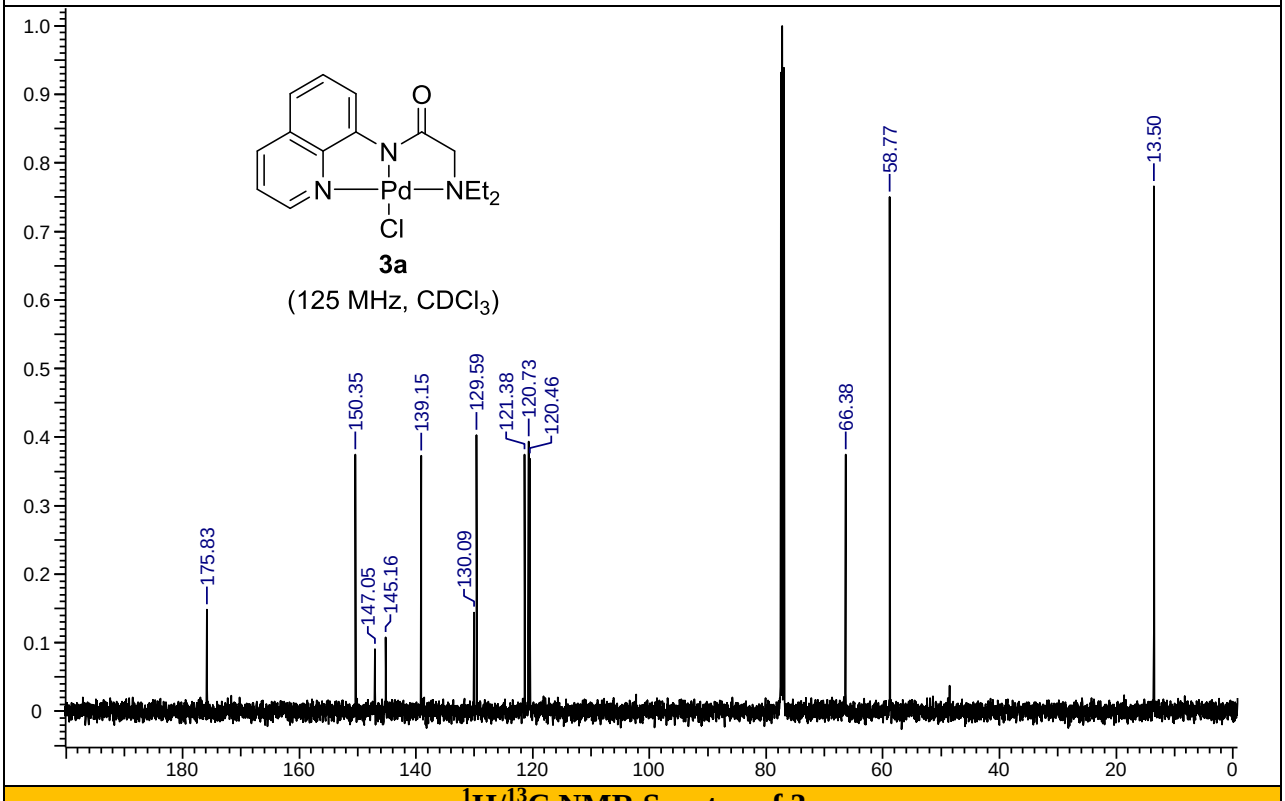

**$^{1}H/^{13}C$ NMR Spectra of 2b**



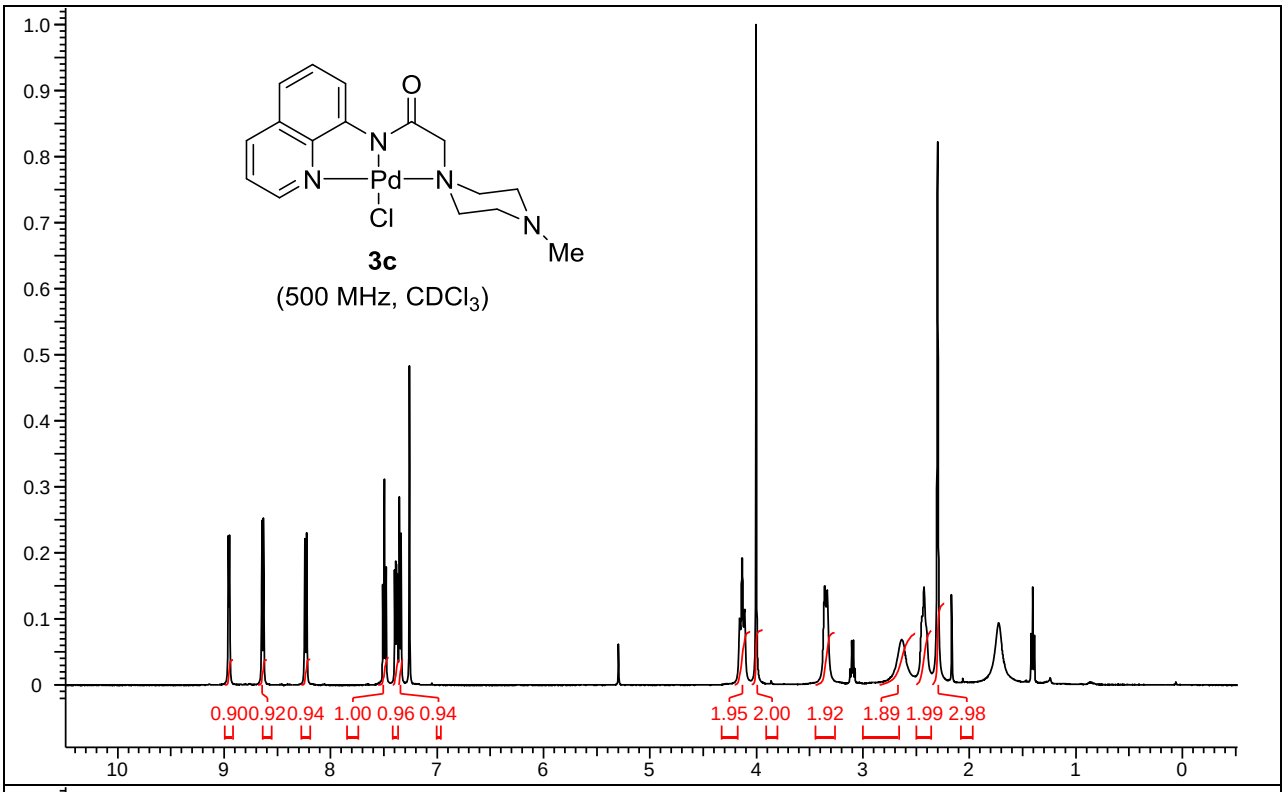



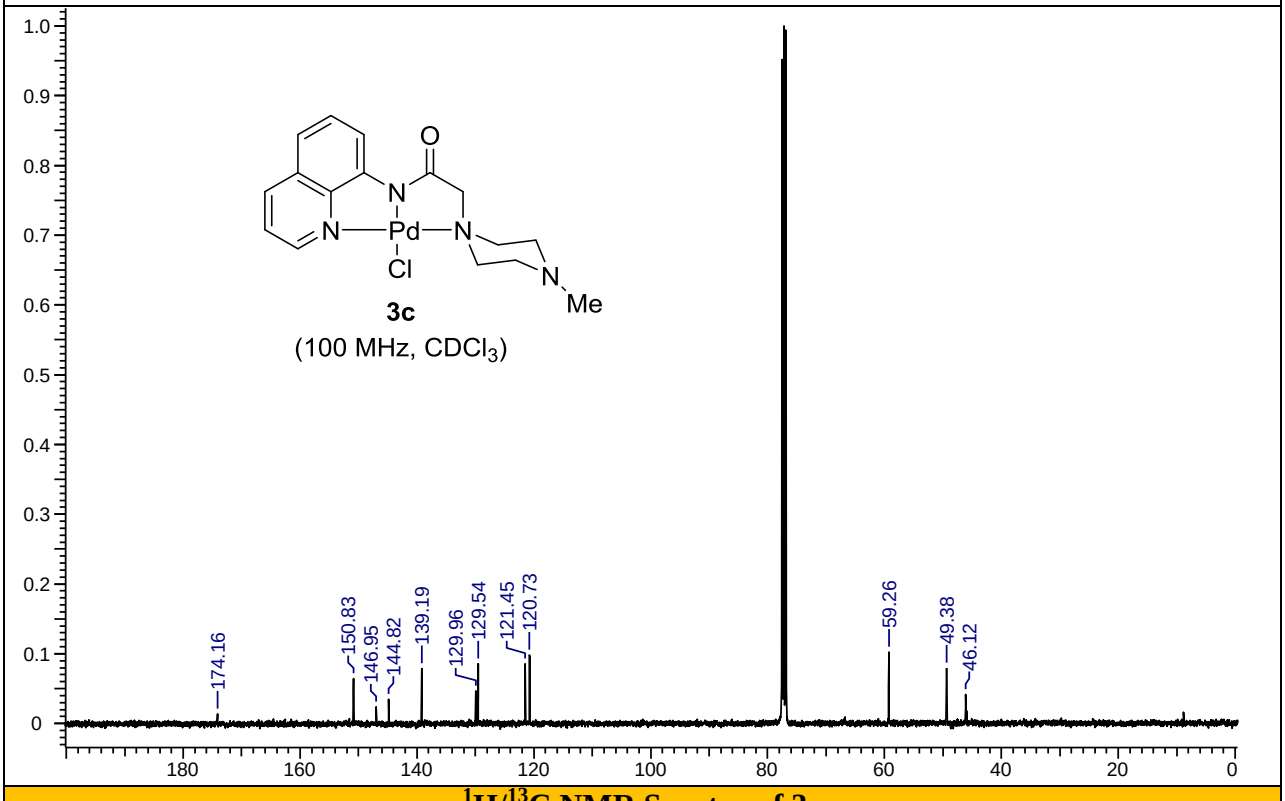

**$^{1}H/^{13}C$ NMR Spectra of 2c**



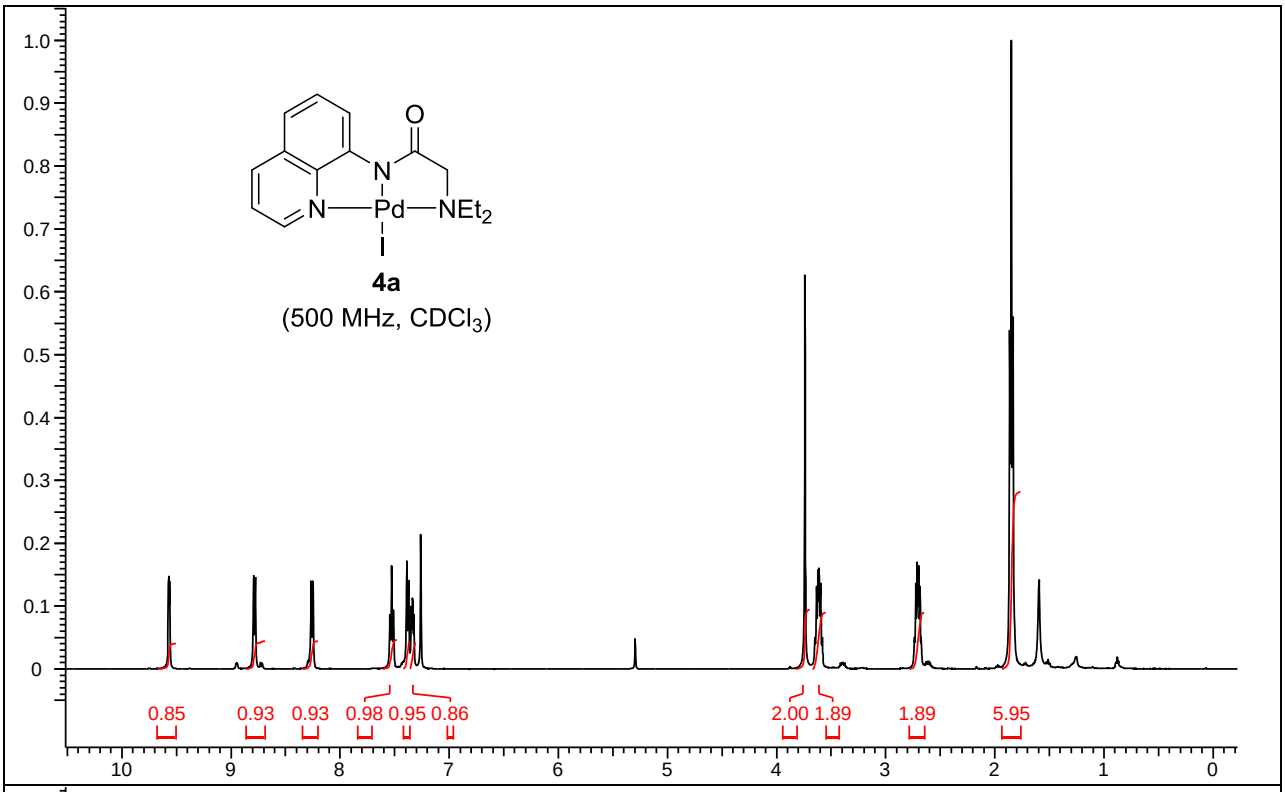



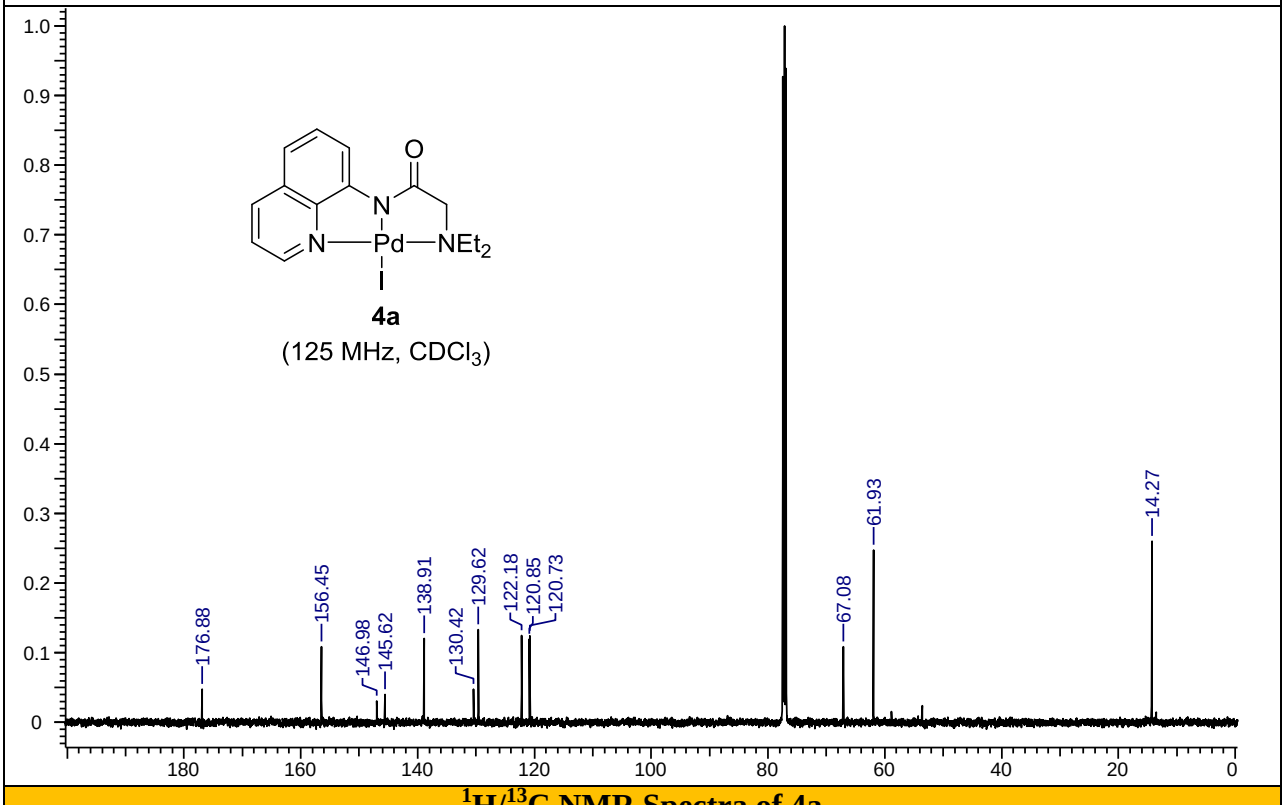

**$^{1}H/^{13}C$ NMR Spectra of 3a**



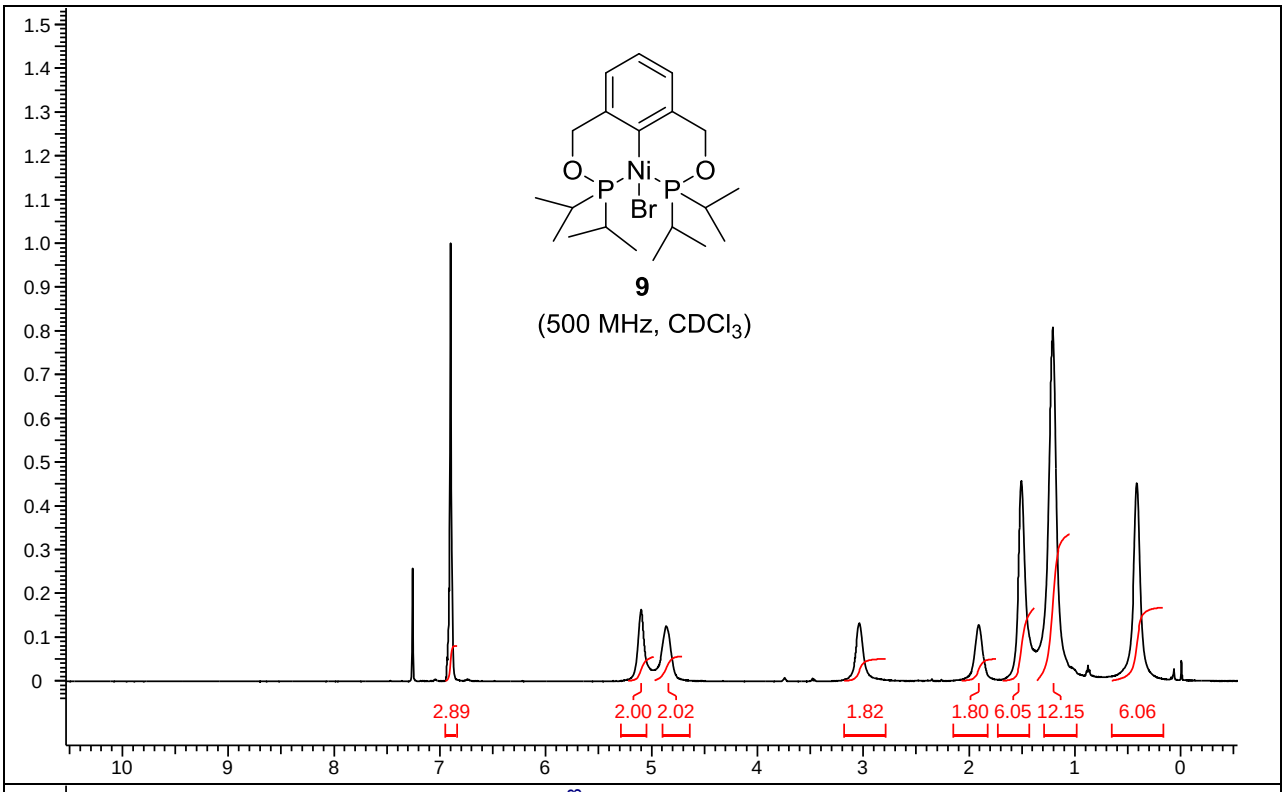



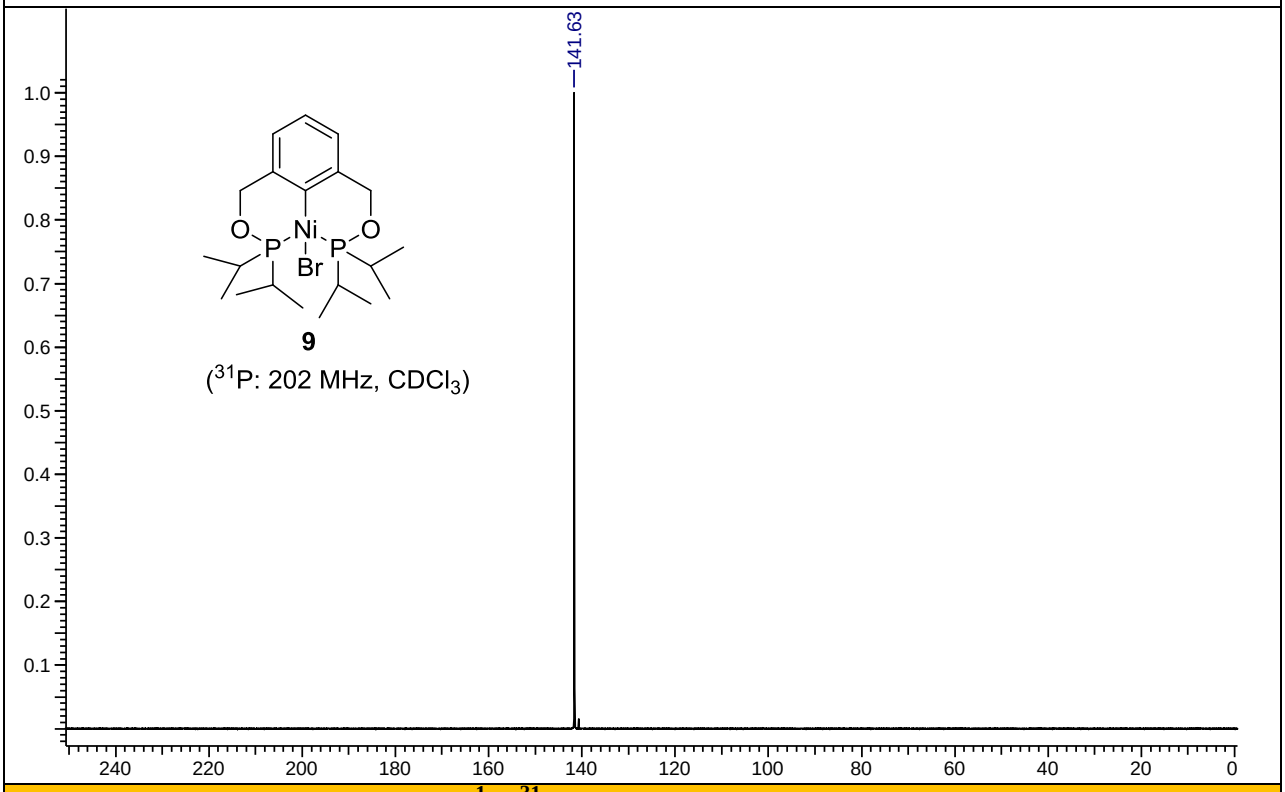

