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Development of N-Heterocyclic Carbenes as Organic Catalysts and Efficient Ligands in Palladium Mediated Transformations

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Development of N-Heterocyclic Carbenes as Organic Catalysts and Efficient Ligands in Palladium Mediated Transformations

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To my Parents, for their love and support

Mrs. Neera Singh and Dr. R. P. Singh

Mrs. Sukhvinder Kaur and Dr. Paramjit Singh

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ABSTRACT

N-Heterocyclic carbenes (NHCs) have emerged as appropriate replacements for phosphines in transition metal catalyzed cross-coupling chemistry. The advantages of NHCs over phosphines include ease of handling, minimal toxicity, stability and powerful electron donating properties. Improvement of catalytic processes has become increasingly relevant in light of prospective applications of organic transformations in industry as well as in synthetic laboratories. To that end, NHCs represent an important class of catalysts and catalyst modifiers which mandate continued research efforts. Prospective applications of processes catalyzed by NHCs and NHC-metal catalysts provide a strong impetus to develop them and related methodologies.

This dissertation focuses on the development of NHCs and NHC ligated metal complexes in various catalytic transformations. NHC ligated palladium catalysts were synthesized in simplified protocols amenable to large-scale industrial applications. The catalysts were utilized in developing different valuable coupling methodologies. Significant advances were achieved in Suzuki-Miyaura, α-arylation of ketones and Kumada-Tamao-Corriu cross coupling reactions. The focus of the work was to make the synthesized catalysts and their activity in these methodologies acceptable to wider range of applications.

The strongly nucleophilic nature and easily tunable steric and electronic properties of NHCs have been exploited to mediate organic transformations by utilizing NHCs as catalysts. The metal-free catalysis has an added advantage of being more environmentally friendly. NHCs have proven to be excellent transesterification catalysts

for reactions of alcohol and esters. An efficient catalytic system, widening the scope of *N*-heterocyclic carbenes catalyzed transesterification/acylation reaction of alcohols is described. The methodology has been expanded to include secondary alcohols as well as phosphorus based esters.

Keywords: Palladium, Carbenes, Cross-Coupling, Organic-Catalysis

CHAPTER 1

INTRODUCTION

1.1. Catalysis

The word catalysis was first coined in 1835 by a Swedish chemist Jons Jakob Berzelius who realized that certain chemicals aid in speeding up the rate of a reaction.[1] Ever since, catalysis has grown to be one of the most important tools in applied chemistry and amounts for more than 80% of all manufactured chemicals. The importance of catalysis can be gauged from the fact that catalysts contribute about 17% of the value of manufactured goods in industrialized countries. Of the twenty most important chemicals, thirteen involve catalysis in their preparation.[2] Catalysis is one of the most active fields of research in sciences since better catalytic systems for production of high volume synthetic chemicals as well as low volume fine chemicals are desirable to make industrial processes more efficient.[3]

Catalysis can be divided into four major classes: Heterogeneous Catalysis, Homogeneous Catalysis, Organocatalysis and Enzymatic Catalysis. While enzymatic catalysis is generally utilized to achieve chiral specificity, organocatalysis is fast gaining momentum as a viable environmentally-friendly option. Although known for many years as organic catalysis,[4] this field of catalysis received a fresh impetus after McMillan coined the term organocatalysis in 2000.[5] However, most of the production processes utilize heterogeneous and homogeneous catalysis.[6] In

this report, homogeneous catalysis, especially pertaining to organotransition metal complexes is of more relevance. Organocatalysis will also be discussed in section 1.4 of this manuscript.

Homogeneous catalysis amounts for about 15% of all catalytic industrial processes. Some of the more popular examples of homogeneously catalyzed reactions are hydroformylation and Ziegler-Natta polymerization. Hydroformylation also known as the oxo-process is used for the synthesis of aldehydes and alkenes. It is considered one of the premier achievements of the twentieth century.[7] Similarly, Ziegler-Natta polymerization is also considered a very significant transformation in industrial processes. Karl Ziegler and Giulio Natta were awarded Nobel Prize in Chemistry (1963) for their efforts in developing this catalytic system.[8]

Achievable high selectivity and good activity under a mild set of conditions are amongst the major advantages of homogeneous catalysis. Another major advantage of homogeneous catalysis is that generally the pre-catalyst is well-defined which gives a better possibility for conducting mechanistic studies of the active catalyst. Mechanistic understanding of the catalytic process is paramount for the development of the system since it can lead to a rational design of the catalyst and reasonable steps can be taken to improve the catalyst and the catalytic system. However the main disadvantages associated with homogeneous catalysis are deactivation of the catalyst because of tendency of metal species to achieve a state of high nuclearity and lower thermal stability as compared to heterogeneous systems. Moreover, homogeneous catalysts pose environmental questions because of the difficulties associated with the separation of the catalyst and product, recovery of catalyst from the reaction mixture and disposal of large amounts of waste produced. These factors may also affect the purity of the ultimate product.

To minimize these effects, one popular tool in the arsenal of chemists is the judicious utilization of ancillary ligands. Ancillary ligands attached to the metal center play a very

important role in the final activity of the catalyst in homogeneous catalysis. The major functions an ancillary ligand can perform to maximize the catalytic activity are: prevention of aggregation to keep the nuclearity of the metal low, providing vacant coordination sites through dissociation, stabilization of intermediates and bringing a positive effect on the selectivity and reactivity of the system via alteration of steric and electronic factors.[9] Ideally a catalyst could go on to catalyze a given reaction indefinitely. However, a number of factors prevent this from happening. The most common reasons in this regard are degradation of the catalyst and catalyst poisoning. A well documented example of such a case is use of tertiary phosphines in transition metal catalyzed transformations. While tertiary phosphines have been the main-stay ligands for a number of metal catalyzed reactions, their biggest nemesis is transition metal catalyzed phosphorus-carbon bond severance leading to rapid deactivation.[10] Generally to overcome this drawback of phosphines, use of an excess concentration of the ligand is necessitated. However, this brings an economical and environmental burden on the catalytic process by often elevating the costs associated with ligands and clean-up, which are even higher than the cost of the precious transition metals itself.[3]

In light of the problems associated with homogeneous catalysis, there is an urgent need of continued efforts directed towards the betterment of catalytic processes in terms of both economics and environment-friendliness. Therefore, the basic goals of catalysis and methodology development should be designing more active and increasingly selective catalysts, designing and/or finding inexpensive alternatives to existing catalysts, achieving prolonged catalytic activity of the catalyst by improving the stability of the ligands and aiming for better catalyst separation from the product, perhaps even recycling the catalyst for achieving environmentally-friendly outcomes. To achieve these goals, research efforts are being constantly

moved towards development of a different class of compounds: N-heterocyclic carbenes as efficient ligands.

1.2. *N*-Heterocyclic Carbenes

Existence of the simplest carbene, CH_2 (methylene), was proposed in 1930s but definite evidence for its existence came much later.[11] The carbenic carbon usually adopts sp^2 hybridization with two non-bonding orbitals and generally has a bent geometry. One orbital remains largely p-character ($p\pi$) and the other assumes stability via significant sp^2 character (σ). Singlet nucleophilic *N*-heterocyclic carbenes (NHCs) are neutral compounds which have a divalent carbon atom with two non-bonding electrons.[12] Wanzlick and co-workers studied chemistry of *N*-heterocyclic carbenes (NHCs) as intermediates and reported formation of dimeric olefin product from carbene species in 1960's (Figure 1.1).[13] They further confirmed the existence of these reactive species by trapping experiments.[14] However, they were not able to isolate the carbenes. The first major advances in isolation of a free *N*-heterocyclic carbene were reported about thirty years later by Arduengo[15] and Bertrand.[16] The first NHC which was stable enough to be isolated and characterized, was 1,3-bis(adamantly)-imidazol-2-ylidene (IAd) reported by Arduengo in 1991 (Figure 1.2).

Figure 1.1. Wanzlick Carbene Dimer

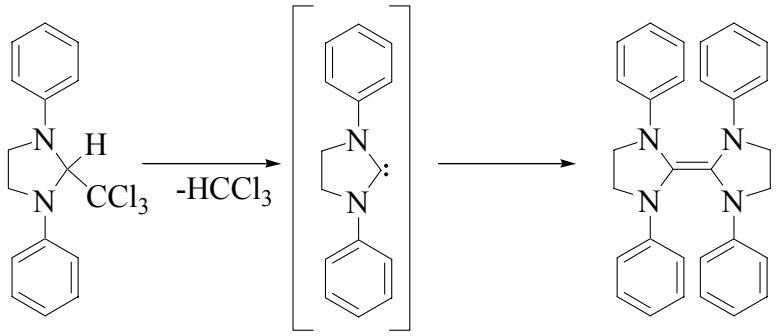
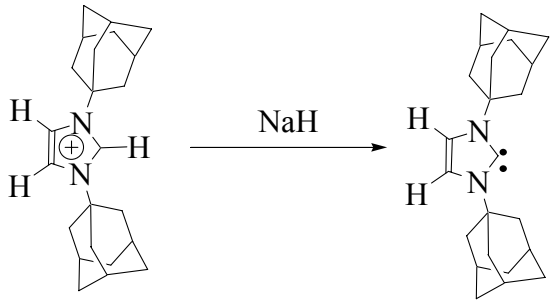


Figure 1.2. Arduengo's carbene: 1,3-Bis(adamantyl)-imidazol-2-ylidene (IAd)

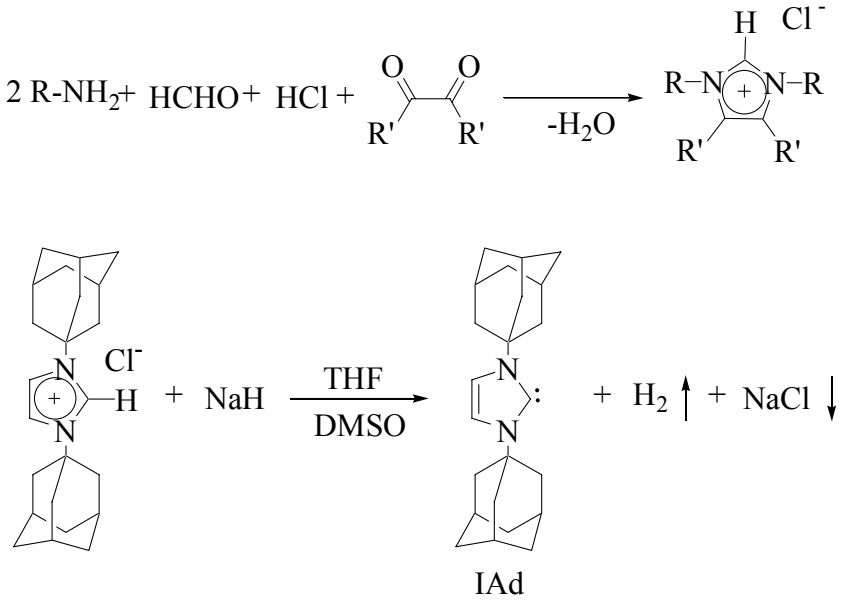


Initially, the steric effect from the sterically bulky adamantyl groups flanking the imidazolium backbone were deemed indispensable for the stability of the carbene preventing decomposition of the carbene by dimerization. However, later it was demonstrated that steric interactions did not have influential significance in determining the stability of the carbene as replacement of bulky adamantyl groups by methyl groups led to formation of a less stable but isolable carbene.[17] A myriad of studies analyzing the cause of stability and nature of the carbenic moieties were carried out.[18] Electronegativity effects of the imidazole nitrogens, π-interaction in the imidazole ring and the large singlet-triplet gap in imidazole-2-ylidenes were also studied.[19] The studies indicated that the major contribution to NHC stabilization is the pπ-pπ electron

donation from the nitrogen electron-pairs into the formally vacant pπ orbital of the carbenic carbon. This makes the carbenic carbon more nucleophilic.[20] Studies revealed that the resonance stabilization of the carbene is not a very important factor, especially since NHCs with saturated imidazolium framework were synthesized and isolated.[21] The ab initio studies also indicated that π-back bonding is not a significant factor in determining stability of these species.[22] It has been accepted that the decisive factor in determining the stability of NHCs is the push-pull synergistic effect of the amino groups.[12]

1.2.1. Synthesis and Characteristics of NHCs

Scheme 1.1. Synthesis of IAd



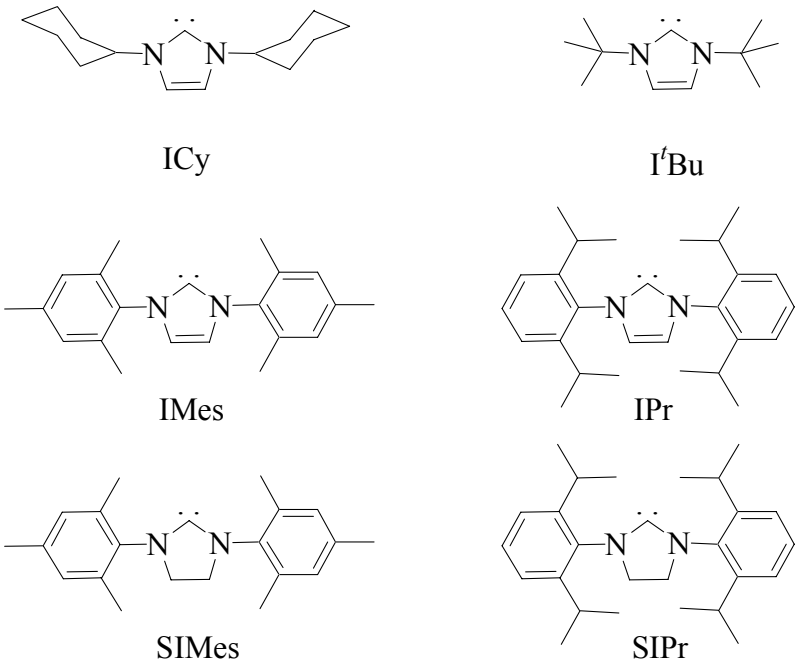
IAd

The initial procedure for the synthesis of NHCs reported by Arduengo et al furnished IAd from the corresponding imidazolium salt. The imidazolium salt was prepared by a one-step

synthesis by reacting 1-adamantanamine, formaldehyde, glyoxal and hydrochloric acid. The deprotonation of 2-carbon of the imidazolium salt by a base gave the free carbene (Scheme 1.1).

Other methods reported for the synthesis of carbenes include deprotonation of the corresponding salts in liquid ammonia by Herrmann,[23] thermal elimination of methanol from a triazolium-methoxide adduct to form triazol-2-ylidene by Enders,[24] reaction of potassiummetal and imidazol-2-thiones by Kuhn.[25] However Arduengo's method is still one of the most popular methods for synthesis of carbenes owing to its easy applicability to a large number of N-substituents giving a unique choice of tunable sterics and electronics in NHCs. The most often-utilized carbenes are depicted in Figure 1.3.

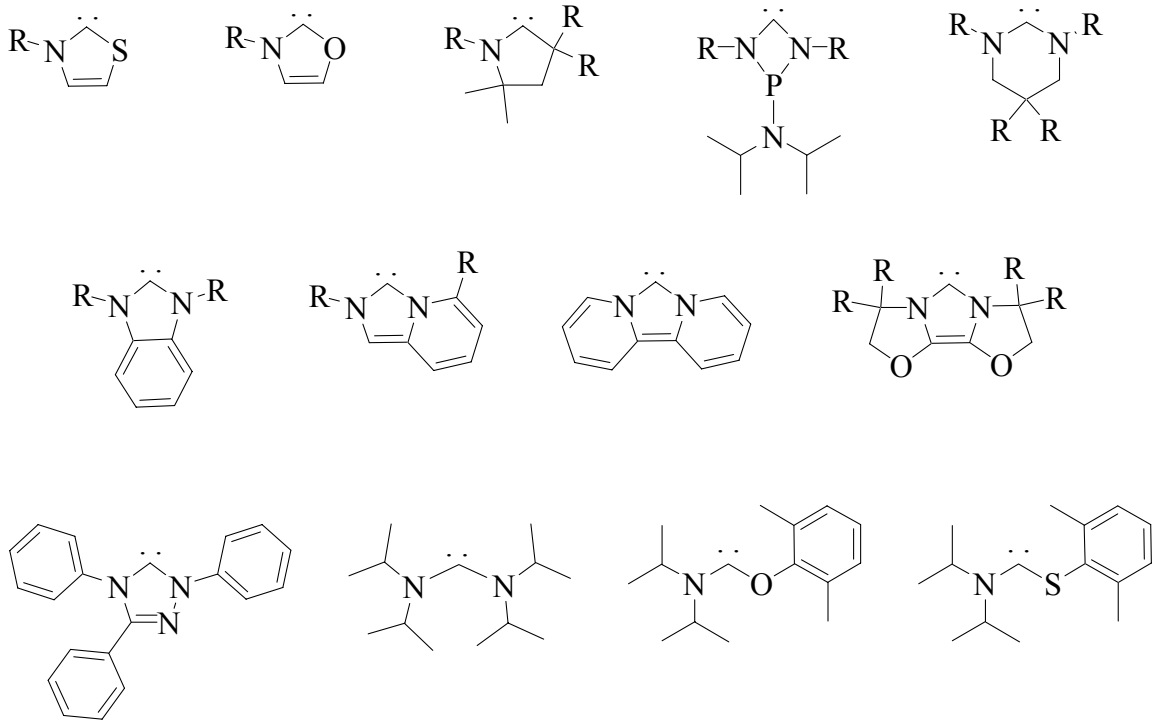
Figure 1.3. Most Popular NHCs: Tunable Sterics and Electronics



The pioneering methods for the synthesis of NHCs mentioned above led to the development of a variety of heterocyclic and acyclic carbenes including some mixed heterocyclic

carbenes as shown in Figure 1.4. However, NHCs derived mostly from imidazolium or imidazolinium salts have found wide-spread applications in homogeneous catalysis.[26]

Figure 1.4. Various Heterocyclic and Acyclic Carbenes

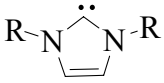
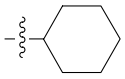
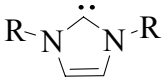
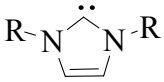
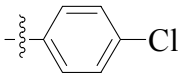
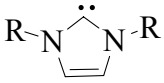
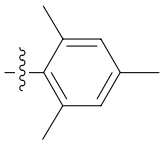
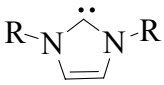
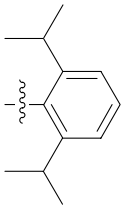
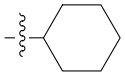


NMR spectroscopy provides an easy tool to characterize and study NHCs. The electron rich carbenic carbon usually shows a signature peak within 200-260 ppm in ^{13}C-NMR. The saturated imidazol backbone containing NHCs (eg SIPr, SIMes) usually demonstrate the same signal 15-25 ppm downfield as compared to their unsaturated congeners. Amongst other features of note is the N_1-$C_{carbenic}$-N_2 bond angle of 100-106^o and partial double bond character between one $C_{carbenic}$-N1. This bond is slightly shorter in length as compared to the other $C_{carbenic}$-N_2. The ligand-properties of NHCs have also been studied with various techniques such as infra-red spectroscopy and solution calorimetery.

Initially Herrmann laid the ground for comparison between NHCs and phosphines with reference to their ligand properties.[27] The binding properties of NHCs as compared to phosphines were subsequently studied by making calorimetric measurements on NHC-Ru complexes (Table 1.1).[28] The thermochemical and structural studies demonstrated that NHCs were better donors than phosphines.[29]

Table 1.1. Thermochemical Studies on NHC-Ru Complexes

$[Cp^*RuCl]_4 + 4L \xrightarrow[30\ ^oC]{THF} 4\ Cp^*Ru(L)Cl$

entry	L	R	$-\Delta H_{rxn}$ (kcal/mol)
1			85.0
2			75.3
3			74.3
4			62.6
5			44.5
6	PR_3		10.5
7	PR_3		9.4

In a recent infra-red spectroscopic study, (NHC)Ni(CO)$_3$ complexes were synthesized and the effect of electron donation by NHC on the metal-CO bond was studied by recording the IR frequency of CO.[30] A good electron donor ligand increases the electron density on Nickel and forces the CO frequency to a lower value. A comparative study of CO frequencies in NHC complexes with corresponding Ni-phosphine complexes was carried out.[31] Lower IR frequency values of NHCs confirmed that NHCs are indeed better donors than phosphines (Table 1.2).[32]

Table 1.2. Comparison of CO Infra-red frequencies in (NHC)Ni(CO)$_3$ Complexes

entry	complex	ν_{CO} (A_1, cm^{-1})	ν_{CO} (E, cm^{-1})
1	Ni(CO)$_3$(IPr)	2051.5	1970.0
2	Ni(CO)$_3$(SIPr)	2052.2	1971.3
3	Ni(CO)$_3$(IMes)	2050.7	1969.8
4	Ni(CO)$_3$(SIMes)	2051.5	1970.6
5	Ni(CO)$_3$(PPh$_3$)	2068.9	1990
6	Ni(CO)$_3$(P*t*Bu$_3$)	2056.1	1971
7	Ni(CO)$_3$(P*i*Pr$_3$)	2059.2	1977

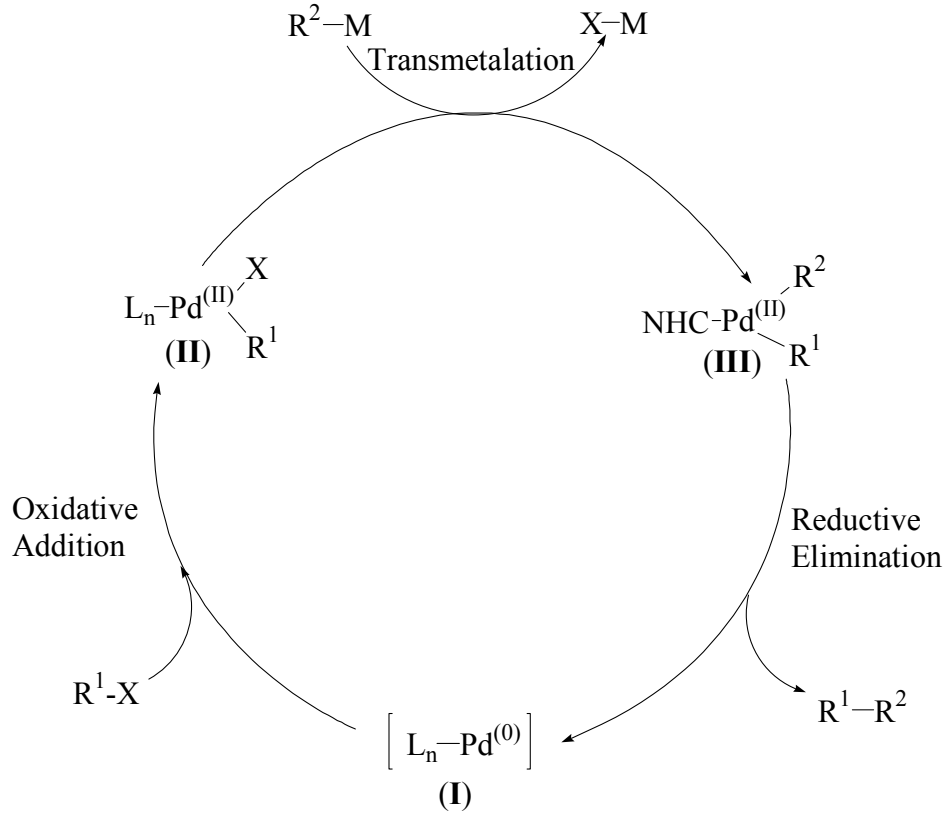
1.2.2. Ligand Properties of NHCs

Electron rich and bulky phosphines are the most commonly employed ligands in transition metal catalyzed C-C bond forming reactions especially with palladium. The tendency of phosphines to stabilize Pd(0) intermediates has been the prime motivation for their

employment in a wide array of cross-coupling reactions.[33] It has been postulated that while electron-rich nature of phosphines such as P(*t*Bu)$_3$ and P(*o*-tol)$_3$ promotes oxidative addition in the mechanistic cycle of transition metal catalyzed C-C bond forming cross-coupling reactions (Scheme 1.2),[34] the steric bulk around the metal center facilitates reductive elimination.[35] The steric bulk increases energy of the higher coordinated species (**III**) thus making it more susceptible to undergoing elimination.[36,37] Significant advances in terms of mild reaction conditions and couplings of less reactive halides (chlorides) as chemical feedstock have been achieved in catalytic systems with bulky phosphines ligated palladium complexes.[38] A pertinent example of phosphine based catalyst in C-C coupling reaction is an air stable phosphines/arene-ligated-palladium-dimer complex prepared from treatment of bis(2-(dicyclohexylphosphino)-2',6'-dimethoxybiphenyl)$PdCl_2$ with $AgBF_4$ as reported by Barder.[39]

However, as mentioned earlier, despite the effective control over reactivity in organometallic chemistry, especially homogeneous catalysis, phosphines suffer from a number of shortcomings. Namely, the tendency of phosphines to undergo degradation at elevated temperatures via P-C bond cleavage and generally their air-sensitive nature are two major drawbacks from which application of phosphines to C-C bond forming coupling reactions suffer.[40] These shortcomings necessitate the use of excess ligand concentration. Employment of higher phosphine concentrations not only have direct consequences on the economics of the catalytic processes but also have a negative effect on the environment because of unrecoverable nature of the ligand.

Scheme 1.2. Mechanistic Cycle for Metal Catalyzed Cross-Coupling Reactions



Interestingly, a remarkable similarity between phosphine and NHC ligands is the possibility of tuning the steric and electronic properties of the ligand by incorporating specific substituents. However, direct attachment of these substituents to the donor atom in phosphines, limits the flexibility of distinctly modifying the steric and electronic properties. Contrastingly, in NHCs the steric and electronic properties are independent from each other since the substituents are attached to the nitrogens of the heterocycle and hence in principle are less direct in affecting the electronic density of the species.[41] Therefore NHCs provide a more flexible approach to incorporating a certain set of required properties in a ligand.[42] In light of all the drawbacks presented by phosphine ligands,[43] focus was turned towards employing NHCs as ligands in

transition metal catalyzed C-C bond forming coupling reactions.[44] Ligand properties in terms of structure, bonding and reactivity of NHCs as ligands have been studied at length.[45]

Transition metal carbene complexes have been long-known for their exhaustive applications in organic synthesis.[46] Initially, Lappert et al reported utilization of carbene-ligated complexes of rhodium to mediate olefin metathesis reactions in 1972.[47] Later Hill[48] and Lappert,[49] demonstrated further applications of rhodium-carbene complexes in separate works. The field of metal-carbene chemistry went through a period of dormancy after these reports until Herrmann realized the potential of these reactive species and presented a report with Heck reaction catalyzed by Pd-carbene complexes.[50] Herrmann noticed the absence of deposition of catalytically inactive metallic palladium in the reactions catalyzed by NHC-Pd catalyst. This was in complete contrast to the palladium-phosphine systems which often show such a behavior owing to P-C bond cleavage and subsequent phosphine decomposition. This discovery re-ignited the interest in metal-carbene chemistry and led to an emergence of a plethora of reports in following years. Palladium-NHC catalysts were extensively employed in catalysis of Heck coupling[51,52] with a report by Calo with thiazolium carbene-palladium catalyst for Heck coupling.[53] Herrmann further exploited his discovery by exploring NHC ligated complexes with Pd and Ni in Heck,[54] Suzuki[55] and Stille[56] coupling reactions. C-N coupling was also achieved utilizing Pd-NHC species.[57]

1.2.3. Palladium and NHCs

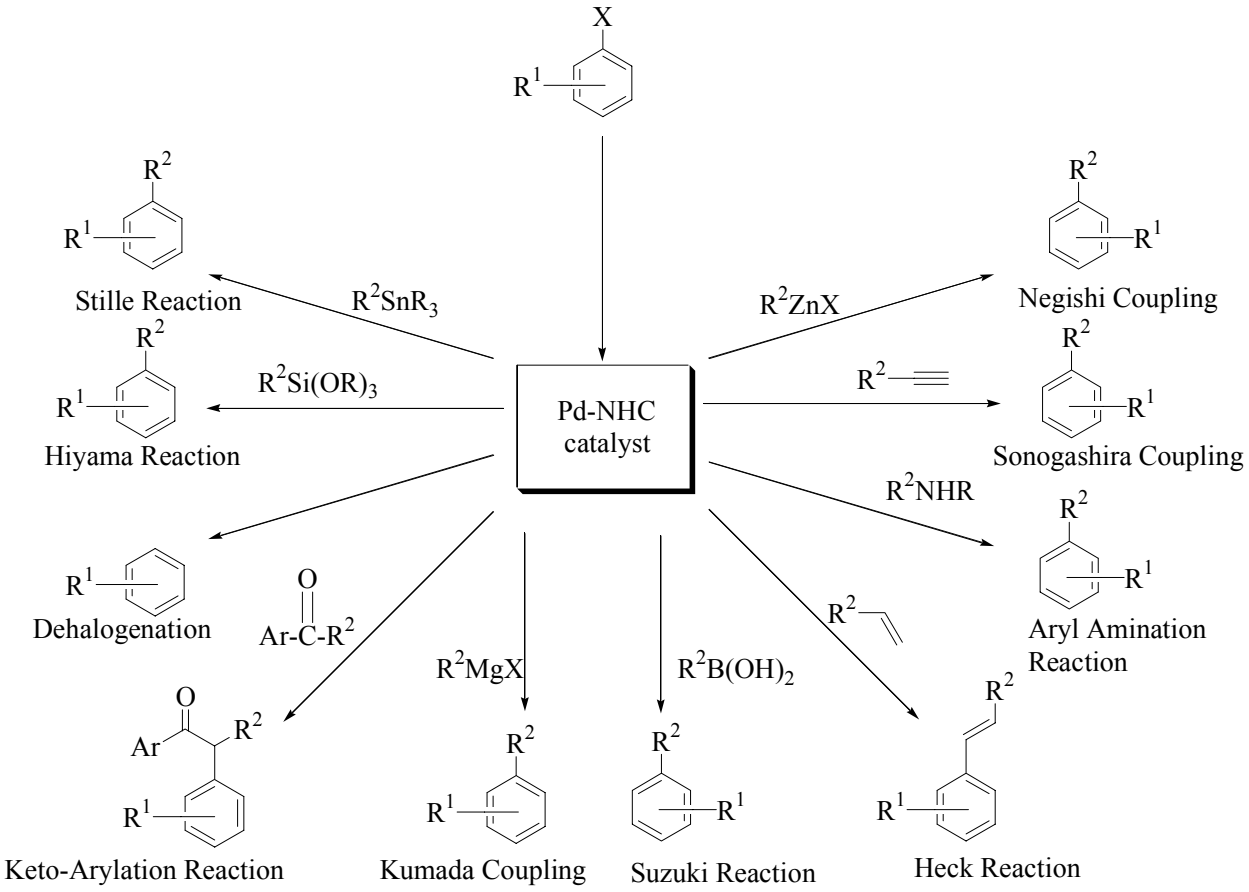
Palladium represents one of the most multifaceted metals in transition metals utilized for catalyzing various transformations.[58] Palladium catalyzed coupling reactions between organic

electrophiles and organometallic reagents are reliable and versatile tools for the regioselective formation of carbon-carbon bonds involving two sp^2-hybridized carbons.[59] It is utilized extensively in C-C bond forming cross-coupling reactions in both laboratory as well as industrial processes.[60] Apart from C-C bond formation palladium mediated systems have also been devised for C-H, C-P, C-N, C-O and C-S bond formation reactions.[61] An important feature of palladium is its redox chemistry. Palladium is more stable at a low oxidation state (0) rather than in higher oxidation state of (+2). Hence, tendency of palladium catalysts to achieve a lower oxidation state provides a supplemental driving force towards formation of C-C and C-heteroatom bonds by aiding reductive elimination. In its low oxidation state palladium (0) can be stabilized by introducing ligands which are good σ-donors. As represented in Scheme 1.2, presence of an electron rich ligand assists in oxidative addition of the electrophilic moiety in a coupling reaction by cleaving the R-X bond (X = halide / pseudo halide). The oxidative addition leads to formation of the palladium (II) species which can then undergo transmetalation with an organometallic substrate consisting of a more electropositive metal. Usually such a resultant higher coordinate species with palladium (II) is higher in energy and unstable. Tendency of palladium to achieve an oxidation state of (0) in conjunction with steric bulk, if provided by the ligand aids in eliminating the coupling product. The formation of C-C or C-heteroatom coupled product regenerates the catalyst by bringing palladium back to oxidation state of (0).

