# Sulfonated *N*-Heterocyclic carbenes and their importance in Palladium catalyzed Cross-Coupling Reactions in Water

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*For my Parents…….*

*and sisters Dipika & Ritika.*

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## *Table of Contents*

## *Abbreviations*

| | | | |
|---|---|---|---|
| AcO | acetate | IR | infra-red |
| Ad | adamantyl | $KO^tBu$ | potassium-*tert*-butoxide |
| ADMET | acyclic diene metathesis polymerization | L | ligand |
| | | LAH | lithium aluminium hydride |
| Ar | aryl | m | multiplet |
| br | broad signal | Me | methyl |
| cat. | catalyst | MHz | Mega-hertz |
| CM | cross metathesis | mol % | mol percent |
| COD | 1,5-cyclooctadiene | MTBE | methyl-*tert*-butyl ether |
| Conc. | concentrated | max. | maximum |
| Cy | cyclohexyl | NHC | *N*-heterocyclic carbene |
| d | doublet | NMR | nuclear magnetic resonance |
| dba | dibenzylidene acetone | $^i$Pr | isopropyl |
| DCM | dichloromethane | Ph | phenyl |
| DMF | dimethylformamide | ppm | part per million |
| Eqv. | equivalent | py | pyridine |
| ESI-MS | electro-spray ionization mass spectrometry | RCM | ring closing metathesis |
| | | ROMP | ring opening metathesis polymerization |
| Et | ethyl | | |
| EtOH | ethanol | RP | reverse phase |
| $Et_2O$ | diethyl ether | RT | room temperature |
| GC | gas chromatography | s | singlet |
| HR-MS | high resolution mass spectrometry | SIMes | 1,3-bis(2,4,6-trimethylphenyl) imidazolin-2-ylidine |
| IAd | 1,3-bis(adamantly)imidazole-2-ylidene | SIPr | 1,3-bis(2,6-diisopropylphenyl) imidazolin-2-ylidine |
| $I^tBu$ | 1,3-bis(tert-butyl)imidazole-2-ylidine | SM | Suzuki-Miyaura |
| ICy | 1,3-bis(cyclohexyl)imidazole-2-ylidine | T | temperature |
| | | TfO | trifluoromethanesulfonate |
| IMes | 1,3-bis(2,4,6-trimethylphenyl) imidazole-2 ylidene | TLC | thin layer chromatography |
| | | TMS | trimethylsilyl |
| IPr | 1,3-bis(2,6-diisopropylphenyl) imidazole-2ylidene | TPPTS | triphenylphosphine-m-trisulfonate |

# 1 Introduction

## 1.1 N-Heterocyclic Carbenes (NHCs)

*N*-Heterocyclic carbenes (NHCs) were first prepared by independently *Wanzlick* and *Schönherr*[1] and *Öfele*[2] in 1968. It attracted much attention after the discovery of first stable, crystalline NHC by *Arduengo* in 1991 [1,3-bis(adamantly)imidazole-2-ylidene, IAd].[3] The potential of this class of compounds to serve as spectator ligands was recognized in 1995 by *Herrmann et al*.[4] Soon thereafter, the exploitation of the potential of NHC ligands in catalysis began. The significant advancement occured in the development of a variety of NHC ligands[5] and their transition-metal complexes were utilized in the several catalytic reactions. However, only NHCs derived from imidazolium or, 4,5-dihydroimidazolium salts were found wide-spread application in homogeneous catalysis. The most important example was the ruthenium metathesis catalyst developed by *Grubbs and co-workers*, for which the Nobel Prize was awarded in 2005.[6] The ruthenium based bis-(tricyclohexylphosphine)alkylidene complex known as *Grubbs first generation catalyst*, is of a great importance due to its functional group tolerance property in a wide range. The replacement of one of the tricyclohexyl phosphine by *N*-heterocyclic carbene of the type imidazole-2-ylidene in *Grubbs I catalyst* led to the significant improvements in catalytic activity as well as stability. This is well-known as Grubbs second generation catalyst.

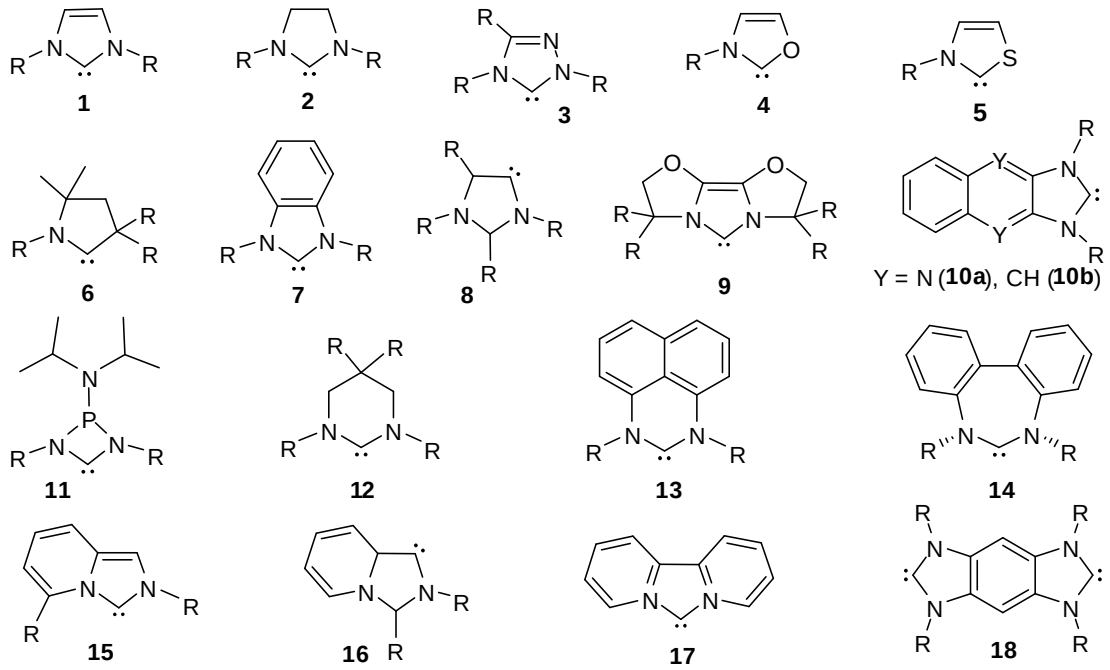



***Figure 1.1*** *Different types of N-heterocyclic carbenes (*R *= alkyl or aryl groups)*

Until now there is a large number of *N*-heterocyclic carbene frameworks known in the literature, ranging from five membered to seven membered rings, including, imidazolium(**1**), imidazolinium (**2, 8**),[7] triazolium (**3**),[10] oxazolium (**4**),[9] thiazolium (**5**),[8] pyrrolidium (**6**),[11] benzimidazolium (**7**),[12] bisoxazoline (**9**),[13] quinoxaline (**10a**),[14] naphtha annulated imidazolium (**10b**),[15] diazaphosphetidin amine (**11**),[16] pyrimidine (**12**),[17] perimidine (**13**),[18] dibenzo(1,3)diazepine (**14**),[19] imidazo[1,5-a]pyridine (**15, 16**),[20] 2,2'-bipyridine derived imidazolium (**17**),[21] bisimidazolium with arene backbone (**18**)[22] etc.

## *1.2 Comparison between NHCs and Phosphines*

Both ligand classes phosphines and *N*-heterocyclic carbenes have played crucial role in designing various catalytic systems as well as new synthetic methodologies in organic and organometallic transformations. But nowadays, NHCs play more valuable contribution than phosphines because of their strong donor abilities as ligands and stabilities of the resulting metal complexes.

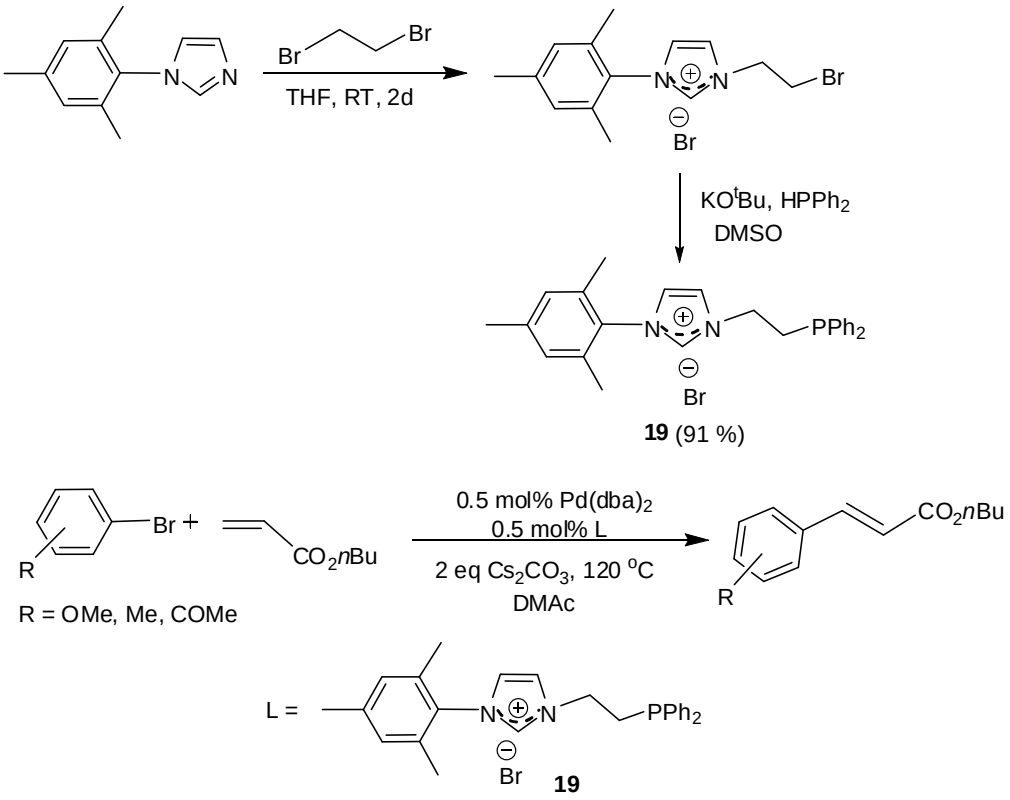
*Herrmann* first reported the similarities between NHCs and tertiary phosphines in terms of electronic properties.[23] The ease of reaction of sterically demanding NHCs with an electron-deficient ruthenium complex $[Cp^*RuCl]_4$ (Cp* means pentamethylcyclopentadienyl) proved the better nucleophilic character (means strong donation) than phosphines.[24] Recently, the steric and electronic parameters of NHCs were analysed from the nickel-carbonyl complexes of the formula $(NHC)Ni(CO)_3$.[25] The more electron-donating ligands contributed increased electron density on nickel center which allowed the increased back-donation into π-accepting ligand such as CO. This resulted in the lower value of carbonyl frequencies. The infrared carbonyl frequency value of the Ni-complexes confirmed the better donor ability for NHC compared to the most donating tertiary phosphines.

## *1.3 Pincer type N-heterocyclic ligands*

The ease of functionalization of imidazolium or imidazolinium salts led to the incorporation of *N*-heterocyclic carbenes as donor ligands into poly-dentate structures by attaching classical donor ligands, such as phosphines, alkenes, amines, thiols etc.[26] This type of pincer ligands in combination of different donor moieties allowed a tuning of the metal coordination sphere. While the strongly bound carbenes remained intact in the metal coordination sphere, the heteroatom donor groups can reversibly dissociate from the metal center to generate vacant coordination site for the substrate for binding in the catalytic process.

### *1.3.1 Phosphine/N-Heterocyclic Carbene Pincer Ligand*

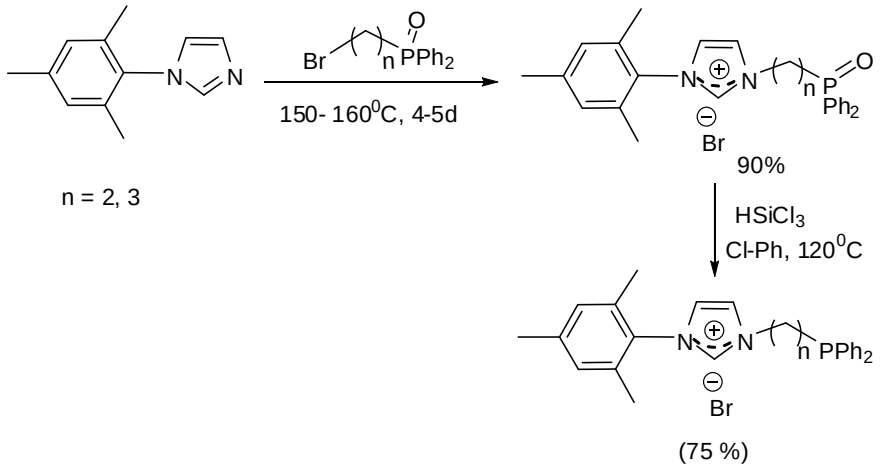
The first classical donor functionalized NHC, comprising of saturated imidazolin-2-ylidene with phosphine by C3 linker was reported by *Lappert.*[27] The successful application of pincer-type phosphine-tagged carbene ligand was shown by *Nolan's* group by utilizing *Heck coupling reaction* of deactivated aryl bromides with *n*-butylacrylate (***Scheme 1.1***). [28]



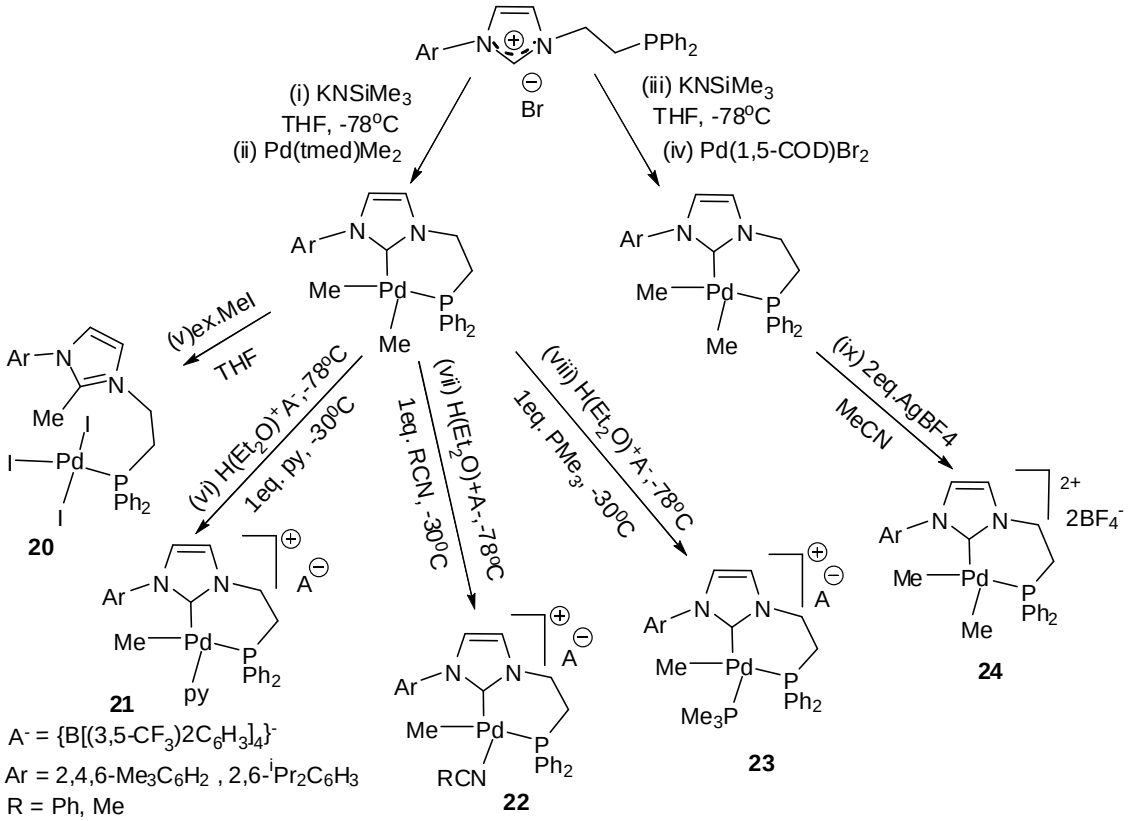

***Scheme 1.1*** *Synthesis of pincer-type phosphine-tagged NHC ligands*

In 2003 *Danopoulos and coworkers* reported various palladium complexes of diphenylphosphino–alkyl imidazole-2-ylidene complexes.[29] They synthesized ligands by using neat reaction of phosphine oxide and 1-arylimidazole at 150 to 160 $^{o}$C and followed by reduction of phosphine oxide to obtain diphenylphosphino-alkyl-imidazolium ligands (***Scheme1.2***). The palladium complexes were synthesized from in situ generated carbene in THF, followed by addition of suitable palladium precursors, such as Pd(TMEDA)(Me)$_2$ or Pd(1,5-COD)Br$_2$ (***Scheme 1.3***). Although NHC ligands which were much better σ–donors than trialkylphosphines should exert higher *trans* influence, but it was not revealed from the

experimental data. However, the reactivity of two *cis* methyl groups in dimethylpalladium complex was kinetically different.




***Scheme 1.2*** *Synthesis of pincer-type phosphine-tagged NHC ligands using phosphine-oxide*

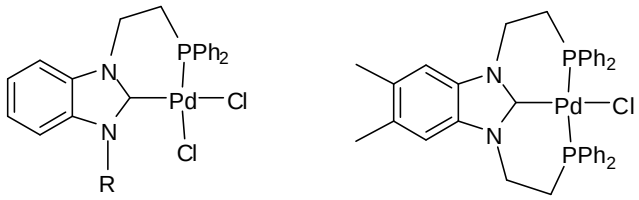



***Scheme 1.3*** *Synthesis of palladium complexes with phosphine-tagged NHCs*

To explain the reactivity of dimethylpalladium complex, it was reacted with methyl iodide which led to the formation of palladium complex having one imidazolium functionalized phosphine, one chloro and two iodo ligands. But the detailed mechanism of formation of this complex was not clear. The reaction of dimethylpalladium complex with donor ligand, such as pyridine revealed that pyridine would be *trans* to the phosphine. The reason for this was not because of *trans* influence of this ligand but due to steric demand of two electronically dissimilar parts of the ligand. The steric bulk created by the phosphine end could hinder the coordination of a donor ligand, thus making the attack to the methyl *trans* to phosphine was more kinetically favorable.

Another structural motif having bi-dentate phosphine as well as NHC of the type PCP-pincer ligand was reported by *Lee and coworkers*.[30] At first 1,3-bis(2-chloroethyl)-3H-imidazole-1-ium chloride was made and then it was converted to 1,3-bis(2-diphenylphosphanyl-ethyl)-3H-imidazol-1-ium chloride ($PC^{NHC}P.HCl$). The palladium complex was easily obtained either by reacting with $PdCl_2$ and $PC^{NHC}P.HCl$ ligand or through transmetalation with silver complex. Then it was converted to cationic acetonitrile complex which was proved to be a good catalyst for Heck coupling reaction of aryl bromides and iodides.

Similar type of structural moiety with benzimidazole (***Figure 1.2***) was reported by *Hahn and coworkers*.[31] They also tested palladium complexes of such ligands in the *Heck coupling reaction* of *para*-functionalized aryl bromides with styrenes. The reactivities of bi-dentate mixed phosphine/ carbene ligands were better catalyst than the more sterically demanding tri-dentate pincer-type P-C-P ligand.

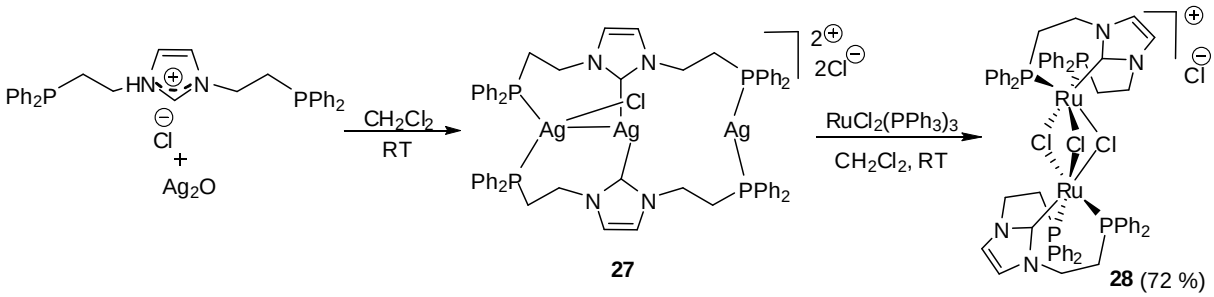



**25**; R = Et, *n*-Pr, *n*-Bu **26**

***Figure 1.2*** *Different coordination modes of phosphine-tagged NHCs*

In 2005 *Lee and coworkers* reported the synthesis of ruthenium complex of pincer type phosphine/NHC ligand.[32] The silver complex was used as a carbene transfer agent to make ruthenium complex. The usual reaction of silver complex with ruthenium chloro-tris(triphenyl-phosphine), $[RuCl_2(PPh_3)_3]$ in dichloromethane resulted in the formation of a facial isomer, such as the triply chloro-bridged diruthenium complex, $[Ru_2(\mu\text{-}Cl)_3(PC^{NHC}P)_2]Cl$. The structure of the

complex was confirmed by NMR as well as X-crystallographic study. There was no more studies regarding catalytic activities of such type of ruthenium complexes were reported.

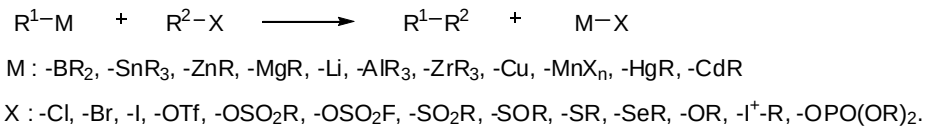



***Scheme 1.4*** *Synthesis of ruthenium complexes with phosphine-tagged NHCs*

There are very few literatures reported related to such type of pincer ligands having NHC and other functionality simultaneously. From the point of view of catalytic study even less is known. Therefore, this type of ligand class would be highly important in future to synthesize robust and highly active catalysts for various types of transformations.

## *1.4 Palladium Catalyzed Cross-coupling Reactions*

Palladium catalyzed carbon-carbon, carbon-heteroatom bond forming reactions are widely used and powerful tools in organic synthesis.[33] The typical processes are recognized as *Heck* reaction and cross coupling and related reactions where aryl halides or pseudohalides are coupled with a nucleophilic partner. In cross coupling reactions the coupling of organometallic compounds with organic halides or related organic electrophiles occurred in the presence of transition metal catalysts.[34] The *Heck* reaction, which does not involve organometals as substrate may not be considered as a cross-coupling reaction. The cross coupling reaction can be represented as below.

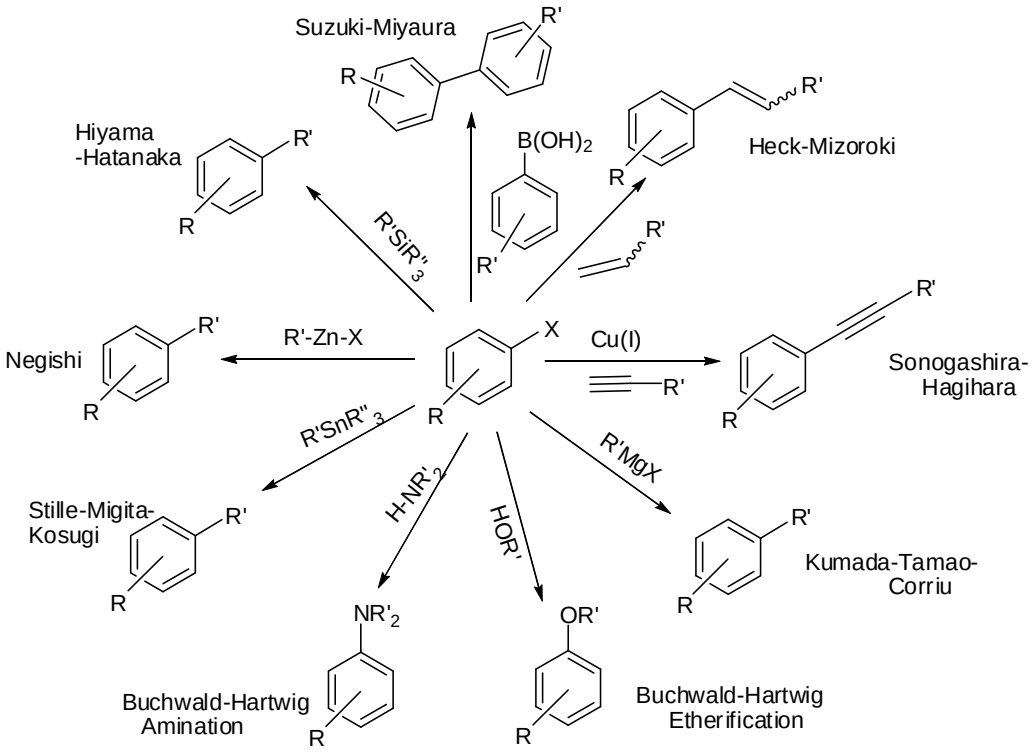



***Scheme 1.5*** *Generalized cross-coupling methodology*

### *1.4.1 Early History*

The early history of the transition metal catalyzed cross-coupling methodology was reported in 1941 by *kharasch and coworkers* from the interaction of *Grignard reagents* with organic halides.[35] The intensive research in this area was begun after the issue of a series of papers published by *Tamura and Kochi* since 1971.[36] They observed that cross coupling reactions of *Grignard reagents* with organic halides were effective in the presence of iron, silver and copper salts. In 1972 *Kumada and coworkers*[37] and *Corriu and Masse*[38] reported independently the cross coupling reactions of *Grignard reagents* with aryl and alkenyl halides using nickel complexes as catalysts. The use of palladium in such type of cross coupling protocol was first reported by *Murahasi and coworkers*[39] and this methodology was extrapolated by *Negishi* by using organo-aluminium, zinc and zirconium reagents.[40] Afterwards, many other organometallic reagents were used as effective nucleophiles for the cross coupling reactions, e.g., organolithiums by *Murahashi*,[41] organostannanes by *Migita*[42] and *Stille*,[43] 1-alkynylcopper by *Normant*,[44] organosilicon compounds by *Hiyama*.[45] The alkyne version of the *Heck reaction* using Cu(I) salts and Pd complexes as catalysts was reported by *Sonogashira*[46]during the same period. In 1978, *Negishi* first reported the coupling of iodoarenes with lithium 1-hexenyl(tributyl)borate through palladium catalyzed addition-elimination sequence.[47] However, the cross coupling reaction involving organoboron reagents underwent transmetalation to Pd(II) species which was the key step and proceeded smoothly by activation of suitable base was found by groups of *Suzuki and Miyaura*.[48]

Still now many variants of C-C coupling reactions[49] are known in the literature, among them the *Suzuki-Miyaura* (boron-mediated),[50] *Corriu-Kumada-Tamao* (magnesium-mediated),[51] *Kosugi-Migita-Stille* (tin-mediated),[52] *Negishi* (zinc-mediated),[53] *Sonogashira-Hagihara* (copper-mediated),[54] *Heck-Mizoroki* (Pd-mediated),[55] and *Hiyama* (Si-mediated)[56] coupling reactions and other C-heteroatom coupling reactions[57] are well-studied.




***Scheme 1.6*** *Palladium catalyzed coupling reactions.*

## *1.4.2 Palladium-N-Heterocyclic Carbene Catalysts for Cross-coupling Reaction*

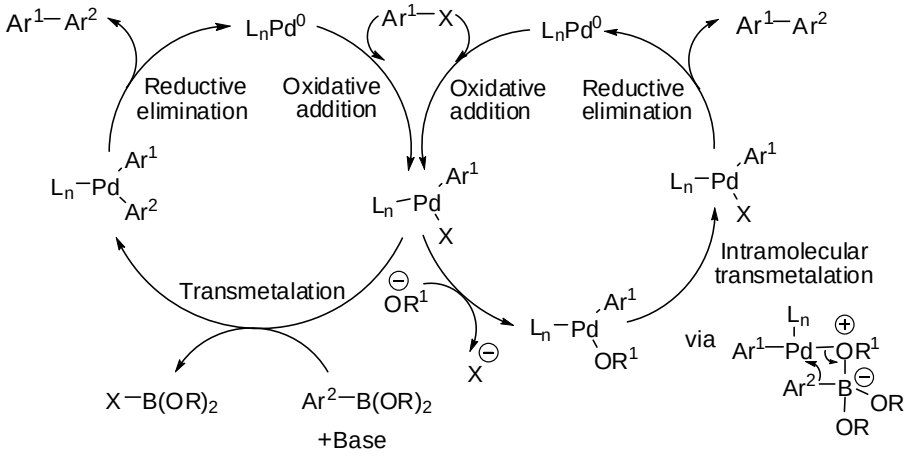
*N*-heterocyclic carbenes are highly promising and versatile ligand alternatives to phosphines in the area of cross-coupling catalysis.[58] Even though a number of metals have been used to mediate this process, the versatility of palladium compounds has remained unsurpassed.[59] The advantages of using NHCs as ligands in Pd mediated reactions are: (1) the strong σ-donating ability of NHCs into Pd center makes easier the process of oxidative addition in traditionally less reactive chloroarenes or alkyl halides; (2) the steric bulk of NHCs facilitates reductive elimination; and (3) the strong Pd-NHC bond and limited decomposition in solution make it more attractive than phosphines.

### *1.4.3 The Suzuki-Miyaura Reaction*

The cross-coupling of organoboron derivatives with aryl halides (*Suzuki-Miyaura reaction*)[60] is currently the most widely used cross-coupling protocol because of the ease of commercial availability and air-moisture-tolerant boronic acids. In addition, the reactions proceed in a wide range of solvents, including alcohol and water and are tolerant to a wide range of functional groups present in the complex substrates. The by-products formed during the reaction are non-toxic and easily separable.

### *1.4.4 Mechanism of Suzuki-Miyaura Cross-Coupling Reaction*

A general catalytic cycle for the cross coupling reactions involved oxidative addition followed by transmetalation and at the end reductive elimination of product.[61] The catalytic cycle was initiated by the oxidative addition of organic halide to the Pd(0) species. The role of bases also played important contributions in SM cross coupling. Firstly, base helped to generate a more labile Pd(II) intermediate from the oxidative addition intermediate such as aryl-Pd(II)-halide species. Secondly, base helped to activate boronic acid or alkyl borate in the form of alkoxy-borate so that transmetalation process would be facilitated. In the final step the reductive elimination of product biaryl regenerated the catalyst Pd(0) again.[62]

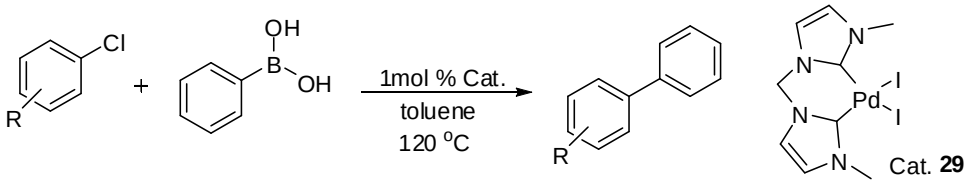



***Scheme 1.7*** *General catalytic cycle for Suzuki-Miyaura coupling reaction*

## *1.4.5 Palladium-NHC Catalyzed Suzuki-Miyaura Cross-Coupling Reaction*

### *1.4.5.1 Bis-Chelating N-heterocyclic carbene-Pd complexes*

Arylboronic acids were the most frequently used nucleophilic partners in the *Suzuki-Miyaura* (*SM*) coupling reaction. Pd-NHC catalysts produced *in situ* from imidazolium salts and common Pd sources were shown high activity in cross-coupling reactions of simple aryl chlorides and arylboronic acids. *Herrmann and coworkers*[63] first reported *SM* cross-coupling of NHC as ancillary ligand involving deactivated aryl bromides and activated aryl chlorides. The bis-chelating NHC-palladium complex was used for the study of catalytic activities.




***Scheme 1.8*** *Suzuki-Miyaura coupling with chelating bis-NHC*

### *1.4.5.2 Mixed N-heterocyclic carbene-Phosphine-Pd complexes*

Further study from *Herrmann's* group[64] revealed that the catalytic activity of mixed NHC-phosphine complexes were better than bis-phosphine and bis-NHC complexes. There were several Pd-complexes of these types (***Figure 1.3***) but the mixed palladium complex containing diiodo[1,3-di(1-phenylethyl)imidazolin-2-ylidene](tricyclohexylphosphino)palladium(II) complex showed better catalytic activity compared to others.

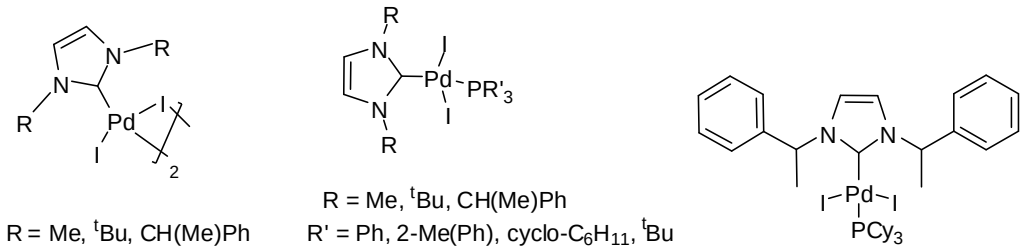
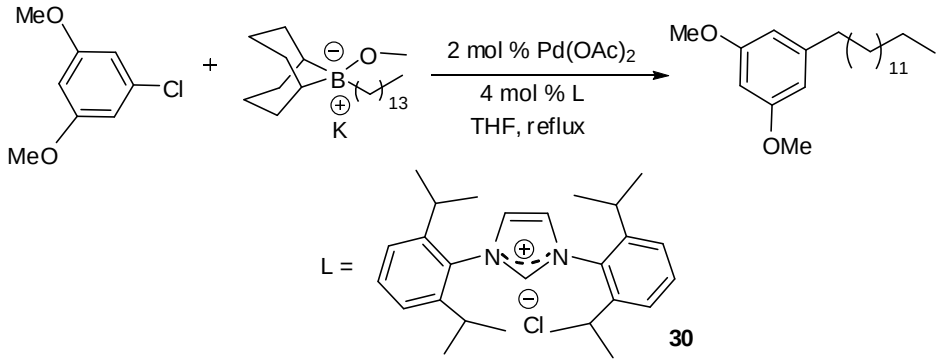



***Figure 1.3*** *Mixed NHC-phosphine complexes of palladium*

### *1.4.5.3 SM coupling with Alkyl-, Allyl-, Alkenyl-, Alkynyl-borane-derivatives*

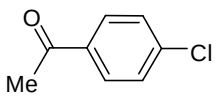
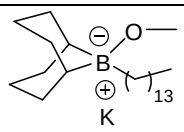
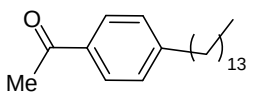
Another interesting methodology of *Suzuki-Miyaura* coupling reaction was observed by *Fürstner and coworkers*.[65] Instead of aryl boronic acid, B-alkyl, B-alkenyl, B-allyl and B-alkynyl, B-cyclopropyl derivatives were used as nucleophilic partners. These boron compounds transferred their organic residue into the C-Cl bond of aryl chlorides in the presence of *in situ* generated catalysts from $Pd(OAc)_2$ and imidazolium salts. It was observed that 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (IPr.HCl) (**30**) in combination with $Pd(OAc)_2$ was superior catalyst to 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (IMes.HCl) (**31**) counterpart. The catalyst optimization study was carried out for B-alkyl borate derivatives formed from 1-tetradecene, 9-H-9-BBN and potassium methoxide and 3,5-dimethoxy chlorobenzene. The catalyst generated from imidazolium salt IPr.HCl (**30**, 4 mol%) with $Pd(OAc)_2$ (2 mol%) led to the desired product in good (81%) yield.




***Scheme 1.9*** *Suzuki-Miyaura coupling of alkyl-borane derivative*

The following table represents cross-coupling reaction of some electron rich and electron-poor chloroarenes under optimized condition in presence of KOMe or NaOH as bases.

***Table 1.1*** *Suzuki-Miyaura coupling of alkyl-, allyl-, alkynyl-borane derivatives*

| Entry | Aryl chloride | Boron derivative | Product | Yield (%) |
|---|---|---|---|---|
| 1 |  |  |  | 98* |

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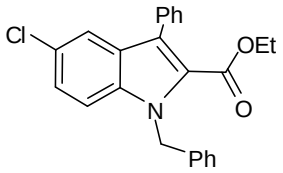
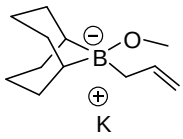
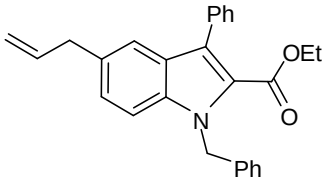
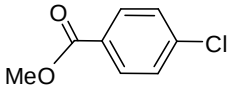
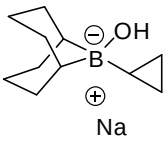
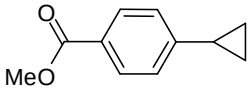
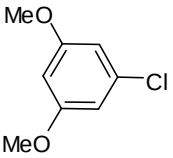
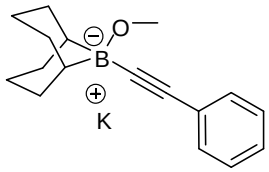
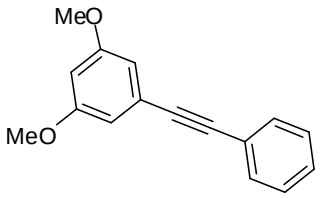
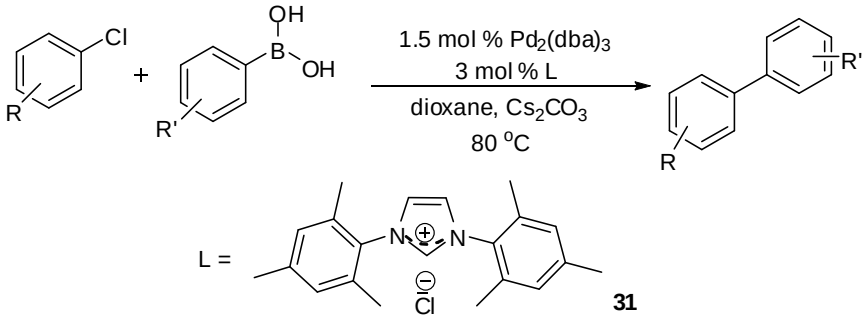
| 2 |  |  |  | 84 |
| 3 |  |  |  | 61 |
| 4 |  |  |  | 84** |

*1 mol% $Pd(OAc)_2$ and 2 mol% IPr.HCl ; **4 mol% $Pd(OAc)_2$ and 8 mol% IPr.HCl

### *1.4.5.4 In situ generated N-heterocyclic carbene-Pd (1:1) complexes*

In 1999 *Nolan and co-workers*[66] reported the use of zero-valent $Pd_2(dba)_3$ as palladium source and 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride (IMes.HCl) as a potential ancillary ligand for the cross-coupling of 4-chlorotolene with phenylboronic acid. The catalytic protocol was simplified by the use of air-stable imidazolium chloride which was deprotonated *in situ* using cesium carbonate and the isolated yield of cross-coupled product was above 90%.




***Scheme 1.10*** *Suzuki-Miyaura coupling with IMes*

In 2002 *Nolan's* detailed study[67] on SM cross-coupling reaction revealed the optimized condition by exploring different reaction parameters such as different types of imidazolium salts, bases, stoichiometry of catalyst and different catalyst precursors, different types of

substrate and reaction time etc. The different kinds of imidazolium salts, namely, 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene (IMes.HCl) (**31**), 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene (IPr.HCl) (**30**), 1,3-bis(adamantly)imidazole-2-ylidene (IAd.HCl) (**35**), 1,3-bis(2,6-dimethylphenyl)imidazole-2-ylidine (IXy.HCl) (**33**), 1,3-bis(cyclohexyl)imidazole-2-ylidene (ICy.HCl) (**34**), 1,3-bis(4methylphenyl)imidazole-2-ylidene (ITol.HCl) (**32**), and 1-ethyl-3-methylimidazole-2-ylidene (IEtMe.HCl) (**36**) were used for the study of reactivity in SM cross-coupling reaction. The overall reactivity of IPr.HCl and IMes.HCl in combination with $Pd_2(dba)_3$ or $Pd(OAc)_2$ showed promising results for electron-poor aryl chlorides and tosylates with respect to functional group tolerance. More precisely, from the point of view of functional group tolerance and substrate scope, isopropylimidazolium-Pd system worked even better than

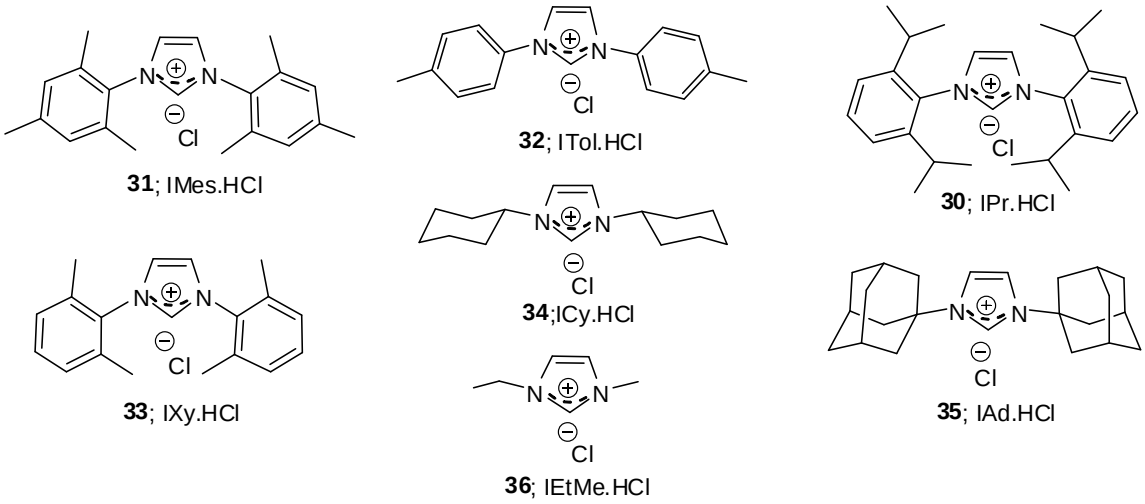
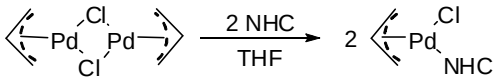



***Figure 1.4*** *Symmetrical and unsymmetrical aryl- and alkyl-substituted imidazolium chlorides*

others. Different types of organic and inorganic bases were used whereas cesium carbonate showed best reactivity and complete conversion within short interval of time (1 to 2 hours). Another noticeable point was the effect of metal to ligand ratio during the course of reaction which showed that 1:1 palladium-ligand ratio afforded faster reaction rate for both IPr.HCl and IMes.HCl reactions.

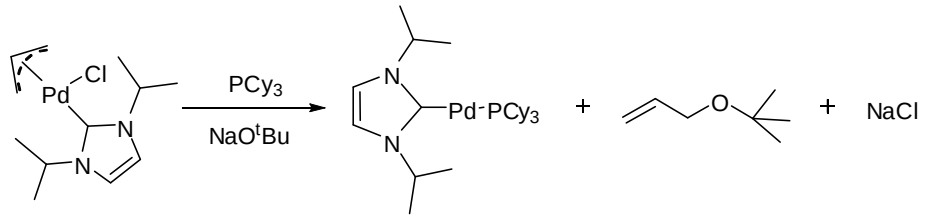
### *1.4.5.5 π-Allyl Palladium complexes: [(NHC)Pd(allyl)Cl]*

The further development in the cross-coupling methodology was reported by *Nolan's* group.[68] The various types of palladium(allyl)NHC complexes were synthesized and structurally characterized by reacting NHC with (allyl)chloro-palladium dimer precursor.




***Scheme 1.11*** *Synthesis of palladium-allyl-NHC complxes*

The detailed study on the reaction pathway was predicted the nature of catalytically active Pd(0) species which was *in situ* generated from Pd(allyl)NHC complexes. The usual inorganic bases like cesium carbonate, cesium fluoride, potassium phosphate and sodium acetate led to the formation of no product involving the reaction of aryl chlorides and benzene boronic acid. These bases simply failed to activate the precatalyst. In the presence of strong bases, like sodium *tert*-butoxide ($NaO^tBu$), in stoichiometric or catalytic amount along with other bases the reaction led to a complete conversion (95%) of the desired product. This was indicated that strong base like $NaO^tBu$ needed to generate the catalytically active Pd(0) species. It was observed from the $^1H$ NMR study that the reaction of Pd(allyl)NHC complex with $NaO^tBu$ at room temperature within few minutes led to a mixture of two species. When it was warmed to 40 $^oC$ for one hour, one species was converted to the second species exclusively. The finally formed allyl species, allyl *tert*-butyl ether was confirmed by comparing with the authentic sample.[69] In palladium allyl systems, there were precedents for nucleophilic attack by an alkoxide base either at the allyl[70] or at palladium center.[71] It was postulated that two possible pathways for the activation of Pd(allyl)NHC complex led to the formation of allyl ether. Either there was a direct attack at allyl or attack at Pd center by butoxide led to formation of Pd-complex which might undergo reductive elimination at higher temperature. Regardless of the activation route, an NHC-Pd(0) species was formed that was confirmed by the trapping experiment with $PCy_3$.[72]



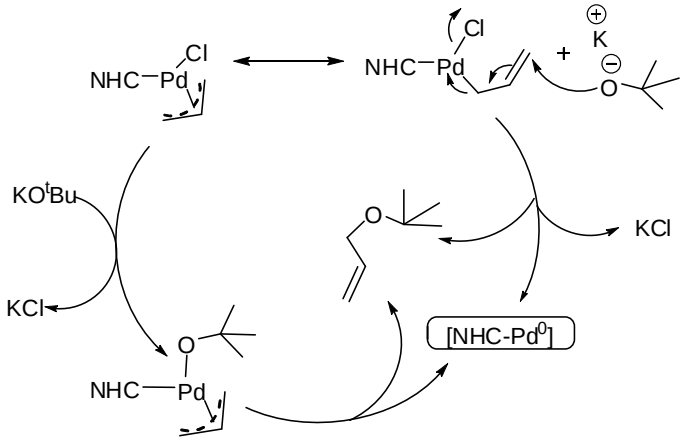

***Scheme 1.12*** *Synthesis of mixed NHC-phosphine complexes of palladium(0)*

It was assumed that the new species formed was (NHC)Pd(allyl)($O^tBu$) complex. The formation of such species would be the result of a simple metathesis reaction between (NHC)Pd(allyl)Cl and $NaO^tBu$. In either alkoxide attack at allyl position or metathetical alkoxide replacement, the new NHC-Pd species was formed. The reductive elimination of ether from Pd(II) complex generated the Pd(0) active species.

The further extension of the study on Pd(allyl)NHC complexes was reported in 2004[73] by the same group and the Pd(allyl)NHC system was thoroughly investigated as a substitute for phosphine based systems in *SM* cross coupling reaction. The study revealed that the strong bases like $NaO^tBu$ and $KO^tBu$ were more effective than commonly used bases, such as KF, $Cs_2CO_3$ etc. Next study was to find the suitable ancillary NHC ligand in this system. Several (NHC)Pd(allyl)Cl catalytic systems were studied: (IMes)Pd(allyl)Cl; (SIMes)Pd(allyl)Cl [SIMes = {1,3-bis(2,4,6-trimethylphenyl)4,5-dihydroimidazole}-2-ylidene]; (IPr)Pd(allyl)Cl; (SIPr)Pd(allyl)Cl [SIPr = {1,3-bis(2,6-diisopropyl)4,5-dihydroimidazole}-2-ylidine]; ($I^tBu$)Pd(allyl)Cl [$I^tBu$ = 1,3-bis(tert-butyl)imidazole-2-ylidene] etc. As observed in the earlier *in situ* catalyst generated from palladium and imidazolium salts bearing IPr and IMes displayed the best catalytic behavior. The use of (IPr)Pd(allyl)Cl led to complete conversion of 4-chlorotoluene after 1 h at 80 $^oC$ in dioxane. For Pd/imidazolium system, a shorter reaction time was required using the well-defined catalyst system compared to *in situ* system. An induction period was usually observed for *in situ* generated catalyst system because a time-interval was required to generate free NHC ligands which would combine with palladium-counterpart to produce active catalyst. But for (NHC)Pd(allyl)Cl system the active Pd(0) species was formed rapidly by reacting with the alkoxide. There was no indication of catalyst decomposition as no Pd-black was formed. Moreover, *SM* cross-coupling protocol was used for microwave assisted heating using such Pd-allyl complexes.