**$^{1}H/^{13}C$ NMR Spectra of 3c**



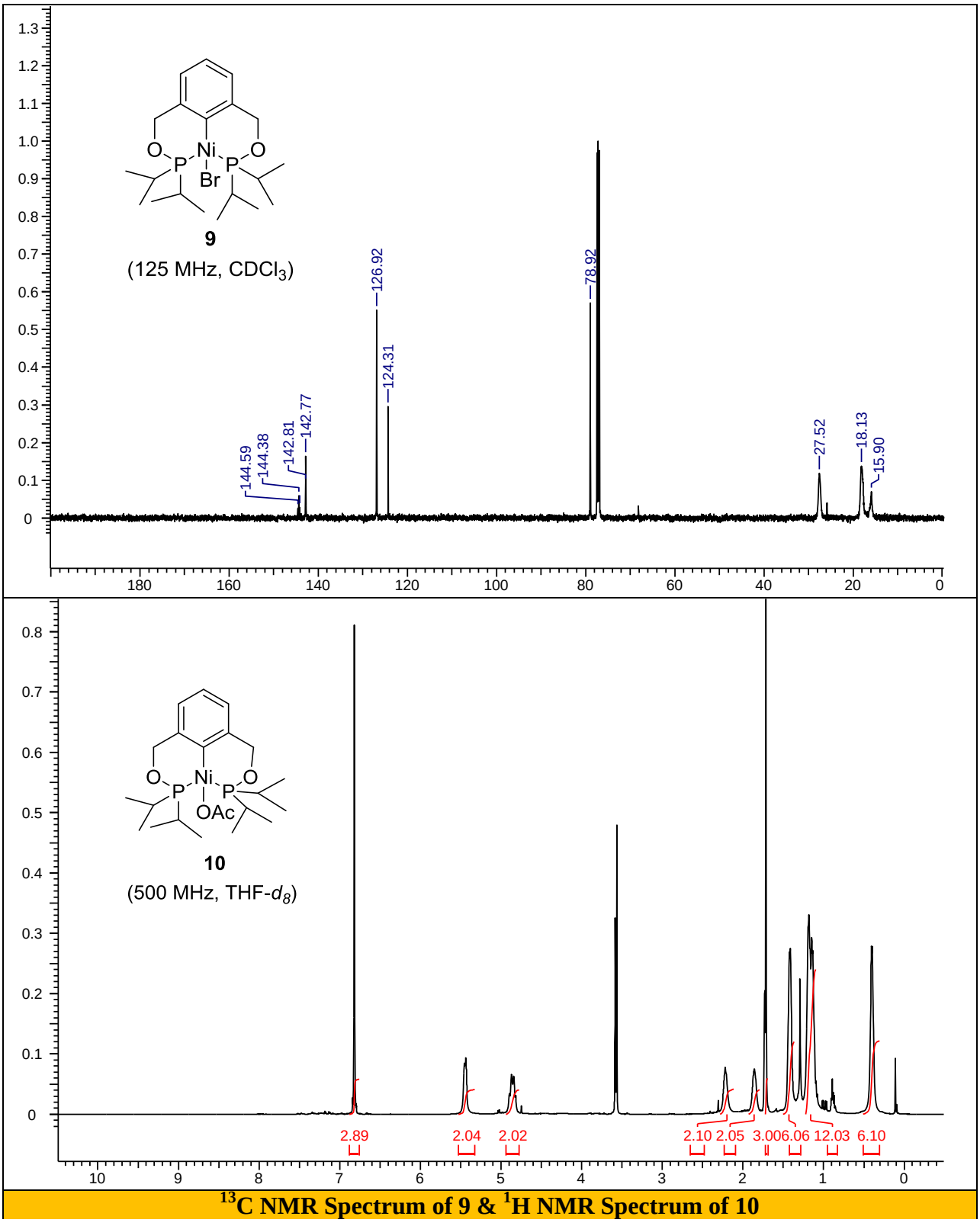




**$^{1}H/^{13}C$ NMR Spectra of 4a**

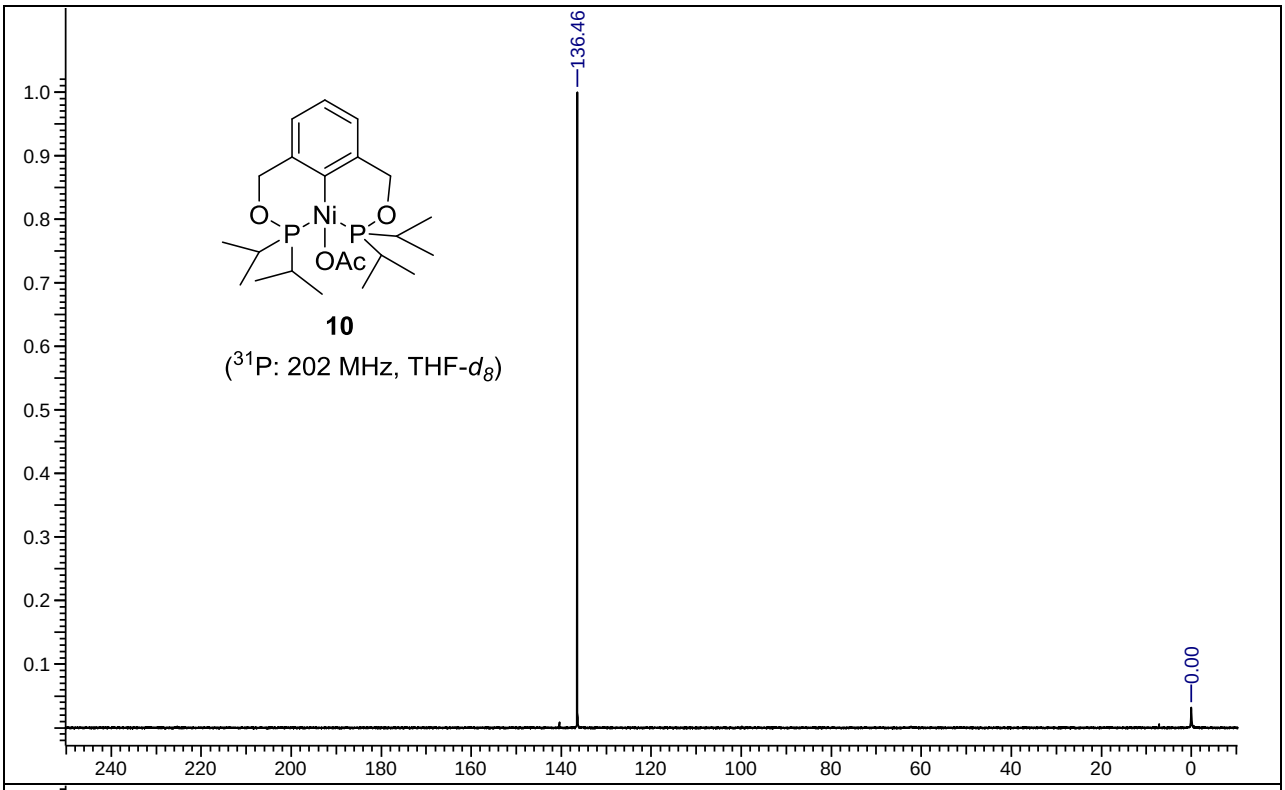


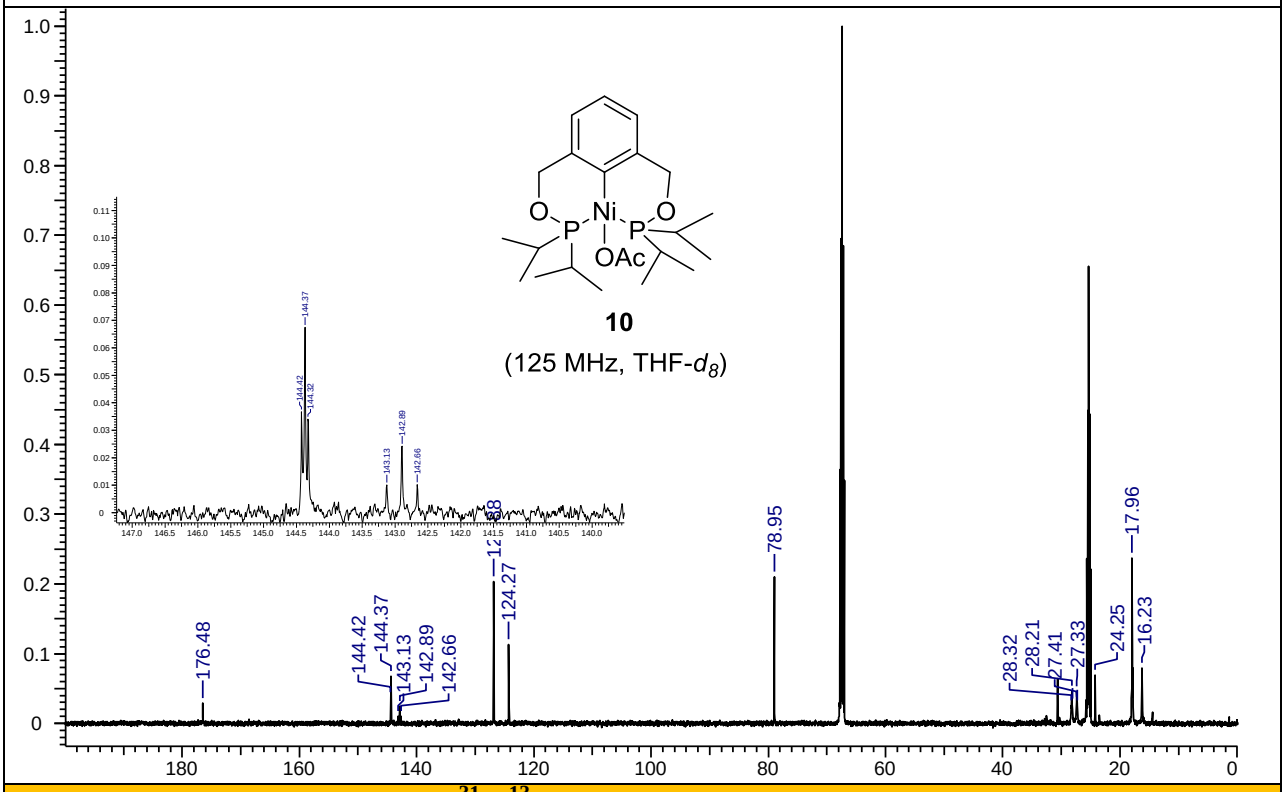




**$^{1}H/^{31}PNMR$ Spectra of 9**

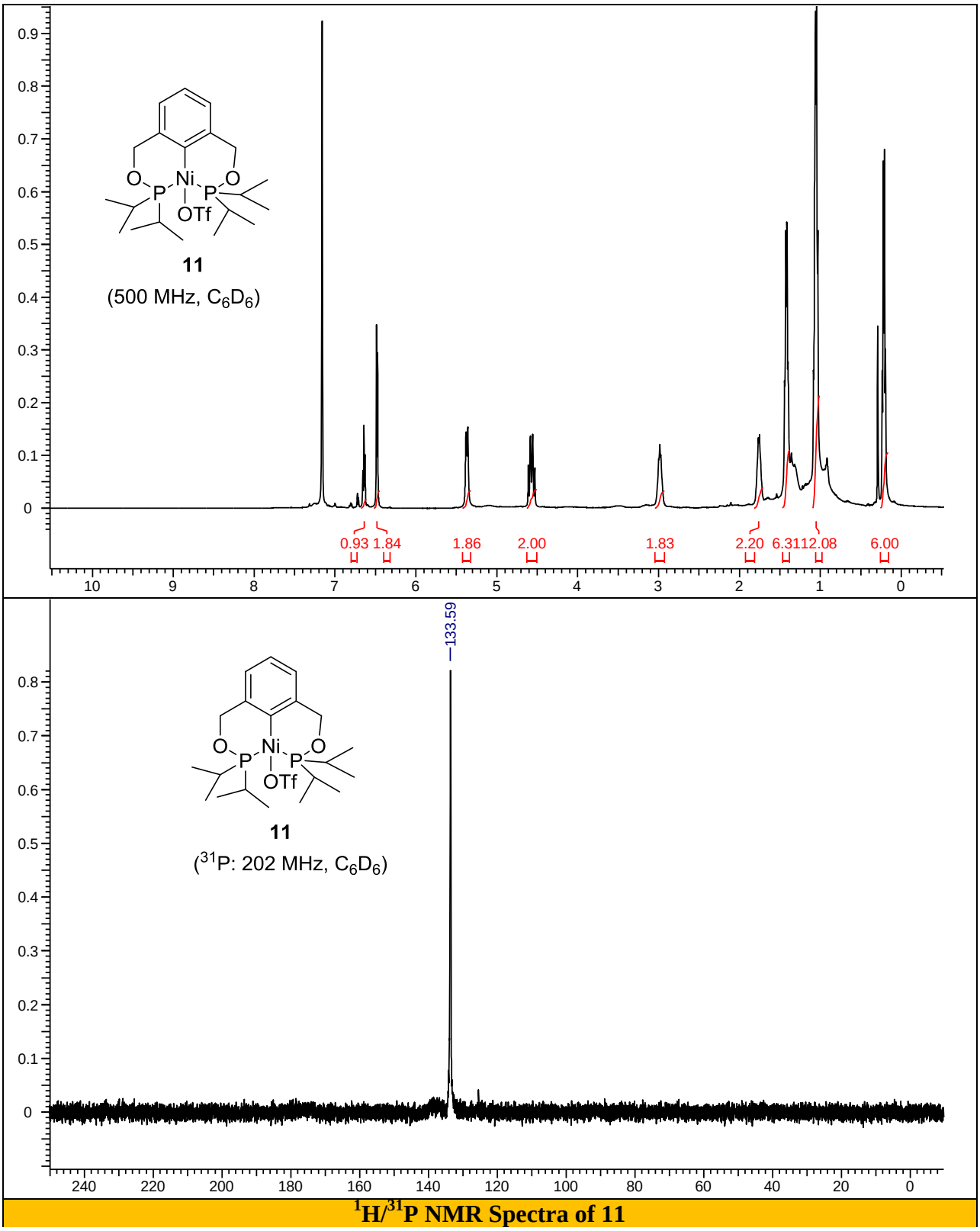



**$^{13}$C NMR Spectrum of 9 & $^{1}$H NMR Spectrum of 10**

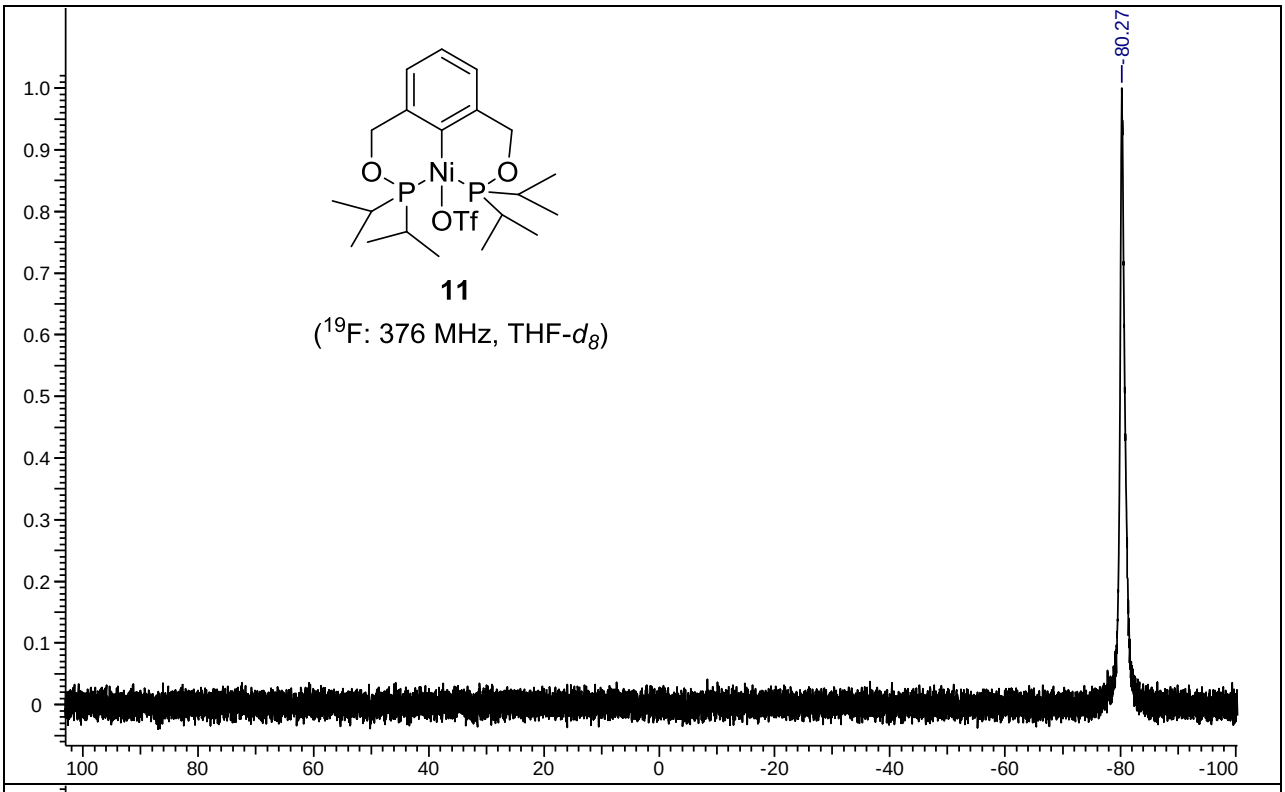


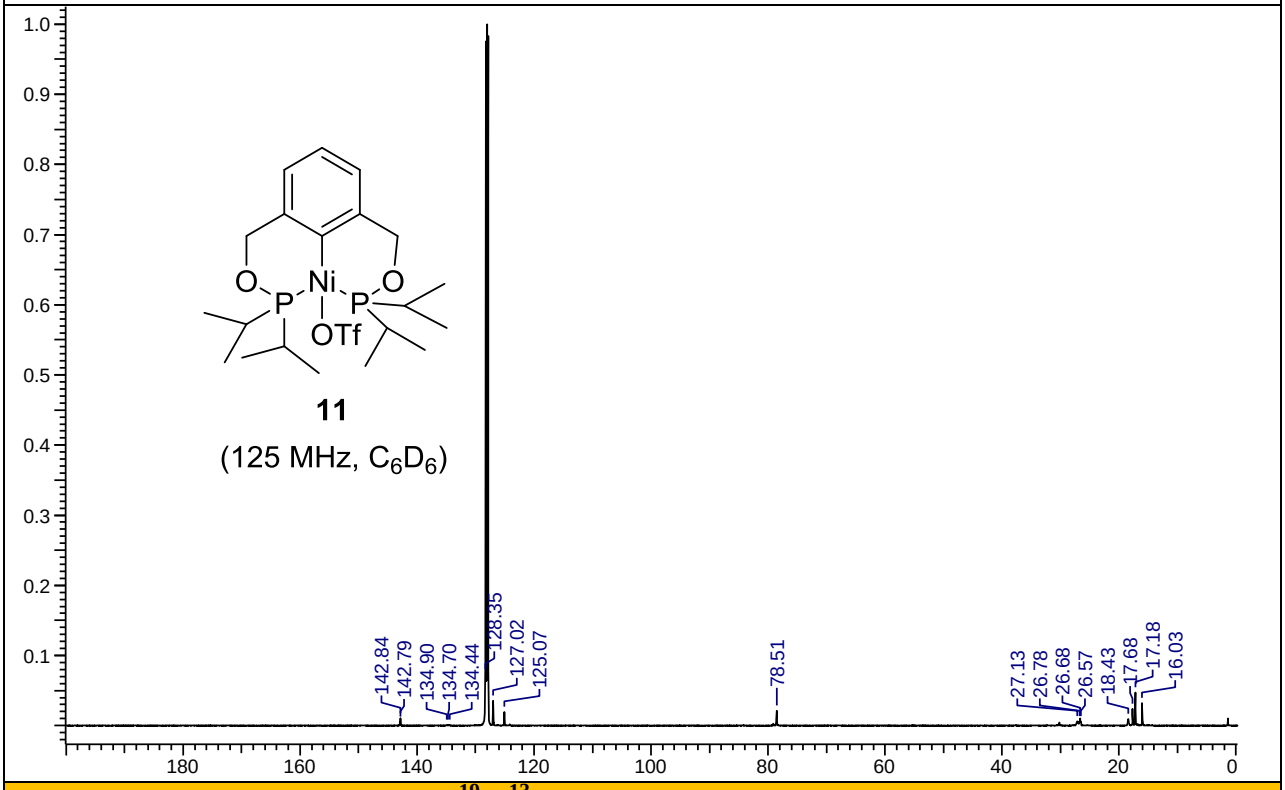