Emergence of cross-coupling chemistry as one of the ubiquitous features in organic synthesis has led to exhaustive study of the scope of this field.[62] The extent of exploitation of palladium in C-C as well as C-heteroatom (N, O and S) can be gauged from the fact that palladium catalyzed processes have been utilized in applications as varied as synthesis of

polymers,[63] nano-complexes,[64] liquid crystals,[65] biological relevant peptide mimics,[66] pharmaceutically relevant species[67] and natural products.[68]

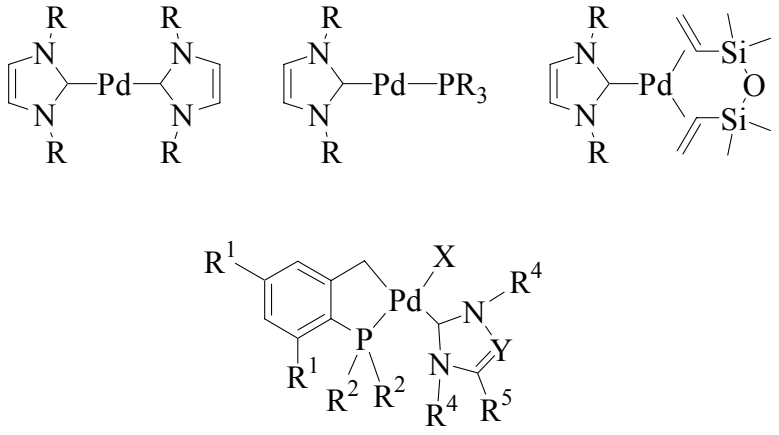
Scheme 1.3. Various Palladium Catalyzed Cross-Coupling Reactions



These transformations provide a huge advantage from the point of view of their applicability to organic synthesis and industrial utilization by employing easily available and cheap feedstock – aryl halides or psudohalides and main group transmetalating agents (Scheme 1.3).[69] Broad functional group tolerance provides another dimension to the utility of palladium catalyzed C-C and C-heteroatom bond formation.[70]

A number of palladium-NHC catalysts have been synthesized and utilized for catalyzing various transformations. These include complexes of NHCs and palladium (0),[71] *bis*-carbene-palladium complexes[72] mixed carbene-palladium-phosphine complexes,[73] and NHC-phospha-palladacycles.[74] A few representative examples of various Pd-NHC complexes are presented in figure 1.5.

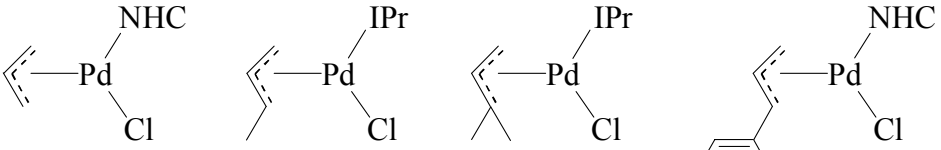
Figure 1.5. Examples of Various Pd-NHC Complexes



The Nolan group has synthesized a variety of different well-defined palladium-NHC complexes from commercially available palladium sources. These complexes include NHC-Pd-olefins,[75] NHC-Pd-carboxylates,[76] NHC-Pd-acetylacetonate[77] NHC-palladacyclic complexes[78] and NHC-Pd-chloride dimers[79] (Figure 1.6) and have been employed in catalyzing various transformations such as Suzuki-Miyaura coupling and Buchwald-Hartwig amination.[80]

Figure 1.6. Various Well-Defined Pd-NHC Derivatives Developed by Nolan et al.

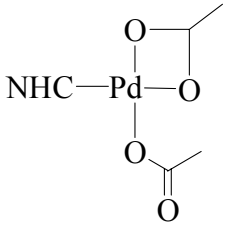
(a) NHC-Pd-allyl Derivatives



NHC = IPr
SIPr
IMes
SIMes
I*t*Bu
ICy
IAd

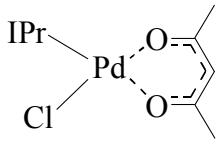
NHC = IPr
SIPr

(b) NHC-Pd-carboxylate Derivatives

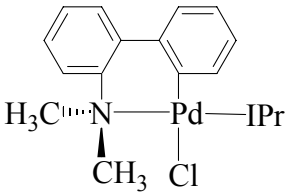


NHC = IPr
IMes

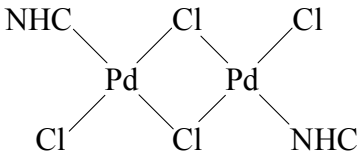
(c) IPr-Pd-acetylacetonate Derivative



(d) IPr-Palladacycle Derivative



(d) NHC-Pd-Dimer Derivative



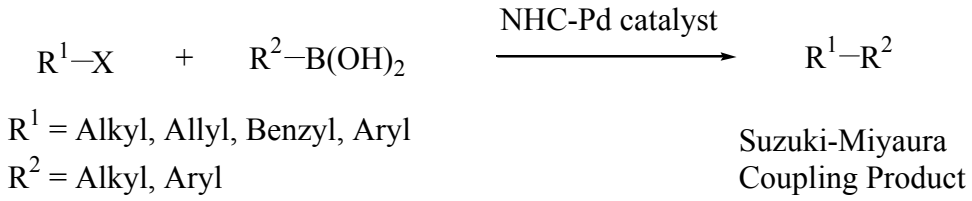
NHC = IPr
SIPr

1.3. Palladium-NHC Catalysis: Methodologies Relevant to this Study

As depicted in Scheme 1.3, palladium acts as mediator in a number of important cross coupling reactions. Although historically phosphine has been used for a majority of palladium-catalyzed coupling reactions, it has been demonstrated that NHC-palladium catalysts are capable of catalyzing all of the transformations presented in Scheme 1.3. Moreover, Pd-NHC systems have provided better results in these transformations as compared to Pd-phosphine systems. The overview of reactions relevant to the work being presented: (1) Suzuki-Miyaura Cross-Coupling Reaction (2) α-Arylation of Ketones and (3) Kumada-Tamao-Corriu Cross-Coupling Reaction, is provided in the following sections.

1.3.1. Suzuki-Miyaura Cross-Coupling Reaction

Scheme 1.4. Suzuki-Miyaura Cross-Coupling Reaction

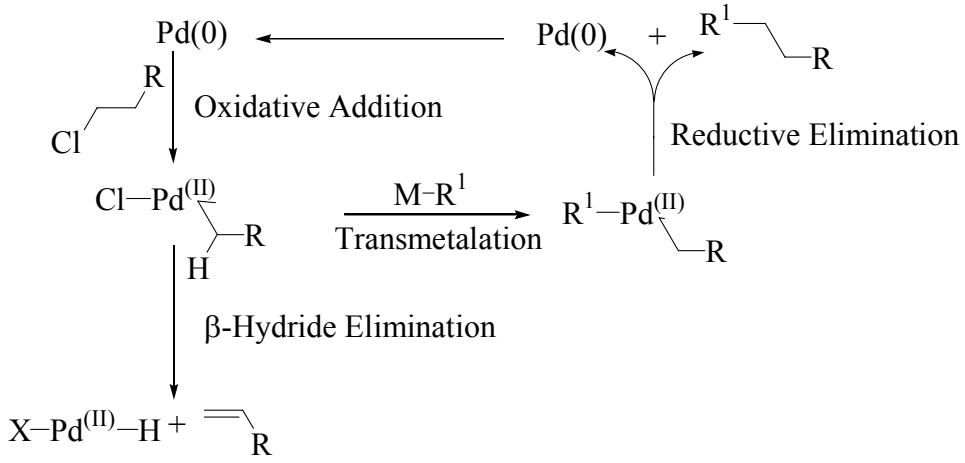


Suzuki, Miyaura and Yamada discovered that alkenyl boronates underwent coupling reaction with alkenyl and alkynyl halides and introduced this important coupling reaction to the organic synthetic methodologies in 1979.[81] In the following years they have done seminal work underscoring the utility of this reaction.[82] The versatility of this reaction has increased manifolds

since these early reports.[83] Arguably, it has become the most important metal-catalyzed C-C bond forming reaction (Scheme 1.4).[84]

The major advantage Suzuki-Miyaura cross-couplings offer is the employment of very user-friendly organometallic coupling partners – organoboron reagents.[85] Organoboron reagents offer many advantages such as air- and moisture stability, ready availability, minimal toxicity, thermal stability and tolerance towards functional groups.[86] Usually boronic acids are used for the reaction.[87] Molander has also reported the use of fluoroborates in the Suzuki-Miyaura coupling with halides.[88]

Figure 1.7. Possible Mechanistic Pathways for Suzuki-Miyaura Reaction

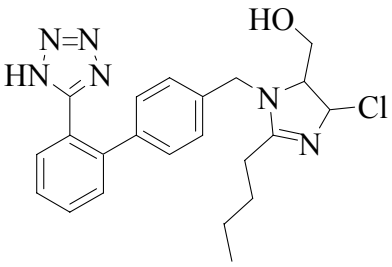


However, in terms of the electrophilic coupling partner, much development needs to be done as attempts of employing the cheap and more user-friendly chlorides were mostly unsuccessful.[89] In that regard, Fu et al has made significant advances in coupling chemistry especially with β-hydrogen containing substrates.[90] Although the examples of coupling of difficult substrates at mild reaction conditions being utilized in Suzuki-Miyaura coupling are rather rare,[91] new discoveries are being made and a large volume of research efforts are directed

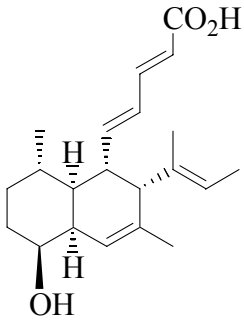
towards making the Suzuki-Miyaura methodology a better option for organic synthetic chemists as well as for widely acceptable industrial applications.[92] Possible mechanistic pathway for β-hydrogen containing substrates is presented in Figure 1.7.

Recent developments in applications of Suzuki-Miyaura towards synthesis of drugs,[93] natural products,[94] polymers[95] and therapeutic agents[96] have rendered this methodology indispensable in the arsenal of an organic chemist (Figure 1.8).

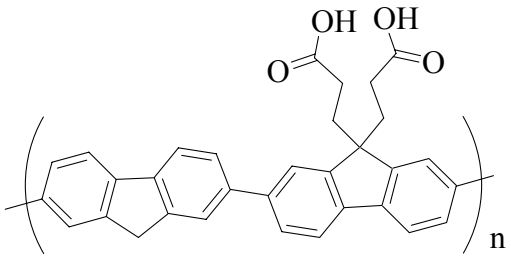
Figure 1.8. Utilization of Suzuki-Miyaura Coupling in Synthesis of Various Classes of Compounds



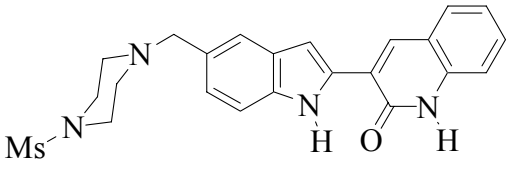
Losartan



(+)-Phomopsidin



PF-DA

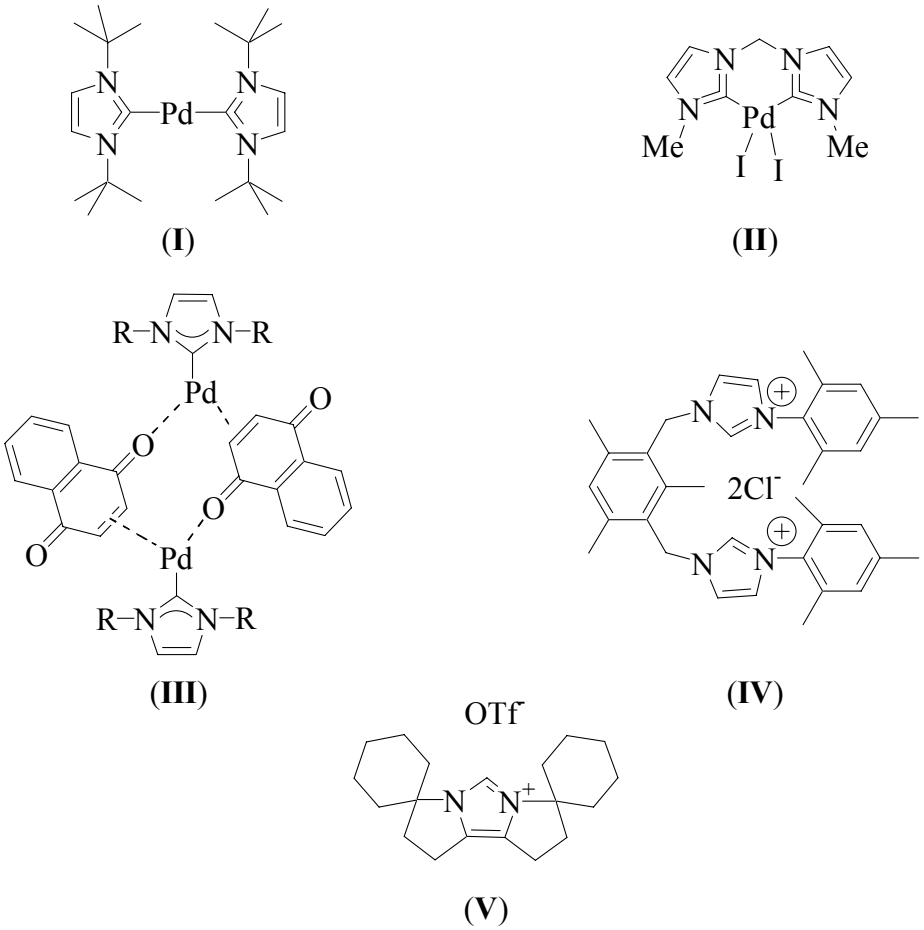


KDR Kinase Inhibitor

A few examples of the most popular NHC ligands and palladium catalysts utilized in Suzuki-Miyaura cross-coupling reaction have been presented in Figure 1.9. The most common palladium sources used in these systems are $Pd(OAc)_2$ and $Pd_2(dba)_3$. The figure also depicts the bis-imidazolium salt ((**IV**), Figure 1.9) which was utilized by Trudell et al[97] for coupling of aryl

chlorides. Glorius demonstrated use of ligand (**V**) for the coupling of electron rich chlorides.[98] Both the systems used $Pd(OAc)_2$ as the palladium source in conjunction with the respective ligands.

Figure 1.9. Various NHC Ligands and NHC-Pd Catalysts Utilized in Suzuki-Miyaura Cross-Coupling Reaction



In the work being presented, easy synthesis and catalytic activity of two different sets of NHC-palladium catalysts in Suzuki-Miyaura reaction will be discussed. The aim of the work was to simultaneously develop NHC-palladium catalysts along with the betterment of Suzuki-

Miyaura methodology. Using first class of compounds, (NHC-Pd-carboxylate) coupling of β-hydrogen containing activated chlorides was achieved. Sterically hindered substrates also coupled with boronic acids under mild conditions. The efforts to develop the methodology necessitated a survey of a broad spectrum of parameters. The reaction conditions were optimized to a protocol that is user-friendly and environmentally benign. The catalyst loadings were reduced substantially, as was concentration of the alkoxide base. The protocol did not necessitate use of any additives such as tetrabutyl ammonium bromide and technical grade solvents were employed for the coupling process making it a very attractive protocol. The second set of NHC-palladium catalysts comprised of (NHC)Pd$(Cl)_2$-(X-pyridine) complexes. The activity of these complexes was studied in Suzuki-Miyaura reaction and scope and limitations of the protocol were analyzed.

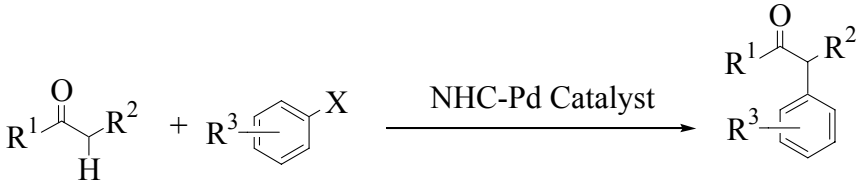
1.3.2. α-Arylation of Ketones

As discussed above, development of efficient and selective catalytic C-C bond formation reactions has been a subject of vital interest in organic and organometallic chemistry.[99] Catalytic conversion of C-H bond to a C-C bond is an important sub-group of such C-C bond forming reactions. The coupling of enolizable ketones and aryl halides despite its promising synthetic value has not been explored exhaustively and vast potential of this coupling remains un-trapped.[100]

Finding a proficient and dependable catalytic method to form a bond between an arene and carbon α to a carbonyl group is an exigent problem.[101] The use of aryl halides for direct

arylation of ketones at the carbon α to the carbonyl group has proven to be a transformation of great utility in synthesis of fine chemicals,[102] pharmaceutical, agrochemical and organic synthesis.[103]

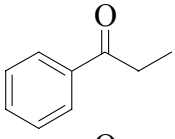
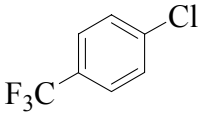
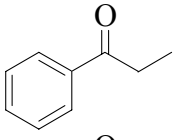
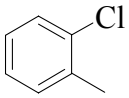
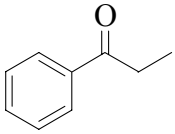
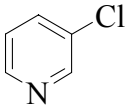
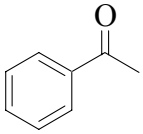
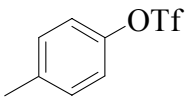
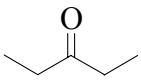
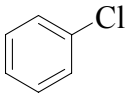
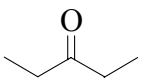
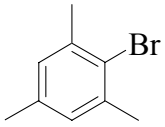
Scheme 1.5. α-Arylation of Ketones



The initial metal mediated coupling protocols of enolates employed the use of stoichiometric amounts of metal complexes.[104] The under-developed protocol also involved the use of less readily available carbonyl alternatives.[105] However, in concurrent work, Buchwald,[106] Hartwig[107] and Miura[108] reported the first examples of direct, catalytic, α-arylations of ketones in 1997. Since then, a myriad of reports from these and other groups have helped establish the catalytic α-arylation of ketones as a very significant transformation.[109] The enolate form of the ketone can be generated efficiently in situ and acts as a transmetalating agent in catalytic transformations. Although a side-reaction in which condensation of two ketone molecules to form a α-hydroxyketone is a possibility, various ways have been devised to avoid this problem.[110] The reaction leads to the formation of new sp^2-sp^3 bonds and displays good regioselectivity.[111] Usually the catalyst supporting ligands are tertiary phosphines, as mentioned above; they are susceptible to thermal degradation and are often difficult to remove from products.

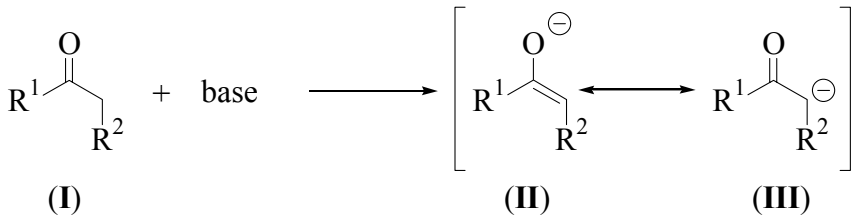
A few years ago, we reported on efficient mediation of α-arylation of ketones by (NHC)Pd(allyl)Cl catalysts.[112] The catalyst was prepared from a reaction of NHC with [(η^3-allyl)Pd(Cl)]$_2$[113] The activation of the catalyst involved nucleophilic attack on the allyl moiety by a base which generated the active species.[114] The catalyst was found to be very efficient in coupling aryl chlorides, bromides and triflates with ketones, under a mild set of conditions and with very low catalyst loading. A few examples of coupling from the protocol are presented in Table 3. The protocol afforded coupling product with functionalized (entry 1), sterically hindered (entries 2 and 6), heterocyclic (entry 3) and triflate (entry 4) coupling partner.

Table 1.3. α-Arylation of Ketones catalyzed by (SIPr)Pd(allyl)Cl Catalyst[112]

entry	ketone	halide/triflate	temperature (^{o}C)	time(h)	yield (%)
1			70	1	81
2			60	1	87
3			50	1	60
4			60	1.5	88
5			70	0.2	88
6			60	0.5	68

The presence of a basic moiety is of prime importance since the base deprotonates the ketone at the α-position thus forming the reactive species: enolate. The enolate can then enter the catalytic cycle and react with Pd(II) species formed after oxidative addition of the halide/pseudohalide coupling partner.

Scheme 1.6. Activation of Ketone via Action of the Base



(I) **(II)** **(III)**

In the work being presented, a convenient protocol underscoring the activity of $(IPr)Pd(OAc)_2$ catalysts in the α-arylation of ketones will be discussed. The protocol was found to be amenable to large-scale synthesis. A wide array of functionalized halides has been investigated in an effort to better understand the bearings of electronics and sterics on the reaction. Coupling of heterocyclic and sterically hindered substrates at optimum temperatures were also achieved. Bearing of sterics and electronics on the mechanistic pathway was also analyzed by studying the coupling of various functionalized halides.

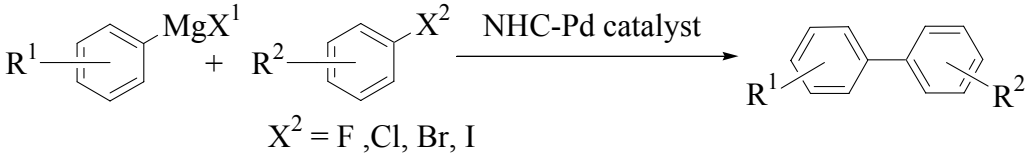
1.3.3. Kumada-Tamao-Corriu Cross-Coupling Reaction

Organomagnesium compounds have been a very important class of synthetic tools in organic chemistry ever since their discovery by Grignard.[115] Transition metal catalyzed cross-coupling of organomagnesium compounds[116] has been utilized for the synthesis of structural

building blocks for complex molecules in natural product synthesis,[117] liquid crystals, polymers and ligands.[118] Grignard reagents were minitially utilized in exploring the reactivity of Grignard reagents with vinyl halides.[119] In separate works, Kumada[120] and Corriu[121] reported that the reaction of Grignard reagents with alkenyl or aryl halides could be catalyzed by Nickel (II) complexes.

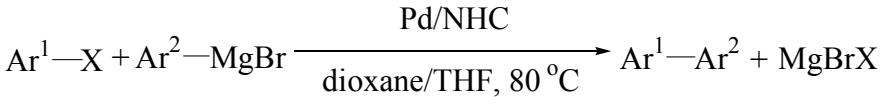
Simple preparation of Grignard reagents from organohalides and magnesium provides this reaction with a major advantage in terms of substrates. Although, questionable functional group tolerance of the Grignard reagents handicaps the utility of this coupling methodology, low toxicity and cost of magnesium makes Kumada-Tamao-Corriu coupling reaction a very useful process.[122]

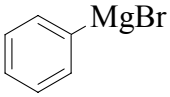
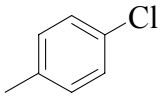
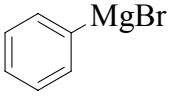
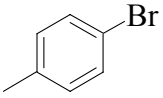
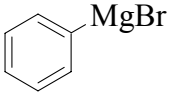
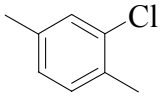
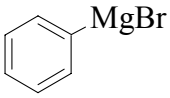
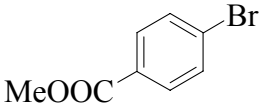
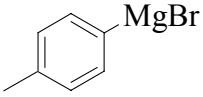
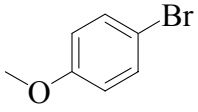
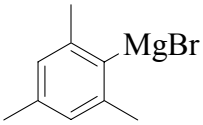
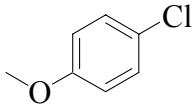
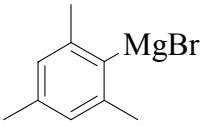
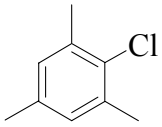
Scheme 1.7. Kumada-Tamao-Corriu Coupling Reaction



The Nolan group presented the first report utilizing NHC-palladium system for mediating the Kumada-Tamao-Corriu coupling reaction.[123] Pd_2dba_3 was employed as the palladium source. Aryl chlorides, aryl bromides and aryl iodides were demonstrated to work well in the methodology with nearly quantitative yields obtained in the reactions (Table 1.4). Interestingly, while di-*ortho* substituted products (entry 6) were achieved with good results in the protocol, attempts to synthesize more sterically hindered tetra-*ortho* substituted products (entry 7, Table 1.4) did not furnish the desired product.

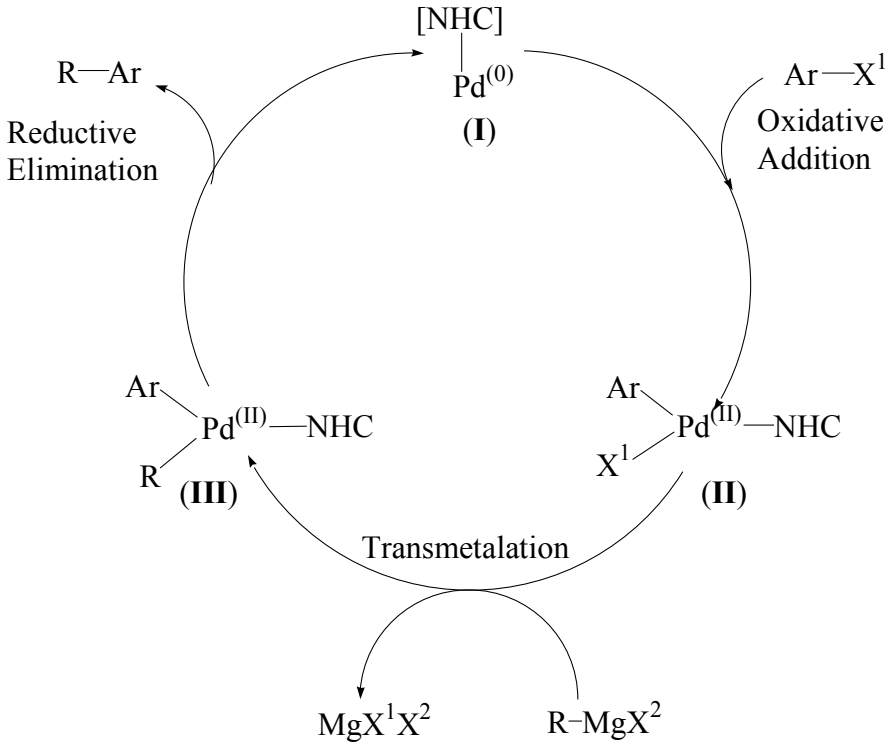
Table 1.4. K-T-C Coupling in a Pd-NHC System[123]



entry	ketone	halide	time(h)	yield (%)
1			3	99
2			1	99
3			3	85
4			5	69
5			3	99
6			3	95
7			24	0

A putative mechanistic cycle for K-T-C coupling is presented in Scheme 1.8. While presence of steric hindrances around the reaction center can act as deterrent towards oxidative addition or transmetalation in the catalytic cycle (Scheme 1.8), on the contrary it can facilitate the reductive elimination leading to the formation of the desired coupling product.