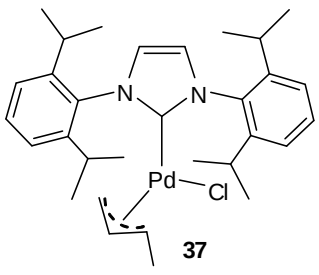
Again the extensive study on Pd(allyl)NHC catalysis was made by designing the new mono-ligated palladium(allyl)NHC complex of type (NHC)Pd(R-allyl)Cl, possessing a modified allyl moiety.[74] These precatalysts could be easily activated at room temperature in a short time interval to obtain an increased concentration of catalytically active Pd(0) species. In the case of (NHC)Pd(allyl)Cl, the activation mode occured through a chloride/ alkoxide–metathesis followed by reductive elimination, liberating in both cases a [(NHC)Pd(0)] species.

Proposed Activation Pathway…

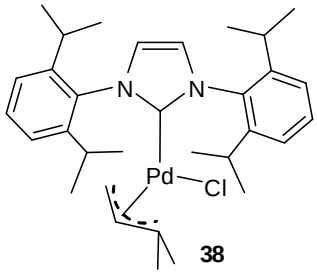



***Scheme 1.13*** *Activation of palladium-allyl-NHC complxes*

Palladium(allyl)NHC complexes having advantage as they could be synthesized in a straightforward way from the commercially available allyl-palladium-chloride dimer.[75] But they still required the activation at higher temperature to generate the active catalyst. To overcome this sluggish activation step, new types of allyl moiety were used. The substitution on the allyl moiety decreased the overall stability by increasing the steric bulk around the Pd center and decreasing the back-bonding from the Pd to olefin. Thus the less tightly bound allyl moiety would be more prone to nucleophilic attack and to reductive elimination. Thus the activation process of Pd-allyl precatalysts would be easier by tuning the substitution on allyl scaffold. By using different allyl derivatives, four different Pd-allyl-NHC complexes were synthesized and fully characterized : (IPr)Pd(crotyl)Cl (crotyl = 3-methylallyl) (**37**), (IPr)Pd(prenyl)Cl (prenyl =3,3-dimethylallyl) (**38**), (IPr)Pd(cinnanyl)Cl (cinnamyl = 3-phenylallyl) (**39**) and (SIPr)Pd(cinnmyl)Cl (**40**) etc.




**37**




**38**

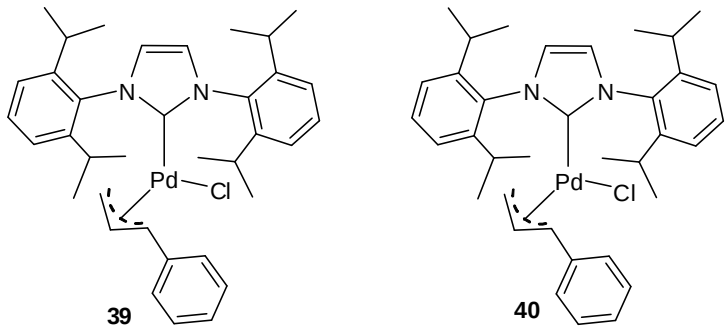
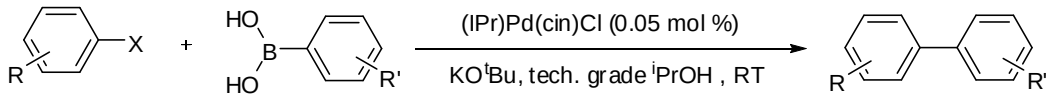



***Figure 1.5*** *Different types of palladium(allyl)NHC complexes*

The effect of terminal substitution on the allyl moiety increased bond distance from Pd-center remaining other allyl-end to Pd distance intact. Both the electronic and steric factors played role to increase the dissymmetry in the coordination of allyl moiety. From X-ray crystal structure, it was observed that the terminal phenyl substitution resulted more dissymmetry to Pd center which made easier the activation process.

The reactivity studies of these complexes towards *SM* cross coupling reaction of 4-chloro-toluene and phenylboronic acid revealed that the substituted allyl complexes were effective at room temperature. Even in the case of sterically hindered substrates, like 2,6-dimethylphenyl chloride was used to couple with naphthaleneboronic acid at room temperature. The cinnamyl and prenyl-derivatives showed maximum reactivity in all cases. The systems were also compatible with unactivated aryl bromides and triflates. The representative examples are depicted below by using (cinnamyl)Pd complex.

***Table 1.2*** *Suzuki-Miyaura cross-coupling reaction using Pd-allyl complexes*




X= OTf, Br, Cl

| Entry | Aryl halide | Boronic acid | Product | Time (h) | Yield (%) |
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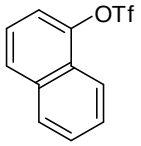
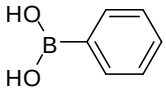
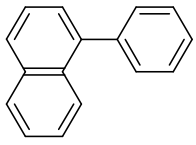
| 1 |  |  |  | 2.5 | 88 |

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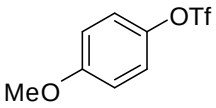
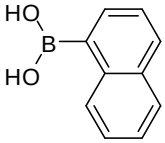
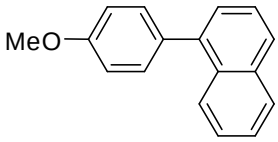
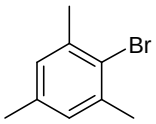
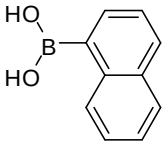
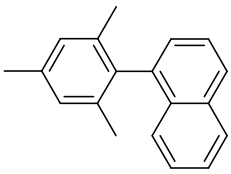
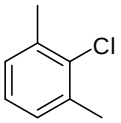
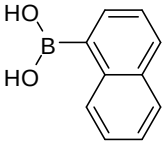
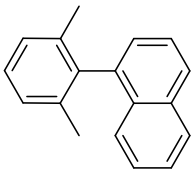
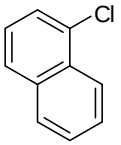
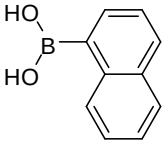
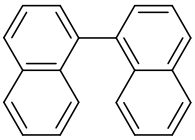
| 2 |  |  |  | 2.5 | 85 |
| 3 |  |  |  | 3.5 | 89 |
| 4 |  |  |  | 15 | 94 |
| 5 |  |  |  | 15 | 96 |

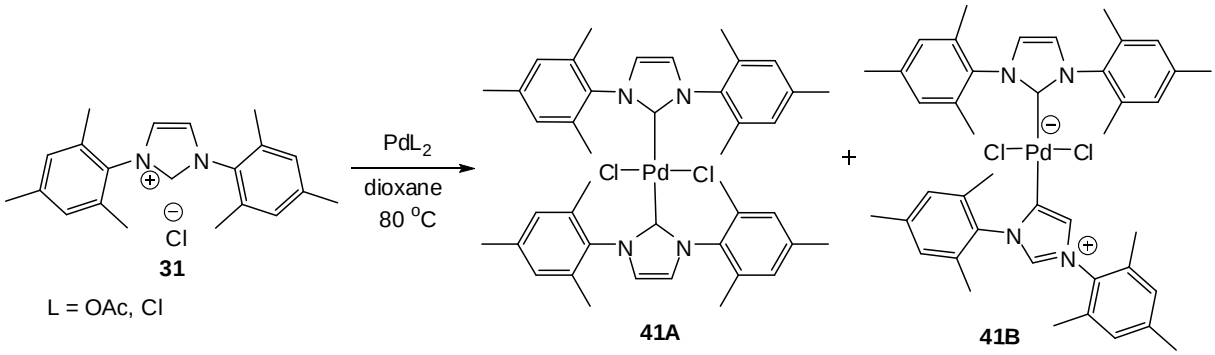
Both aryl bromides and triflates were more reactive substrates than the corresponding chlorides which could be coupled using as little as 0.05 mol % of (IPr)Pd(cinnamyl)Cl catalyst at room temperature. When catalyst loading was decreased to as low as 50 ppm, the increase in temperature was required to obtain complete conversion. Again at higher temperature (IPr)Pd(cinnamyl)Cl and simple allyl complex showed comparable reactivity.

### *1.4.5.6 Bis-N-heterocyclic carbene-Pd complexes*

Another interesting study was reported from *Nolan's group* where the well-defined catalyst system was compared with the *in situ* generated catalytic system.[76] The palladium(II)NHC complex was prepared from $Pd(OAc)_2$ and imidazolium salt by following the literature procedure.[77] A single product (41B) was obtained after mixing two equivalents of IMes.HCl with one equivalent of $Pd(OAc)_2$ in dioxane at 80 $^{o}$C. The NMR data of the complex was confirmed the unusual coordination mode of NHC ligand to the Pd-center. It was also further proved from the X-ray crystallographic data. Surprisingly, when an additional base, such as cesium carbonate was used in the previous condition, no abnormal complex was formed, the only normal coordinated bis(NHC)chloro-palladium complex (41A) was formed together with

bis(NHC)di(acetate)palladium complex, $(IMes)_2Pd(OAc)_2$. Pd-complex (41B) was exclusively formed when $PdCl_2$ was used as the precursor.

The reactivity of these two isolated complexes was compared to the *in situ* formed catalyst [from $Pd(OAc)_2$ (1 equiv.) and IMes.HCl (2 equiv.)] in SM reaction. The complex (41A) was inactive while complex (41B) led to the formation of desired coupling product. But the reactivity of (41B) is less than the *in situ* generated catalyst obtained from two equivalents of IMes.HCl and one equivalent of palladium acetate.




| | | |
|---|---|---|
| $Pd(OAc)_2$, dioxane, 80 °C | <1 % | 74 % |
| $PdCl_2 + Cs_2CO_3$, dioxane, 80 °C | 68 % | <1 % |

***Scheme 1.14*** *Synthesis of bis-NHC-palladium complexes*

## *1.4.5.7 Palladium-N-heterocyclic-bis(oxazoline) system*

*Glorius and coworkers* reported a new family of NHCs derived from bisoxazolines (IBiox).[13,78] Those ligands were electron rich, sterically demanding with tricyclic core structure and having restricted flexibility from the substituents on tricyclic core. This structural diversity was utilized in cross-coupling type reactions.

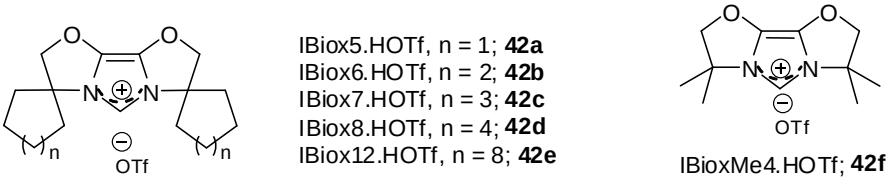
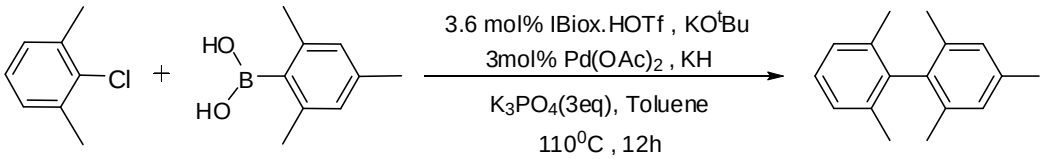



***Figure 1.6*** *Structure of IBiox salts*

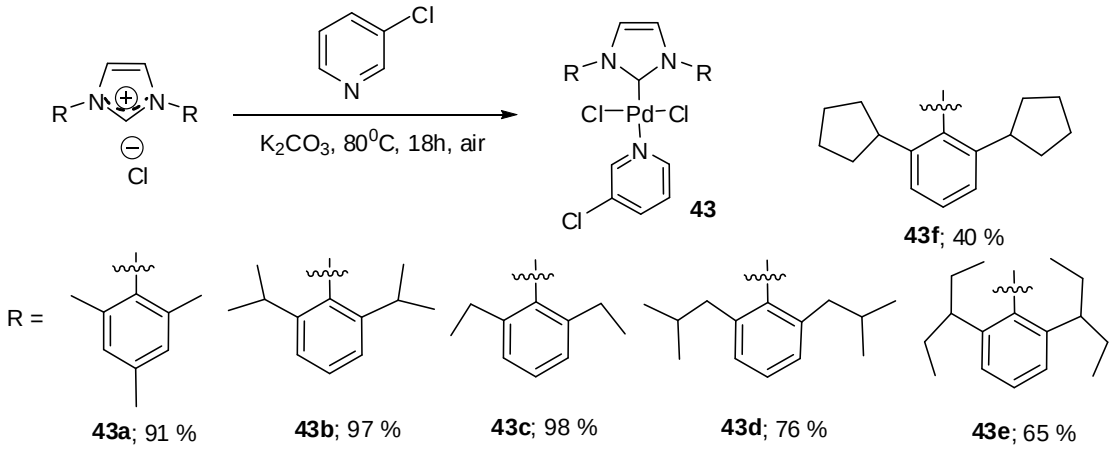
These ligands were found to be useful in the formation of tetra-ortho-substituted biaryls using aryl chlorides via Suzuki-Miyaura coupling reactions. Preliminary experiment of SM coupling reaction revealed that the coupling between 1-chloro-2,6-dimethylbenzene and 2,4,6-trimethyl -benzeneboronic acid was effective by using potassium *tert*-butoxide in toluene. Using this system, a combination of $Pd(OAc)_2$ and IBiox12.HOTf gave maximum yield of product (96%). The small ring systems were not so effective and IBiox7 & IBiox8 displayed better reactivities than smaller analogue. The IBiox12.HOTf system was also applicable for preparing several such type of sterically hindered substrates. The use of strictly anhydrous condition was required for tetra-ortho-substituted biarys to minimize the proto-deboration of arylboronic acid.




***Scheme 1.15*** *Formation of tetra-ortho-substituted biaryls*

### *1.4.5.8 Pyridine-containing Palladium complexes :*

*Organ and coworkers* recently synthesized and developed[79] the pyridine adduct of mono-dentate NHC-contaning Pd(II) compounds of the general formula $[(NHC)PdCl_2(py)]$ utilizing the loosely bound two-electron donor ligand of third generation *Grubbs catalyst*. Prolonged heating of IPr.HCl with palladium(II) dichloride in neat 3-chloropyridine led to the formation of py-Pd-NHC complex (PEPPSI complex means pyridine enhanced precatalyst, preparation, stabilization and initiation) in high yield.

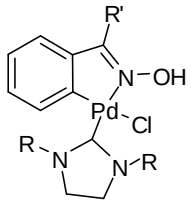



***Scheme 1.16*** *Pyridine-derived palladium-NHC complexes*

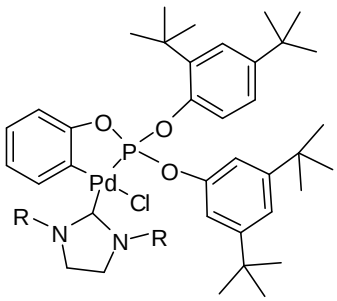
These pyridine adducts, and especially the IPr-containing (**43b**), showed good activity in the SM reaction, enabling the coupling of heteroaromatics and the formation of tri-ortho-substituted biaryls under mild conditions. Further developments in PEPPSI type complex[80] was based on the modification of steric crowding surrounding NHC, utilizing *iso*-butyl, *iso*-pentyl, cyclo-pentyl types of moiety in the aromatic ring attached to N-atoms of NHC. These catalysts were tested for SM cross coupling reaction to synthesize tetra-*ortho*-substituted biaryls. The *iso*-pentyl substituted catalyst showed better activity than earlier disclosed *iso*-propyl analogous. A number of sterically encumbered chloro- and bromo-aromatic compounds were used for cross-coupling with sterically demanding and highly substituted phenyl/naphthyl/anthracenyl boronic acids to obtain desired biaryls in good to excellent yields.

### *1.4.5.9 Palladacycles :*

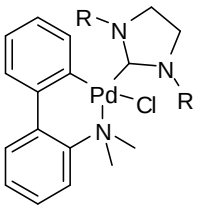
Palladacycles had recently gained more importance in catalysis because of their flexible framework and robustness. Until now the conjugation of palladacyclic scaffold and NHC had scarcely been studied. In 2003, *Iyer* described the synthesis and application of oxime-based palladacycles containing NHC.[81] By using this catalyst in *Suzuki-Miyaura* cross coupling reaction, aryl bromides were suitable coupling partners but aryl chlorides were reluctant to couple. *Bedford and coworkers* reported the formation of phosphite-based palladacycles[82] and studied their activity in the *SM* reaction. Overall, the reactivity of these catalysts was poor and could only couple unhindered and activated aryl bromides.




R = Ph, R' = Me (**44a**), Ph (**44b**)




R = Ph (**45a**), Mes (**45b**)



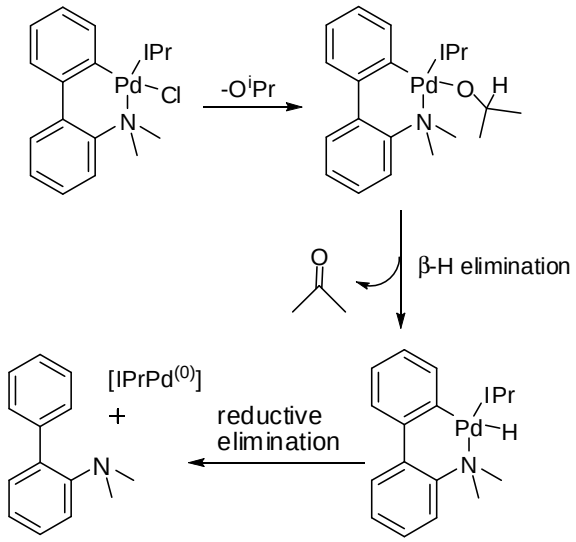

R = Mes (**46a**), 2,6-$Pr_2C_6H_2$(**46b**)

***Figure 1.7*** *Different types of Palladacycles*

In 2003 *Nolan and coworkers* reported the synthesis of amino-palladacycles (**46a**) and (**46b**) (***fig. 1.7***).[83] The activity of the most efficient one, IPr-containing (**46b**) was investigated in Suzuki-Miyaura reaction. Using IPr-palladacycle catalyst deactivated aryl chlorides and phenyl boronic acid were coupled in technical grade 2-propanol with $NaO^tBu$ as a base (1.2

equivalents) to obtain the products like di- and tri-*ortho*-substituted biaryls in high yields in short time intervals at room temperature. To gain the mechanistic insight of the reaction, the catalyst palladacycle and $NaO^tBu$ was put together in *iso*-propanol which led to the quantitative formation of 2-(dimethylamino)biphenyl. Based on this, it was proposed that liberation of organic fragment from the catalyst initiate the initial activation to obtain Pd(0) species. In the absence of base, the palladacycle remained intact.

Plausible mechanism for the activation of palladacycle(**46a/b**)




***Scheme 1.17*** *Plausible mechanism of activation of palladacycles*

It was further assumed that activation pathway led to the formation of palladacycle-hydride species which was subsequently undergone reductive elimination to obtain the biphenyl moiety. The [(IPr)Pd] species was generated then used for oxidative addition of aryl chlorides and initiates the catalytic cycle. Though this catalyst system showed impressive performance to synthesize di- and tri-*ortho*-substituted biaryls from aryl chlorides and triflates and tetra-substituted biaryls could not be produced.

There is still high demand to develop a new catalytic system having special features with higher reactivity using moderate conditions and within short time limits. The special features in the catalyst frameworks are designed on the basis of using environmentally benign, cheap, low toxic chemicals as well as solvents. Sometimes, the special characteristics might help the catalyst to work in aqueous phase which is cost-effective as well as reducing toxicity. Moreover, purification of organic substances is easier from aqueous system after finishing the reaction. The special characteristics might help catalysts to work in ionic liquids or in supercritical

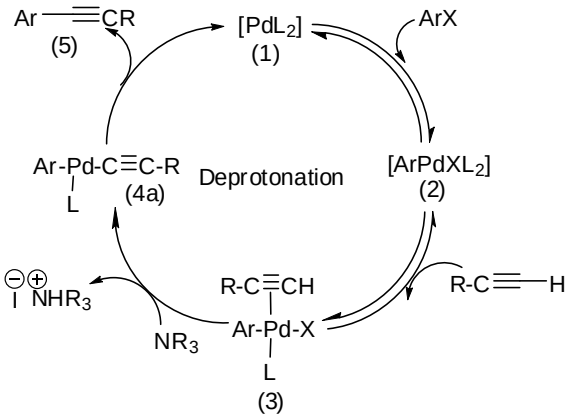
solvents. To improve the purification process polymer-attached catalysts could also be developed. This type of biphasic catalysts are helpful in regeneration process after finishing the catalytic cycle.

## *1.5 Cross-Coupling with Terminal Alkyne: the Sonogashira Reaction*

The coupling of terminal alkynes with aryl or alkenyl halides provided a straightforward methodology in the synthesis of arylalkynes and conjugated enynes. The most widely used protocol was based on using palladium catalyst and copper(I) salts as cocatalysts in the presence of amine bases. Since the discovery of copper-assisted reaction by *Sonogashira* in 1975,[46] it had widespread applications in the synthesis of diverse materials such as natural products, non-linear active compounds, molecular wire etc.[84] However, the copper additives might be problematic in the reaction outcome of certain substrates and under certain circumstances.[85] To overcome this problem, copper-free condition had also been developed. The reaction under such condition was known as the *Heck* alkynylation or as a copper-free *Sonogashira reaction*, depending on the conditions and substrates.

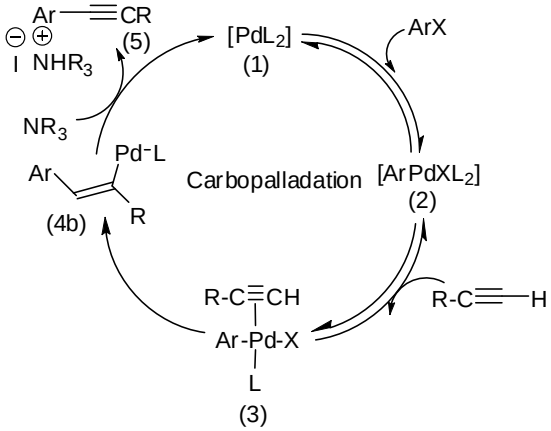
### *1.5.1 Mechanism*

In the literature two mechanistic pathways were described for copper-free *Sonogashira* mechanism.[86] Both catalytic cycles commenced on by generating catalytically active colloidal nature and/or low-ligated $Pd^0$-species (1), stabilized by coordinated ligands, base and solvent molecules. In the first step oxidative addition of aryl halides or vinyl halides was occurred to produce $Pd^{II}$-species (2). In the second step, a reversible coordination of alkyne to (2) was occurred to form Pd-alkyne complex (3). Up to this point both cycles were similar. In the deprotonation type mechanism, the base then removed a proton from coordinated alkyne to form palladium-acetylide complex (4a), from which the cross-coupled product (5) was expelled and active $Pd^0$-species was recovered by reductive elimination.




***Scheme 1.18*** *Catalytic cycle for Sonogashira coupling reaction (Deprotonation type mech.)*

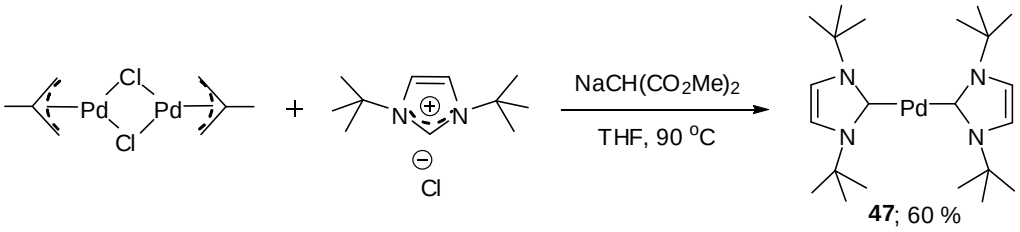
In the carbopalladation type mechanism, the Pd-Ar complex coordinated to the alkyne was added over the triple bond, forming carbene complex (4b), and the cross-coupled product was generated (5) by the treatment of a base and active catalyst was recovered through β–hydride elimination.




***Scheme 1.19*** *Catalytic cycle for Sonogashira coupling reaction (Carbopalladation mech.)*

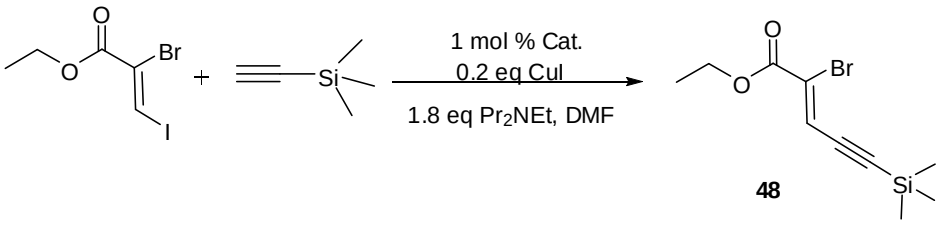
## *1.5.2 N-Heterocyclic Carbene Catalyzed Sonogashira Coupling Reaction*

*Herrmann and coworkers*[63] first reported Sonogashira coupling reaction of NHC as ancillary ligand involving activated aryl bromides and phenyl acetylene. The bis-chelating NHC-palladium-iodo complex was used for the catalytic study. The further study on *Sonogashira* coupling reaction was seen in 2001 when *Caddick and coworker* used a well-defined palladium(0)bis-NHC complex for this type of reaction.[87]



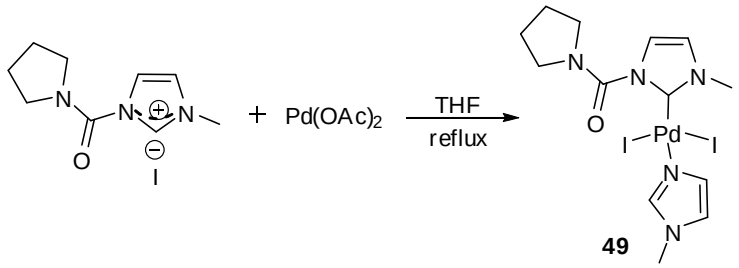

***Scheme 1.20*** *Bis-NHC-palladium(0)complex for Sonogashira coupling reaction*

The palladium(0) complex was made by reaction of palladium-allyl precursor with two equivalents of 1,3-bis(*tert*-butyl)imidazole-2-ylidine in the presence of sodium dimethylmalonate base. The complex was able to couple ethyl-2-iodo-3-bromopropionate with trimethylsilylacetylene to afford 85% yield of the product.



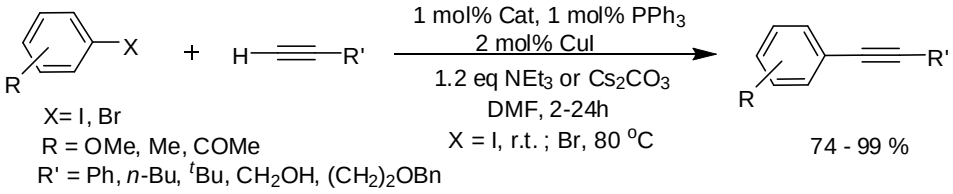

***Scheme 1.21*** *Sonogashira coupling reaction*

*Batey and coworkers* used electron-withdrawing carbomyl substituted NHC-palladium complex for studying the *Sonogashira reaction* in detail.[88] Two equivalents of *N*-carbamoyl-substituted imidazolium salt and $Pd(OAc)_2$ were refluxed together in THF in the formation of the desired palladium complex. The exact mechanism of the formation of this unique palladium complex was unknown. The formation of Pd-bound carbamoyl imidazole-2-ylidine was accompanied by the release of acetic acid, which rapidly reacted with the second equivalent of carbamoyl imidazolium salt to form *N*-acetylpyrrolidine. The byproduct of the nucleophilic attack, *N*-methyl imidazole then coordinates with the palladium center to form the observed Pd-complex.



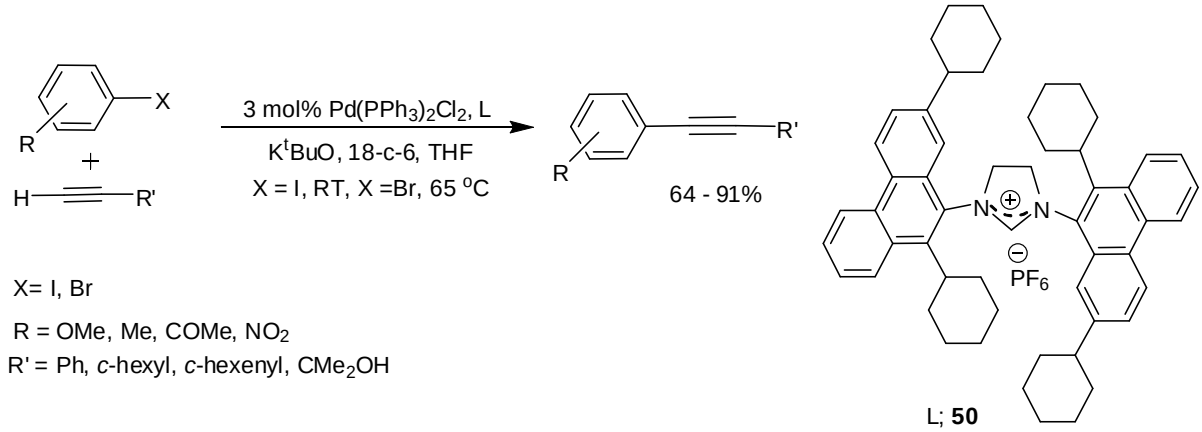

***Scheme 1.22*** *Palladium complex for Sonogashira coupling reaction*

The palladium complex was then used in the *Sonogashira* reaction by modifying the standard reaction condition. Instead of using large excess of amine base as solvent, stoichiometric amount of cesium carbonate or triethyl amine was used as a base in DMF for coupling of aryl bromides and iodides respectively. In addition, $PPh_3$ (1 mol %) was used to the Pd catalyst to avoid byproduct formation and increase functional group tolerance power.



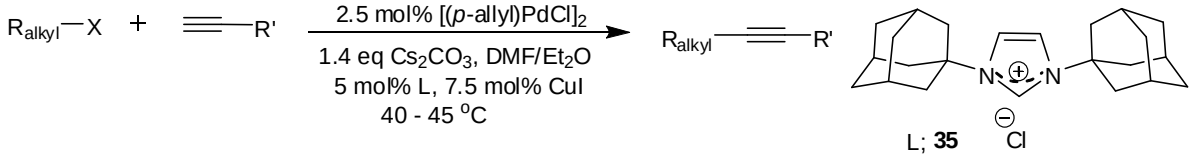

***Scheme 1.23*** *Sonogashira coupling reaction protocol*

*Andrus and coworkers* reported[89] the copper-free coupling of bromo- and iodo-arenes and alkenes with terminal acetylenes using sterically bulky 1,3-bis(2,9-dicyclohexyl-10-phenanthryl)-imidazole-2-ylidine ligand with palladium-phosphine complex, potassium *tert*-butoxide as a base and in the presence of 18-crown-6. Electron-rich and -deficient substrates were coupled with equal success.




***Scheme 1.24*** *Copper-free Sonogashira coupling reaction*

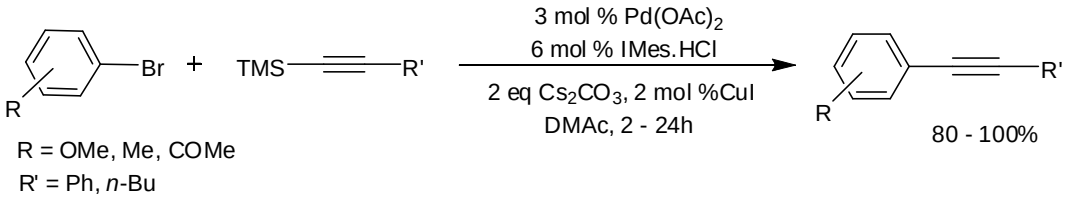
An interesting application of *N*-heterocyclic carbene in the coupling of alkyl electrophile with copper acetylides was reported by Fu and coworkers. The reaction of n-nonyl bromide with 1-octyne in the presence of phosphines, palladium and copper complex were ineffective. But the reactivity of NHC, such as sterically bulky ligands, 1,3-bis-(2,6-diisopropylphenyl)imidazole-2-ylidine, 1,3-bis(tert-butyl)imidazole-2-ylidine, 1,3-bis(adamantly)imidazole-2-ylidine were effective in the presence of palladium-allyl precursor and CuI.




***Scheme 1.25*** *Alkyl-version of Sonogashira coupling reaction*

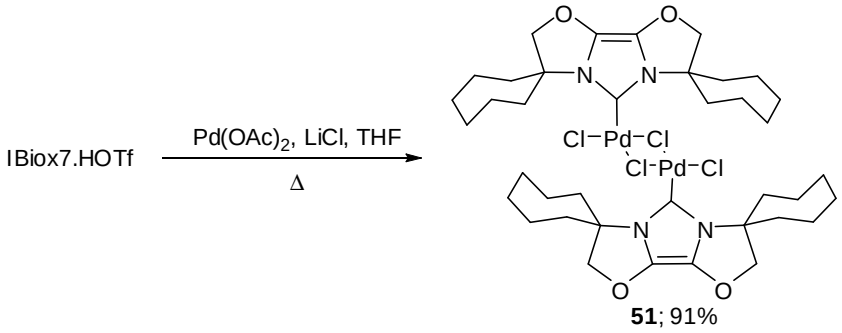
In 2002 *Nolan and coworkers*[90] reported the *Sonogashira* coupling using deactivated aryl bromides and alkynylsilane mediated by Pd-NHC which was *in situ* generated from Pd-precursors and imidazolium salts. The rate of reaction was accelerated in the presence of CuI and also trimethylsilyl-protected acetylene was used to suppress the side reaction of homo-coupling product formation. The use of $Cs_2CO_3$ as a base worked in two-fold ways; first to generate active catalyst and secondly, to make deprotection of silyl group. Within the most

commonly used imidazolium salts, 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride was the most active species.

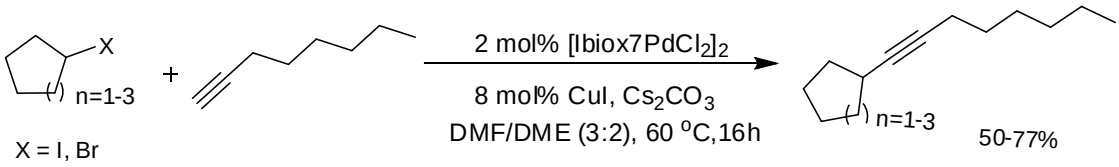



***Scheme 1.26*** *Sonogashira coupling with protected alkyne*

The most interesting application of NHC was reported by *Glorius and coworkers*[91] in the cross-coupling of secondary alkyl bromides and iodides with unactivated alkyne. The use of electron-rich donor bis-oxazoline system with sterically demanding as well as flexible frame-work showed appreciable reactivity in alkyl-alkyl cross-coupling reaction. The use of cesium carbonate as a base along with the catalyst system resulted in the formation of the desired product in a good yield. Within bisoxazoline ligand system, Ibiox6 and Ibiox7 worked better than the others and also as preformed Pd-complex compared to *in situ* generated. The addition of catalytic amount of 1,2-diaminocyclohexane was sometimes helpful to increase the reactivity of catalyst. After following the *Fu's* reaction condition only low amount of desired product was formed and most of them were homo coupling product of the alkyne.




***Scheme 1.27*** *Synthesis of palladium-Ibiox complex*



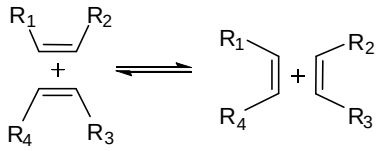

***Scheme 1.27*** *Alkyl-version of Sonogashira coupling reaction*

The *Sonogashira* coupling protocol was applicable to different secondary alkyl halides, such as cyclo-pentyl, -hexyl, -heptyl and -octyl bromides and iodides as well as challenging acyclic alkyl bromides. The reaction condition was well acquainted with alkyl bromides having a variety of functional group, such as acetyl protected alcohol, ester, epoxide, olefin, aromatic ring on the alkyl chain.

*N*-heterocyclic carbenes are more promising ligands compared to phosphine with respect to *Sonogashira* coupling reaction. Until now there is not so much emphasis on NHCs regarding this coupling reaction. The detailed study regarding the catalytic activity and the mechanistic aspects related to NHCs are still scare to highlight the field of cross-coupling. Although only a limited number of reports incorporating NHCs in the field of cross-coupling are known but they show superior activity compared to other ligands with respect to reactivity, recycling of catalysts, stability in solution state as well as towards air and moisture etc. Moreover, NHCs are usually synthesized as stable salts, and generated *in situ* and sometimes in the course of reaction metal-NHC complexes are produced. Thus easy handling also makes an advantage over highly sensitive phosphine ligands. The NHCs are cheap, as they are made from cheap starting materials, such as aniline derivatives and without doing much precaution of air and moisture. They are more promising as ancillary ligands not only in the field of palladium but also other transition metal catalyzed transformations.

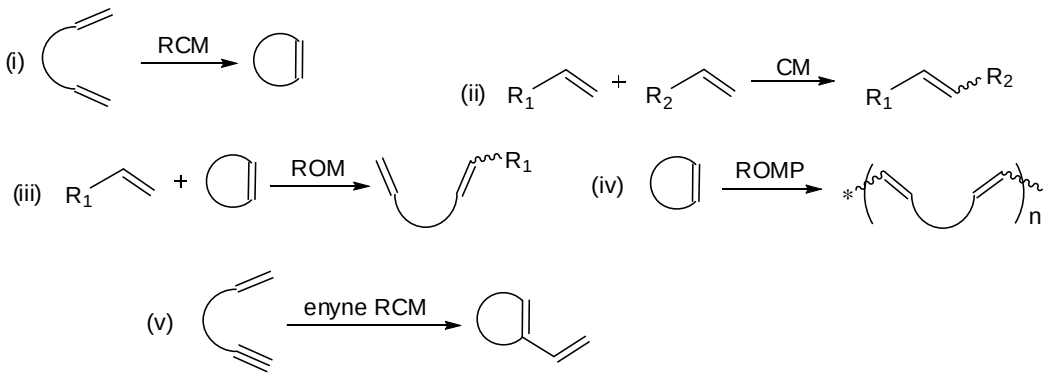
## *1.6 Olefin Metathesis*

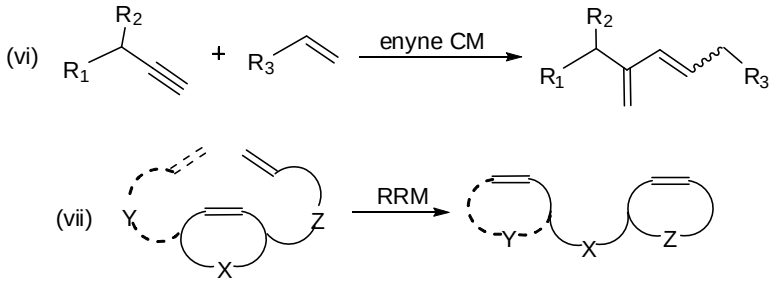
Olefin metathesis is a fundamental chemical reaction involving the rearrangement of carbon-carbon double bonds, and can be used to couple, cleave, ring-close, ring-open, or polymerize olefinic molecules.[92] Among the various types of transition metal catalyzed C-C bond forming reactions, olefin metathesis has become one of the most important reactions in recent years owing to the wide range of transformations that are possible with commercially available and easily handled catalysts. Consequently olefin metathesis is now widely considered as one of the most powerful synthetic tools in organic chemistry. With the evolution of new catalysts, the selectivity, efficiency, and functional group compatibility of this reaction have improved to a level that was unimaginable just few years ago.




***Scheme 1.28*** *Olefin metathesis (bond breaking and making process)*

Although the double-bond scrambling reactions were reported in the mid 1950s, the term "olefin metathesis" was introduced by Calderon and coworkers afterwards in 1967.[93] The metal catalyzed redistribution of carbon-carbon double bonds was utilized in a variety of transformations which might be included ring-closing metathesis (RCM), ring-opening metathesis (ROM), ring-opening metathesis polymerization (ROMP), acyclic diene metathesis polymerization (ADMET), and cross-metathesis (CM) and more recently ring-rearrangement metathesis. The extension of this reaction to the version of triple bonds was made possible and termed as ene-yne and alkyne metathesis (***Scheme 1.29***).






***Scheme 1.29*** *Different types of olefin metathesis reactions*

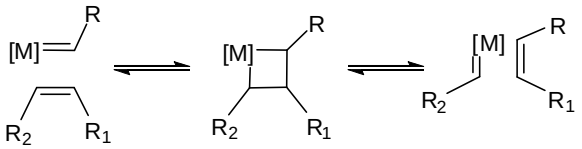
## *1.6.1 Historical Background*

### *1.6.1.1 Origins*

The origin of olefin metathesis was stemmed from the polymer chemistry research when researchers were interested to find new type of well-defined Ziegler-type catalysts to synthesize characteristics polymers.[94] Although double-bond scrambling reactions were initially reported in the mid-1950's, after several years the term "olefin metathesis" was introduced by Calderon and coworkers of such type of reactions.[93] The early days of olefin metathesis catalysts were based on poorly defined, multicomponent homogeneous and heterogeneous systems consisting of transition metal salts combined with the main group alkylating agents. Some of the classic combinations include $WCl_6/Bu_4Sn$, $WOCl_4/EtAlCl_2$, $MoO_3/SiO_2$ and $Re_2O_7/Al_2O_3$ among many others.[95] These catalysts were however limited to their use because of long initiation periods and harsh reaction conditions and the presence of strong Lewis acids which were incompatible with most functional groups.

### *1.6.1.2 Mechanistic Aspects*

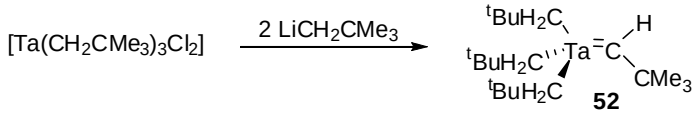
To circumvent the problems associated with the metathesis reaction several research groups were interested to understand in detail of it, including mechanistic studies. Many schemes were proposed over the years, however ultimately, the scheme developed by Chauvin was found to be the most consistent with experimental evidence and till now well accepted. The proposed mechanism of olefin metathesis was involved the interchange between an olefin and metal alkylidene. This process was believed to occur via an intermediate, namely metallacyclobutane species which was formed by [2 + 2] cycloaddition between an olefin and metal alkylidene and subsequently fragmented to a new metal alkylidene and a new olefin, thus propagating the catalytic cycle.[96]



***Scheme 1.30*** *Chauvin's mechanism in alkene metathesis*

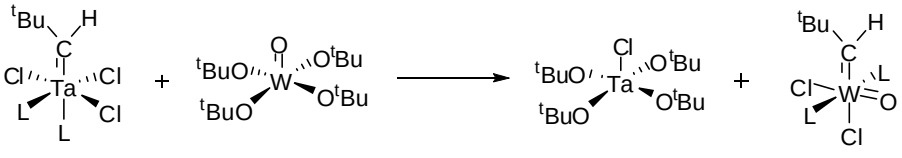
### *1.6.1.3 Early tantalum (Ta) and tungsten (W) complexes*

In the mid of 1970s the first well-defined tantalum-based methylidene complexes were emerged. Early work based on the synthesis of stable species of the type $TaMe_nCl_{5-n}$, where the complex with n = 3 gave the maximum number of methyl groups for stable complexes.[97] The attempted synthesis of penta(neopentyl)tantalum through the addition of $[LiCH_2CMe_3]$ to $[Ta(CH_2CMe_3)_3Cl_2]$ was resulted in the formation of first stable "tantalum-ylide"- kind species $[(Me_3CCH_2)_3Ta{=}CHCMe_3]$.[98] This new electron-deficient, high oxidation state, stable species was different from "*Fischer carbene*" and known as "*Schrock Carbene*". The noticeable metathesis activity was observed by using tantalum-alkylidene complex with chloro and phosphine alkoxy ligands.[99] It was proposed that *tert*-butoxide ligands prevent the reduction of metal and promote metathesis. These ideas were extended to the tungsten chemistry as tungsten and tantalum were relatively stable in higher oxidation state. Afterwards, the tungsten-alkylidene methodology was developed by using "*Wittig*"-like reaction between a tantalum alkylidene and a tungsten oxo complex. It was observed that an unanticipated oxo neo-pentylidene complex of tungsten showed metathesis activity in presence of a trace of $AlCl_3$, which helped to produce vacant coordination site at the metal.[100]

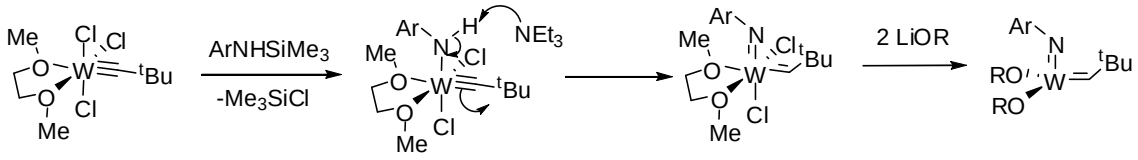


**52**

***Scheme 1.31*** *First example of Schrock carbene*



***Scheme 1.32*** *Synthesis of tungsten-based Schrock carbene*

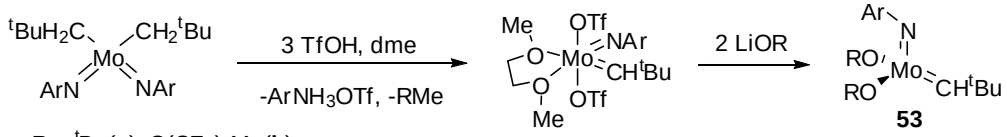


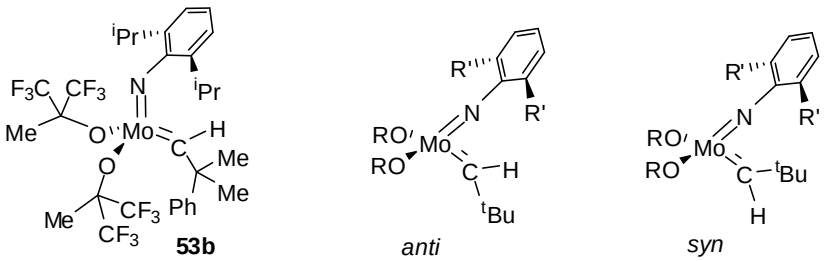

***Scheme 1.33*** *Synthesis of tungsten-based Schrock catalyst*

The oxo-group present in the tungsten-based catalyst was unsuitable because it underwent bimolecular decomposition. The introduction of an isoelectronic aryl imido group, instead of oxo-group in the tungsten-based catalyst significantly slowed down the rate of bimolecular decomposition and increased the metathesis activity. In particular, catalysts having bulky substituents on imido group such as 2,6-diisopropylphenyl moiety making it more stable and highest reactivity was observed for electron withdrawing alkoxy ligands such as hexafluoro-*tert*-butoxide.[101]

### *1.6.1.4 Molybdenum Complexes*

Afterwards, the more attention was focused upon molybdenum catalysts with the goal of achieving the stable and functional group-tolerant catalysts. The synthesis of molebdenum-imido-alkylidene complexes were carried out by the treatment of bis-imido complexes with triflic acid in 1,2-dimethoxyethane (dme), providing the stable 18-electron imido alkylidene complexes, via α–hydrogen abstraction and loss of the alkyl group. When these complexes were treated with various lithium alkoxides, the bis(alkoxide)imido-alkylidene molybdenum complexes were formed.[102] It was also observed that two isomers were possible for such type of Mo complexes depending upon the location of substituents on alkylidene group with respect to imido group. If it was closer to imido-group was known as *syn* and further from it as *anti*. The *anti*-isomer was more reactive than *syn.* Because of steric reason the hexa-fluoro-*tert*-butoxide molybdenum complex (**53b**) remained exclusively in anti-form which were more reactive compared to *tert*-butoxide due to interconversion between *syn* and *anti* to the later.[103]






***Scheme 1.34*** *Synthesis and structure of molybdenum-based Schrock catalyst*

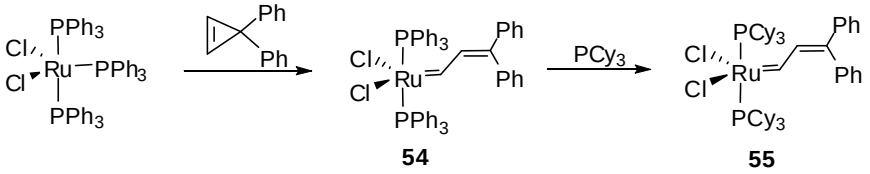
The more electron withdrawing nature of hexafluoro-*tert*-butoxide group and bulky aryl-imido group reduced the intra-molecular C-H activation and thus stabilize these molybdenum-based 'Schrock catalysts'. All these molybdenum- and tungsten-based catalysts were oxophilic and require handling under schlenk conditions.