**$^{31}$P/$^{13}$C NMR Spectra of 10**

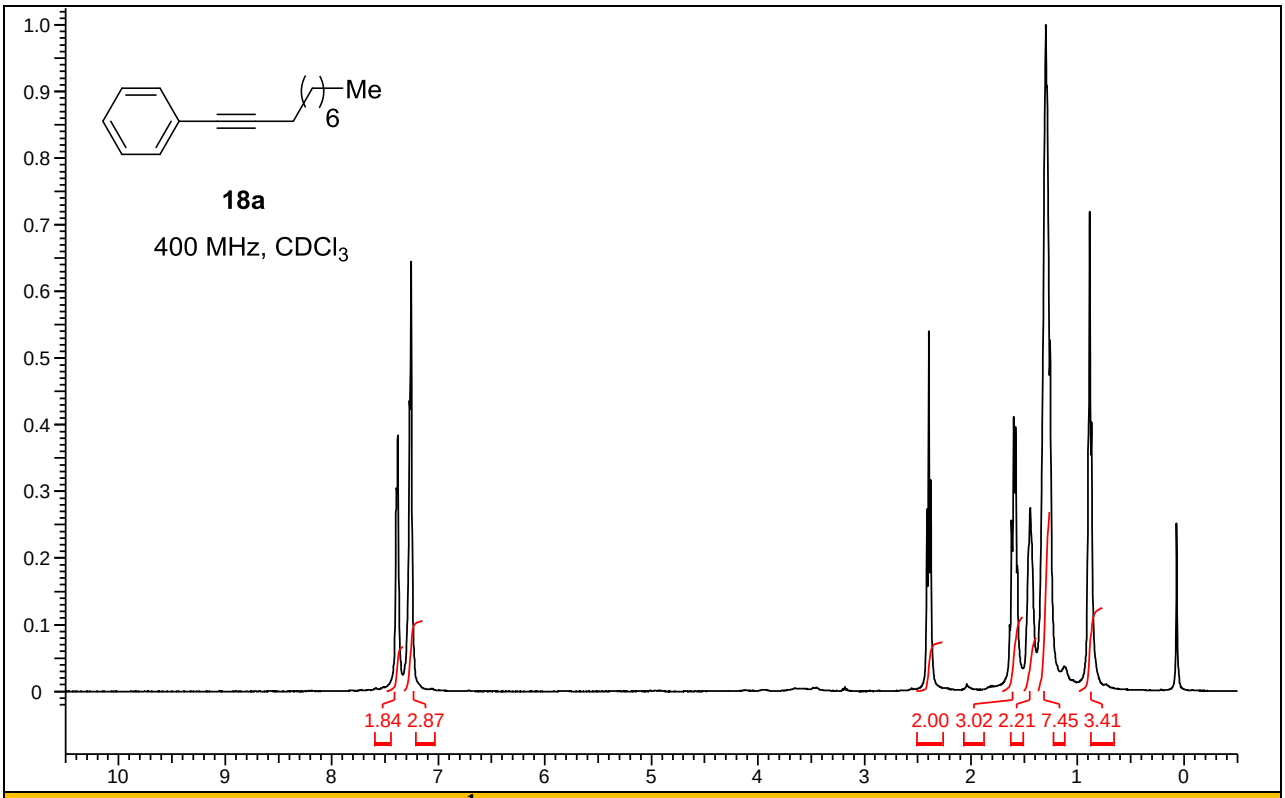



**$^{1}H/^{31}P$ NMR Spectra of 11**

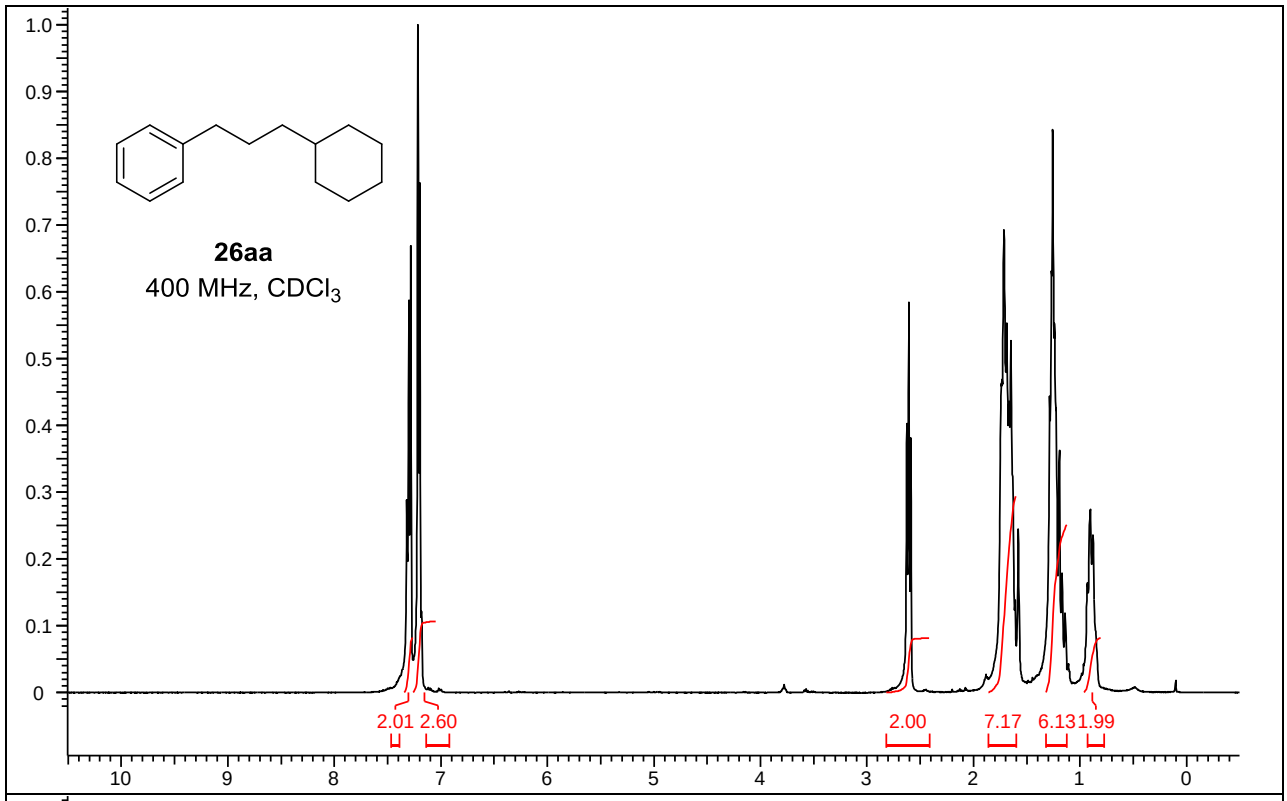


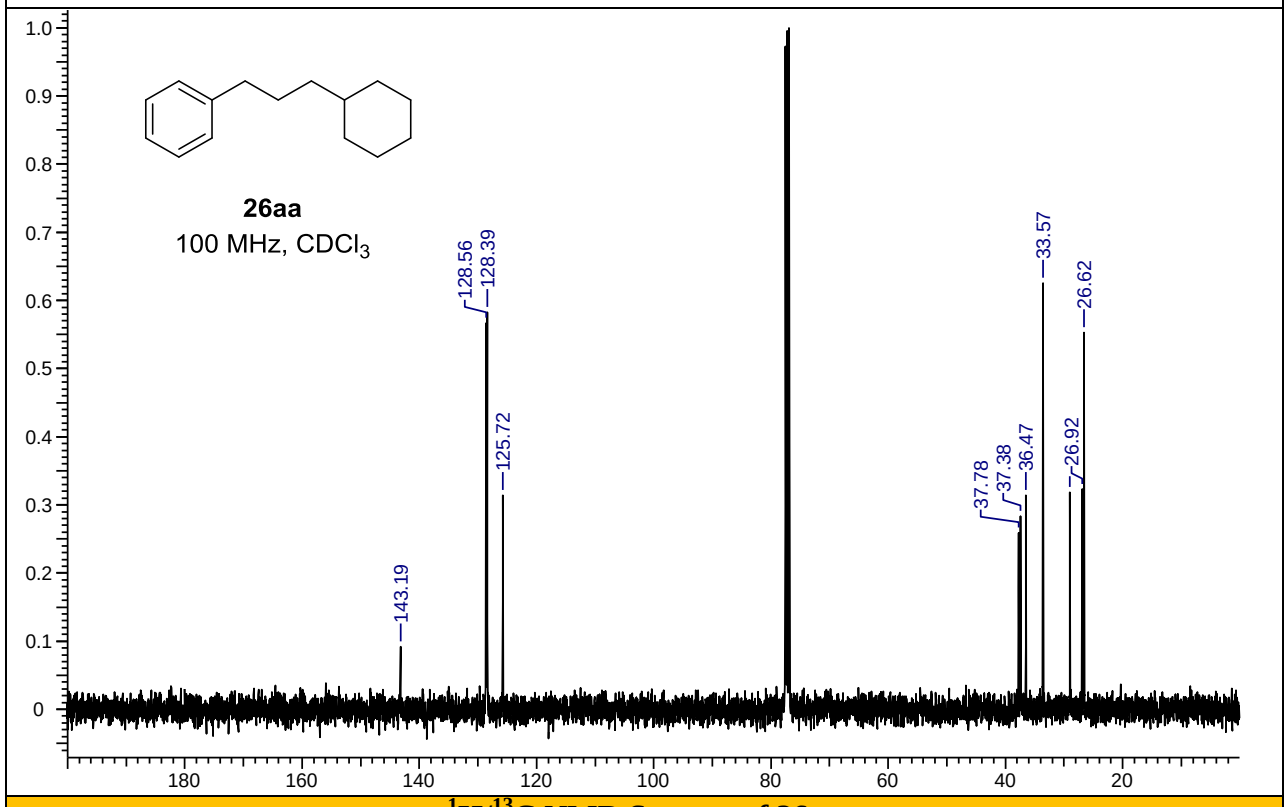




**$^{19}$F/$^{13}$C NMR Spectra of 11**

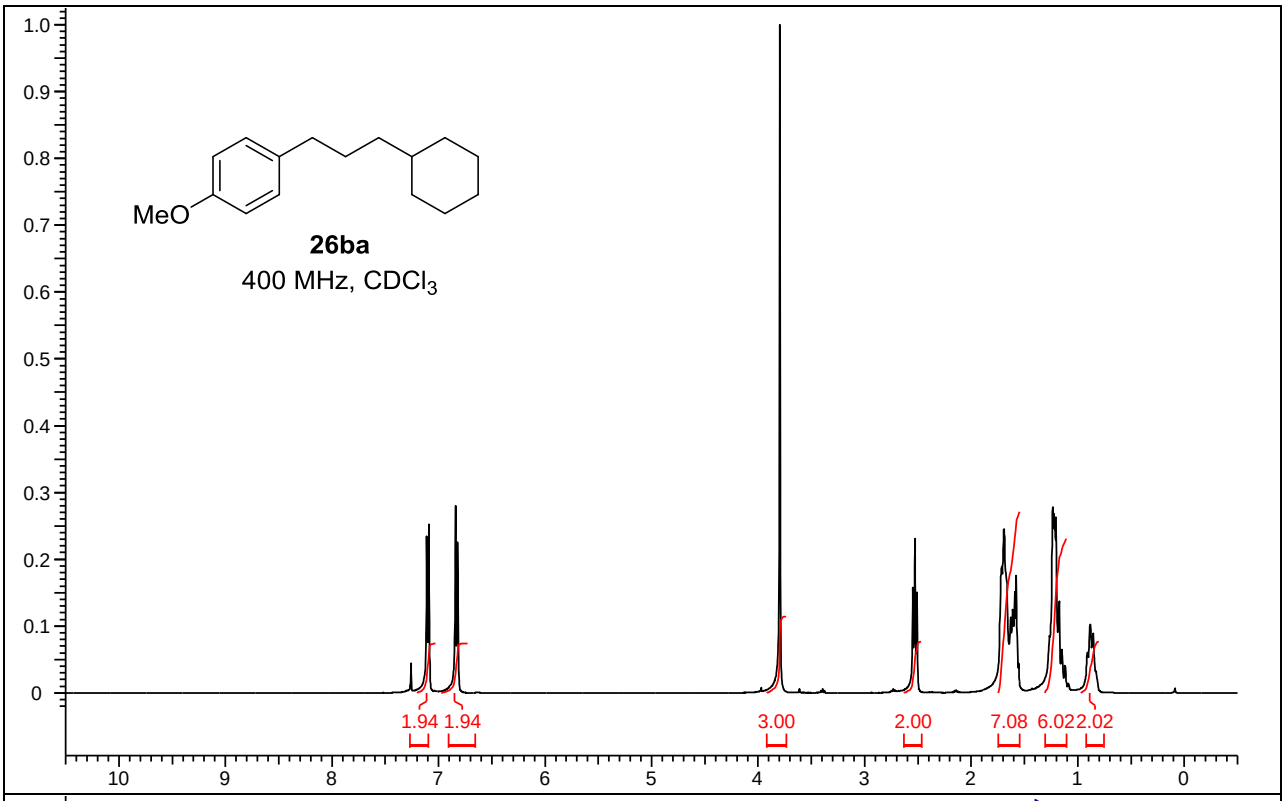


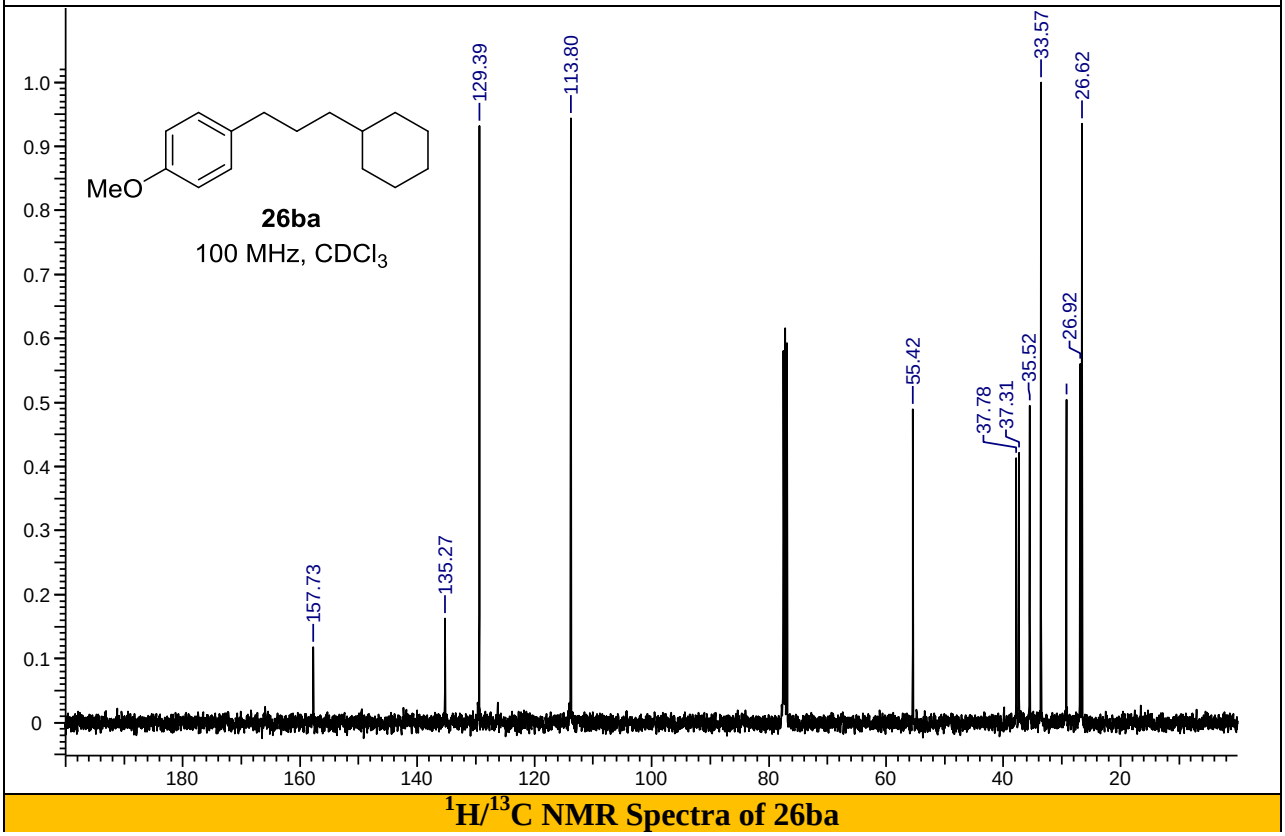

**$^{1}$H NMR Spectrum of 18a**



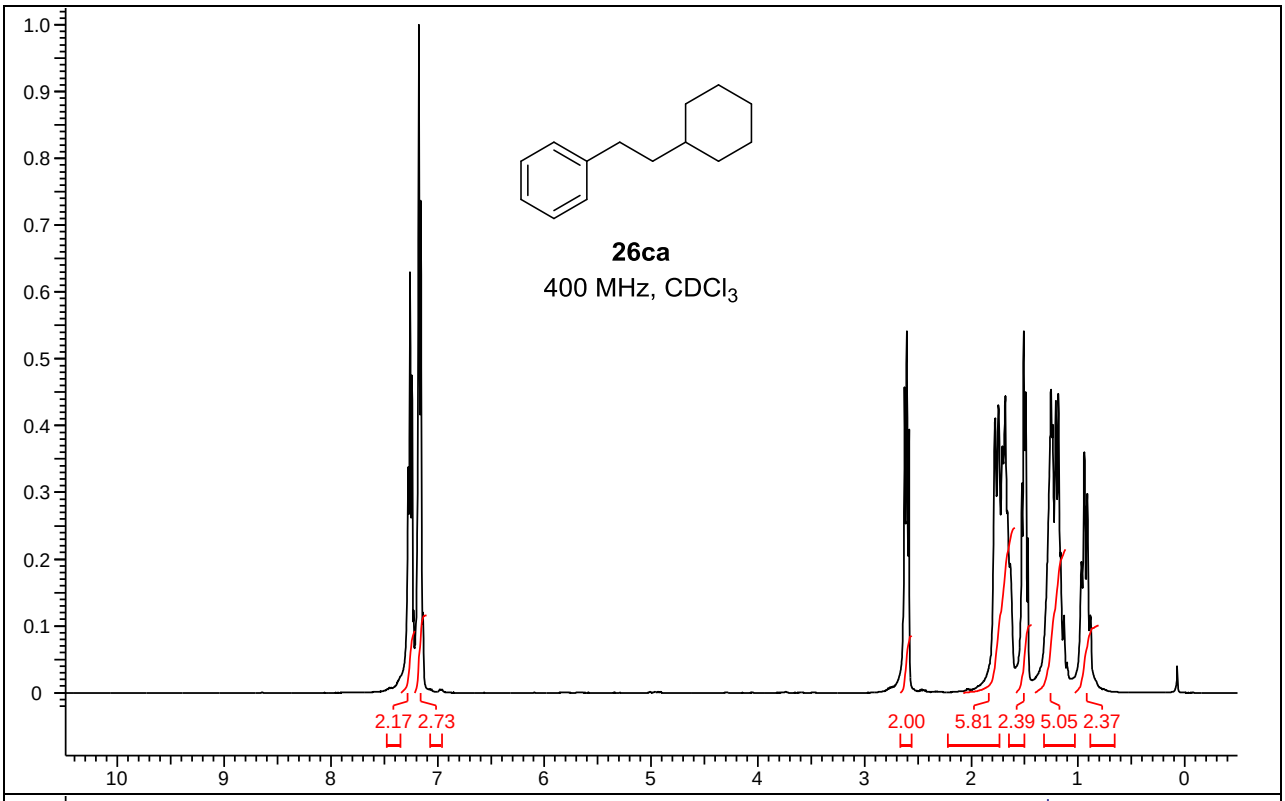



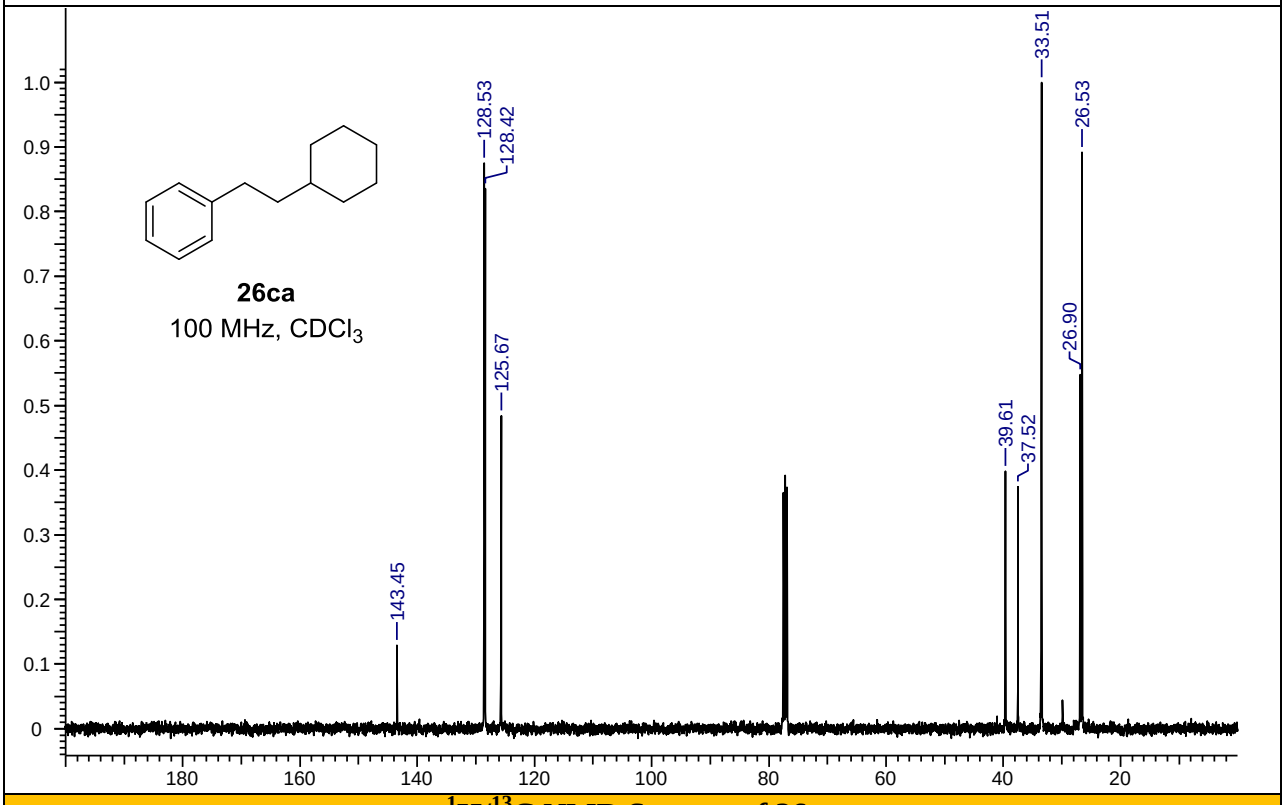