Scheme 1.8. Catalytic Cycle for K-T-C coupling



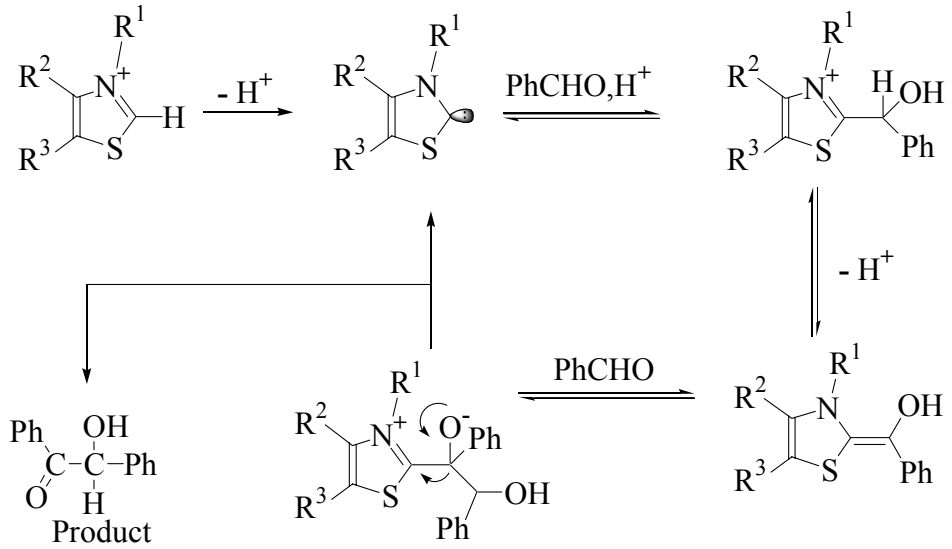
In the work being presented, significant advances in development of Kumada-Tamao-Corriu methodology are discussed. High activity profile of the catalyst allowed coupling of various halides with very low catalyst loadings. The process was also shown to be viable for applications in industry and synthetic laboratories by achieving excellent yields in scale-up experiments. Furthermore, best conditions for a palladium-NHC system in C-F bond activation of unactivated aryl fluoride were also presented.

1.4. Organic Catalysis

Starting from first examples of nucleophilic catalysis of benzoin condensation by Wohler and Liebig,[124] organocatalysis has come a long way and is fast gaining momentum as a viable environmentally-friendly mode of catalysis. McMillan's seminal work[125] has revived this field of catalysis.[126]

Building upon Lapworth's work on cyanide catalyzed benzoin condensation,[127] Ukai and co-workers discovered thiazolium catalyzed benzoin condensation and reported initial examples of organic catalysis.[128] Based on Lapworth's work, Breslow proposed a mechanism for thiazolium catalyzed benzoin condensation in 1958 (Scheme 1.9).[129]

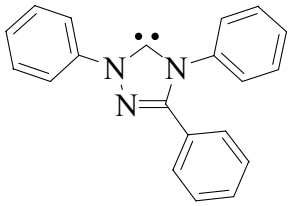
Scheme 1.9. Breslow's Mechanism for Thiazolium Catalyzed Benzoin Condensation



The major feature of Breslow's mechanism was proposal of thiazol-2-ylidene species. These carbene intermediates were a class of highly reactive species having a divalent carbon

atom. As discussed above, Wanzlick and co-workers studied the chemistry of *N*-heterocyclic carbenes (NHCs) as intermediates and later Arduengo synthesized stable free carbenes. Today, these NHCs have been extensively utilized as nucleophilic catalysts by various groups including major advances reported by Teles and Enders who have worked with triazole-based carbenes.[130] Their triazole-carbene became the first commercially available *N*-heterocyclic carbene (Figure 1.3).[131]

Figure 1.10. First Commercially Available Triazolium-Based Carbene

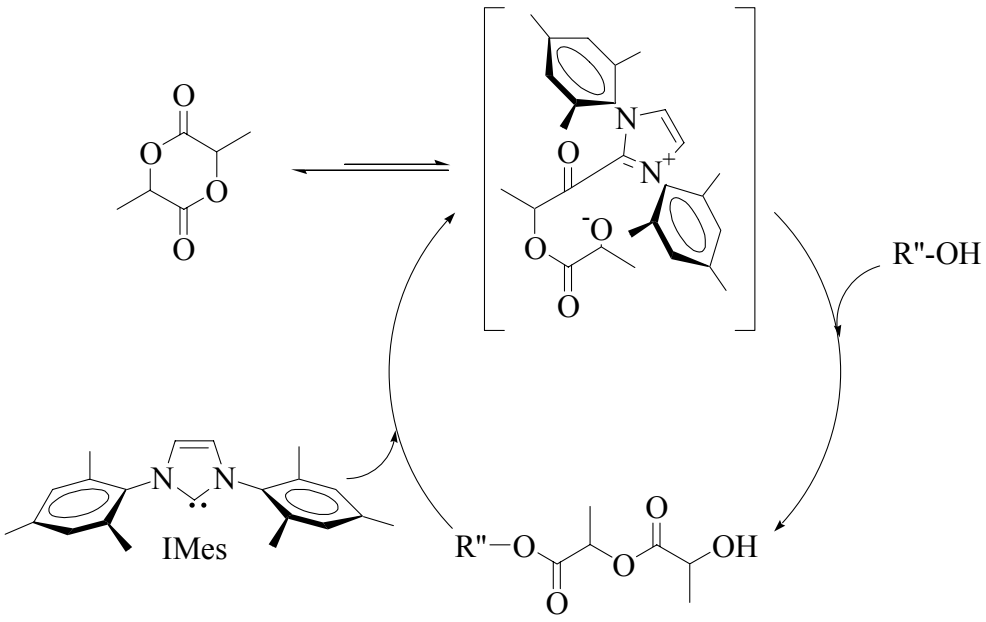


Tunable sterics and electronics and non-pyrophoric, non-toxic nature of NHCs has helped establish them as very important and useful organic catalysts. Some major advances in utilizing NHCs as organic catalysts are: cyclotrimerization of isocyanates,[132] preparation of γ-butyrolactams,[133] kinetic resolution of secondary alcohols,[134] amidation of unactivated esters with amino alcohols,[135] trifluoromethylation of carbonyl compounds,[136] conversion of α,β-unsaturated aldehydes into saturated esters via an umpolung reaction[137] and one-step assembly of functionalized γ–butyrolactones from benzoins or benzaldehydes via an NHC-mediated tandem reaction.[138]

Hedrick et al. described the use of NHCs as organic catalysts for ring opening polymerization of cyclic esters (Scheme 1.10)[139] and further extension of his work.[140] This

method was reported as a useful means to free polymers of the metal contaminants, which are present in the usual metal catalyzed processes.[141]

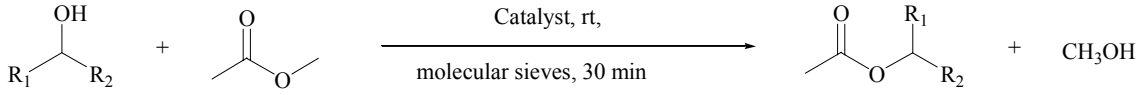
Scheme 1.10. NHC Catalyzed Ring Opening Polymerization of Lactones

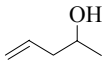
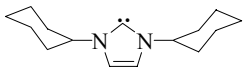
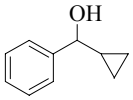
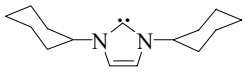
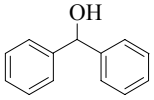
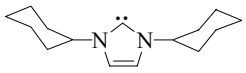
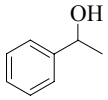
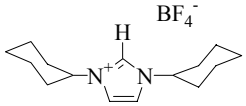
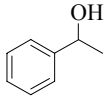
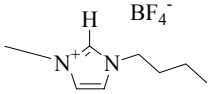


Congruent to Hedrick's report, Nolan reported NHC catalyzed transesterification with vinyl acetate and more difficult to cleave, methyl esters as substrates.[142] The scope of the reaction was studied[143] and later work was extended to include secondary alcohols (Table 1.5).[144]

In the work being presented, the extension of this methodology to phosphorus-esters will be discussed. Various parameters affecting the reaction will also be presented. A possible application of the methodology to an important issue of detoxification of chemical weapons such as VX has also been addressed.

Table 1.5. NHC Catalyzed Transesterification of Secondary Alcohols[144]



entry	alcohol	catalyst	catalyst loading	yield (%)	inference
1			5 mol%	85	Functional gp compatibility
2			5 mol%	94	Absence of free radical mech.
3			5 mol%	81	Sterically bulky substrate
4			10 mol%	60	In situ generated carbene
5			5 mol%	80	In situ generated carbene: Commercially available precursor

1.5. Dissertation Outline and Objectives

N-Heterocyclic Carbenes (NHCs) have emerged as a very promising new class of catalyst modifiers in a large number of metal-mediated transformations. NHCs have also proven to be a very important class of organic-catalysts. Some advantages associated with NHCs are thermal stability, powerful electron donation properties, minimal toxicity, non-dissociative tendencies, and remarkable air- and moisture-stability in conjunction with metals. These advantages make NHCs very attractive for applications in organic synthesis and for broader acceptance in industrial applications. For example the instability of phosphines translates to higher costs of the

catalytic process because an excess of the ligand has to be added to the reaction. However, use of NHCs circumvent such a need and hence bring the cost of the process down, thus making it attractive for wider applications. A large volume of research efforts are being directed towards exploring the utility of NHCs in organometallic and organic chemistry. The main goals of the work being presented in this dissertation have been development of methodologies involving NHCs as efficient ligands in palladium-catalyzed reactions and as organic catalysts in metal-free reactions. The development of methodologies has been carried with an aim of making these protocols amenable to wider acceptance in the scientific community, both laboratorial and industrial.

The main objectives of this study are:

(1) Synthesis and investigation of behavior of NHCs as ancillary ligands in cross-coupling reactions.

(2) Development and study of NHC-palladium complexes as efficient catalysts.

(3) Development of methodology in NHC-palladium catalyzed Suzuki-Miyaura, α-arylation of ketones and Kumada-Tamao-Corriu cross-coupling reactions.

(4) Investigation of scope of NHCs as nucleophilic organic-catalysts in the transesterification reaction.

1.6. References

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CHAPTER 2

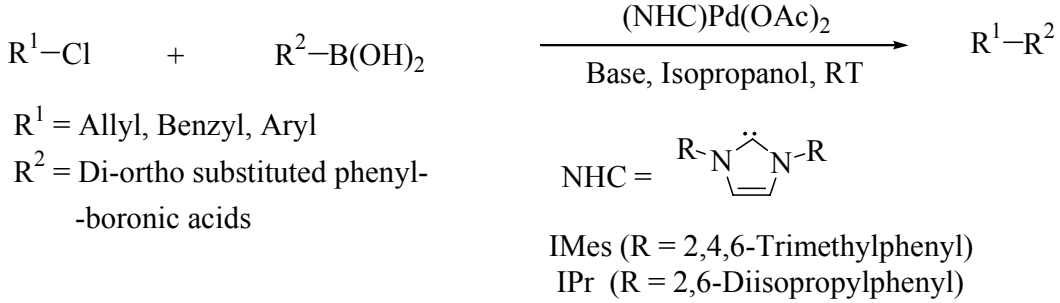
SIMPLE (IMIDAZOL-2-YLIDENE)-Pd-ACETATE COMPLEXES AS EFFECTIVE PRECATALYSTS FOR STERICALLY HINDERED SUZUKI-MIYAURA COUPLINGS*

2.1. Introduction

A simplified synthesis of N-heterocyclic carbene (NHC)Pd-carboxylate complexes and their activity in Suzuki-Miyaura cross coupling reactions are described. Coupling of sterically hindered aryl and activated alkyl chlorides bearing β-hydrogens has been successfully achieved.

The versatility of Suzuki-Miyaura reaction has greatly progressed since its early reports.[1] It serves as one of the most useful cross-coupling tools in synthetic chemistry.[2] Remarkable progress in both, volume of work and mechanistic investigations, has been achieved in recent years. However, barring a few recent advances, the attempts to use alkyl halides (especially chlorides) as electrophile partners have been largely unsuccessful.[3] Moreover, examples of mild reaction conditions are rare when the desirable coupling products are sterically hindered di-ortho or tri-ortho substituted biaryls.[4,5]

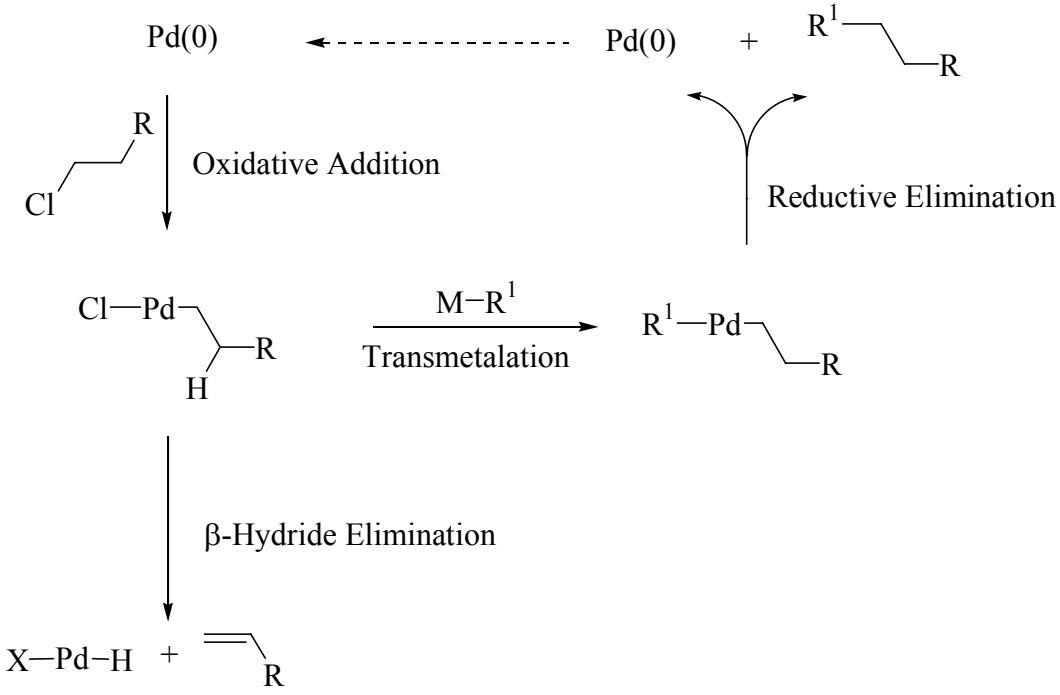
Scheme 2.1. Simple (Imidazol-2-ylidene)-Pd-Acetate Complexes as Effective Precatalysts for Sterically Hindered Suzuki-Miyaura Couplings



The major impediment in Suzuki-Miyaura coupling of alkyl halides is the presence of a facile β-hydride elimination pathway (Scheme 2.2). This undesired side reaction competes with the transmetalation step hindering a productive coupling process.

Extensive studies by a number of groups have helped this area take new strides.[6] Elegant work by Fu has helped expand the scope of this reaction by including alkyl chlorides and secondary alkyl bromides as substrates.[7] The Suzuki-Miyaura reactions utilizing C(sp^3)-chlorides reported so far, have been either with boranes as coupling partners[8] or catalyzed by phosphine ligands. However, both classes of compounds suffer from drawbacks. Air sensitivity and commercial non-availability of boranes increases the number of steps required to perform the coupling reaction. The boronic acids have been widely accepted as the more convenient transmetalating agents for this reaction. Furthermore, toxic and pyrophoric phosphines can be replaced by user friendly *N*-heterocyclic carbenes (NHCs).[9]

Scheme 2.2. Competing Pathways in Suzuki-Miyaura Coupling



In previous studies, we have highlighted the use of *N*-heterocyclic carbenes as efficient ligands in various cross-coupling reactions including the Suzuki-Miyaura reaction.[10] In a recent communication, we reported the synthesis of (imidazol-2-ylidene)$Pd(OAc)_2$ complexes.[11,12] The complexes were found to be active catalysts for the hydroarylation of alkynes.

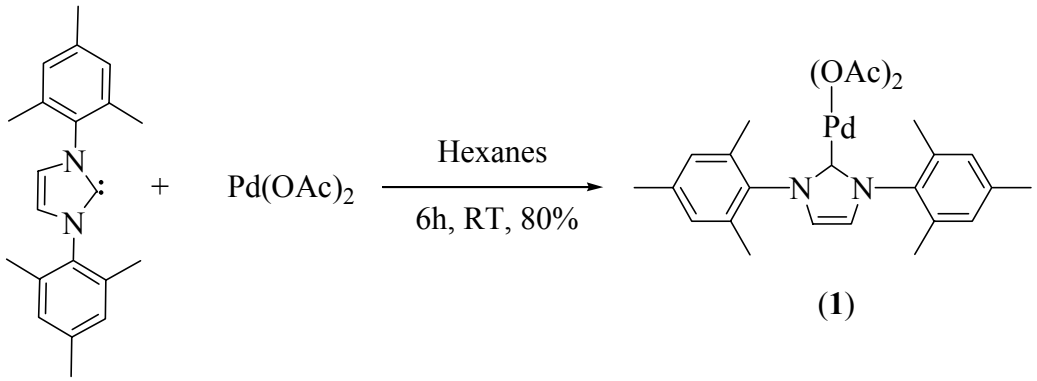
2.2. Synthesis of (Imidazol-2-ylidene)$Pd(OAc)_2$ Complexes

In conjunction with extensive previous work with $Pd(OAc)_2$ as the palladium source for the Suzuki-Miyaura reaction,[10c,13] we examine here the activity of (NHC)$Pd(OAc)_2$ complexes in this important transformation. We now describe a simplified procedure for the synthesis of

(NHC)Pd(OAc)$_2$ complexes and Suzuki-Miyaura reaction involving coupling of activated, β-hydrogens containing C(sp^3)-Cl with boronic acids. The system also allows for synthesis of highly sterically hindered, di-ortho and tri-ortho substituted biphenyls under mild conditions.

We have improved upon our previously reported synthesis of (NHC)Pd(OAc)$_2$ complexes (Scheme 2.3).[14]

Scheme 2.3. Synthesis of (IMes)Pd(OAc)$_2$



(**1**)

2.3. (Imidazol-2-ylidene)Pd(OAc)$_2$ Catalyzed Suzuki-Miyaura Cross Coupling

To analyze the activity of this complex in mediating the Suzuki-Miyaura reaction, coupling of phenylboronic acid and 4-chlorotoluene was examined. The reaction proceeded to furnish a 97% yield of the desired product in 1 hour at room temperature. Surprisingly, the IPr analogue, (IPr)Pd(OAc)$_2$ did not show appreciable formation of coupling product at room temperature. However, on raising the temperature 40 °C, it provided quantitative yield in 45 minutes. To circumvent the inconvenience of previously reported slow-addition of halides,[4b] the

reactions were tested with normal rate of addition of the halide substrate (for experimental details see supporting information). No formation of dehalogenation by-products rendered the slow-addition protocol obsolete.

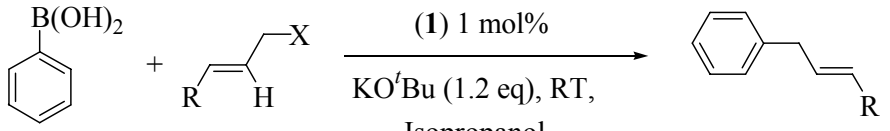
Our previous work emphasizing the important role played by the solvent in the reaction system, prompted us to screen various alcohols as solvents. Screening of alcohols indicated that isopropanol (IPA) was the best solvent for these systems.[15] Use of technical grade isopropanol, without prior drying renders this protocol quite practical and amenable to large scale synthesis.

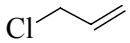
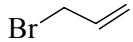
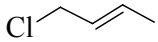
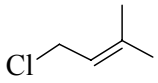
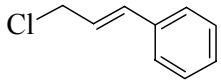
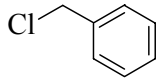
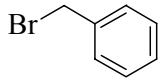
To increase the scope of the reaction, various bases were also screened.[16] In general, alkoxide bases yielded the best results at room temperature. Milder bases such as Cs_2CO_3 and K_3PO_4 performed moderately well (see experimental section).

As mentioned earlier, C(sp^3)-chlorides suffer from poor activity in Suzuki-Miyaura coupling. Apart from difficulty in transmetalation step, the low reactivity of chlorides in this reaction is attributable in part to the strength of the C–Cl bond.[17] However, recently a few systems which allow oxidative addition of alkyl chlorides have been reported.[18] Our desire to contribute to solving the problem of coupling of chloride substrates with β-hydrogens led us to explore this aspect in Suzuki-Miyaura coupling.

In this regard, our efforts with unactivated C(sp^3) chlorides such as lauryl and hexyl chloride did not result in the desired coupling products. In these attempts, formation of dehalogenation products was observed, indicating a problem at the transmetalation step rather than oxidative addition of the alkyl chloride to the palladium center.

Table 2.1. Screening of activated C(sp^3)-Chlorides[a]



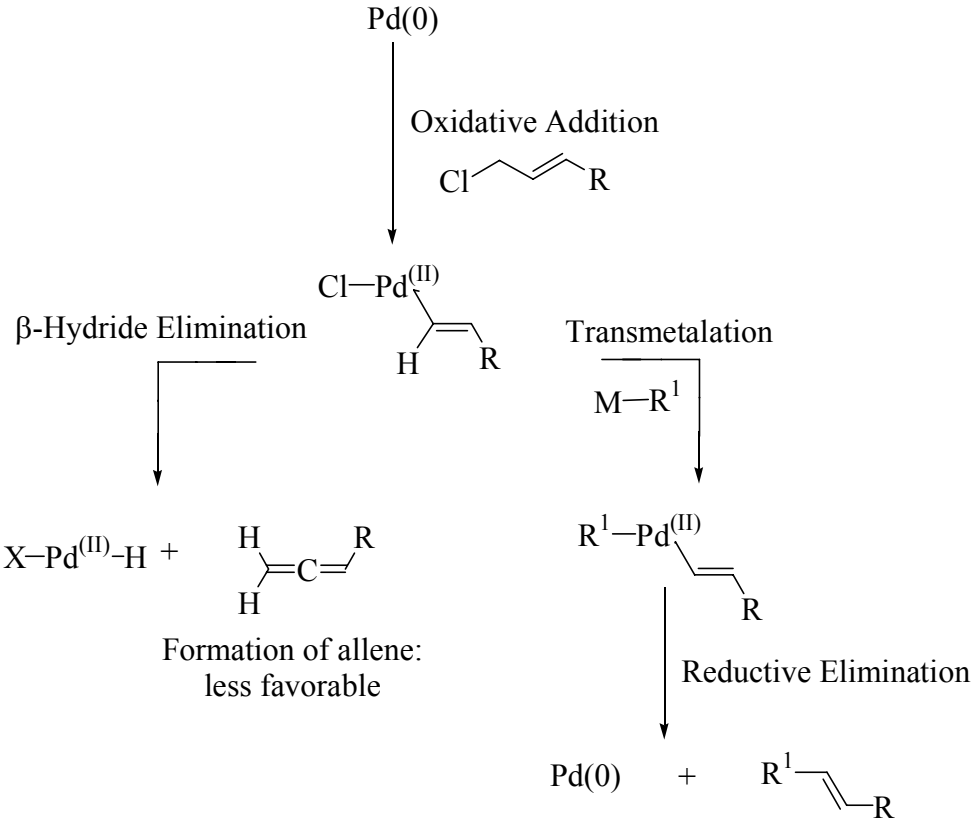
entry	halide substrate	time (h)	yield (%)[b]
1		0.5	80(72)
2		2	100(93)
3		0.5	78(74)
4		-	NR[c]
5		0.5	78(72)
6		3	98(86)
7		1	85(58)

[a]Reaction conditions: 1 mol% of $(IMes)Pd(OAc)_2$, 1 mmol of halide, 1.1 mmol of phenylboronic acid, 1.2 mmol of KOtBu, 2 mL of IPA. [b]GC yield (isolated yield), average of two runs. [c]Unidentified mixture of products.

However, reactions of activated C(sp^3)-chlorides (allylic and benzylic) proceeded to give excellent yields of coupling products despite the presence of β-hydrogens in the allylic substrates (Table 2.1).

Conceivably, for allylic substrates, the transmetalation step is more favored relative to the β-hydride elimination, which if favored would lead to formation of allenes (Scheme 2.4). Hence the final outcome is the coupling of the substrates rather than dehalogenation of the chlorides.

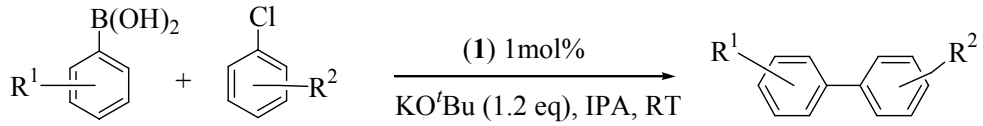
Scheme 2.4. Competing Pathways in Suzuki-Miyaura Coupling of Allylic Substrates

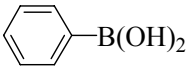
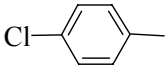
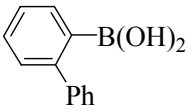
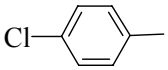
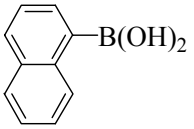
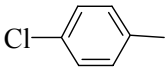
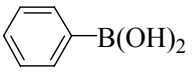
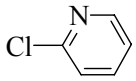
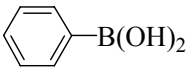
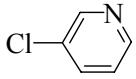
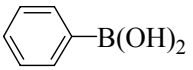
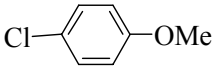
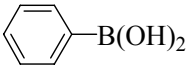
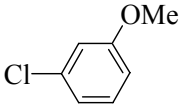
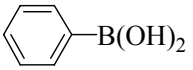
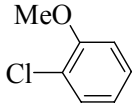
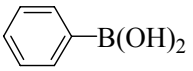
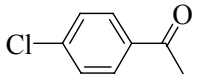
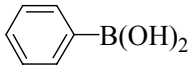
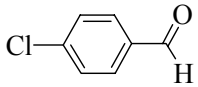


As mentioned earlier, boronic acids serve as excellent transmetalating agents. To test the limits of compatibility of various functionalities using our protocol, various boronic acids were tested for activity. Excellent yields were obtained in most cases including reactions leading to formation of ortho-substituted products (Entries 2, 3 and 8, Table 2.2). Functional group variance on the halides was also studied (Entries 4-10, Table 2.2).

We were able to achieve coupling of electron-donating (Entries 6, 7 and 8, Table 2.2) as well as electron-withdrawing (Entries 9 and 10, Table 2.2) group containing chlorides. Formation of 2-phenylpyridine and 3-phenylpyridine (Entries 4 and 5, Table 2.2) demonstrated compatibility of hetero-aromatic aryl chlorides in the coupling process.

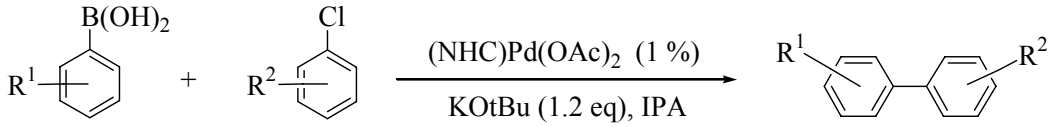
Table 2.2. Substrate Screening

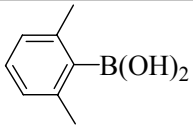
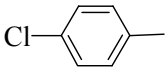
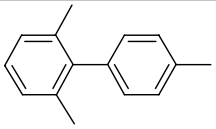
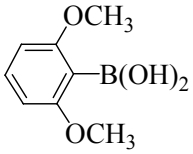
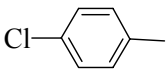
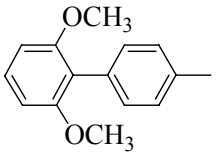
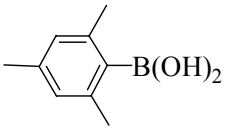
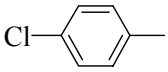
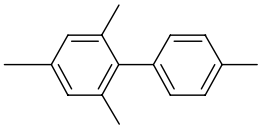
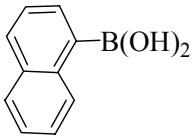
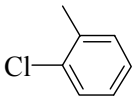
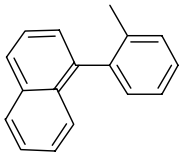
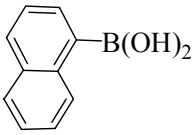
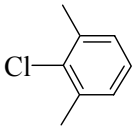
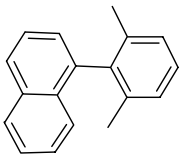
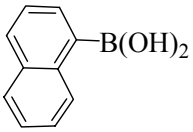
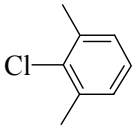
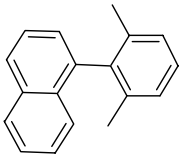
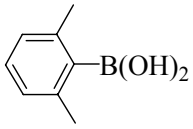
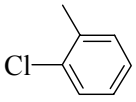
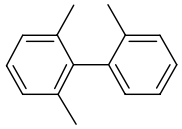


entry	boronic acid	halide	time (h)	yield (%)[b]
1			1	97(94)
2			2	100(94)
3			2	100(91)
4			20	63(61)
5[c]			7	77(74)
6			3	90(81)
7			2	72(68)
8			2	90(85)
9			24	93(88)
10			2	65(63)

[a]Reaction conditions: 1 mol% of $(IMes)Pd(OAc)_2$, 1 mmol of halide, 1.1 mmol of boronic acid, 1.2 mmol of KOtBu, 2 mL of IPA; [b]GC yield (isolated yield), average of two runs; [c]T = 40 °C.