## *1.6.2 Ruthenium Complexes*

From 1960s there were several reports on ROMP of norbornene derivatives using $RuCl_3$ (hydrate) in refluxing aqueous ethanol, though yields were small.[104] In the late 1980s and later there were more studied reports on $RuCl_3$[105] which revealed that ROMP was initiated in water very quickly but was inhibited in anhydrous condition. Thus, water was not only compatible with this catalyst system but also having beneficial role to the initiation process. Next $Ru(H_2O)_6(tos)_2$ complex was studied for ROMP in water but showed limitation to the strained ring substrates.[106]

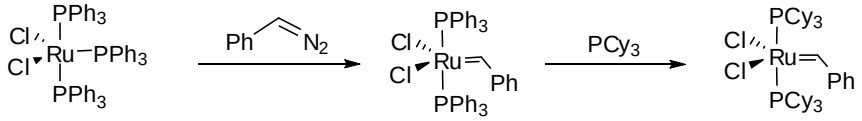
The major break-through was occurred when the methodology for synthesizing tungsten alkylidenes by using 3,3-disubstituted cyclopropenes as carbene precursors, was applied to the synthesis of a Ru-alkylidene catalyst. The addition of diphenylcyclopropene to $[RuCl_2(PPh_3)_3]$ led to the formation of (**54**; ***Scheme 1.35***), the first well-defined, metathesis active ruthenium alkylidene complex.[107] Further modification was done by using the more basic phosphines which exerted the greater metathesis activity and stability of the catalyst.[108] The catalyst (**55**) bearing tricyclohexylphosphine ($PCy_3$) ligands was much more versatile catalyst due to its activity towards acyclic olefins and ROMP of lower strained substrates and functional group tolerant. This catalyst was air-stable solid and retained its activity even exposed to water, alcohols or acids. The difficulty of synthesizing diphenylcyclopropene put limitation to the synthesis of these type ruthenium alkylidene complexes.

The true turning point in ruthenium metathesis catalysis occurred when Grubbs' group utilized diazolkanes as carbene source instead of cyclopropene derivatives for the synthesis of new Ru-carbene complexes.[109] The ruthenium-chloro-tris(triphenylphosphine) complex was treated with phenyldiazomethane, followed by ligand exchange with more basic tricyhexylphosphine ($PCy_3$) resulted in the formation of a robust catalyst, known as '*Grubbs first generation'* catalyst (*Grubbs I*) (**57**; ***Scheme 1.36***). This catalyst is highly active, functional group tolerant, stable towards air and moisture and used in various types of metathesis, particularly RCM and cross metathesis and various organic syntheses.




**54** **55**

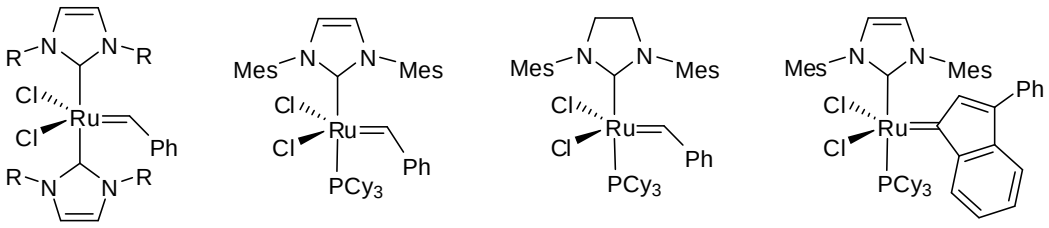
***Scheme 1.35*** *The first stable and active ruthenium-based metathesis catalyst*




**56** **57**

***Scheme 1.36*** *Synthesis of Grubbs I catalyst*

Further modification of *Grubbs I* was observed by introducing one labile and one strong σ-donor ligands attached to the ruthenium center which enhanced the formation and stability of the intermediates in the metathesis processes. It was assumed that *N*-heterocyclic carbenes (NHC) would be a better choice to fulfill such criteria. *Herrmann and coworkers* were first reported the use of NHC-ruthenium complex for metathesis.[110] They synthesized bis-NHC complex (**58**) by replacing both phosphines by NHC. Unfortunately, it showed no significant improvements in metathesis activity but NHC unit conferred stability. Afterwards, Nolan[111], Grubbs[112] and Herrmann[113] pursued the idea of combining a labile phosphine in combination with a stabilizing NHC ligand to make better catalysts. These complexes showed remarkable activity and stability. The complex in which 1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene substituted either of the two phosphines from *Grubbs I* complex was most stable and showed better activity compared to others. These types of mixed phosphine-NHC ruthenium alkylidene complexes were known as *Grubbs II* complexes (**59**; **60**). *Nolan and coworkers* developed indenylidene-type ruthenium complexes (**61**) which showed higher metathesis reactivity and stability even in high temperature and drastic conditions.[114]

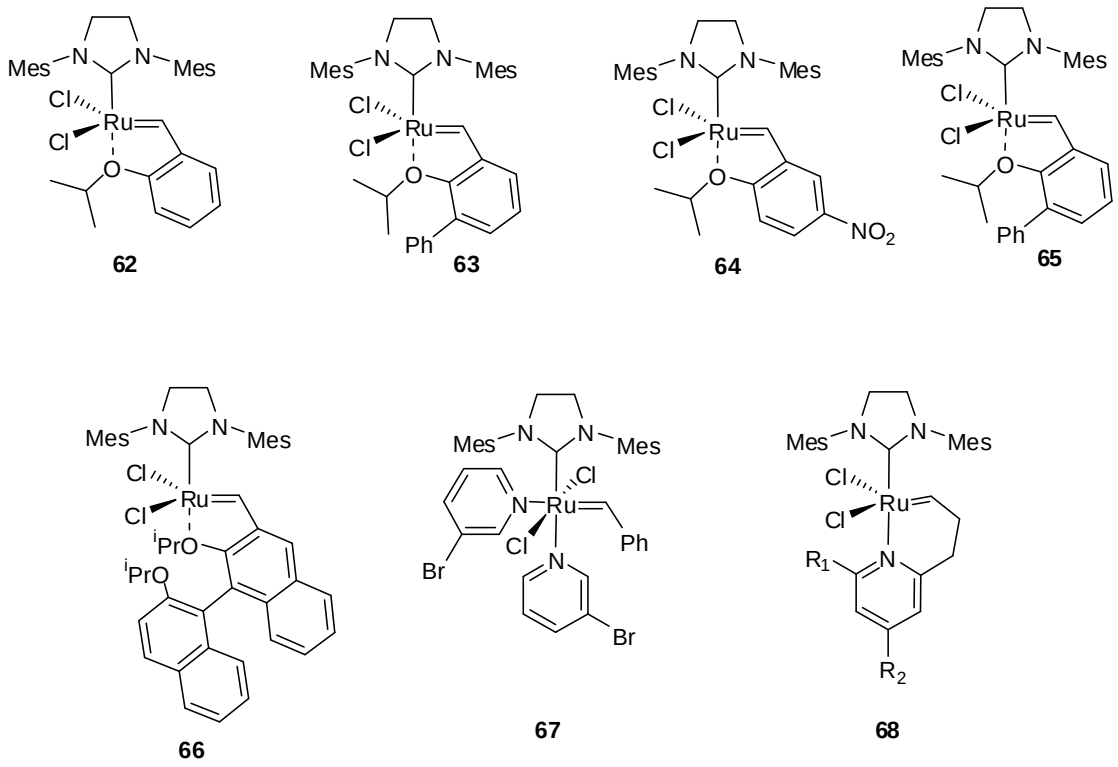



**58** **59** **60** **61**

***Scheme 1.37*** *N-heterocyclic carbene-based catalysts*

### *1.6.2.1 Phosphine-free Ruthenium Catalysts :*

In 1997, it was first observed that certain styrene ethers could form stable cyclic ruthenacarbenes with *Grubbs*-type systems in a bidentate fashion.[115] Subsequently, catalyst bearing an isopropoxystyrene ligand with phosphine to the *trans*-coordination of isopropoxy group showed good metathesis activity together with air- and moisture tolerance as well as stability to silicagel chromatography.[116] In 2000, the group of *Hoveyda*[117] and *Blechert*[118] simultaneously reported phosphine-free catalysts where one phosphine was replaced by NHC and another phosphine by isopropoxystyrene (**62**) and 3-phenyl-isopropoxystyrene (**63**) derivatives respectively. This so-called '*Hoveyda-Grubbs'* catalyst showed improved reactivity for CM of electron-deficient alkenes, such as acrylonitriles, fluorinated alkenes and others and RCM of tri-substituted alkenes. This catalyst was very stable to air and moisture and also reusable. This catalyst framework was subsequently used as a template to modify the steric and electronic property to obtain better catalysts. Grela and coworkers synthesized nitro-styrere derivative of this *Hoveyda*–type catalyst (**64**), which showed enhanced activity due to the electron withdrawing *p*-nitro-group reduced the electron donation power of isopropoxy-unit towards ruthenium center.[119] There were several other catalysts synthesized by Blechert's group where steric properties were varied to destabilize the five-membered ruthenacycle formed by isopropoxy-styrene moiety in the precatalyst.[120] All these catalysts showed better reactivity than the parent compound. Grubbs and coworkers developed ruthenium complex bearing two neutral 3-bromopyridine ligands (**67**) making the precatalyst one of the fastest initiating precatalysts known.[121] This was known as *Grubbs-third generation (Grubbs III)* catalyst. Further modification from Grubbs' group made by using tethered pyridyl moiety into the ruthenium center[122] (**68**) which was mostly useful in ROMP reaction.




***Scheme 1.38*** *Structure of phosphine-free catalysts*

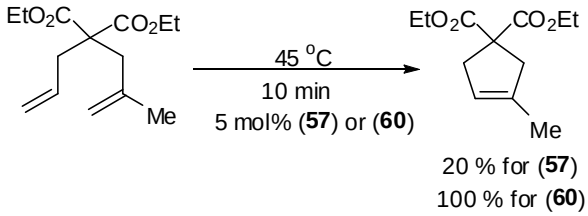
## *1.6.3 Applications of Ruthenium-based Catalysts*

### *1.6.3.1 Ring Closing Metathesis (RCM)*

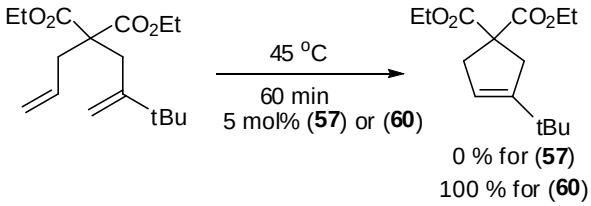
In ring closing metathesis the intramolecular mutual exchange between two olefin fragments promoted by metal-carbene complexes was occured. There were two main possibilities to do metathesis intramolecularly to obtain cyclic compounds. One possibility was just simple metathesis between two olefinic fragments and another ene-yne ring closing where one alkyne fragment metathesized with another alkene fragment intramolecularly, also known as broadly classified group enyne metathesis.

In simple RCM reactions, *Grubbs II* catalyst (**60**) showed increased activity compared to *Grubbs I* (**57**) in forming cyclopentene derivatives (***Scheme 1.39***).[123] The improved reactivity of (**60**) could be exemplified in the metathesis reaction of sterically more crowded and more challenging substrate where catalyst (**60**) proved its superiority over catatyst (**57**) under the

same catalytic condition (***Scheme 1.40***).[124] It was a general trend that bulky substituents in the allylic position or directly at the double bond, significantly slowed down the metathesis reactions. For other demanding substrate such as macrocycles, catalyst (**60**) proved the importance of RCM.

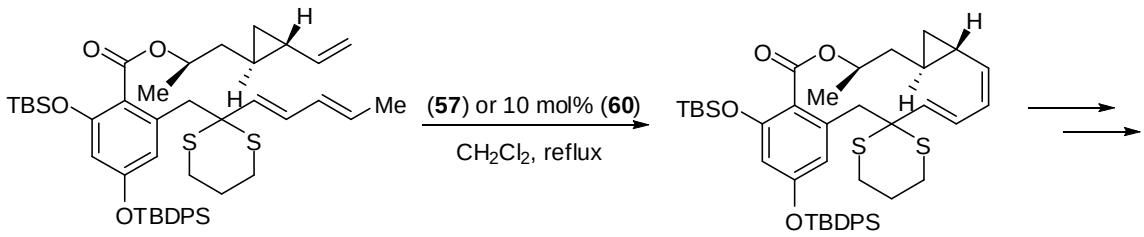



***Scheme 1.39*** *Ring closing metathesis of substituted olefin*




***Scheme 1.40*** *Ring closing metathesis of substituted olefin*

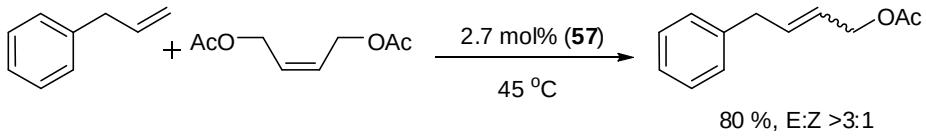
Comparison between *Grubbs II* (**60**) and *Grubbs I* (**57**) was exemplified by *Danishefsky and coworkers* in the course of synthesis of radicicol, where the intermediate macrocycle was formed in 60% yield by using (**60**) but only traces of compound with (**57**) (***Scheme 1.41***).[125] Another example was the synthesis of aspercyclide C by Fürstner and coworkers where (**59**) showed reactivity towards RCM to form macrocycle but (**57**) showed poor reactivity, even using 50 mol % catalyst loading.[126]



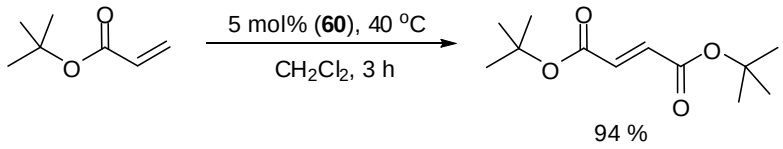

***Scheme 1.41***

### *1.6.3.2 Cross Metthesis (CM)*

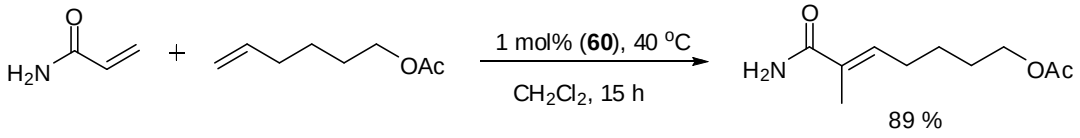
Olefin cross metathesis could be described as the intermolecular mutual exchange of carbene fragments between two olefins promoted by metal-alkylidene complexes.[127] There were three main variations in this category: (a) cross metathesis, (b) ring opening cross metathesis and (c) intermolecular enyne metathesis.[128] Cross metathesis was benefited as there were more substrate scope to expand the rapidly growing metathesis field. Only unhindered, electron-rich olefins could be used for *Grubbs I* type catalyst and sterically hindered and electron deficient olefins failed to couple.[129] *Grubbs and coworkers* showed that by using second generation catalysts a large variety of functionalized and substituted olefins could be coupled successfully through cross metathesis, such as, α, β-unsaturated carbonyl compounds,[130] vinyl phosphonates[131] and vinyl sulfones[132] etc. By using *Grubbs II*, the highly substituted double bonds could be obtained very easily in high yield. The introduction of prenyl groups in natural product could be efficiently achieved by using 2-methyl-2-butene as cross metathesis partner. This method was followed in the synthesis of natural products namely, garsubellin A [133] and flustramine B.[134]




***Scheme 1.43*** *Cross metathesis with Grubbs I cat.*




***Scheme 1.44*** *Cross metathesis with Grubbs II cat. (homodimerization)*




***Scheme 1.45*** *Cross metathesis with Grubbs II cat.*

For simple olefins, the reaction yield was limited to only 50 % if the reaction partners were used as 1 : 1 ratio. To overcome this problem *Grubbs and coworkers* developed an empirical guidelines to predict the outcome of the cross metathesis reactions based on the reactivity of

various olefins for a particular metathesis catalyst.[127] This classification was based on the different rates at which functionalized olefins undergo self-metathesis. Olefins were classified into four categories from rapid homodimerization (class 1), over slow homodimerization (class 2) and no homodimerization (class 3), to spectators to cross metathesis (class 4).

**Table** Olefin categories for selective metathesis

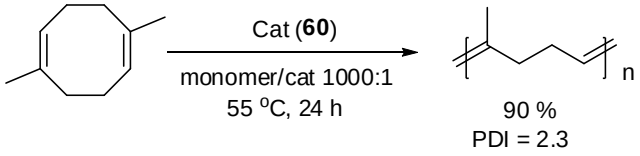
| *Olefin type* | *Grubbs I* | *Grubbs II* |
|---|---|---|
| Class 1 (fast homodimerization) | Terminal olefins, Allyl silane | Terminal olefins, allyl silanes, $1^{o}$ allylic alcohols, styrenes. |
| Class 2 (slow homodimerization) | Styrene, $2^{o}$ allylic alcohols | Styrenes (large *ortho* substituents), acrylates, acrylamides, vinyl ketones |
| Class 3 (no homodimerization) | Vinyl siloxanes | 1,1-Disubstituted olefins, trisubstituted olefins, $3^{o}$ allylic alcohols |
| Class 4 (spectators to CM) | 1,1-Disubstituted olefins, disubstitued α,β-unsaturat--ed carbonyls | Vinyl nitro olefins |

The most important factors for olefin classification were due to steric reason at the allylic position or directly on the double bond. It was observed that the least substituted and most electron-rich double bonds were most active.

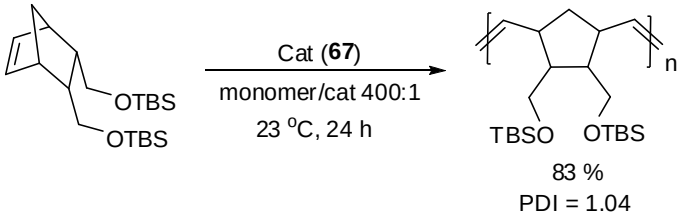
### *1.6.3.3 Ring-Opening Metathesis Polymerization (ROMP)*

It was a chain-growth polymerization process in which a cyclic olefin was converted to polymer. This process was driven by the release of ring strain which provided the main driving force to overcome the unfavorable entropy change in polymerization.[135] ROMP was employed in the synthesis of a wide range of well-defined polymer architectures. Polymerization process was commenced on the initiation of catalyst through the dissociation of phosphine ligand such as $PCy_3$ in the *Grubbs-type* ruthenium catalysts. The polydispersity index (PDI) was a measure of the distribution of molecular mass in a polymer sample and usually measured as a ratio of the

weight average molecular weight to the number average molecular weight. The PDI would have a value always greater than 1, as the polymer chains approached uniform chain length, the PDI would approach unity (1). In *Grubbs I* and *Grubbs II* type complexes the propagation rate was faster than initiation so that the PDI ratios obtained were generally broad. As in *Grubbs III complex* 3-bromopyridine ligand dissociation was faster, the rate of initiation and propagation of polymerization were significantly increased and the PDI of polymers obtained from strained olefins were close to unity and also in high yield (***Scheme 1.47***).[136]



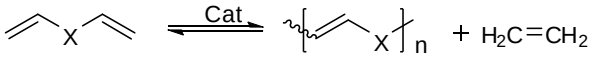

***Scheme 1.46*** *Ring opening metathesis polymerization of cyclooctadiene*




***Scheme 1.47*** *Ring opening metathesis polymerization of norbornene-derivative*

## *1.6.3.4 Acyclic Diene Metathesis Polymerization (ADMET)*

When cross metathesis was carried out on acyclic diolefins, resulted in the formation of polymers. This process was known as acyclic diene metathesis polymerization.[137] This was a step-growth polymerization process driven by the release of small molecule condensate, e.g., ethylene. The equilibrium of ADMET polymerization was forced towards the high polymer structure by using reduced pressure to remove ethylene from bulk reaction mixture.[138]



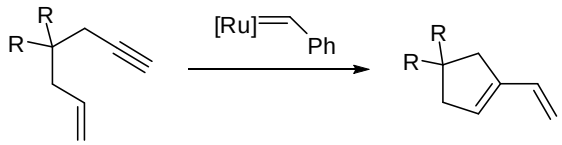

***Scheme 1.48*** *Acyclic diene metathesis polymerization*

ADMET offered a synthetic route to strictly linear, functionalized polyethylenes through the polymerization of α, ω-diene followed by exhaustive hydrogenation. The sequence was controlled and truly random copolymers could be obtained by using almost equally reactive diolefins. If the sequence was not controlled gradient polymers were formed. Both highly active

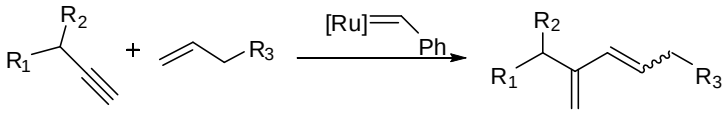
ruthenium and molybdenum-based catalysts proved as valuable tools for the production of novel structured polymeric materials.

### *1.6.3.5 ENYNE Metathesis*

Enyne metathesis could be explained as a process in which the reorganization of covalent bonds between an alkene and an alkyne resulted in the formation of conjugated 1,3-diene species. Enyne metathesis was divided into two categories depending on the molecularity of the reaction. In ring closing enyne metathesis 1,n-enyne intramolecularly metathesize to form a 1-vinyl-cycloalkene. The intermolecular or cross enyne produced diene from alkyne and alkene fragments.[139]



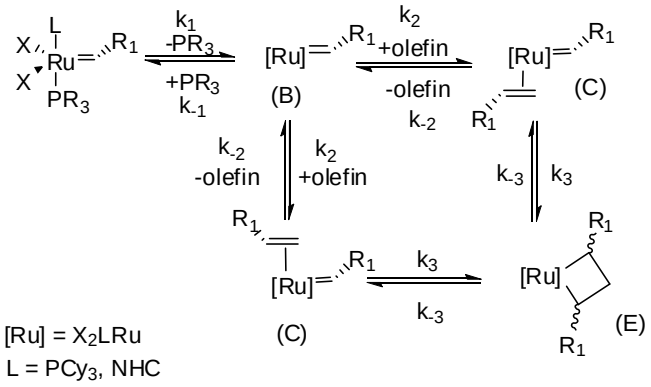

***Scheme 1.49*** *Enyne ring-closing metathesis*



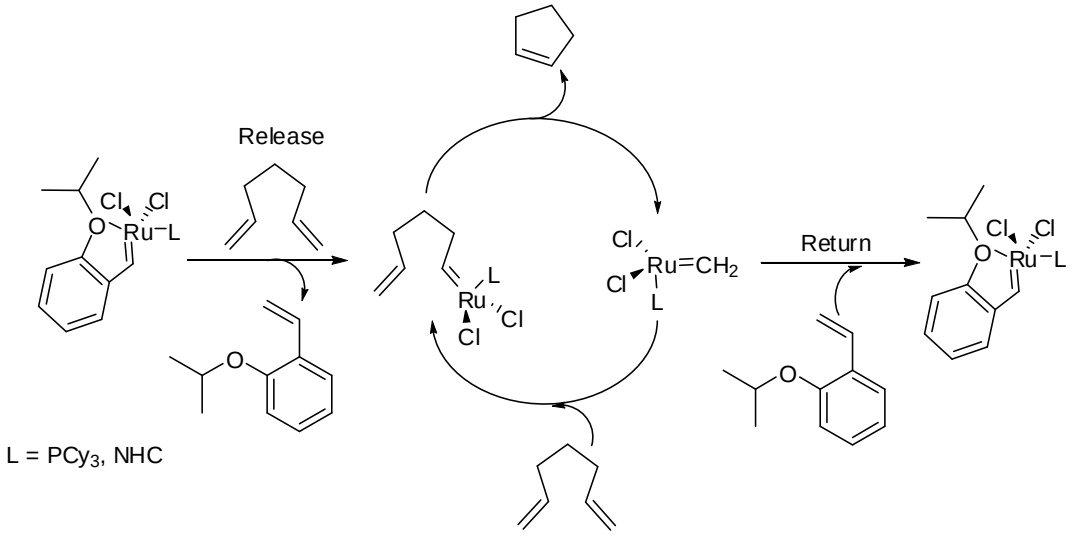

***Scheme 1.50*** *Enyne-cross metathesis*

### *1.6.4 Mechanistic Considerations of Ruthenium-based Catalysts*

From the mechanistic study, it was revealed that the initiation of catalysis involved by dissociation of phosphine or tethered iso-propoxy coordination from 16-electron ruthenium pre-catalysts to obtain 14-electron active catalysts (B). This 14-electron low-coordinated Ru-species was bound to the olefinic substrates *trans* to the remaining phosphine or NHC. Then rearrangement between the Ru-alkylidene and olefin was occurred to form the ruthanacyclobutane intermediate (E) followed by cleavage of the bonds to release the metathesis product. Hence the catalytic cycle initiated by the formation of ruthenium-alkylidene species and upon complete consumption of olefins, initially dissociated phosphine or iso-propoxy-styrene regenerated the pre-catalysts back.[140]




***Scheme 1.51*** *Proposed Catalytic cycle of Grubbs I & II type complexes*



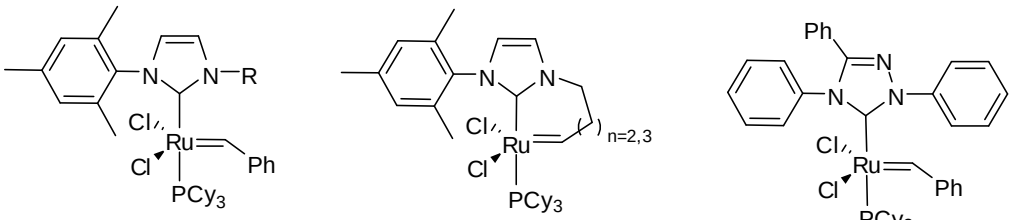

***Scheme 1.52*** *Catalytic cycle of Hoveyda-type catalyst*

In the case of *Hoveyda* type system the activity of the catalyst was much greater, as the release/return mechanism operating properly whereas in the presence of phosphine the ruthenium-alkylidene catalyst was deactivated (***Scheme 1.52***).[141]

## *1.6.5 Structural Diversity and Ruthenium-NHC complexes*

The *N*-heterocyclic carbene moiety could be manipulated in different possible ways either substitution on *N*-atoms of imidazole or 4,5-dihydroimidazole system or the backbone or the heteroatoms. *Mol and coworkers* reported the use of sterically bulky *N*-2,6-diisopropylphenyl

groups on *N*-atoms increased the reactivity.[142] The backbone variation was occurred by using chloro-substituents in the unsaturated imidazole system. *Fürstner and coworkers* reported unsymmetrically substituted catalysts containing one aromatic and one alkyl chain on the *N*-atoms of imidazole motif (**69**), showed moderate to good metathesis reactivity.[143] Another interesting ruthenium pre-catalyst was mentioned in the same paper where *N*-heterocyclic carbene and regular carbene unit of Ru=CHR were tethered together to form metallacycle (**70**). The idea for making such type of system was to regenerate catalysts after reacting with the consumed substrate quantitatively. The structure of these complexes was established from NMR studies as well as x-ray crystallography. Additionally, it was revealed from structure of the complexes that aromatic rings of NHC preferred to sit in close proximity facing the ruthenium benzylidene ring, suggesting conformational restraint by π-π interactions. The triazole-containing catalyst (**71**) was reported by Fürstner exhibited good metathetic activity for simple systems but limited lifetime in solution restricted use for sterically demanding systems. With sterically demanding adamantyl substituted unsymmetrical NHC, the ruthenium complex displayed lower reactivity, most likely due to steric congestion around the active Ru-center.[144]



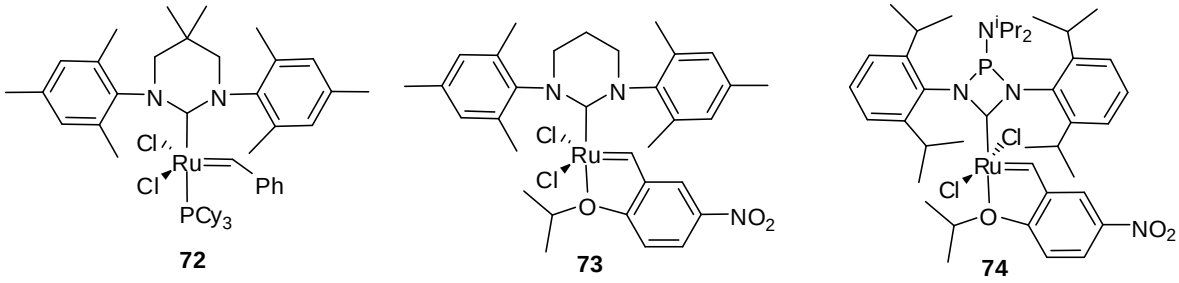

**69a**; R = $(CH_2)_nCH=CH_2$
**69b**; R = $(CH_2)_2OTBS$
**69c**; R = $(CH_2)_2(CF_2)_5CF_3$

**70**

**71**

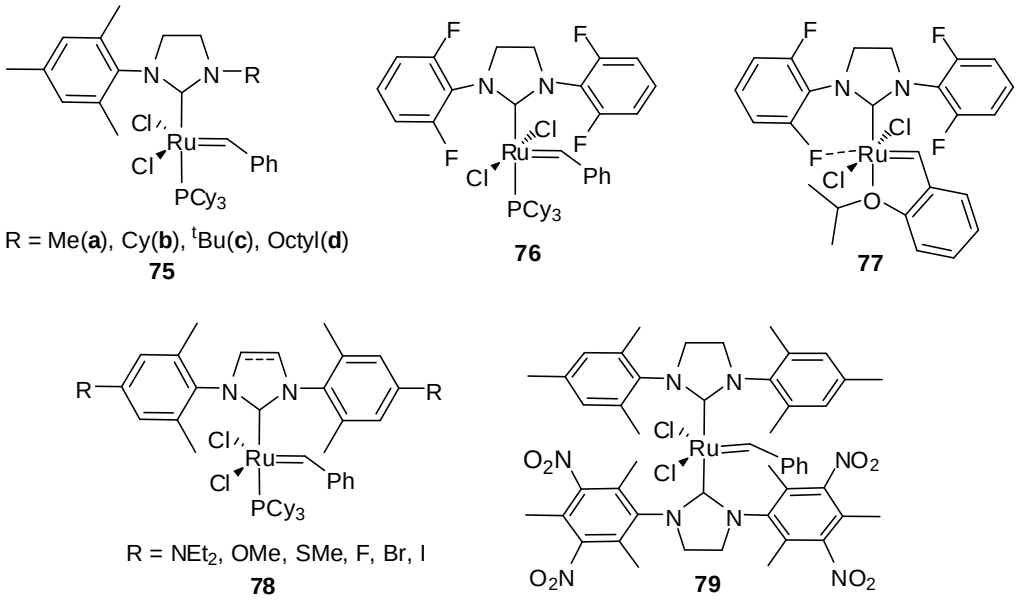
***Scheme 1.53*** *Unsymmetrical NHCs (**69**; **70**) and triazole-NHC (**71**)*

However, *Ledoux and coworkers* reported several Ru-unsymmetrical NHC systems containing different sterically hindered substituents.[145] Among these the least steric-bulk methyl-substituted catalyst showed higher reactivity compared to others. Recent reports on four and six-membered NHC systems from Grubbs's[146] and Buchmeiser's[147] groups had revealed no significant effect of ring size on catalysis.




***Scheme 1.54*** *Variation of ring-size of NHC*

Plenio and coworkers reported correlation between the effect of para-substitution of aromatic rings directly attached to N-atoms to the electron donation powers to the ruthenium center (**78**) and more explicitly the rate of metathesis.[148] More recently, another variation of *bis*-NHC-ruthenium-alkylidene complex (**79**) was found by Plenio and coworkers.[149] There were two different structural motifs of NHCs were coordinated trans to each other in the ruthenium center. These ruthenium pre-catalysts were highly active for metathesis reaction at higher temperature using strically demanding tetra-substituted olefins. Another interesting structural feature of NHCs was utilized by *Grubbs and coworkers* where ruthenium complexes of {bis1,3-(2,6-difluorophenyl)4,5-dihydroimidazole-2-ylidene} in *Grubbs II* (**76**) and *Hoveyda* type (**77**) catalysts showed different reactivity.[150]




***Scheme 1.55*** *Variation in aryl substituents in NHC*

The phosphine analogous Ru-complex was more reactive than conventional mesityl *Grubbs II* and *Hoveyda* catalysts. But the isopropoxystyrene congener of fluoro-derivative NHC showed slower reactivity due to Ru….F interaction caused by twisting of aromatic ring and thus slowed down the initiation rate of catalyst.

In general, NHC variations in the aryl rings could have beneficial effect on the reactivity in metathesis. However, research in this area is still now ongoing and future generations of NHC-based systems may play important role in producing highly active catalysts for multiple reactions.

# *2 Strategic Plans*

## *2.1 Strategy for Designing New N-Heterocyclic Carbene Ligands: C-C bond forming methodology*

Among the transition metal catalyzed carbon-carbon or carbon-hetero atoms bond formation reactions, palladium catalyzed cross-coupling and ruthenium catalyzed olefin metathesis reactions are two major classes of transformations which are nowadays extensively used both in the laboratory as well as in the industry. The rapid progress in these fields are also accelerated by the use of *N*-heterocyclic carbene ligands which enhance the activities as well as stabilities of the catalysts and making the scope of the catalysis even larger. Hence the rational design of NHC ligands is an important factor to introduce desired novel properties in new catalysts.

Palladium catalyzed coupling reactions, such as *Heck*, *Suzuki*, *Sonogashira* and *Hartwig-Buchwald* amination reactions are widely used synthetic methodologies. But the use of homogeneous catalysts is associated with several problems, such as the separation of catalysts and products after finishing the reaction. So in industry there is strong preference to heterogenize the homogeneous catalysts by solid support. Unfortunately, the synthesis of solid-supported catalysts is challenging and often results in the decreased efficiency of the catalyst. There is another possibility to use biphasic medium where products and catalysts reside in two different immiscible systems, usually in liquid medium. During the reactions, catalyst and reactant phases are brought together in contact by stirring or heating or sonication or using microwave etc. After completion of reaction the two phases are separated easily and catalysts phase can be reused as such or after regeneration of the catalysts. A variety of organic immiscible solvents have been used which include water, fluorous solvents, supercritical carbon-di-oxide and ionic liquids.

Water is a green, environmentally benign, safe solvent and an attractive alternative to traditional organic solvents because it is inexpensive, nontoxic, inflammable and environmentally sustainable. Water is unique due to its high structured nature enforced by intermolecular hydrogen bonding. Water can accelerate the organic reactions because of its hydrophobic effect.[151] Water is a Lewis base which accelerate the reaction of compounds having polar groups by solvation, ion-pair formation and dissociation. Reactions carried out in water provide the opportunity to finely tune the pH of the system which might cause the change in reactivity and selectivity of the system. After all, water can act as acid, base,

nucleophilic reagents and hydrogen source which might serve as a better convenient solvent than conventional system.

The most convenient approach to construct a catalyst into aqueous phase reaction has been to design ligands containing hydrophilic substituents. The hydrophilic functionality would cause sufficient solubility in water as well as provides necessary steric and electronic properties to give desired stability, activity and selectivity. Most commonly used ionic substituents are sulfonate, carboxylate, phosphate, ammonium etc. and examples of non-ionic hydrophilic substituents, such as polyols, carbohydrates and polyethers etc. A major challenge in aqueous phase catalysis is to increase the miscibility of water-soluble catalyst and reacting components together. If the reacting components are to some extent soluble in water, the reaction can occur in the bulk of the water through the interaction of water-soluble catalyst and dissolved substrates. For less soluble substrates the reaction rate will be decreased because of lower concentration in water. One approach to overcome this problem is to use water miscible organic cosolvents (i.e., alcohols, acetonitrile, DMF) to increase the solubility of hydrophobic substrates in water. Another approach is to use surfactants or phase transfer agents (cyclodextrins or calixarenes) by the formation of water soluble miscelles. Although the high water solubility of catalyst is desirable to facilitate the reaction in aqueous phase but the increased water solubility often leads to lower activity due to poor interaction of hydrophilic catalyst with hydrophobic substrates. Thus, there is an increased demand to obtain such type of catalysts which might keep balance between the reactivity and solubility in the aqueous phase and ultimately fulfill the desired goal.

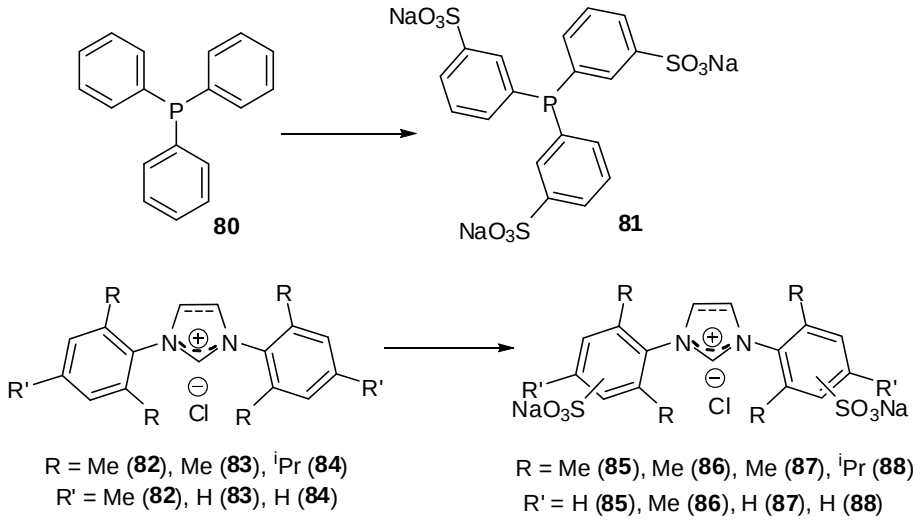
## *2.2 Design of Ligands and catalytic protocol*

The first and commonly used water solubilizing substituent is the sulfonate group. *Chatt* first reported the sulfonation of triphenylphosphine using 25% sulfur-tri-oxide ($SO_3$) in sulfuric acid ($H_2SO_4$) to the monosulfonated triphenylphosphine derivative (m-TPPMS) in modest yield.[152] The trisulfonated derivative, m-TPPTS was first prepared by *Kuntz* at Rhône-Poulenc from the reaction of triphenylphosphine in 20% oleum at 40 $^{o}$C for 24h followed by neutralization with sodium hydroxide (NaOH).[153] And the utilization of such water-soluble ligand was occurred in the rhodium catalyzed hydroformylation propene in industrial scale. Since that time there was an increasing demand to develop new catalysts as well as catalytic reactions in water. Among the recent work on cross-coupling reactions, Buchwald's group has developed sulfonated dialkyl(2-biphenyl)phosphine ligands for Suzuki-Miyaura and Sonogashira reactions.[154] The very recent work from our group showed that sterically demanding sulfonated 9-

fluorenyldialkyl-phosphines are excellent catalysts for Suzuki-Miyaura and Sonogashira coupling reactions in water.[155]

*Nolan and coworkers* reported the extensive studies on palladium catalyzed cross-coupling reactions using common NHC ligands, like 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidine and 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidine. Further studies from this group revealed that synthesis of Pd(allyl)NHC complex shows increased stability of precatalyst along with enhanced reactivity.[68, 73, 74]

In our laboratory we have designed, synthesized and developed a new class of sulfonated *N*-heterocyclic carbene ligands and their exploitation in cross-coupling catalysis, namely *Suzuki-Miyaura* and *Sonogashira* coupling reactions in water. These ligand systems are utilized as *in situ* generated catalysts by using sodium tetra-chloro-palladate ($Na_2PdCl_4$), a palladium source as well as isolated complex, such as palladium(allyl)NHC complex.




***Scheme 2.1*** *Introduction of sulfonate group to make water-soluble.*

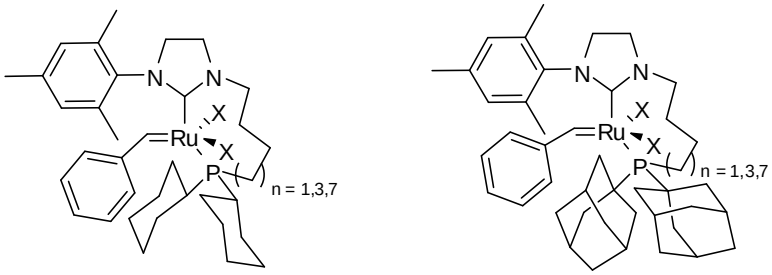
The *in situ* generated precatalyst from $Na_2PdCl_4$ and sulfonated-NHC shows higher reactivity towards *Suzuki-Miyaura* coupling reaction for the coupling of electron rich and sterically demanding chloro-aromatic substrates with aryl boronic acids only in water. Though the substrate chloroaromatic compounds are insoluble in water but the other component boronic acid is water soluble. At higher reaction temperature (90 to 100 $^{o}$C) both type of substrates and catalyst form homogeneous mixture. After formation of product the reaction mixture is cooled down at room temperature and product is separated out from the aqueous layer which is dissolved in some organic solvent and collected as almost pure product leaving the catalyst

remained in the aqueous phase. The palladium(allyl)NHC complexes are also highly active precatalysts for difficult substrates in water and alcohol mixed solvent system. In *Sonogashira* reaction only *in situ* generated catalyst system shows efficient reactivity. For all these systems product purification is the same and very simple compared to the conventional organic solvent system.

## *2.3 Strategy for designing pincer-type phosphine-tagged NHC ligands: C=C double-bond forming methodology*

The tremendous advances in carbon-carbon bond forming methodology is occurred mainly due to the enormous contributions from ruthenium catalyzed olefin metathesis reaction which is further boosted by the incorporation of *N*-heterocyclic carbene ligand instead of phosphine. In this C=C bond forming methodology, rearrangement of C=C double bonds is occurred in the ruthenium catalyst which ultimately leads to couple, cleave, ring-closing, ring-opening or polymerization. The *Grubbs first generation* catalyst is based on a ruthenium complex, surrounded by five ligands, namely two phosphines (*trans* to each other), two halides and one alkylidene moiety. In *Grubbs second generation* catalyst either of two phosphines is substituted by a better σ–donating *N*-heterocyclic carbene ligand which makes the other *trans*-phosphine ligand more labile. After the discovery in 1999, *Grubbs II* systems have rapidly evolved as a large family of ruthenium complexes by varying the steric and electronic properties of NHC ligands. The ruthenium-complex bearing one 1,3-bis(2,4,6-trimethyl-phenyl)imidazolin-2-ylidene trans to one tricyclohexylphosphine shows better stability and reactivity compared to other NHC-Ru-phosphine complexes. This catalyst system has been widely utilized to facilitate the new type of transformations and applications in synthesis of natural products and macromolecules and different types of polymers. Until now, several research groups have made a large contribution in the development and designing of *Grubbs II* type NHC-based ruthenium catalysts. From the mechanistic study of olefin metathesis, it is revealed that generation of low-coordinated, 14-electron ruthenium species is a catalytically active species. The faster the dissociation of phosphine or other ligand *trans* to NHC in ruthenium coordination sphere, the faster is the initiation of catalyst, i.e., higher is coordination with olefins and overall efficiency. Another thing, if the σ–donation from NHC is increased, higher will be the stabilization of 14-electron intermediate. Regeneration and recycling of catalyst depend upon the stability of labile dissociated ligand, such as phosphine which will recombine after the catalytic process is finished. In our laboratory, we have designed and trying to develop the phosphine tethered *N*-heterocyclic carbene ruthenium complexes where the coordination mode of two different donor functionalities could be tuned, so that catalytic activity and stability of the systems could be modulated. The ligand variation is made by using different functionalized phosphines which

are attached with flexible length of alkyl chain and contains one *N*-heterocyclic carbene at the other end. The better σ-donating NHC ligand might stabilize the ruthenium complex in precatalyst as well as active catalyst and consequently the loosely held phosphine such as alkyl-dicyclohexyl and alkyl-diadamantyl phosphine systems would dissociate faster to make room for substrate olefin in the catalytic cycle. By decreasing the alkyl-chain length it would be possible to disturb the *trans*-phosphine fashion to *cis*-coordination modes and thus affecting in the catalytic process.




X = Cl (**89**), I (**90**) X = Cl (**91**), I (**92**)

***Figure 1.1*** *Mode of attachment of Pincer type (P-C) ligands to Ru-center.*

In the tethered NHC ligands, alkyl chains used are decyl, hexyl and butyl and the chain length might cause the end-phosphine group to shift from *trans* to *cis*-coordinating mode at the ruthenium center and also give space for olefinic substrate at the *trans*-position. By designing such type of catalysts we hope to tune catalytic activity and simultaneously correlate the activity and stability with the structure of ruthenium complex.

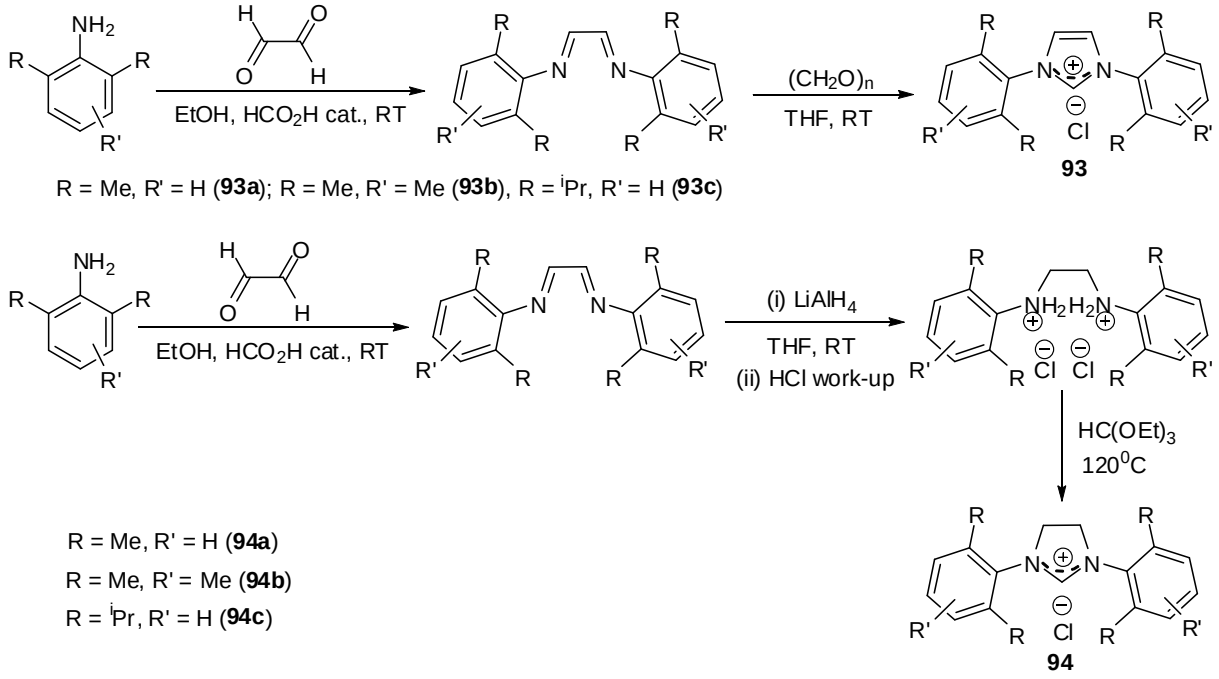
# 3 Results and Discussion

There are a large number of parameters in the *Suzuki-Miyaura* and *Sonogashira* coupling reactions, e.g., palladium source, ligands, additives, solvents, temperature etc. and correspondingly a large number of protocols to accomplish such transformations depending upon the structure of the reactants.