**$^{1}H/^{13}C$ NMR Spectra of 26aa**



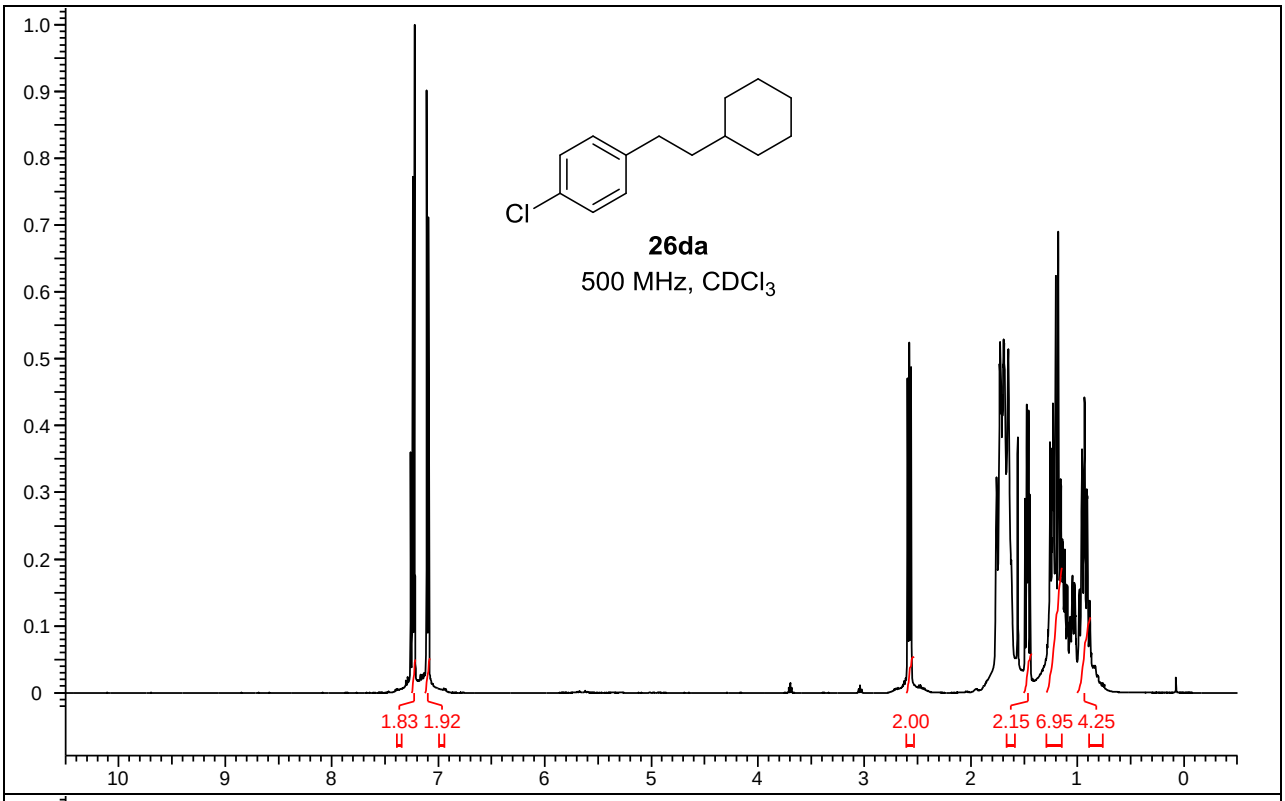



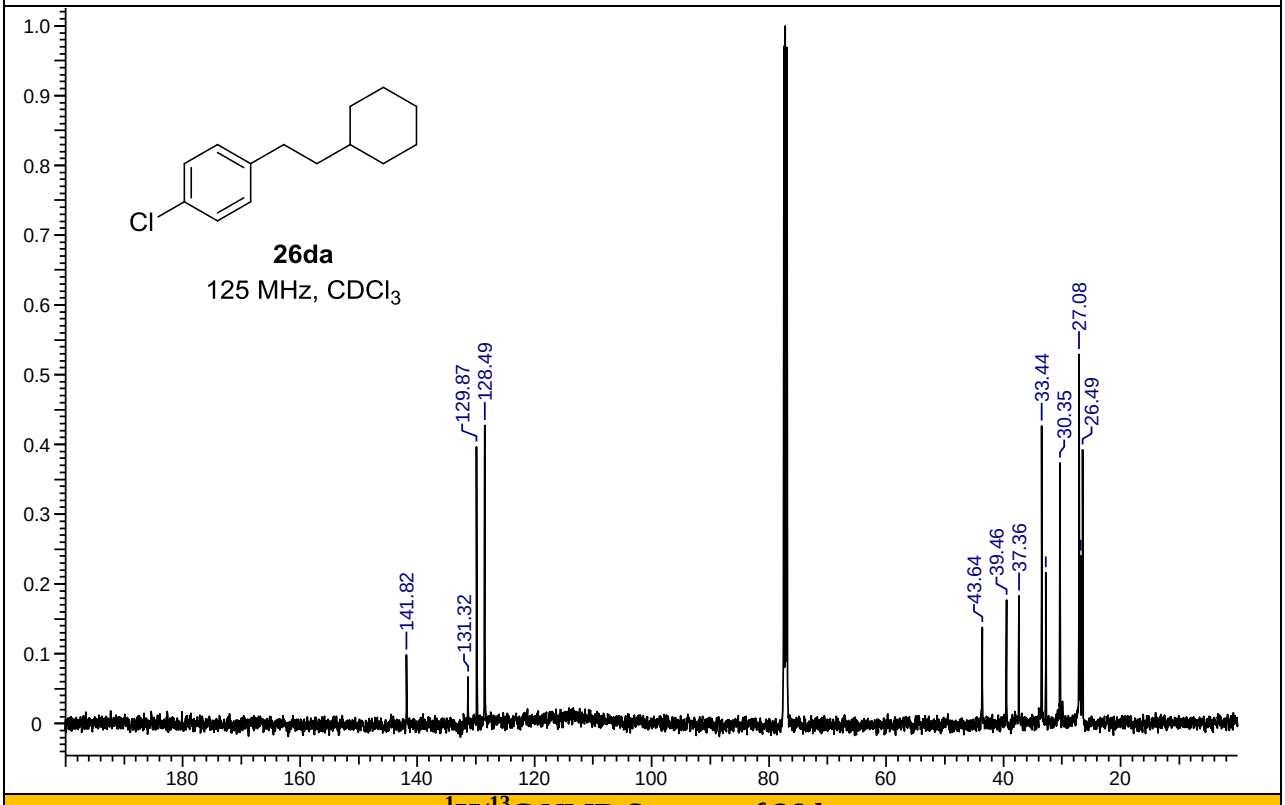

**$^{1}H/^{13}C$ NMR Spectra of 26ba**



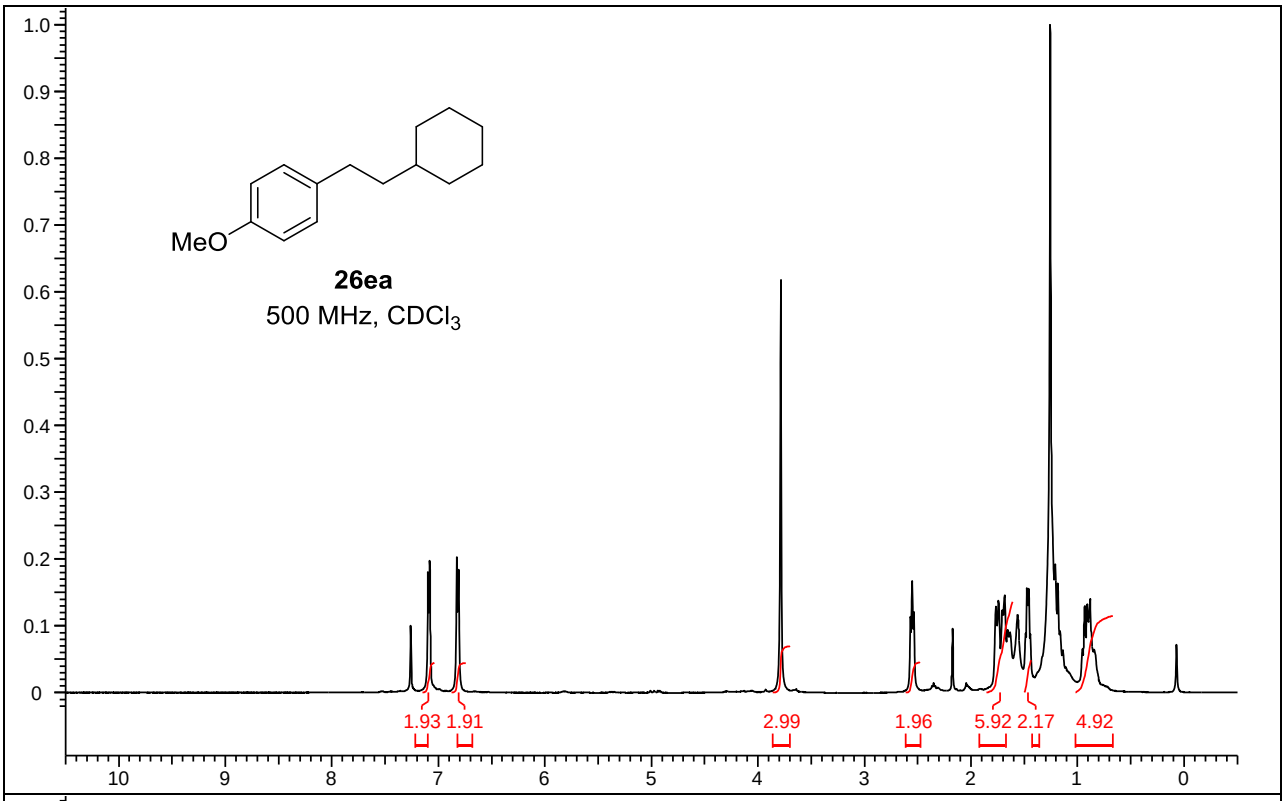



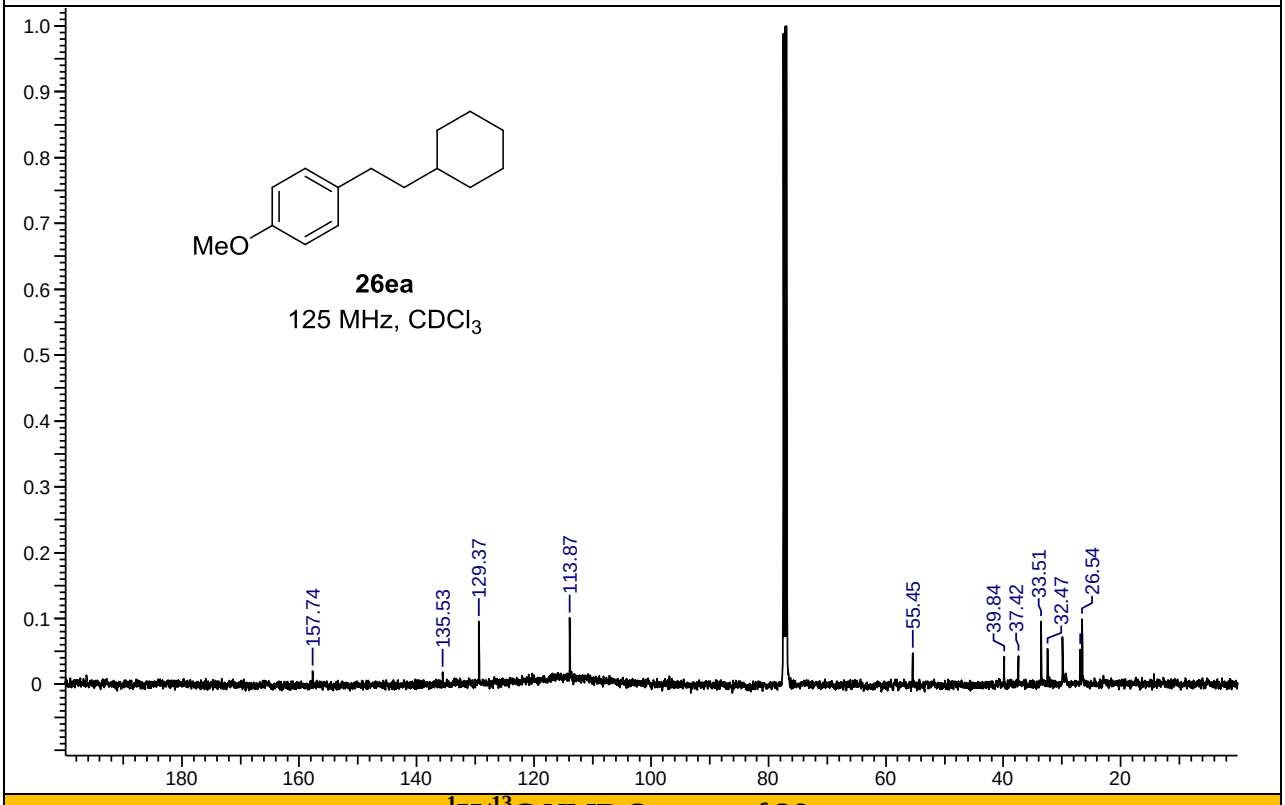

**$^{1}H/^{13}C$ NMR Spectra of 26ca**



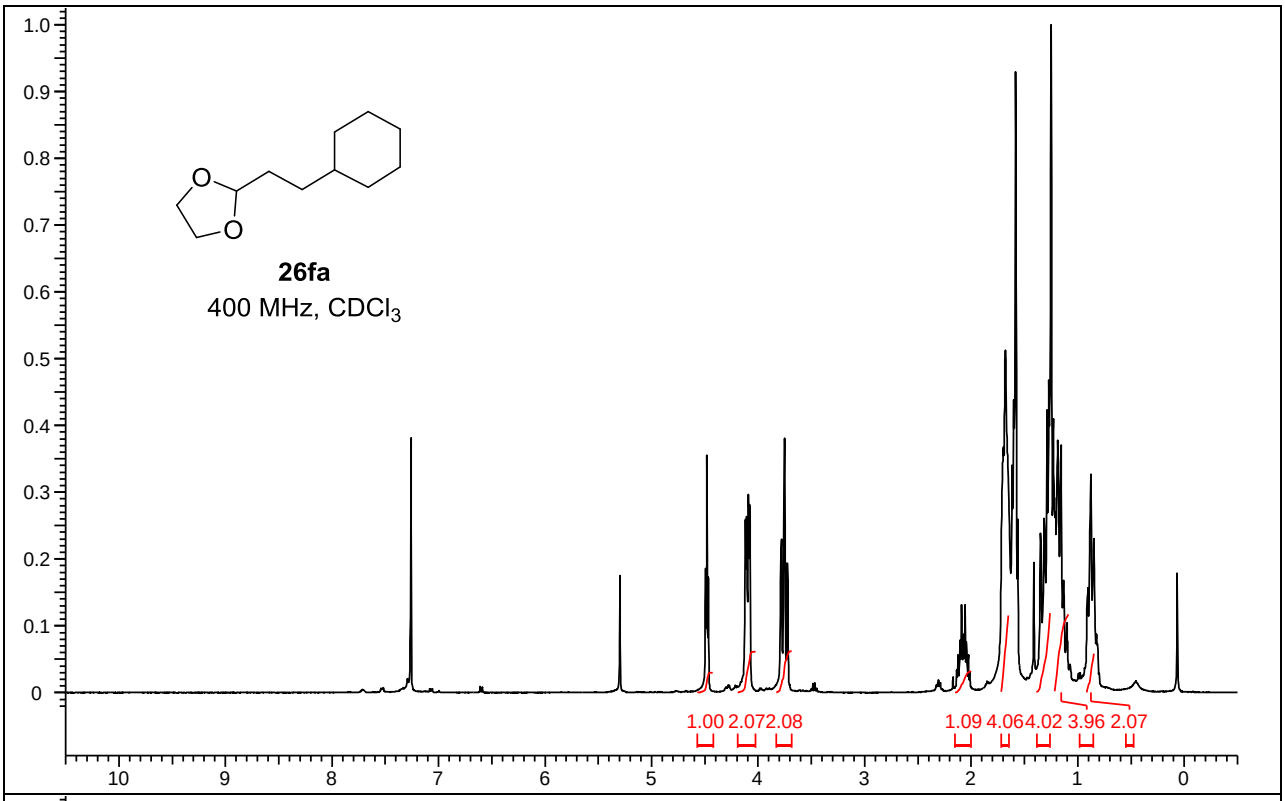



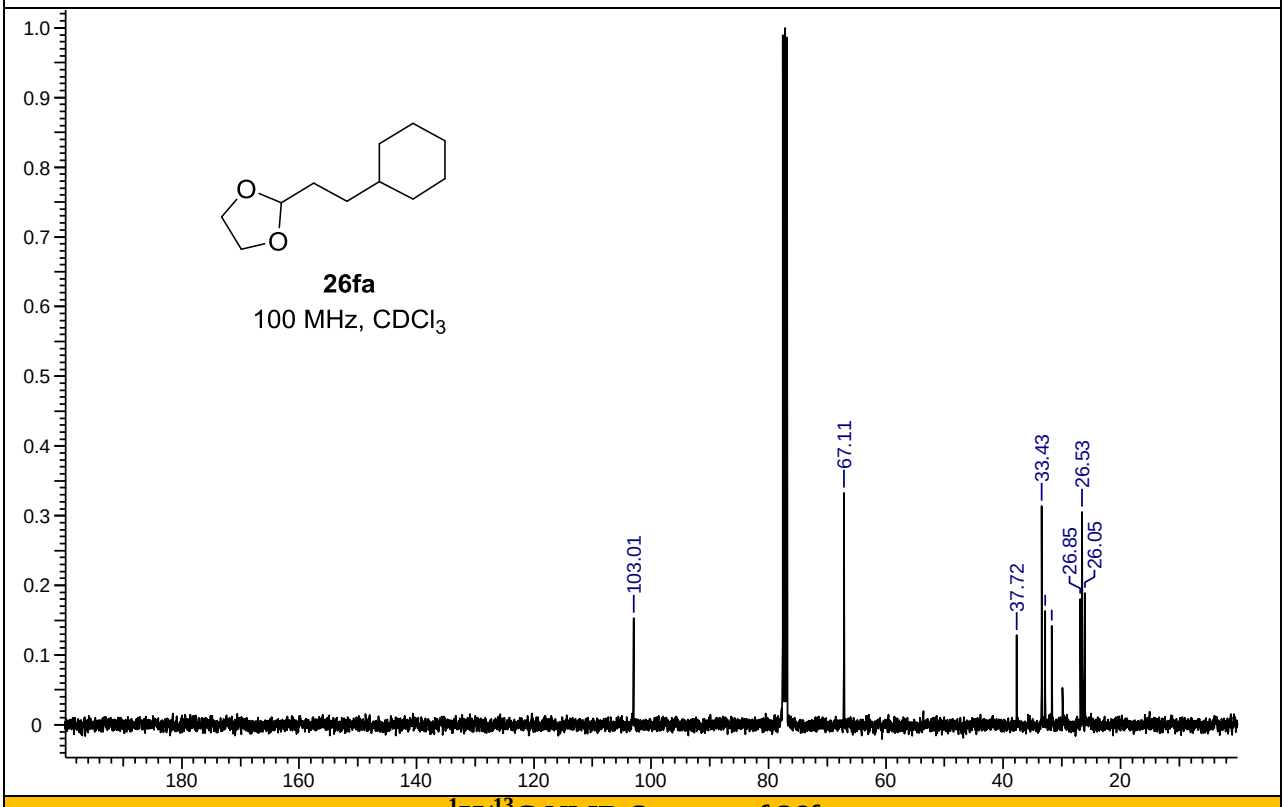

**$^{1}H/^{13}C$ NMR Spectra of 26da**



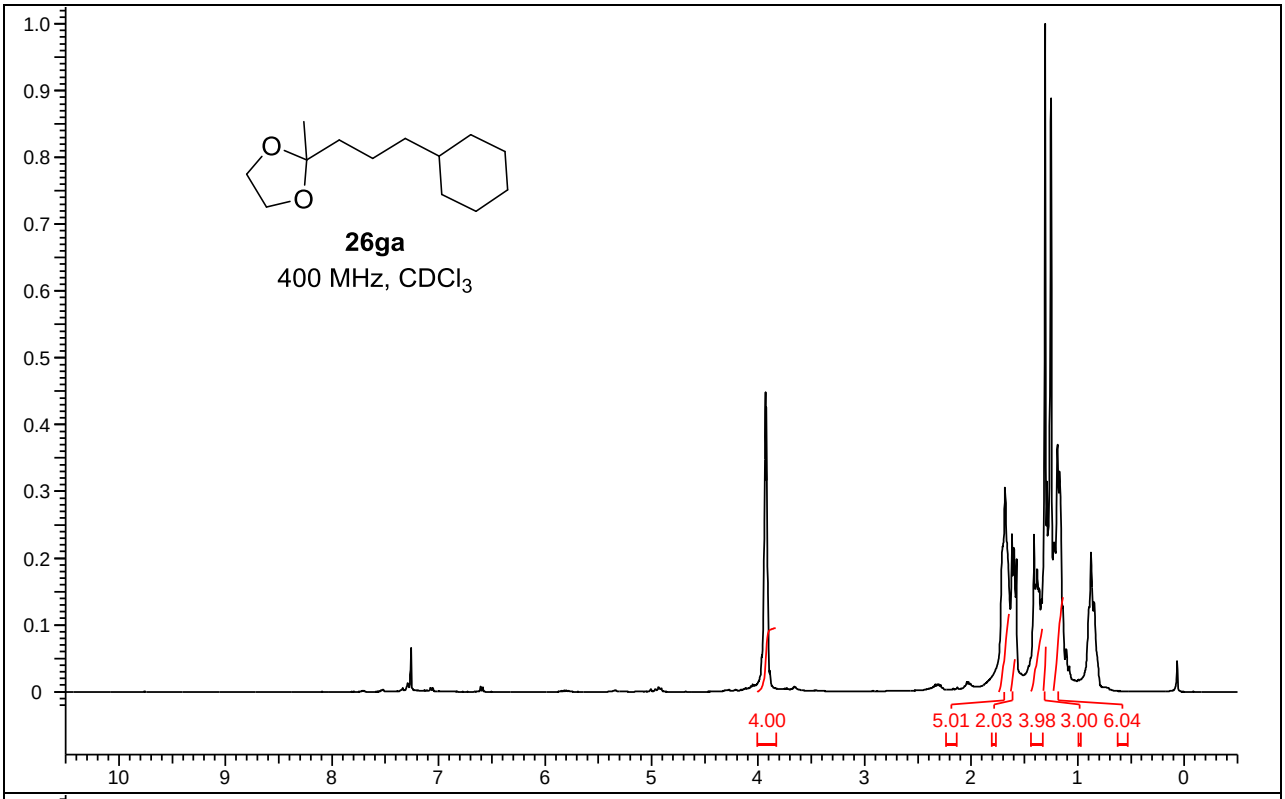