Table 2.3 Synthesis of Di- and Tri-ortho Substituted Biaryls[a]



entry	boronic acid	Ar-chloride	product	method[b]	time (h)	yield (%)[c]
1				A	2	80(75)
2				A	2	92(81)
3				A	2	78(72)
4				A	1	91(89)
5				A	-	NR[d]
6				B	3	100(91)
7				B	6	90(88)

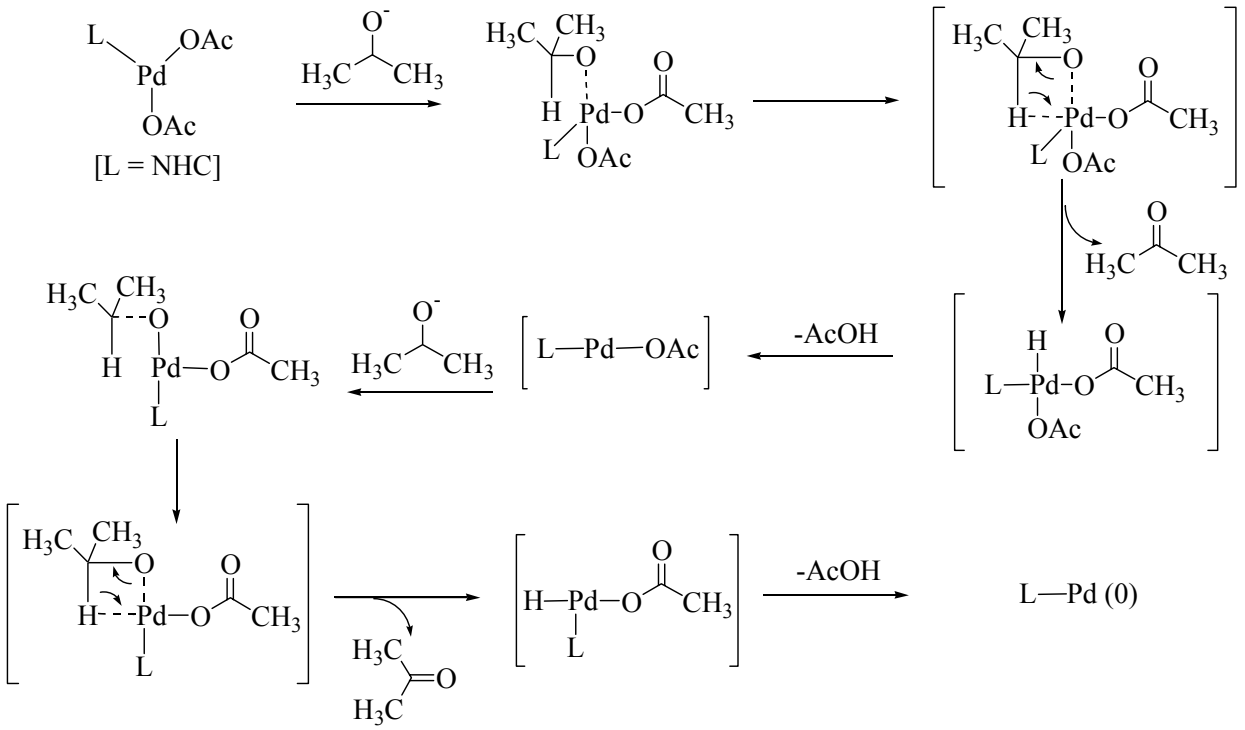
[a]Reaction conditions: 1 mmol of halide, 1.1 mmol of boronic acid, 1.2 mmol of KOtBu, 2 mL of IPA; [b]Method A: 1 mol% of $(IMes)Pd(OAc)_2$, RT; Method B: 1 mol% of $(IPr)Pd(OAc)_2$, 40 °C. [c]GC yield (isolated yields), average of two runs. [d]Unidentified mixture of products.

Synthesis of sterically hindered products was also achieved using this system. While preparation of di-ortho biphenyls proceeded at room temperature, the tri-ortho biphenyls required

temperature of 40 °C and proceeded in excellent yields using (IPr)Pd(OAc)$_2$ as the catalyst (Compare entries 5 and 6, Table 2.3).

A pathway for the activation of the catalyst is proposed (Scheme 2.4). Initial deprotonation of isopropyl alcohol (IPA) by the base (KO*t*Bu) can generate an isopropoxide anion which can attack the (NHC)Pd(OAc)$_2$ complex. Analogous to previously reported β-hydride elimination from a palladium coordinated isopropoxide, formation of a Pd-hydride species with elimination of a molecule of acetone can be envisaged.[4b]

Scheme 2.5. Proposed Activation of the Catalyst



Next, elimination of acetic acid from H-Pd(OAc)$_2$ can generate a (NHC)Pd(OAc) species. Sigman has previously proposed this type of pathway in the oxidation of alcohols.[19] The mono acetate species, (NHC)Pd(OAc) can then undergo a second isopropoxide anion attack,

with subsequent elimination of a molecule of acetone and acetic acid. This could finally generate the required NHC-Pd(0) species available for oxidative addition of the halide substrate.

2.4. Conclusions

In summary, we have described a convenient synthetic protocol for preparation of imidazol-2-ylidene based palladium acetate complexes. We have established these complexes as efficient mediators of Suzuki-Miyaura coupling. A broad spectrum of parameters has been surveyed, optimizing reaction conditions to a protocol which is user-friendly and environmentally benign.[20] The protocol has been used to couple β-hydrogen containing activated C(sp^3)-chlorides with boronic acids providing an alternative to the Friedel-Crafts reaction for synthesis of allylic-aromatics.[21] Sterically hindered substrates have also been coupled using mild conditions. Ongoing studies are directed towards further expanding the scope of these reactions.[22]

2.5. Experimental Section

2.5.1. General Considerations

- All reactions were carried out in an MBraun glovebox containing dry argon or using standard Schlenk techniques under an atmosphere of dry argon.

- Solvents for synthesis were distilled from appropriate drying agents or were passed through an alumina column in an MBraun solvent purification system.
- Technical grade solvents were used for screening in Suzuki-Miyaura cross-coupling and were used *as is* without any prior drying. Technical grade isopropanol was used for base, halide and boronic acid screening. Solvents for NMR spectroscopy were degassed with argon and dried over molecular sieves.
- NMR spectra were collected on 300 or 400 MHz Varian Gemini spectrometers.
- Flash chromatography was performed on silica gel 60 (230-400 mesh) (Natland International Corporation). IMes = *N,N'*-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene and IPr = *N,N'*-bis(2,6-diisopropyl)imidazol-2-ylidene were synthesized according to the literature procedures.[23]
- **NOTE:** Although the reactions were performed inside a dry-box, the reaction protocol can also be followed with equal efficiency without using a glove-box. For performing the coupling of phenylboronic acid and 4-chlorobenzaldehyde, Schlenk techniques were used without any apparent decrease in activity (Table 3.2, Entry 10).

2.5.2. Synthesis of (IMes)Pd(OAc)$_2$

In a 25 ml Schlenk flask, a suspension of $Pd(OAc)_2$ (recrystallized from benzene, 225 mg, 1 mmol) in dry hexanes (10 mL) was prepared by heating at 40 °C. A solution of IMes (304 mg, 1 mmol) in dry hexanes (5 mL) was added to the $Pd(OAc)_2$ solution. Stirring at room temperature for 30 minutes afforded a dark colored solution. Continued stirring for 6 hours, afforded precipitates of the product. The suspension was then filtered under an atmosphere of

argon. The resulting precipitates were washed with hexanes (10 x 2 mL) and dried *in vacuo* to yield the product in 80% (423 mg) yield.

^{1}H-NMR ($CDCl_3$): δ = 6.88 (singlet, 4H, C*H*-aromatic), 6.73 (singlet, 2H, C*H*-imidazole), 2.43 (singlet, 6H, Ph-(*p*-CH_3)$_2$), 1.94 (singlet, 12H, Ph-(*o*-CH_3)$_2$), 1.24 (singlet, 6H, (OOC-CH_3)$_2$), ^{13}C-NMR ($CDCl_3$): δ = 18.4, 21.2, 22.6, 104.3, 122.3, 128.8, 136.0, 137.5, 169.5, 175.3, 183.9. Elemental analysis calcd. for $C_{25}H_{30}N_2O_4Pd$: C, 56.24; H, 5.72; N, 5.29. Found: C, 55.86; H, 5.70; N, 4.96.

2.5.3. Representative Procedure for Suzuki-Miyaura cross-coupling

In a dry-box, 1.2 mmol of base was added to a screw-cap vial charged with 1 mol% of (NHC)Pd(OAc)$_2$ complex. 1.1 mmol of the boronic acid was added and the vial sealed with a rubber septum. Outside the dry-box, 2 mL of technical grade solvent was injected in the vial with a syringe and the reaction mixture allowed to shake on a Lab-Line Orbit Shaker (set at 25 °C or 40 °C – J-Kem Scientific, Kem-Lab Controller) for catalyst activation. After 15 minutes, 1 mmol of the halide was added to the vial and the reaction mixture was allowed to shake for indicated time. The reactions were monitored by gas chromatography. After maximum conversion, the solids were filtered and washed with copious amounts of acetone and hexanes. Solvent was evaporated *in vacuo* and the concentrated reaction mixture purified by flash chromatography.

2.5.4. Solvent Screening

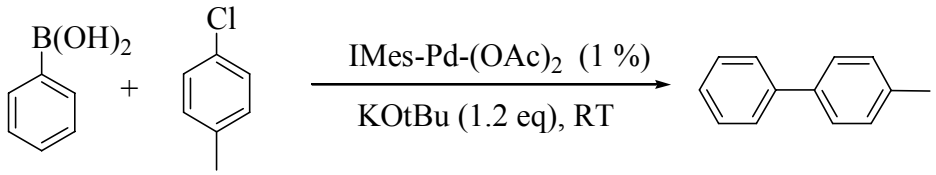
General Procedure for Screening of Solvents in Suzuki-Miyaura Reaction:

In a dry-box, KO^{t}Bu (1.2 mmol, 135 mg) was loaded in a screw-cap vial charged with (IMes)Pd(OAc)$_2$ (0.01 mmol, 5.3 mg). Phenyl boronic acid (1.1 mmol, 133 mg) was added and the vial sealed with a rubber septum. Outside the dry-box, technical grade solvent (2 mL) was injected in the vial with a syringe and the mixture allowed to shake on a Lab-Line Orbit Shaker [set at 25 °C (J-Kem Scientific, Kem-Lab Controller)] for catalyst activation. After 15 minutes, 4-chlorotoluene (1 mmol, 118 μl) was added to the vial with a syringe and the reaction mixture was allowed to shake for the indicated time. The reactions were monitored by gas chromatography

Discussion:

Various alcohols were screened as solvents in the Suzuki-Miyaura cross-coupling reaction. The best result was obtained with isopropyl alcohol as solvent (Entry 1, Table 2.4). Both methyl alcohol and ethyl alcohol did not perform well, giving poor yields (Entries 2 and 3, Table 2.4). *n*-Butanol, *tert*-butanol and *tert*-amyl alcohol did not show formation of the coupling products (Entries 4, 6 and 7, Table 2.4). 2-Butanol, which is similar in structure to isopropanol, performed well giving 91 % conversion in 3 hours (Entry 5, Table 2.4).

Table 2.4. Solvent Screening[a]



entry	solvent	time (h)	yield (%)[b]
1	Isopropanol	1	97
2	Methanol	2	35
3	Ethanol	6	21
4	Butanol	-	NR
5	2-Butanol	3	91
6	*tert*-Butanol	-	NR
7	*tert*-Amyl Alcohol	-	NR

[a]Reaction conditions: 1 mol% of $(IMes)Pd(OAc)_2$, 1 mmol of chlorotoluene, 1.1 mmol of phenylboronic acid, 1.2 mmol of KOtBu, 2 mL of solvent. [b]GC yields, average of two runs.

2.5.5. Base Screening

General Procedure for Screening of Bases in Suzuki-Miyaura Reaction:

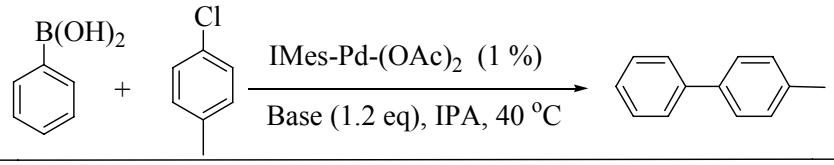
In a dry-box, base (1.2 mmol) was loaded in a screw-cap vial charged with $(IMes)Pd(OAc)_2$ (0.01 mmol, 5.3 mg). Phenyl boronic acid (1.1 mmol, 133 mg) was added and the vial sealed with a rubber septum. Outside the dry-box, technical grade isopropanol (2 mL) was injected in the vial with a syringe and the mixture allowed to shake on a Lab-Line Orbit

Shaker [set at 25 °C or 40 °C (J-Kem Scientific, Kem-Lab Controller)] for catalyst activation. After 15 minutes, 4-chlorotoluene (1 mmol, 118 μl) was added to the vial with a syringe and the reaction mixture was allowed to shake for the indicated time. The reactions were monitored by gas chromatography.

Discussion:

To expand the scope of the reaction and analyze its limitations various bases were screened for activity in coupling of 4-chlorotoluene and phenyl boronic acid. Alkoxide bases (^{t}butoxide, ^{t}amylate, methoxide and ethoxide) performed exceedingly well in the reaction (Entries 2-8, Table 2.5). The best result was obtained with KO*t*Bu, giving quantitative conversion within 1 hour. KOH and KH also performed well in the reaction (Entries 9 and 11, Table 2.5). Weaker bases (phosphates and carbonates) showed moderate conversions (Entries 16 and 18, Table 2.5) or no reaction (Entries 20 and 22, Table 2.5) at room temperature. However on increasing the temperature to 40 °C, K_3PO_4 and Cs_2CO_3 proceeded to provide good yields. K_2CO_3 and Na_2CO_3 continued to be minimally active even at higher temperatures.

Table 2.5. Base Screening



entry	base	temp (°C)	time (h)	yield (%)[b]
1	-	RT	-	NR
2	KO^{t}Bu	RT	1	97
3	NaO^{t}Bu	RT	3	94
4	KO^{t}Am	RT	1	86
5	KOMe	RT	1	73
6	NaOMe	RT	3	40
7	NaOMe	40	3	70
8	NaOEt	RT	4	60
9	KOH	RT	2	81
10	NaOH	RT	12	12
11	KH	RT	1	95
12	NaH	RT	3	46
13	$NaPF_6$	40	-	NR
14	KOAc	RT	-	NR
15	KOAc	40	-	NR
16	K_3PO_4	RT	3	43
17	K_3PO_4	40	22	85
18	Cs_2CO_3	RT	12	47
19	Cs_2CO_3	40	21	92
20	K_2CO_3	RT	-	NR
21	K_2CO_3	40	22	48
22	Na_2CO_3	RT	-	NR
23	Na_2CO_3	40	-	NR

[a]Reaction conditions: 1 mol% of IMes-Pd-$(OAc)_2$, 1 mmol of chlorotoluene, 1.1 mmol of phenylboronic acid, 1.2 mmol of base, 2 mL of IPA. [b]GC yield, average of two runs.

2.5.6. General Procedure for Screening of Activated C(sp^3)-chlorides in Suzuki-Miyaura Reaction:

In a dry-box, KO^{t}Bu (1.2 mmol) was loaded in a screw-cap vial charged with (IMes)Pd(OAc)$_2$ (0.01 mmol, 5.3 mg). Phenyl boronic acid (1.1 mmol, 133 mg) was added and the vial sealed with a rubber septum. Outside the dry-box, technical grade isopropanol (2 mL) was injected in the vial with a syringe and the mixture allowed to shake on a Lab-Line Orbit Shaker [set at 25 °C (J-Kem Scientific, Kem-Lab Controller)] for catalyst activation. After 15 minutes, the halide (1 mmol) was added in the vial with a syringe and the reaction mixture was allowed to shake for the indicated time. The reactions were monitored by gas chromatography. After maximum conversion, the solids were filtered and washed with copious amounts of acetone and hexanes. Solvent was evaporated *in vacuo* and the concentrated reaction mixture purified by flash chromatography (hexanes or 10% ethyl acetate in hexanes). Identity of the products was confirmed by comparison with literature spectroscopic data.

Isolated Products:

Allyl benzene[24] (Table 2.1, Entry 1) The procedure afforded 85 mg (72 %) of the title compound.

Allyl benzene[24] (Table 2.1, Entry 2): The procedure afforded 110 mg (93 %) of the title compound.

But-2-enyl-benzene[25] (Table 2.1, Entry 3): The procedure afforded 97 mg (74 %) of the title compound.

(3-Phenylprop-1-enyl)benzene[26] (Table 2.1, Entry 5): The procedure afforded 140 mg (72 %) of the title compound.

Diphenylmethane[27] (Table 2.1, Entry 6): The procedure afforded 144 mg (86 %) of the title compound.

Diphenylmethane[27] (Table 2.1, Entry 7): The procedure afforded 98 mg (58 %) of the title compound.

2.5.7. General Procedure for Screening of Various Substrates in Suzuki-Miyaura Reaction

In a dry-box, KO^{t}Bu (1.2 mmol) was loaded in a screw-cap vial charged with (IMes)Pd(OAc)$_2$ (0.01 mmol, 5.3 mg). Boronic acid (1.1 mmol) was added and the vial sealed with a rubber septum. Outside the dry-box, technical grade isopropanol (2 mL) was injected in the vial with a syringe and the mixture allowed to shake on a Lab-Line Orbit Shaker [set at 25 °C or 40 °C (J-Kem Scientific, Kem-Lab Controller)] for catalyst activation. After 15 minutes, the halide (1 mmol) was added in the vial with a syringe and the reaction mixture was allowed to shake for the indicated time. The reactions were monitored by gas chromatography. After

maximum conversion, the solids were filtered and washed with copious amounts of acetone and hexanes. Solvent was evaporated *in vacuo* and the concentrated reaction mixture purified by flash chromatography (hexanes or 10% ethyl acetate in hexanes). Identity of the products was confirmed by comparison with literature spectroscopic data.

Note: Schlenk techniques were employed for reaction of phenylboronic acid and 4-chlorobenzaldehyde (Table 2.2, Entry 10).

Isolated Products:

4-Methylbiphenyl[24] (Table 2.2, Entry 1): The procedure afforded 158 mg (94 %) of the title compound.

4-Methyl-2'-phenylbiphenyl[28] (Table 2.2, Entry 2): The procedure afforded 230 mg (94 %) of the title compound.

1-(4-Methylphenyl)naphthalene[29] (Table 2.2, Entry 3): The procedure afforded 199 mg (91 %) of the title compound.

2-Phenylpyridine[30] (Table 2.2, Entry 4): The procedure afforded 94 mg (61 %) of the title compound.

3-Phenylpyridine[31] (Table 2.2, Entry 5): The procedure afforded 114 mg (74 %) of the title compound.

4-Methoxybiphenyl[24] (Table 2.2, Entry 6): The procedure afforded 149 mg (81 %) of the title compound.

3-Methoxybiphenyl[32] (Table 2.2, Entry 7): The procedure afforded 125 mg (68 %) of the title compound.

2-Methoxybiphenyl[24] (Table 2.2, Entry 8): The procedure afforded 156 mg (85 %) of the title compound.

1-(4-Biphenylyl)ethanone[33] (Table 2.2, Entry 9): The procedure afforded 172 mg (88 %) of the title compound.

4-Formylbiphenyl[34] (Table 2.2, Entry 10): The procedure afforded 114 mg (63 %) of the title compound.

2.5.8. General Procedure for Synthesis of Di-ortho and Tri-ortho Substituted Biphenyls

Method A:

In a dry-box, KO^{t}Bu (1.2 mmol) was loaded in a screw-cap vial charged with (IMes)Pd(OAc)$_2$ (0.01 mmol, 5.3 mg). Boronic acid (1.1 mmol) was added and the vial sealed with a rubber septum. Outside the dry-box, technical grade isopropanol (2 mL) was injected in the vial with a syringe and the mixture allowed to shake on a Lab-Line Orbit Shaker [set at 25 °C (J-Kem

Scientific, Kem-Lab Controller)] for catalyst activation. After 15 minutes, the halide (1 mmol) was added in the vial with a syringe and the reaction mixture was allowed to shake for the indicated time. The reactions were monitored by gas chromatography. After maximum conversion, the solids were filtered and washed with copious amounts of acetone and hexanes. Solvent was evaporated *in vacuo* and the concentrated reaction mixture purified by flash chromatography (hexanes or 10% ethyl acetate in hexanes). Identity of the products was confirmed by comparison with literature spectroscopic data.

Method B:

In a dry-box, KO^{t}Bu (1.2 mmol) was loaded in a screw-cap vial charged with (IPr)Pd(OAc)$_2$ (0.01 mmol, 6.1 mg). Boronic acid (1.1 mmol) was added and the vial sealed with a rubber septum. Outside the dry-box, technical grade isopropanol (2 mL) was injected in the vial with a syringe and the mixture allowed to shake on a Lab-Line Orbit Shaker [set at 40 °C (J-Kem Scientific, Kem-Lab Controller)] for catalyst activation. After 15 minutes, the halide substrate (1 mmol) was added in the vial with a syringe and the reaction mixture was allowed to shake at 40 °C for the indicated time. The reactions were monitored by gas chromatography. After maximum conversion, the solids were filtered and washed with copious amounts of acetone and hexanes. Solvent was evaporated *in vacuo* and the concentrated reaction mixture purified by flash chromatography (hexanes or 10% ethyl acetate in hexanes). Identity of the products was confirmed by comparison with literature spectroscopic data.

Isolated Products:

4-Methyl-2',6'-dimethylbiphenyl[35] (Table 2.3, Entry 1): The procedure afforded 145 mg (75 %) of the title compound.

4-Methyl-2',6'-Dimethoxybiphenyl[36] (Table 2.3, Entry 2): The procedure afforded 185 mg (81 %) of the title compound.

4-Methyl-2',4',6',-trimethylbiphenyl[37] (Table 2.3, Entry 3): The procedure afforded 152 mg (72 %) of the title compound.

1-(2-Methylphenyl)naphthalene[38] (Table 2.3, Entry 4): The procedure afforded 194 mg (89 %) of the title compound.

1-(2,6-Dimethylphenyl)naphthalene[39] (Table 2.3, Entry 6): The procedure afforded 211 mg (91 %) of the title compound.

2-Methyl-2',6'-dimethylbiphenyl[40] (Table 2.3, Entry 7): The procedure afforded 173 mg (88 %) of the title compound.

2.6. Acknowledgements

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2.7. References and Notes

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15. For screening of solvents (Table 2.4) see the Experimental Section.

16. For detailed table of base screening (Table 2.5) and discussion see Experimental Section.

17. The stronger C-Cl bond as compared to C-Br and C-I in alkyl halides makes the alkyl chlorides more resistant to oxidative addition. Initially, only the use of vinyl or aromatic substrates allowed for the use of chlorides in this reaction: (The bond-dissociation energy values: CH_3–Cl = 227 kcal/mol, CH_3–Br = 219 kcal/mol, CH_3–I = 212 kcal/mol, CH_2=CH–Cl = 207 kcal/mol, Ph–Cl = 219 kcal/mol). Morrison, R. T.; Boyd, R. N. *Organic Chemistry*, 6th ed.; Prentice Hall, New York, 1996, p-22.

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CHAPTER 3

AN EFFICIENT AND MILD PROTOCOL FOR THE α-ARYLATION OF KETONES MEDIATED BY AN (IMIDAZOL-2-YLIDENE)PALLADIUM(ACETATE) SYSTEM*

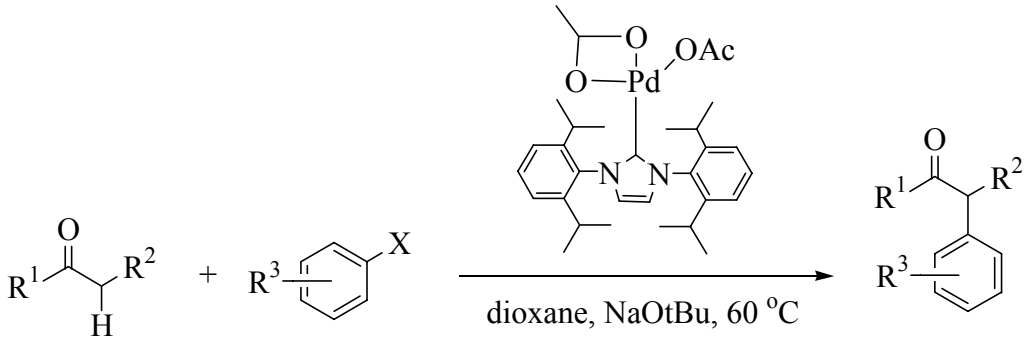
3.1. Introduction

Transition metal catalyzed cross-coupling reactions are a popular means of adding a variety of carbon nucleophiles to aryl halides.[1] Development of efficient and selective catalytic reactions for C-C bond formation has been a subject of paramount interest in organic and organometallic chemistry. Catalytic conversion of C-H bond to a C-C bond is an important subgrouping of such transformations. During the past years, numerous reactions involving C-H bond transformations have been developed.[2] Among these, palladium-catalyzed conversion of C-H bonds to form C-C bonds via coupling of aryl halides or pseudo aryl halides with carbon nucleophiles is one of the most widely employed transition metal catalyzed reaction.[3] Finding an efficient and reliable catalytic method to form a bond between an arene and carbon α to a carbonyl group is a challenging problem.[4] The use of aryl halides for direct arylation of ketones at the carbon α to the carbonyl group has proven to be a transformation of great utility in pharmaceutical, agrochemical and organic synthesis.[5] It has also found an increasing interest in the synthesis of fine chemicals.[6]

The increased acidity of a proton on a carbon α to a carbonyl group helps in its abstraction and generation of an enolate. The simplicity in methodology offered by *in situ* generation of an enolate via deprotonation is an added advantage of this approach. Initially, the metal mediated coupling of enolates was achieved by use of stoichiometric amounts of metal complexes.[7] Moreover some of the procedures involved use of less readily available carbonyl alternatives.[8] However, in concurrent work, Buchwald[9], Hartwig[10] and Miura[11] reported the first examples of direct, catalytic, α-arylations of ketones in 1997. Since then, a myriad of reports from these and other groups have helped establish the catalytic α-arylation of ketones as an indispensable synthetic tool.[12-15]

Since the discovery of stable *N*-heterocyclic carbenes (NHCs), a number of groups have utilized them in catalysis.[16] In the past several years, a number of NHC-metal complexes serving as efficient catalysts for a number of reactions have been reported.[17] Such examples include the palladium-catalyzed α-arylation of ketones.[18] More recently, we and others[19] have reported on the synthesis and unambiguous characterization of (imidazol-2-ylidene)palladium acetate complexes. The complexes were tested for activity in the hydroarylation of alkynes[20] and in the Suzuki-Miyaura cross-coupling reaction.[17a] Encouraged by the very attractive reactivity profile in these transformations mediated by (NHC)$Pd(OAc)_2$ complexes, the results of catalytic study dealing with α-arylation of ketones with various chlorides as coupling partners are reported here (Scheme 3.1).

Scheme 3.1 (NHC)Pd(OAc)$_2$ Catalyzed α-Arylation of Ketones



The model reaction involving propiophenone with 4-chlorotoluene revealed the complex (IPr)Pd(OAc)$_2$ [IPr = N,N'-(2,6-diisopropyl phenyl) imidazol-2-ylidene] to be an active mediator, furnishing quantitative yield of product in 3 hours at 60^{o}C. This catalytic transformation is very appealing, especially since the catalyst is very easy to synthesize.[21] With an aim to prove this protocol practical and amenable to wider laboratory and industrial applications we wish to provide a detailed report of our studies regarding the optimization, scope and applicability of α-arylation of ketones.

3.2. Results and Discussion

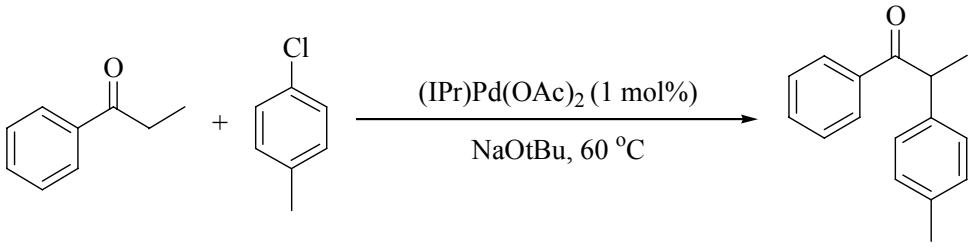
For the initial optimization studies we chose to focus on reactions of propiophenone, since it provides only one site for a possible deprotonation by the base and avoids potential complications arising from multi-arylations. For halide coupling partner, we primarily made use of chlorides. This decision was motivated in part by our realization that so far very few reports

have been published which employ chlorides.[15c,12c,13e] Although aryl chlorides have lower costs and are available in broader diversity as compared to bromides and iodides, as a general trend they tend to be less active towards oxidative addition in metal mediated couplings.[22] We therefore initiated an investigation of the utility of chlorides in α-arylation of ketones.[18] For optimization studies, 4-chlorotoluene was chosen as the halide coupling partner. Initially, an analysis of various solvents as reaction media was carried out (Table 3.1).