## *3.1 Synthesis of imidazolium/imidazolinium salts*

### *3.1.1 Convenient Route of Synthesis of Imidazolium and imidazolinium salts:*

The first step of the synthesis of imidazolium salt was condensation of two equivalents of aniline with one equivalent of glyoxal in slightly acidic medium to obtain a diimine. Next, diimine was reacted with paraformaldehyde in anhydrous acidic condition to obtain an imidazolium salt that is precipitated out from the reaction mixture. Next, for making imidazolinium salt the previous diimine was reduced with lithium aluminium hydride to obtain a diamine which was isolated as a salt using an acidic work-up of the reaction mixture. This diamine-salt was refluxed in triethylorthoformate ester to obtain imidazolinium salt. Following this method symmetrical imidazolium and imidazolinium salts could be obtained in good yield.

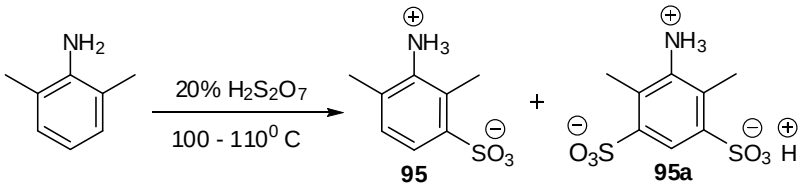



***Scheme 3.1*** *General synthetic route of Imidazolium and Imidazolinium salts.*

### *3.1.2 Synthesis of meta-sulfonated Aniline*

There were several procedures for the sulfonation of aniline in the literature depending upon the substitution on the aromatic ring as well as on the number of sulfonation groups to be introduced. Usually direct sulfonation by concentrated sulfuric acid and oleum (sulfur tri-oxide in $H_2SO_4$) and chlorosulfonic acid might cause oxidation of aniline which was avoided by using sulfonation under vacuum or inert atmosphere (argon). For the synthesis of *meta*-substituted 2,6-dimethyl-aniline 20 to 30% oleum was used and reaction mixture was heated up to 100 to 110 $^{o}$C under inert atmosphere. When it was cooled down to room temperature, anilinium-sulfonic acid was poured into water slowly to neutralize excess acid used, the product precipitated out. It was filtered off to collect anilinium sulfonic acid whose solubility in water is very little because of formation of zwitter ion.

The problem for the sulfonation reaction using either of concentrated sulfuric acid or oleum was to make selective substitution in the aromatic ring. It was always obtained as a mixture of *mono*-(**95**), di-*meta*-sulfonated products (**95a**) and those were very similar in physical properties. So it was not possible to separate the desired product from the mixture by simple method. Even after converting to sodium salts of sulfonated aniline, it was not possible to separate those two compounds. Moreover, neutralization of the reaction mixture was resulted the formation of a lot of soluble sodium salts, like sodium sulfate along with sulfonated aniline-salt. All these are water soluble which again created problem in the separation of desired product.

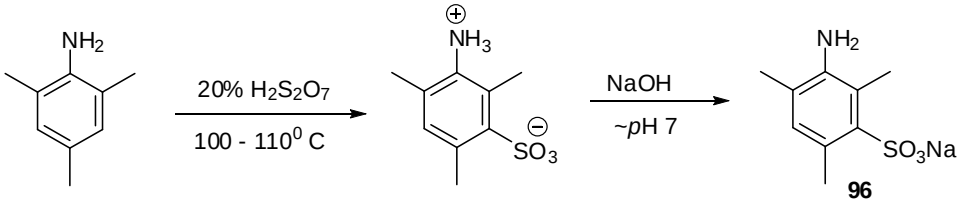



***Scheme 3.2*** *Sulfonation of 2,6-dimethylaniline*

This problem was overcome by slowly crystallizing the reaction mixture of aniline sulfonic acid from water over a longer period of time. During the course of time, aniline *mono-m*-sulfonic acid was only crystallized out as needle. This was neutralized to obtain pure *mono-m*-sulfonated aniline sodium salt. But the crystallization process was a very time-consuming process because of slow evaporation of water.

In order to avoid such type of double-sulfonation byproduct and also to form selective substitution at single *meta*-position, another methyl group was introduced at the *para*-position.

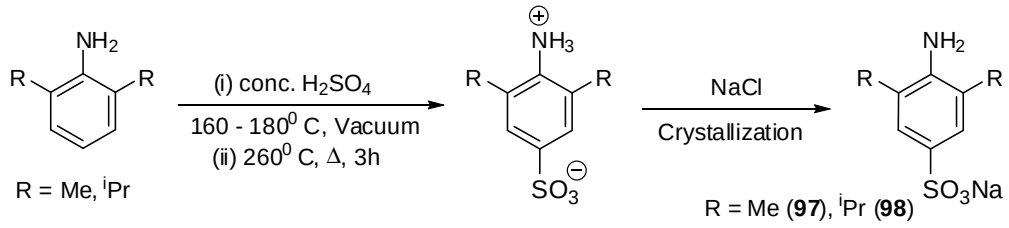
The same sulfonation procedure was repeated for 2,4,6-trimethylaniline and selectively mono meta-sulfonated aniline was recovered after finishing the work-up procedure.




***Scheme 3.3*** *Sulfonation of 2,4,6-trimethylaniline.*

## *3.1.3 Synthesis of para-sulfonated-Aniline*

The sulfonation reaction in aniline occurred mainly at *meta*-directing substitution, as in acidic solution aniline was converted as anilinium ion which was *meta*-directing in nature. So formation of *meta*-substitution was kinetically favorable process. In order to obtain the *para*-substituted product drastic condition was required. In concentrated sulfuric acid and small amount of water aniline was added and heated up to 180 $^{o}$C under vacuum to evaporate the water completely. Therefore, the reaction mixture was contained only sulfur-tri-oxide and aniline which might react at higher temperature 260 $^{o}$C for the complete conversion of para-sulfonated product (thermodynamically controlled product). This reaction condition was very important to obtain solely *para*-product. So, the complete evaporation of water from the sulfuric acid and aniline mixture was necessary condition to obtain pure $SO_3$ in order to accelerate the backing of aniline with $SO_3$ to obtain *para*-product. Otherwise, the baking process would not occur at all. 2,6-Dimethylaniline led to analogous *p*-sulfonated product which was slowly oxidized during the course of work-up and dark pink solution was formed. The use of activated charcoal and filtered off in hot condition was helpful for the purification of product. Sodium chloride was added and cooled to 0 $^{o}$C to isolate in crystallized form of *p*-sulfonated aniline sodium salt.

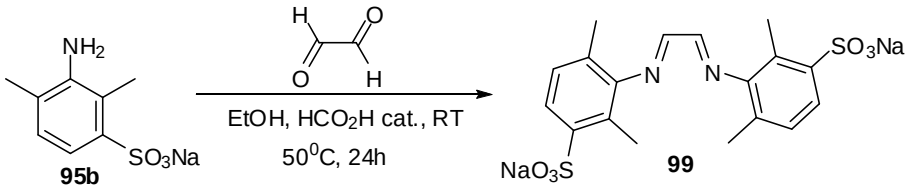



***Scheme 3.4*** *Para-selective sulfonation of 2,6-disubstituted anilines*

Sometimes the crystallization process took longer time. Then the compound might form more oxidized product in solution. To avoid crystallization process, anilinium sulfonic acid was neutralized with stoichiometric amount of sodium methoxide in anhydrous methanol. The 2,6-diisopropylaniline analogous was relatively stable and was possible to isolate by crystallization method in pure form.

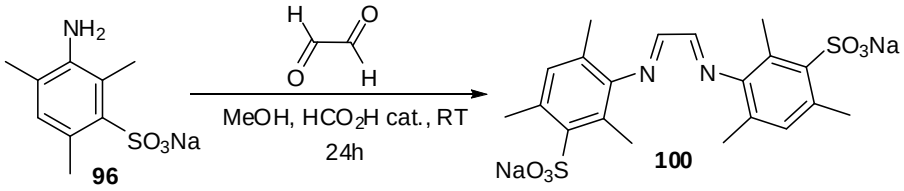
## *3.1.4* Synthesis of *meta*-sulfonated Diimines

According to the normal procedure, diimines (**99**) of *m*-sulfonated anilines were formed by reacting with aqueous 40% glyoxal (0.5 equivalents) in alcoholic solution in the presence of a catalytic amount of formic acid. For 2,6-dimethyl-3-sulfonated aniline a large amount of ethanol was required in order to obtain complete conversion because of the poor solubility of the starting aniline. Moreover, reaction at 50 $^{o}$C led to a better progress than at room temperature.




***Scheme 3.5*** *Synthesis of diimine from 2,6-dimethyl-3-sulfonated aniline*

However, this reaction always led to the formation of some unavoidable impurities. Even the formation of impurities could not be avoided using a complete anhydrous condition using 2,3-dihydroxy-1,4-dioxane was used as anhydrous adduct of glyoxal in inert atmosphere. The crystallization technique did not work as during the course of time starting material was precipitated out from the solvent. As the imine formation was a reversible reaction in which water would be eliminated, it could not be used as a solvent though the solubility of sulfonated anilines was a maximum in water. To overcome the solubility problem, tetra-*n*-butylammonium, lithium salts of sulfonated aniline were used. But this led to no improvement of product formation instead of making more complication in detecting the signals of the starting material and product separately in NMR spectra. By reacting with lithium hydroxide, sulfonated-lithium salt of aniline was not formed properly. In order to make diimine of 2,4,6-trimethyl-3-sulfonated aniline a methanolic solution and aqueous glyoxal were used to utilize greater solubility in methanol than ethanol. But again there was formation of unassignable impurities along with the product which were difficult to separate by commonly used method.

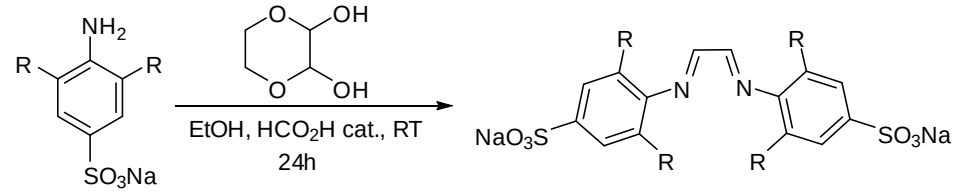



***Scheme 3.6*** *Synthesis of diimine from 2,4,6-trimethyl-3-sulfonated aniline*

The complete anhydrous condition using 2,3-dihydroxy dioxane led to no improvement in the purity of diimine formation. Although the starting materials were pure in nature as were obtained from crystallized form of sulfonic acid derivatives of aniline, the product formation did not show the pure product in either of the procedures. The role of solvent played more importance in both the sulfonated anilines. And the solubility of respective compounds in ethanol and methanol differed greatly so that the product formation was also affected.

## *3.1.5 Synthesis of p-Sulfonated Diimines*

The normal course of synthesis of diimine from *p*-sulfonated aniline by reacting with aqueous glyoxal was not fruitful because of the incomplete conversion of the product. The reason for incomplete conversion is the reversible nature of the reaction in which both starting materials and products were insoluble in ethanol and water mixture. Basically the imine formation was occurred by eliminating water molecule from reactants in slightly acidic media (*p*H ~ 4 to 6). In case of *p*-sulfonated aniline the equilibrium was much favored in the reverse direction which led to the incompleteness in the product formation and sometimes decomposition observed. The reaction was modified by using anhydrous glyoxal derivative like 2,3-dihydroxy-dioxane in anhydrous solvent in slightly acidic medium. The reaction proceeded smoothly by the formation of yellow precipitate of diimine product (**101**, **102**) and impure by-products remained in the solution.




R = Me (**97**), $^{i}$Pr (**98**)

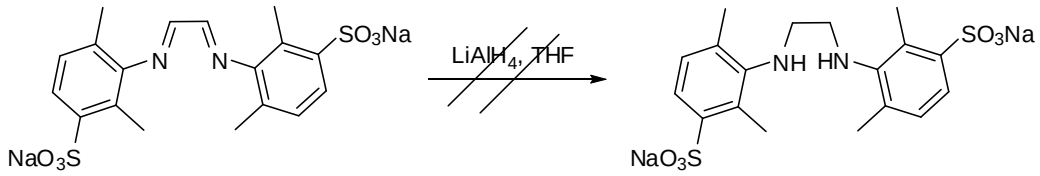
R = Me (**101**), $^{i}$Pr(**102**)

***Scheme 3.7*** *Synthesis of p-sulfonated diimines*

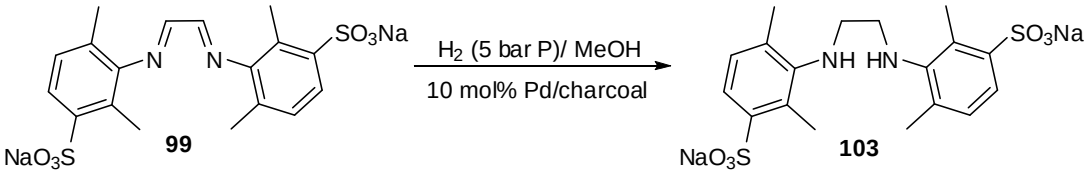
The product diimine formation was highly effective by following using dry solvent and the anhydrous derivative of glyoxal. The product obtained was reasonably pure product for both *p*-sulfonated derivatives of aniline.

### *3.1.6 Synthesis of meta-sulfonated Diamines*

The usual course of reduction of diimine with lithium aluminium hydride (LAH) led to the formation of incomplete conversion of product. The reason for that might be the poor solubility of the substrate in THF, a commonly used solvent for LAH reduction. Gratifyingly, the reduction with molecular hydrogen ($H_2$) with high pressures (5 to 7 bar) and palladium on charcoal as catalyst (10 mol %) led to the formation of the desired hydrogenated product (**103**). As diimine was getting hydrolyzed to the starting material aniline in the presence of little water, the use of dry methanol required to obtain full conversion of the product. The product diamine was preserved under inert atmosphere, as it was prone to oxidation, leading to a pink coloration.



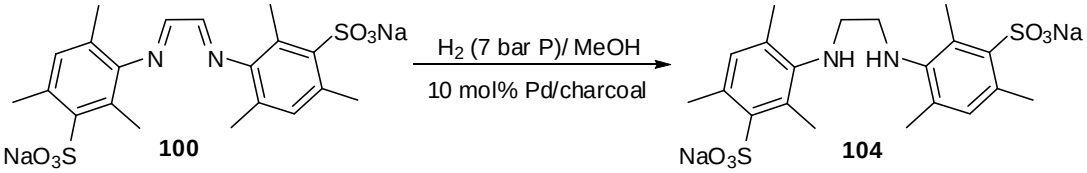

***Scheme 3.8*** *Problem in the synthesis of m-sulfonated diamines*




***Scheme 3.9*** *Synthesis of m-sulfonated diamines*

The formation of product diamine from diimine was not very pure. Because of impurities from the previous step in diimine was carried into the product diamine. By using different solvent, it was not possible to seperate out the impurity from the product. It was not suitable to crystallize the product as it was decomposed very easily. It was also not possible to convert diamine to the corresponding diammonium salts as in the presence of acid the sulfonated sodium salt could be converted to the sulfonic acid.

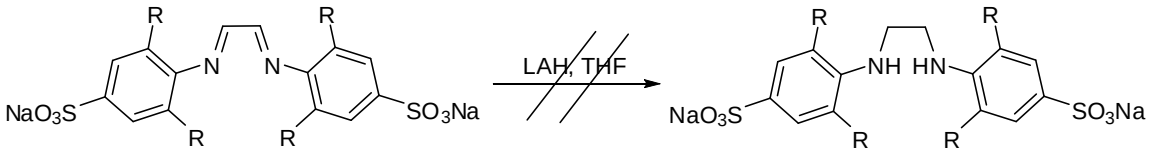
For the reduction of bis(2,4,6-trimethyl-3-sulfonatophenyl)diimine derivative with hydrogen in the presence of palladium/charcoal (10 mol %) catalyst led to the formation of diamine with difficulty. The product diamine always contaminated with starting diimine even using dry methanol as solvent. The longer reaction time (more than 8 h) was also unable to produce pure product. The problem might be associated with the very poor solubility of starting material as well as product. Another thing was sensitivity of the diamine towards moisture. The impurity in product diamine was also carried out from the previous step.



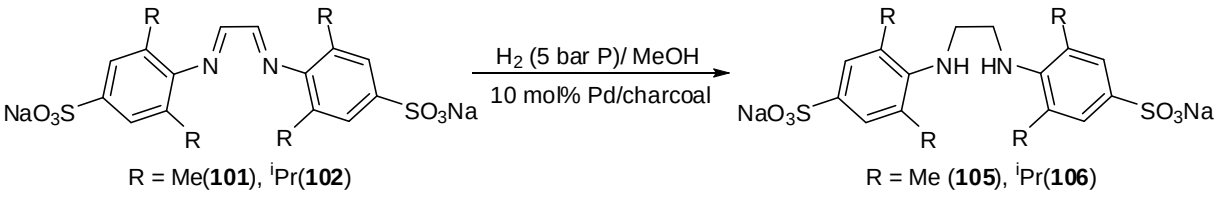

***Scheme 3.10*** *Synthesis of m-sulfonated diamines*

## *3.1.6 Synthesis of para-sulfonated Diamines*

The conventional method of diimine reduction using LAH did not give complete conversion to the desired *p*-sulfonated-diamine product. The problem was again poor solubility in THF which caused the less interaction between the reactants together. However, the desired product was formed using hydrogen in the presence of palladium catalyst and charcoal as activator, and the reaction was finished within few hours.




***Scheme 3.11*** *Problem in the synthesis of p-sulfonated diamines*

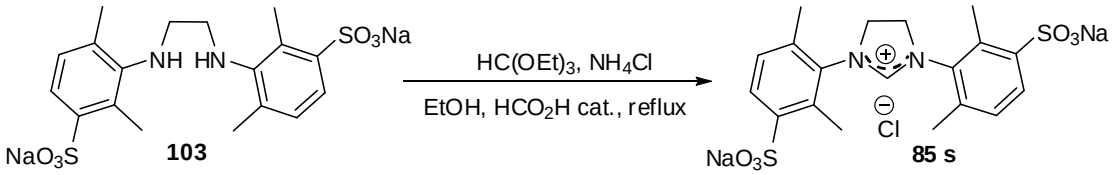



***Scheme 3.12*** *Synthesis of p-sulfonated diamines*

In this method *p*-sulfonated diamines were formed in relatively pure form. Another thing was during the course of work-up diamines become pinkish because of aerial oxidation. But the main problem for *p*-sulfonated derivative was water. Anhydrous solvent, such as dry methanol was used to follow the reaction. In the presence of water, there was always equilibrium between starting materials and obtained product. In this case, starting material anilines, diimines and product diamines were maintained the equilibria, so that the product diamines were not possible to obtain. The *iso*-propyl-derivatives showed better solubility than the methyl-analogue.

### *3.1.7 Synthesis of meta-sulfonated Imidazolinium salts*

According to the literature procedure, imidazolinium salts were obtained from the reaction of hydrochloride salts of diamines with triethylorthoformate or trimethylorthoformate ester under refluxing condition in the presence of a catalytic amount of formic acid. In case of sulfonated-diamines the main problem was to generate diammonium salts from diamines. The acid which was essential for making diammonium salts would react with the sulfonated-sodium salt to form sulfonic acid. So there would be an undesired mixture of sulfonic acid derivatives as well as sulfonated salt analogue. To overcome this problem a weak-basic salt, such as ammonium halide as additive was used in the course of the reaction. The reaction did not proceed at all when ammonium chloride in refluxing triethylorthoformate ester was used. The reaction mixture was only changed to a brown color suggesting a complete deterioration of the diamine. In general, the ring-closing reaction of diamine by using triethylorthoformate ester proceeded with the formation of ethanol as a by-product. Sometimes, it was needed to distill out by-product ethanol from the reaction-mixture in order to proceed in the forward direction. In this particular case, the equilibrium of the reaction was shifted smoothly towards forward direction by using ethanol as solvent along with the triethylorthoformate ester. The only reason was the better miscibility of the reactant components using polar solvent like ethanol.

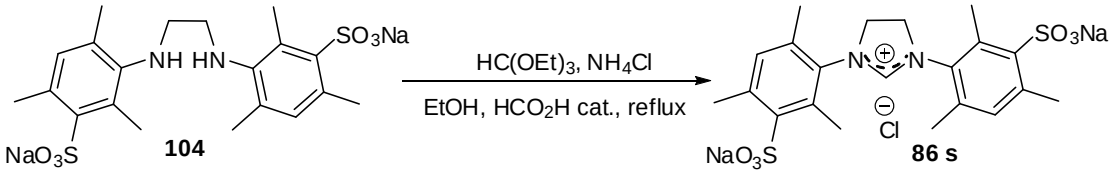



***Scheme 3.13*** *Synthesis of m-sulfonated imidazolinium salt*

The imidazolinium salt obtained in this procedure was sufficiently pure, except a trace amount of impurity carried out from diimine formation step. The imidazolinium salt was precipitated out from the reaction mixture and it was easily separated by simply doing filtration. This

reaction was earlier tried in MeOH and trimethylorthoformate ester as most of the rectants were showed better solubility in MeOH compared to ethanol. But it was difficult to isolate product by this method. Finally the product, imidazolinium salt was purified by using a reverse-phase (HP 20) column chromatography, using a mixture of methanol and water as eluant. After concentrating the elute solvent, it was possible to obtain pure imidazolinium salts as zwitter ionic species of mono-sodium sulfonated salt form. The product obtained by making column chromatography (HP 20) was highly pure but the yield was less.

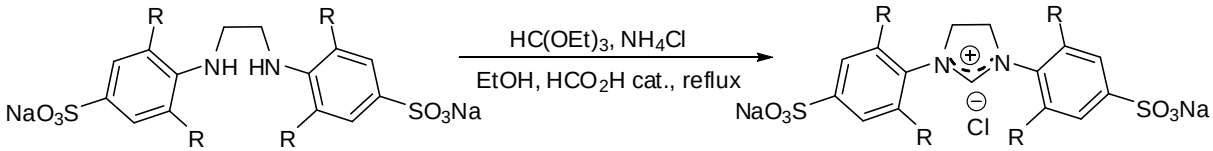
The above mentioned method for ring closing of diamine was used for 2,4,6-trimethyl-3-sulfonato-diamine analogous. In the presence of ethanol, triethylorthoformate ester and $NH_4Cl$ were used for ring closing of diamine. After formation of product, it was purified by using reverse phase column chromatography and water/methanol (7:3) as eluant.




***Scheme 3.14*** *Synthesis of m-sulfonated imidazolinium salt*

## *3.1.8 Synthesis of para-sulfonated Imidazolinium salts*

For the formation of *p*-sulfonated imidazolinium salts again the same problem was appeared similar to *m*-sulfonated derivatives. The problem was solved by following the previous method of ring closing reaction. The use of ethanol as solvent was really helpful in the conversion of product. The slight pinkish tinge of diamines went off immediately after the start of the reaction and a white product was precipitated out during the course of reaction.

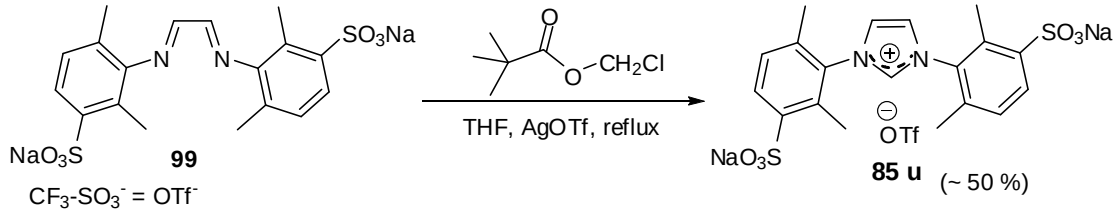



***Scheme 3.15*** *Synthesis of p-sulfonated imidazolinium salt*

The *p*-sulfonated imidazolinium salts produced by this method were sufficiently pure but one problem was that 2,6-dimethyl analogous was not sufficiently stable to preserve for longer time. There was no suitable explanation for the instability of the 2,6-dimethyl analogous.

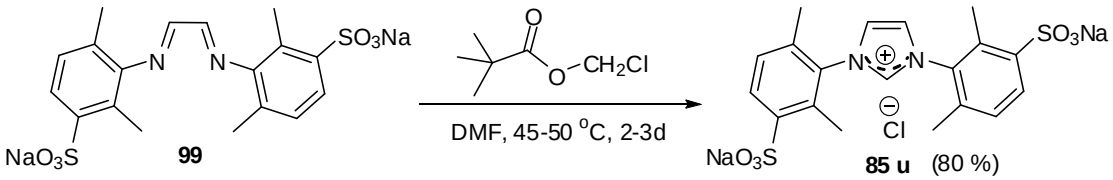
### *3.1.9 Synthesis of meta-sulfonated Imidazolium salts*

It was not possible to synthesize the imidazolium salt of *m*-sulfonated derivative from the respective diimine following the literature procedure of paraformaldehyde reaction in THF.[165] No desired product was formed in this method. As this reaction was carried out in acidic medium using 4 (M) HCl in dioxane, there was some decomposition of diimine observed, as sulfonated sodium salts became protonated. There was another report in the literature, where chloromethyl pivalate ester was used along with silver triflate in THF to isolate imidazolium triflate salt. The problem was again lower solubility of diimine in THF which caused incomplete the conversion. It was a maximum of 50 % conversion of product observed using a large amount of solvent (THF).




***Scheme 3.16*** *Synthesis of m-sulfonated imidazolium salt*

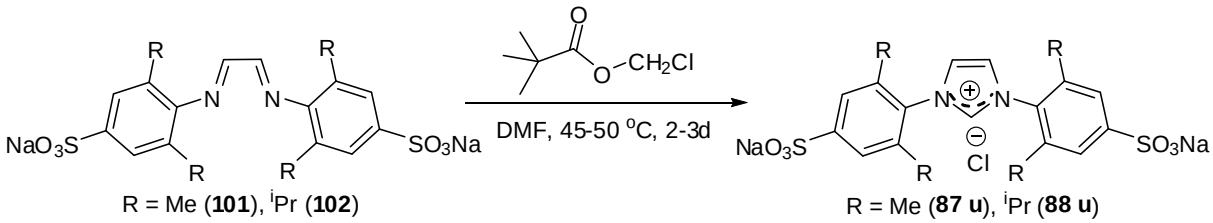
It was not possible to purify the diimines either of the any conventional methods. Next this reaction was tried in polar solvents, like ethanol or methanol. But no better result was observed except decomposition. Then the similar reaction of diimines with chloromethyl pivalate ester was tried in polar DMF solvent and was heated at 40 to 50 $^{o}$C for 2 to 3 days. The yellow color of diimine slowly changed to light brown color. The solvent was removed completely under vacuum to obtain off-white solid. The compound was purified either by using reverse phase column chromatography (HP 20) or by stirring over ethyl acetate for 3 to 5 times for a longer period of time.




***Scheme 3.17*** *Synthesis of m-sulfonated imidazolium salt (modified method)*

### *3.1.10 Synthesis of para-sulfonated Imidazolium salts*

The *p*-sulfonated imidazolium salts were obtained by following the same method like earlier. The appropriate diimines were reacted with chloromethyl pivalate ester in DMF around 40 to 50 $^{o}$C for 3 days. By this time color change occurred from yellow to light brown. After evaporation of solvent, products were purified like earlier.




***Scheme 3.18*** *Synthesis of p-sulfonated imidazolium salt*

The synthesis of imidazolium and imidazolinium salts from sulfonated anilines was time-consuming and difficult task. In every step, there was problem due to the solubility of the starting materials as well as product which might intervene in the further progress in catalysis. In large scale synthesis the problem would be more and the amount of impurity would be even higher. This was another disadvantage to follow such multi-step synthesis. Another thing, the use of reverse phase column chromatography was not much worthy as the yield was decreased drastically. To solve this problem the direct method of sulfonation of imidazolium and imidazolinium salts were introduced. In this method the unsubstituted imidazolium or imidazolinium salts were sulfonated by single step using chlorosulfonic acid and after completion of work-up procedure pure product was obtained.

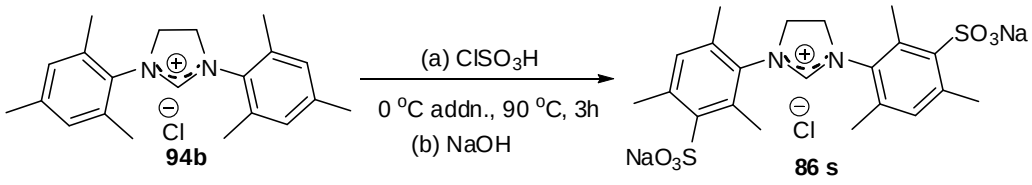
## *3.2 Direct method of Sulfonation of imidazoli(ni)um salts*

### *3.2.1 Synthesis of m-sulfonated-bis(2,4,6-trimethyl)imidazolinium chloride*

The direct method of synthesis of sulfonated imidazolium and imidazolinium salts was an easy access to obtain the pure sulfonated salts only by using a single step from the appropriate unsubstituted imidazolium or imidazolinium salts.

The reaction of 1,3-bis(2,4,6-trimethylphenyl)imidazolinium chloride in neat chloro-sulfonic acid at 100 to 110 $^{o}$C was resulted in the formation of 1,3-bis(2,4,6-trimethyl-3-chlorosulfonyl-phenyl) imidazolinium chloride which was hydrolysed in ice at -20 $^{o}$C followed by filtration and washing with ice-cold water. Then it was evaporated *in vacuo* to remove water. During this time the solid was usually converted to sulfonic acid derivative at room temperature. After

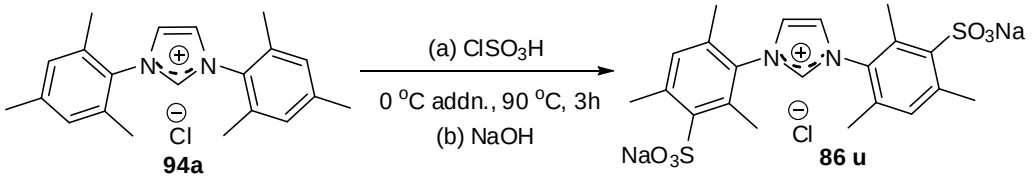
neutralization with NaOH and followed by heating at 50 to 60 $^{o}$C the desired sulfonated imidazolinium chloride (**86 s**) was obtained.




***Scheme 3.19*** *Synthesis of m-sulfonated imidazolinium salt*

## *3.2.2 Synthesis of m-sulfonated-bis(2,4,6-trimethyl)imidazolium chloride*

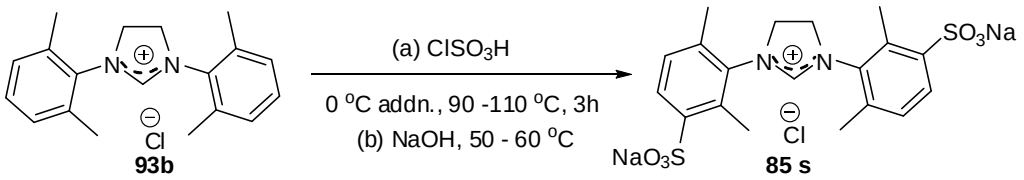
The mixture of 1,3-bis(2,4,6-trimethylphenyl)imidazolium chloride and chloro-sulfonic acid was heated up to 90 $^{o}$C to obtain the sulfonyl chloride derivative of the corresponding imidazolium salt which after ice-water work-up at -20 $^{o}$C and neutralization with sodium hydroxide followed by heating at 50 to 60 $^{o}$C resulted in the formation of sulfonated imidazolium salt.




***Scheme 3.20*** *Synthesis of m-sulfonated imidazolium salt*

## *3.2.3 Synthesis of meta-sulfonated-bis(2,6-dimethyl)Imidazolinium chloride*

The direct sulfonation of 1,3-bis(2,6-dimethylphenyl)imidazolinium chloride in neat chloro-sulfonic acid at high temperature at 100 to 110 $^{o}$C resulted in the formation of the corresponding meta-chlorosulfonyl derivative. After hydrolysis of chlorosulfonic acid at low temperature (-20 $^{o}$C, using ice-water bath), it was filtered to obtain as a white solid. It was converted to sulfonic acid derivative when slowly warm up to room temperature. Afterwards, acid was neutralized with NaOH and heated for sometimes at a given temperature.

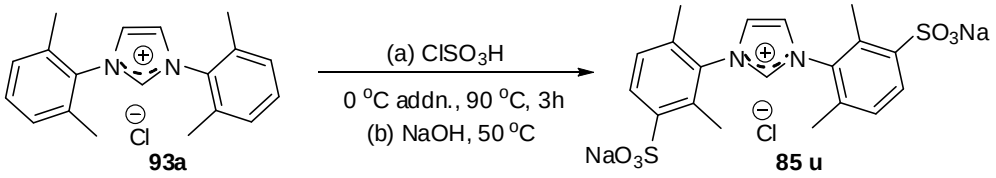



***Scheme 3.21*** *Synthesis of m-sulfonated imidazolinium salt*

By following this method, the pure sulfonated derivatives were obtained. The removal of acid from sulfonic acid derivative of imidazolium and imidazolinium salts was easier. It was stirred 4 to 5 times with ethyl acetate for longer time (usually 5 to 6 h every time) to get rid off rest of the acid remaining in the sulfonic acid derivatives.

### *3.2.4 Synthesis of meta-sulfonated-bis(2,6-dimethyl)Imidazolium chloride*

The meta-sulfonated derivative of 2,6-dimethyl imidazolium chloride was obtained by following the previous method. In this case reaction condition was much easier and chloro-sulfonation occurred at 90 $^{o}$C within 30 min. and the product was formed in almost pure form.



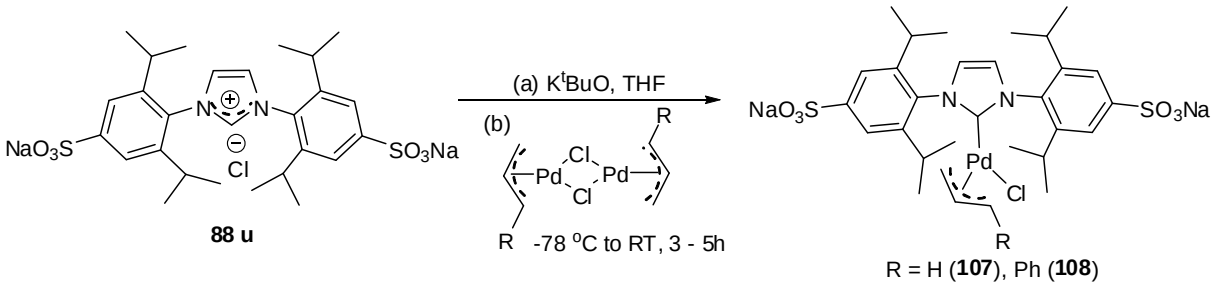

***Scheme 3.22*** *Synthesis of m-sulfonated imidazolium salt*

However, the direct sulfonation method has several limitations. First of all, this sulfonation method was not selective for 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride and 1,3-bis(2,6-diisopropylphenyl)imidazolinium chloride. Another thing drastic condition was used. The reaction work-up and purification process was quiet tricky due to the presence of an excess of unreacted chlorosulfonic acid. In the work-up process, hydrolysis at -20 $^{o}$C and afterwards usually sulfonyl chloride derivatives of the corresponding imidazolium or imidazolinium chlorides were formed. But during the separation and filtration process at room-temperature, it was converted to the sulfonic acid derivatives. The sulfonic acid derivatives were easily purified by stirring several portions of ethyl acetate for longer time. After complete removal of acid, it was neutralized with aqueous dilute sodium hydroxide solution at 50 to 60 $^{o}$C. For the sulfonation of 1,3-bis-(2,6-diisopropylphenyl)imidazole(ni)um the sulfonation reaction yielded a mixture of possible combination of *meta*- and *para*-sulfonated derivatives of the analogous compounds. Afterwards, it was impossible to separate each other from the mixture of compounds by using usual technique. The problem was that the sulfonated compounds have similar properties. So common technique like column chromatography, even using reverse-phase column chromatography, it was not possible to purify the particular sulfonated product from the mixture.

## *3.3 Palladium-π-allyl(NHC) complexes*

### *3.3.1 Palladium-π-allyl complexes of sulfonated N-heterocyclic Carbene*

The palladium(allyl)NHC complexes of imidazolium salts were of a great importance as they were highly reactive, easy to synthesize and stable towards air and moisture. The most convenient method of synthesis of such complexes were deprotonation of imidazolium salts using potassium *tert*-butoxide or sodium *tert*-pentylate in THF followed by addition of allyl-palladium chloride dimer. The reaction mixture was stirred for 4 to 5 h to obtain complete conversion of the product. The work-up was done by dissolving in degassed methanol and filtered under argon through celite to remove inorganic salts as by-products. The simple allyl-Pd-NHC complexes were not so stable and could not be stored for longer time as they were slowly decomposed (within one week). The solution of simple allyl-palladium complexes was decomposed within few hours as revealed from NMR study using degassed deuterated solvent. The (phenyl-allyl)Pd analogous complexes were stable enough to store even under ordinary condition and without exclusion of air. All these complexes in solution were not very stable. In normal organic solvents like dichloromethane, diethyl ether etc., the complexes decomposed into starting NHC salt and unknown palladium rest.




***Scheme 3.23*** *Synthesis of palladium π-allyl-NHC complexes*

## *3.4 Catalytic Study: Palladium catalyzed Cross-coupling Reactions*

Palladium catalyzed cross-coupling reactions are very important methodologies for the formation of carbon-carbon (C-C) and carbon-heteroatom (C-N, C-O, C-S etc.) bonds. Among the various cross-coupling reactions *Suzuki-Miyaura* coupling reaction and *Sonogashira* reaction played major roles because of the versatility and easy accessibility and wide applicability of these protocols. These two reactions were studied here in the light of sulfonated *N*-heterocyclic carbene ligands either as *in situ* generated palladium catalytic systems or isolated palladium-

(allyl)NHC systems. The individuality of these reaction protocols were based on their applicability in eco-friendly, environmentally benign and greener aqueous system. The reaction conditions were mild and products were easily separated by extracting with some organic solvents and the catalyst remained in the aqueous layer which could be recycled further.

## *3.5 Suzuki-Miyaura Coupling reaction*

It was worthy to study the reactivity of *in situ* generated catalyst from sulfonated NHC in combination with sodium tetra-chloropalladate in water for *Suzuki-Miyaura* (*SM*) coupling reaction. The study of *SM* coupling reactions was elaborated on the variation of substrate scope, compatibility with functional groups and low catalyst loading in aqueous media.

### *3.5.1 Substrate Scope*

Aryl halides and aryl/alkyl boronic acids are two important components in the SM cross-coupling reactions. The use of aryl iodides, bromides and tosylates were common in cross-coupling reactions whereas the use of aryl chlorides and fluorides were uncommon. The reactivity of haloarenes followed the order ArI> ArBr> ArCl> ArF, which was consistent with the bond strength of the respective halides. From the literature, it was found that bond dissociation energy of Ar-X bonds are 65, 81, 96, 126 Kcal $mol^{-1}$ at 298 K for iodide to fluoride respectively.[156] Thus the initiation of catalysis, the oxidative addition process in which aryl-halogen bond cleavage occurred was highly dependent on the bond strength. The stronger the bond, the lesser was initiation rate and poorer the catalytic activity. Unfortunately, the more reactive iodo-and bromo-arenes are more expensive whereas fluorides are both costly and inactive. Thus aryl chlorides are most attractive for synthetic applicability as they are inexpensive and readily available in bulk quantities.

### *3.5.2 Nature of Aromatic ring*

It was well-known that aryl halides having electron-withdrawing groups gave higher rates of oxidative addition than those containing electron-donating groups. The presence of electron-withdrawing groups made the aryl-halide bond more electron-deficient and more susceptible to oxidative addition. The stronger carbon-halide bond resulted in larger energy barriers in the oxidative addition. It was observed that when electron-withdrawing substituents were present on the aryl bromides, the oxidative addition process became approximately 100 times more

reactive than aryl chloride analogue and the electron-donating groups made the difference in reactivity by a factor in between 2 and 3.[156]

### *3.5.3 Nature of Boronic acid*

The introduction of electron-donating group in the *ortho* or *para* position of an arylboronic acid increased the nucleophilicity of the carbon atom connected to the boron atom, while an electron-withdrawing group in the same position decreased the nucleophilicity. Comparably, an electron-donating group in the *meta* position of an arylboronic acid decreased the nucleophilicity. The stronger the nucleophilicity the more active is the arylboronic acid.

### *3.5.4 Reaction Condition*

The *SM* reaction can be carried out using various catalysts, bases, solvents and their combinations might affect significantly in the yield and selectivity of the product formation.

### *3.5.5 Catalyst Scope (In situ generated vs. Isolated Pd-complex)*

There were several new *N*-heterocyclic carbene ligands designed and synthesized to obtain highly efficient and selective catalysts in order to expand the scope of the reaction. The reactivity of ligands was directly correlated on the efficiency in generating and stabilizing the catalytically active palladium(0) species, as the stoichiometry of ligand to palladium and the bulkiness or donating ability of ligands might change the reactivity of the catalysts towards oxidative addition, transmetalation, and reductive elimination.

### *3.5.6 Nature of Ancillary Ligands*

The σ-donor ligands attached to the metal facilitated the oxidative addition step and π-acceptors tend to reduce or suppress the process. The electron richness of ancillary ligands (phosphines, NHCs) might facilitate the oxidative addition of the aryl-halide bond to active Pd(0) species and the steric demand of ligands might favor ligand dissociation to afford an active mono-ligated-Pd(0) species. The steric bulk of the ligand in the catalyst enhanced the rate of the reductive elimination.

### *3.5.7 Effect of Bases*

The addition of bases played an important role in *Suzuki-Miyaura* coupling reaction. It was believed that the bases help to accelerate the rate of transmetalation between aryl-palladium-

halides ($Ar^1$-Pd-X) and oraganoboronic acid or trialkylboranes. The quarternization of boranes or boronic acid by negatively charged base enhanced the nucleophilicity of organic residue on boron and thus activating arylation/alklation of $Ar^1$-Pd-X. The *p*Ka of phenylboronic acid is 8.8, whereas the aryl/ alkylboronate species $[Ar^2B(OH)_3]^-$ was formed at *p*H over 9. Indeed, there would be always equilibrium between boronic acid and boronate species depending upon the concentration of bases. It should also be noted that higher concentration of bases (*p*H over 11) strongly retarded the reaction.

### *3.5.8 Effect of Solvents*

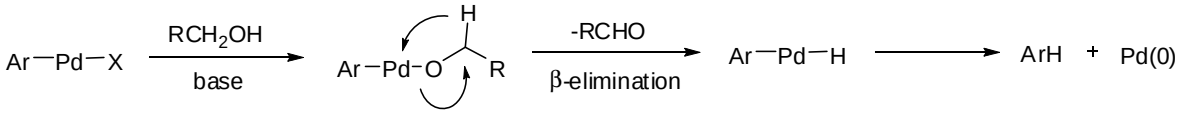
The cross-coupling reactions of organoboronic acids with organic halides require the presence of a negatively charged nucleophilic base which could easily be obtained in the presence of water. The rate of formation of aryl/ alkyl-boronate species was accelerated by the use of hydrated inorganic bases, preferably in the presence of water. Another fact was the facile dehydration of organoboronic acids led to formation of boroxine derivatives with the elimination of water. On the other hand, the reaction would not be completed under strictly anhydrous conditions. The reaction under aqueous conditions sometimes produced undesired product due to competitive hydrolytic B-C bond cleavage. Such type of cleavage was even more accelerated in the presence of *ortho*-substituents, and significant in hetero-aryl boronic acids.

### *3.5.9 Effect of Reaction Temperature/Time/Other factors*

There was a tremendous effect of temperature on the reactivity of precatalyst. To generate the catalytically active palladium(0) species in *Suzuki-Miyaura* coupling reactions thermal or photochemical energy was required. The most convenient way to obtain that was to use thermal agitation of the reaction mixture. Another thing was the stabilization of catalytically active species which would also be a temperature dependent parameter.

To obtain the maximum efficiency of the catalysts, reaction time was also an important factor in combination with temperature and other factors. The reaction condition should be strictly maintained oxygen-free inert atmosphere, as arylboronic acids were coupled to give homo-coupling product. In neutral condition, the formation of homo-coupling product was slow, but is rapid in the presence of an aqueous base.

The cross-coupling reactions often resulted in dehalogenation of aryl halides, particularly when alcohol was used as a solvent. The Pd-hydride species was generated from the β-hydride elimination of Ar-Pd-$OCH_2R$, yielding Ar-Pd-H and RCHO. This type of side reaction might be observed in the reactions of arylboronic esters.



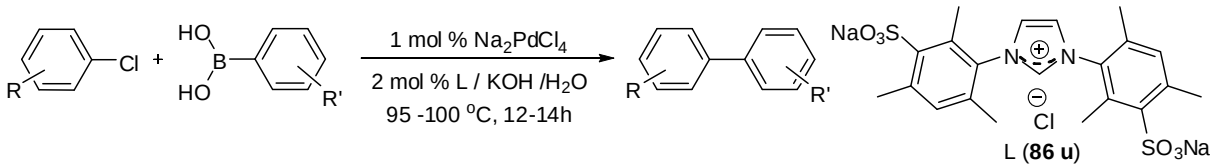

***Scheme 3.24*** *Dehalogenation of aryl halides*

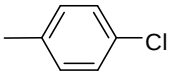
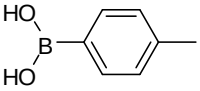
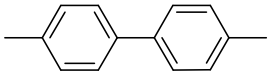
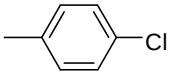
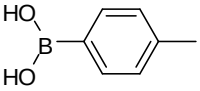
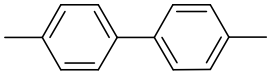
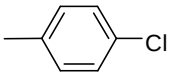
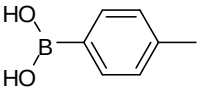
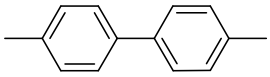
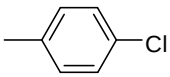
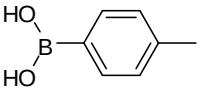
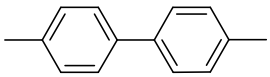
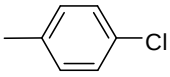
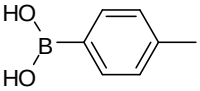
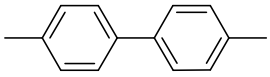
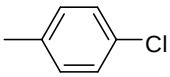
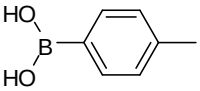
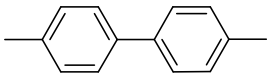
## *3.5.10 Catalytic Studies in Water (in situ generated catalysis)*

The main objective of the present work was to study the effect of sulfonated-*N*-heterocyclic carbene ligands in *Suzuki-Miyaura* coupling reaction in the form of *in situ* generated catalyst, using sodium tetra-chloro-palladate as palladium precursor in water. The metal-ligand stoichiometry played a crucial role to the *in situ* generated catalytic system. The precatalyst formation and afterwards active catalyst generation were highly dependent on the metal to ligand ratio. It was observed that metal to ligand ratio 1:2 showed highly effective catalyst compared to 1:1 and 1:3 ratios. On the basis of above fact it was assumed that the formation of catalytically active Pd(0) species might possess two NHC ligands in its coordination sphere which would oxidatively add to aryl chloride. Another thing was the formation of bis-NHC-Pd complex that was generated with the assistance of base as it was indicated from the study of concentration dependence of base. It might happen that in basic aqueous medium the dissociation of chloride and generation of carbene was easier.