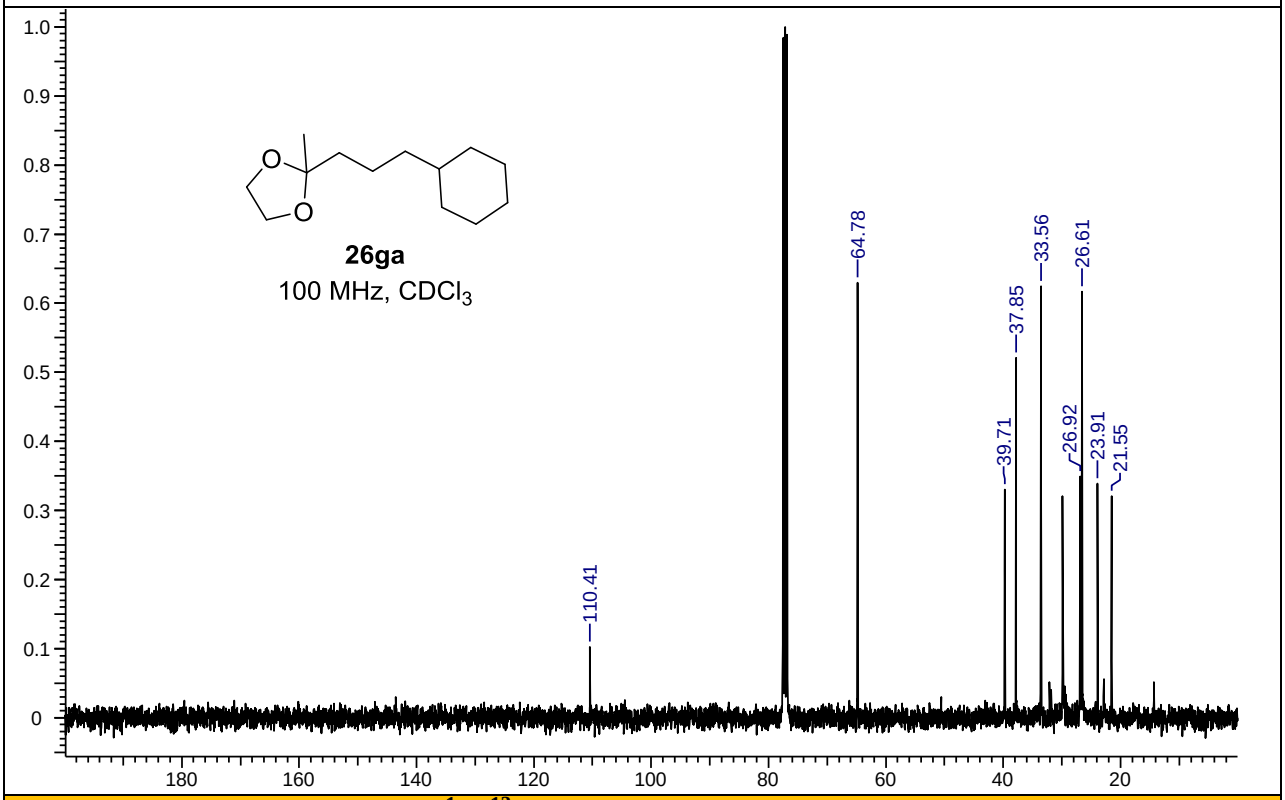

**$^{1}H/^{13}C$ NMR Spectra of 26ea**



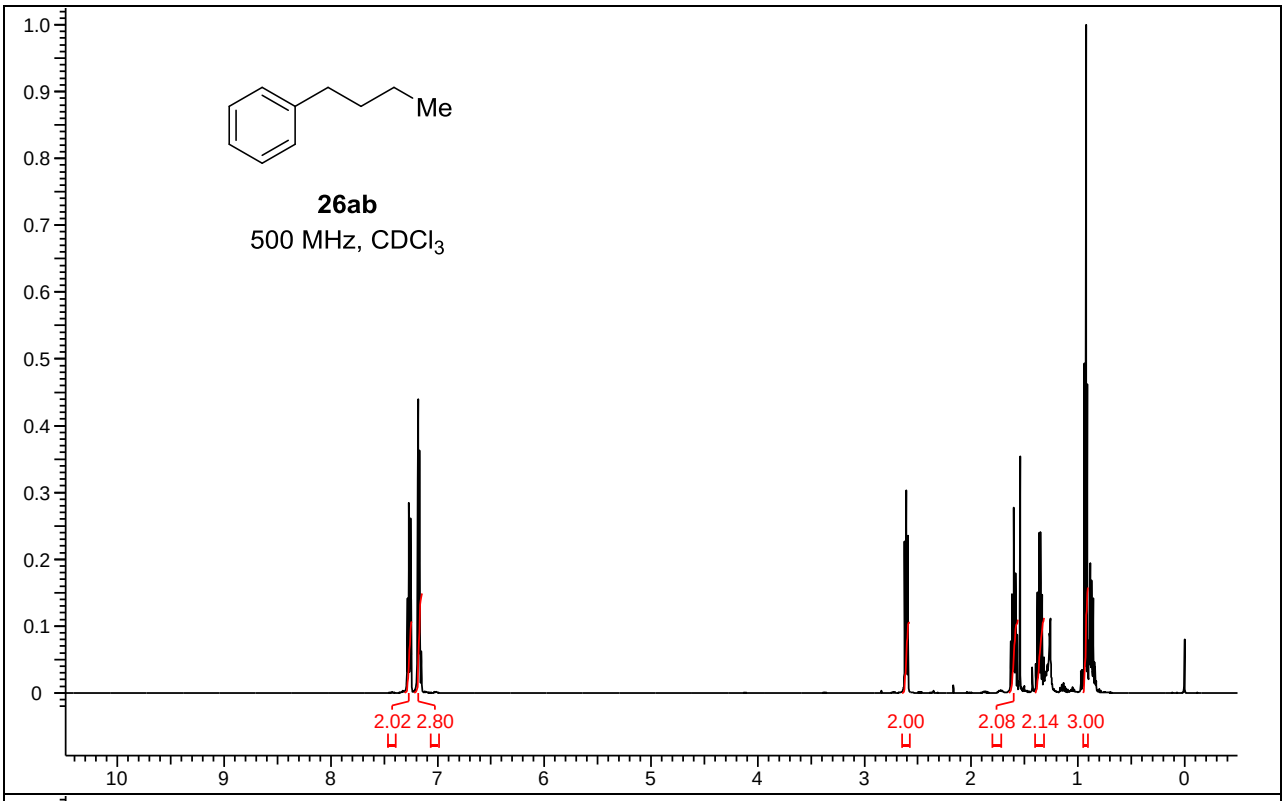



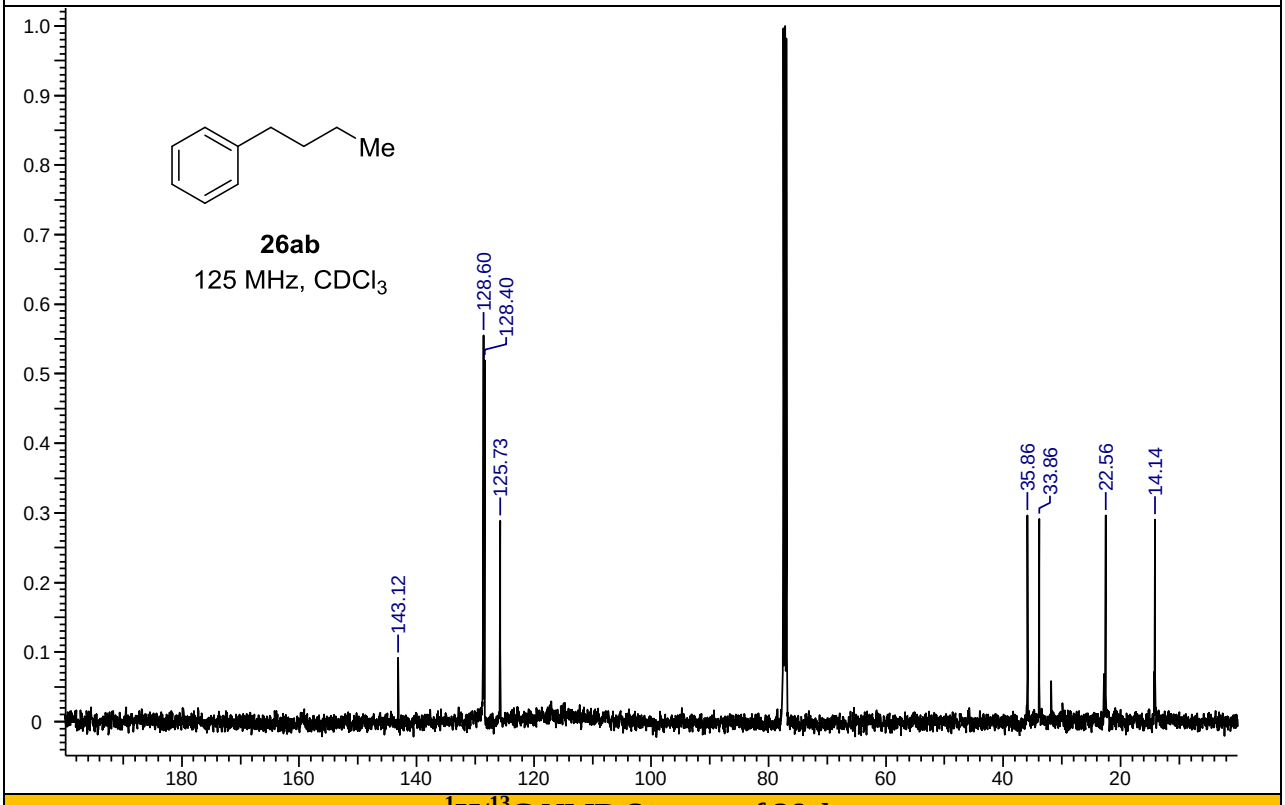

**$^{1}H/^{13}C$ NMR Spectra of 26fa**



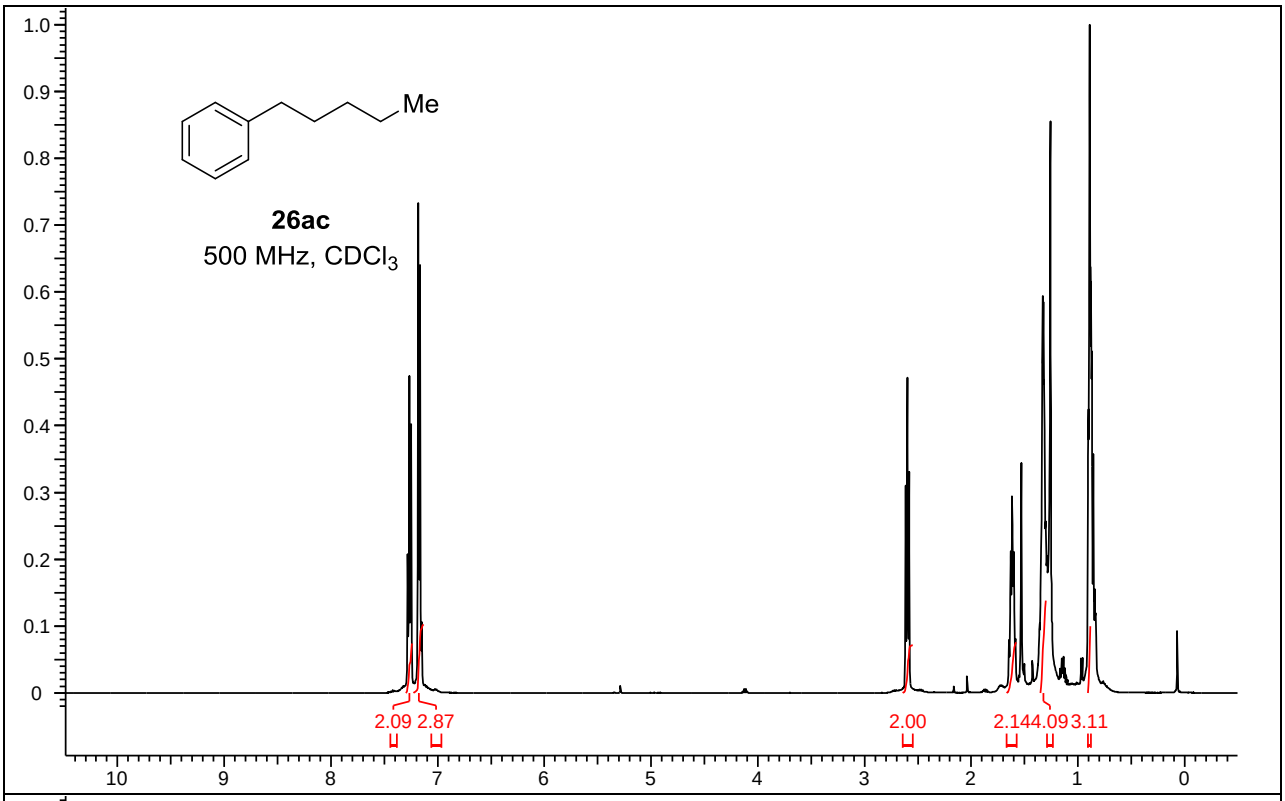



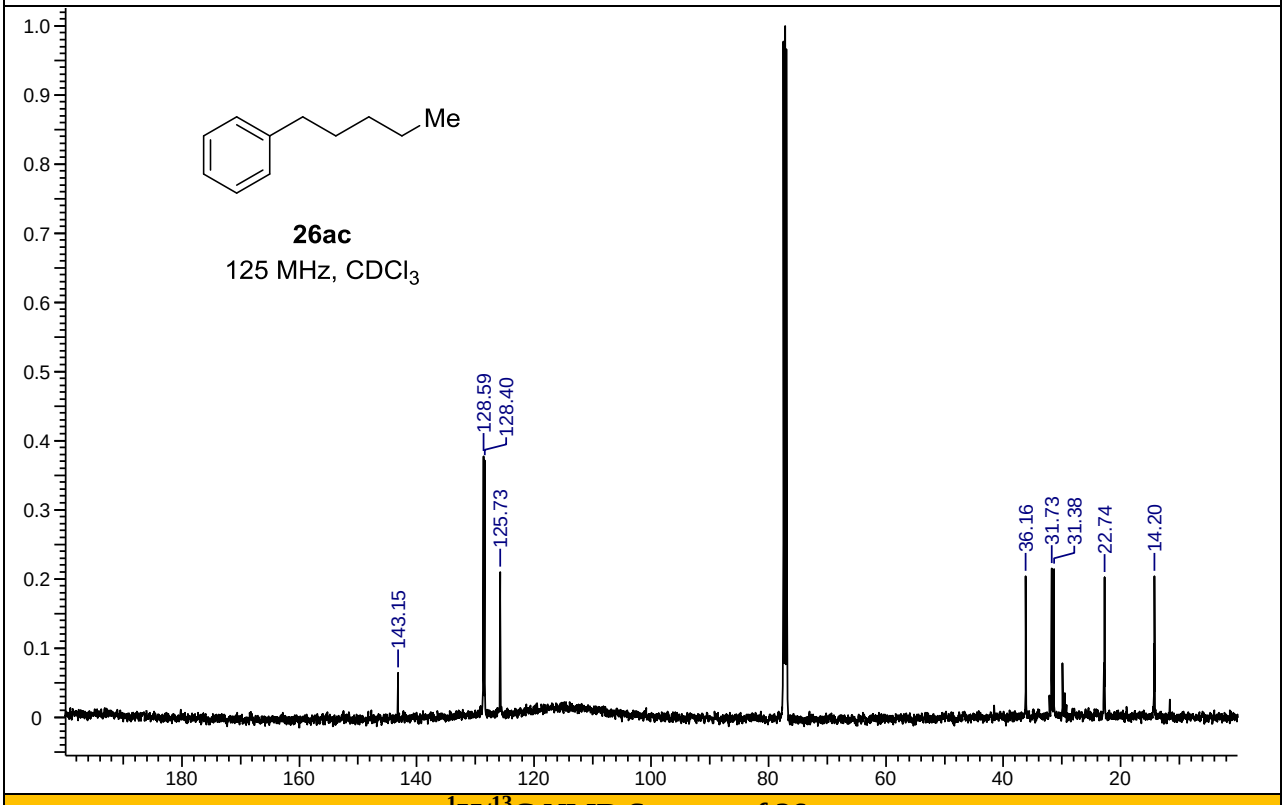

**$^{1}H/^{13}C$ NMR Spectra of 26ga**



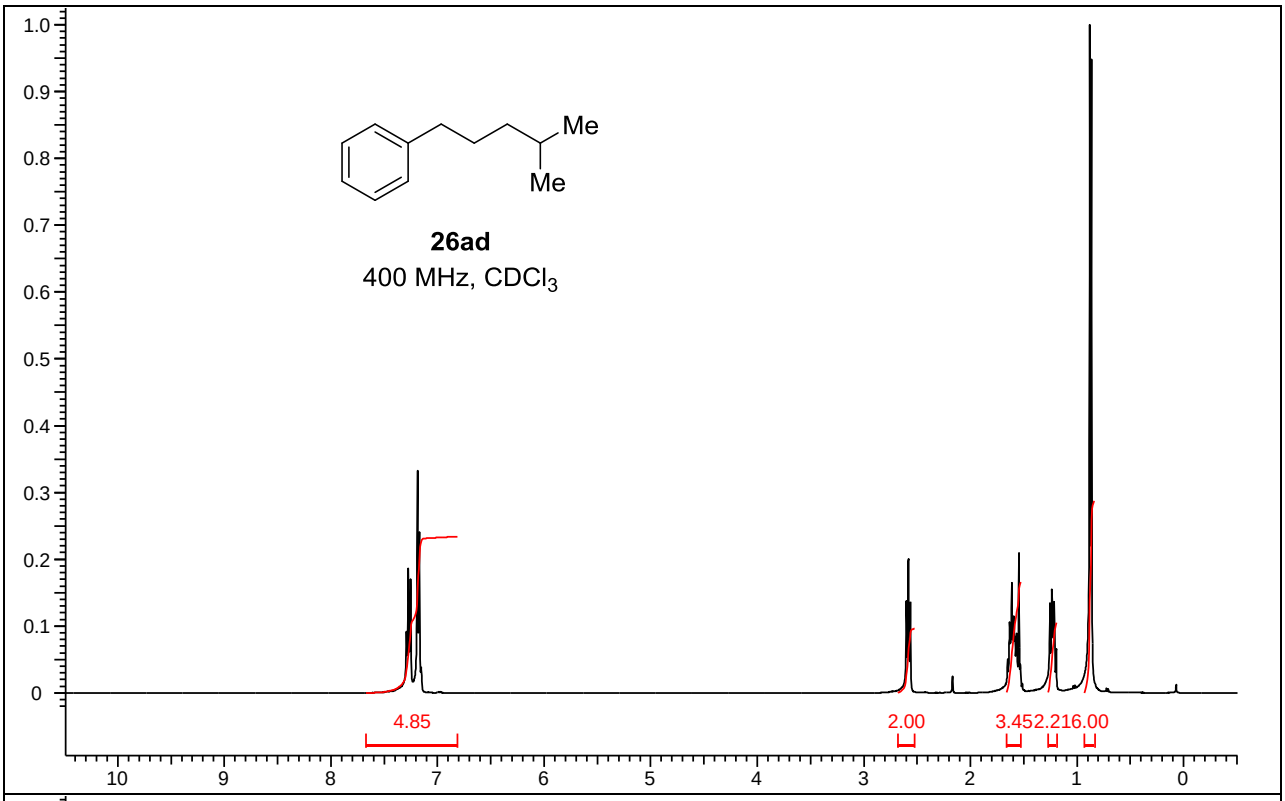



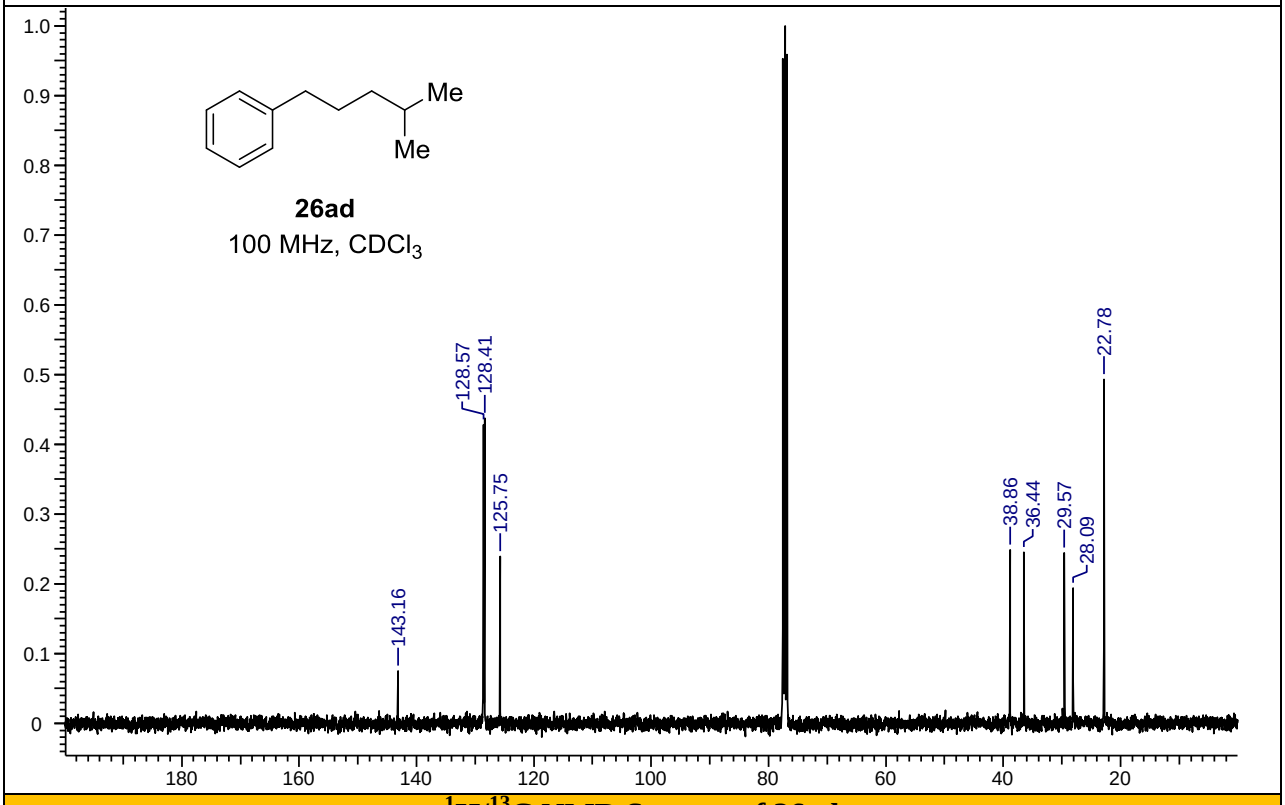