3.2.1. Solvent Screening

As a generic reaction, 4-chlorotoluene was reacted with propiophenone in the presence of 1 mol% of (IPr)Pd(OAc)$_2$ and 1.5 equivalents of base (sodium *tert*-butoxide) at 60^{o}C. Among various solvents tested for activity, isopropyl alcohol and *N, N*-dimethylacetamide failed to furnish appreciable quantities of product. However, excellent yields were obtained with other solvents and 1,4-dioxane was found to provide quantitative conversion in minimum time, making it most suitable for our protocol.[23]

Table 3.1. Solvent Screening



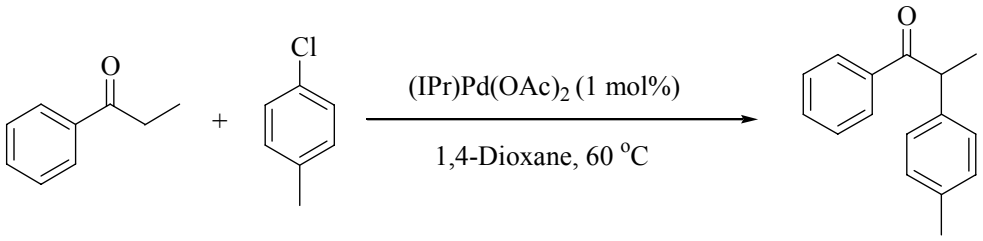
entry	solvent	time (h)	yield (%)[b]
1	Toluene	1	77
2	DME	2	85
3	Dioxane	1	87
4	THF	1	84
5	Isopropanol	-	NR
6	MTBE	1	82
7	DMAc	-	NR

[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of propiophenone, 1 mmol of 4-chlorotoluene, 1.5 eq of NaOtBu, 1.5 mL of solvent, 60 °C. [b]GC yields, average of two runs.

3.2.2. Base Screening

With the dual influence of base in consideration (generation of active catalytic Pd species and deprotonation of ketone to generate enolate), various commercially available standard alkali metal bases were investigated in the model reaction (Table 3.2). Among the productive bases, NaO*t*Bu was found to be the most affordable and convenient.

Table 3.2. Base Screening



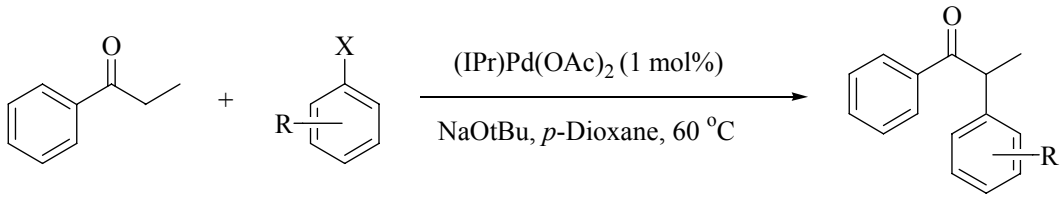
entry	base	time (h)	yield (%)[b]
1	NaO^tBu	3	96
2	KO^tBu	4	85
3	NaH	2	85
4	KH	12	78
5	Cs_2CO_3	3	10
6	KOMe	5	60
7	K_3PO_4	3	27

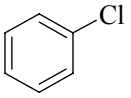
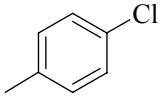
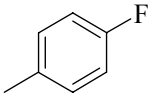
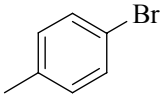
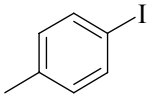
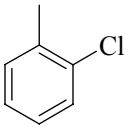
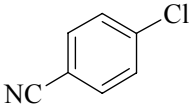
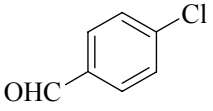
[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of propiophenone, 1 mmol of 4-chlorotoluene, 1.5 eq of base, 1.5 mL of 1,4-dioxane, 60 °C. [b]GC yields, average of two runs.

3.2.3. Reactions of various halides with propiophenone

With optimum conditions in hand, a survey of reactions between propiophenone and various aryl halides under catalytic conditions was performed. The details are provided in Table 3.3.

Table 3.3. α-Arylation of Various Halides with Propiophenone[a]



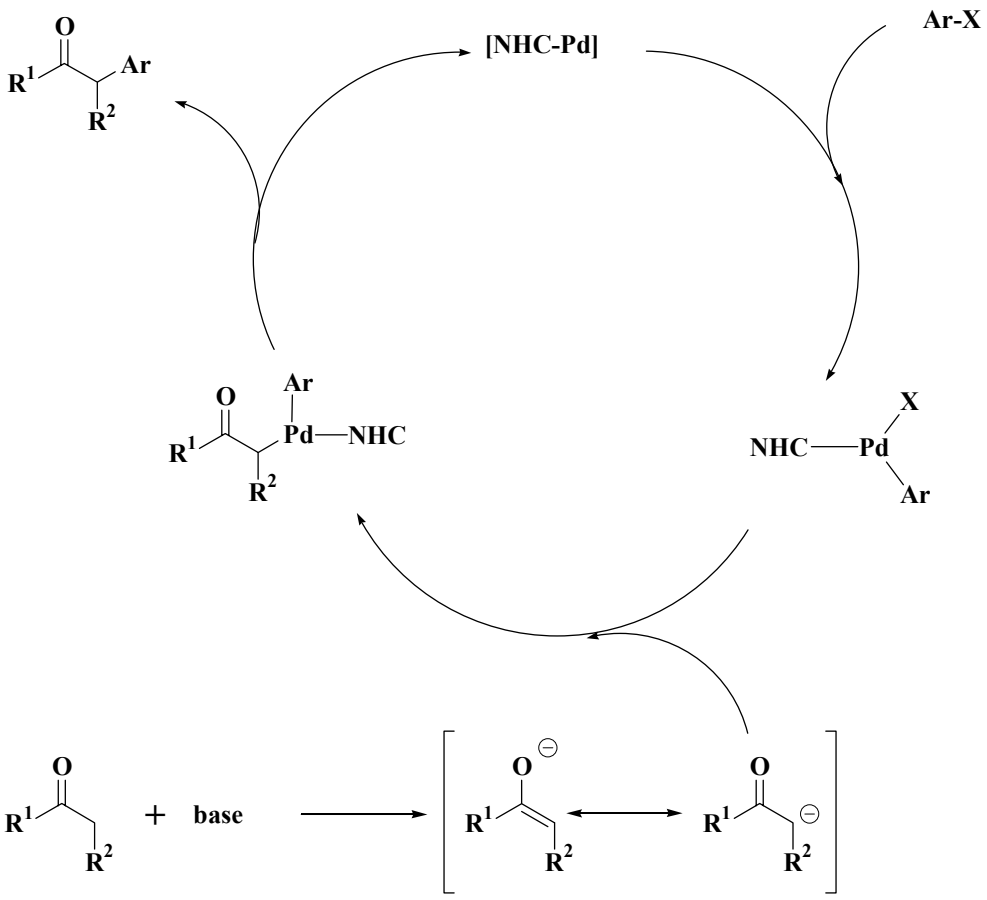
entry	aryl halide	time (h)	yield (%)[b]
1		6	80 (71)
2		3	96 (92)
3		-	NR
4		1	92 (88)
5		1	96 (83)
6		2	96 (90)
7		-	NR
8		-	NR

[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of propiophenone, 1 mmol of aryl halide, 1.5 eq of NaOtBu, 1.5 mL of 1,4-dioxane, 60 °C. [b]GC yields (isolated yields in parentheses), average of two runs.

Reactions of *para*-bromo- and *para*-iodotoluene proceeded to furnish quantitative yields within 1 hour (Table 3.3, entries 4 and 5). More difficult substrates, chlorobenzene and *para*-chlorotoluene also performed well giving good yields (Table 3.3, entries 1 and 2). A stronger C-F bond in aryl-fluorides prevents its oxidative addition to the palladium center. Therefore, the

reaction of *para*-fluorotoluene with propiophenone under the standard conditions failed to furnish the product in appreciable quantity (Table 3.3, entry 3).

Scheme 3.2. Proposed Catalytic Cycle for α-Arylation of Ketones in (NHC)Pd(OAc)$_2$ System



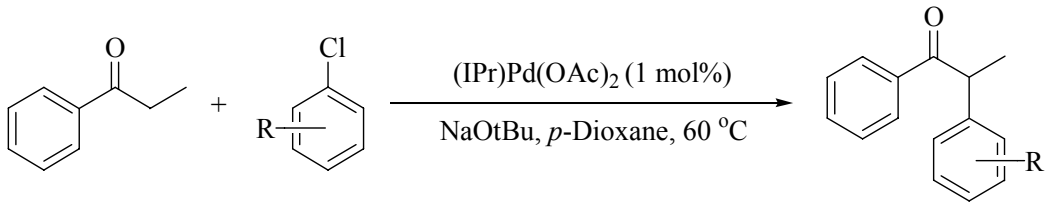
Reaction of *ortho*-chlorotoluene proceeded to give complete conversion in less time than *para*-chlorotoluene (Table 3.3, entry 6), indicating a favorable effect of presence of steric bulk around the reaction center. The increase in steric bulk around the palladium center in the catalytic cycle (Scheme 3.2) can help the reaction by expediting the reductive elimination.[24] Increase in steric bulk around the metal center increases the energy of the stable, higher co-

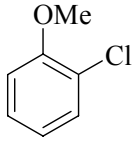
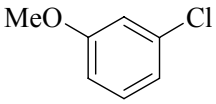
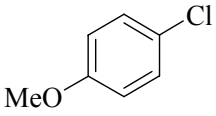
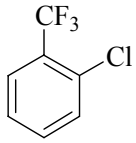
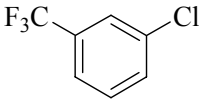
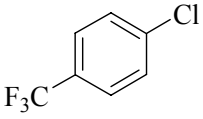
ordinate species prompting it to undergo reductive elimination.[25, 13a] Moreover, the presence of sterically hindering moiety in the final product can act as a deterrent for multi-arylations.

3.2.4. Study of ortho-, meta- or para- substitution on aryl chlorides with both electron-donating and electron-withdrawing groups

To obtain some insight into the substrate scope of this reaction, we investigated effect of electron-donating and electron-withdrawing groups at various positions on the aryl chlorides. Hence, reactions of *ortho*-, *meta*- and *para*- substituted chloroanisoles and chloro(trifluoromethyl)phenyls were performed under the standard reaction conditions. The substrates with electron donating methoxy substituent performed exceedingly well, furnishing excellent yields in short times (Table 3.4, entries 1, 2 and 3). However, reactions involving the electron-withdrawing trifluoromethyl substituted chlorophenyls failed to perform well. While *ortho*- and *para*-chloro(trifluoromethyl)phenyls furnished moderate yields in longer time periods (Table 3.4, entries 4 and 6), the *meta*-substituted, 3-chloro(trifluoromethyl)phenyl failed to undergo coupling (Table 3.4, entry 5). These results represent an interesting trend, since it is known that usually electron-rich aryl halides are difficult to activate towards oxidative addition with palladium.[25]

Table 3.4. Substituent Effect on Aryl Chlorides in α-Arylation with Propiophenone



entry	aryl halide	time (h)	yield (%)[b]
1		1	98 (94)
2		1	91 (81)
3		3	96 (90)
4		12	75 (71)
5		-	NR
6		12	71 (69)

[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of propiophenone, 1 mmol of aryl halide, 1.5 eq of NaO^tBu, 1.5 mL of 1,4-dioxane, 60 °C. [b]GC yields (isolated yields in parentheses), average of two runs.

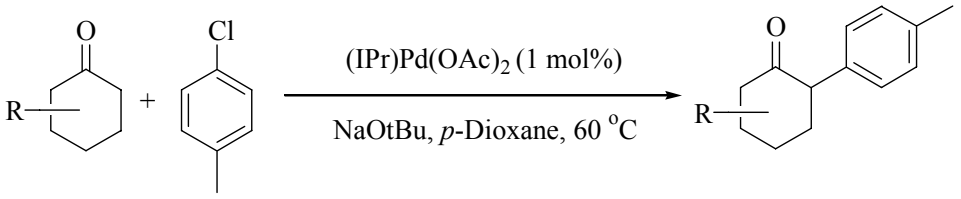
Conceivably, the oxidative addition does not affect the overall rate of the reaction and is not the rate determining step. Although in most cross-coupling reactions of haloarenes, the reaction rates are usually believed to be controlled by the rate of oxidative addition[22b] and usually the transmetalation and reductive elimination are more rapid[26], non-involvement of

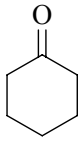
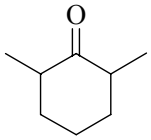
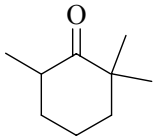
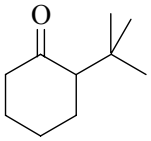
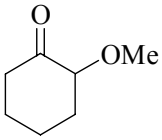
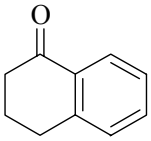
oxidative addition in determining the rate of a reaction is not unprecedented.[27] Since the presence of electron withdrawing groups around the metal center should activate it towards transmetalation with an enolate, it is possible that the presence of electron withdrawing group (especially at *meta*- position) deactivates the substrates towards reductive elimination.

3.2.5. Study of effect of introduction of steric bulk on position α to carbonyl group in substituted cyclohexyl ketones

Given the fact that sterics play an important role in the α-arylation of ketones, an investigation of effect of bulk around the ketone, on generation of enolate was carried out. To this effect, a limited study with various substituted cyclohexyl ketones was performed (Table 3.5). Unsubstituted, cyclohexyl ketone performed well under the standard conditions, furnishing good yield in 2 hours. However, poor conversion due to presence of methyl groups around the carbonyl carbons in 2,6-dimethylcyclohexanone and 2,2,6-trimethylcyclohexanone was observed. This is indicative of sensitivity of generation of enolate in the reaction towards presence of sterically hindering groups around the carbonyl group. Furthermore, 2-*tert*-butylcyclohexanone yielded a poor conversion while aryl fused cyclohexanone derivative (α-tetralone) fared better giving good conversion in 6 hours. It is worth mentioning that both these substrates have an unsubstituted carbon α- to the carbonyl group. However, electronics come into play when 2-methoxycyclohexanone is used. In spite of an unsubstituted carbon α to the carbonyl group, the electron donating nature of the methoxy group attenuates acidity of the ketone, deactivating it towards deprotonation.

Table 3.5. Effect of Steric Bulk in Generation of Enolates in Cyclohexyl Ketone Derivatives[a]



entry	ketone	time (h)	yield (%)[b]
1		2	73 (67)
2		-	NR
3		-	NR
4		12	20
5		-	NR
6		6	90 (83)

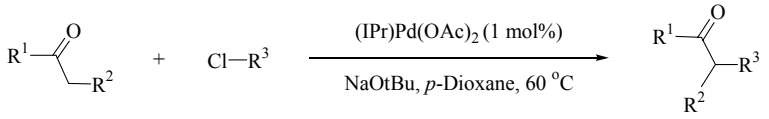
[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of ketone, 1 mmol of 4-chlorotoluene, 1.5 eq of NaOtBu, 1.5 mL of 1,4-dioxane, 60 °C. [b]GC yields (isolated yields in parentheses), average of two runs.

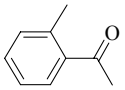
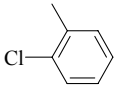
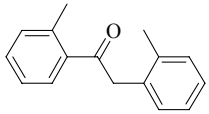
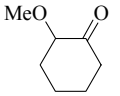
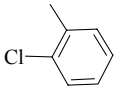
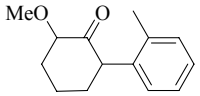
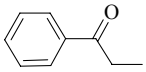
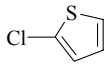
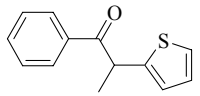
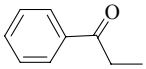
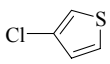
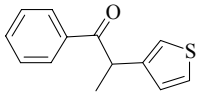
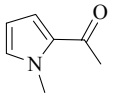
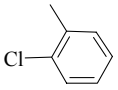
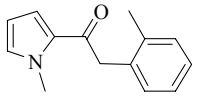
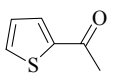
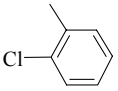
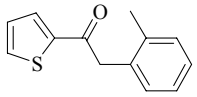
It is worthy of note that reactions involving cyclohexyl ketone derivatives demonstrated excellent regioselectivity. In spite of availability of additional sites for arylation, only trace amounts of diarylations were observed in these reactions.

3.2.6. α-Arylation of various substrates including heterocyclic ketones and chlorides

With an aim on expanding the scope of the reaction and broadening the base of usable substrates, we explored various chlorides in the α-arylation of ketones.

Table 3.6. α-Arylation of Various Substrates Including Heterocyclic Ketones and Chlorides[a]



entry	ketone	aryl halide	product	time (h)	yield (%)[b]
1				24	80 (75)
2				12	17
3				12	42
4				24	36
5				6	46
6				12	13

[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of ketone, 1 mmol of aryl halide, 1.5 eq of NaOtBu, 1.5 mL of 1,4-dioxane, 60 °C. [b]GC yields(isolated yields in parentheses), average of two runs.

Since synthesis of heterocyclic compounds is of significant importance to synthetic and medicinal chemists, we wished to explore the compatibility of heterocyclic substrates with the present protocol. Moderate success was achieved in this venture on coupling 2- and 3-chlorothiophene with propiophenone and 2-acetyl-1-methylpyrrole with 2-chlorotoluene (Table

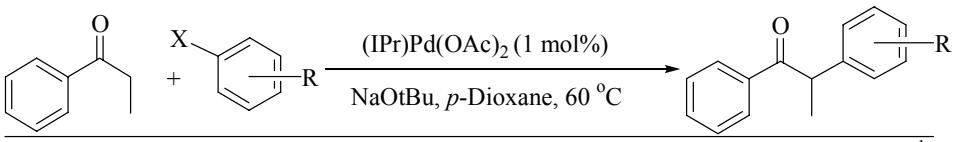
3.6, entries 3, 4 and 5). 2-Acetylthiophene did not furnish a good yield in the reaction with 2-chlorotoluene.

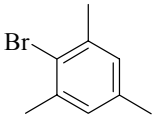
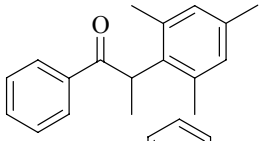
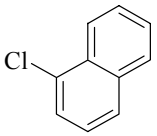
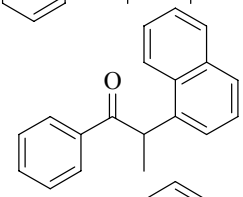
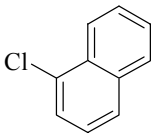
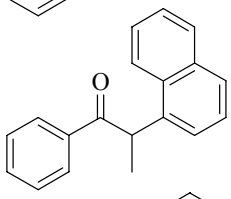
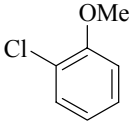
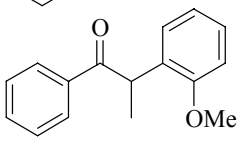
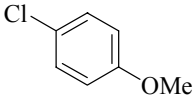
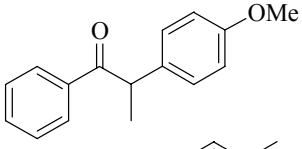
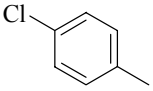
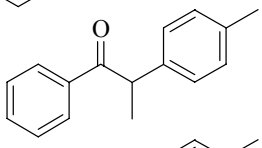
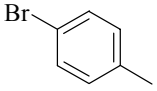
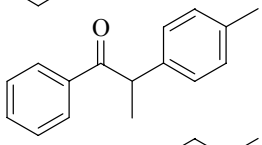
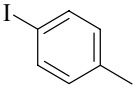
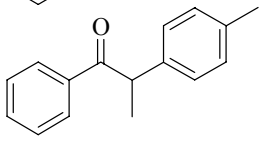
3.2.7. α-Arylation of sterically hindered substrates and optimum reaction temperature

At this stage we were pleased that our objective of effecting couplings of non-activated chlorides in a synthetically oriented protocol could be accomplished. On the other hand, we were not satisfied with the scope of the process and aspired to further expand it. Given our past experience,[17a,17f] we wished to pursue sterically hindered substrates as prospective coupling partners in this reaction. The use of bromomesitylene in arylating the ketone in excellent yield was achieved within a very short time (Table 3.7, entry 1). Unactivated, *ortho*-substituted chlorides performed well under our reaction protocol (Table 3.7, entries 2, 3 and 4). In particular, bulky naphthylchloride gave quantitative yield within 1 hour at 60^{o}C. Furthermore, on testing the performance of catalyst at optimum temperature in this reaction, we were happy to discover formation of arylated product. Only a few examples of α-arylation of ketones, performed at room temperature have been reported so far. However, these elegant reports by Hartwig[13e] and Buchwald[12a] have only utilized more reactive bromides. To the best of our knowledge, no reports of room temperature α-arylation of ketones with chlorides have been reported to date.

To further explore this aspect of our reaction protocol, we carried out reactions of various halides at room temperature. Herein we wish to report the first examples of α-arylation of ketones with chlorides at room temperature. Reactions of propiophenone progress well with 1-chloronaphthalene, 2-chloroanisole and 4-chloroanisole (Table 3.7, entries 3, 4 and 5). Reaction

Table 3.7. α-Arylation of Sterically Hindered Substrates[a]



entry	aryl halide	product	temp(°C)	time (h)	yield (%)[b]
1			60	0.5	92 (83)
2			60	1	100 (93)
3			25	12	80 (75)
4			25	12	78 (71)
5			25	18	73 (67)
6			25	24	41
7			25	12	42
8			25	12	75 (70)

[a]Reaction conditions: 1 mol% of $(IPr)Pd(OAc)_2$, 1.2 mmol of ketone, 1 mmol of 4-chlorotoluene, 1.5 eq of NaOtBu, 1.5 mL of 1,4-dioxane, 60 °C. [b]GC yields (isolated yields in parentheses), average of two runs.

of 4-iodotoluene proceeds cleanly to provide the product in good yield (Table 3.7, entry 8). However, when 4-chlorotoluene and 4-bromotoluene are used, the product is obtained in

moderate yields (Table 3.7, entries 6 and 7). Nevertheless, the activity of (IPr)Pd(OAc)$_2$ at room temperature provides a new dimension to the use of this protocol towards more universal laboratory and industrial applications.

3.3.Conclusions

In summary, we have described a convenient protocol for the α-arylation of ketones utilizing an easy to synthesize (imidazol-2-ylidene)palladium acetate complex as catalyst. The best reaction conditions obtained via optimization studies revealed compatibility with a commercially available, inexpensive and convenient base, as well as solvent making the reaction protocol amenable to large-scale synthesis. A wide array of functionalized halides has been investigated in an effort to better understand the bearings of electronics and sterics on the reaction. Coupling of heterocyclic substrates has also been achieved. In view of the paucity of examples of reactions at lower temperatures using unactivated aryl chlorides (particularly *ortho*-substituted chlorides), we believe these observations are noteworthy. Efforts aimed at developing effective catalyst systems for a broad range of substrates under mild conditions, as well as initiating investigations of mechanistic aspects at play are ongoing.[28]

3.4. Experimental Section

4.4.1. General considerations

- All aryl halides and ketones were used as received (Aldrich, Acros). Bases were stored under argon in an MBraun glovebox.
- All solvents were distilled from appropriate drying agents or were passed through an alumina column in an MBraun solvent purification system.
- The catalyst was prepared according to the reported procedures.[17a,20,29]
- All reactions were carried out under an atmosphere of argon in screw-cap vials.
- ^{1}H- and ^{13}C-NMR spectra were recorded using a Varian-400 or Varian-300 MHz spectrometer at ambient temperature in $CDCl_3$ (Cambridge Isotope Laboratories, Inc.). The solvent for NMR spectroscopy was stored over molecular sieves.
- Flash chromatography was performed on silica gel (230-400 mesh) (Natland International Corporation).

3.4.2. Representative procedure for α-arylation of ketones

In a drybox, 1.5 mmol of base was added to a screw-cap vial charged with 1 mol% of $(IPr)Pd(OAc)_2$ complex. 1.5 mL of solvent was added and the vial sealed with a rubber septum. Outside the drybox, 1.2 mmol of ketone was injected in the vial with a syringe. 1 mmol of aryl

halide was injected last. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate in an oil bath set at 60 ^{o}C for the indicated time. The reactions were monitored by gas chromatography. After reaching maximum conversion, the reaction mixture was allowed to cool to room temperature and it was then quenched with water. The organic layer was extracted with methyl *tert*-butyl ether or diethyl ether and dried over magnesium sulfate. The solvent was then evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel.

3.4.3. Screening of solvents in α-arylation of ketones

In a drybox, NaO^{t}Bu (1.5 mmol, 144 mg) was loaded in a screw-cap vial charged with (IPr)Pd(OAc)$_2$ complex (0.01 mmol, 6.1 mg). 1.5 mL of solvent was added and the vial sealed with a rubber septum. Outside the drybox, propiophenone (1.2 mmol, 160 μl) was injected in the vial with a syringe. Lastly, 4-Chlorotoluene (1 mmol, 118 μl) was injected into the vial. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate in an oil bath set at 60 ^{o}C for the indicated time. The reactions were monitored by gas chromatography.

3.4.4. Screening of bases in α-arylation of ketones

In a drybox, 1.5 mmol of base was loaded in a screw-cap vial charged with (IPr)Pd(OAc)$_2$ complex (0.01 mmol, 6.1 mg). 1.5 mL of dioxane was added and the vial sealed with a rubber septum. Outside the drybox, propiophenone (1.2 mmol, 160 μl) was injected in the vial with a syringe. Lastly, 4-Chlorotoluene (1 mmol, 118 μl) was injected to the vial. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate in an oil bath set at 60 ^{o}C for the indicated time. The reactions were monitored by gas chromatography

3.4.5 α-Arylation of various ketones with aryl halides

In a drybox, NaO^{t}Bu (1.5 mmol, 144 mg) was loaded in a screw-cap vial charged with (IPr)Pd(OAc)$_2$ complex (0.01 mmol, 6.1 mg). 1.5 mL of dioxane was added and the vial sealed with a rubber septum. Outside the drybox, 1.2 mmol of ketone was injected in the vial with a syringe. 1 mmol of aryl halide was injected last. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate (at room temperature or in an oil bath set at 60 ^{o}C) for the indicated time. The reactions were monitored by gas chromatography. After the maximum conversion had been reached, the reaction mixture was allowed to cool to room temperature and quenched with water. The organic layer was extracted with methyl *tert*-butyl ether or diethyl ether and dried over magnesium sulfate. The solvent was then evaporated *in vacuo*. When necessary, the product was

purified by flash chromatography on silica gel. Identity of the products was confirmed by comparison with literature spectroscopic data.

Isolated Products:

1,2-Diphenyl-propan-1-one (Table 3.3, entry 1) The procedure afforded 149 mg (71 %) of the compound.

1-Phenyl-2-*p*-tolyl-propan-1-one (Table 3.3, entry 2) The procedure afforded 206 mg (92 %) of the compound.

1-Phenyl-2-*p*-tolyl-propan-1-one[30] (Table 3.3, entry 4) The procedure afforded 197 mg (88 %) of the compound.

1-Phenyl-2-*p*-tolyl-propan-1-one[30] (Table 3.3, entry 5) The procedure afforded 185 mg (83 %) of the compound.

1-Phenyl-2-*o*-tolyl-propan-1-one[30] (Table 3.3, entry 6) The procedure afforded 202 mg (90 %) of the compound.

2-(2-Methoxy-phenyl)-1-phenyl-propan-1-one[31] (Table 3.4, entry 1) The procedure afforded 225 mg (94 %) of the compound.

2-(3-Methoxy-phenyl)-1-phenyl-propan-1-one[13e] (Table 3.4, entry 2) The procedure afforded 194 mg (81 %) of the compound.

2-(4-Methoxy-phenyl)-1-phenyl-propan-1-one[10] (Table 3.4, entry 3) The procedure afforded 216 mg (90 %) of the compound.

1-Phenyl-2-(2-trifluoromethyl-phenyl)-propan-1-one[32] (Table 3.4, entry 4) The procedure afforded 197 mg (71 %) of the compound.

1-Phenyl-2-(4-trifluoromethyl-phenyl)-propan-1-one[32] (Table 3.4, entry 6) The procedure afforded 192 mg (69 %) of the compound.

2-*p*-Tolyl-cyclohexanone[33] (Table 3.5, entry 1) The procedure afforded 126 mg (67 %) of the compound.

2-*p*-Tolyl-3,4-dihydro-2H-naphthalen-1-one[34] (Table 3.5, entry 6) The procedure afforded 196 mg (83 %) of the compound.