To find a suitable base for *SM* coupling reaction was an important matter in water catalysis protocol. Firstly, the formation of low-coordinated catalytically active Pd(0) species could be obtained by ligand displacement through the nucleophilic attack of bases and secondly the nucleophilicity of boronic acid was enhanced by adding bases. Several bases, such as cesium carbonate, potassium carbonate, sodium carbonate, potassium phosphate, potassium hydroxide etc. were used for catalysis protocol in water. All these bases did not show greater reactivity than potassium hydroxide itself. For most of the bases around 15 to 20 % conversion was observed. There was no cesium effect observed in such type of sulfonated-NHC catalyzed cross-coupling protocol. The higher conversion was also observed for potassium and sodium carbonate (50 to 80 %) bases. But the excellent reactivity was observed for using certain equivalents (3 equivalents) of potassium hydroxide. There was a good correlation observed between the equivalents of base used to the conversion of product. The following table indicated such type of correlation study. It was observed that in our catalystic condition certain amount (3 equivalents) of KOH gave optimum result and by decreasing and increasing the concentration gradual decrease of product formation observed.

***Table 3.1*** *Suzuki-Miyaura coupling of aryl chlorides with tolylboronic acid: effect of KOH*




| Entry | Aryl Chloride | Boronic acid | Product | Base (Equivalent) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 1.5 | 11 |
| 2 |  |  |  | 2.0 | 38 |
| 3 |  |  |  | 2.5 | 83 |
| 4 |  |  |  | 3.0 | ≥99 |
| 5 |  |  |  | 3.5 | 85 |
| 6 |  |  |  | 4.0 | 74 |

*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

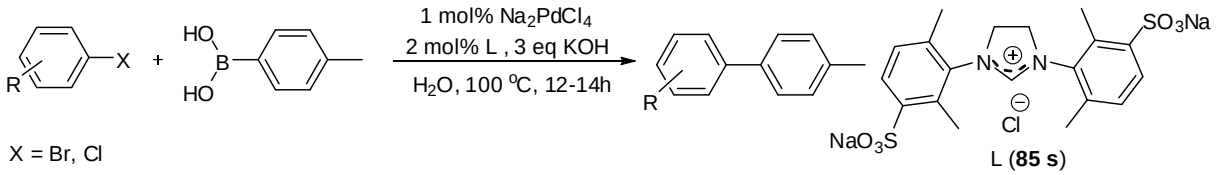
In water catalysis the main problem was the miscibility of substrates and catalyst. Among the palladium precursors, sodium *tetra*-chloro-palladate and palladium acetate were more soluble in water, but the use of sodium *tetra*-chloro-palladate was more cost-effective. The solubility of sulfonated NHCs was moderate. But when water was heated up, two equivalents of sulfonated-NHCs and one equivalent palladium resulted in the formation of water soluble bi-coordinated NHC-Pd complex *in situ* which might play crucial role to generate the catalytically active Pd(0) species and initiation of the catalytic cycle. It was not possible to characterize such type of

active catalyst or precatalyst by simple NMR technique because of the high sensitivity towards oxygen and solubility in water at room temperature and also other experimental restrictions. When this *in situ* generated catalyst was added to the reaction mixture of substrate components in basic aqueous media, the initiation did not occur. Again there was a problem associated with solubility. When reaction mixture was heated at the boiling point of water in a sealed schlenk tube, formation of the active catalyst was occurred and also catalytic cycle initiated due to better solubility of aryl halides at this temperature. The effect of temperature was crucial as it affected the yield of product formation as well as the rate of conversion of the product. The product formation was drastically decreased at 80 $^{o}$C or at even lower temperature. There was not much improvement of rate of conversion observed at even longer period of time at lower temp (80 $^{o}$C or below). The main problem in water catalysis was to generate catalytically active Pd(0) species which demanded high activation energy.

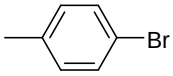
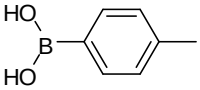
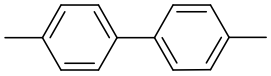
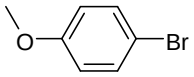
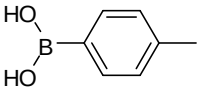
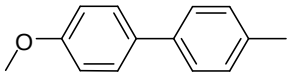
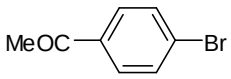
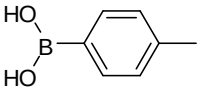
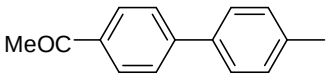
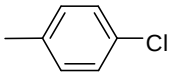
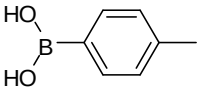
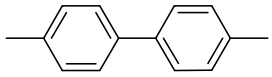
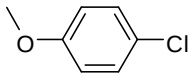
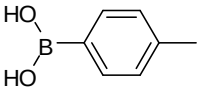
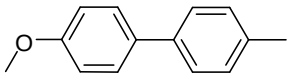
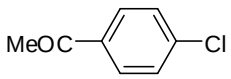
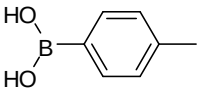
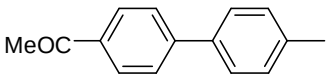
The reaction protocol was very simple. The catalyst was prepared from one equivalent of palladium precursor and two equivalents of NHCs, heated in degassed water in the presence of excess (almost 10 equivalents) base, KOH at 50 to 60 $^{o}$C for 2 h. This catalyst stock solution was used in the next step for *SM* screening reaction for coupling of aryl boronic (1.1 equivalents) with various electron-rich and electron-deficient aryl chlorides.

At first the screening reaction was made to test the catalytic activity of saturated NHC system, i.e., 1,3-bis(2,6-dimethyl-3-sulfonatophenyl)imidazolinium chloride (**85 s**) in combination with sodium tetra-chloropalladate in simple water. The reactivity for bromo-substituents was expectedly excellent. Only few substrates 4-bromoanisole, 4-bromotoluene and 4-bromoacetophenone were studied and full conversion was observed. Next the reactivity of such system towards electron rich chloro aromatic substrates was studied. Almost full conversion was observed for 4-chloroacetophenone, 4-chlorotoluene and 4-chloroanisole. But the conversion was drastically reduced with lowering the catalyst loading.

***Table 3.2*** *Suzuki-Miyaura coupling of aryl chlorides with tolylboronic acid: substrate scope*



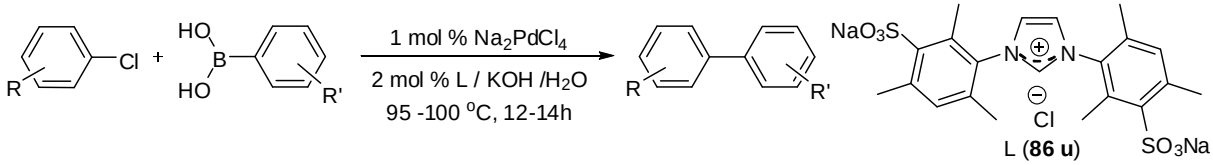

| Entry | Aryl Halide | Boronic acid | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|

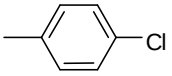
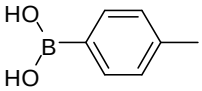
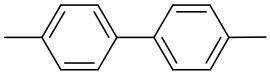
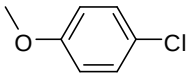
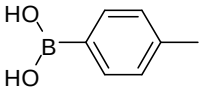
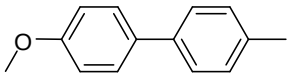
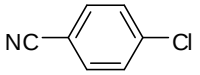
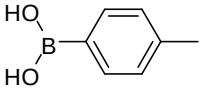
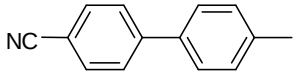
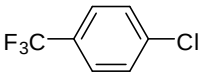
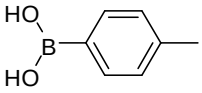
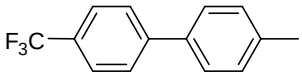
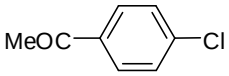
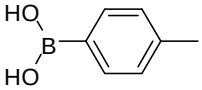
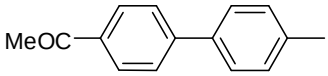
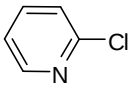
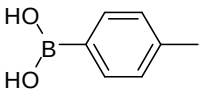
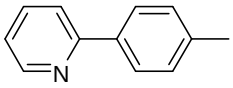
| | | | | | |
|---|---|---|---|---|---|
| 1 |  |  |  | 1.0 | ≥99 |
| 2 |  |  |  | 1.0 | ≥99 |
| 3 |  |  |  | 1.0 | ≥99 |
| 4 |  |  |  | 1.0 | ≥99 |
| 5 |  |  |  | 1.0 | ≥99 |
| 6 |  |  |  | 1.0 | ≥99 |

*Best of two runs: the conversion determined *via* GC using an internal heptadecane standard.

Next the screening experiment was carried out using 1,3-bis(m-sodiumsulfonated-2,4,6-trimethylphenyl)imidazolium chloride (**86 u**) as the ligand and $Na_2PdCl_4$ as the palladium source. The coupling of 4-tolylboronic acid with different aryl halides, such as 4-tolylchloride, 4-anisole, 4-cyano-chlorobenzene, 4-chloro-benzotrifluoride, 4-chloro-acetophenone, 2-chloropyridine etc. resulted complete conversion to respective biaryls at 95 to 100 $^{o}$C using this system. The following table represented the observed data for the formation of biaryls using the *in situ* generated catalyst. The electron-rich to electron-poor all chloroarenes gave complete conversion to the corresponding biaryl products with 1 mol % catalyst loading. Further decrease in the catalyst loading led to the lower conversion of the product. In all these substrates there was no significant amount of homo-coupling product was observed.

***Table 3.3*** *Suzuki-Miyaura coupling of aryl chlorides with tolylboronic acid: substrate scope*

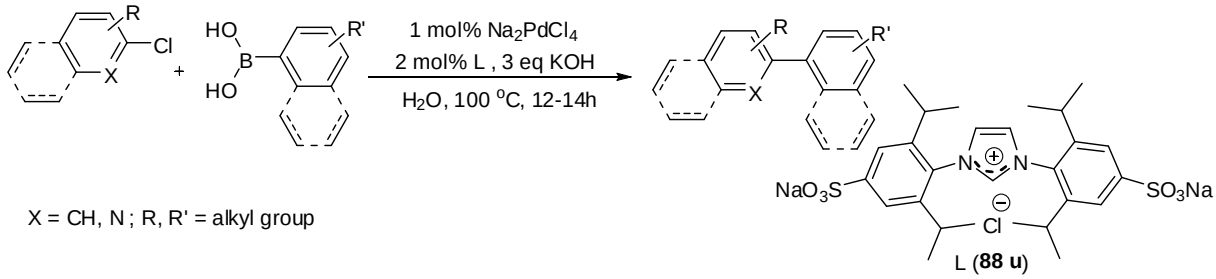


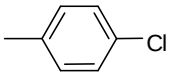
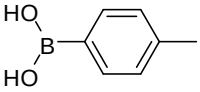
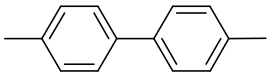
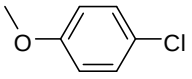
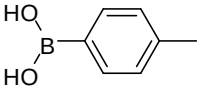
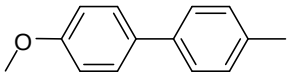
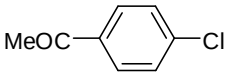
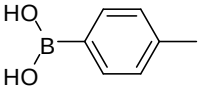
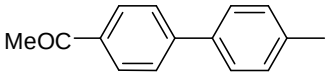
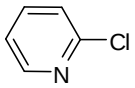
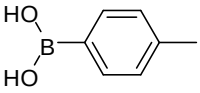
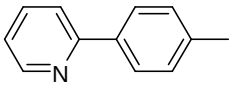
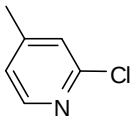
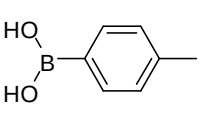
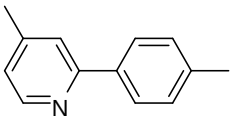
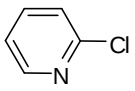
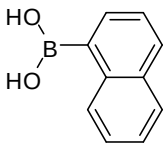
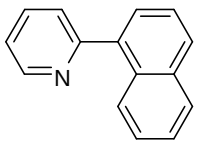
| Entry | Aryl Chloride | Boronic acid | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 1.0<br>0.5<br>0.1 | ≥99<br>84<br>40 |
| 2 |  |  |  | 1.0<br>0.1 | ≥99<br>70 |
| 3 |  |  |  | 1.0 | ≥99 |
| 4 |  |  |  | 1.0 | ≥99 |
| 5 |  |  |  | 0.1 | ≥99 |
| 6 |  |  |  | 1.0<br>0.1 | ≥99<br>59 |

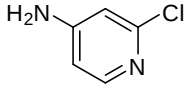
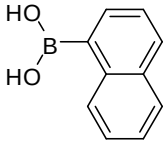
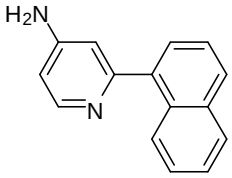
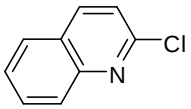
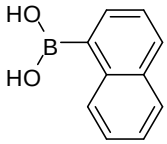
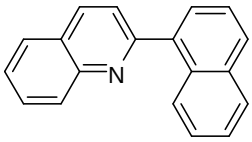
*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

It was obvious from the two types of closely similar ligand systems that reactivity and reproducibility of unsaturated sulfonated NHC system showed better effects in product formation. Therefore, next emphasis of the biaryl formation was focused on the unsaturated 1,3-bis(2,6-diisopropyl-4-sodiumsulfonato-phenyl)imidazolium chloride (**88 u**) as an ancillary ligand for the *in situ* catalyst generation. For electron-rich substrates, like 4-chlorotoluene, 4-chloroanisole, the excellent to good conversion of coupled product was obtained using 1 mol% catalyst loading or less (0.1 mol%).[167] By using other heteroaryl substrates, such as 2-chloropyridine, 4-methyl-2-chloropyridine, chloro-quinoline, 4-amino-2-chloropyridine etc. the cross-coupling reaction of tolyl- and naphthyl boronic acids was easily accomplished using a very minute amount of catalyst (0.1 to 0.5 mol%) in water.

***Table 3.4*** *SM coupling of hetero-aryl chlorides with tolyl- and naphthyl-boronic acid: substrate scope*




| Entry | Aryl Chloride | Boronic acid | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 1.0<br>0.1 | ≥99<br>89 |
| 2 |  |  |  | 1.0<br>0.1 | ≥99<br>74 |
| 3 |  |  |  | 0.1 | ≥99 |
| 4 |  |  |  | 0.1 | ≥99 |
| 5 |  |  |  | 1.0 | ≥99 |
| 6 |  |  |  | 0.5 | ≥99 |

| | | | | | |
|---|---|---|---|---|---|
| 7 |  |  |  | 1.0 | ≥99 |
| 8 |  |  |  | 0.5 | ≥99 |

*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

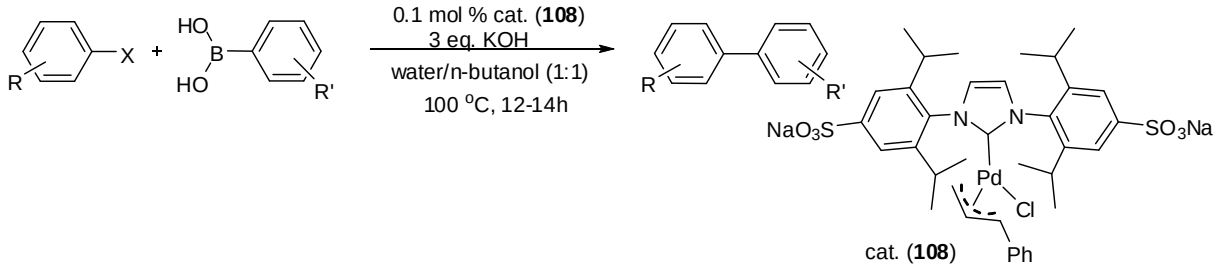
From the above catalytic study, it was observed that the 4-sulfonated-2,6-diisopropyl imidazolium chloride ligand is more effective ancillary ligand compared to sulfonated-mesityl imidazolium chloride analogous.

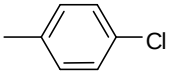
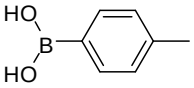
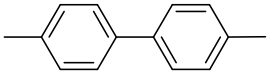
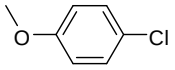
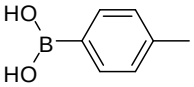
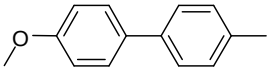
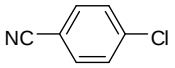
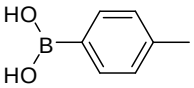
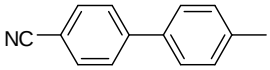
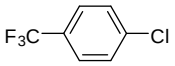
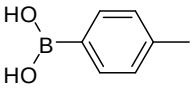
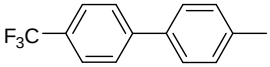
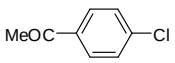
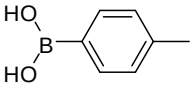
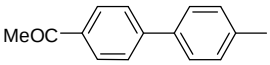
### *3.5.11 Catalytic Studies in $H_2O$/n-BuOH mixture (1:1): Using Pd-π-allyl complex*

The reactivity study of *in situ* generated Palladium/sulfonated *N*-heterocyclic carbenes motivated us to elaborate and extend the *Suzuki-Miyaura* cross-coupling protocol using isolated pre-catalyst. The *in situ* generated catalytic system was restricted to a strict control of Pd/ligand ratio. Palladium(π-allyl)NHC complexes provided a good opportunity to study *SM* cross-coupling reactions in water/alcohol mixture in the presence of base (KOH). This method was effective for the coupling of different electron-rich aryl chlorides and hetero-aryl chlorides with 4-tolyl- and 1-naphthyl- boronic acids using as low as 0.1 mol % catalyst loading at 95 to 100 $^{o}$C in aqueous/ *n*-butanol mixture.

From the earlier studies on *in situ* generated catalysis, it was revealed that the 1,3-bis(2,6-diisopropyl-4-sodiumsulfonated-phenyl)imidazolium chloride (**88 u**) showed better reactivity compared to the others. Now the catalytic screening study was made by using palladium(cinnamyl)-(diisopropylphenyl-imidazolene) (**108**) for most commonly used electron-rich and electron deficient aryl chlorides, such as 4-chloro-toluene, 4-chloroanisole, 4-cyanochlorobenzene, 4-tri-fluoromethylchlorobenzene, 4-chloroacetophenone etc. It was observed that coupling of all these substrates with tolylboronic acid gave excellent yield with only 0.1 mol % catalyst loading. But for simple palladium(allyl)NHC (**107**) complex was not effective under this same condition. Besides this, there was no appreciable amount of homo-coupling product was observed.

***Table 3.5*** *SM coupling of aryl chlorides with tolylboronic acid: Pd(cinnamyl)NHC complex*

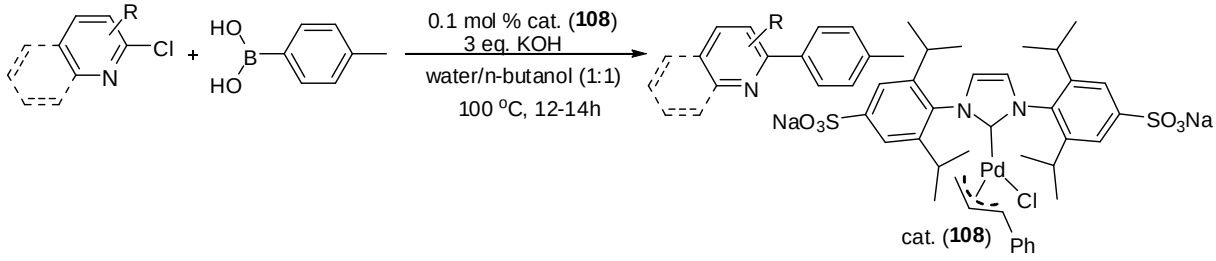


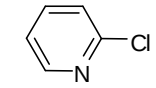
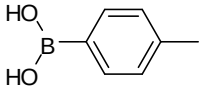
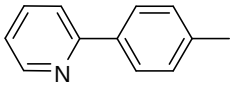
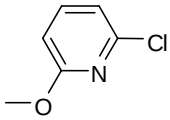
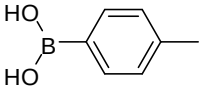
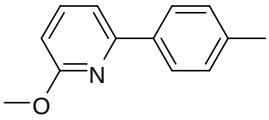
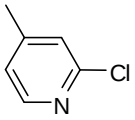
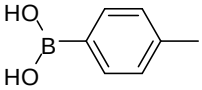
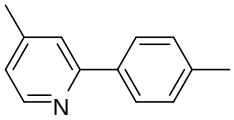
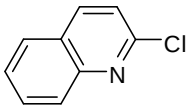
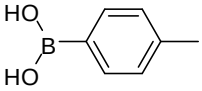
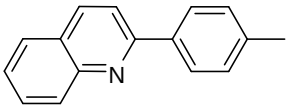
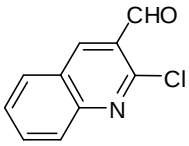
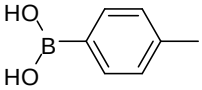
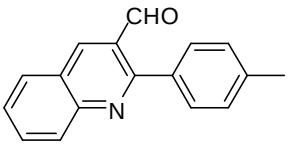
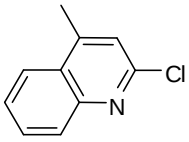
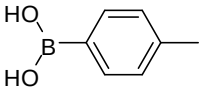
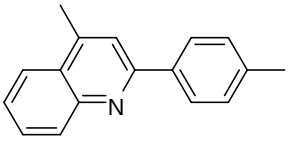

| Entry | Aryl Chloride | Boronic acid | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.1 | 89 |
| 2 |  |  |  | 0.1 | 85 |
| 3 |  |  |  | 0.1 | ≥99 |
| 4 |  |  |  | 0.1 | ≥99 |
| 5 |  |  |  | 0.1 | ≥99 |

*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

Moreover, this palladium-(cinnamyl)-sulfonated-isopropyl-NHC system (**108**) had displayed excellent reactivity towards heterocyclic arenes. The reaction of 2-chloropyridine with tolylboronic acid resulted in the quantitative conversion of the cross-coupled product. The more deactivated *N*-heterocycles like 2-chlorolepidine and 2-chloro-6-methoxypyridine quantitatively coupled under the similar reaction condition. The reaction of 2-chloroquinoline, 2-chloroquinoline-3-carbaldehyde, 2-chloro-4-methylquinoline etc with tolylboronic acid gave nearly full conversion of the respective product using the similar protocol. There was no catalyst deactivation observed due to coordination of hetero-atom to palladium center of the catalyst.

***Table 3.6*** *SM coupling of hetero-aryl chlorides with tolylboronic acid: Pd(cinnamyl)NHC complex*



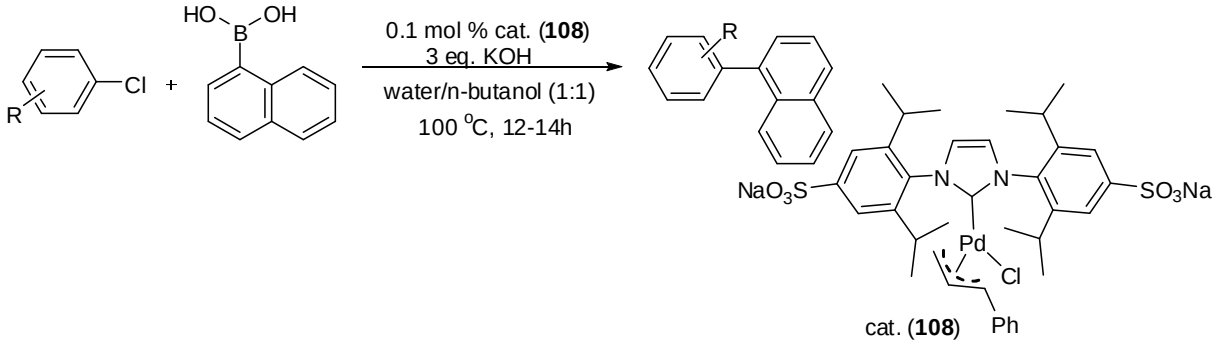

| Entry | Aryl chloride | Boronic acid | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.1 | ≥99 |
| 2 |  |  |  | 0.1 | ≥99 |
| 3 |  |  |  | 0.1 | 99 |
| 4 |  |  |  | 0.1 | ≥99 |
| 5 |  |  |  | 0.1 | 87 |
| 6 |  |  |  | 0.1 | ≥99 |

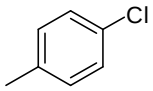
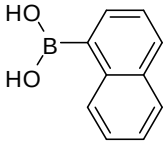
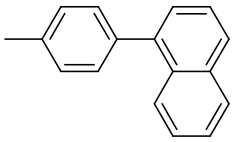
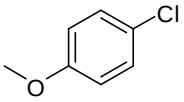
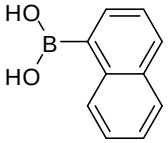
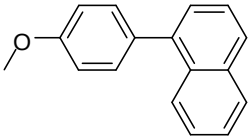
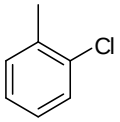
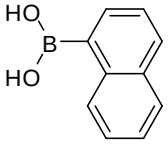
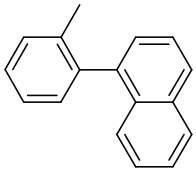
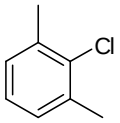
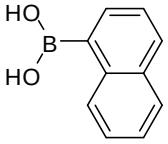
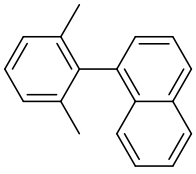
*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

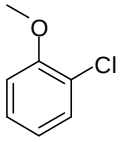
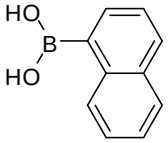
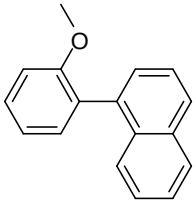
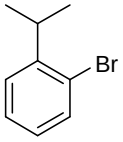
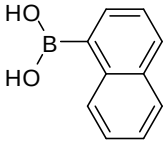
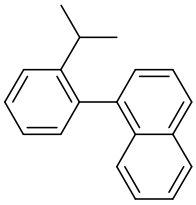
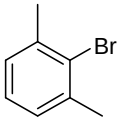
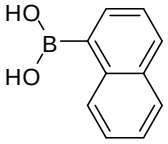
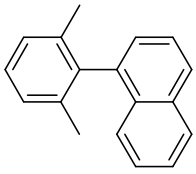
Further extension and elaboration of this catalytic system revealed that sterically hindered and electron-rich 1-naphthylboronic acid successfully reacted to a large number of aryl halides

(chlorides and bromides) and heteroaryl chlorides. By using electron-rich and sterically demanding substrates such as 4-tolyl chloride, 4-chloroanisole, 2-tolyl chloride, 2-chloroanisole, 2,6-dimethylphenyl chloride, 2,6-dimethylphenyl bromide, 2-isopropylphenyl bromide etc. and very good to excellent yield of the respective cross-coupled products were obtained.

***Table 3.7*** *SM coupling of aryl chlorides with naphthylboronic acid: Pd(cinnamyl)NHC complex*



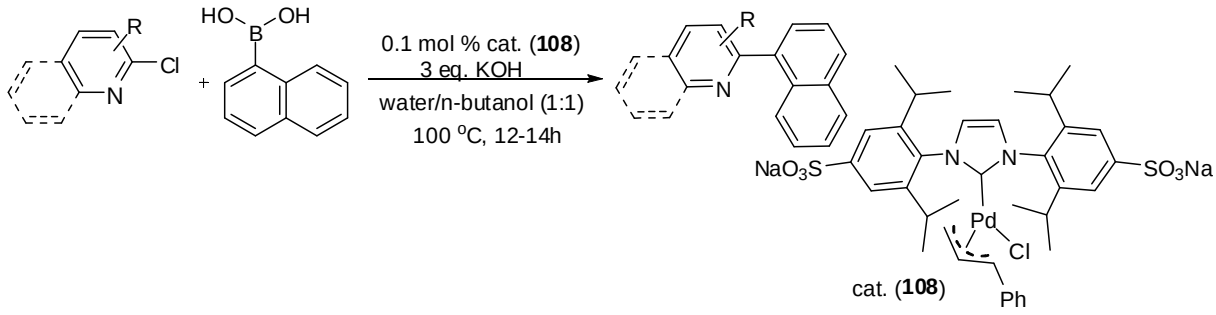

| Entry | Aryl halide | Boronic acid | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.1 | 98 |
| 2 |  |  |  | 0.1 | ≥99 |
| 3 |  |  |  | 0.1 | 87 |
| 4 |  |  |  | 0.2 | ≥99 |

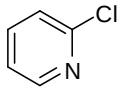
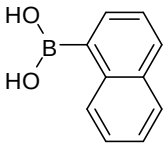
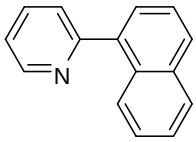
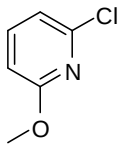
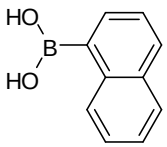
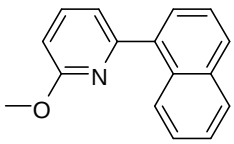
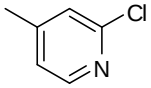
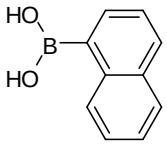
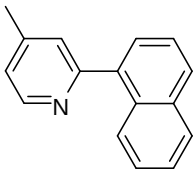
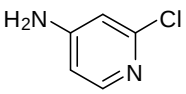
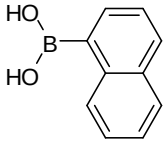
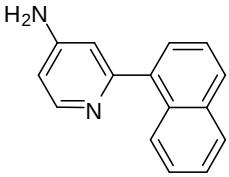
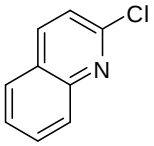
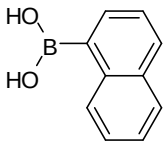
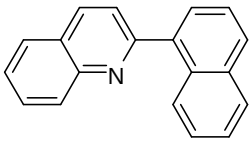
| | | | | | |
|---|---|---|---|---|---|
| 5 |  |  |  | 0.1 | 84 |
| 6 |  |  |  | 0.1 | 97 |
| 7 |  |  |  | 0.1 | 80 |

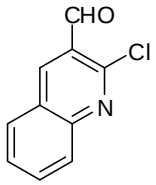
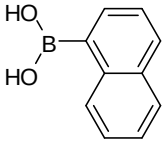
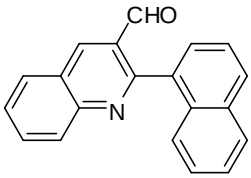
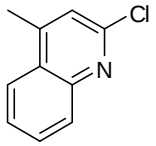
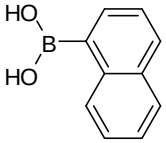
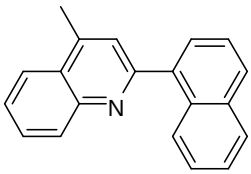
*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

This Pd(cinnamyl)-NHC precatalyst was successfully applied in the synthesis of heteroaryl derivatives of naphthylene. The normal substrates such as 2-chloropyridine, 2-chloroquinoline were coupled with naphthylboronic acid very easily using as low as 0.1 mol % catalyst loading. By using electron-rich deactivated substrates, namely 6-methoxy-2-chloropyridine, 4-lepidine, 4-aminopyridine etc. the corresponding naphthyl derivatives were obtained very easily. By following the same protocol, 2-chloroquinoline-3-carbaldehyde, 2-chloro-4-methylquinoline provided the analogous naphthyl derivatives in excellent yield (94 to ≥99 %). There was no catalyst deactivation occurred due to the coordination of pyridine type substrates with the palladium catalyst. In aqueous media, it was more likely that water molecule coordinated with the palladium in stead of the the pyridine sunbstrate which led to the formation of smooth cross-coupling product. It was observed that naphthyl boronic acid showed better reactivity compared to the tolyl boronic acid with respect to the substrate scope as well as conversion of product. Though there was more steric effect in naphthyl boronic acid but there might be the distribution of π-electron density in the naphthyl ring which might play role in the cross-coupling of such type of system.

***Table 3.8*** *SM coupling of het-aryl chlorides with naphthylboronic acid: Pd(cinnamyl)NHC complex*




| Entry | Aryl chloride | Boronic acid | Product | Cat. (mol %) | Conversion (%) |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.1 | ≥99 |
| 2 |  |  |  | 0.1 | 99 |
| 3 |  |  |  | 0.1 | ≥99 |
| 4 |  |  |  | 0.2<br>0.1 | ≥99<br>94 |
| 5 |  |  |  | 0.1 | 97 |

| | | | | | |
|---|---|---|---|---|---|
| 6 |  |  |  | 0.1 | 87 |
| 7 |  |  |  | 0.1 | ≥99 |

*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

## *3.5.12 Conclusion and Outlook*

In the above study there was a great advancement in the aqueous phase catalytic reaction, namely *Suzuki-Miyaura* coupling reaction using sulfonated *N*-heterocyclic carbene ligands, a better substitute of toxic and sensitive phosphine ligands. The methods developed were very simple and versatile as the *in situ* generated catalyst from sodium tetrachloropalladate and easy accessible Pd(π-allyl)NHC complexes. These protocols were successfully applied to challenging substrates like deactivated and sterically demanding aryl chlorides and heteroaryl chlorides in combination with different boronic acids. Another advantage was the separation of product from the catalyst phase by using simple organic solvent to extract the product after finishing the reaction. The catalyst remained in the aqueous phase might be recycled further.

There was still needed the further development of the new catalytic system which would be easy to synthesis and robust to use solely in aqueous phase without addition of any organic cosolvents. The catalyst might be versatile to use for various sterically encumbered substrates to obtain more *ortho*-substituted biaryls and hetero-biaryls. The reaction conditions would be amenable so that heating at higher temperature (boiling water) and longer reaction time could be avoided. The mechanistic study for the detailed reaction pathways should needed to be highlighted to obtain the actual visualization of catalytic interactions with substrates. With the vivid knowledge of the mechanism, it would be really helpful to obtain our cherished goal in near future.

## *3.6 Sonogashira Coupling Reaction*

The sulfonated-*N*-heterocyclic carbene catalyzed aqueous phase cross-coupling methodology was further extended to the *Sonogashira* coupling reaction where aryl and heteroaryl halides were successfully coupled with aryl as well as alkyl acetylenes. The relevance of this reaction protocol was based on the variation of the substrates using a very low catalyst loading (0.25 mol %) in water and iso-propanol mixture (1:1) and in the absence of copper(I) co-catalysts. This process was cost-effective as potassium hydroxide was used in aqueous/alcohol media avoiding the use of amine bases in cost-effective organic solvents.

### *3.6.1 Substrate Scope*

From the mechanistic study, it was difficult to conclude which step in the catalytic cycle would be rate-determining. However, the nucleophilic attack or alkyne addition was appeared to be almost insensitive to the nature of halide substituent of the activated aromatic halide. On the other hand, the rate of oxidative addition was extremely susceptible to the nature of halides (ArI > ArBr >> ArCl), as was often the overall efficiency of the catalysts. The oxidative addition process was facilitated if the electron density of the C-halide bond was reduced in the presence of electron-withdrawing groups attached to the aromatic ring. And electron donating groups on the aromatic ring behaved in the reverse way.

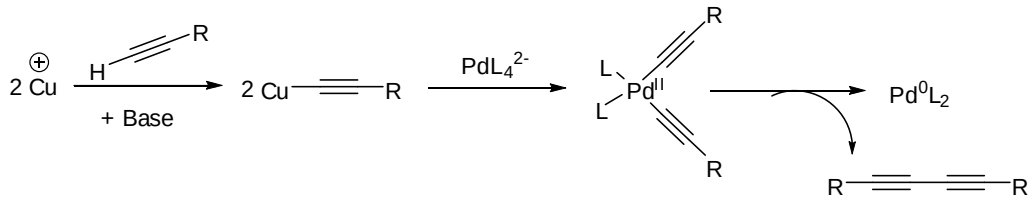
### *3.6.2 Nature of acetylene derivatives*

The *Sonogashira* reaction is generally applicable to terminal alkynes. The acetylenic C-H bond was cleaved in the course of reaction and new C-aryl or C-alkyl bond was formed, depending on the aryl or alkyl halides used. In the copper-free *Snonogashira* protocol nature of acetylenic derivatives might influence the reactivity of the alkyne-C-H bond as from the mechanism it was assumed that alkyne coordination to the palladium center occurred prior to the dissociation. The presence of electron-rich center attached to the other end of alkyne might reduce the electron-density in the alkyne bond. The alkyl substituents were less favored compared to the aryl substituents.

### *3.6.3 Reaction Condition*

The addition of copper salts as co-catalysts in the typical *Sonogashira* coupling reaction also had some drawbacks. The copper(I) acetylides formed *in situ* could undergo oxidative dimeriza-tion to give diaryl diacetylenes when they were exposed to air or an oxidant (a reaction known as Glaser Coupling). In normal palladium catalysis, copper(I) acetylides form bi-coordinated

acetylides-palladium intermediate in basic medium which reductively eliminate to give palladium(0) active species and diaryl diacetylenes. The byproducts would generally cause problem to separate from the desired products. Furthermore, copper acetylides are potential explosive reagents.




***Scheme 3.24*** *Formation of diacetylene derivatives*

## *3.6.4 Catalyst Scope*

From the most accepted reaction mechanism of *Sonogashira* reaction, the catalytically active palladium(0) species was 14-electron bi-ligated Pd(0) species which might participate in oxidative addition process by reacting with aryl halides. By using Sodium tetra-chloropalladate and sulfonated NHC catalyst, it was observed that the ligand to metal 2:1 ratio was most effective compared to other stoichiometry in water/alcohol mixture. Moreover, the isolated palladium(allyl)sulfonated-NHC complexes showed really poor reactivity towards the formation of desired coupling product. It was well-known from the literature that in the presence of base, palladium(allyl)NHC complexes usually converted to mono-ligated NHC-Pd(0) species which might not be so effective in Sonogashira catalytic cycle. From the observed data of sulfonated-NHC-palladium *in situ* generated catalysis, it might support in favor of the formation of bis-NHC-Pd(0) species as catalytically active species (as catalyst decomposition is not as fast as phosphine complexes, so ligand to metal stoichiometry would remain more or less similar). The further evidence to support this view from NMR study was not possible because of solubility problem in $D_2O$ at room temperature. Another thing was the isolation of *in situ* low-ligated catalyst that was not favorable because of sensitivity, concentration or other factors.

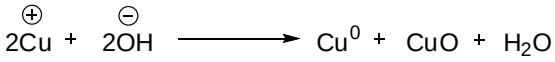
## *3.6.5 Nature of Ancillary Ligands*

The electron-rich and sterically bulk ligands around the palladium center would increase the σ-donation proper of the ligands which facilitated the oxidative addition. For NHC ligands, 1,3-bis-(2,6-diisopropylphenyl)imidazolium chloride showed better reactivity because of greater steric hindrance. It was also observed that unsaturated NHC systems worked better compared to saturated system for Sonogashira coupling reaction.

### *3.6.6 Effect of Solvents and other parameters*

There was a large influence of solvent in the *Sonogashira* coupling reaction using sulfonated NHC as ancillary ligands. The more soluble sodium tetra-chloropalladate as a precursor in water was chosen for the catalytic study. But the lower solubility of aryl or heteroaryl halides and acetylene derivatives in water made the coupling process less significant. The use of iso-propanol or n-butanol increased the solubility of the reacting components and subsequently productivity of the coupling reaction. The use of iso-propanol compared to n-butanol showed slight better reactivity in the formation of the product. The catalyst was not effective at ambient temperature. By heating the reaction mixture at 90 to 95 $^{o}$C, the optimum reactivity of catalyst was observed with a high yield of product.

The use of potassium hydroxide as a base, better reactivity was observed compared to common bases, such as cesium carbonate, potassium carbonate, potassium phosphate etc. But the concentration of base (KOH) also played an important role to determine the conversion of the desired product into maximum yield. The use of copper(I) salt in basic aqueous media was problematic as it underwent disproportion reaction to form copper oxide and precipitation of metallic copper.




***Scheme 3.25*** *Decomposition of Cu(I) in water*

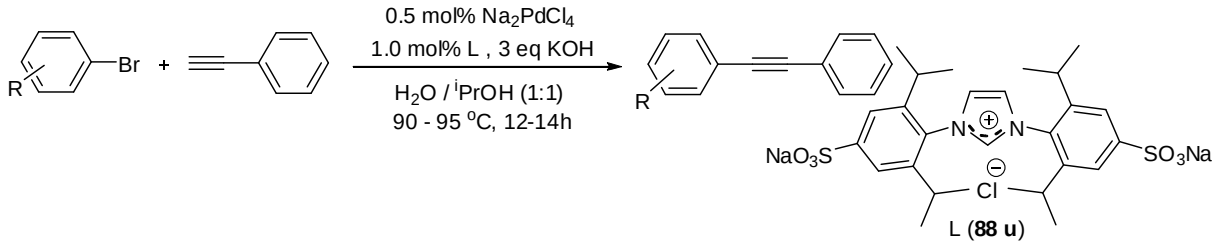
The terminal alkynes involved in the coupling reaction could also play an important role. In copper-free catalytic cycle, the carbon-carbon triple bond might coordinate to the palladium center. If the rate of oxidative addition was faster than alkyne coordination, then the cross-coupling product was favored. However, for aryl chlorides and deactivated aryl bromides, it might happen that the rate of oxidative addition was slower than alkyne coordination which resulted in the catalytic reaction less efficient. In this case, the alkyne would be able to coordinate with palladium(0) active complex prior to oxidative addition step, therefore producing a decelerating effect by formation of ($\eta^2$-RC$\equiv$CH)$Pd^0L_2$ complexes. The use of slight excess of alkyne (only 1.05 equivalents) to aryl halides avoided the formation of deactivating alkyne-palladium complexes.

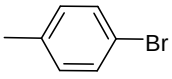
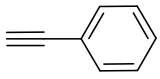
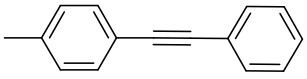
### *3.6.7 Catalytic studies in $H_2O$/iso-Propanol mixture (1:1) (In situ generated catalysis)*

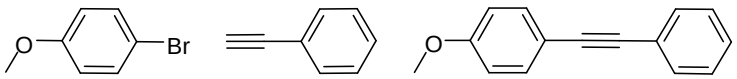
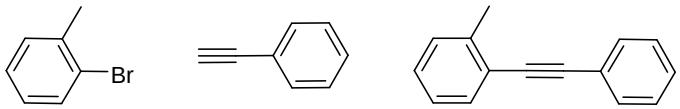
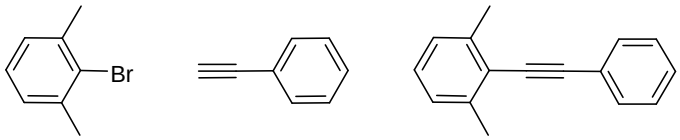
The newly developed *in situ* generated catalytic system based on sulfonated *N*-heterocyclic carbenes and sodium tetra-chloropalladate showed greater efficiency in the copper-free *Sonogashira* reaction protocol by using different aryl and hetero aryl halides coupled with aryl and alkyl acetylenes in water and iso-propanol mixture. By using 1,3-bis(2,6-diisopropyl-4-sulfonato)imidazolium chloride ligand along with $Na_2PdCl_4$, the maximum reactivity was observed compared to other sulfonated imidazolium system. Therefore, it was rationalize to use this ligand exclusively in the further development of the *Sonogashira* reaction protocol. The catalyst was prepared from the reaction of one equivalent of Pd-precursor with two equivalents of NHCs in 8 to 10 equivalents of KOH in water at 50 to 60 $^{o}$C (two hours reaction time). Next step this stock catalyst solution was used for the screening of catalysis using different aryl and hetero-aryl halides in aqueous-iso-propanol mixture at 90 to 95 $^{o}$C for 12 to 14 h.

The commonly used aryl bromides having electron-donating group at the *para*-position to the aromatic ring, i.e., deactivating substrates, such as *p*-tolyl bromides and *p*-bromoanisole showed good reactivity towards phenyl acetylene using as low as 0.5 mol% catalyst loading in water and iso-propanol mixture. The reaction was not sensitive to steric hindrance, as 2-tolyl bromide also showed better conversion to the desired product. When 2,6-dimethylphenyl bromide was employed as substrate, a good yield (86%) of the product was also obtained.

***Table 3.9*** *Sonogashira coupling reaction of electron-rich aryl bromides with phenyl acetylene*



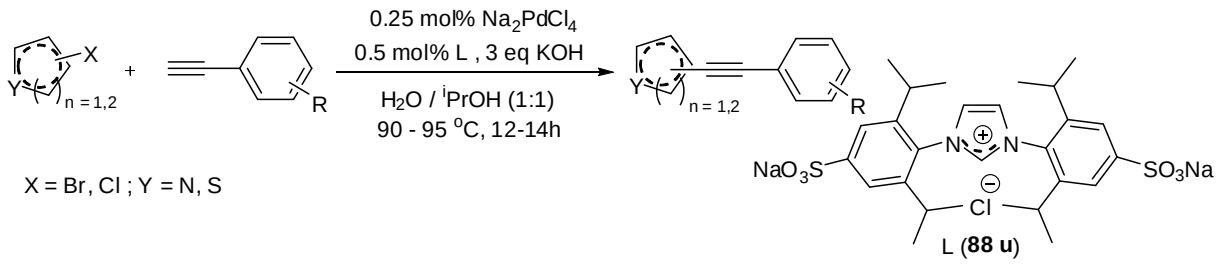

| Entry | Aryl halide | Alkyne | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.5 | 83 |

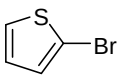
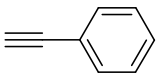
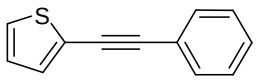
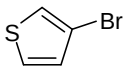
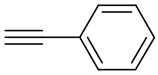
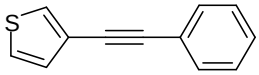
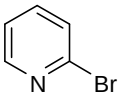
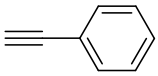
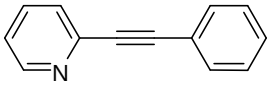
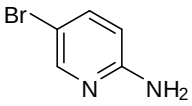
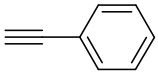
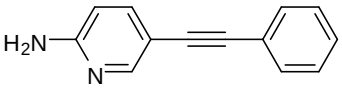
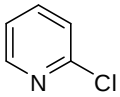
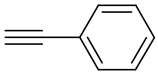
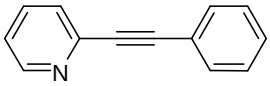
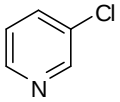
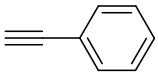
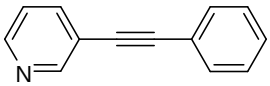
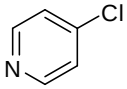
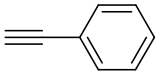
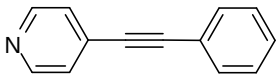
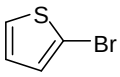
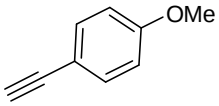
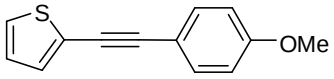
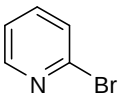
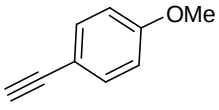
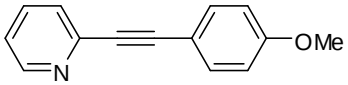
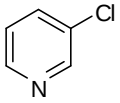
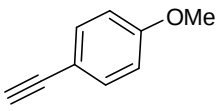
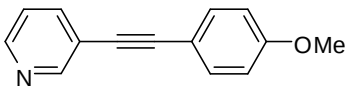
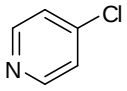
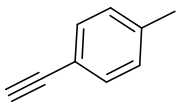
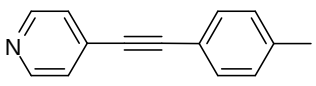
| | | | | |
|---|---|---|---|---|
| 2 |  | | 0.5 | 82 |
| 3 |  | | 0.5 | 83 |
| 4 |  | | 0.5 | 86 |

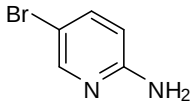
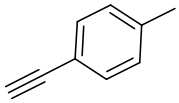
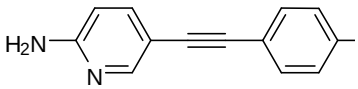
*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

The *Sonogashira* coupling protocol was more suitably applicable to heteroaromatic systems. The *N*- and *S*-based heterocyclic chlorides and bromides were widely used to couple to phenyl acetylene as well as electron-rich *p*-methoxyphenyl acetylene and *p*-tolyl acetylene using this protocol. This protocol was very efficient by using as low as 0.25 mol % and even lower (0.1 mol %) catalyst loading. The use of normal heteroaromatic substrate, like 2-bromo thiophene, 3-bromothiophene, 2-bromopyridine etc. yielded full conversion over a time period of 12 to 14 hours. The use of 2-bromo-5-aminopyridine as a difficult substrate with a free amino group was successfully coupled with phenyl and tolyl acetylenes with nearly quantitative conversion. The same reaction condition was also successfully applied to the chloropyridine derivatives, such as, 2-, 3- and 4-chloropyridines. Except 2-chloropyridine where 0.5 mol % catalyst loading was needed, the other heteroaryl halides led to nearly complete conversion with low catalyst loading (0.25 mol %). For 3-chloropyridine, the reaction gave a slightly lower yield of around 76 % with 4-methoxyphenyl acetylene as coupling partner. After all, the excellent reactivity was obtained for almost all substrates using 1,3-bis(2,6-diisopropyl-4-sulfonatophenyl)imidazolium chloride ligand with sodium tetrachloro palladate in water/iso-Propanol media.