**$^{1}H/^{13}C$ NMR Spectra of 26ab**



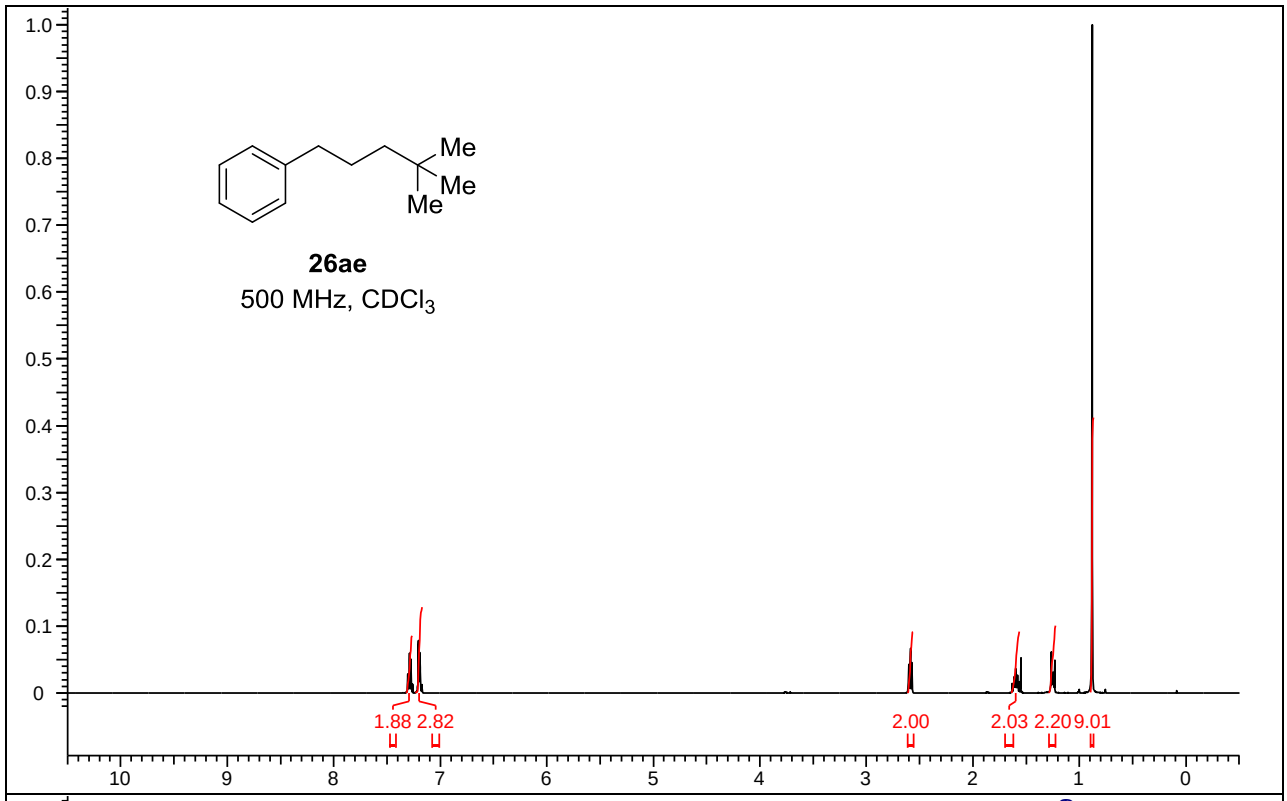



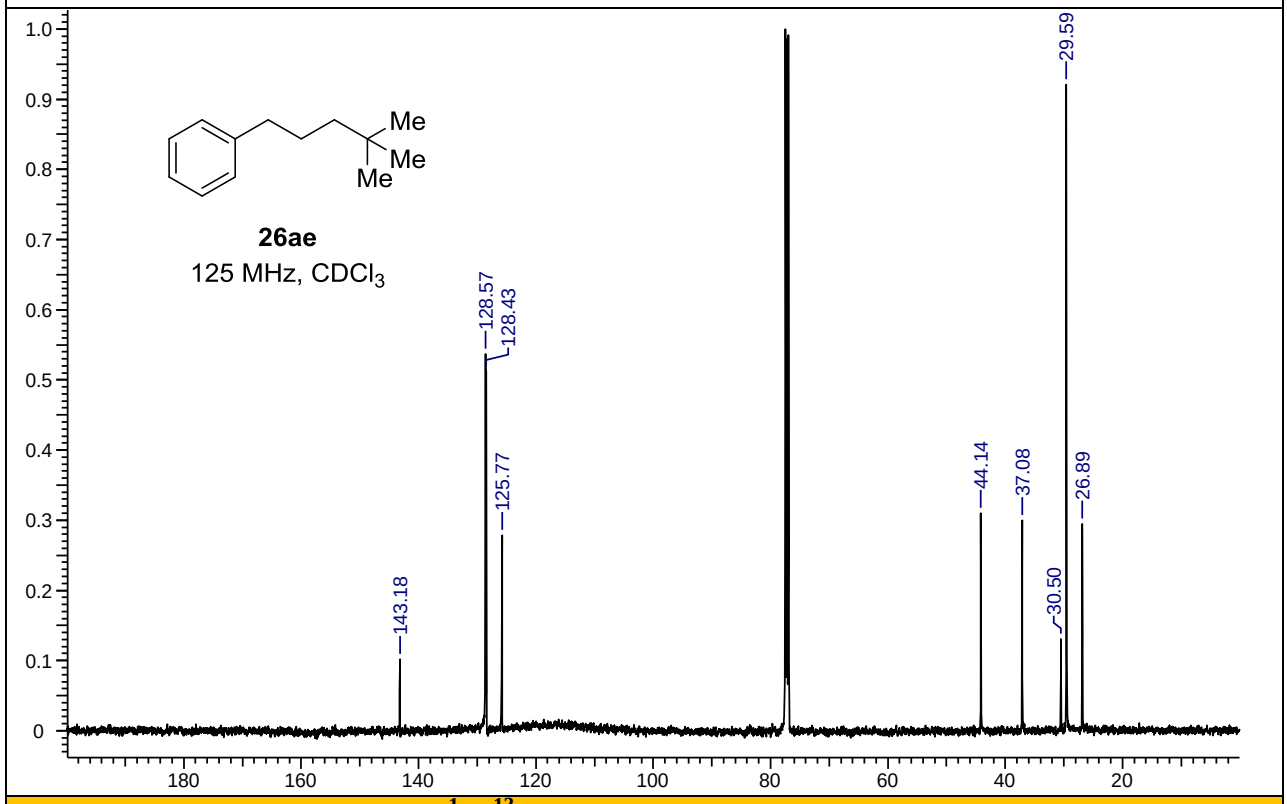

**$^{1}H/^{13}C$ NMR Spectra of 26ac**



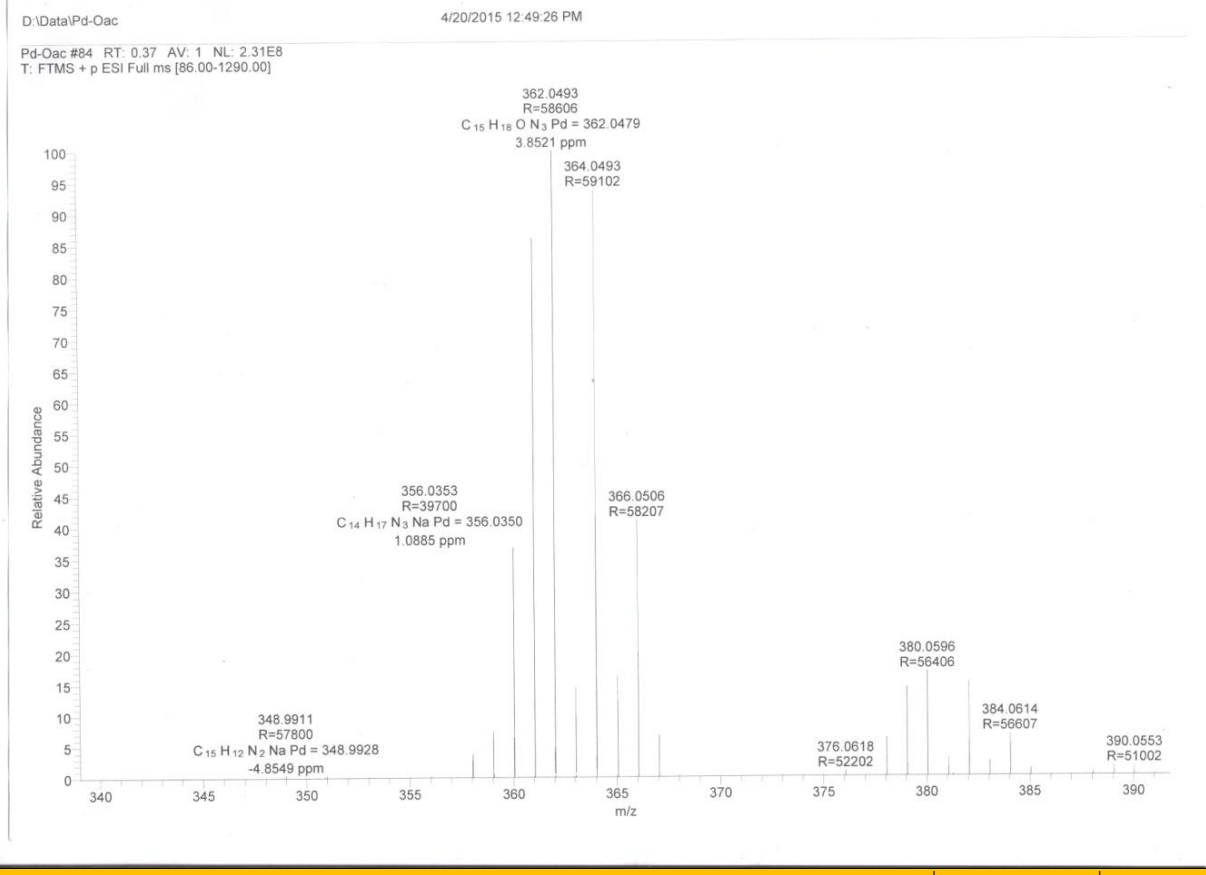

**$^{1}H/^{13}C$ NMR Spectra of 26ad**



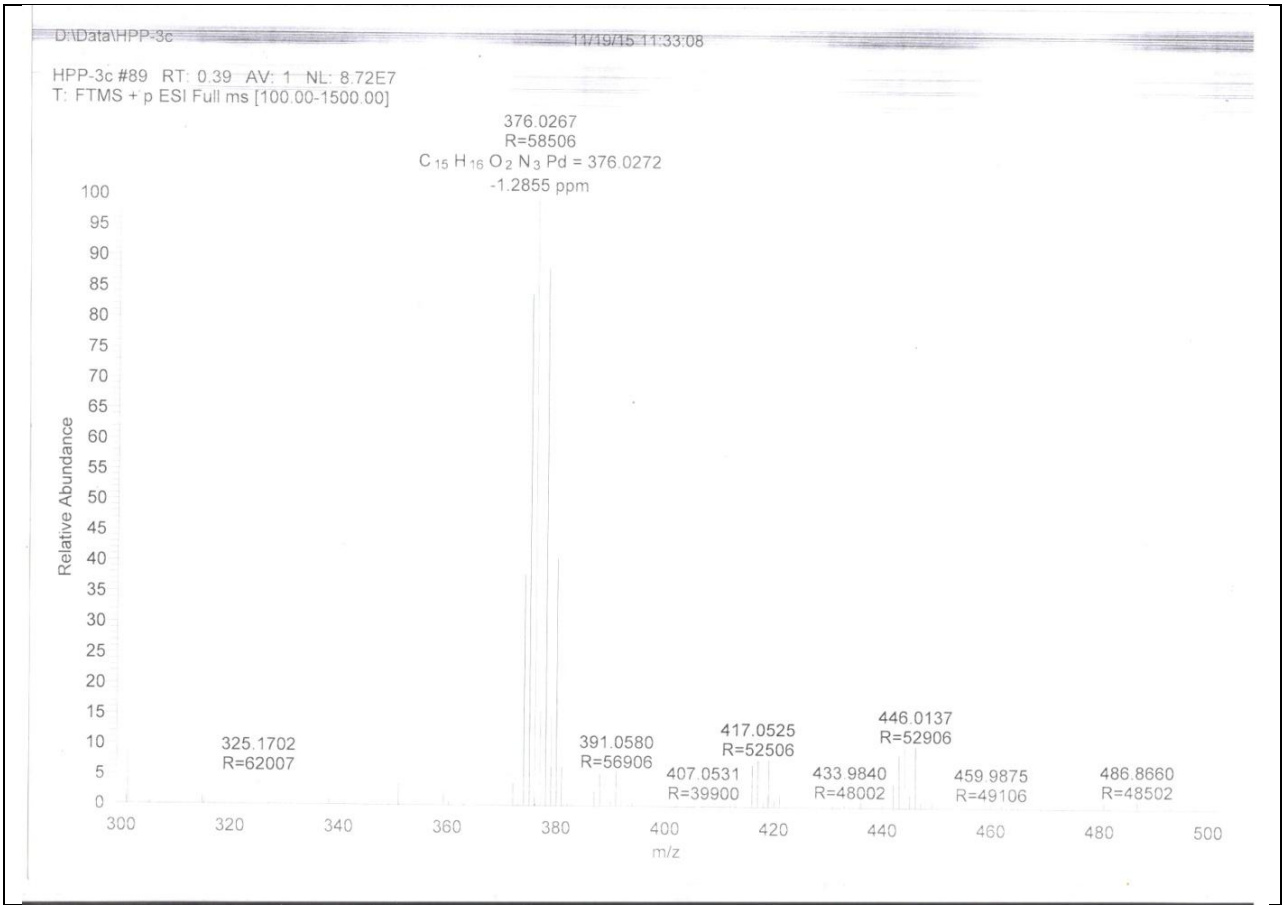




**$^{1}H/^{13}C$ NMR Spectra of 26ae**

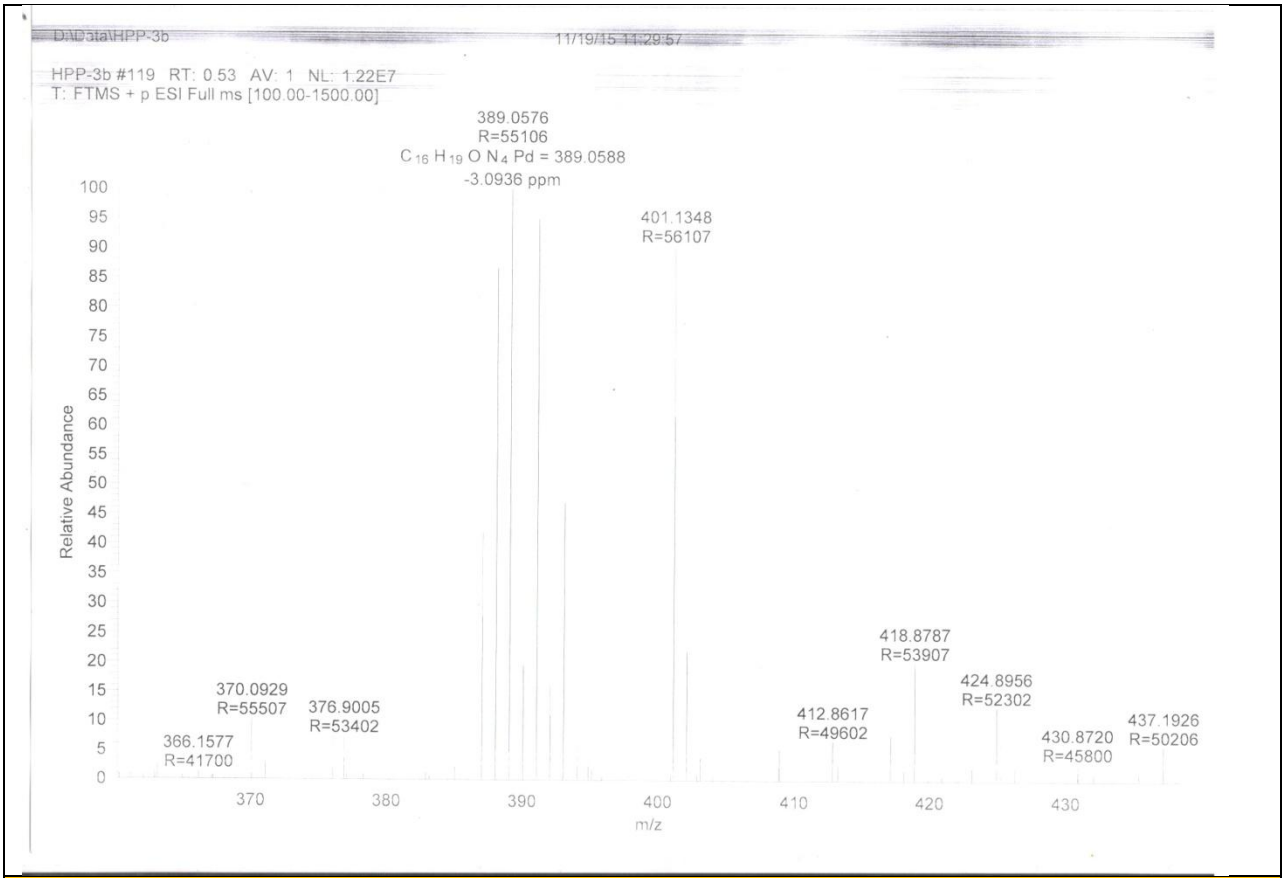
## HRMS and MALDI Spectra of Representative Complexes