1,2-Di-*o*-tolyl-ethanone[35] (Table 3.6, entry 1) The procedure afforded 168 mg (75 %) of the compound.

1-Phenyl-2-(2,4,6-trimethyl-phenyl)-propan-1-one[36] (Table 3.7, entry 1) The procedure afforded 209 mg (83 %) of the compound.

2-Naphthalen-1-yl-1-phenyl-propan-1-one[37] (Table 3.7, entry 2) The procedure afforded 242 mg (93 %) of the compound.

2-Naphthalen-1-yl-1-phenyl-propan-1-one[37] (Table 3.7, entry 3) The procedure afforded 195 mg (75 %) of the compound.

2-(2-Methoxy-phenyl)-1-phenyl-propan-1-one[31] (Table 3.7, entry 4) The procedure afforded 170 mg (71 %) of the compound.

2-(4-Methoxy-phenyl)-1-phenyl-propan-1-one[10] (Table 3.7, entry 5) The procedure afforded 161 mg (67 %) of the compound.

1-Phenyl-2-*p*-tolyl-propan-1-one[30] (Table 3.7, entry 8) The procedure afforded 156 mg (70 %) of the compound.

3.4 Acknowledgements

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CHAPTER 4

SIMPLE SYNTHESIS OF N-HETEROCYCLIC CARBENE $[(NHC)Pd(Cl)_2]_2$ COMPLEXES AND THEIR USE IN KUMADA-TAMAO-CORRIU CROSS-COUPLING REACTIONS*

4.1. Introduction

The activity of well-defined N-heterocyclic carbene $[(NHC)Pd(Cl)_2]_2$ complexes has been studied in the Kumada-Tamao-Corriu (KTC) coupling of Grignard reagents with various halides. The results show a high activity profile, allowing for the coupling of various halides with low catalyst loadings. The use of hindered and heterocyclic substrates provides an avenue for convenient synthesis for motifs frequently encountered in organic synthetic chemistry. The scalability of the reaction and the optimum conditions for KTC coupling of fluoride substrates are also discussed.

Since their discovery by Grignard, organomagnesium compounds have become an indispensable tool in an organic chemist's arsenal[1]. Transition metal catalyzed cross-coupling of organomagnesium compounds[2] is a useful tool for the synthesis of substituted biaryls, which are important structural building blocks for the synthesis of complex natural product molecules,[3] liquid crystals, polymers and ligands.[4] Fuchs and co-workers laid the groundwork for the use of Grignard reagents in their reactivity studies with vinyl halides.[5] In separate efforts, Kumada and

Corriu reported that the reaction between Grignard reagents with alkenyl or aryl halides could be catalyzed by nickel (II) complexes.[2a,2b]

Palladium-catalyzed coupling reactions between organic electrophiles and organometallic reagents are reliable and versatile tools for the regioselective formation of carbon-carbon bonds involving two sp^2-hybridized carbons.[6] Usually aryl triflates, aryl bromides and aryl chlorides are employed as electrophiles.[7] Use of chlorides is especially attractive because their low cost and availability allow both laboratory scale syntheses and industrial applications.[8] The palladium catalyzed version of the Kumada-Tamao-Corriu (KTC) cross-coupling reaction was first reported by Murahashi in 1975.[9] The report explored reactivity of vinyl halides with Grignard reagents.

However, questionable functional group tolerance of Grignard reagents led to a greater emphasis on a search for less nucleophilic partners for coupling with aryl halides. Consequently, exciting progress was described in the development of coupling chemistry of organotin,[10] organoboron,[11] organosilane[12] and organozinc[13] reagents as related substitutes. Nevertheless, Grignard reagents have found a wide range of applicability in the synthesis of organic functionalities such as aldehydes, ketones, carboxylic acids esters, amides and alcohols and are also deemed amongst the most versatile reagents for formation of C-C bonds.[14] Interestingly, since organoboron compounds are generally prepared from organomagnesium compounds, the use of Grignard reagents in coupling chemistry offers the benefit of reducing the number of steps required to achieve the targeted coupling products.[4,15,16] Less tedious preparation of the relevant product achieved via smaller number of steps is especially relevant for cost-effective industrial applications of the methodology.

A few years ago, we reported on the synthesis of air stable (NHC)Pd(Cl_2)-palladium dimeric species, [(NHC)$PdCl_2$]$_2$.[17] Since then, Sigman has extensively utilized these and similar

species in oxidation reactions.[18] Cognizant of the need for synthetically useful catalysts, we believe that these Pd dimers should be excellent precatalysts for C-C and C-N bond formation. This role has scarcely been exploited for this dimeric architecture.[17,18] As part of a program aimed at the development of palladium catalyzed couplings, we decided to address the challenge of broadening the scope and utility of these species in catalytic coupling chemistry. In this report we describe our progress in that direction by reporting $[(NHC)Pd(Cl)_2]_2$ mediated KTC cross-coupling reactions and the development of this useful methodology.

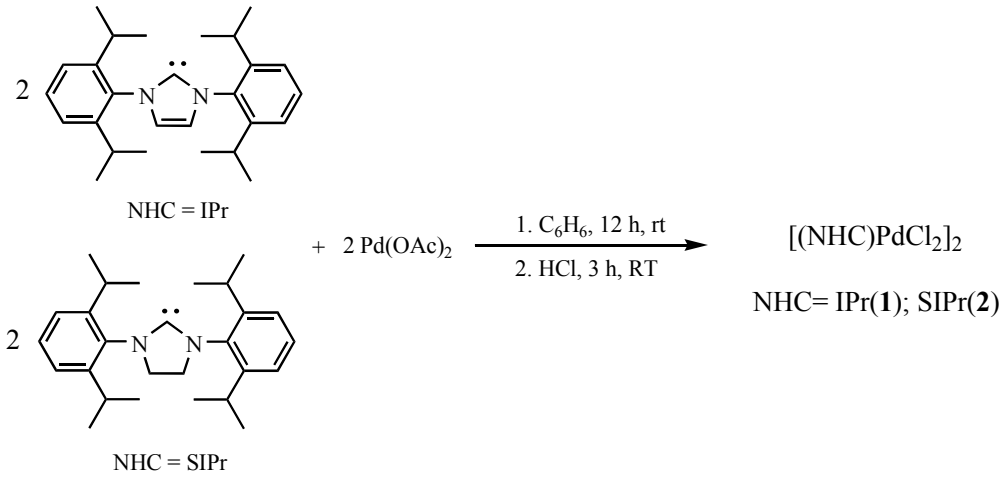
4.2 Results and Discussion

As a first step towards achieving our goal, we explored a more user-friendly and general synthetic route leading to the desired $[(NHC)Pd(Cl)_2]_2$ complexes. The reported methods for synthesis of these reactive species suffer from extreme conditions[18a] or lack of molecule economy.[17] Other methods include utilizing (IPr)Pd(allyl)Cl as the precursor for the synthesis[19] but it effectively increases the number of steps required to synthesize the dimer complex since (IPr)Pd(allyl)Cl itself is synthesized from $PdCl_2$. Hence, a simpler method with fewer steps, utilizing moderate reaction conditions, is highly desirable. To that end, we wish to report our synthetic protocol achieving synthesis of two $[(NHC)PdCl_2]_2$ complexes bearing generally used NHC, in a one pot protocol, utilizing $Pd(OAc)_2$ as the palladium source (Scheme 4.1).

The synthetic procedure involves a simple addition of the NHC to $Pd(OAc)_2$ under argon in a 1:1 ratio. Followed by addition of HCl to yield $[(IPr)PdCl_2]_2$ (**1**) where IPr = 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene and in a similar fashion $[(SIPr)PdCl_2]_2$ (**2**) when SIPr is used [SIPr = 1,3-bis(2,6-diisopropylphenyl)-imidazolin-2-ylidene]. Complex **2** was

unequivocally characterized by X-Ray crystallography.[20] This simple synthetic route affords the products in high yields and can be scaled up without reduction in yields.

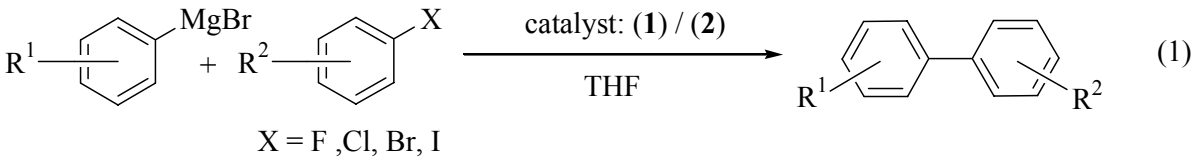
Scheme 4.1. One-pot Synthesis of $[(NHC)PdCl_2]_2$



4.2.1. KTC Cross Coupling Reaction

We have reported remarkable advances in various transformations as part of our studies highlighting the utility of *N*-heterocyclic carbenes as efficient ligands with various metals,[21] especially palladium,[22] copper,[23] nickel,[24] gold[25] and silver.[26] We have extensively explored the use of NHC-ligated metal catalysts in cross-coupling reactions[27-32] including a report making significant advances regarding the Kumada-Tamao-Corriu Cross Coupling Reaction.[33] Interesting work by Ackermann[34] Herrmann,[35] Beller[36] and others[37] has helped KTC coupling reaction take new strides. Some of the major advances reported are employment of fluorides,[35,38] aryl tosylates[39] and alkyl chlorides[36b] as coupling partners. Herein, we wish to report the first examples of KTC cross-coupling reaction in an $[(NHC)PdCl_2]_2$ mediated system (Scheme 4.2).

Scheme 4.2. $[(NHC)Pd(Cl)_2]_2$ Catalyzed Kumada-Tamao-Corriu Cross Coupling Reaction



(1)

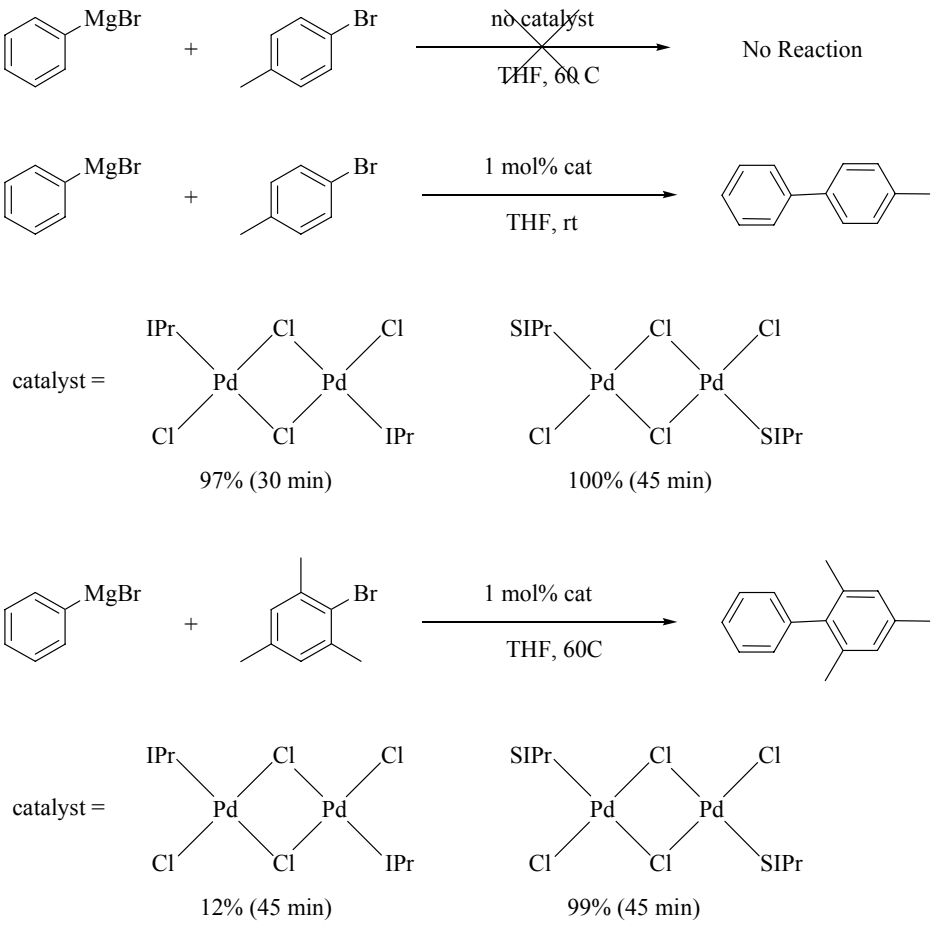
4.2.2. Screening of Catalyst and Optimization of Reaction Conditions

Catalyst Screening:

Our initial efforts to develop the reaction were centered on screening of the catalyst. Initially, a control experiment in absence of the catalyst was performed. Not surprisingly, the reaction did not afford any coupling product. Thereafter, we moved on to utilization of both SIPr and IPr dimer species in mediating the generic reaction of bromotoluene (1 mmol) with 3 mmol phenylmagnesium-bromide in THF (3 mL).[40] Initially the reactions were loaded with 1 mol% catalyst. Both the catalysts were found to be highly active in performing the transformation (Scheme 4.3). The product was received in quantitative yields in very short times.

To analyze the relative activity of both IPr dimer and SIPr dimer, we decided to test them in reaction of a more difficult substrate. Sterically challenging 2-bromo-1,3,5-trimethyl benzene was chosen as a suitable substrate. The reaction warranted elevated temperature because of the difficult nature of the substrate. On performing the reaction it was found that the SIPr analogue worked significantly better (99% in 45 min.) as compared to the IPr analogue (12% in 45 min.). The IPr analogue took exceedingly long reaction time to achieve an isolable reaction yield (67% in 12 hours) thus making SIPr counterpart the catalyst of choice for rest of the investigations

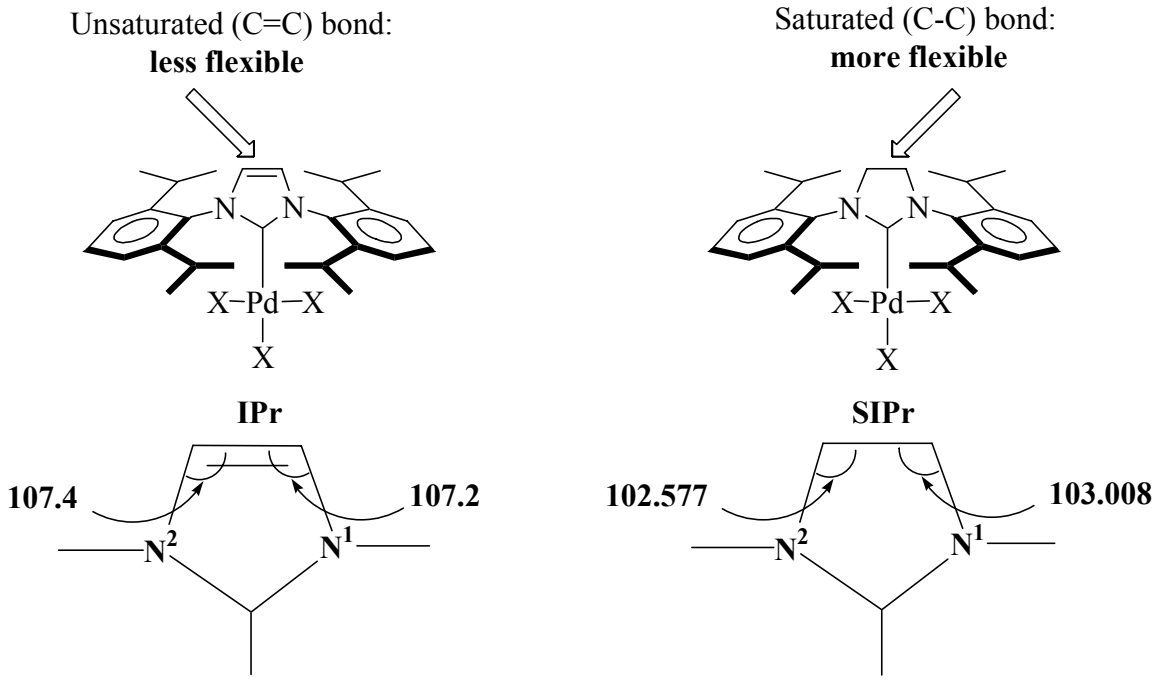
Scheme 4.3. Screening of Catalyst



While the difference in structures of SIPr and IPr seems very nominal, it is implicit that saturated C-C bond backbone provides more flexibility than the unsaturated counterpart IPr.[41] Indeed, on comparing the bond angle values (deg) for C(15)-C(14)-N(1) and C(14)-C(15)-N(2) of the IPr dimer (107.2 and 107.4 respectively)[17] with the SIPr dimer (103.008 and 102.577 respectively) it is evident that there is more deviation in SIPr dimer as compared to the IPr dimer. While the difference in bond angle values for IPr dimer suggest rigidity in the imidazolium structure, the deviation in SIPr dimer bond angle values indicates towards a more flexible

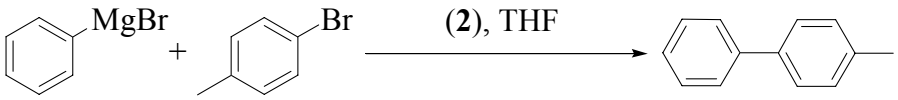
structure. Although the mechanistic implications of the positive effects afforded to a reaction-outcome by flexibility of the NHC backbone are not yet fully understood, the fact that the saturated complex is significantly more active in catalysis is not unprecedented. We and others have observed a similar difference in catalyst-performance between IPr and SIPr in previous studies.[42]

Scheme 4.4. Difference in Flexibility and Structural Profile of IPr and SIPr Complexes[17, 20]



Optimization of Catalyst Loadings:

Table 4.1. Optimization of Catalyst Loading[a]



entry	catalyst loading	temperature (^{o}C)	time (h)	yield (%)[b]
1	1 mol%	25	0.75	100
2	0.5 mol%	25	12	47
3	0.5 mol%	60	0.5	64
4	0.25 mol%	60	6	61
5	0.1 mol%	60	24	45

[a]Reaction conditions: 1 mmol of bromotoluene, 3 mL of THF, 3 mmol of phenylmagnesiumbromide. [b]GC yields (average of two runs).

For metal catalyzed transformations, costs associated with the amount of metal used are a major concern. Moreover the environmental factors also warrant consideration while developing a methodology.[43] Constant efforts are being directed towards addressing such drawbacks.[44] We also focused our efforts towards this conclusion by optimization of reaction conditions. To make the protocol more compatible with large-scale and industrial applications, we set out to explore the optimal catalyst loadings. On observing highly potent activity of the catalyst at 1 mol% concentration, the catalyst loading was subsequently decreased as demonstrated in Table 4.1. Expectedly, the decrease in catalyst loadings leads to loss of some activity and has to be compensated by other factors. A compromise is achieved by subjecting the reactants to higher

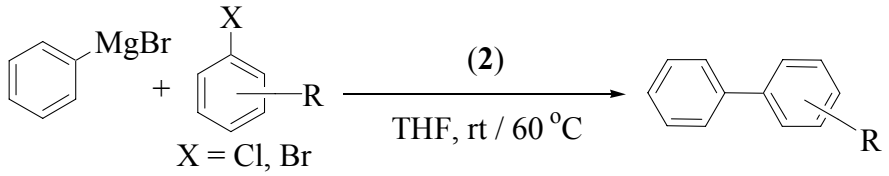
temperature and/or longer reaction times. We found the loading of 0.5 mol% to be optimal for our methodology development purposes. Interestingly, albeit longer reaction time assumes significance, the product is obtained even at catalyst loading as low as 0.1 mol% making it a very attractive protocol for applications in both industrial and academic processes.

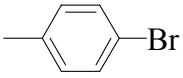
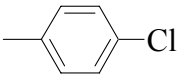
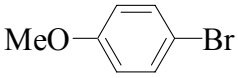
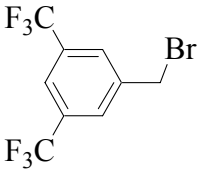
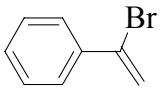
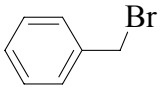
4.2.3. Halide Substrate Screening in Reactions with Phenylmagnesium-bromide in Kumada-Tamao-Corriu Coupling

With optimum catalyst loading and reaction conditions in hand, a survey of reactions of phenylmagnesium-bromide with various aryl halides and C(sp^3)-halides was performed. The details are provided in Table 3. Reactions of *para*-bromotoluene and *para*-chlorotoluene proceeded to furnish the coupling product in excellent yields (Table 4.2, entries 1 and 2). However, the contrast in reaction time required to achieve such yields is considerable amongst the chloro- and bromo- congeners. Stronger C-Cl bond in *para*-chlorotoluene (bond dissociation energy: 219 kcal/mol) as compared to the C-Br bond in *para*-bromotoluene (bond dissociation energy: 210 kcal/mol)[45] translates to the difference in reaction times between the two substrates.

Interestingly, although Grignard reagents are susceptible to homocoupling, in our protocol very minimal homocoupling activity was observed. As illustrated in Table 4.2, 1-bromomethyl-3,5-bis(trifluoromethyl)benzene and (1-bromo-vinyl)-benzene proceed to provide the product in exceedingly good yields within minutes (Table 4.2, entries 4 and 5).

Table 4.2. Halide Substrate Screening in Reactions with Phenylmagnesium-bromide in KTC Coupling[a]



entry	halide	temperature (°C)	time	yield (%)[b]
1		60	30 m	84 (81)
2		60	24 h	95 (91)
3		60	12 h	68 (66)
4		60	5 m	100 (93)
5		25	5 m	100 (94)
6		25	15 m	100 (92)[c]

[a]Reaction conditions: 0.5 mol% of catalyst, 1 mmol of halide, 3 mL of THF, 3 mmol of phenylmagnesiumbromide. [b]GC yields (isolated yields in parentheses) - average of two runs. [c]catalyst loading 1 mol%.

Trifluoromethyl aromatic derivatives are amongst the most important family of fluorinated intermediates which have found extensive use in agrochemical and pharmaceutical industry.[46] However, safety issues related with utilization of trifluoromethylphenyl Grignard

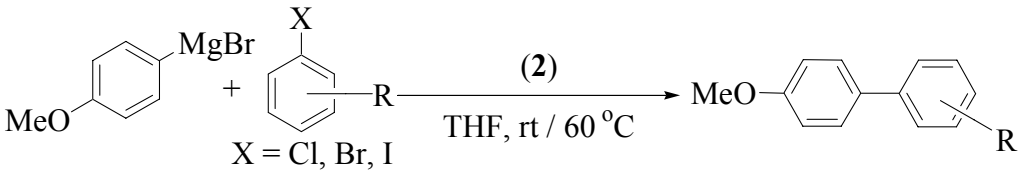
reagents in synthesis of trifluoromethyl aromatic derivatives[47] has led to development of alternate strategies[48] The strategy of using the trifluoromethylphenyl-halide instead of trifluoromethylphenyl-Grignard reagent is an example of a safe alternative route to achieve the synthesis of trifluoromethyl aromatic derivatives. Successful coupling of 1-bromo-vinylbenzene indicates towards the compatibility of the process with olefin functionality and demonstrates the versatility of the protocol (Table 4.2, entry 5). The reaction of $C(sp^3)$ containing benzyl bromide with phenylmagnesium-bromide (Table 4.2, entry 6) under the given conditions showed formation of side products. To push the reaction in favor of the desired product, the concentration of the catalyst was increased to 1 %. The desired product was obtained in quantitative yield in 15 minutes.

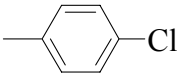
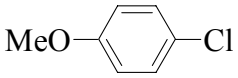
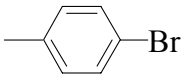
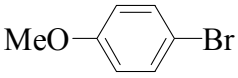
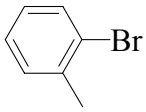
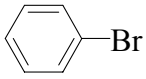
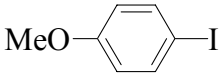
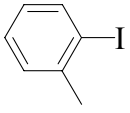
4.2.4. Substrate Screening in KTC Coupling Reaction

Capitalizing on the easily-executable reaction protocol, we decided to study the activity of *para*-methoxy-phenylmagnesium-bromide under the aforementioned reaction conditions. A wide range of halides were employed as coupling partners of the Grignard reagent (Table 4.3). Expectedly, *para*-bromotoluene performed better than *para*-chlorotoluene (Table 4.3, entries 1 and 3). The scope of the reaction was expanded by inclusion of iodide substrates (Table 4.3, entries 7 and 8). As illustrated in table 4.3 (entries 5 and 8), SIPr-dimer mediates the coupling of sterically challenging substrates, *ortho*-bromotoluene and *ortho*-chlorotoluene. The catalyst performed exceedingly well even with room temperature reactions and furnished the products in

quantitative yields in very short reaction times augmenting the support for general applicability of this protocol.

Table 4.3. Substrate Screening in KTC Coupling Reaction[a]



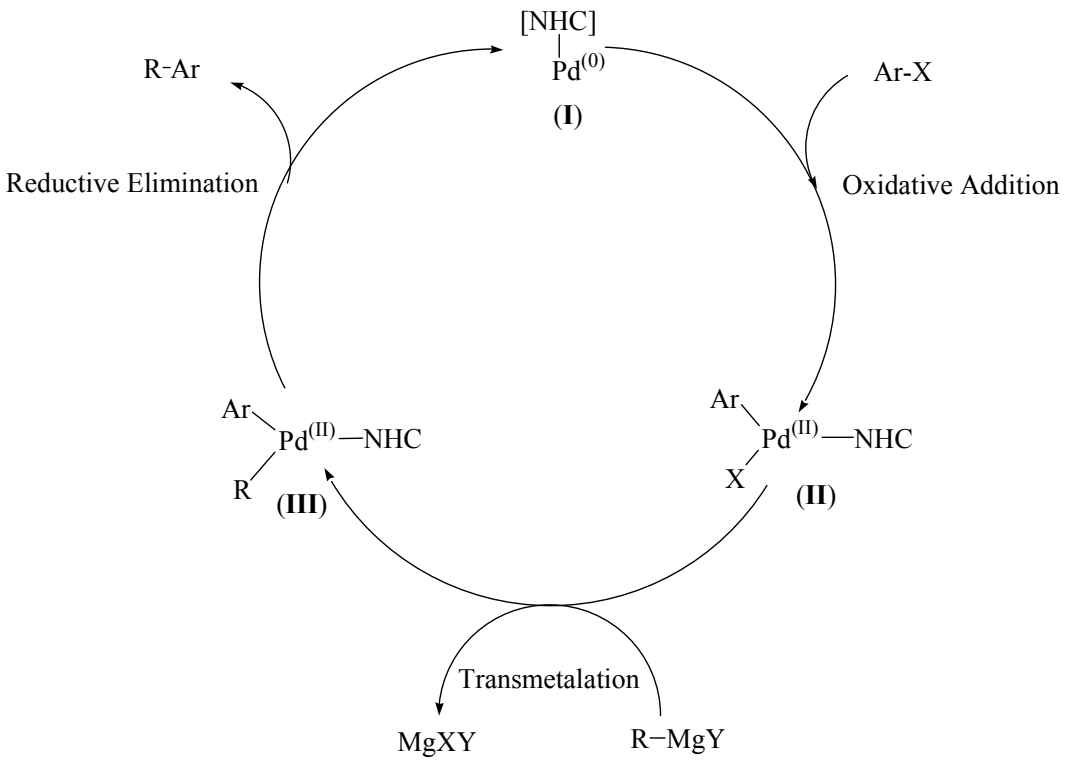
entry	halide	temperature (°C)	time (h)	yield (%)[b]
1		60	24	90 (87)
2		25	0.5	100 (96)
3		60	3	93 (89)
4		60	24	75 (73)
5		60	0.5	100 (89)
6		25	3	98 (94)
7		25	0.5	93 (90)
8		60	0.25	100 (92)

[a]Reaction conditions: 0.5 mol% catalyst, 1 mmol of halide, 3 mL of THF, 3 mmol of 4-methoxy-phenylmagnesium-bromide. [b]GC yields (isolated yields in parentheses) - average of two runs.