***Table 3.10*** *Sonogashira coupling of hetero- aryl halides with aryl acetylene*



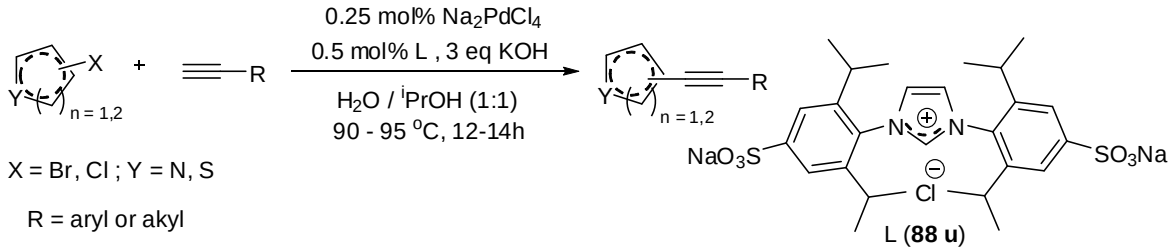
| Entry | Aryl halide | Alkyne | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.25 | ≥99 |
| 2 |  |  |  | 0.25 | ≥99 |
| 3 |  |  |  | 0.25 | ≥99 |
| 4 |  |  |  | 0.25 | ≥99 |
| 5 |  |  |  | 0.5 | 94 |
| 6 |  |  |  | 0.25 | 91 |
| 7 |  |  |  | 0.25 | ≥99 |
| 8 |  |  |  | 0.25 | ≥99 |
| 9 |  |  |  | 0.25 | 96 |
| 10 |  |  |  | 0.25 | 76 |
| 11 |  |  |  | 0.25 | ≥99 |

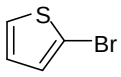
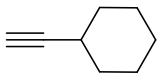
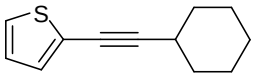
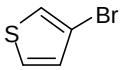
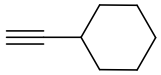
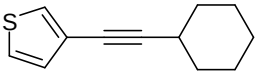
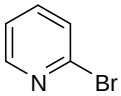
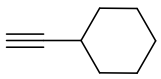
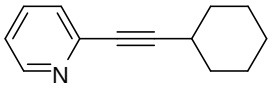
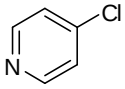
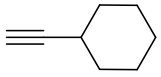
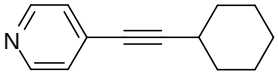
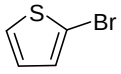
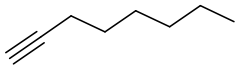
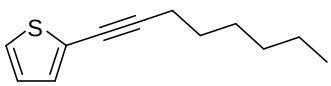
| | | | | | |
|---|---|---|---|---|---|
| 12 |  |  |  | 0.25 | ≥99 |

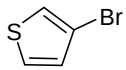
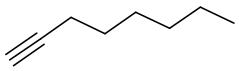
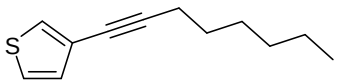
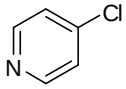
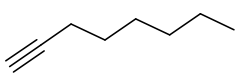
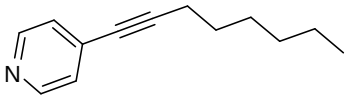
*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

The same reaction methodology was further generalized for the coupling of less reactive alkyl acetylene derivatives, such as n-hexyl- and cyclohexyl-acetylenes. The simple substrates, such as bromothiophenes, 2-bromopyridine and 4-chloropyridine were successfully applied for this coupling reaction to obtain unsymmetrically substituted hateroaryl-alkyl acetylene compounds.

***Table 3.11*** *Sonogashira coupling of hetero-aryl halides with alkyl acetylene*




| Entry | Aryl halide | Alkyne | Product | Cat. (mol %) | Conversion (%)* |
|---|---|---|---|---|---|
| 1 |  |  |  | 0.25 | ≥99 |
| 2 |  |  |  | 0.25 | ≥99 |
| 3 |  |  |  | 0.25 | ≥99 |
| 4 |  |  |  | 0.25 | ≥99 |
| 5 |  |  |  | 0.25 | ≥99 |

| | | | | | |
|---|---|---|---|---|---|
| 6 |  |  |  | 0.25 | 90 |
| 7 |  |  |  | 0.25 | ≥99 |

*Average of two runs: the conversion determined *via* GC using an internal heptadecane standard.

## *3.6.8 Conclusion and Outlook*

The copper-free *Sonogashira* coupling reaction protocol developed here is highly effective and promising for the development of aqueous phase catalysis. The protocol is very simple and useful by using a low catalyst loading (0.25 to 0.1 mol %) excellent yields are obtained for the coupling of heroaryl electrophiles with aryl and alkyl acetylenes. The reaction protocol showed a really good activity even for electron rich and sterically demanding aryl electrophiles. The reaction protocol was cost effective as *in situ* generated catalyst was obtained from sulfonated NHC and sodium tetrachloropalaldate. After an end of the reaction, product would be easily isolated by extracting the aqueous phase with organic solvent, remaining the catalyst intact in water. That aqueous phase might be recycled further.

It is still required to find a suitable catalyst to accomplish aqueous phase *Sonogashira* reaction protocol which could utilize the opportunity with a variety of electron rich and sterically demanding electrophiles, especially aryl chlorides. It would be highly beneficial to obtain the detailed mechanistic aspects of the aqueous phase copper-free *Sonogashira* coupling reaction which might fulfill our desire for making new robust excellent catalyst. These sulfonated-NHC ligands in combination with metal precursors would help to develop further new catalytic protocols, such as Heck coupling reactions, reductive coupling reaction, coupling reaction through C-H activation etc. in aqueous media.

## *4 Ruthenium Catalyzed C=C double bond forming methodology: Olefin metathesis*

The synthesis of ruthenium-alkylidene complexes bearing new NHC ligands is a fascinating and demanding field for the development of olefin metathesis catalysis. The new type of NHCs may create structural uniqueness with coordination flexibility which ultimately causes the great influence in the reactivity.

### *4.1 Design and Synthesis of Ligands*

The present study was to develop pincer type bi-dentate C-P donor ligands where *N*-heterocyclic carbene donor center was attached with the phosphine donor through a long alkyl chain. Then two types of donor center would be attached to the ruthenium center of alkylidene complex in such a fashion that both would be *trans* to each other. The advantage of such type of coordination behavior would favor the binding of olefin by detaching only the labile phosphine center during the metathesis process. Another thing would be after completing the catalytic cycle the catalyst might be regenerated by the attachment of the labile phosphine back to the ruthenium center. That was meant the recycling process would be more effective for this type of ligand system. These types of ligands were tuned by two ways- firstly by varying the type of phosphine ligands and secondly by changing the chain-length. Two types of phosphines, namely diadamantylphosphine and dicyclohexylphosphine were used in combination of alkyl chain having decyl, hexyl and butyl groups connecting to the NHC nitrogen atom. So these types of six ligands were prepared to study the model system.

(a) 1-decyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenyl)imidazolium iodide

(b) 1-hexyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenyl)imidazolium iodide

(c) 1-butyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenyl)imidazolium iodide

(d) 1-decyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolium iodide

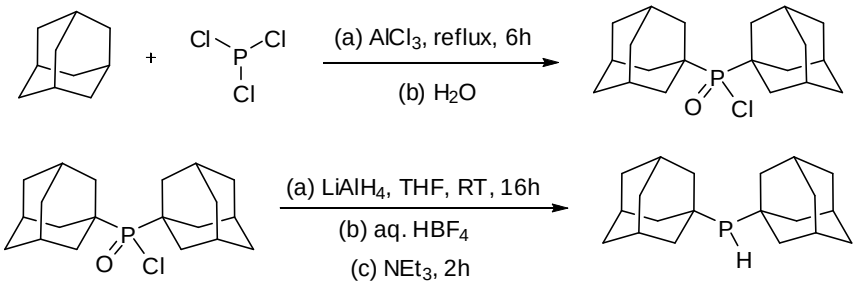
(e) 1-hexyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolium iodide

(f) 1-butyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolium iodide.

### *4.2 Synthesis of diadamantylphosphine[160]*

Diadamantylphosphine was prepared from the reduction of diadamantylphosphine-oxychloride with lithium aluminium hydride in tetrahydrofuran (THF).[160] At first adamantane was reacted with phosphorus trichloride ($PCl_3$) by following Friedel-Craft reaction in presence of aluminium

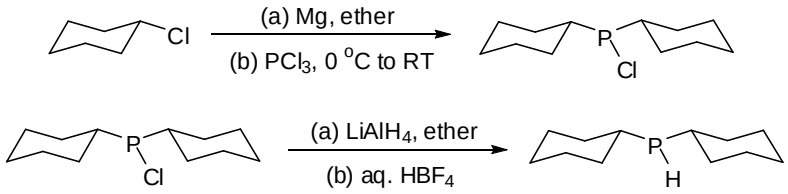
trichloride ($AlCl_3$). Finally, water hydrolysis led to the formation of diadamantyl-phosphinic chloride which was extracted with chloroform. The diadamantylphosphinic chloride was then reduced with an excess of lithium aluminium hydride in dry THF and the product was isolated and purified as phosphonium tetrafluoroborate salt that was stable towards air and moisture. The phosphonium salt was stirred with common organic base, such as triethylamine to remove fluoroboric acid and the phosphine was isolated as pure form.




***Scheme 4.1*** *Synthesis of diadamantylphosphine*

## *4.3 Synthesis of dicyclohexylphosphine*

Dicyclohexylphosphine was prepared from the reduction of chlorodicyclohexyl phosphine with lithium aluminium-hydride in ether. The starting material chlorodicyclohexylphosphine was prepared from the Grignard reaction of chlorocyclohexane with phosphorus trichloride. First Grignard reagent was made from chlorocyclohaxane (around 2 equivalents) to form cyclohexyl-magnesium chloride which then reacted with $PCl_3$ (1 equivalent) to form chloro-dicyclohexylphosphine. The formation of Grignard reagent from chlorocyclohaxane was tricky and the addition of cyclohexyl-magnesium chloride to $PCl_3$ was highly exothermic which might cause oxidation of phosphine. Finally the product chlorodicyclohexylphosphine was purified under vacuum distillation (yield 70 to 85 %).




***Scheme 4.2*** *Synthesis of dicyclohexylphosphine*

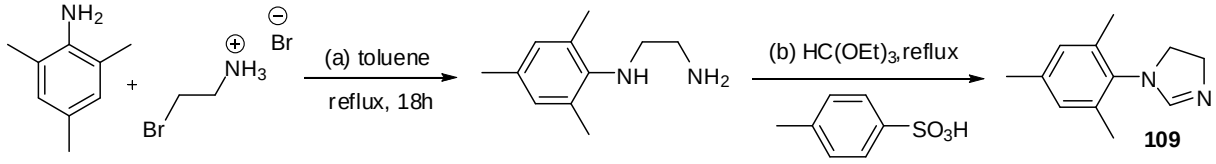
The chlorodicyclohexylphosphine was reduced with lithium aluminium-hydride in ether solution. The work-up procedure was quite tricky as the highly sensitive dicyclohexylphosphine

got oxidized and decomposed very easily. The isolation of phosphonium tetrafluoro-borate salt was not helpful as it is also a sensitive compound. So further purification of phosphonium salt made it more complicated to purify. The incomplete hydrolysis of reduction mixture of ether solution with aqueous fluoroboric acid led to hydrolyze excess LAH as insoluble solid, leaving phosphine in the ether phase. The ether layer was filtered through a pad of celite under argon to obtain pure phosphine product.

## *4.4 Synthesis of N-heterocyclic carbene precursors[161]*

### *4.4.1 Synthesis of 1-(2,4,6-trimethylphenyl)imidazolidine*

The mixture of an excess of 2,4,6-trimethylaniline and 2-bromoethylamine hydrobromide in refluxing toluene resulted in the formation of N-2,4,6-trimethylphenyl-1,2-diaminoethane which was separated from unreacted aniline via vacuum distillation. This diamine was cyclized with the help of triethylorthoformate ester in acid catalyzed refluxing condition. The compound was easily purified by acid/ base work up using the basic nature of this compound. In basic medium compound was extracted from aqueous layer and impurity remained in the aqueous phase. Similarly by making the compound acidic, it was redissolved in aqueous phase and impure materials were separated by extracting with organic solvent. Then again the compound was regenerated in basic medium.



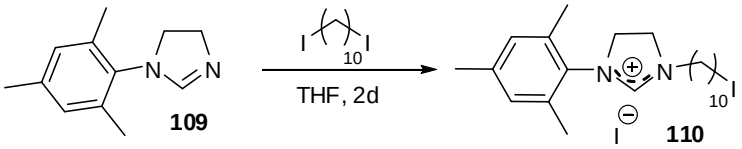

***Scheme 4.3*** *Synthesis of 1-mesitylmidazolidine*

## *4.5 Synthesis of iodo-alkyl-mesitylimidazolidinium iodides*

### *4.5.1 Synthesis of 1-iododecyl-3(2,4,6-trimethylphenyl)imidazolinium iodide*

Initially several attempts were made to synthesize 1-bromo-decyl-3-(2,4,6-trimethyl-phenyl)imidazolinium bromide from the reaction of commercially available 1,10-dibromo decane and 1-(2,4,6-trimethylphenyl)imidazolidine. The reaction between these two compounds in neat condition in presence of excess 1,10-dibromodecane also did not result in

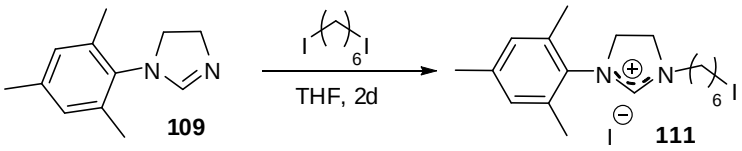
the desired compound. The reaction in toluene and DMF did not give selectively mono alkylated product. It was always resulted in a mixture of mono- and di-alkylated products. The reaction in tetrahydrofuran led to the formation of selectively mono alkylated product but the problem is the purification of unreacted 1,10-dibromodecane from the product. Most of the starting materials were removed by washing with diethyl ether or methyl-*tert*-butyl ether. But the easy accessible method to modify this protocol was to convert the bromo analogue to iodo-counterpart. The dibromo- decane was easily converted to diiodo-decane by stirring with a large excess of sodium iodide in acetone by following Finkelstein reaction. Then mesitylimidazolidine was reacted with almost four equivalents excess 1,10-diiodo decane in THF to form the desired iodo-decyl-imidazolinium salt which was purified very easily with ether wash.




***Scheme 4.4*** *Synthesis of 1-iododecylmesitylimidazolinium iodide*

## *4.5.2 Synthesis of 1-iodohexyl-3(2,4,6-trimethylphenyl)imidazolinium iodide*

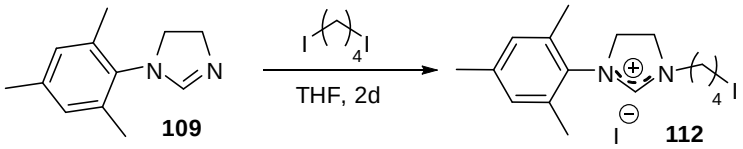
The reaction of 1,6-diiodo hexane with mesitylimidazolidine in THF resulted in the formation of 1-iodo-hexyl-3-(2,4,6-trimethylphenyl)imidazolinium iodide by following the analogous method of decyl derivative.




***Scheme 4.5*** *Synthesis of 1-iodohexylmesitylimidazolinium iodide*

## *4.5.3. Synthesis of 1-iodobutyl-3(2,4,6-trimethylphenyl)imidazolinium iodide*

By following the method discussed for decyl-derivatives, the reaction of 1,4-diiodo butane with mesitylimidazolidine resulted in the desired 1-iodobutyl-3-mesitylimidazolinium iodide.

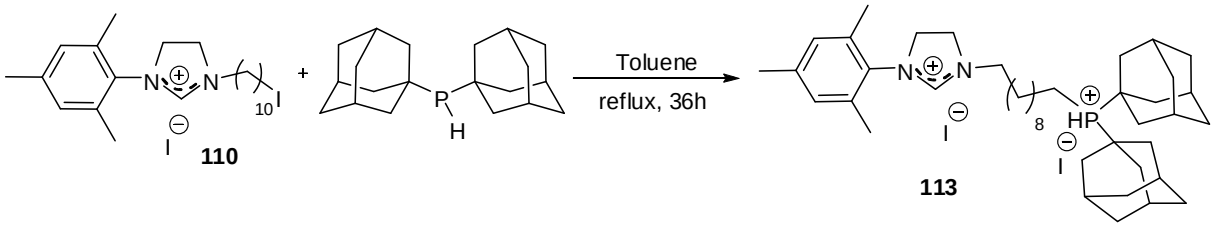



***Scheme 4.6*** *Synthesis of 1-iodobutylmesitylimidazolinium iodide*

## *4.6 Synthesis of (phosphonium-alkyl)-mesitylimidazolidinium diiodides*

### *4.6.1 Synthesis of 1-decyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

The reaction between diadamantylphosphine and 1-iododecyl-3-mesitylmidazolinium iodide was seemed to occur in DMSO as both the imidazolinium iodide and phosphine were soluble in polar solvent. So the first attempt was made to do reaction in DMSO at 100 to 110 $^{o}$C with overnight stirring. But in reality, instead of forming 1-decyl-phosphonium imidazolinium salt, 1-decyl-phosphine oxide of corresponding imidazolinium salt was observed and the reaction mixture became sticky brown oily solid after removal of DMSO. To avoid the difficulty associated with its work-up process and then again further reduction, this reaction was tried in other solvent such as THF and toluene. Although reacting components were not better soluble at room temperature but the miscibility was occurred at high temperature under refluxing condition. In refluxing THF, the reaction did not reach to the completion. In the case of toluene refluxing condition, reaction was completed within 36 hours in closed schlenk condition.




***Scheme 4.7*** *Synthesis of 1-decyl(diadamantylphosphino)mesitylimidazolinium iodide*

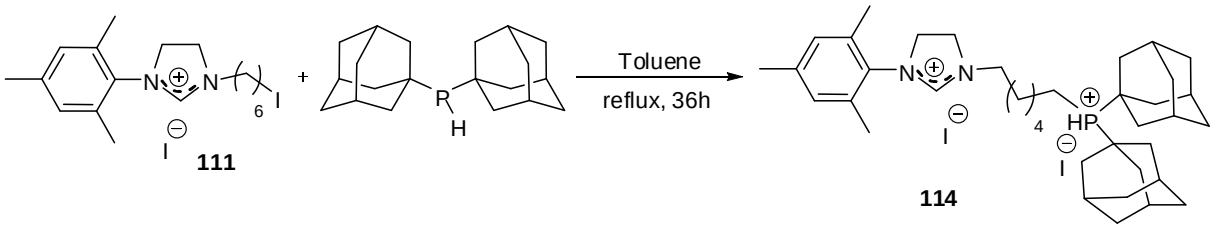
There were several factors in the reaction which might influence the purity in product formation. The stoichiometry of starting materials might have great influence in the completion of reaction or formation of side product. When iodo-decyl imidazolinium iodide and phosphine were used in nearly equimolar ratio, the incomplete conversion of product was observed. When the ratio was more of imidazolinium iodide to phosphine was around 1.25 to 1.5 the

maximum purity of product was obtained. The more equivalents of phosphine led to the decomposition of phosphine generating impurities which were inseparable from the product. There was obviously a great problem to purify this doubly charged Imidazolinium salts from the impurities which were most often phosphine derivatives along with bis-imidazolidine derivatives. There were several other factors such as temperature, reaction time, quantity of solvent (i.e., concentration of substrates) and scale of the reaction etc. It was observed that the reaction proceeded smoothly to complete conversion in refluxing toluene condition. By decreasing the reaction temperature, it would not proceed to completion even after longer period of time. Both the substrates were less soluble in toluene at ambient temperature. When the temperature was raised to around 80 $^{o}$C, miscibility of the components was observed. The larger amount of solvent (100 mg in 100 ml solvent) might help in the dissolution process. As the reaction gradually proceeded, the product formed was precipitated out as viscous oil at the bottom of the schlenk tube. So the precipitation of product might be assisted by the presence of large amount of non-polar solvent, like toluene. The duration of reaction was also an important factor to obtain full conversion of the product. From the observed NMR data it was revealed that almost 90 % conversion was occurred within 12 hours but the full conversion was observed only after one and half day. It seemed that the reaction was getting gradually slower during the course of time. That might be because of immiscibility of the reacting components into the reaction mixture. The reaction worked better only for small scale, like 250 mg to 500 mg of starting iodo-imidazolidinium salt. Further scaling up of the reaction caused the generation of unavoidable impure product. The obtained product as phosphonium salt was very stable in solid state and could be preserved under air without any exclusion of air and moisture. There was an attempt to make 1-decyl-diadamantylphosphine analogous from the phosphonium salt by neutralizing one equivalent HI. But the attempts to make such phosphine derivative were failed. The reason for that might be the selective deprotonation of only phosphonium salt without interrupting the imidazolinium counterpart. So there was always a mixture of phosphine-derivative, phosphonium salts with imidazolinium cation or salts. It was also true fact that because of solubility problem, the complete deprotonation was not possible. Another thing was the sensitivity of phosphine-derivative which also made it impossible to isolate a pure product.

### *4.6.2 Synthesis of 1-hexyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

The synthesis of hexyl analogous of phosphonium salt was synthesized by following the previous method like decyl derivatives, only starting material was differed. Instead of iodo-

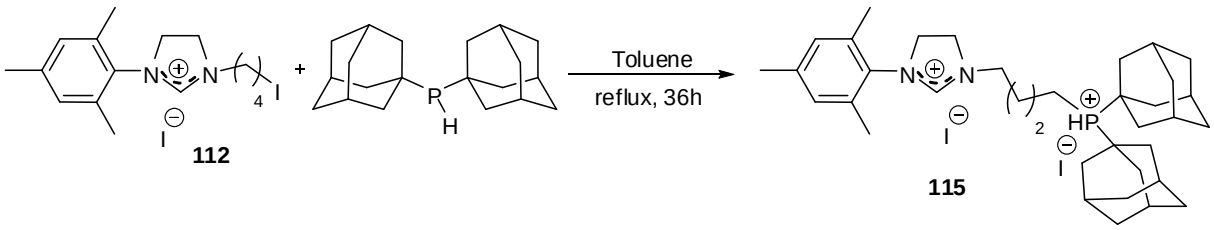
decyl-imidazolinium salt, iodo-hexyl-imidazolinium salt was used to react with required quantity of diadamantylphosphine.




***Scheme 4.8*** *Synthesis of 1-hexyl(diadamantylphosphino)mesitylimidazolinium iodide*

## *4.6.3 Synthesis of 1-butyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

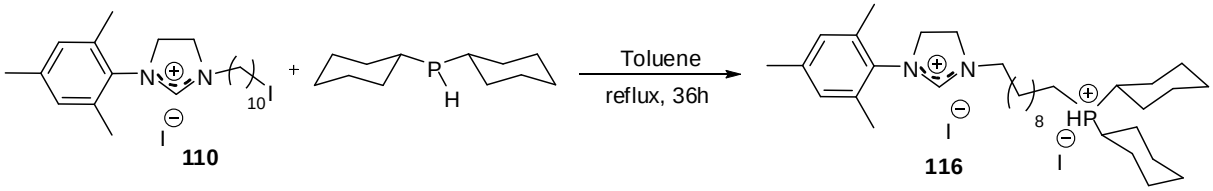
The butyl analogous diadamantylphosphonium salt was synthesized from the reaction of the iodo-alkylimidazolidinium salt with diadamantylphosphine in refluxing toluene such as the decyl-derivative as mentioned above.




***Scheme 4.9*** *Synthesis of 1-butyl(diadamantylphosphino)mesitylimidazolinium iodide*

## *4.6.4 Synthesis of 1-decyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

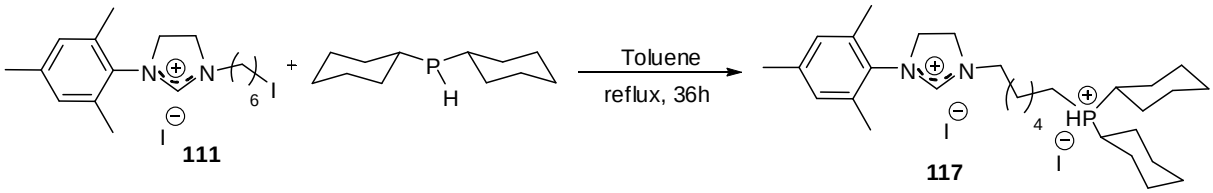
There was a similar method to diadamantylphosphine-analogous that was followed for the synthesis of dicyclohexylphosphonium-decyl-imidazolinium salt. The reaction procedure and other experimental parameters were similar. But the formation of pure product was rather improbable because of the higher sensitivity of dicyclohexyl phosphine towards air, moisture etc.




***Scheme 4.10*** *Synthesis of 1-decyl(dicyclohexylphosphino)mesitylimidazolinium iodide*

## *4.6.5 Synthesis of 1-hexyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

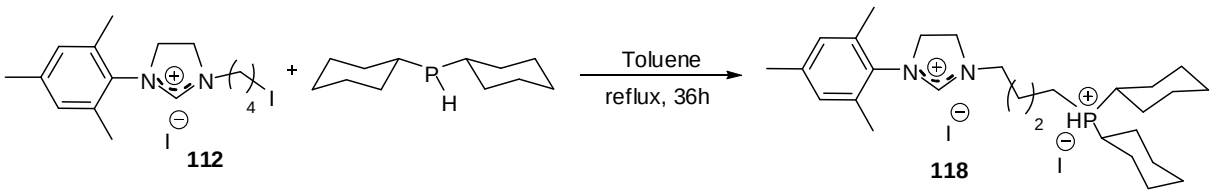
The same procedure was repeated once again by taking hexyl-iodoimidazolidine salt instead of decyl-iodoimidazolidine salt for making hexyl-dicyclohexylphosphine derivative of imidazolidine compound. The precaution and restriction were followed like earlier mentioned.




***Scheme 4.11*** *Synthesis of 1-hexyl(dicyclohexylphosphino)mesitylimidazolinium iodide*

## *4.6.6 Synthesis of 1-butyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

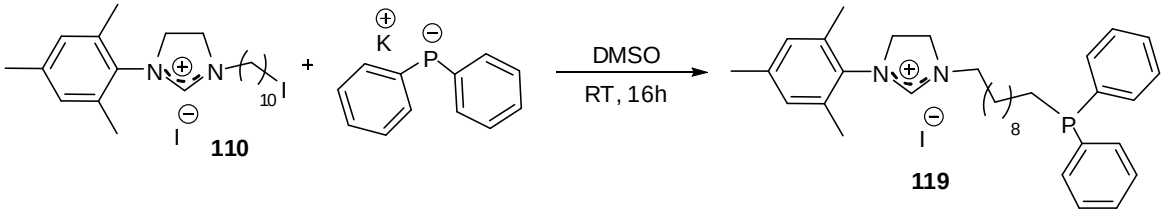
The butyl analogous compound was also prepared like usual procedure by reacting dicyclohexyl –phosphine with appropriate proportion of butyl-iodoimidazolidine salt in toluene refluxing condition. The sensitivity and selectivity of the product formation was similar as mentioned for earlier compounds. There was still the problem associated with the minute amount of inseparable impurity which cannot be avoided after taking all the precaution. So it became case-sensitive. Sometimes it was possible to observed pure and sometimes not although exactly same procedure was used. It might be due to the experimental set-up or manipulation.




***Scheme 4.12*** *Synthesis of 1-butyl(dicyclohexylphosphino)mesitylimidazolinium iodide*

## *4.6.7 Synthesis of 1-decyl-(diphenylphosphine)-3-(2,4,6-trimethylphenyl) imidazolinium iodide*

A mixture of potassium diphenylphosphide and 1-iododecyl-3(trimethylphenyl)imidazolidine was reacted in DMSO at ambient temperature for overnight to result in the formation of highly sensitive product.




***Scheme 4.13*** *Synthesis of 1-decyl(diphenylphosphino)mesitylimidazolinium iodide*

It was not possible to purify the product by removing byproduct potassium iodide from the reaction mixture. The compound was not possible to isolate in the form of salt so that further step would be easier.

## *4.7 Formation of Ruthenium(Phosphine-tagged Carbene pincer ligand)(alkyledene) complexes:*

### *4.7.1 Direct Method*

(a) From *Grubbs I* type complex $[Ru(PCy_3)_2Cl_2(=CH\text{-}Ph)]$

(b) From *Grubbs III* type complex $[Ru(PCy_3)(py)_2Cl_2(=CH\text{-}Ph)]$

(c) From *Grubbs I* type complex $[Ru(PPh_3)_2Cl_2(=CH\text{-}Ph)]$

### *4.7.2 Indirect Method*

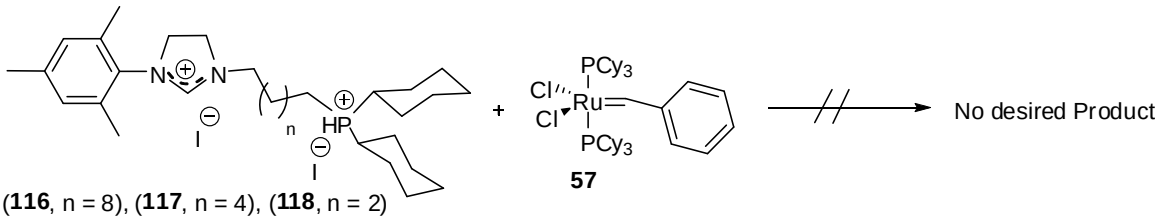
(d) Formation of Silver complex

(e) Formation of Ru-indenylidene complex

### *4.7.1 Direct Method*

(a) From *Grubbs I* type complex $[Ru(PCy_3)_2Cl_2(=CH\text{-}Ph)]$

The general method for synthesizing (NHC)Ru-alkylidene complexes was based on the generation of NHC from imidazolinium salt followed by addition to the *Grubbs I* precursor $[Ru(PCy_3)_2Cl_2(=CH\text{-}Ph)]$. The carbene usually generated by deprotonation of imidazolinium salt with strong base, like potassium *tert*-butoxide ($KO^tBu$), sodium amylate ($NaOC_5H_{11}$) in Toluene or THF solvent. These pincer type phosphine-tagged imidazolinium salts were deprotonated with either of these two strong bases. Then the resulting solution was added to the $PCy_3$-analogous *Grubbs I* complex, i.e., $[Ru(PCy_3)_2Cl_2(=CH\text{-}Ph)]$. But from $^{31}$PNMR data there was no trace of product observed and only oxidized phosphorus peak. The problem was associated with the deprotonation of two types of protons by base. The phosphine deprotonation was sensitive and most of the cases only oxidized product was obtained. When this mixture was poured into *Grubbs I* complex, the $PCy_3$ was also getting oxidized. Thus the resulting NMR spectrum only indicated the presence of oxidized substances. The replacement of both phosphines from the ruthenium-coordination sphere by phosphine-tagged NHC was also difficult. The replacement of one phosphine might be feasible by NHC but the second $PCy_3$ by other phosphine was quite unusual. So there was a need to change ruthenium precursor also to make the condition more convenient.




(**116**, n = 8), (**117**, n = 4), (**118**, n = 2)

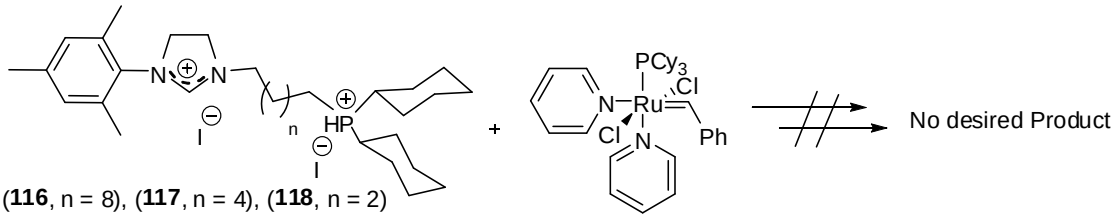
**57**

***Scheme 4.14*** *Attempt to synthesis of ruthenium-alkylidene(phosphine-tagged-NHC) complexes*

(b) From *Grubbs III* type complex $[Ru(PCy_3)(py)_2Cl_2(=CH\text{-}Ph)]$

There was one small modification of the *Grubbs I* type that was made by replacing either of the tricyclohexylphosphines by loosely bound pyridine ligand. This was known as *Grubbs III*

complex. When excess of pyridine was added to the *Grubbs I* complex, one of the phosphine was replaced by pyridine but the resulting complex became octahedral in geometry with two pyridine ligands, one of them is *trans* to phosphine, another is *trans* to alkylidene moiety. When deprotonation of phosphine-tagged NHC was made following the previous method using potassium *tert*-butoxide in toluene and then the resulting carbene was transferred to the *Grubbs III* complex at cold condition (0 $^{o}$C), a red-brown solution was formed. After purification by silica-gel column chromatography with diethylether and pentane (1 to 4 ratios) as eluant under argon atmosphere, it was possible to obtain very less yield (10 to 20 %) of purified compound. From $^{1}$H NMR study, it was observed that there were two signals at δ 20.3 ppm and δ 19.9 ppm and in $^{31}$P NMR at δ 37.8 and δ 36.3 ppm. The two types of $^{1}$H NMR signals might be indicative of a mixture of ruthenium-alkylidene products due to the presence of chloro and iodo ligands. It was also possible to convert both complexes into either of the product chloro-complex or iodo-complex. The product mixture was stirred into a dichloromethane ($CH_2Cl_2$) solution of a large excess of *N*-butylammonium chloride or iodide for overnight to obtain selectively either of the products. By using 1-decyl(dicyclohexylphosphine)-3-mesitylimidazolinium iodide and as well other butyl and hexyl analogous, same type of $^{1}$H NMR and $^{31}$P NMR spectra were observed. Sometimes only slight ppm difference was observed because of the NMR time-scale. Another thing was other series of compounds like 1-decyl(diadamantylphosphino)-3-mesitylimidazolinium iodide and butyl and hexyl analogous also showed similar type of NMR pattern. Another thing was this NMR pattern was similar to the *Grubbs I* type complex, the starting material of *Grubbs III* type, i.e., Ru-py(alkylidene) complex. The explanation of the above fact might be the reason of the instability associated with new type of phosphine-tagged NHC ligands.



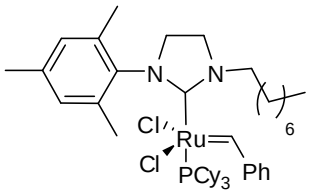

(**116**, n = 8), (**117**, n = 4), (**118**, n = 2)

***Scheme 4.15*** *Attempt to synthesis of Ru-alkylidene(phosphine-tagged-NHC) complexes*

It might happen that pyridine ligand could be easily replaced by carbene-carbon center but the dangling phosphine part cannot get attached with the ruthenium center. Thus this type ruthenium complex was unstable as phosphine part easily decomposed during the course of reaction. In solution it might happen that free $PCy_3$ which was much more stable than NHC and dangling phosphine part, could reattach with the pyridine-ruthenium-complex center by

replacing loosely bound pyridine. That was the reason why *Grubbs I* type complex was recurred as the final product. The mixed halogen complex of *Grubbs I* was formed which also indicated that in solution ligand replacement and ligand exchange (halide) were possible. When the reaction was made in low temperature (-78 $^{o}$C) to avoid decomposition of phosphine part of the phosphine-tagged-NHC ligand, a green colored complex was formed. For diadamantylphosphine analogous ligands, it was possible to purify through silica-gel short column with pentane and ether (4 to 1 ratios) as eluant under argon. From $^{1}$H NMR data only one benzylidene proton (δ 18.68 ppm) was observed and from $^{31}$P NMR, two phosphorus peaks δ 32.1 and δ 26.1 ppm were observed along with two more impure peaks of free $PCy_3$ (δ 11.2 ppm) and tricyclohexylphosphine oxide ($O=PCy_3$, δ 49.7 ppm). The $^{31}$P NMR data at δ 26.1 ppm indicated the presence of free adamantyl-phosphine phosphorus and the peak at δ 32.1 ppm was indicative of coordinated $PCy_3$ ligand *trans* to the carbene carbon. It was clear from the spectral data that pincer diadamantayl-phosphine part was not able to decoordinate $PCy_3$ from the ruthenium center and remained as dangling tertiary phosphine. Now the question was how the nature of the halide ligands in ruthenium complex. From the literature study,[163] it was known that $PCy_3$ analogous Grubbs-I type Ru-complexes with dichloro and diiodo ligands showed $^{1}$H NMR and $^{31}$P NMR spectra (in $CDCl_3$) at δ 19.93 (*H*C=C-Ph) and 20.3 (*H*C=C-Ph) and 35.6 ($PCy_3$) and 37.8 ($PCy_3$) ppm respectively. For *Grubbs II* type complexes with dichloro and diiodo ligands showed $^{1}$H NMR and $^{31}$P NMR spectra (in $CD_2Cl_2$) at δ 20.02 (*H*C=C-Ph) and 19.09 (*H*C=C-Ph) and 36.6 ($PCy_3$) and 30.8 ($PCy_3$) ppm respectively.[163] From this study, it was noted that the presence of iodo ligands in *Grubbs I* complex made benzylidene proton down-field shift compared to chloro complex. But for *Grubbs II* type complexes, the benzylidene proton showed reverse effect. The chloro cmplex showed low-field compared to iodo analogous. From $^{31}$P NMR study, it was observed that *Grubbs I* (iodo) showed downfield shift compared to *Grubbs I* (chloro) complex. And the reverse thing was observed for Grubbs-II complexes. These NMR data were not helpful to get any conclusive idea regarding the effect of halide ligands in the ruthenium complexes. There was another literature [145a] where the unsymmetrically substituted octyl-mesityl-NHC was used to make ruthenium complex of *Grubbs II* type. It was mentioned that $^{1}$H NMR and $^{31}$P NMR spectra (in $CDCl_3$) of that chloro-complex showed the benzylidene proton and phosphine phosphorus at δ 18.99 (*H*C=C-Ph) and 32.6 ($PCy_3$) ppm respectively. These values were in comparison with the Ru-complex obtained from pincer NHC-adamantylphosphine ligand which might have similar structural features with the previous literature complex. Thus it could be concluded from the fact that Ru-NHC($PAd_2$) complex might be dichloro complex in nature. There was another thing, the generation of carbene by deprotonation with base at -70 $^{o}$C led to a clear solution leaving a white insoluble sodium iodide

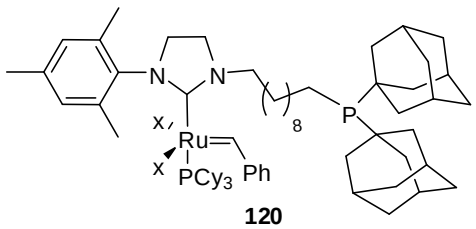
at the bottom. The carbene solution was then transferred to the Ru-(chloro)-pyridine complex to synthesize the product.



**75d**

$^{1}$H NMR δ 18.99 (*H*C=C-Ph) ppm

$^{31}$P NMR δ 32.6 ($PCy_3$) ppm

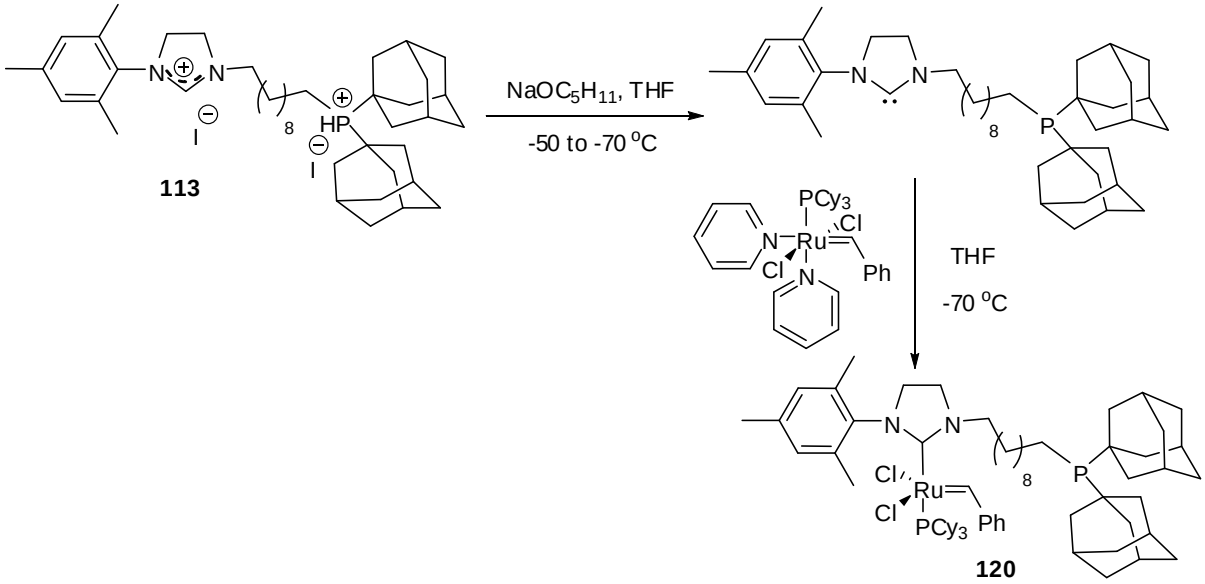


**120**

$^{1}$H NMR δ 18.68 (*H*C=C-Ph) ppm

$^{31}$P NMR δ 32.1 ($PCy_3$) and 26.1 ($PAd_2$) ppm

***Figure:*** *Comparison of newly formed ruthenium complex to literature reported complex*




**113**

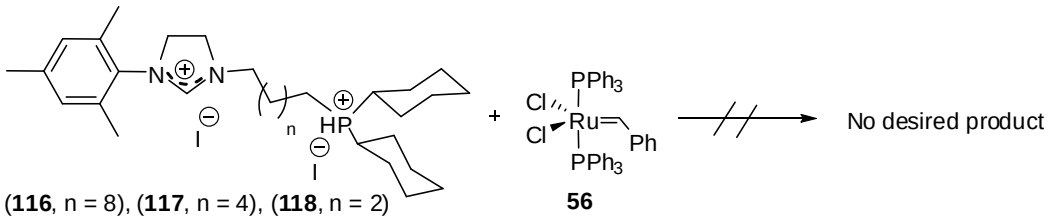
**120**

***Scheme 4.16*** *Attempt to synthesis of Ru-alkylidene(phosphine-tagged-NHC) complexes*

This complex slowly decomposed within two to three days though preserved under argon atmosphere. The instability of the product mixture was due to the free dangling phosphine part which was not able to attach to the ruthenium center because of the strong coordination ability of $PCy_3$. For dicyclohexylphosphine-analogous ligand, same type of green product was observed but no further work-up or study was possible because of the instability associated with dicylohexylphosphine moiety.

(c) From *Grubbs I* type complex [$Ru(PPh_3)_2Cl_2(=CH\text{-}Ph)$]

From the earlier study on tricyclohexylphosphine analogous of *Grubbs I*, it was observed that the ruthenium-$PCy_3$ bond was so strong that replacement of $PCy_3$ was impossible which might cause the instability of the pincer ligand to attach to the ruthenium center. To avoid such problem, weakly coordinating triphenylphosphine coordinated *Grubbs I* complex was used as a ruthenium precursor to synthesize the desired alkylidene-NHC complex.




(**116**, n = 8), (**117**, n = 4), (**118**, n = 2) **56**

***Scheme 4.17*** *Attempt to synthesis of Ru-alkylidene(phosphine-tagged-NHC) complexes*

The reaction condition was maintained at low temperature -78 $^{o}$C, like earlier and after addition of pincer ligand phosphine-tagged carbene to the *Grubbs I*, a pink coloration was formed. But it was not possible to check by thin layer chromatography (TLC), as compound was decomposed on TLC plate. The reason of decomposition might be two-fold. First thing, it might be repetitive case like earlier where either of the triphenylphosphine was replaced by carbene leaving the dangling phosphine moiety free and again the ruthenium coordination became unstable because of the presence of weakly binding nature of $PPh_3$. So there were two effects worked simultaneously to destabilize the complex. Another thing was, it might be assumed that both the $PPh_3$ groups were replaced by one carbene and another pincer phosphine whose nature would be unstable. So it was really difficult to conclude about such type complexes as there was no NMR data.

## *4.7.2 Indirect Method*

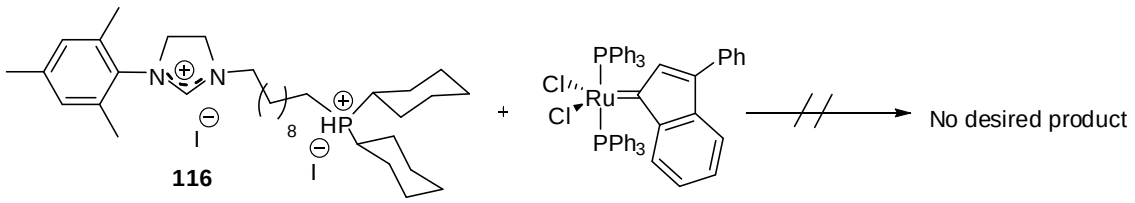
(d) Formation of Silver complex

As it was observed that no direct method was fruitful to obtain ruthenium-alkylidene complex of newly developed pincer-type phosphine-tagged NHC ligands, the indirect method was followed by making silver complex which could be used as transfer agent to form ruthenium complex. The commonly used method for synthesizing silver-NHC complex was followed by reacting with silver oxide ($Ag_2O$) in dry and degassed dichloromethane. When ligand to silver oxide ratio 2 to 1 was used only phosphine-bound silver complex was formed and imidazolinium proton remain as it was. It was thought that because of phosphonium salt, two

silver atoms were used up and relatively hard imidazolinium-proton remained unreacted. Then ligand to silver oxide ratio 1 to 1 or slight excess was used and complicated $^{31}P$ NMR was observed which might be indicative of the presence of more than two products. So it was not desirable to use such type of mixture of products to use in the next step to make ruthenium complex. The reaction was repeated in other solvent like dichloroethane (DCE), THF etc but did not change the pattern of $^{31}P$ NMR spectra. Next to obtain the single and clean product phosphonium salt was deprotonated with base to make imidazolinium-phosphine which might be subsequently purified and reacted with silver oxide to obtain desired product. Again there was a problem arisen, the deprotonation with weak base like triethylamine did not work well for all the ligands. The only ligand which worked better was butyl-diadamantylphosphine analogous. The reaction usually occurred initially at -50 to -70 $^{o}$C for 4 hours and longer period of time to obtain complete deprotonation (room temperature). Afterwards, work-up was done and ethanol was used to purify under celite filtration. For other ligands, the reaction did not reach to completion even after stirring at ambient temperature for two days. There was another problem for stirring longer time as phosphine was decomposed over the period of time. So to generalize the reaction condition for all ligands and to make the reaction faster, strong base such as sodium *tert*-pentylate was used at -70 $^{o}$C in THF. From the NMR spectra it was observed that deprotonation from imidazolinium as well as phosphonium salts were occurred. But again there was problem of formation of silver complex which might be the stability reason. It might happen that at low temperature the silver complex was formed and at room temperature it was getting decomposed. Another way it could be explained that the nature of phosphine bound the metal center made it unstable to isolate.