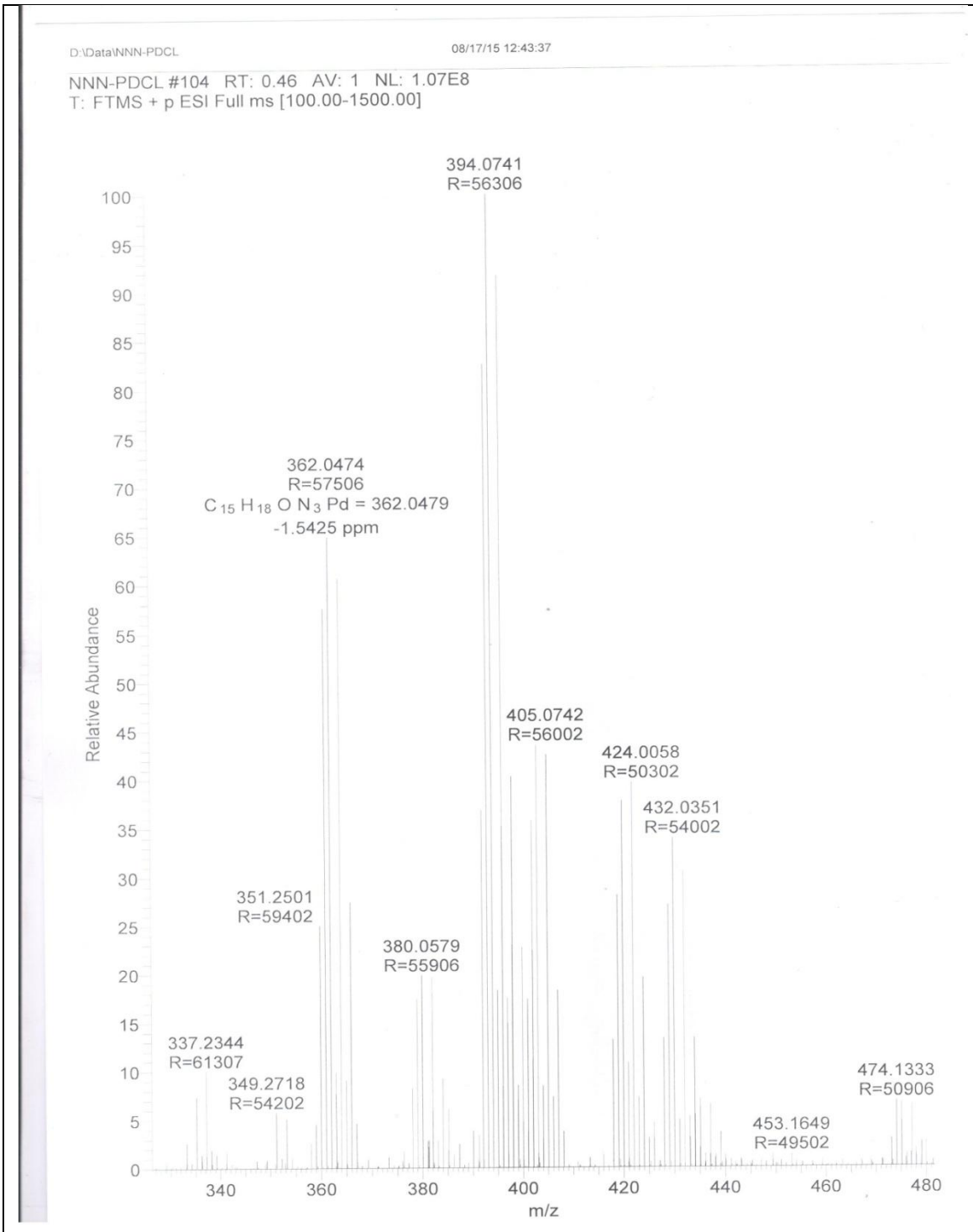

**HRMS Spectrum of Complex 2a**: *m/z* calcd. for $C_{17}H_{21}N_3O_3Pd - OAc^+$ $[M - OAc]^+$ 362.0479, found 362.0493.



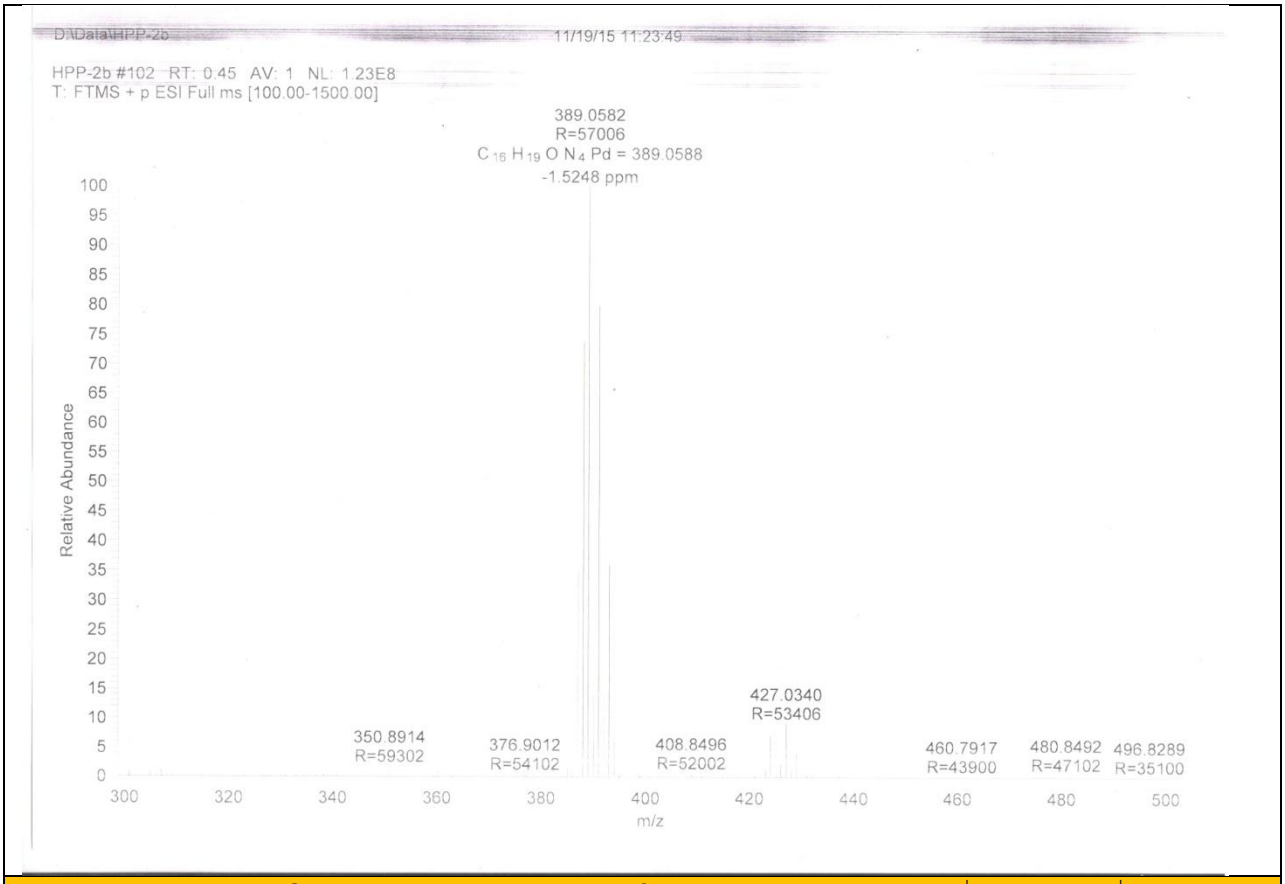

**HRMS Spectrum of Complex 2b**: *m/z* calcd. for $C_{17}H_{19}N_3O_4Pd - OAc^+$ $[M - OAc]^+$ 376.0272, found 376.0267.



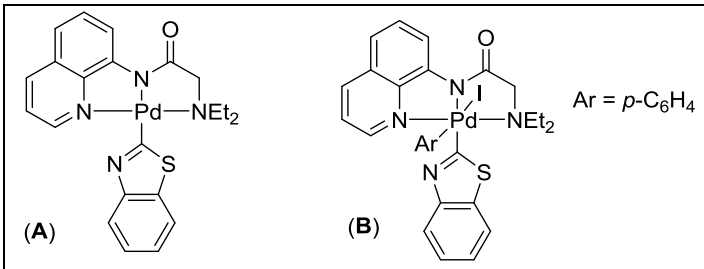

**HRMS Spectrum of Complex 2c**: *m/z* calcd. for $C_{18}H_{22}N_4O_3Pd - OAc^+$ $[M - OAc]^+$ 389.0588, found 389.0576.

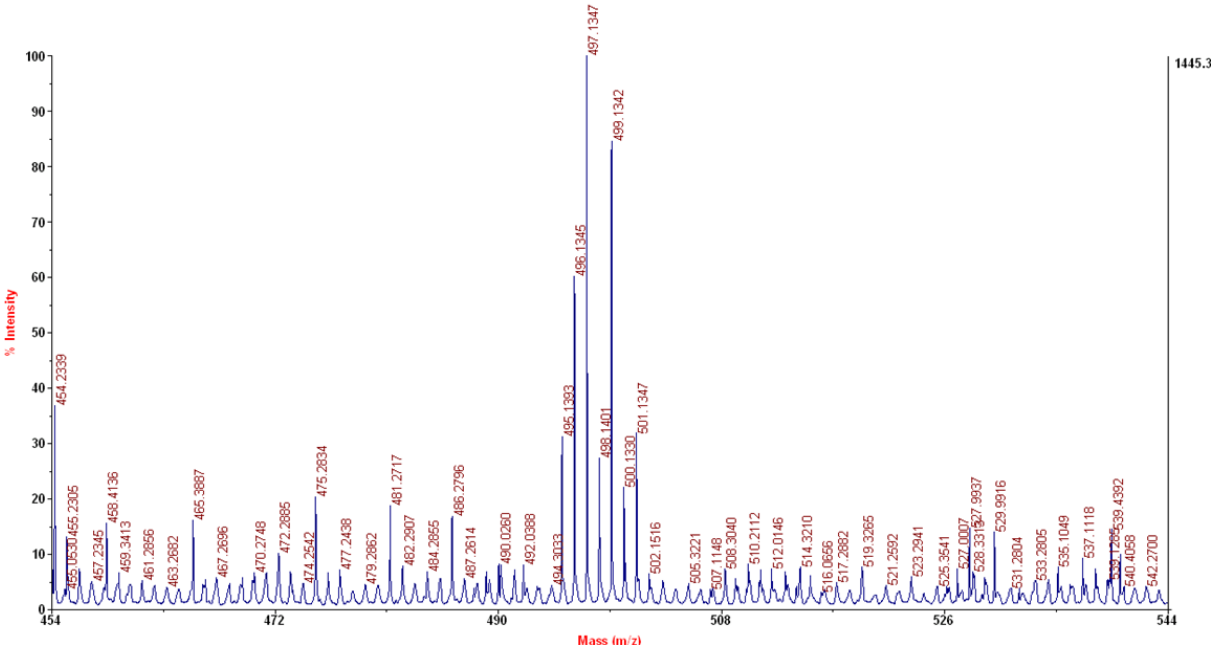


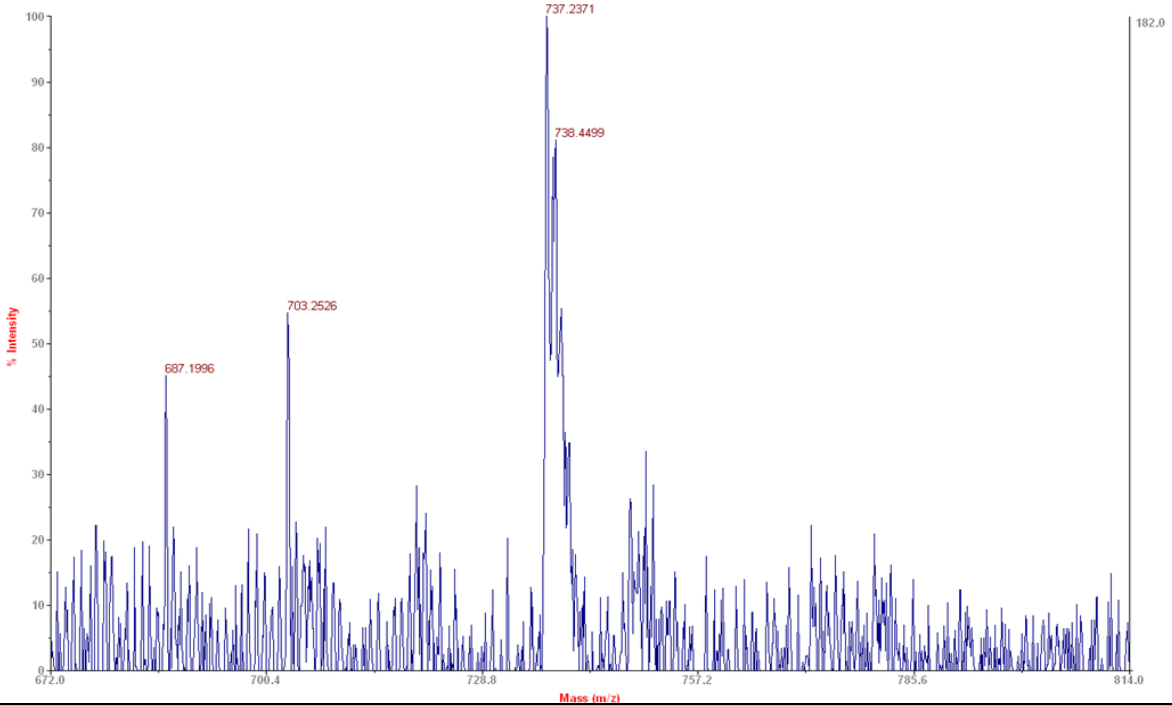

**HRMS Spectrum of Complex 3a**: *m/z* calcd. for $C_{15}H_{18}ClN_3OPd - Cl^+$ $[M - Cl]^+$ 362.0479, found 362.0474.



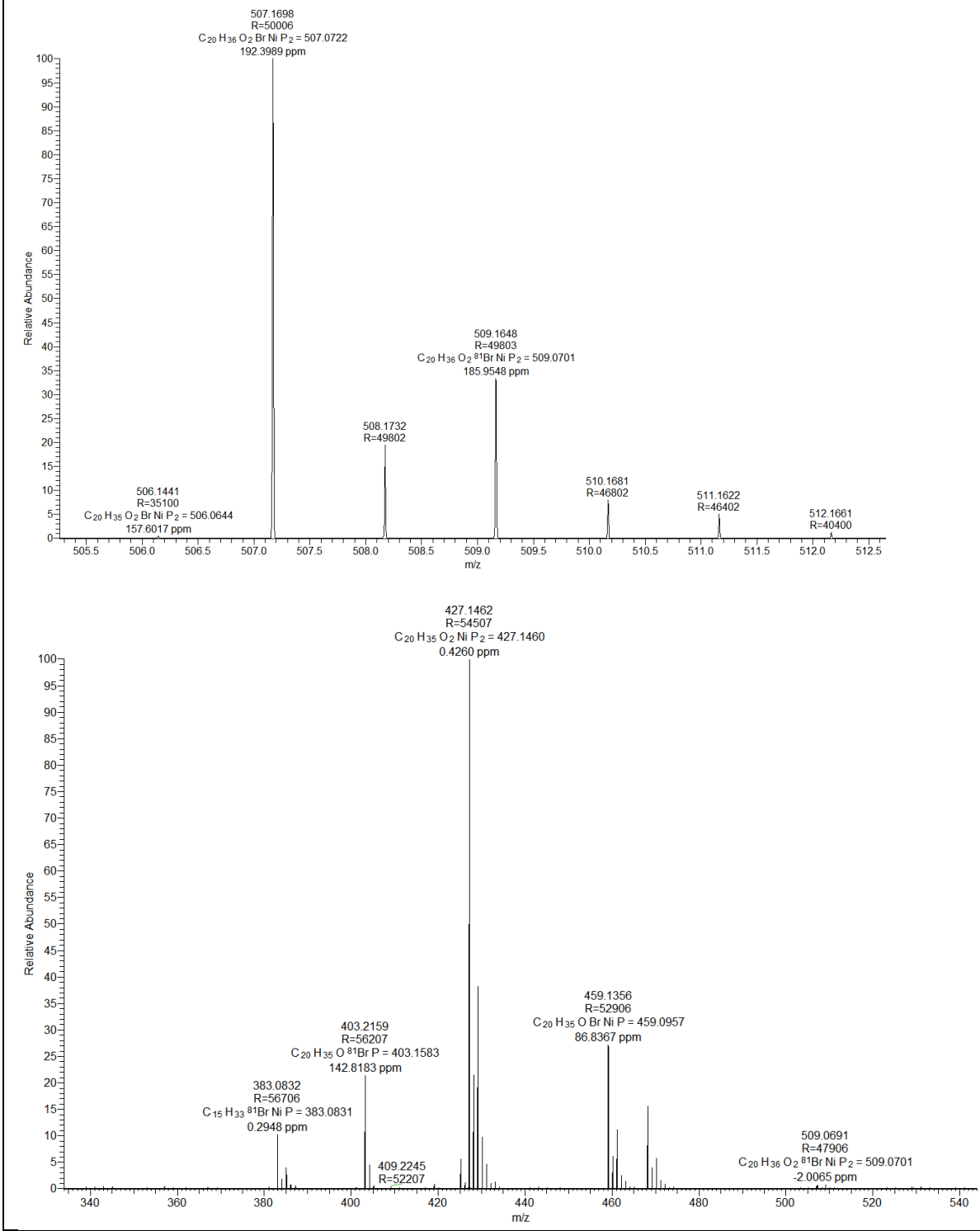

**HRMS Spectrum of Complex 3c**: *m/z* calcd. for $C_{16}H_{19}ClN_4OPd - Cl^+$ $[M - Cl]^+$ 389.0588, found 389.0582.



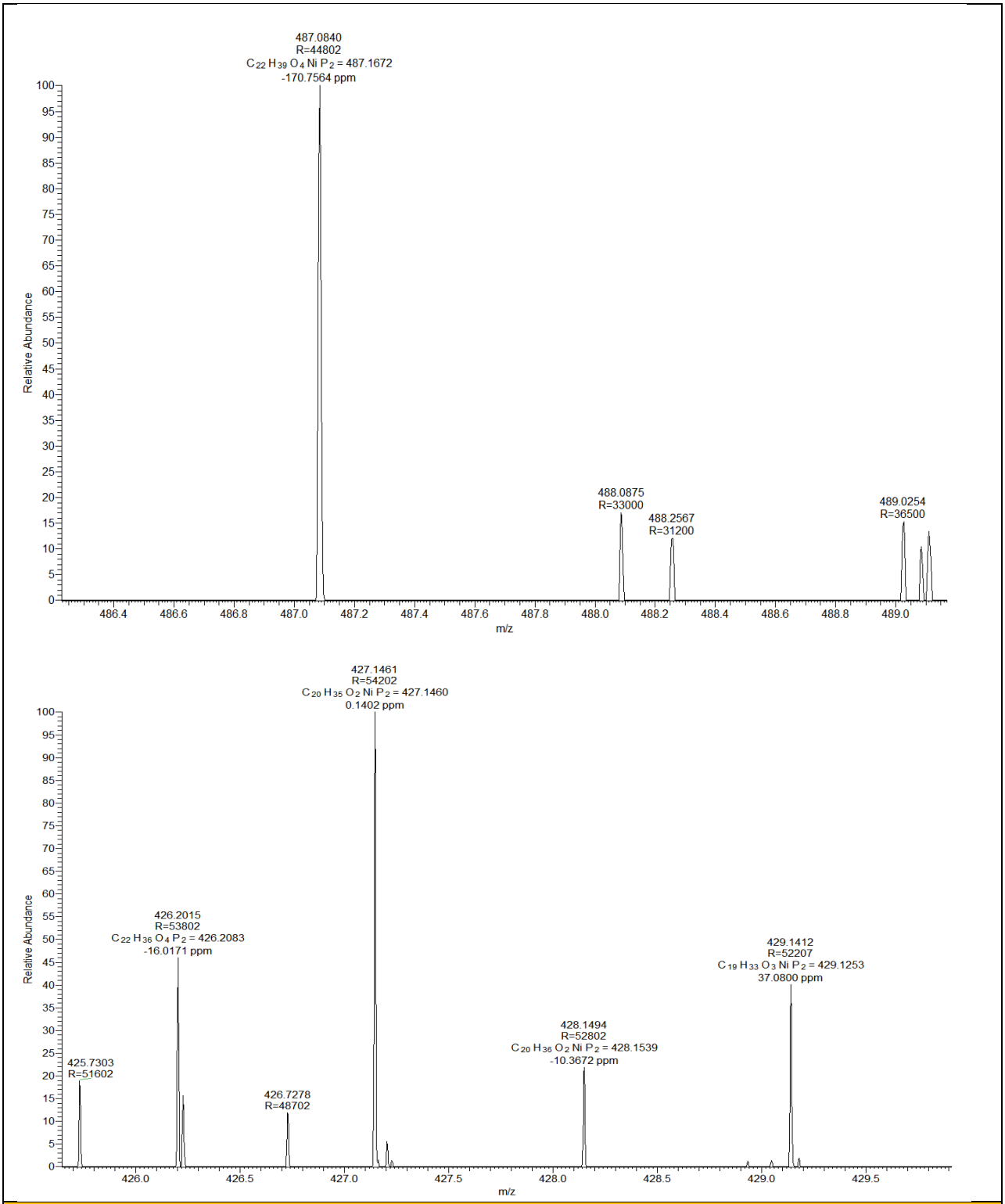



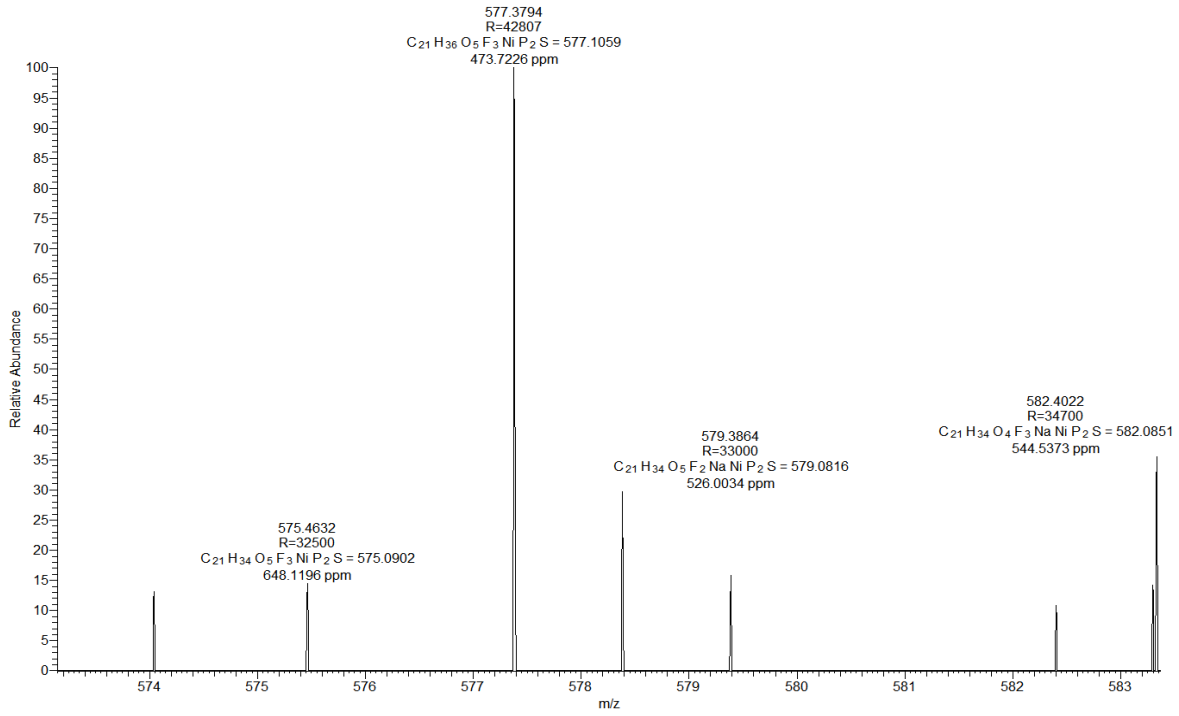

**MALDI-TOF Spectra for the Reaction Mixture of Arylated Benzothiazole.**

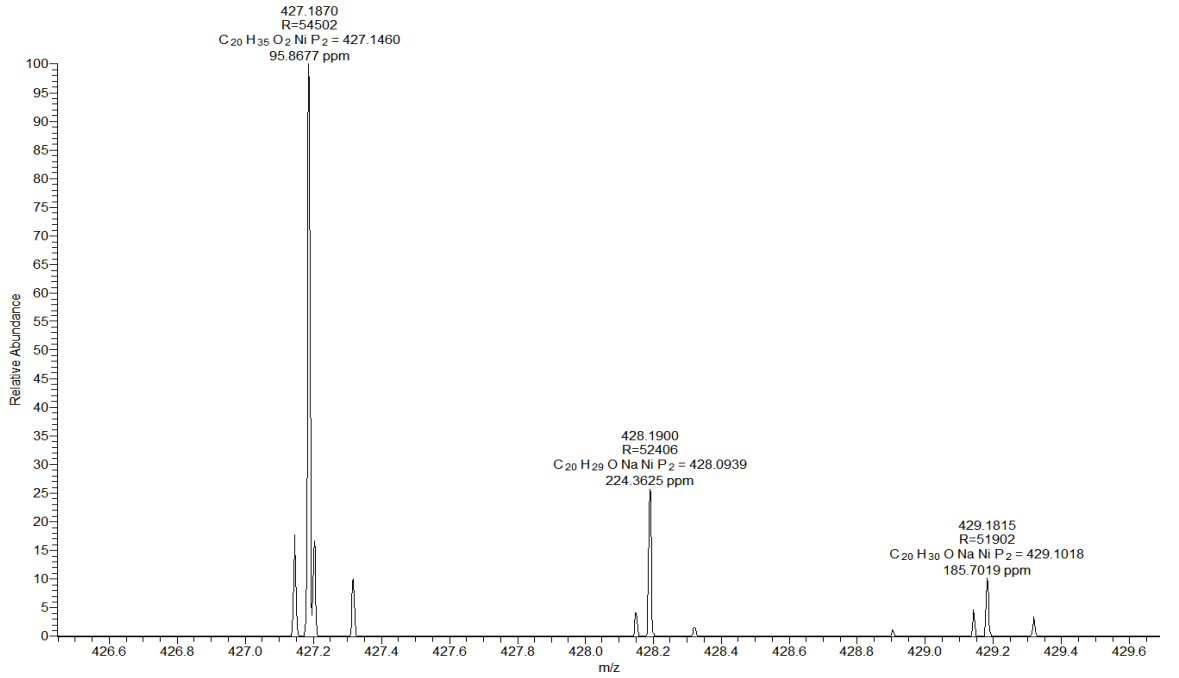



**HRMS Spectra of Complex 9**: *m/z* calcd. for $[C_{20}H_{35}O_2P_2BrNi+H]^+$ $[M+H]^+$ 507.0722 and 509.0701; found 507.1698 and 509.1648; $[C_{20}H_{35}O_2P_2BrNi - Br]^+$ $[M - Br]^+$ 427.1460, found 427.1462

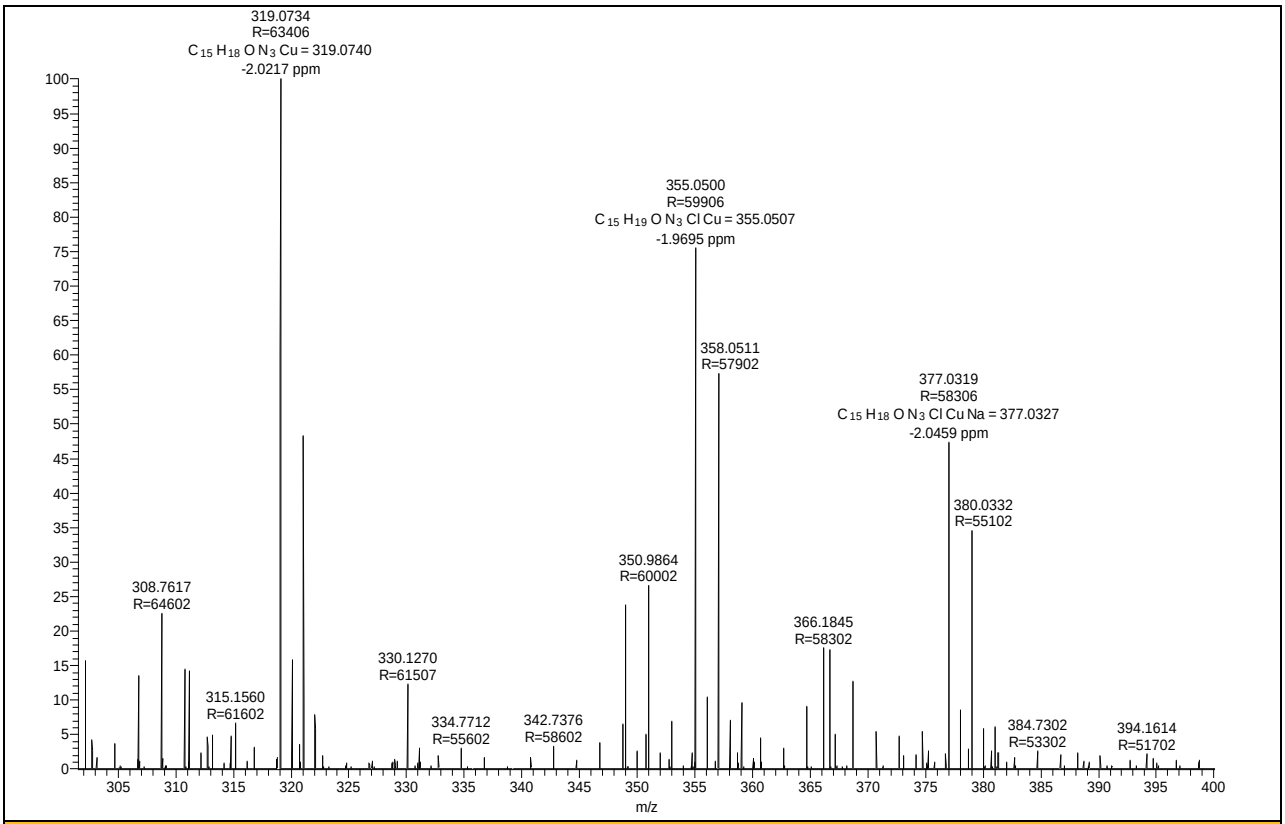



**HRMS Spectra of Complex 10**: *m/z* calcd. for $[C_{22}H_{38}O_4P_2Ni+H]^+$ $[M+H]^+$ 487.1672, found 487.0840; $[C_{22}H_{38}O_4P_2Ni-OAc]^+$ $[M-OAc]^+$ 427.1460, found 427.1461.