4.2.5 Kumada-Tamao-Corriu Coupling of Hindered Substrates

Encouraged by the excellent results obtained with coupling of sterically hindered substrates *ortho*-bromotoluene and *ortho*-chlorotoluene and with a desire to expand the scope of this coupling methodology, we decided to address the challenge of effecting Kumada coupling of hindered substrates by application of (SIPr)Pd$(Cl)_2$-dimer catalyst as mediator for the transformation. While presence of steric hindrances around the reaction center can act as deterrent towards oxidative addition or transmetalation in the catalytic cycle (Scheme 4.5), on the contrary it can facilitate the reductive elimination leading to formation of the desired coupling product.[49] The steric bulk increases energy of the higher coordinated and usually stable species (**III**) thus making it more susceptible to undergoing the elimination.[50,51] A comparison of entries 3 and 5 in table 4.3 suggests that such a positive role is indeed possibly being played by steric bulk. The presence of methyl group around the metal center in *ortho*-bromotoluene facilitates reductive elimination thus furnishing the coupling product in significantly reduced time as compared to the *para*-bromtoluene substrate. Following the elimination, the reduced oxidation state of the metal center exposes it to oxidative addition by attack from another molecule of the halide thus completing the catalytic cycle. Furthermore, the role of the ligand (SIPr) cannot be denied in facilitating the successful couplings of sterically hindered substrates since sterically bulky ligands are known to be of assistance in such demanding transformations.[52]

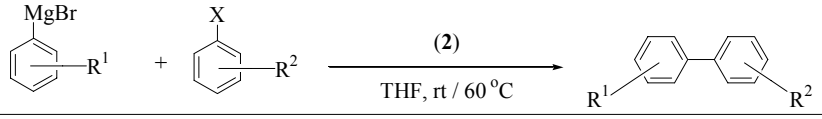
Scheme 4.5. Mechanistic Pathway for Kumada-Tamao-Corriu Coupling

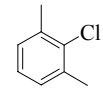
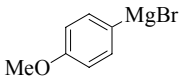
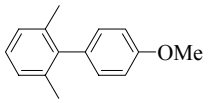
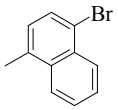
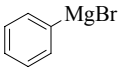
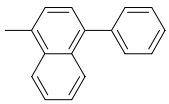
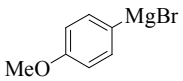
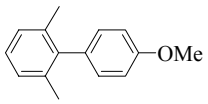
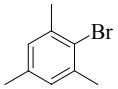
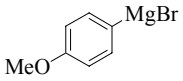
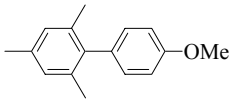
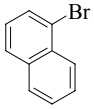
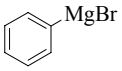
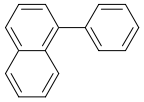
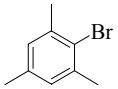
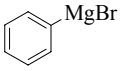
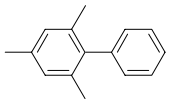
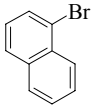
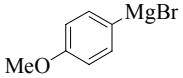
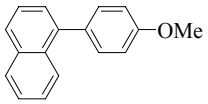
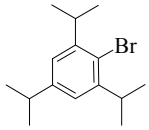
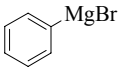


To capitalize on this interesting mechanistic profile, we subjected various sterically hindered substrates to our reaction protocol (Table 4.4). Expectedly, the mono-*ortho* substituted substrates 1-bromo-4-methyl-naphthalene and 1-bromonaphtahlene (Table 4.4, entries 2, 5 and 7) performed better than the di-*ortho* substituted chloro-*m*-xylene, bromo-*m*-xylene and bromomesitylene (Table 4.4, entries 1, 3, 4 and 6).

In all the reactions excellent yields were obtained making the protocol an attractive tool for further applications in synthesis. However, 2-bromo-1,3,5-triisopropylbenzene did not furnish the desired product and a mixture of compounds was obtained. The analysis of reaction mixture confirmed decomposition of the Grignard reagent as the competing processes after prolonged heating of reaction mixture under the given conditions.

Table 4.4. Kumada-Tamao-Corriu Coupling of Hindered Substrates[a]



entry	halide	Grignard	product	temperature (°C)	time (h)	yield (%)[b]
1				60	24	75 (73)
2				25	0.25	100 (96)
3				60	24	90 (84)
4				60	3	93 (89)
5				60	0.25	100 (91)
6				60	3	94 (90)
7				60	0.25	100 (89)
8			-	-	-	NR[c]

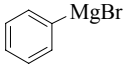
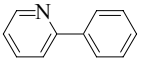
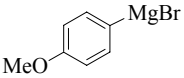
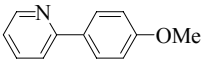
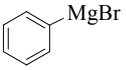
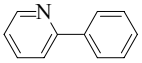
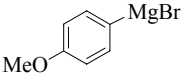
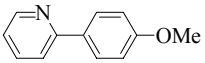
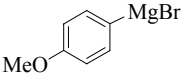
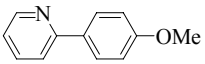
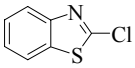
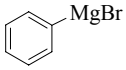
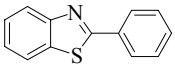
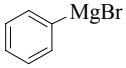
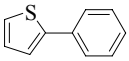
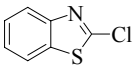
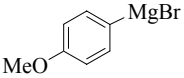
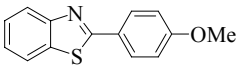
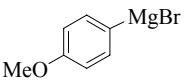
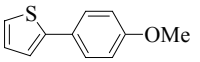
[a]Reaction conditions: 0.5 mol% catalyst, 1 mmol of halide, 3 mL of THF, 3 mmol of Grignard reagents. [b]GC yields (isolated yields in parentheses) - average of two runs. [c]side-products obtained.

4.2.6. KTC Coupling of Heterocyclic Substrates

Having achieved our goal of developing the KTC methodology to a large extent, we shifted our focus towards heterocyclic substrates. No cross-coupling methodology can claim acceptance in medicinal and synthetic chemistry unless this very important class of compounds

is included as possible coupling reagents. Cognizant of such a need, we set out to explore Kumada coupling of various nitrogen and sulphur heterocycles under our set of conditions.

Table 4.5. Kumada-Tamao-Corriu Coupling of Heterocyclic Substrates[a]

entry	halide	Grignard	product	temperature (°C)	time (h)	yield (%)[b]
1				60	0.25	93 (87)
2				25	24	75 (73)
3				60	0.5	80 (76)
4				25	18	85 (81)
5				60	1	100 (92)
6				60	0.25	100 (93)
7				60	0.25	88 (86)
8				60	6	100 (94)
9				60	0.25	100 (97)

[a]Reaction conditions: 0.5 mol% catalyst, 1 mmol of halide, 3 mL of THF, 3 mmol of the Grignard reagent. [b]GC yields (isolated yields in parentheses) - average of two runs.

Indeed, the reactions of various chloro- and bromo-heterocyclic compounds were efficiently catalyzed by the $[(NHC)PdCl_2]_2$ catalyst (Table 4.5). The short reaction times required

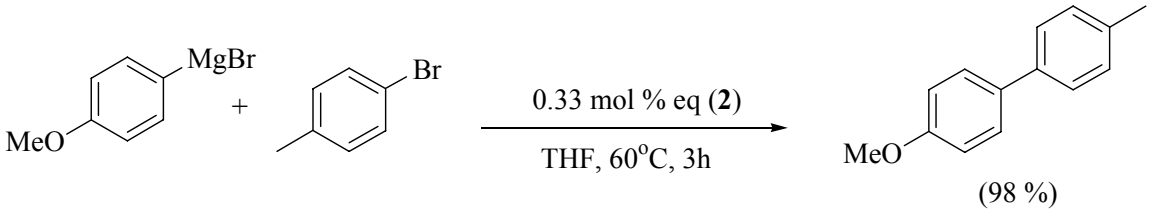
for these important couplings are a notable feature of the protocol. Effective couplings can be performed in reaction time as little as a few minutes with the given set of conditions. Positive results were achieved on exploring the prospects of effecting the couplings at optimum temperature. However, the reaction times have to be prolonged if the reaction is performed at a lower temperature. This difference is quite evident on comparison of entries 4 and 5 (Table 4.5). On reacting 2-chloropyridine with *para*-methoxy-phenylmagnesium-bromide at elevated temperatures, the product is obtained in quantitative yields within 1 hour. However, at optimum temperature, the reaction proceeds to furnish 85% product in 18 hours. Successful coupling reactions of 2-chlorobenzothiazole (Table 4.5, entries 6 and 8) support our efforts to make this protocol attractive for medicinal and synthetic applications, as reactions of bulky heterocyclic substrates are of vital significance for them.[42]

4.2.7. Scalability of KTC Coupling Reaction - Gram Scale Reaction with Lower Catalyst Loading

During our methodology development efforts, we focused our attention on potential utility of the protocol in industrial applications. Difference in outcome of a reaction (especially in terms of yields obtained) is a common problem faced when laboratorial processes are metamorphosed to bigger scale applications in the industry. To that end, we examined the impact of scaling-up the reaction to gram scale under our set of conditions. For a representative demonstrative reaction, 0.74 mL (6 mmols) of *para*-bromotoluene was coupled with excess *para*-methoxy-phenylmagnesium-bromide (Scheme 3). The effective catalyst loading was further reduced from 0.5 mol% to 0.33 mol%. Within 3 hours the reaction proceeded to furnish

the product in excellent yield. 4'-methoxy-3-methyl-biphenyl was isolated in 98% yield (1.18 grams). The flexible scalability of the procedure, demonstrated by successful transformation of our microscale protocol to gram-scale synthesis further supports our claim of this protocol being susceptible to wider applications.

Scheme 4.6. KTC Coupling in a Gram Scale Reaction

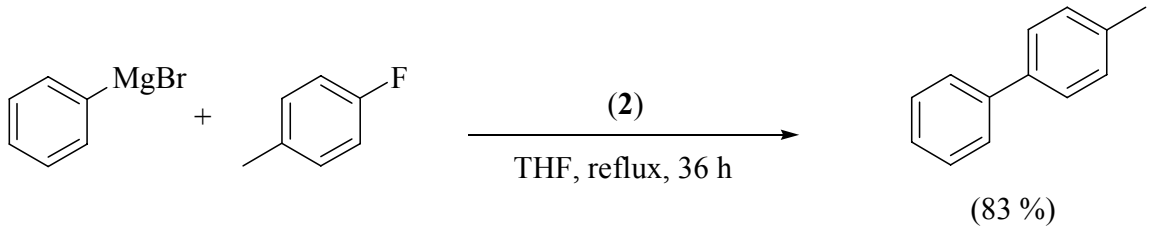


4.2.8. C-F Bond Activation in Kumada Coupling of an Unactivated Aryl Fluoride

Amongst the various metal catalyzed coupling reactions, the aryl halides are the most often employed class of electrophilic partners owing to their ease of handling, ready availability and low costs. However, within this class of compounds, aryl fluorides are known to be the least reactive towards customary coupling protocols.[35,53-56] The aversion of fluorides to actively participate in coupling reactions is rooted in the inherent strength of the carbon-fluorine bond.[57] However, contrary to case of other coupling reactions, Kumada coupling of fluoride electrophiles were developed from the very beginning.[53] As mentioned earlier, significant advances were reported later by Herrmann[35] and others.[38] In the major developments reported in this regard, nickel catalysts have been employed for mediating the transformation. Although Dankwardt has reported a few examples with palladium, the reaction required extreme conditions.[58] Herein we wish to report the best conditions for C-F activation in unactivated fluorides with an NHC-Pd

catalyst system (Scheme 4). The reaction of phenylmagnesium-bromide with *para*-fluorotoluene was performed in THF with an increased catalyst loading of 2 mol%. The coupling product was isolated in excellent yield after refluxing the reaction mixture for 36 hours.

Scheme 4.7. C-F Bond Activation in KTC Coupling of an Unactivated Aryl Fluoride



4.3. Conclusions

In summary, we have made significant advances in development of the Kumada-Tamao-Corriu cross-coupling methodology. Capitalizing on the easily accessible catalytic species, we have studied action of various substrates under our reaction conditions. The results showed a high activity profile, allowing for the coupling of various halides. The reactions were demonstrated to work with catalyst loadings as low as 0.1 mol%. The efficient couplings of bulky hindered and heterocyclic substrates provided an attractive and convenient process for prospective applications in synthetic and medicinal chemistry. Gram-scale synthesis and the best conditions for C-F bond activation in fluoride substrates by an NHC-ligated palladium catalyst were also achieved making the protocol susceptible to wider applicability.

4.4 Experimental Section

4.4.1 General considerations

- All aryl halides, alkyl halides and Grignard reagents were used as received (Aldrich, Acros).
- Solids were stored under argon in an MBraun glove-box.
- The solvents for synthesis and catalysis were distilled from appropriate drying agents or were passed through an alumina column in an MBraun solvent purification system.
- The *N*-heterocyclic carbenes (SIPr and IPr) were prepared according to the reported procedures.[59]
- All reactions were carried out under an atmosphere of argon, either in screw-cap vials or in a Schlenk flask.
- ^{1}H- and ^{13}C- nuclear magnetic resonance spectra were recorded using a Varian-400 MHz spectrometer at ambient temperature in $CDCl_3$ (Cambridge Isotope Laboratories, Inc.). The solvent for NMR spectroscopy was stored over molecular sieves.
- Flash chromatography was performed on silica gel (230-400 mesh) (Natland International Corporation).

NOTE: Although the reactions were performed in a dry-box, the reaction protocol can also be followed with equal efficiency without using a dry-box. The scalability experiment and the C-F bond activation experiment were performed using Schlenk techniques without any adverse effect on activity (Schemes 4.6 and 4.7).

4.4.2 Procedure for One-pot Synthesis of (SIPr)Pd(Cl)$_2$-dimer

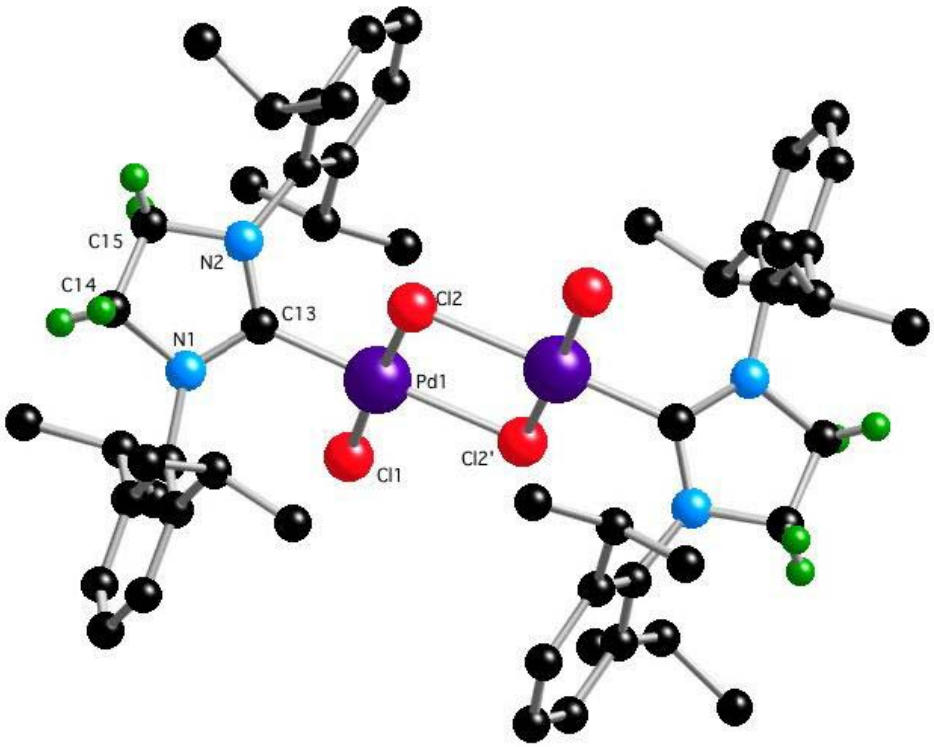
In a 25 ml Schlenk flask, a suspension of $Pd(OAc)_2$ (recrystallized from benzene, 225mg, 1 mmol) in anhydrous benzene (5 mL) was prepared by stirring at room temperature. 1 mmol of *N*,*N*'-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene – (SIPr) – (390 mg, 1 mmol) was then added to the Schlenk flask under an atmosphere of argon. The mixture was allowed to stir for 12 hours at room temperature. Solvent was then removed *in vacuo* and 5 mL of HCl solution (in diethyl ether) was added via syringe. The reaction mixture was allowed to stir at room temperature for 6 hours. The solvent was then removed *in vacuo*. The residue was washed with hexanes. The product was triturated with pentane and the liquid decanted. The residual product was dried under vacuum to obtain the final product. The procedure furnished the SIPr dimer in 80 % (453 mg) yield. Identity of the compound was confirmed by comparison with literature spectroscopic data.[19] The SIPr complex was further characterized by X-ray crystallography.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.45-7.41 (multiplet, 2H, aromatic), 7.27-7.24 (multiplet, 2H, aromatic), 7.20 (doublet, *J* = 8.0, 2H, aromatic), 3.87 (singlet, 4H, C*H*$_2$-imidazolin), 3.29 (triplet, *J* = 6.8, 2H, methine), 3.0 (triplet, *J* = 6.8, 2H, methine), 1.42 (doublet, *J* = 6.4, 6H, HC(C*H*$_3$)$_2$), 1.33 (doublet, *J* = 6.4, 6H, HC(C*H*$_3$)$_2$), 1.18 (doublet, *J* = 6.8, 6H, HC(C*H*$_3$)$_2$), 1.10 (doublet, *J* = 6.8, 6H, HC(C*H*$_3$)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 180.4, 147.6, 147.2, 134.7, 129.8, 124.8, 53.9, 28.9, 26.9, 24.5. Elemental Analysis Calcd. for $C_{27}H_{38}Cl_2N_2Pd$: C – 57.10, H – 6.74, N – 4.93. Found: C – 57.26, H – 6.96, N – 4.90.

4.4.3 X-Ray Structure of (SIPr)Pd(Cl)$_2$-dimer

The crystals for single crystal X-ray diffraction analysis were grown by slow diffusion in a mixture of dichloromethane and hexanes. The ball and stick representation is presented in figure 1. The hydrogen atoms on *N,N'*-(2,6-disiopropyl)phenyl fragments have been removed for clarity. The study confirmed that the molecule has 2 bridging chlorines. The molecule sits on an inversion center, so only 1/2 of the formula unit is contained in the asymmetric unit.

Figure 4.1. Ball and Stick Representation of [(SIPr)Pd(Cl)$_2$]$_2$. Hydrogen atoms omitted for clarity.[60]



Provided courtesy of Prof. Edwin D. Stevens

4.4.4 Procedure for One-pot Synthesis of (IPr)Pd(Cl)$_2$-dimer

In a 25 ml Schlenk flask, a suspension of $Pd(OAc)_2$ (recrystallized from benzene, 225mg, 1 mmol) in anhydrous benzene (5 mL) was prepared by stirring at room temperature. 1 mmol of *N*,*N*'-bis(2,6-diisopropylphenyl)imidazol-2-ylidene – (IPr) – (388 mg, 1 mmol) was then added to the Schlenk flask under an atmosphere of argon. The mixture was allowed to stir for 12 hours at room temperature. Solvent was then removed *in vacuo* and 5 mL of HCl solution (in diethyl ether) was added via syringe. The reaction mixture was allowed to stir at room temperature for 6 hours. The solvent was then removed *in vacuo*. The residue was washed with hexanes. The product was triturated with pentane and the liquid decanted. The residual product was dried under vacuum to obtain the final product. The procedure furnished the IPr dimer in 92 % (519 mg) yield. Identity of the compound was confirmed by comparison with literature spectroscopic data.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.55 (br, 2H, aromatic), 7.34 (br, 4H, aromatic), 6.99 (singlet, 2H, C*H*-imidazole), 2.92 (singlet, 2H, methine), 2.59 (singlet, 2H, methine), 1.36 (singlet, 12H, 2 x (HC(CH_3)$_2$), 1.06 (singlet, 12H, 2 x (HC(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 148.2, 146.5, 134.5, 130.7, 125.5, 124.5, 53.9, 28.9, 26.5, 23.5. Elemental Analysis Calcd. for $C_{27}H_{36}Cl_2N_2Pd$: C – 57.30, H – 6.41, N – 4.95. Found: C – 57.51, H – 6.70, N – 4.79.

4.4.5 Catalyst Screening

In a dry-box, 1 mol% of the indicated catalyst was loaded to a screw-cap reaction vial equipped with a stirring bar. The solvent was added and the vial sealed with a screw-cap

equipped with rubber septum. Outside the dry-box, 123 μL (1 mmol) of *para*-bromotoluene or bromomesitylene was injected through the rubber septum, inside the vial with a syringe. It was followed by addition of 3 mmol of phenylmagnesium-bromide via syringe. The *para*-bromotoluene reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 25 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate, for the indicated time. For bromomesitylene reactions, the reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or in an oil bath set at 60 ^{o}C for the indicated time. The reactions were monitored by Agilent 6890N or Agilent 6890Plus gas chromatographs.

4.4.6 Optimization of Catalyst Loadings

In a dry-box, the indicated concentration of (SIPr)Pd(Cl)$_2$-dimer catalyst was loaded to a screw-cap reaction vial equipped with a stirring bar. The solvent was added and the vial sealed with a screw-cap equipped with rubber septum. Outside the dry-box, 123 μl (1 mmol) of *para*-bromotoluene was injected through the rubber septum, inside the vial with a syringe. It was followed by addition of 3 mmol of phenylmagnesium-bromide via syringe. For room temperature reactions, the reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 25 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate, for the indicated time. For high temperature reactions, the reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or in an oil bath set at 60 ^{o}C for the indicated time. The reactions were monitored by Agilent 6890N or Agilent 6890Plus gas chromatographs.

4.4.7 Representative procedure for Kumada-Tamao-Corriu coupling

In a dry-box, the indicated concentration of catalyst was loaded to a screw-cap reaction vial equipped with a stirring bar. The solvent was added and the vial sealed with a rubber septum equipped screw-cap. Outside the dry-box, 1 mmol of the halide substrate was injected inside the vial with a syringe. For solid halide substrates, the addition to vial is done inside the dry-box. It was followed by addition of indicated Grignard reagent via syringe. The reaction mixture was then allowed to shake on a Lab-Line Orbit Shaker (set at 25 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate, for the indicated time. For high-temperature reactions, the reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 60 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or in an oil bath set at 60 ^{o}C for the indicated time. The reactions were monitored by Agilent 6890N or Agilent 6890Plus gas chromatographs. After maximum conversion the reaction mixture was allowed to cool down to room temperature and hydrolyzed with dilute HCl (1.0 M). The organic layer was extracted with methyl-*tert*-butyl ether or diethyl ether. The organic layer extracts were combined and washed with saturated $NaHCO_3$ solution and saturated saline solution, and then dried over magnesium sulfate. The solvent was then evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel (hexanes or 5 % ethyl acetate in hexanes). The ^{1}H- and ^{13}C-NMR spectra for all the coupling products, were found to be in agreement with previously reported spectroscopic data.

Isolated products:

4-Methyl-biphenyl[61] (Table 4.2, entry 1) The procedure afforded 136 mg (81 %) of the product.

4-Methyl-biphenyl[61] (Table 4.2, entry 2) The procedure afforded 152 mg (91 %) of the product.

4-Methoxy-biphenyl[62] (Table 4.2, entry 3) The procedure afforded 121 mg (66 %) of the product.

1-Benzyl-3,5-bis(trifluoromethyl)benzene[63] (Table 4.2, entry 4) The procedure afforded 282 mg (93 %) of the product.

1,1-Diphenylethylene[64] (Table 4.2, entry 5) The procedure afforded 169 mg (94 %) of the product.

Diphenylmethane[65] (Table 4.2, entry 6) The procedure afforded 154 mg (92 %) of the product.

4'-Methoxy-4-methyl-biphenyl[66] (Table 4.3, entry 1) The procedure afforded 172 mg (87 %) of the product.

4,4'-Dimethoxy-biphenyl[66] (Table 4.3, entry 2) The procedure afforded 205 mg (96 %) of the product.

4'-Methoxy-4-methyl-biphenyl[66] (Table 4.3, entry 3) The procedure afforded 176 mg (89 %) of the product.

4,4'-Dimethoxy-biphenyl[66] (Table 4.3, entry 4) The procedure afforded 156 mg (73 %) of the product.

4'-Methoxy-2-methyl-biphenyl[67] (Table 4.3, entry 5) The procedure afforded 176 mg (89 %) of the product.

4-Methoxy-biphenyl[62] (Table 4.3, entry 6) The procedure afforded 172 mg (94 %) of the product.

4,4'-Dimethoxy-biphenyl[66] (Table 4.3, entry 7) The procedure afforded 192 mg (90 %) of the product.

4'-Methoxy-2-methyl-biphenyl[67] (Table 4.3, entry 8) The procedure afforded 182 mg (92 %) of the product.

4'-Methoxy-2,6-dimethyl-biphenyl[68] (Table 4.4, entry 1) The procedure afforded 154 mg (73 %) of the product.

1-Methyl-4-phenyl-naphthalene[69] (Table 4.4, entry 2) The procedure afforded 209 mg (96 %) of the product.

4'-Methoxy-2,6-dimethyl-biphenyl[68] (Table 4.4, entry 3) The procedure afforded 178 mg (84 %) of the product.

4'-Methoxy-2,4,6-trimethyl-biphenyl[70] (Table 4.4, entry 4) The procedure afforded 201 mg (89 %) of the product.

1-Phenyl-naphthalene[71] (Table 4.4, entry 5) The procedure afforded 185 mg (91 %) of the product.

2,4,6-Trimethyl-biphenyl[72] (Table 4.4, entry 6) The procedure afforded 176 mg (90 %) of the product.

1-(4-Methoxy-phenyl)-naphthalene[73] (Table 4.4, entry 7) The procedure afforded 208 mg (89 %) of the product.

2-Phenyl-pyridine[74] (Table 4.5, entry 1) The procedure afforded 134 mg (87 %) of the product.

2-(4-Methoxy-phenyl)-pyridine[75] (Table 4.5, entry 2) The procedure afforded 135 mg (73 %) of the product.

2-Phenyl-pyridine[74] (Table 4.5, entry 3) The procedure afforded 117 mg (76 %) of the product.

2-(4-Methoxy-phenyl)-pyridine[75] (Table 4.5, entry 4) The procedure afforded 149 mg (81 %) of the product.

2-(4-Methoxy-phenyl)-pyridine[75] (Table 4.5, entry 5) The procedure afforded 170 mg (92 %) of the product.

2-Phenyl-benzothiazole[76] (Table 4.5, entry 6) The procedure afforded 196 mg (93 %) of the product.

2-Phenyl-thiophene[77] (Table 4.5, entry 7) The procedure afforded 137 mg (86 %) of the product.

2-(4-Methoxy-phenyl)-benzothiazole[78] (Table 4.5, entry 8) The procedure afforded 226 mg (94 %) of the product.

2-(4-Methoxy-phenyl)-thiophene[77] (Table 4.5, entry 9) The procedure afforded 184 mg (97 %) of the product.

4.4.8 Procedure for the Scalability Experiment of Kumada-Tamao-Corriu Coupling Reaction - Gram Scale Reaction with Lower Catalyst Loading

In a dry-box, 56 mg (1 mol % - 0.33 eq) of the catalyst was loaded to 25 mL Schlenk flask equipped with a stirring bar. 2 mL of THF was then added to the flask and the flask sealed with a rubber septa. Outside the dry-box, 0.738 mL (6 mmol) of *para*-bromotoluene was injected inside the flask with a syringe. It was followed by addition of 15 mL (7.5 mmol) of 0.5 M solution of *para*-methoxy-phenylmagnesium-bromide in THF, with a syringe. The flask was allowed to stir in an oil bath set at 60 ^{o}C for 3 hours. The reaction was monitored by Agilent 6890Plus gas chromatograph. After 3 hours the reaction mixture was allowed to cool down to room temperature and hydrolyzed with dilute HCl (1.0 M). The organic layer was extracted with diethyl ether. The organic layer extracts were combined and washed with saturated $NaHCO_3$ solution and saturated saline solution, and then dried over magnesium sulfate. The solvent was then evaporated *in vacuo*. The final product 4'-methoxy-4-methyl-biphenyl was obtained as a light green powder. The ^{1}H- and ^{13}C-NMR spectra of the compound were found to be in agreement with previously reported spectroscopic data.

4'-Methoxy-4-methyl-biphenyl[66] (Scheme 4.6) The procedure afforded 1.18 gm (99 %) of the product.

4.4.9 Procedure for C-F Bond Activation in Kumada Coupling of an Unactivated Aryl Fluoride

In a dry-box, 113 mg (2 mol %) of the catalyst was loaded to 25 mL long necked Schlenk tube equipped with a stirring bar. 3 mL of THF was then added to the tube and the tube sealed with a rubber septa. Outside the dry-box, 110 μL (1 mmol) of *para*-fluorotoluene was injected in the tube with a syringe. It was followed by addition of 3 mL (3 mmol) of 1 M solution of phenylmagnesium-bromide in THF, with a syringe. The reaction mixture was refluxed by heating in an oil bath. The reaction was monitored by Agilent 6890Plus gas chromatograph. After 36 hours the reaction mixture was allowed to cool down to room temperature and hydrolyzed with dilute HCl (1.0 M). The organic layer was extracted with methyl-*tert*-butyl ether. The organic layer extracts were combined and washed with saturated $NaHCO_3$ solution and saturated saline solution, and then dried over magnesium sulfate. The solvent was then evaporated *in vacuo*. The final product 4-methyl-biphenyl was obtained as an off white powder. The ^{1}H- and ^{13}C-NMR spectra of the compound were found to be in agreement with previously reported spectroscopic data.

4-Methyl-biphenyl[61] (Scheme 4.7) The procedure afforded 140 mg (83 %) of the product.