(e) Formation of Ru-indenylidene complex

There was another possibility to make ruthenium alkylidene complex through the formation of ruthenium-indenylidene complex which might be cross-metathesize with styrene to obtain desired alkylidene complex. For making such type of complex, ruthenium-bis(triphenylphosphine)chloro(indenylidene) complex was taken as starting material. The deprotonated phosphine-tagged carbene at -70 $^{o}$C was added to the precursor and then stirred at room temperature. There was no as such good NMR spectra was observed except the decomposed phosphine. It might be the difficulty of the carbene and phosphine simultaneously to coordinate to the sterically encumbered ruthenium center in indenylidene complex.




***Scheme 4.18*** *Attempt to synthesis of Ru-indenylidene(phosphine-tagged-NHC) complexes*

### *4.7.3 Synthesis of Ru[1-decyl-(diphenylphosphino)-3-(2,4,6-trimethylphenyl) imidazolinidine]dichloro(alkylidene)] complex*

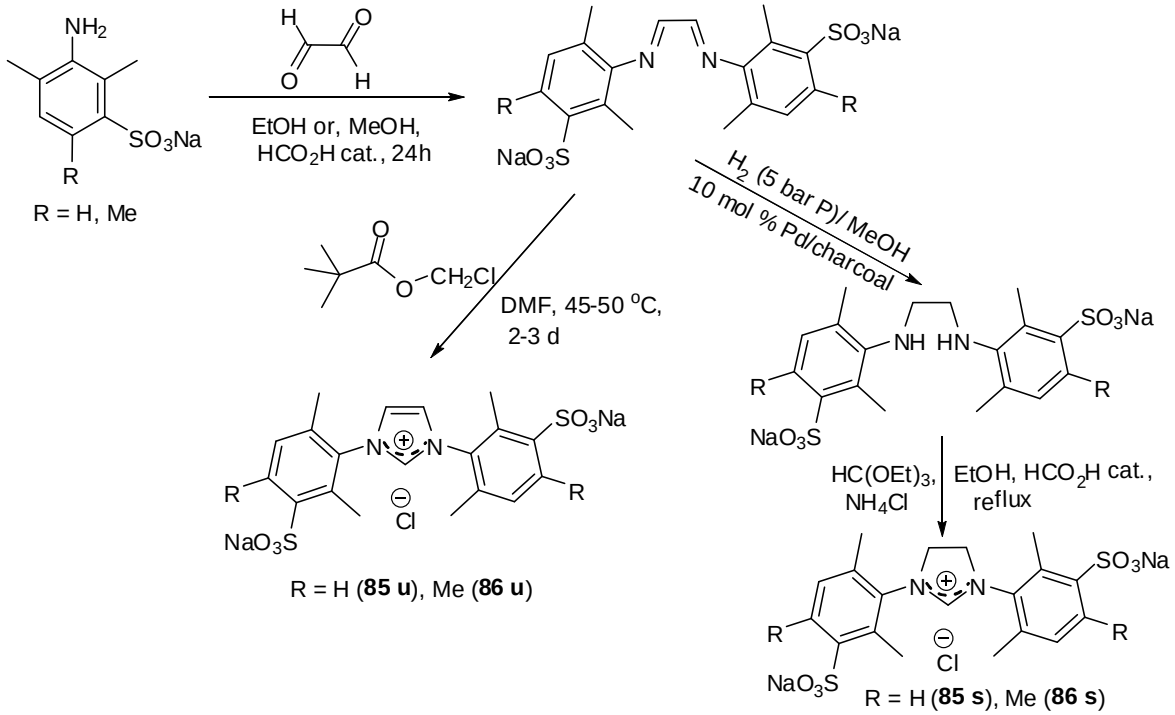
The deprotonation reaction of decyl(diphenylphosphine)imidazolinium chloride was carried with potassium tert-butoxide in toluene of THF followed by addition of *Grubbs I* or *Grubbs III* complex might result in the formation of ruthenium-alkylidene complex. But it was really difficult to handle the ligand as well as the resulting complex. It was not possible to take even NMR or made TLC of such type complex to characterize the product.

### *4.7.4 Conclusion and Outlook*

The idea of developing pincer type phosphine-tagged *N*-heterocyclic carbene ligands and their utilization in the ruthenium alkylidene complexes were really novel and useful. There is still a lot of synthetic knowledge as well as mechanistic study needed to collect information regarding reactivity and stability of such type of complexes. The chelating phosphine tagged NHC ligands are interesting structural motif to visualize the actual reaction pathway during the metathesis catalysis. The unsymmetrical nature with one alkyl substituent and other aromatic substituent on NHC structure could be a reason for unstable nature of the ruthenium complexes. Another thing is the stability of phosphine moiety attached to the NHC ligands. Because of that the replacement of triphenylphosphine or tricyclohexylphosphine from *Grubbs I* type complexes was not possible. The indirect method through silver complex formation was not as hopeful as there was no particular type of complex was formed. By using such mixture of unknown complex might create complicacy in the next step by reacting with *Grubbs I* type complexes. Though silver works as a good phosphine scavenger as well as ligand transfer agent, but for this type of ligand system is completely ineffective. These types of ligands and their complexes could be important structural motif in theoretical study. The various interactions with metal to ligands in different kinds of mode of attachment and bond-energy calculations could bring a shower of light to illuminate this still obscure topic. So the further development in synthesis and catalytic studies and structure-reactivity correlations would be challenging topics to develop new field.

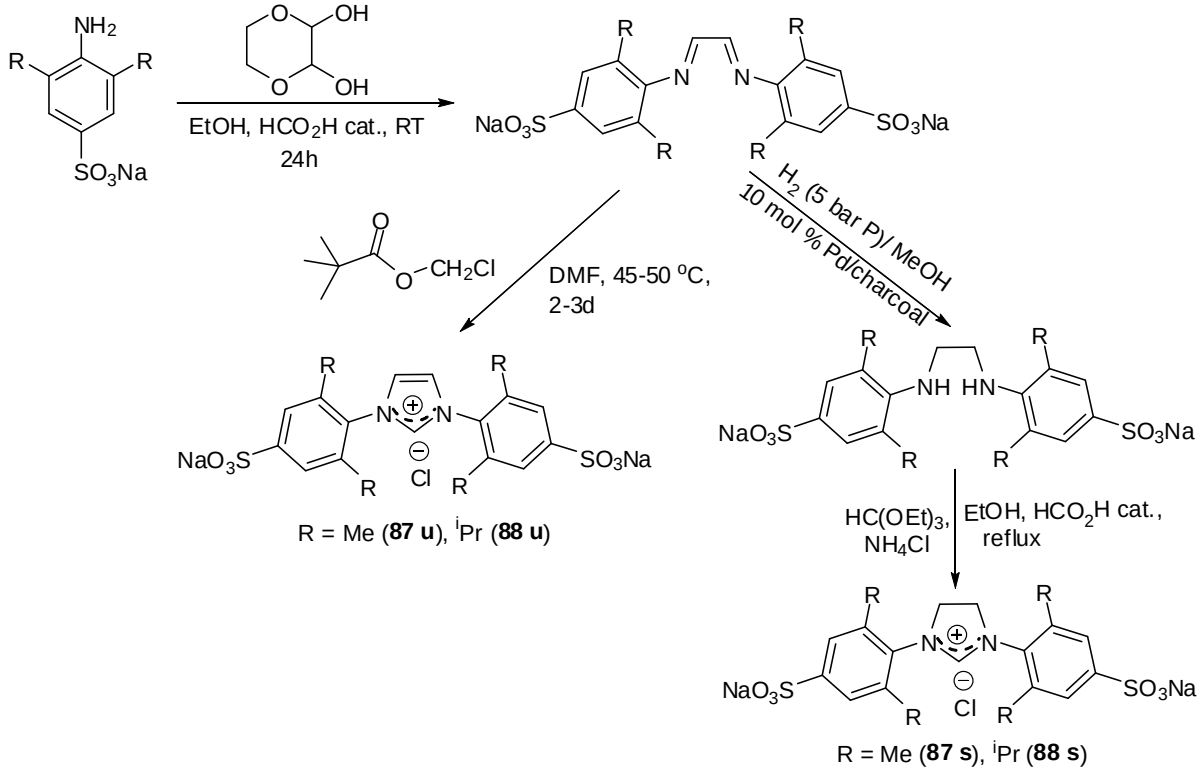
## *5 Summary and Outlook*

This thesis concerns with the development of new type of sulfonated *N*-heterocyclic carbene ligands and their application in the cross-coupling reactions in water. Besides this, another class of pincer type phosphine-tagged *N*-heterocyclic carbene ligands and their ruthenium complexes are synthesized. At first the synthesis of the sulfonated-NHC ligands are studied along with their proper characterization data. There are two methods concerning the synthesis of sulfonated-NHC ligands. In indirect method, sulfonated anilines are synthesized starting from commercially available aniline derivatives by reacting with concentrated sulfuric acid or oleum. Then the common route of synthetic procedure for imidazolium and imidazolinium salts is followed. In this method of synthesis of sulfonated-imidazolium salt, firstly diimine is made followed by the ring closing reaction with chloromethylpivalate ester to obtain the desired imidazolium salt as a product. For the synthesis of sulfonated-imidazolinium salt, first diimine, followed by the reduction ($H_2$/ Pd-charcoal catalyst) of it to obtain diamine and finally ring-closure is done by triethylorthoformate ester. For *meta*-substituted imidazolium and imidazolinium salts are usually obtained by this procedure. Thus by following this procedure bis(2,6-dimethyl-3-sulfonatophenyl)imidazolium/imidazolinium salts (**85 u**, **85 s**) and bis(2,4,6-trimethyl-3-sulfonatophenyl)imidazolium/imidazolinium salts (**86 u, 86 s**) are prepared.




***Scheme 5.1*** *Indirect method of synthesis of m-sulfonated imidazolium and imidazolinium salts*

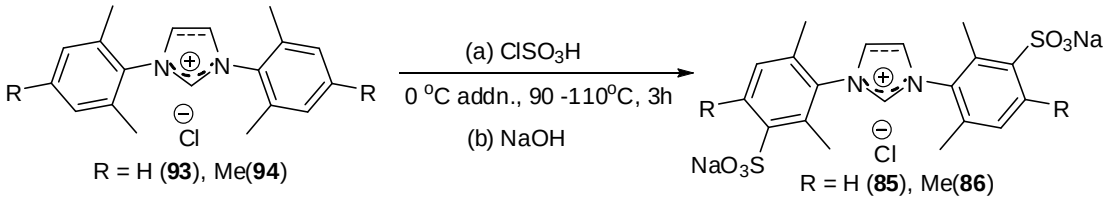
The *para*-substituted imidazolium and imidazolinium derivatives are obtained by following slightly modified procedure. Usually, anhydrous conditions are preferred to obtain high yield and pure product. Otherwise, there is always a mixture of product and starting materials. The diimine formation is effective by using anhydrous glyoxal derivatives, i.e., 2,3-dihydroxy-1,4-dioxane. For making diamine, palladium/charcoal catalyzed hydrogenation (pressure 5 to 7 bar) is used anhydrous methanol.




***Scheme 5.2*** *Indirect method of synthesis of p-sulfonated imidazolium and imidazolinium salts*

This procedure is having some drawbacks as purification of the desired product is difficult. Another thing is multi-step synthesis is always time consuming and overall yield is always low. So the direct method is evolved. In the direct method, sulfonation reaction is done with easily available imidazolium and imidazolinium salts, reacting with chlorosulfonic acid at 90 to 110 $^{o}$C for 1.5 to 3 h and the purification problem is avoided. By following this method, bis(2,6-dimethyl-3-sulfonatedphenyl)imidazolium/imidazolinium chlorides (**87 u, 87s**) and bis(2,4,6-trimethyl-3-sulfonatedphenyl)imidazolium/imidazolinium chlorides (**88 u, 88 s**) are obtained. But this method is having limitation because of the regioselectivity of product is not always restored. For synthesizing sulfonated-2,6-diisopropylimidazolium and imidazolinium salts, there is always a mixture of *para*- and *meta*-sulfonated product obtained. The sulfonated products

are separated by using reverse phase column chromatography. But this type of purification method suffers from low yield.




***Scheme5.3*** *Direct method of synthesis of m-sulfonated imidazolium and imidazolinium salts*

## *Suzuki-Miyaura (SM) Coupling Reaction*

Next these sulfonated imidazolium and imidazolinium salts are properly utilized in palladium-catalyzed aqueous phase cross coupling reaction, namely *Suzuki-Miyaura* (*SM*) and copper-free Sonogashira Reactions. In case of *Suzuki-Miyaura* coupling protocol, at first *in situ* generated palladium-NHC complexes are utilized. It is observed that imidazolium systems in combination with sodium tetra-chloro-palladate are more suitable match for cross-coupling protocol compared to the corresponding imidazolinium analogous which is already known from the systematic study in the literature. Moreover, bis(2,6-diisopropyl-4-sulfonatedphenyl)-imidazolium chloride shows better reactivity compared to the other imidazolium salts.Next this *Suzuki-Miyaura* coupling protocol is further extended in a variety of substrate, like different electron-rich chloro arenes and chloropyridine derivatives along with tolyl and naphthyl boronic acid by using bis(2,6-diisopropyl-4-sulfonatophenyl)imidazolium chloride as ligand.

In the quest of a better catalyst, palladium(allyl)NHC complexes are prepared from bis(2,6-diisopropyl-4-sulfonatophenyl)imidazolium chloride and palladium-allyl dimer. It is observed that the (cinnamyl)palladium-NHC complex display greater reactivity compared to the simple allyl-Pd-NHC complex in water/alcohol mixture with reduced catalyst loading (0.1 mol %). This may be due to the generation of active catalysts from Pd(allyl)NHC pre-catalyst in basic water/butanol media. Another interesting point is this palladium(phenylallyl)NHC complex shows even excellent reactivity with naphthyl boronic acid by reacting with sterically demanding ortho-substituted chloroarenes.

## *Sonogashira Reaction*

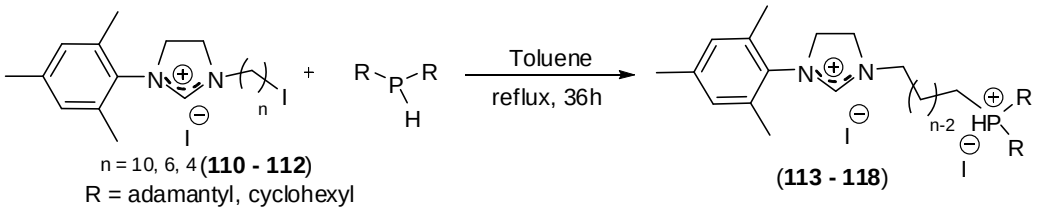
Further utilization of the sulfonated-NHC ligands is applied to *Sonogashira* reaction protocol where *in situ* generated catalyst from sodium tetrachloro-palladate and sulfonated-diisopropyl-imidazolium chloride shows good to excellent reactivity with electron-rich bromo-arenes as

well as chloro- and bromo-heteroarenes in water/isopropanol media without copper additive. The coupling of heteroaryl bromides and chlorides, like thiophene and furan-derivatives with different electron-rich phenyl acetylenes and alkyl acetylenes even better reactivity is observed using as low as 0.25 mol % catalyst loading.

## *Pincer-type Phosphine-tagged NHCs and ruthenium complexes*

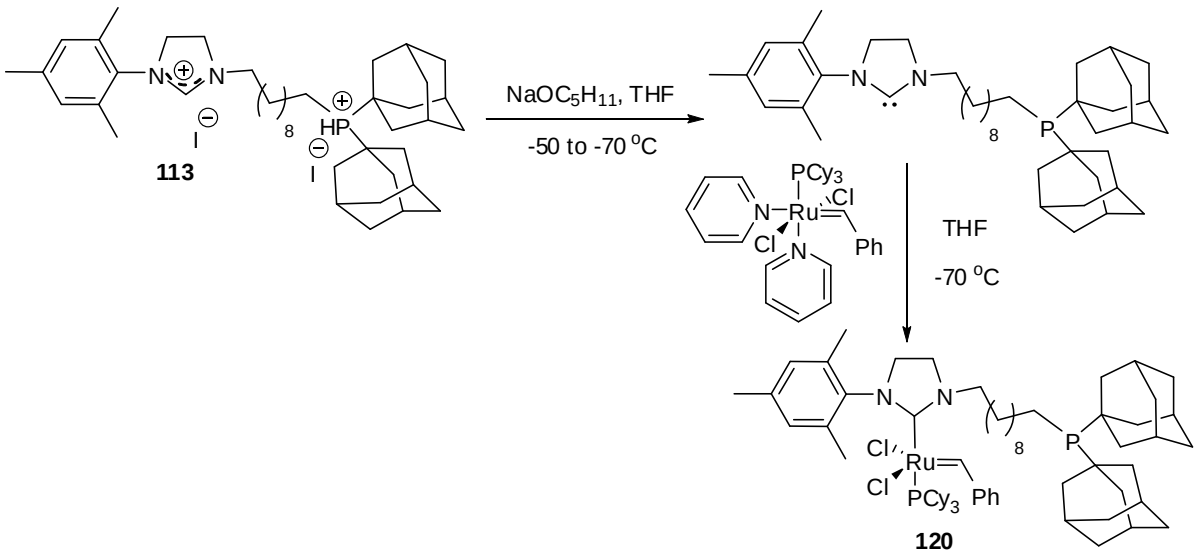
Another class of P-C pincer type ligands is synthesized where NHC ligand is attached with phosphine part through a long alkyl chain. The purpose of such type of ligand design is to synthesize ruthenium-alkylidene complex where NHC and phosphine parts would be *trans* to each other, like *Grubbs II* system. It is known from mechanistic study of olefin metathesis that the initiation of the catalysis occurred by breaking the phosphine-part and olefin is coordinated in that position and again termination of catalysis occurs by recoordination of the phosphine and thus catalyst is recycled. From this pincer-type NHC-phosphine ligand would be a model system of the *Grubbs II* type complex where the initiation and regeneration of the catalyst would be easier and also the stability of the system would be greater compared to usual *Grubbs II* type system. The reactivity of such type of complex to the olefin catalysis is a curious query.

The ligand is synthesized from the iodo-alkyl imidazolinium salts with diaryl or dialkyl phosphine either as alkylated form or directly. By following this method dicyclohexylphosphonium-imidazolinium diiodo salt and diadamantylphosphonium-imidazolinium diiodo salts are obtained.




***Scheme 5.4*** *Synthesis of phosphine-tagged imidazolinium salts*

This type of ligands is attempted in several ways to synthesize the ruthenium-alkylidene complexes. By following direct method, imidazolinium-phosphonium salts are *in situ* deprotonated with strong bases, like potassium tert-butoxide or sodium-tert-pentylate and followed by addition to *Grubbs I* type complexes ($PPh_3$ and $PCy_3$ analogue). But in all these cases desired bi-coordinated complex is not formed. In case of *Grubbs I* ($PCy_3$) complex for diadamantyl, it was possible to obtain NHC-coordinated and dangling diadamantylphosphine of ruthenium complex but the unstable nature put the limit to the further extensive study.




***Scheme 5.4*** *Synthesis of ruthenium-NHC-dangling phosphine complex*

By following other indirect method, such as silver complex formation or ruthenium-indenylidene complex synthesis, it was not possible to obtain desired goal.

From the above mentioned study of cross-coupling reaction and *Grubbs II* type model system, some points could be rationalized in the future plan of work.

There is still demand for making new type of *N*-heterocyclic carbene ligands which could show its reactivity in solely aqueous media at ambient condition with ppm or ppb level of catalyst loading irrespective of the nature of the substrate in cross-coupling reaction. The synthesis and purification process would be easier and cost-effective to make universally accepted for large-scale synthesis. The catalyst must be robust so that the stable nature of catalyst could be viable to use in open air without rigorous restriction of inert atmosphere and recycling process could be maintained very effectively. In case of *Sonogashira* reaction the protocol should be much more sustainable to lower catalyst loading with various chloroarenes or chloroalkyl and alkyl-acetylenes as partners.

This type ruthenium catalysis protocol might be helpful in the point of view of theoretical and mechanistic study. There is still thorough investigation needed to find a suitable system which could fulfill our desired attempt. It would be a really great job if such type of stable and recyclable catalyst could be synthesized for olefin metathesis reaction.

# 6 Experimental Part

## 6.1 General Considerations

Solvents and Reagents and Reaction Condition

Almost all reactions except few starting materials were carried out under an atmosphere of argon using standard Schlenk techniques. The solvents were purchased as reagent grade and dried either by passing through a column with dry alox with argon pressure or distilled from appropriate drying reagents such as sodium, potassium, phosphorus pent-oxide and condensed under argon atmosphere. The high boiling solvents, like DMSO, DMF were used as very dry with sealed bottle, like crown-cap category. All chemicals were purchased as reagent grade from commercial sources and used without further purification, unless it was mentioned. Arylboronic acids were prepared from the corresponding aryl bromides according to the commonly reported procedures and purified as described by Espinet.[157]

Nuclear Magnetic Resonance Spectroscopy (NMR)

$^{1}H$ NMR, $^{13}C$ NMR and $^{31}P$ NMR spectra were recorded on Bruker DRX 500 at 500 MHz for $^{1}H$, 126 MHz for $^{13}C$ and 202 MHz for $^{31}P$ respectively and Bruker DRX 300 at 300 MHz for $^{1}H$, 75 MHz for $^{13}C$ and 121 MHz for $^{31}P$ respectively and on Bruker AM 200 at 200 MHz for $^{1}H$ and 81 MHz for $^{31}P$ respectively. The chemical shifts were measured in parts per million (ppm) on the delta scale (δ) and were referenced to tetramethylsilane ($^{1}H$, $^{13}C$ NMR 0 ppm) or the residual solvent peak. $^{31}P$ NMR was referenced to $H_3PO_4$ (65% aq. 0 ppm) or $PMe_3$ (-63 ppm). Abbreviations for NMR data: s for singlet; d for doublet; t for triplet; q for quartet; sep for septet; m for multiplet; bs for broad signal; arom for aromatic protons.

Infrared Spectroscopy (IR)

IR spectra were recorded on a Perkin-Elmer 1600 IR spectrometer as a film between KBr palates.

Gas Chromatography (GC)

GC analysis was performed on Virian CP-Sil 8 CB column (length 15m, diameter 0.25mm, $d_F$ 1.0 µm) with Perkin Elmer Clarus 500 GC Auto System.

Mass Spectrometry (MS)

HR-MS (EI) was recorded on a Finnigan MAT95 mass spectrometer.

Thin Layer Chromatography (TLC)

Thin layer Chromatography (TLC) was performed using silica gel 60 F 254 (0.2 mm) on aluminium plates and reversed phase HP 20 TLC plates were used.

Flash Column Chromatography

For preparative chromatography E. Merck silica gel 60 F 254 (0.20 to 0.063 mm) on aluminium plates was used and reversed phase column chromatography was prepared with HP-20 polymer.

The following reagents were purchased from by general chemical suppliers:

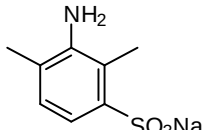
2,4,6-Trimethylaniline, 2,6-Dimethylaniline, 2,6-diisopropylaniline, glyoxal (aq. 40 %), paraformaldehyde, lithium aluminiumhydride, tricyclohexylphosphine, silver oxide ($Ag_2O$), tri-ethylorthoformate ester, chloromethyl pivaluate ester, 4-chlorotoluene, 4-chloroanisole, 4-chloroacetophenone, 4-chloronitrobenzene, 4-chlorobenzo-trifluoride, 4-chlorobenzonitrile, 2,6-dimethylchlorobenzene, 2-chlorotoluene, 2-isopropylbromobenzene, 4-bromotoluene, 4-bromoanisole, 2-bromotoluene, 2,6-dimethylbromobenzene, chloropyridines, chloropyridine derivatives, 2-chloroquinoline, chloroquinoline derivatives, 2-bromopyridine, bromopyridine derivatives, phenyl acetylene, 4-methoxyphenyl acetylene, 4-methylphenyl acetylene, n-hexyl acetylene, cyclohexyl acetylene, cinnamyl bromide etc.

The following reagents were synthesized according to literature procedure:

N,N'-bis(2,4,6-trimethylphenyl)imidazolium chloride[164, 165], N,N'-bis(2,4,6-trimethylphenyl) imidazolinium chloride[164, 165], N,N'-bis(2,4,6-trimethylphenyl)ethane-1,2-diamine[164, 165], N,N'-bis(2,4,6-trimethylphenyl)ethane-1,2-diimine[164, 165], N,N'-bis(2,6-dimethylphenyl)imidazolium chloride[164, 165], N,N'-bis(2,6-dimethylphenyl)imidazolinium chloride[164, 165], N,N'-bis(2,6-diisopropylphenyl)imidazolium chloride[164, 165], N,N'-bis(2,6-diisopropylphenyl)imidazolinium chloride[164, 165], (allyl)chloro-palladium(II) dimer[76], (cinnamyl)chloro-palladium(II) dimer[76], *Grubbs I* catalyst[109], *Grubbs I* Catalyst ($PPh_3$ analogous)[109], Ruthenium-indenyl complex[166], *Grubbs-III* catalyst[162a] etc.

## *6.2 Synthesis of Aniline derivatives*

**(A) 2,6-Dimethyl-3-sulfonatedaniline sodium salt** (modified literature procedure)[158]



**95b**

In 2,6-dimethylaniline (24.2 g, 200 mmol), 100 ml 20% oleum ($SO_3$ in $H_2SO_4$) was dropwise added slowly over a period of 2 hours under inert atmosphere so that the reaction mixture temperature remained around room temperature. It was then heated up to 110 $^{o}$C and stirred at this temperature for 1.5 hour. Afterwards, it was cooled down and poured slowly into 150 g ice and whole system kept cool using ice-water bath. The product was precipitated out and filtered off and washed with ice-cold water to remove most of the acid. Now the product would not be completely pure as it might contain double sulfonated aniline. Then it was dried and redissolved in water and kept it for slow crystallization at ambient condition. The mono-meta- aniline sulfonic acid was selectively crystallized out. The desired product was separated and filtered and washed with ice-cold water.

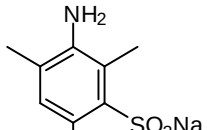
The product was neutralized with dilute sodium hydroxide (NaOH) solution and at the neutralization point it became a clear solution. The solution was concentrated by evaporating water and finally became off-white solid product.

**$^{1}$H NMR** (300MHz, DMSO-$d_6$) δ [ppm] 7.01 (d, 1H, ArH, *J* = 9 Hz), 6.73 (d, 1H, ArH, *J* = 9 Hz), 4.45 (s, 2H, $NH_2$), 2.29 (s, 3H, $CH_3$), 2.06 (s, 3H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 144.5, 144.1, 125.6, 121.9, 118.2, 115.0, 17.9, 14.1.

**(B) 2,4,6-Trimethyl-3-sulfonatedaniline sodium salt**

The procedure was similar to the above mentioned. There was only change that 2,4,6-trimethyl –aniline was taken instead of 2,6-dimethylaniline and the same course of steps were repeated.

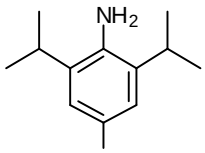


**96**

**$^{1}$H NMR** (300MHz, DMSO-$d_6$) δ [ppm] 6.58 (s, 1H, ArH), 4.23 (s, 2H, $NH_2$), 2.40 (s, 3H, $CH_3$), 2.37 (s, 3H, $CH_3$), 2.03 (s, 3H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 142.9, 142.5, 130.4, 122.7, 121.0, 119.9, 22.7, 17.7, 15.4.

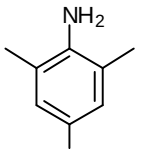
**(C) 2,6-Diisopropyl-4-sulfonatoaniline sodium salt** (modified literature procedure)



**98**

In a 500 ml two-necked round bottomed flask 2,6-diisopropylaniline (43.5 g, 245 mmol) was added slowly to a mixture of 15 ml conc. Sulfuric acid and 44 ml water. Then water was removed completely under vacuum by heating upto 160 to 180 $^{o}$C using metal-bath. Afterwards, the reaction temperature was raised to 260 $^{o}$C for 3 h. The resulting grey solid was allowed to cool up to 100 $^{o}$C and NaOH solution (35 ml of 30 % and little amount of water if needed) was poured cautiously and then stirred for 15 min at 90 to 100 $^{o}$C. Then it was filtered off in hot condition and acidified with conc. HCl to pH 2 and cooled down. The precipitated solid was separated by filtration and again it was suspended in water and 20 % sodium carbonate ($Na_2CO_3$) solution was added and heated to 90 $^{o}$C. The solution should be basic (pH around 8) and activated charcoal (2 g) was added to it and filtered in hot condition. In the hot filtrate 40g of NaCl was added and the solution was allowed to stand overnight in cold condition. The product was separated as crystalline solid and filtered off and dried a white solid. Yield: 40.2 g (58.5 %). The NMR data was identical with the literature reported data.[159]

**(D) 2,6-Dimethyl-4-sulfonatoaniline sodium salt**

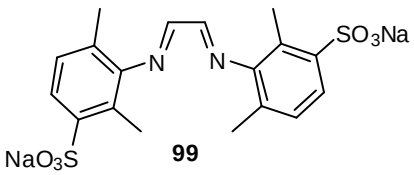


**97**

The procedure was similar like diisopropyl-sulfonatoaniline and the scale of the reaction was different. 2,6-dimethylaniline (12.2 g, 100.7 mmol) and 2.5 ml conc. $H_2SO_4$ etc. Yield: 14.0 g (68.7 % , sulfonic acid form) and 15.0 g (67.1%, sulfonated sodium salt ). The NMR data was similar to the literature report. [159]

## *6.3 Synthesis of Diimine derivatives*

***(E) N,N'*-bis(2,6-dimethyl-3-sodium-sulfonatophenyl)ethane-1,2-diimine**



**99**

In a 500 ml round bottom flask the sulfonated aniline (10 g, 44.8 mmol) was dissolved in 250 ml ethanol by stirring 30 min. Then glyoxal (2.6ml, 22.4mmol, 40 % aq.) was added dropwise to the solution followed by the addition of 5 to 6 drops of formic acid. The reaction mixture was stirred overnight at room temperature and then stirring was continued for 24 h at 50 $^{o}$C. A yellow solid

was precipitated out, filtered off and washed with cold methanol and dried *in vacuo*. Yield: 6.1 g (68.7 %).

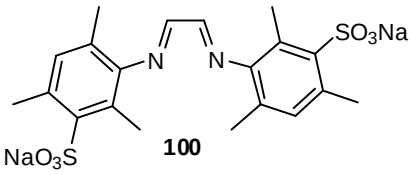
**$^{1}$H NMR** (300 MHz, DMSO-$d_6$) δ [ppm] 8.10 (s, 2H, CH), 7.53 (d, 2H, ArH, *J* = 9 Hz), 7.05 (d, 2H, ArH, J = 9 Hz), 2.32 (s, 6H, $CH_3$), 2.08 (s, 6H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 163.9, 150.2, 144.9, 126.4, 125.9, 123.9, 123.0, 18.0, 14.8.

HRMS calcd for $C_{18}H_{18}N_2S_2O_6Na$ (M-NaCl) 445.0504; found 445.0509.

***(F) N,N'*-bis(2,4,6-trimethyl-3-sodium-sulfonatophenyl)ethane-1,2-diimine**

The above mentioned procedure was followed to synthesize this compound with slight alteration. Sulfonated aniline (8.35 g, 33 mmol) was reacted with aqueous glyoxal (19.2 ml, 16.6 mmol) in 500 ml methanol instead of ethanol like earlier. At first aniline should dissolves in methanol and then stirring was carried out at room temperature for 2 days. The yellow precipitate was collected by filtration and washed with cold methanol to obtain product. Yield: 3.6 g (44 %).



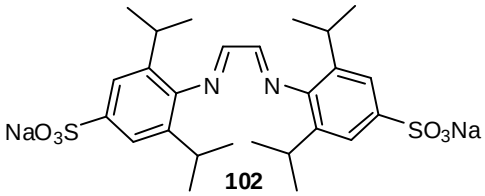
**100**

**$^{1}$H NMR** (300 MHz, DMSO-$d_6$) δ [ppm] 8.04 (d, 2H, CH, J = 1.2 Hz), 6.89 (s, 2H, ArH), 2.52 (s, 3H, $CH_3$), 2.36 (s, 3H, $CH_3$), 2.03 (s, 3H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 163.7, 148.5, 143.7, 131.8, 131.0, 125.5, 124.5, 22.8, 17.8, 16.6.

***(G) N,N'*-bis(2,6-diisopropyl-4-sodium-sulfonatophenyl)ethane-1,2-diimine**

In a 250 ml round bottomed flask 2,6-diisopropyl-4-sulfonatoaniline sodium salt (4.7 g, 14.9 mmol) was dissolved in 100 ml of dry ethanol (dried over calcium hydride and distilled off) and 2,3-dihydroxy-1,4-dioxane (0.90 g, 7.5 mmol) was added followed by the addition of formic acid (6 to 7 drops). The reaction mixture was continued stirring and the clear



**102**

solution started becoming turbid because of the precipitation of diimine. The reaction mixture was stirred for 2 days at ambient condition to get complete conversion of product. The yellow product was separated, filtered and washed with cold ethanol and dried in vacuo to afford pure powdery product. Yield: 3.5 g (80.9 %).

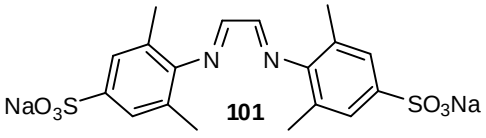
**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 8.15 (s, 2H, CH), 7.45 (s, 4H, ArH), 2.86 (sept, 4H, CH, $^{3}J$ = 6.9 Hz), 1.15 (d, 24H, $CH_3$, $^{3}J$ = 6.9 Hz).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 163.8, 148.3, 144.9, 135.6, 120.8, 28.0, 23.4.

ESI-MS: m/z calcd for $C_{26}H_{34}N_2Na_2O_6S_2$ ($M^{\bullet+}$ + Na) 603.6; found 603.7 and (M -$Na^{+}$) 557.2; found 557.3.

***(H) N,N'*-bis(2,6-dimethyl-4-sodium-sulfonatophenyl)ethane-1,2-diimine**

The procedure was similar like the diisopropylaniline analogous as described above. 2,6-dimethyl-4-sulfonatoaniline sodium salt ( 5.0 g, 22.4 mmol), 2,3-dihydroxy-1,4-dioxane (1.32 g, 11.0 mmol) in 150 ml dry ethanol and 8 to 10 drops formic acid catalyst.



**101**

Yield: 2.6 g (49.5 %).

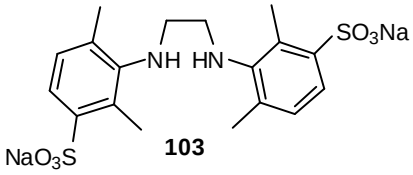
**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 8.15 (s, 2H, CH), 7.37 (s, 4H, ArH), 2.12 (s, 12H, $CH_3$).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 164.1, 150.0, 144.5, 125.8, 125.5, 18.2.

## *6.4 Synthesis of Diamine derivatives*

***(I) N,N'*-bis(2,6-dimethyl-3-sodium-sulfonatophenyl)ethane-1,2-diamine**

The dimethyl-sulfonated diimine (5.0 g, 10.2 mmol) was suspended in 120 ml of dry methanol in an autoclave flask and palladium/charcoal (1.13 g, Pd: 10 % (w/w)) was added. The mixture was hydrogenated for 3 h at 5 to 7 bar $H_2$



**103**

pressure. Afterwards, the reaction mixture was filtered off through a pad of celite to remove the catalyst and the solution was evaporated to afford white (sometimes pinkish tinge) solid product. Yield: 3.1 g (64 %).

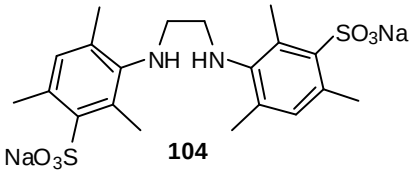
**$^{1}$H NMR** (300 MHz, DMSO-$d_6$) δ [ppm] 7.32 (d, 2H, ArH, *J* = 9 Hz), 6.86 (d, 2H, ArH, *J* = 9 Hz), 3.0 (s, 4H, $CH_2$), 2.43 (s, 6H, $CH_3$), 2.20 (s, 6H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 146.8, 144.6, 130.8, 127.9, 126.3, 120.4, 48.5, 18.5, 14.8.

HR-MS: m/z calcd for $C_{19}H_{21}N_2S_2O_6Na$ (M-NaCl) 483.0636; found 483.0627.

***(J) N,N'*-bis(2,4,6-trimethyl-3-sodium-sulfonatophenyl)ethane-1,2-diamine**

The trimethyl-sulfonated diimine (1.0 g, 2 mmol) was suspended in 160 ml dryl MeOH and with molecular sieves (2g, 4 Å) and Pd/C (0.20 g, Pd: 10 % (w/w)) were used. The hydrogenation time was very long almost 7 to 8 hours to obtain complete hydrogenated product.



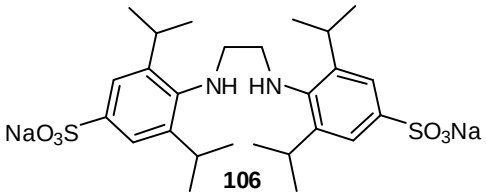
**104**

Yield: 0.95 g (94.9 %).

**$^{1}$H NMR** (200 MHz, DMSO-$d_6$) δ [ppm] 6.67 (s, 4H, ArH), 4.07 (m, br, 2H, NH), 2.90 (s, 4H, $CH_2$), 2.56 (s, 3H, $CH_3$), 2.39 (s, 3H, $CH_3$), 2.15 (s, 3H, $CH_3$).

***(K) N,N'*-bis(2,6-diisopropyl-4-sodium-sulfonatophenyl)ethane-1,2-diamine**

The diisopropyl-sulfonated diimine (5.0 g, 8.6 mmol) was used in 150 ml dry MeOH and Pd/C (1.0 g, Pd: 10 % (w/w)). The mixture was hydrogenated for 6 h at 7 bar pressure. Yield: 4.1 g (81.5 %).



**106**

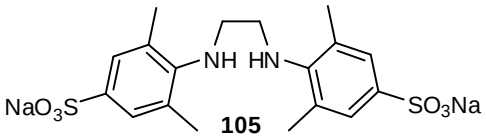
**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 7.33 (s, 4H, ArH), 3.92(s, br, 2H, NH), 3.40 (m, 4H, CH), 1.17 (d, 24H, $CH_3$, $^{3}J$ = 6.9 Hz).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 144.4, 143.1, 141.6, 121.1, 52.1, 27.3, 24.6.

ESI-MS: m/z calcd for $C_{26}H_{38}N_2Na_2O_6S_2$ ($M^{\bullet+}$ + Na) 607.2; found 607.4 and ($M-Na^+$) 561.2; found 561.2.

***(L) N,N'*-bis(2,6-dimethyl-4-sodium-sulfonatophenyl)ethane-1,2-diamine**

The dimethyl-4-sulfonated diimine (1.01 g, 2.16 mmol) was similarly hydrogenated by using Pd/C (0.15 g, Pd: 10 % (w/w)) in 180 ml dry MeOH containing molecular sieves (3 g, 4 Å). Yield: 0.75 g (73.5 %).



**105**

**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 7.18 (s, 4H, ArH), 4.06 (s, br, 2H, NH), 3.07 (s, 4H, $CH_2$), 2.20 (s, 12H, $CH_3$).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 147.7, 142.1, 128.9, 127.3, 49.3, 19.9.

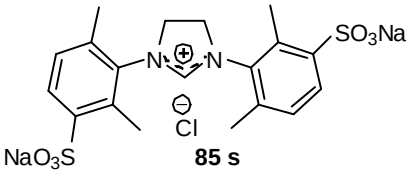
## *6.5 Synthesis of Imidazolinium salts*

### 6.5.1 General procedure for the synthesis of sulfonated imidazolinium chlorides

The corresponding sulfonated diamine (1 eq) and ammonium chloride (NH4Cl, 1 eq) were taken in a round bottomed flask, equipped with reflux condenser. Then a mixture of triethylortho-formate ester ($HC(OEt)_3$, 10 eq) and ethanol (10ml/mmol)was added to the flask along with one drop of formic acid. The reaction mixture was refluxed for one day. It was cooled to room temperature and the product was precipitated out from the solution. The off-white solid product was filtered off and washed with ethyl acetate to obtain almost pure product. In case the product was not pure, then purification was done by using reverse phase column chromatography (HP-20) and water/methanol mixture as eluant.

***(M) N,N'*-bis(2,6-dimethyl-3-sulfonatophenyl)imidazolinium disodium chloride**

Bis(2,6-dimethyl-3-sulfonatophenyl)diamine (1.67 g, 3.5 mmol), $NH_4Cl$ (0.19 g, 3.5 mmol) and $HC(OEt)_3$ (20 ml) and ethanol (30 ml) refluxed together. Yield: 1.40 g (77 %).




**85 s**

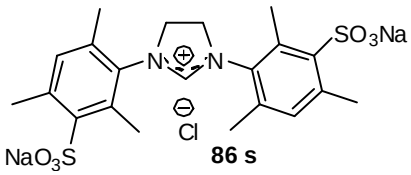
**$^1$H NMR** (300 MHz, DMSO-$d_6$) δ [ppm] 9.12 (d, 1H, CH, *J* = 6 Hz), 7.82 (d, 2H, ArH, *J* = 9 Hz) 7.22 (d, 2H, ArH, *J* = 9 Hz), 4.47 (s, 4H, $CH_2$), 2.61 (s, 6H, $CH_3$), 2.37 (s, 6H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 160.5, 145.9, 145.7, 136.3, 133.9, 128.1, 127.4, 50.9, 17.5, 14.6.

HRMS calcd for $C_{18}H_{22}N_2S_2O_6Na$ (M-NaCl) 449.0817; found 449.082.

***(N) N,N'*-bis(2,4,6-trimethyl-3-sulfonatophenyl)imidazolinium disodium chloride**

Bis(2,4,6-trimethyl-3-sulfonatophenyl)diamine (0.95 g, 1.89 mmol), $NH_4Cl$ (0.10 g, 1.89 mmol) and $HC(OEt)_3$ (20 ml) and ethanol (30 ml) refluxed together. Yield: 0.87 g (84 %).




**86 s**

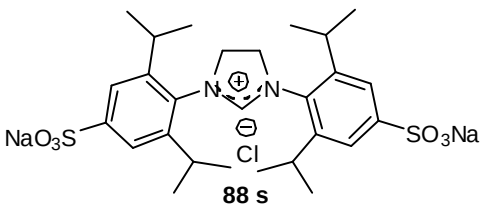
**$^1$H NMR** (500 MHz, $D_2O$) δ [ppm] 8.55 (d, 1H, CH, *J* = 2.4 Hz), 7.19 (s, 2H, ArH, *J* = 9 Hz), 4.46 (s, 4H, $CH_2$), 2.59 (s, 6H, $CH_3$), 2.54 (s, 6H, $CH_3$), 2.34 (s, 6H, $CH_3$).

**$^{13}$C NMR** (125.8 MHz,$D_2O$) δ [ppm] 160.5, 145.9, 145.7, 136.3, 133.9, 128.1, 127.4, 51.6, 22.7, 17.5, 16.4.

ESI-MS: m/z calcd for $C_{21}H_{25}N_2Na_2O_6S_2Cl$ ($M\text{-}Cl^-$) 511.1; found 511.3 and ($M\text{-}Cl^-\text{-}2Na^+$) 465.1; found 465.1.

***(O) N,N'*-bis(2,6-diisopropyl-4-sulfonatophenyl)imidazolinium disodium chloride**

Bis(2,6-dimethyl-4-sulfonatophenyl)diamine (1.5 g, 3.2 mmol), $NH_4Cl$ (0.17 g, 3.2 mmol) and $HC(OEt)_3$ (20 ml)




**88 s**

and ethanol (30 ml) refluxed together. Yield: 0.87 g (52 %).

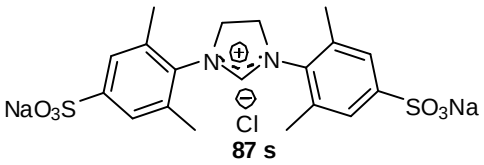
**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 9.49 (s, 1H, CH), 7.58 (s, 4H, ArH), 4.53 (s, 4H, $CH_2$), 3.12-3.04 (m, 4H, CH), 1.34 (d, 12H, $CH_3$, $^{3}J$ = 6.8 Hz), 1.19 (d, 12H, $CH_3$, $^{3}J$ = 6.8 Hz).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 159.7, 150.2, 145.2, 129.2, 121.2, 53.1, 27.7, 24.4, 22.8.

ESI-MS: m/z calcd for $C_{27}H_{37}N_2Na_2O_6S_2Cl$ (M-$Cl^-$) 595.2; found 595.4 and (M-$Cl^-$-2$Na^+$) 549.2; found 549.2.

***(P) N,N'*-bis(2,6-dimethyl-4-sulfonatophenyl)imidazolinium disodium chloride**

Bis(2,6-diisopropyl-4-sulfonatophenyl)diamine (0.90 g, 3.2 mmol), $NH_4Cl$ (0.17 g, 3.2 mmol) and $HC(OEt)_3$ (20 ml) and ethanol (30 ml) refluxed together. Yield: 0.87 g (52 %).



**87 s**

**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 9.05 (s, 1H, CH), 7.47 (s, 4H, ArH), 4.48 (s, 2H, $CH_2$), 2.40 (s, 12H, $CH_3$).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 160.6, 150.0, 135.7, 133.5, 126.4, 51.2, 17.7.

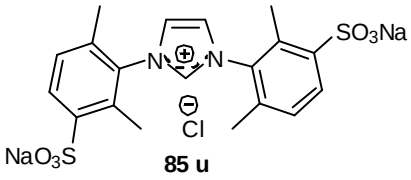
## *6.6 Synthesis of Imidazolium salts*

### 6.6.1 General procedure for the synthesis of sulfonated imidazolium chlorides

In a 25 ml Schlenk tube, the respective sulfonated diimine (1.0 eq) was suspended in dry DMSO and chloromethylpivalate (1.1 eq) was added to it through syringe. The reaction mixture was stirred at 45 $^{o}$C for 2 to 3 days. By this time, the reaction mixture turned brownish tinge solution from starting yellow color. Then it was cooled to room temperature and DMSO was removed *in vacuo* to leave a brownish/off-white solid. It was stirred with several portions of ethylacetate for longer time (5x 50 ml for 5 to 6 h) to remove the impurities completely. Alternatively, purification with reverse-phase column (HP-20) and water/methanol eluant was also could be used but yield would be less.

***(Q) N,N'*-bis(2,6-dimethyl-3-sulfonatophenyl)imidazolium disodium chloride**

Bis(2,6-dimethyl-3-sulfonatophenyl)diimine (1.35 g, 2.8 mmol) and chloromethylpivalate ester (0.477 g, 0.46 ml, 4.6 mmol) in 12 to 15 ml DMSO reacted for 2 to 3 days at 45 $^{o}$C. Yield: 1.15 g (77.3 %).