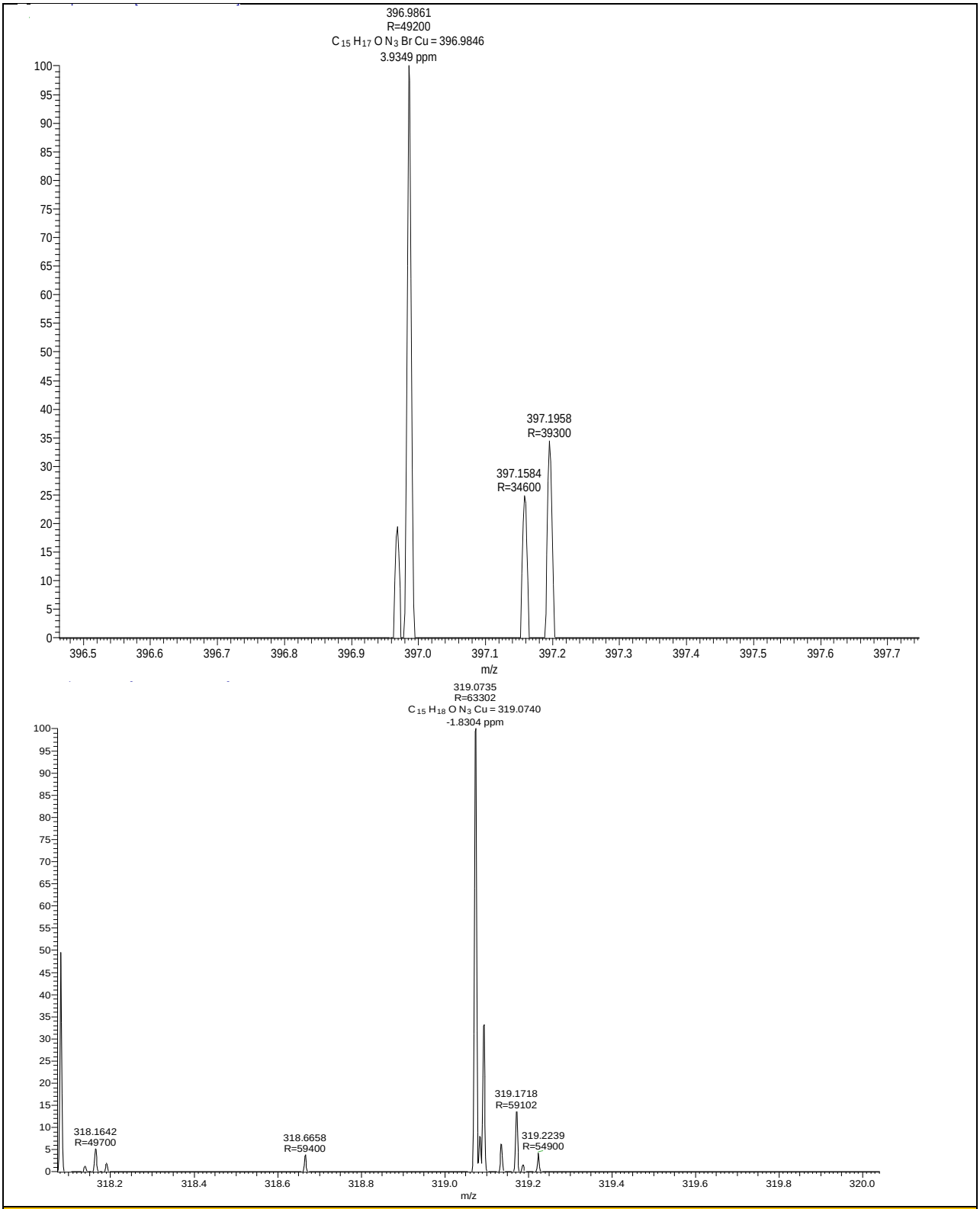


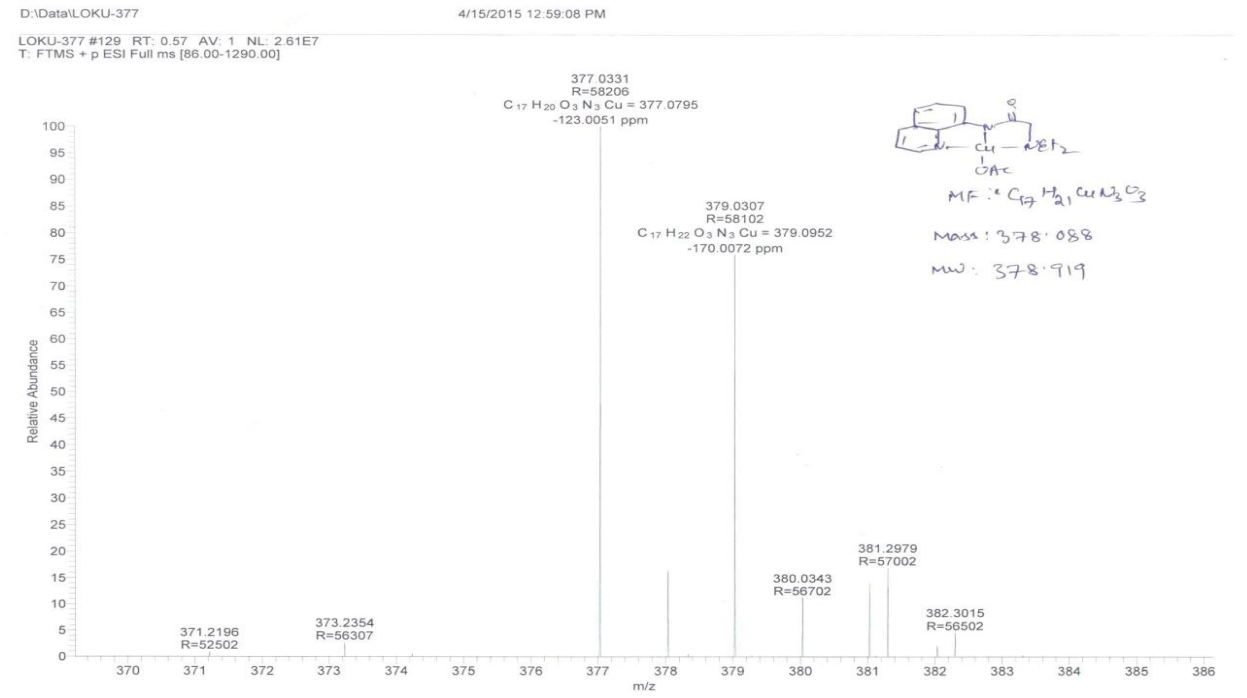

**HRMS Spectra of Complex 11**: *m/z* calcd. for $[C_{21}H_{35}O_5F_3NiP_2S+H]^+$ $[M+H]^+$ 577.1059, found 577.3794; $[C_{21}H_{35}O_5F_3NiP_2S-OTf]^+$ $[M-OTf]^+$ 427.1460, found 427.1870

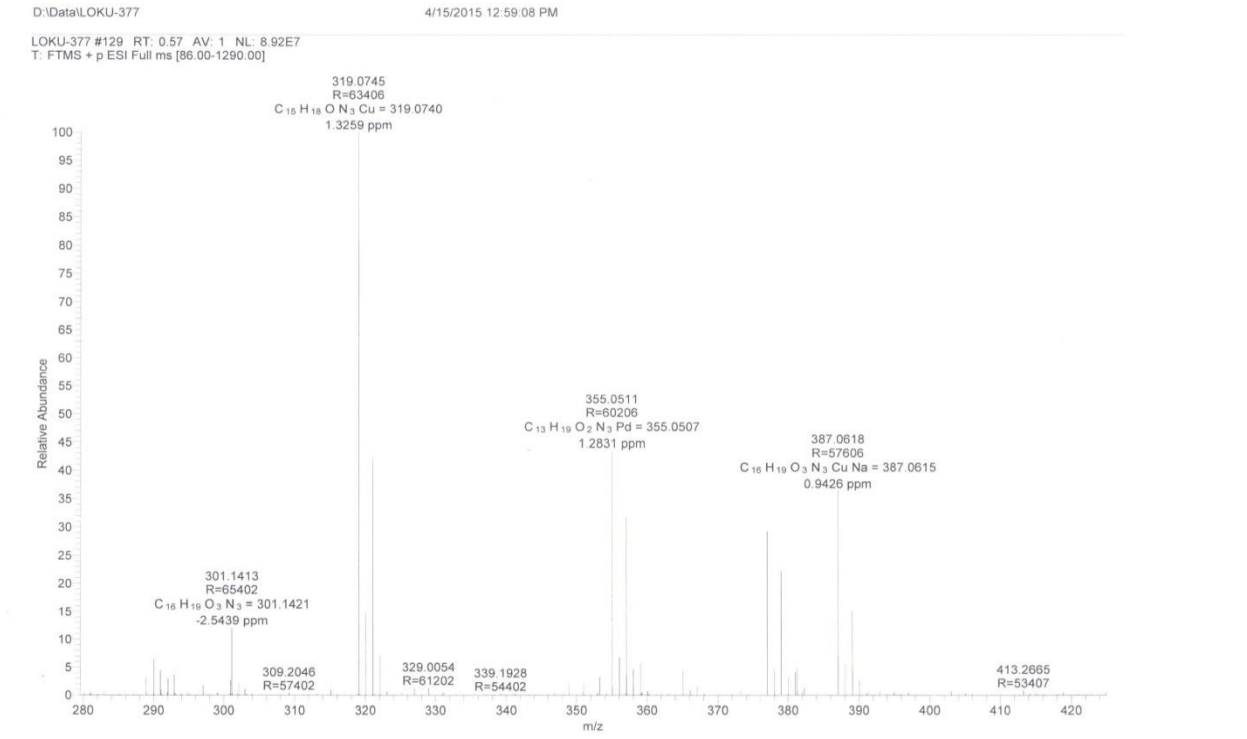



**HRMS Spectrum of Complex 20**: *m/z* Calcd. for $C_{15}H_{18}ON_3ClCu+H^+$ $[M+H]^+$ 355.0507, found 355.0500 and $C_{15}H_{18}ON_3ClCu–Cl^+$ $[M–Cl]^+$ 319.0740, found 319.0734

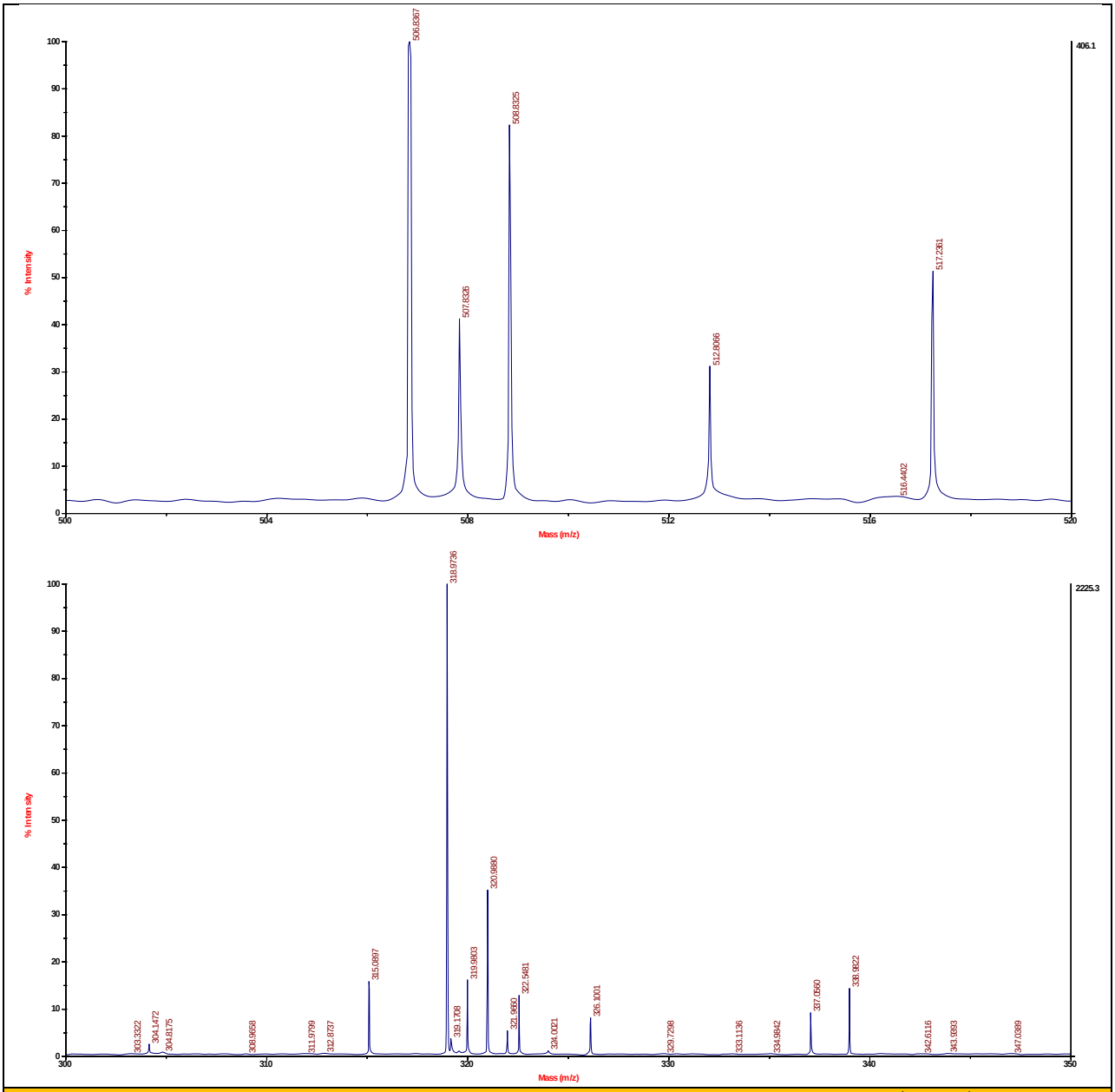



**HRMS Spectra of Complex 21**: *m/z* calcd. for $C_{15}H_{18}ON_3BrCu–H^+$ $[M–H]^+$ 396.9846, found 396.9861; and $C_{15}H_{18}ON_3BrCu–Br^+$ $[M–Br]^+$ 319.0740, found 319.0735.

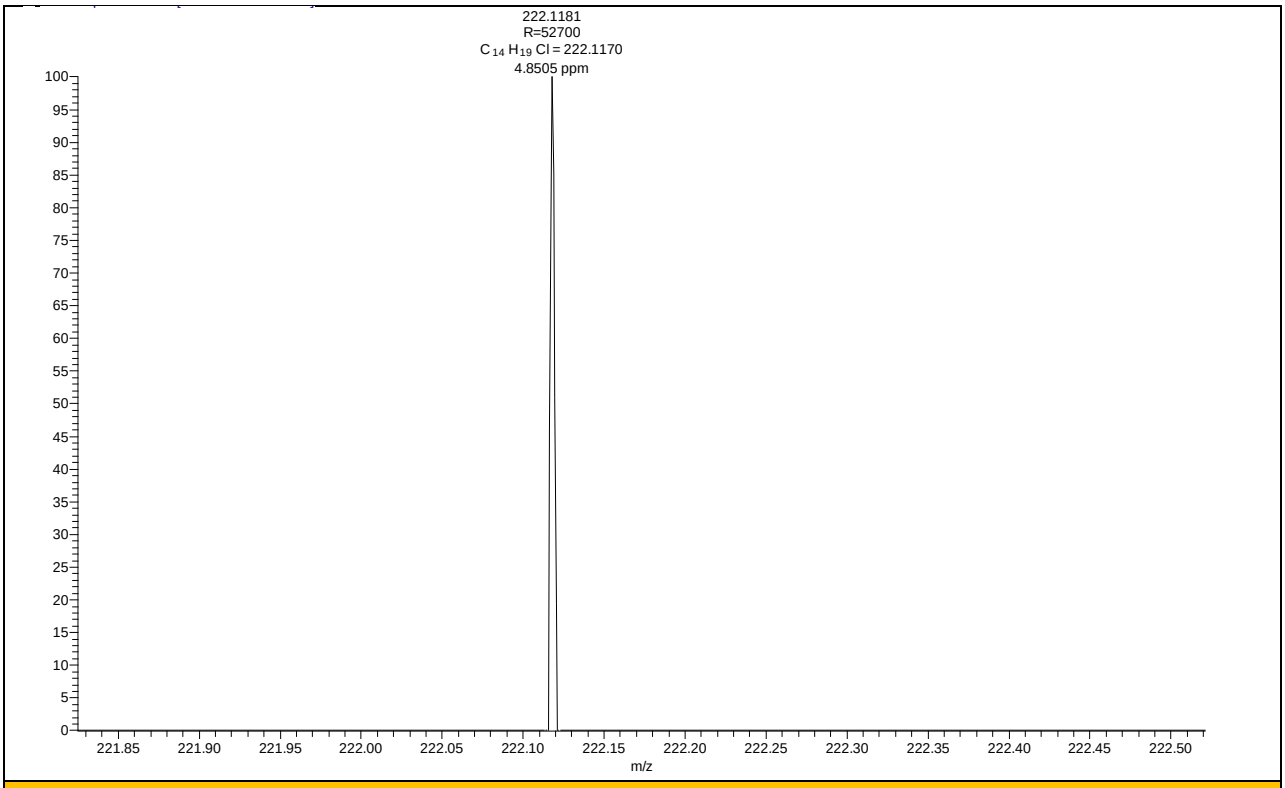


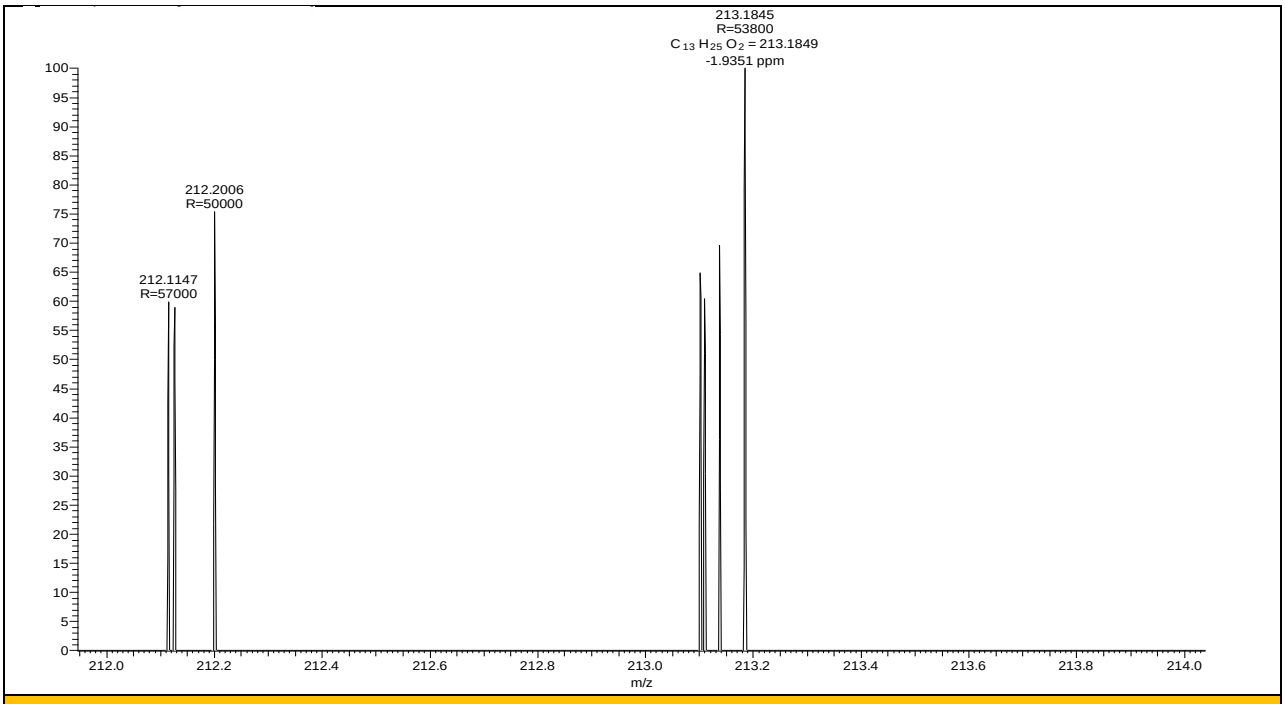

**HRMS Spectra of Complex 22.$(H_2O)_{0.5}$**: *m/z* calcd. for $C_{17}H_{22}O_{3.5}N_3Cu–(H_2O)_{0.5}+H^+$ $[M–(H_2O)_{0.5}+H]^+$ 379.0952, found 379.0307 and $[C_{17}H_{22}O_{3.5}N_3Cu–\{OAc+(H_2O)_{0.5}\}]^+$ $[M–\{OAc+(H_2O)_{0.5}\}]^+$ 319.0740, found 319.0745.




**MALDI-TOF Spectra of Complex 23**: *m/z* calcd. for $[C_{18}H_{21}O_4N_4F_3SCu]^+$ $[M]^+$ 509.0532, found 508.8325 and $[C_{18}H_{21}O_4N_4F_3SCu–(CH_3CN+OTf)]^+$ $[M–(CH_3CN+OTf)]^+$ 319.0740, found 318.9736




**HRMS Spectrum of 1-Chloro-4-(2-cyclohexylethyl)benzene (26da)**




**HRMS Spectrum of 2-(3-Cyclohexylpropyl)-2-methyl-1,3-dioxolane (26ga)**

## List of Publications

1. **Pandiri, H.;** Soni, V.; Pandey, D. K.; Samal, P. P.; Punji, B. "Development of quinolinamine-based NNN-pincer nickel complexes for Sonogashira cross-coupling of phenylacetylene with alkyl halides", *Manuscript under preparation*.
2. **Pandiri, H**.; Gonnade, R. G.; Punji, B. "Synthesis and Characterization of Pincer-based Copper(II) Complexes: Application for Kumada Coupling of Alkyl Halides", *Manuscript communicated*.
3. **Pandiri, H**.; Sharma, D. M.; Gonnade, R. G.; Punji, B. "Synthesis and characterization of six-membered pincer nickelacycles and application in alkylation of benzothiazole", *J. Chem. Sci*. **2017**, *129*, 1161-1169.
4. **Pandiri, H**.; Soni, V.; Gonnade, R. G.; Punji, B. "Development of (Quinolinyl)amido-based Pincer Palladium Complexes: A Robust and Phosphine-Free Catalyst System for C-H Arylation of Benzothiazoles", *New J. Chem.* **2017**, *41*, 3543-3554.

**Response to the Comments:**

**Q1**: As discussed in chapter 2, if the phosphine free-Ni catalysts are good/better, then why phosphine based catalysts are developed and reported in chapter 3?

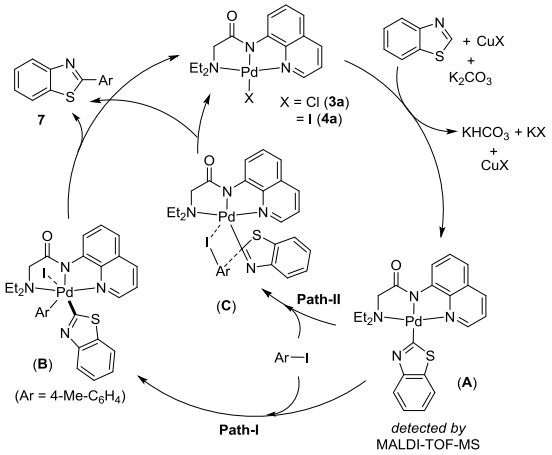
**Response**: The phosphine-based POCCCOP-pincer nickel complexes (chapter 3) were synthesized and applied as catalysts for the alkylation of benzothiazole, prior to the exploration of NNN-based pincer palladium complexes (chapter 2). Synthesis of these phosphine-based ligands as well as the corresponding complexes needs to be performed under the argon atmosphere, as they are air- and moisture-sensitive. Hence, we have synthesized robust and phosphine-free NNN-pincer palladium complexes as catalysts for the arylation of benzothiazoles.

**Q2**: Why six-membered Ni(Br)($^{iPr4}$POCCCOP) showed to be superior than 5-membered (PCP)NiBr or (POCOP)Ni(OAc)?

**Response**: POCCCOP-pincer nickel complexes have the flexible pincer backbone, which can readily give vacant site for the coordination of benzothiazole, whereas the five-membered PCP/POCOP-pincer nickel complexes have the comparatively less flexible backbone. Hence, 6-membered ($^{iPr4}$POCCCOP)NiBr complex showed superior activity than the 5-membered ($^{iPr4}$PCP)NiBr or ($^{iPr4}$POCOP)Ni(OAc) complex.

**Q3**: As predicted in chapter 4, why the mechanism was not predicted in chapter 2?

**Response**: There are well known mechanism for azole arylation reaction using palladium complexes, hence, the mechanistic prediction was not included before. We have now included the mechanistic prediction. The same has also been reported in published work (*New J. Chem.* **2017**, *41*, 3543).




**Q4**: Why $Cu^{2+}$ pincer chemistry should be compared with $Ni^{2+}$ pincer chemistry?

**Response**: We mentioned that the NNN-pincer nickel complexes were previously developed in our group and the same NNN-ligand was explored for the synthesis of NNN-pincer copper complexes. This is what we mean to say, but have not compared their pincer chemistry.

**Q5**: Overall comparison the results and conclusion are missing, why?

**Response**: We have provided the conclusion/summary in the individual chapters about the advancement of the work comparing the literature precedents. Hence, overall summary was not provided.