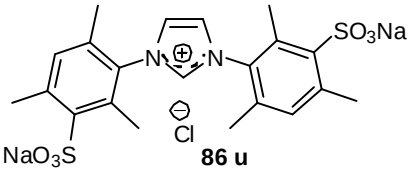

**85 u**

**$^{1}$H NMR** (300 MHz, DMSO-$d_6$) δ [ppm] 9.72 (d, 1H, CH, *J* = 6 Hz), 8.32 (d, 2H, CH, *J* = 6 Hz), 7.93 (d, 2H, ArH, *J* = 9 Hz), 7.32 (d, 2H, ArH, *J* = 9 Hz), 2.33 (s, 6H, $CH_3$), 2.11 (s, 6H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, DMSO-$d_6$) δ [ppm] 161.0, 140.2, 139.9, 138.5, 133.5, 132.5, 17.1, 14.3.

***(R) N,N'*-bis(2,4,6-trimethyl-3-sulfonatophenyl)imidazolium disodium chloride**

Bis(2,4,6-trimethyl-3-sulfonatophenyl)diimine (1.2 g, 2.4 mmol) and chloromethylpivalate ester (0.40 g, 0.38 ml, 2.6 mmol) in 12 to 15 ml DMSO reacted for 2 to 3 days at 45 $^{o}$C. Yield: 0.93 g (71.0 %).




**86 u**

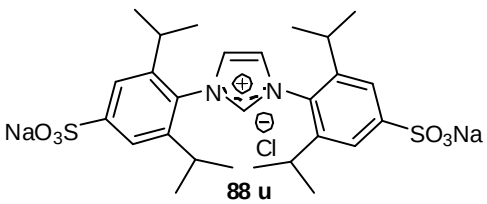
**$^{1}$H NMR** (300 MHz, $D_2O$) δ [ppm] 9.22 (d, 1H, CH), 7.86 (s, 2H, CH), 7.27 (s, 2H, ArH), 2.58 (s, 6H, $CH_3$), 2.33 (d, 6H, $CH_3$, *J* = 6 Hz), 2.11 (d, 6H, $CH_3$, *J* = 3 Hz).

**$^{13}$C NMR** (75.5 MHz,$D_2O$) δ [ppm] 140.4, 139.9, 137.1, 134.0, 132.9, 132.4, 125.2, 22.5, 16.8, 15.8.

ESI-MS: m/z calcd for $C_{21}H_{23}N_2Na_2O_6S_2Cl$ (M-$Cl^-$) 509.1; found 509.2 and (M-$Cl^-$-2$Na^+$) 463.1; found 463.1.

***(S) N,N'*-bis(2,6-diisopropyl-4-sulfonatophenyl)imidazolium disodium chloride**

Bis(2,6-diisopropyl-4-sulfonatophenyl)diimine (1.13 g, 1.9 mmol) and chloromethylpivalate ester (0.322 g, 0.3 ml, 2.1 mmol) in 10 to 12 ml DMSO reacted for 2 to 3 days at 45 $^{o}$C. Yield: 0.90 g (73.3 %).




**88 u**

**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 10.22 (s, 1H, CH), 8.57 (s, 2H, CH), 7.67 (s, 4H, ArH), 2.40-2.34 (m, 4H, CH), 1.26 (d, 12H, $CH_3$, $^{3}J$ = 7.0 Hz), 1.16 (d, 12H, $CH_3$, $^{3}J$ = 8.5 Hz).

(500 MHz, $D_2O$) δ [ppm] 9.57 (s, 1H, CH), 7.96 (s, 2H, CH), 7.69 (s, 4H, ArH), 2.36 (m, 4H, CH), 1.13 (d, 12H, $CH_3$, $^{3}J$ = 6.5 Hz), 1.06 (d, 12H, $CH_3$, $^{3}J$ = 6.6 Hz).

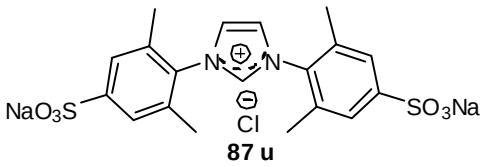
**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 152.6, 145.5, 140.5, 130.9, 127.3, 122.5, 29.7, 25.1, 24.1.

(125.8 MHz, $D_2O$) δ [ppm] 147.1, 146.3, 138.7, 132.3, 126.5, 122.2, 29.4, 23.9, 22.9.

ESI-MS: m/z calcd for $C_{27}H_{35}N_2Na_2O_6S_2Cl$ (M-$Cl^-$) 593.2; found 593.4 and (M-$Cl^-$-2$Na^+$) 547.2; found 547.2.

***(T) N,N'*-bis(2,6-dimethyl-4-sulfonatophenyl)imidazolium disodium chloride**

Bis(2,6-dimethyl-4-sulfonatophenyl)diimine (1.22 g, 2.6 mmol) and chloromethylpivalate ester (0.430 g, 0.4 ml, 2.8 mmol) in 12 to 15 ml DMSO reacted for 2 to 3 days at 45 $^{o}$C. Yield: 0.95 g (70.6 %).




**87 u**

**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 9.73 (s, 1H, CH), 8.32 (s, 2H, $CH_2$), 7.57 (s, 4H, ArH), 2.17 (s, 12H, $CH_3$).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 150.8, 138.9, 134.6, 133.4, 126.2, 17.4.

## *6.7 Direct method of synthesis of Imidazolinium and imidazolium salts*

### 6.7.1 Direct method for the synthesis of sulfonated imidazolinium chlorides

In a two-necked round bottomed flask, equipped with reflux condenser, imidazolinium chloride was taken and the air inside the flask was replaced by argon. Then at cold condition chloro-sulfonic acid (5 ml/g) was added dropwise into the flask. Afterwards, it was warmed upto room-temperature and slowly heated up to 100 to 110 $^{o}$C for 2 to 3 h. Then it was allowed to cool down to ambient temperature and this high viscous material slowly added to ice (using ice-salt

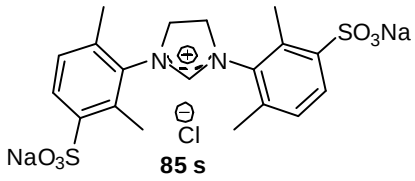
mixture bath at -20 $^{o}$C) and afterwards, stirred slowly to avoid lump formation. The product was finally filtered off and removed water *in vacuo*. There would be still lot of acid in the product which was removed slowly by stirring with several portions of ethyl acetate and filtered off the material as powder. The complete removal of product could be detected from $^{1}$H NMR data.

Finally the product obtained by the above work-up procedure was sulfonic acid derivative of the corresponding imidazolinium salt. This was neutralized with NaOH and heated up to 50 $^{o}$C . Then water was removed completely to obtain the pure sulfonated-sodium salt.

***(U) N,N'*-bis(2,6-dimethyl-3-sodium-sulfonatophenyl)imidazolinium chloride**

N,N'-bis(2,6-dimethylphenyl)imidazolinium chloride (1 g, 3.19 mmol) and $ClSO_3H$ (5 ml).

Yield: 0.77 g (46.5 %).

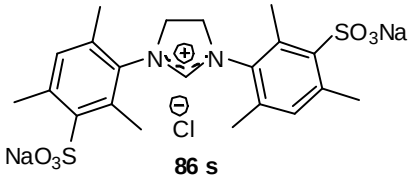



**85 s**

***(V) N,N'*-bis(2,4,6-trimethyl-3-sodium-sulfonatophenyl)imidazolinium chloride**

N,N'-bis(2,4,6-trimethylphenyl)imidazolinium chloride (4.94 g, 14.5 mmol) and $ClSO_3H$ (50 ml).

Yield: 5.5 g (69.3 %) .




**86 s**

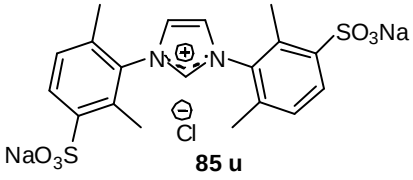
**6.7.2 Direct method for the synthesis of sulfonated imidazolium chlorides**

For imidazolium salt similar procedure like above was used. But the raction temperature was lower to obtain complete conversion of chloro-sulfonated or finally sulfonated product. Finally neutralization with dilute NaOH and heated up to 50 $^{o}$C formed the product as sulfonated-sodium salt. Water was removed and evacuated to obtain pure product.

***(W) N,N'*-bis(2,6-dimethyl-3-sodium-sulfonatophenyl)imidazolium chloride**

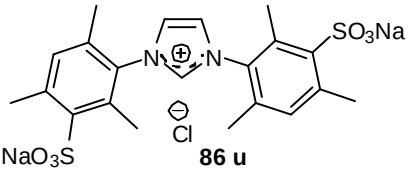
N,N'-bis(2,6-dimethylphenyl)imidazolinium chloride (2.4 g, 7.6 mmol) and $ClSO_3H$ (15 ml).

Yield: 2.32 g (59 %).




**85 u**

***(X) N,N'*-bis(2,4,6-trimethyl-3-sodium-sulfonatophenyl)imidazolium chloride**




**86 u**

N,N'-bis(2,4,6-trimethylphenyl)imidazolinium chloride (4.48 g, 13.2 mmol) and $ClSO_3H$ (50 ml).

Yield: 5.52 g (76.6 %).

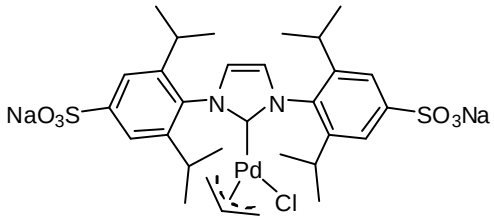
## *6.8 Synthesis of Palladium-allyl-NHC complexes*

### 6.8.1 General procedure for synthesis of palladium-allyl-NHC complexes

In a schlenk tube sulfonated imidazolium salt (2.2 eq) was dissolved in dry and degassed THF and then sodium-*tert*-pentylate (2.1 eq) was added to it dropwise and stirred 30 min. at room temperature. Then it was cooled to -70 $^{o}$C and chloro-palladium-allyl-dimer complex (1.0 eq) was added to it and stirring was continuing 30 min. Afterwards, it was allowed to warm to ambient temperature slowly and stirring was continued for additional 4 to 5 hours. During this time reaction mixture might become black-grey coloration. After completion of the reaction, solvent was evaporated in vacuo to leave grey solid powder. This solid compound was dissolved in small amount of dry and degassed methanol and filtered through celite using schlenk frit. The clear filtrate solution was evaporated to obtain desired palladium-allyl-NHC complex.

**(Y) (allyl){N,N'-bis(2,6-diisopropyl-4-sulfonatophenyl)carbene}(chloro)Palladium(II)**

4-sulfonato-diisopropyl-imidazolium chloride (0.100 g, 0.159 mmol) and sodium tert-pentylate (1.7 M in toluene, 0.1 ml, 0.160 mmol) and palladium-allyl-chloro dimer (0.0275 g, 0.076 mmol).




**107**

Yield: 0.108 g (87.3 %).

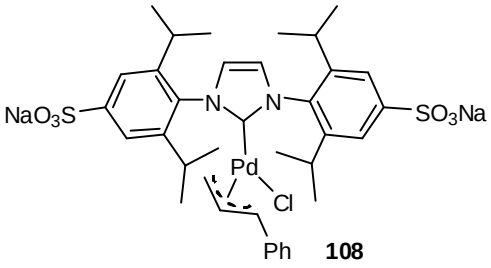
**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 7.67 (s, 2H, CH), 7.49 (s, br, 4H, ArH), 4.79 (m, 1H, CH, $^{3}J$ = 9.0 Hz, $^{3}$J = 6 Hz), 3.55 (d, 2H, $CH_2$, *J* = 7.5 Hz), 2.77 (m, 2H, CH), 2.68 (m, 2H, CH), 2.52 (d, 2H, $CH_3$, *J* = 14 Hz), 1.22- 0.96 (m, 12H, $CH_3$).

**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 183.9, 149.0, 145.6, 144.9, 144.5, 142.5, 135.6, 125.2, 120.6, 113.9, 70.4, 55.8, 49.2, 40.3,39.9, 29.1, 27.9, 23.8, 23.1, 22.4.

ESI-MS: m/z calcd for $C_{31}H_{45}N_2Na_2O_6PdS_2$ ($M^{\bullet+}$-Cl) 757.15; found 757.1.

**(Z) (cinnamyl){N,N'-bis(2,6-diisopropyl-4-sulfonatophenyl)carbene}(chloro)Palladium(II)**

4-sulfonato-diisopropyl-imidazolium chloride (0.150 g, 0.238 mmol) and sodium tert-pentylate (1.7 M in toluene, 0.15 ml, 0.24 mmol) and palladium-allyl-chloro dimer (0.058 g, 0.114 mmol).



**108**

Yield: 0.180 g (88.7 %).

**$^{1}$H NMR** (500 MHz, DMSO-$d_6$) δ [ppm] 7.78 (s, 2H, CH), 7.60 (s, br, 4H, ArH), 7.14 (s, br, 5H, ArH), 5.26 (m, 1H, CH, $^{3}J$ = 9 Hz, $^{3}J$ = 4 Hz), 4.29 (d, 2H, $CH_2$, $J$ = 12.5 Hz), 4.06 (s, br, 1H, CH), 3.58 (s, br, 1H, $CH_2$), 2.91 (m, br, 4H, CH), 1.28 (m, 12H, $CH_3$ J = 6.5 Hz), 1.10 (m, 12H, $CH_3$ J = 6.5 Hz).

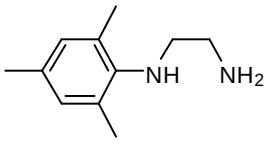
**$^{13}$C NMR** (125.8 MHz, DMSO-$d_6$) δ [ppm] 184.6, 150.6, 146.8, 139.6, 137.6, 130.2, 129.6, 129.5, 129.0, 128.9, 127.9, 127.4, 127.3, 122.5, 110.2, 91.3, 70.5, 47.2, 30.4, 29.7, 27.4, 24.3, 24.2.

ESI-MS: m/z calcd for $C_{37}H_{49}N_2Na_2O_6PdS_2$ ($M^{\bullet+}$-Cl) 833.14; found 833.4.

## *6.9 Synthesis of unsymmetrical Imidazolinium salts*

**6.9.1 1-(2,4,6-trimethylphenyl)imidazolidine** (modified literature procedure)[161]

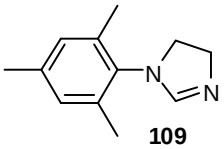
(a) *N*-2,4,6-Trimethylphenyl-(1,2-diaminoethane)




To a suspension of 2-bromoethylamine hydrobromide (10.0 g, 48.8 mmol) in toluene (20 ml), 2,4,6-trimethylaniline (13.2 g, 97.6 mmol) was added and refluxed for 18 h. Then it was cooled and solvent was evaporated completely and made alkaline with 2 (N) NaOH solution and extracted with MTBE (3 x 30 ml). The organic extracts were washed with water and dried over $MgSO_4$ and evaporated to obtain yellow oil. Then it was distilled under reduced pressure to remove most of the starting aniline and last fraction as pure colorless product.

Yeild: 7.3 g (84 %).

(b) 1-(2,4,6-trimethylphenyl)imidazolidine


**109**

A mixture of *N*-2,4,6-Trimethylphenyl-(1,2-diaminoethane) (5 g, 28.07 mmol), triethyl orthoformate ester (20 ml) and p-toluenesulfonic acid (0.25 g) were heated at reflux for 18 h. It was cooled down to room temperature and the made alkaline with NaOH and extracted with chloroform (3 x 50 ml). The extracts were collected and dried over $MgSO_4$ and evaporated to obtain brown oil. This was again acidified with dilute HCl and aqueous layer was washed with MTBE. Then again aqueous layer was made alkaline and extracted with MTBE and dried with $MgSO_4$ and evaporated to obtain brown oil which became brownish-yellow solid at ambient temperature.

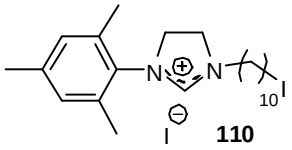
Yield: 4.2 g (79.4 %).

### 6.9.2 General Procedure for synthesizing 1-iodo-alkyl-3(2,4,6-trimethylphenyl)- imidazolinium salt

A mixture of 1-(2,4,6-trimethylphenyl)imidazolidine (1 eq) and diiodo-alkane (4 eq) was stirred in THF for 2 days at room temperature. During this time a white solid was slowly coming out of the reaction mixture. Afterwards, the reaction mixture was kept undisturbed and the supernatant THF was syringed out and rest of the solvent was removed *in vacuo*. To the rest solid, diethylether was added and stirred and filtered of the solvent and the white solid was collected and dried in reduced pressure.

(c) **1-Iododecyl-3-(2,4,6trimethylphenyl)imidazolinium iodide**

1-(2,4,6-trimethylphenyl)imidazolidine (2.00 g, 10.75 mmol) and 1,10-diiododecane (16.96 g, 43.0 mmol) in 150 ml THF.


**110**

Yield: 4.92 g (78.3 %).

**$^1$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.06 (s, 1H, N-C*H*-N), 6.92 (s, 2H, Ar*H*), 4.35 (m, 2H, N-C$H_2$-$CH_2$), 4.22 (m, 2H, N-C$H_2$-$CH_2$), 3.91 (t, 2H, N-$CH_2$-C$H_2$, J = 6.9 Hz), 3.19 (t, 2H, C$H_2$-I, J

= 6.9 Hz), 2.32 (s, 6H, C*H*$_3$), 2.28 (s, 3H, C*H*$_3$), 1.82 (m, 2H, C*H*$_2$), 1.75 (m, br, 2H, C*H*$_2$), 1.36 (m, br, 6H, C*H*$_2$), 1.29 (m, br, 6H, C*H*$_2$).

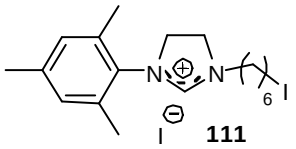
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.9, 140.3, 135.3, 130.4, 128.9, 51.1, 49.5, 48.8, 33.5, 30.4, 29.3, 29.0, 28.4, 27.2, 26.3, 21.0, 18.5.

ESI-MS: m/z calcd for $C_{22}H_{36}N_2I_2$ (M-I$^-$) 455.2; found 455.3.

(d) **1-Iodohexyl-3-(2,4,6trimethylphenyl)imidazolinium iodide**

1-(2,4,6-trimethylphenyl)imidazolidine (2.61 g, 13.86 mmol) and 1,6-diiodohexane (9.14 ml, 55.44 mmol) in 150 ml THF.

Yield: 6.53 g (89.5 %).




**111**

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.12 (s, 1H, N-C*H*-N), 6.92 (s, 2H, Ar*H*), 4.37 (m, 2H, N-C*H*$_2$-CH$_2$), 4.23 (m, 2H, N-C*H*$_2$-CH$_2$), 3.93 (t, 2H, N-CH$_2$-C*H*$_2$, J = 7.2 Hz), 3.20 (t, 2H, C*H*$_2$-I, J = 6.9 Hz), 2.32 (s, 6H, C*H*$_3$), 2.28 (s, 3H, C*H*$_3$), 1.81 (m, 2H, C*H*$_2$), 1.45 (m, br, 2H, C*H*$_2$).

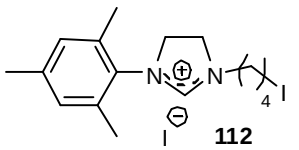
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 158.0, 140.3, 135.3, 130.4, 129.9, 127.9, 120.3, 51.1, 49.5, 48.6, 33.0, 29.8, 27.0, 25.1, 21.0, 18.5.

ESI-MS: m/z calcd for $C_{18}H_{28}N_2I_2$ (M-I$^-$) 399.1; found 399.2.

(e) **1-Iodobutyl-3-(2,4,6trimethylphenyl)imidazolinium iodide**

1-(2,4,6-trimethylphenyl)imidazolidine (2.52 g, 13.38 mmol) and 1,4-diiodobutane (7.1 ml, 53.5 mmol) in 150 ml THF.

Yield: 5.92 g (88.8 %).




**112**

**$^1$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.21 (s, 1H, N-C*H*-N), 6.92 (s, 2H, Ar*H*), 4.38 (m, 2H, N-C$H_2$-$CH_2$), 4.23 (m, 2H, N-C$H_2$-$CH_2$), 4.01 (t, 2H, N-$CH_2$-C$H_2$, *J* = 6.9 Hz), 3.27 (t, 2H, C$H_2$-I, *J* = 6.3 Hz), 2.33 (s, 6H, C$H_3$), 2.29 (s, 3H, C$H_3$), 1.94 (m, 4H, C$H_2$).

**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 158.0, 140.3, 135.3, 130.0, 51.1, 49.5, 47.6, 29.9, 28.0, 21.0, 18.7, 18.5.

ESI-MS: m/z calcd for $C_{16}H_{24}N_2I_2$ (M-$I^-$) 371.1; found 371.1.

## *6.10 Synthesis of pincer-type phosphine-tagged Imidazolinium salts*

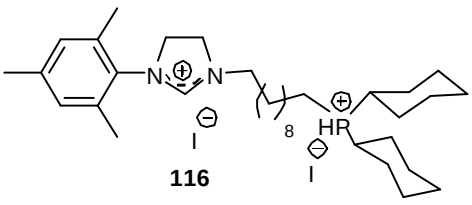
### 6.10.1 General Procedure for synthesizing 1-alkyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolinium hydro-diiodide

In a 25 ml Schlenk tube 1-iodoalkyl(2,4,6-trimethylphenyl)imidazolinium iodide (1 eq) was taken and 15 ml dry degassed toluene was added to it. Then 1.25 to 1.3 eq of dicyclohexylphosphine was added to it and refluxed for 36 h. After completion of reaction, it was cooled to room temperature and the supernatant toluene layer was syringed out. The rest was dried completely *in vacuo* to obtain sticky solid. Then 2x 15 ml of ether was added to it and kept rest for sometimes until the upper ether layer became transparent. The supernatant ether layer was syringe out and the rest was evacuated to obtain white solid powder.

(f) **1-decyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolinium hydro-diiodide**

1-iododecyl(2,4,6-trimethylphenyl)imidazolinium iodide (0.30 g, 0.515 mmol) and dicyclohexyl phosphine (0.12 g, 0.13 ml, 0.64 mmol).

Yield: 0.38 g (94.6 %).




**116**

**$^1$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.14 (s, 1H, N-C*H*-N), 7.23 (dm, 1H, P*H*, $^2J_{P\text{-}H}$ = 470 Hz), 6.84 (s, 2H, Ar*H*), 4.32 (m, 2H, N-C$H_2$-$CH_2$), 4.20 (m, 2H, C$H_2$-$CH_2$-N), 3.87 (t, 2H, N-$CH_2$-C$H_2$, *J* = 4.5 Hz), 2.64 (m, 2H, C$H_2$-P), 2.30 – 1.27 (m, br, 38 H, C$H_2$), 2.26 (s, 6H, C$H_3$), 2.20 (s, 3H, $CH_3$).

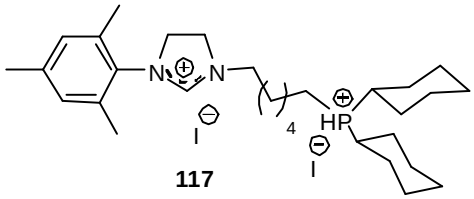
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.0, 139.2, 134.3, 129.6, 128.9, 50.2, 48.6, 47.6, 27.7, 27.6, 27.5, 27.4, 27.3, 26.6, 26.5, 26.1, 26.0, 25.1, 25.0, 24.8, 24.1, 24.0, 17.6.

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 19.3.

(g) **1-hexyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolinium hydro-diiodide**

1-iodohexyl(2,4,6-trimethylphenyl)imidazolinium iodide (0.30 g, 0.57 mmol) and dicyclohexyl phosphine (0.14 g, 0.14 ml, 0.71 mmol).

Yield: 0.383 g (92.0 %).




**117**

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.20 (s, 1H, N-C*H*-N), 7.16 (dm, 1H, P*H*, $^{2}J_{P\text{-}H}$ = 470.5 Hz), 6.89(s, 2H, Ar*H*), 4.39 (m, 2H, N-C$H_2$-$CH_2$), 4.20 (m, 2H, C$H_2$-$CH_2$-N), 3.89 (t, 2H, N-$CH_2$-C$H_2$, *J* = 7.2 Hz), 2.60 (m, 2H, C$H_2$-P), 2.30 – 1.28 (m, br, 30 H, C$H_2$), 2.27 (s, 6H, C$H_3$), 2.20 (s, 3H, $CH_3$).

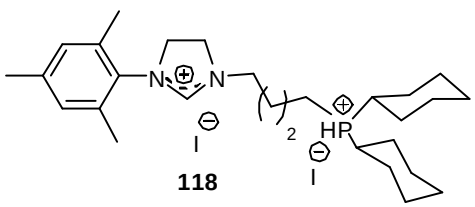
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.1, 139.2, 134.3, 129.6, 128.9, 50.2, 48.7, 47.2, 28.3, 28.2, 27.9, 27.4, 26.6, 26.5, 25.9, 25.4, 25.2, 25.1, 25.0, 24.9, 24.0, 23.9, 22.3, 20.0, 17.8, 13.9.

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 18.9.

ESI-MS: m/z calcd for $C_{30}H_{51}N_2I_2P$ (M-HI-$I^-$) 469.4; found 469.5.

(h) **1-butyl-(dicyclohexylphosphino)-3-(2,4,6-trimethylphenyl)imidazolinium hydro-diiodide**

1-iodohexyl(2,4,6-trimethylphenyl)imidazolinium iodide (0.30 g, 0.60 mmol) and dicyclohexyl phosphine (0.148 g, 0.15 ml, 0.75 mmol).




**118**

Yield: 0.3645 g (87.2 %).

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.35 (s, 1H, N-C*H*-N), 6.97 (dm, 1H, P*H*, $^{2}J_{P\text{-}H}$ = 468 Hz), 6.84 (s, 2H, Ar*H*), 4.49 (m, 2H, N-C$H_2$-$CH_2$), 4.23 (m, 2H, C$H_2$-$CH_2$-N), 4.01 (t, 2H, N-$CH_2$-C$H_2$, *J* = 6.0 Hz), 2.64 (m, 2H, C$H_2$-P), 2.45 - 1.27 (m, br, 26 H, C$H_2$), 2.31 (s, 6H, C$H_3$), 2.20 (s, 3H, $CH_3$).

**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.2, 139.1, 134.2, 129.6, 128.9, 50.2, 48.6, 46.4, 27.7, 27.2, 26.9, 26.6, 26.5, 26.4, 25.9, 25.0, 24.9, 24.0, 20.0, 17.8.

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 21.2.

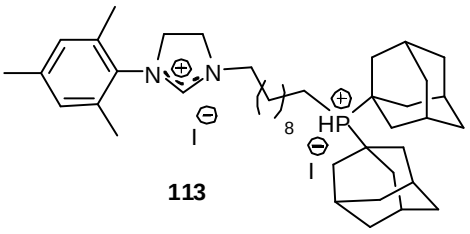
ESI-MS: m/z calcd for $C_{28}H_{48}N_2I_2P$ ($M^{\bullet+}$-2HI) 441.4; found 441.6.

### 6.10.2 General Procedure for synthesizing 1-alkyl-(diadamantyl)-3-(2,4,6-trimethylphenyl)-imidazolinium hydro-diiodide

In a 25 ml Schlenk tube 1-iodoalkyl(2,4,6-trimethylphenyl)imidazolinium iodide (1 eq) was taken and 15 ml dry degassed toluene was added to it. Then 1.5 eq of diadamantylphosphine was added to it and refluxed for 36 h. After finishing the reaction it was cooled to ambient temperature and toluene was decanted and dried. The sticky viscous oily compound was stirred with ether and stood for sometimes to precipitate the solid. The upper ether layer was removed and dried in vacuo. This process repeated twice to remove excess phosphine and other impurity from the product.

(i) **1-decyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenylphosphino)imidazolinium hydro-diiodide**

1-iododecyl(2,4,6-trimethylphenyl)imidazolinium iodide (0.250 g, 0.42 mmol) and diadamantyl phosphine (0.194 g, 0.64 mmol).




**113**

Yield: 0.334 g (89.9 %).

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.15 (s, 1H, N-C*H*-N), 7.27 (dm, 1H, P*H*, $^{2}J_{P\text{-}H}$ = 465.5 Hz),

6.84 (s, 2H, Ar*H*), 4.32 (m, 2H, N-C$H_2$-$CH_2$), 4.20 (m, 2H, C$H_2$-$CH_2$-N), 3.88 (t, 2H, N-$CH_2$-C$H_2$, *J* = 4.5 Hz), 2.26 (s, 6H, C$H_3$), 2.21 (s, 3H, $CH_3$), 2.19 – 1.28 (m, br, 48 H, C$H_2$).

**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.0, 139.0, 134.3, 129.6, 128.9, 50.3, 48.7, 47.7, 36.9, 36.7, 36.5, 34.6, 29.7, 29.6, 27.6, 27.5, 27.4, 27.3, 26.5, 26.4, 26.0, 25.8, 25.7, 24.8, 20.0, 17.6.

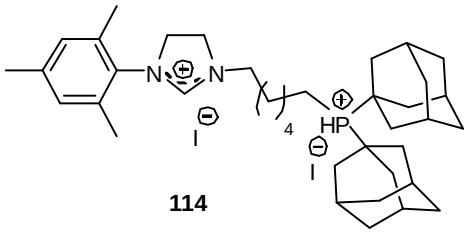
**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 23.8.

ESI-MS: m/z calcd for $C_{42}H_{68}N_2I_2P$ ($M^{\bullet+}$-2HI) 629.5; found 629.7 and $C_{42}H_{68}N_2I_2P$ (M-2$H^+$) 883.3; found 883.4.

(j) **1-hexyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenylphosphino)imidazolinium hydro-diiodide**

1-iodohexyl(2,4,6-trimethylphenyl)imidazolinium iodide (0.200 g, 0.343 mmol) and diadamantyl phosphine (0.155 g, 0.515 mmol).

Yield: 0.266 g (93.6 %).




**114**

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.3 (s, 1H, N-C*H*-N), 7.16 (dm, 1H, P*H*, $^{2}J_{P\text{-}H}$ = 465 Hz), 6.83 (s, 2H, Ar*H*), 4.39 (m, 2H, N-C$H_2$-$CH_2$), 4.21 (m, 2H, C$H_2$-$CH_2$-N), 3.41 (t, 2H, N-$CH_2$-C$H_2$, *J* = 3.3 Hz), 2.27 (s, 6H, C$H_3$), 2.20 (s, 3H, $CH_3$), 2.16 – 1.53 (m, br, 40 H, C$H_2$).

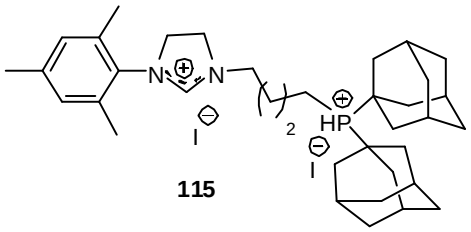
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.0, 139.2, 134.3, 129.6, 128.9, 50.2, 48.6, 47.6, 27.7, 27.6, 27.5, 27.4, 27.3, 26.6, 26.5, 26.1, 26.0, 25.1, 25.0, 24.8, 24.1, 24.0, 17.6.

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 25.0.

ESI-MS: m/z calcd for $C_{38}H_{60}N_2I_2P$ ($M^{\bullet+}$-2HI) 573.4; found 573.7 and $C_{38}H_{60}N_2I_2P$ (M-2$H^+$) 827.2; found 827.3.

(k) **1-butyl-(diadamantylphosphino)-3-(2,4,6-trimethylphenylphosphino)imidazolinium hydrodiiodide**

1-iodobutyl(2,4,6-trimethylphenyl)imidazolinium iodide (0.2049 g, 0.41 mmol) and diadamantyl phosphine (0.186 g, 0.617 mmol).



**115**

Yield: 0.2116 g (64.3 %).

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 9.21 (s, 1H, N-C*H*-N), 7.09 (dm, 1H, P*H*, $^{2}J_{P\text{-}H}$ = 462 Hz), 6.84 s, 2H, Ar*H*), 4.55 (m, 2H, N-C$H_2$-$CH_2$), 4.18 (m, 2H, C$H_2$-$CH_2$-N), 3.95 (t, 2H, N-$CH_2$-C$H_2$, *J* = 6.3 Hz), 2.27 (s, 6H, C$H_3$), 2.20 (s, 3H, $CH_3$), 2.44 – 1.70 (m, br, 36H, C$H_2$).

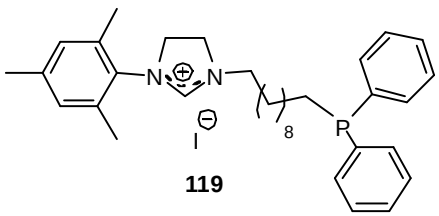
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.1, 139.1, 134.2, 129.6, 128.9, 50.2, 49.3, 46.6, 36.9, 36.5, 35.6, 34.5, 27.4, 27.2, 26.5, 26.4, 22.5, 20.0, 17.6.

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 29.5.

ESI-MS: m/z calcd for $C_{36}H_{56}N_2I_2P$ ($M^{\bullet+}$-2HI) 545.4; found 545.5.

**(l) 1-decyl-(diphenylphosphino)-3-(2,4,6-trimethylphenylphosphino)imidazolinium hydroiodide**

In a schlenk tube, diphenylphosphine (0.1 ml, 0.51 mmol) was added followed by the addition of potassium tert-butoxide (0.029 g, 0.42 mmol) and 3 ml dry DMSO and stirred for 3 h at room temperature. By this time reaction mixture would become red in color. Afterwards, 1-iododecyl-mesityl imidazolinium iodide (0.20 g, 0.34 mmol) was added to the reaction and the red coloration immediately disappeared. The reaction mixture was stirred for overnight. After finishing the reaction the DMSO was evaporated and washed with ether to purify the product. Again it was dissolved in minimum amount of dichloromethane and filtered through celite to remove salt impurity. It evaporated in vacuo to obtain sticky white oily product.



**119**

Yield: 0.185 g (85 %).

**$^{1}$H NMR** (300 MHz, $CDCl_3$) δ [ppm] 8.9 (s, 1H, N-C*H*-N), 7.33 (s, 4H, Ar*H*), 7.24 (s, 2H, Ar*H*), 6.84 (s, 2H, Ar*H*), 4.25 (m, 2H, N-C$H_2$-$CH_2$, *J* = 6 Hz), 4.16 (m, 2H, C$H_2$-$CH_2$-N, *J* = 6 Hz), 3.81 (t, 2H, N-$CH_2$-C$H_2$, *J* = 6 Hz), 2.24 (s, 6H, C$H_3$), 2.20 (s, 3H, $CH_3$).

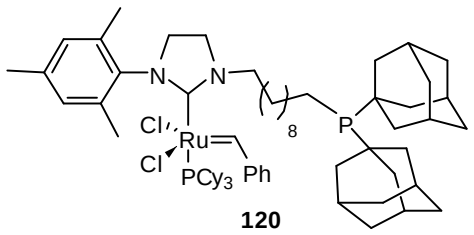
**$^{13}$C NMR** (75.5 MHz, $CDCl_3$) δ [ppm] 157.1, 139.3, 138.0, 137.9, 134.3, 132.0, 131.8, 131.5, 129.7, 129.6, 129.5, 128.9, 128.0, 127.8, 127.7, 127.5, 127.4, 127.3, 50.0, 48.5, 47.9, 40.0, 30.2, 30.0, 28.4, 28.3, 28.2, 28.0, 27.7, 27.6, 27.3, 27.2, 27.0, 26.9, 26.2, 25.9, 25.3, 24.8, 20.0, 17.6.

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] -16.2.

## *6.11 Synthesis of Ruthenium-NHC complex*

### 6.11.1 Synthesis of Ruthenium-NHC complex

In a 25ml Schlenk tube 1-decyl-(diadamantylphosphine)(2,4,6-trimethylphenyl) imidazolinium hydrodiiodide salt (0.25g, 0.283 mmol) was taken and 10 ml dry degassed THF was added and cooled to –70 $^{o}$C using slash bath. Then sodium-tert-pentylate (0.291 ml 1.7 M in toluene, 0.495 mmol) was added to it and stirred for 30 min. At that time the reaction mixture would become clear solution. In a separate Schlenk flask [Ruthenium-alkylidene-$PCy_3$-py] complex (Grubbs-III, 0.165 g, 0.236 mmol) was dissolved in 10 ml of THF and cooled to –70 $^{o}$C. The previous reaction mixture was transferred to ruthenium complex via cannulation and stirring was continued for another 30 min. Then the reaction mixture was warmed at room temperature and stirred for additional 30 min. Afterwards, solvent was evaporated *in vacuo* to obtain dark greenish-brown solid. The solid was purified by silica-gel flash column chromatography under argon using pentane/ether (4 : 1) as eluant.



**120**

Yield: 0.180 g (71 % based on Ru-complex).

**$^{1}$H NMR** (500 MHz, $CDCl_3$) δ [ppm] 18.68 (s, *H*C=CPh), 7.70 (d, 1H, Ar*H*), 7.44 (m, 2H, ArH, J = Hz), 7.04 (s, br, 1H, ArH), 7.00 (t, 1H, ArH, J = Hz), 6.90 (s, 2H, Ar*H*), 3.81 (m, 2H, N-

C*H*$_2$-CH$_2$), 3.73 (m, 2H, N-C*H*$_2$-CH$_2$), 3.59 (t, 2H, N-CH$_2$-C*H*$_2$, *J* = 8 Hz), 2.20 (s, 3H, C*H*$_3$), 1.77 (s, 3H, CH$_3$), 1.65 (s, 3H, CH$_3$), 2.69 – 1.16 (m, br, 81H, C*H*$_2$).

**$^{31}$P NMR** (121.4 MHz, $CDCl_3$) δ [ppm] 32.1 ($PCy_3$), 26.1 ($PAd_2$).

## *6.12 Cross-coupling reaction protocol in water*

### 6.12.1 General Procedure for Cross-Coupling Reactions

All cross-coupling reactions were carried out under argon atmosphere and using degassed solvents. The solvents like water, *n*-butanol and iso-propanol were degassed by bubbling argon for few hours and using freeze and thaw method several times.

### 6.12.2 Suzuki-Miyaura Coupling Reaction

(a) Preparation of catalyst stock solution

Sodium-tetra-chloropalladate (0.05 mmol), imidazolium or imidazolinum salts (0.1 mmol) and KOH (0.5 mmol) were dissolved in 5 ml degassed water in a Schlenk tube under argon. The mixture was stirred at 50 to 55 $^{o}$C for 2 h during which time the solution turned to dark orange color and became clear solution. This stock solution had a concentration of 1 mol %ml$^{-1}$mmol$^{-1}$ aryl halide.

(b) Screening Reaction [in water]

Boronic acid (1.2 mmol) and KOH (3.0 mmol) in water (5 ml) were degassed 2 to 3 times. Then catalyst stock solution (1 ml) was added followed by the addition of respective aryl halide (1 mmol). The reaction mixture was stirred at 100 $^{o}$C in an aluminium block for 12 to 14 h. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (15 ml) and washed with water (10 ml) and organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The product was purified by silica gel column chromatography cyclohexane/ ethyl acetate eluant. Alternatively, the yield was determined by GC analysis with hexadecane or diethylene glycol di-*n*-butyl ether as an internal standard.

(c) Screening Reaction with palladium-allyl-NHC complex [in water/ n-butanol (1:1)]

In a Schlenk tube, boronic acid (0.6 mmol) and KOH (1.5 mmol) in water and *n*-butanol mixture were added and degassed by freeze and thaw. Then Pd-allyl-NHC catalyst (0.4253 mg, 0.0005 mmol in 0.5 ml water: 0.1 mol %ml$^{-1}$mmol$^{-1}$ aryl halide) and respective aryl halide (0.5 mmol) were added to it. Then the reaction mixture was stirred at 100 $^{o}$C in an aluminium block for 12

to 14 h. After cooling down to room temperature, diethyl ether (5 ml) was added to it and washed with water and organic layer was collected and dried over $MgSO_4$, filtered and concentrated in vacuo. The product was either purified by silica gel column chromatography (cyclohexane/ ethyl acetate) or analyzed by GC chromatogram with hexadecane or diethylene glycol di-*n*-butyl ether as an internal standard.

**6.12.3 Sonogashira Coupling Reaction**

(d) Preparation of catalyst stock solution

In a Schlenk tube, sodium-tetra-chloropalladate (8.82 mg, 0.03 mmol), p-sulfonated-diisopropyl imidazolium chloride (37.7 mg, 0.06 mmol) and KOH (13.5 mg, 0.24 mmol) were dissolved in 6 ml degassed water under argon. The mixture was stirred at 50 to 55 $^{o}$C for 2 h during which time the solution turned to dark orange color and became clear solution. This stock solution had a concentration of 0.1 mol % in 0.250 ml using 0.5 mmol aryl halide.

(e) Screening Reaction [in water/ iso-propanol (1:1)]

In a Schlenk tube, KOH (1.5 mmol) was added to water and iso-propanol mixture and degassed by freeze and thaw. Then aryl halide (bromide or chloride, 0.5 mmol) and catalyst (0.25 ml from the above stock solution) were added together and started heating in aluminium block. When reaction temperature would reach to 60 to 70 $^{o}$C, acetylene derivatives (0.55 mmol) was added to it and heated together at 90 to 95 $^{o}$C for 12 to 14 h. After completion of reaction it was allowed to cool to room temperature and diethyl ether was added followed by washing with water and separation of organic layer. The product was isolated either by column chromatography (cyclohexane/ ethyl acetate mixture) or analyzed by GC with hexadecane or diethylene glycol di-*n*-butyl ether as an internal standard.

## *6.13 Appendix*

NMR Data of Cross-coupling Products:

2-p-Tolyl-quinoline-3-carbaldehyde

**$^{1}$H NMR** (500 MHz, $CD_3CN$) δ [ppm] 10.12 (s, 1H, CHO), 8.85 (s, 1H, ArH), 8.12 (m, 3H, ArH), 7.91 (ddd, 1 H, ArH, $^{5}J$ = 1.5 Hz, $^{4}J$ = 7.0 Hz, $^{3}J$ = 8.5 Hz), 7.76 (ddd, 1 H, ArH, $^{5}J$ = 1.5 Hz, $^{4}J$ = 7.0 Hz, $^{3}J$ = 8.5 Hz ), 7.59 (td, 2 H, ArH, $^{4}J$ = 2.0 Hz, $^{3}J$ = 8.0 Hz), 7.41-7.38 (m, 2H, ArH), 2.45 (s, 3H, $CH_3$).

2-Methoxy-6-p-tolyl-pyridine

**$^1$H NMR** (500 MHz, $CDCl_3$) δ [ppm] 7.93 (d, 2H, ArH, $^3J$ = 8.5 Hz), 7.58 (dd, 1H, ArH, $^3J$ = 7.5 Hz, $^3J$ = 8.0 Hz), 7.29 (dd, 1 H, ArH, $^5J$ = 0.5 Hz, $^3J$ = 7.5 Hz,), 7.24 (dd, 2 H, ArH, $^5J$ = 0.5 Hz, $^3J$ = 7.5 Hz,), 6.64 (1H, ArH, $^3J$ = 8.0 Hz), 4.02 (s, 3H, $OCH_3$), 2.39 (s, 3H, $CH_3$).

2-p-Tolyl-pyridin-4-ylamine

**$^1$H NMR** (500 MHz, $CDCl_3$) δ [ppm] 8.25 (d, 1H, ArH, $^3J$ = 5.5 Hz), 7.78 (d, 2H, ArH, $^3J$ = 8.0 Hz), 7.21 (d, 2H, ArH, $^3J$ = 8.0 Hz), 6.85 (s, 1H, ArH), 6.39 (dd, 1H, ArH, $^3J$ = 5.5 Hz, $^4J$ = 2.5 Hz), 4.35 (s, br, 2H, $NH_2$), 2.36 (s, 3H, $CH_3$).

2-Naphthalen-1-yl-quinoline-3-carbaldehyde

**$^1$H NMR** (500 MHz, $CD_3CN$) δ [ppm] 9.74 (s, 1H, CHO), 8.96 (s, 1H, ArH), 8.22 (d, 1H, ArH, $^3J$ = 8.0 Hz), 8.13 (dd, 1H, ArH,$^5J$ = 0.5 Hz, $^3J$ = 8.5 Hz), 8.09 (d, 1H, ArH, $^3J$ = 8.0 Hz), 8.04 (d, 1H, ArH, $^3J$ = 8.0 Hz), 7.96 (ddd, 1 H, ArH, $^5J$ = 1.0 Hz, $^3J$ = 6.5 Hz, $^3J$ = 8.5 Hz), 7.75 (ddd, 1 H, ArH, $^5J$ = 1.5 Hz, $^4J$ = 7.0 Hz, $^3J$ = 8.5 Hz ), 7.67 (dd, 1H, ArH, $^3J$ = 7.0 Hz, $^3J$ = 8.0 Hz), 7.57 (m, 2H, ArH), 7.44 (ddd, 1H, ArH, $^5J$ = 1.5 Hz, $^3J$ = 7.0 Hz, $^3J$ = 8.5 Hz).

2-Naphthalen-1-yl-pyridin-4-ylamine

**$^1$H NMR** (500 MHz, $CDCl_3$) δ [ppm] 8.20 (d, 1H, ArH, $^3J$ = 5.5 Hz), 8.01 (d, 1H, ArH, $^3J$ = 8.0 Hz), 7.76 (t, 2H, ArH, $^3J$ = 9.5 Hz), 7.38 (m, 4H, ArH), 6.47 (d, 1H, ArH, $^4J$ = 2.0 Hz), 6.27 (dd, 1H, ArH, $^3J$ = 5.5 Hz, $^4J$ = 2.5 Hz), 4.37 (s, br, 2H, $NH_2$).

1-(2-Isopropyl-phenyl)-naphthalene

**$^1$H NMR** (500 MHz, $CD_3CN$) δ [ppm] 7.90 (m, 2H, ArH), 7.52 (m, 1H, ArH), 7.48 (m, 1H, ArH), 7.44 (m, 1H, ArH), 7.37 (m, 2H, ArH), 7.25 (m, 1H, ArH), 7.13 (m, 1H, ArH), 2.53 (m, 1H, CH), 1.02 (d, 3H, $CH_3$, $^3J$ = 7 Hz), 1.01 (d, 3H, $CH_3$, $^3J$ = 3 Hz).

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## *Abstract*

Im Rahmen dieser Arbeit werden neuartige sulfonierte *N*-Heterozyklische Carbene in Form von stabilen Imidazolium- und Imidazoliniumsalzen hergestellt und deren katalytische Eigenschaften in Palladium-katalysierten Kreuzkupplungsreaktionen in Wasser getestet. Der Katalysator wird durch Zugabe von sulfoniertem NHC zur Palladiumquelle (Natriumtetrachloropalladat) hergestellt und anschließend bei der *Suzuki-Miyaura* Kreuzkupplung in wässrigem Medium verwendet. Eine Erweiterung des Systems stellt die Verwendung von isolierten Palladium(allyl)-sulfonierten NHC Komplexen dar. Damit ist es möglich, sowohl verschiedene elektronenreiche und sterisch anspruchsvolle Arylchloride als auch Hetereoarylchloride mit Tolyl und Naphthyl-Boronsäuren in einer Mischung von Wasser und Alkohol zu kuppeln. Der *in situ* hergestellte Katalysator wird weiterhin erfolgreich in der *Sonogashira* Reaktion von Arylbromiden und Heteroarylbromiden sowie –chloriden mit Aryl- und Alkyl-Acetylene-Verbindungen in einer Wasser/Alkohol Mischung eingesetzt. Hierzu wurden verschiedene Phosphin-funktionalisierte NHC-Liganden in Form von Imidazoliniumsalzen synthetisiert und versucht, die entsprechenden Ruthenium-Alkyliden-Komplexe (*Grubbs II* Komplexe) zu generieren, was jedoch in keinem Fall zum gewünschten Produkt führte.

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Erklärung

Ich erkläre hiermit, noch keinen Promotionsversuch unternommen zu haben.

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Eidesstattliche Erklärung

Ich erkläre hiermit an Eides Statt, daß ich meine Dissertation selbständig und nur mit den angegebenen Hilfsmitteln angefertigt habe.

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