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CHAPTER 5

EASY SYNTHESIS AND ANALYSIS OF SCOPE AND LIMITATIONS OF N-HETEROCYCLIC CARBENE(NHC)PALLADIUM($Cl)_2$-PYRIDINE DERIVATIVES IN SUZUKI-MIYAURA CROSS-COUPLING REACTION*

5.1. Introduction

N-Heterocyclic(NHC)-palladium($Cl)_2$-pyridine derivative complexes (NHC)Pd($Cl)_2$-(X-pyridine) (X = Cl, Br, H) have been synthesized and characterized. It is established that these complexes serve as catalysts for coupling reactions. The complexes have been screened for activity in Suzuki-Miyaura cross coupling reaction. The efficiency of the catalytic species, in presence of various functionalities has been evaluated. This study also documents the impact of change of various parameters on the coupling reaction. The scope and limitations of the catalysts are discussed. In view of the wide array of reactions that are subject to catalysis by *N*-heterocyclic Carbene (NHC) ligated metal catalysts, there have been numerous studies[1] evaluating NHC-metal complexes and their activity in various transformations.[2] NHCs were first reported by Wanzlick[3] in the 1960s and subsequently NHC–transition metal complexes were reported by Ofele in 1968.[4] In the early 1990s Arduengo and co-workers provided the access to free isolable carbenes from imidazolium salts prepared in a one-step synthesis and brought a renaissance in this field.[5] Numerous reports have demonstrated that NHCs have higher thermal

stability, greater donating properties and generally show better stabilizing effects than most of the commonly utilized phosphines.[6] An appealing design feature of these ligands is the potential to tune their electron donating properties and reactivity through a judicious choice of substituents on nitrogens of the imidazolium framework.[7] Various metals have been utilized to study the behavior of NHCs and a plethora of applications of NHC-metal complexes has been revealed.[8] Among these metals, palladium is one of the most versatile and widely used on both industrial and laboratory scales.[9]

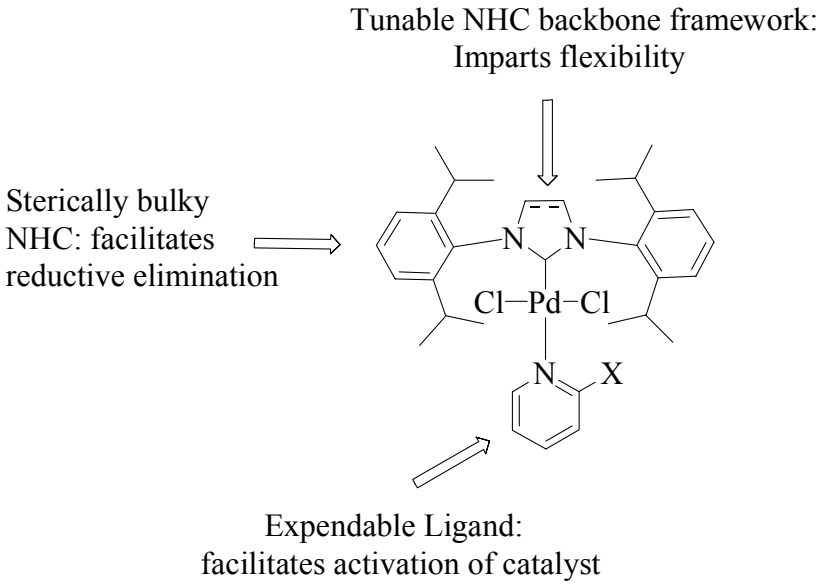
Palladium catalyzed coupling reactions are reliable and versatile tools for the regioselective formation of carbon-carbon bonds.[10] Generally aryl triflates, aryl bromides and aryl chlorides are employed as electrophiles.[11] The use of these organic electrophilic coupling partners is especially attractive because of their easy availability and inexpensive nature which allows both laboratory scale syntheses and industrial applications.[12]

We have reported significant advances in various transformations as part of our studies highlighting the utility of *N*-heterocyclic carbenes as efficient ligands with various metals.[13] We have also extensively explored the use of NHC-ligated metal catalysts in cross-coupling reactions[14] including major advances in Suzuki-Miyaura cross-coupling reaction.[15] One of the major concerns with application of NHC-metal catalysts in synthetic and industrial processes is the air and moisture sensitive nature of the complexes which necessitates drying of solvents and use of special techniques. We[16] and others[17] have reported successful attempts at circumventing these drawbacks by synthesizing stable catalysts and developing protocols utilizing non-anhydrous conditions.

Recently, Organ et al. have documented their attempts to find a *universal* solution to the shortcomings presented by NHC-metal catalysts. To that end, they have reported synthesis of

(NHC)Pd(Cl)$_2$-(3-chloropyridine) complexes and studied their activity in cross-coupling reactions.[18,19] We wished to analyze the structural implications and catalytic activity of such species and consequently initiated a program directed at the design and development of (NHC)Pd(Cl)$_2$-(X-pyridine) (X = Cl, Br, H) derivative catalysts.

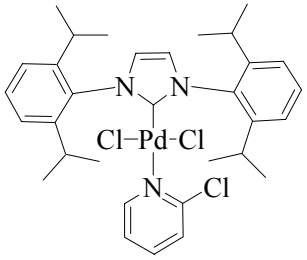
Scheme 5.1. Structural Features of the Catalyst



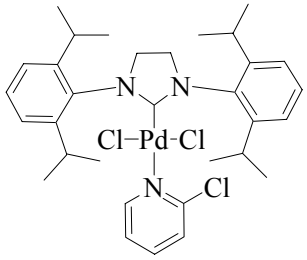
The main structural features (Scheme 5.1) of these complexes are (1) flexibility provided by tunable nature of the NHC, especially the option of unsaturated or saturated backbone of imidazolium framework (2) activation of catalyst by a possibly expendable pyridine ligand (3) steric bulk provided by the NHC ligand which can impart stability against decomposition of the catalyst and provide aid in reductive elimination[20]

To evaluate the consequences of presence of different halide-substituents on the pyridine fragment of the complex, we chose to synthesize and explore different analogues of (NHC)Pd(Cl)$_2$-(X-pyridine) complexes.

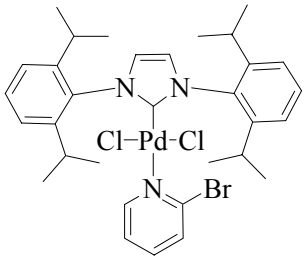
Scheme 5.2. Structure of (NHC)Pd(Cl)$_2$-(X-pyridine) (X = Cl, Br, H) Derivative Catalysts



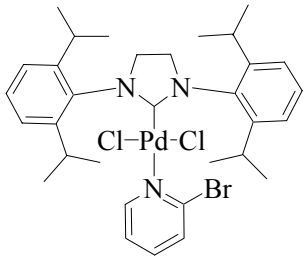
(IPr)Pd(Cl)$_2$(2-chloropyridine)
(**1**)



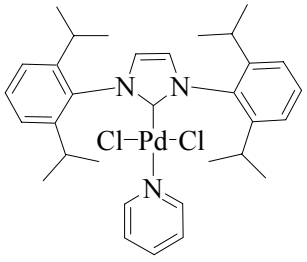
(SIPr)Pd(Cl)$_2$(2-chloropyridine)
(**2**)



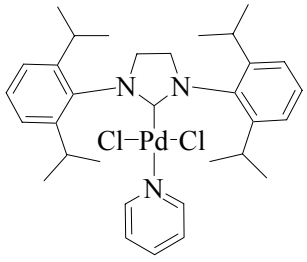
(IPr)Pd(Cl)$_2$(2-bromopyridine)
(**3**)



(SIPr)Pd(Cl)$_2$(2-bromopyridine)
(**4**)



(IPr)Pd(Cl)$_2$(pyridine)
(**5**)



(SIPr)Pd(Cl)$_2$(pyridine)
(**6**)

More specifically, here we present the simple synthesis and catalytic activity study of a series of NHC(palladium)-pyridine derivative complexes: (**1**, (NHC = *N,N'*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene and pyridine substituent = 2-chloropyridine; **2**, (NHC = *N,N'*-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene and pyridine substituent = 2-chloropyridine; **3**, (NHC = *N,N'*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene and pyridine substituent = 2-bromopyridine; **4**, (NHC = *N,N'*-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene

and pyridine substituent = 2-bromopyridine; **5**, (NHC = *N,N'*-bis(2,6-diisopropylphenyl)imidazol-2-ylidene and pyridine substituent = unsubstituted pyridine; **6**, (NHC = *N,N'*-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene and pyridine substituent = unsubstituted pyridine) (Scheme 5.2).

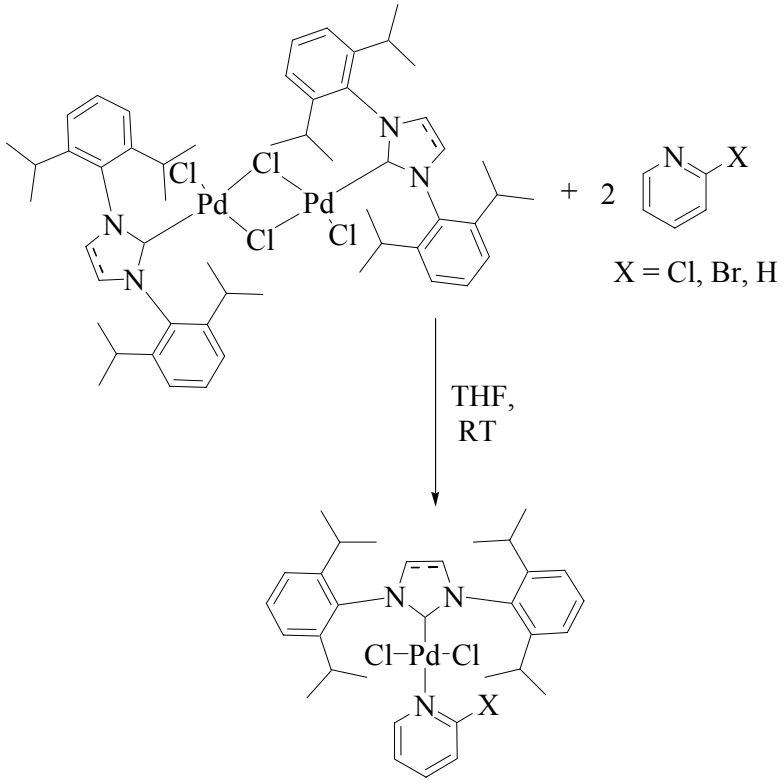
5.2 Results and Discussion

Arguably, one of the most important facets a widely acceptable catalyst should have is ease of availability. It is imperative for a catalyst to be easy to synthesize for acceptance in synthetic and industrial applications. To that end, we set-out to find a user-friendly and easy method to synthesize the targeted (NHC)Pd$(Cl)_2$-(X-pyridine) complexes.

A few years ago we reported on synthesis of air stable (NHC)Pd(Cl_2)-dimer species and their application in catalyzing Buchwald-Hartwig amination.[21] Subsequently, Sigman group made use of these and similar species in developing oxidation reactions.[22] Cognizant of the potential of these dimeric species, we decided to scrutinize their properties more closely. In a separate report, we have revealed easy synthesis of the (NHC)Pd$(Cl)_2$-dimer species and studied their activity in mediating effective Kumada-Tamao-Corriu cross-coupling reactions.[23] Our observation that the cross-couplings proceed particularly well in the presence of (NHC)Pd$(Cl)_2$-dimer catalysts led us to investigate the possibility of utilizing them for achieving positive results towards our goals of arriving at a user-friendly protocol which would be acceptable to both synthetic laboratory as well as industrial applications. We have focused our efforts on these interesting dimeric moieties in part because these catalysts exhibit high stability, good activity and broad applicability in both synthesis and catalysis but also in part due to the fact that the only other method reported for

synthesis of (NHC)Pd(Cl)$_2$-(X-pyridine) complexes uses rather harsh conditions.[18,24] Moreover, the only complexes synthesized were 3-chloropyridine congeners without exploring the possibility of utilizing other pyridine derivatives in such complexes.

Scheme 5.3. Simple Synthesis of (NHC)Pd(Cl)$_2$-(X-chloropyridine) Derivatives from (NHC)Pd(Cl)$_2$-dimers



(NHC)Pd(Cl)$_2$(X-pyridine)

NHC = IPr, SIPr

Herein, we wish to report our simple method of synthesizing (NHC)Pd(Cl)$_2$-(X-pyridine) derivatives from (NHC)Pd(Cl)$_2$-dimers. The procedure involves simple addition of pyridine to the (NHC)-Pd(Cl)$_2$-dimer species without the need of elevated temperatures. The targeted compounds can be achieved in excellent yields within considerably shorter reaction times.[25] (Scheme 5.3).

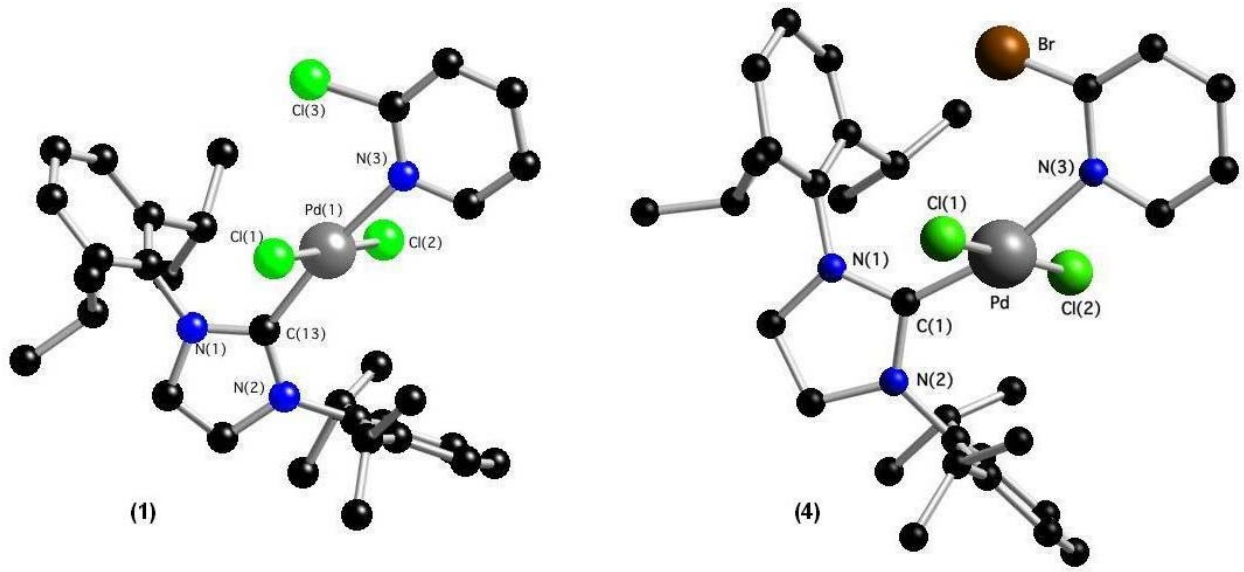
To study structural implications and unambiguously characterize the complexes, single crystal diffraction was performed on the crystals of complexes (**1**),[26] (**4**),[27] (**5**)[28] and (**6**)[29] The crystals for (**1**) were grown by slow diffusion in a mixture of DCM and hexanes, while the crystals for (**4**), (**5**) and (**6**) were grown from mixture of THF and hexanes.

The ball and stick representations for (**1**) and (**4**) are shown in figure 5.1. The hydrogen atoms have been omitted for clarity. All (NHC)Pd$(Cl)_2$-(X-pyridine) complexes have a four-coordinate palladium atom in a square-planar environment. The molecules of (IPr)PdCl_2-(2-chloropyridine) complex (**1**) and (SIPr)PdCl_2-(2-bromopyridine) complex (**2**) were found to be disordered with pyridine fragments having two orientations of unequal occupancy related by an approximate 180 degree rotation about the Pd-N bond. The Flack parameter indicated towards the crystals being racemic twins.

The ball and stick representations for (**5**) and (**6**) are presented in figure 5.2. The hydrogen atoms from *N,N'*-(2,6-diisopropylphenyl) fragments have been omitted. It is interesting to note that generally these complexes are air- and moisture-stable, we found that the (IPr)Pd$(Cl)_2$-(pyridine) complex (**5**) readily absorbed moisture on exposure to air. A distinct signal for water was observed in the ^{1}H-NMR of the complex. On synthesizing the complex in anhydrous conditions, the NMR spectra revealed absence of the same signal. However, on recording the spectra after opening the complex to air, the peak corresponding to water re-appeared in ^{1}H-NMR spectra taken in $CDCl_3$. Interestingly, similar behavior was not observed with the SIPr analogue (**6**), which was found to be stable in open air. This behavior of the complexes indicates towards the importance of choice of NHC in determining the stability of these complexes. Conceivably, it cannot be claimed that all (NHC)Pd$(Cl)_2$-(X-pyridine) complexes are stable but stability of these complexes is rather a function of balance of both

sterics and electronics imparted by the NHC and the pyridine moiety in conjunction with each other.

Figure 5.1. Ball and Stick Representations of (**1**) and (**4**). Hydrogen atoms have been omitted for clarity

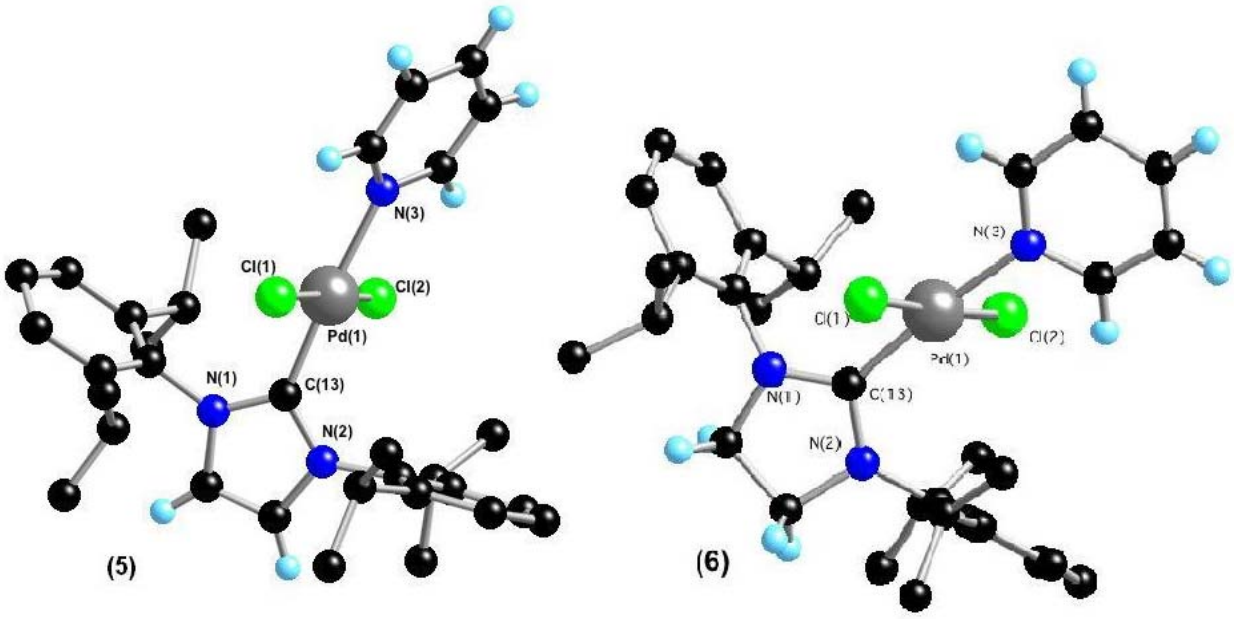


Provided courtesy of Prof. Edwin D. Stevens

Selected bond distances are presented in table 5.1. The palladium-carbenic carbon bond distances are in the range of 1.918 Å – 1.970 Å, which is slightly shorter than that found in most Pd-NHC complexes (around 2 Å).[30] The shortest palladium-carbenic carbon bond distance was found in (**4**) indicating towards a stronger bond between the carbene and palladium in the (SIPr)Pd(Cl)$_2$-(2-bromopyridine) complex (Table 5.1). Also, the palladium-carbenic carbon bond distances were found to be shorter in SIPr complexes ((**4**) = 1.918 Å and (**6**) = 1.961 Å) as compared to the IPr complexes with unsaturated imidazole motif ((**1**) = 1.994 Å and (**5**) = 1.970

Å) indicating towards a stronger bond with saturated NHCs as compared to the unsaturated congeners in these complexes. Interestingly, the longest Pd-$N_{pyridine}$ bond distance was found to be for the most unstable complex (**5**) amongst the four complexes.

Figure 5.2. Ball and Stick representation of (**5**) and (**6**). Hydrogen atoms have been omitted from *N,N'*-(2,6-diisopropylphenyl) fragments for clarity.



Provided courtesy of Prof. Edwin D. Stevens

Table 5.1. Selected Pd-C and Pd-N Bond Distances (Å) in (NHC)Pd(Cl)$_2$-(X-pyridine) Derivatives

(NHC)Pd(Cl)$_2$-(X-pyridine)	Pd(1)—C(13)	Pd(1)—Cl(1)	Pd(1)—Cl(2)	Pd(1)—N(3)
(IPr)Pd(Cl)$_2$-(2-chloropyridine) (**1**)	1.994(7)	2.293(2)	2.296(2)	2.109(5)
(SIPr)Pd(Cl)$_2$-(2-bromopyridine) (**4**)	1.918(11)	2.301(4)	2.293(3)	2.122(7)
(IPr)Pd(Cl)$_2$-(pyridine) (**5**)	1.934(12)	2.301(3)	2.284(4)	2.091(11)
(SIPr)Pd(Cl)$_2$-(pyridine) (**6**)	1.961(7)	2.294(2)	2.300(2)	2.083(7)
(IPr)Pd(Cl)$_2$-(3-chloropyridine)[18]	1.969(3)	2.2897(9)	2.2976(8)	2.137(2)

Selected bond angles are presented in table 2. Cl_1-Pd-C_2 bonds are nearly linear with bond angles ranging from 176.24-178.36. $C_{carbenic}$-Pd-$N_{pyridine}$ bond angles for (**1**), (**5**) and (**6**) are also nearly linear. The biggest deviation is found in the 2-bromopyridine analogue with a $C_{carbenic}$-Pd-$N_{pyridine}$ bond angle of 165.0 degrees (Table 5.2).

Table 5.2. Selected Bond Values (deg) for (NHC)Pd(Cl)$_2$-(X-pyridine) Derivative Complexes

(NHC)Pd(Cl)$_2$-(X-pyridine)	C(13)—Pd—Cl(1)	C(13)—Pd—Cl(2)	C(13)—Pd—N(3)	N(3)—Pd—Cl(1)	N(3)—Pd—Cl(2)	Cl(1)—Pd—Cl(2)
(IPr)Pd(Cl)$_2$-(2-chloropyridine) (**1**)	87.61(17)	94.44(17)	172.6(3)	92.99(18)	84.84(18)	177.68(10)
(SIPr)Pd(Cl)$_2$-(2-bromopyridine) (**4**)	95.6(3)	86.7(3)	165.0(4)	88.0(3)	90.4(3)	176.24(15)
(IPr)Pd(Cl)$_2$-(pyridine) (**5**)	90.6(4)	89.8(4)	179.5(5)	89.7(3)	89.9(3)	178.36(17)
(SIPr)Pd(Cl)$_2$-(pyridine) (**6**)	88.2(2)	94.7(2)	173.2(3)	89.9(2)	87.4(2)	176.72(9)
(IPr)Pd(Cl)$_2$-(3-chloropyridine)[18]	91.47(9)	87.25(9)	176.49(11)	90.98(7)	90.38(7)	177.73(4)

5.2.1 Suzuki-Miyaura Cross-Coupling Catalyzed by (NHC)Pd(Cl)$_2$-(X-pyridine) Derivatives

Suzuki Miyaura cross coupling is arguably the most important Pd-catalyzed C-C bond forming methodology.[31] Moreover, the organo-boron reagents used in the reaction possess positive attributes such as air- and moisture-stability, ease of availability and tolerance towards a wide variety of functionalities. As a consequence of these attractive attributes of Suzuki-Miyaura coupling, it has been actively employed as a very attractive pathway to achieve synthesis of biaryls[32] which can be found in a wide range of natural products.[33] Furthermore, both the boron-containing reagents and generated byproducts of the Suzuki-Miyaura reaction display low toxicity.[34] The vast utility of Suzuki-Miyaura cross-coupling provides a strong impetus to develop effective catalysts for this transformation.[35] In conjunction with extensive previous work with Pd-catalyzed Suzuki-Miyaura reaction, we examine here the activity of (NHC)Pd(Cl)$_2$-(X-pyridine) derivatives in this important transformation (Scheme 5.4).

Scheme 5.4. Suzuki-Miyaura Cross-Coupling Catalyzed by (NHC)Pd(Cl)$_2$-(X-pyridine) Derivatives

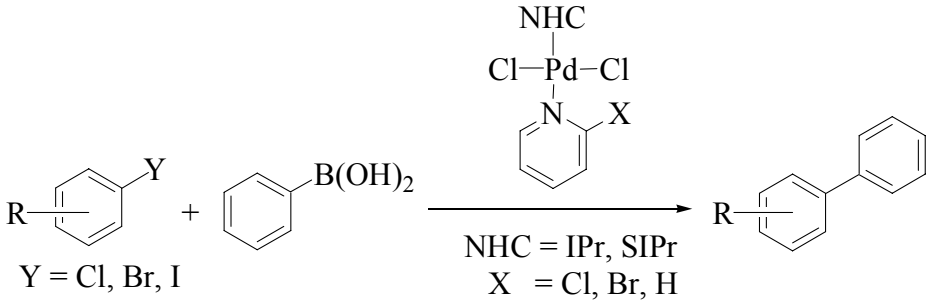
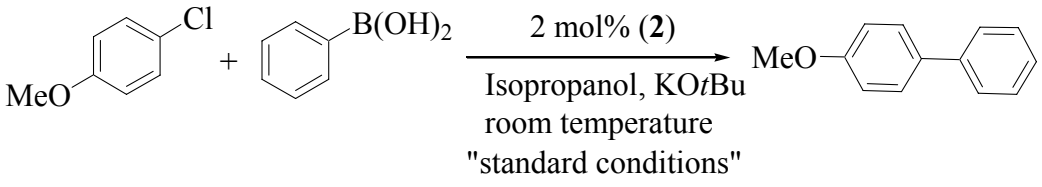


Table 5.3 illustrates the impact of a variation of reaction parameters on the course of the cross-coupling of phenylboronic acid with chloro- substrate *para*-chloroanisole. The standard

conditions consisted of 2% catalyst loading and KO*t*Bu base in technical grade isopropanol solvent. The reactions were performed at room temperature.[36] As depicted in entry 1 (Table 5.3), the reaction proceeded to furnish the coupling biaryl product in 86% yield under the standard conditions. The effect of the base was evaluated by replace alkoxide (KO*t*Bu) by a carbonate base (Cs_2CO_3). The substitution brought about an adverse effect on the outcome of the reaction. A similar result was observed on using *para*-dioxane as the solvent (entry 3, Table 5.3). The reaction furnished poor yield indicating that perhaps our previously reported protocol of alkoxide base in technical grade isopropanol[15b] is better suited for Suzuki-Miyaura cross couplings. Not surprisingly, the standard catalyst system for Suzuki-Miyaura couplings of *para*-chloroanisole was applied without modification to bromide substrate, *para*-bromotoluene (entry 4, Table 5.3). In our previous work, we had introduced a protocol to couple β-hydrogen-containing activated C(sp^3)-chlorides with boronic acids,[15d] providing an alternative to the Friedel-Crafts reaction for synthesis of allylic aromatics.[37] Here, coupling of benzyl bromide was carried out to evaluate the congruity of the (NHC)Pd$(Cl)_2$-(X-pyridine) protocol with the previously reported system. The (IPr)Pd$(Cl)_2$-(2-chloropyridine) catalyst was indeed found to be active for coupling of benzyl bromide with phenylboronic acid furnishing the product in 82% yield. Next we turned our attention towards coupling of sterically hindered bulky substrates. To that effect, *para*-chloroanisole from the standard conditions was replaced by 1-chloronaphthalene as the halide partner. The catalyst was found to be active in performing the coupling and furnished the mono-*ortho*-substituted product albeit in 2 hours.

Table 5.3. Impact of Reaction Parameters on Efficiency of Suzuki-Miyaura Cross Coupling Catalyzed by $(IPr)Pd(Cl)_2$-(2-chloropyridine)



entry	deviation from standard conditions	time (h)	yield (%)[a]
1	none	0.5	86
2	Cs_2CO_3	12	31
3	Dioxane	12	17
4	4-Bromotoluene	0.25	90
5	4-Chlorotoluene	0.5	93
6	Benzyl bromide	2	82
7	1-Chloronaphthalene	2	90
8	Lauryl chloride	-	NR[b]

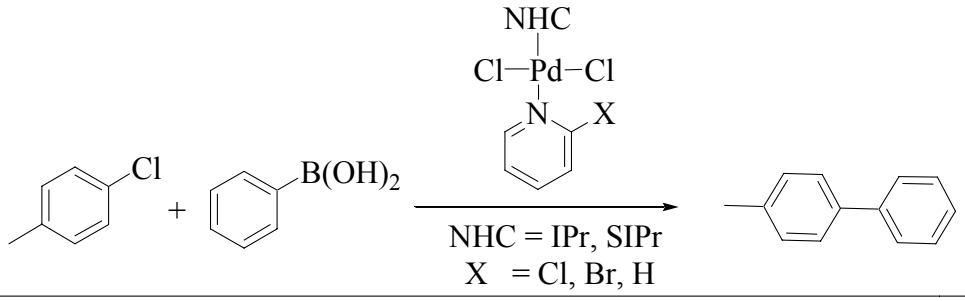
[a]GC yields versus a calibrated internal standard - dodecane (average of two runs). [b]reaction temperature increased to 60°C.

Although remarkable progress in both volumes of work and mechanistic investigations with regard to Suzuki-Miyaura reaction has been achieved in recent years, except a few recent advances,[15d,38] the attempts to use alkyl halides (especially chlorides) as electrophilic partners have been largely unsuccessful.[39] Generally the reluctance of inactivated alkyl halides to add oxidatively to Pd(0) is believed to be one of the hurdles that impedes the development of proficient means to effect couplings in this class of substrates. To evaluate the activity of alkyl halides in the present reaction protocol, coupling of lauryl chloride with phenylboronic acid was

attempted with the standard conditions. However, the catalyst proved inadequate in performing the desired coupling. No reaction was observed even after heating the reaction for prolonged reaction time.

5.2.2 Catalyst Screening

Table 5.4. Screening of Catalysts

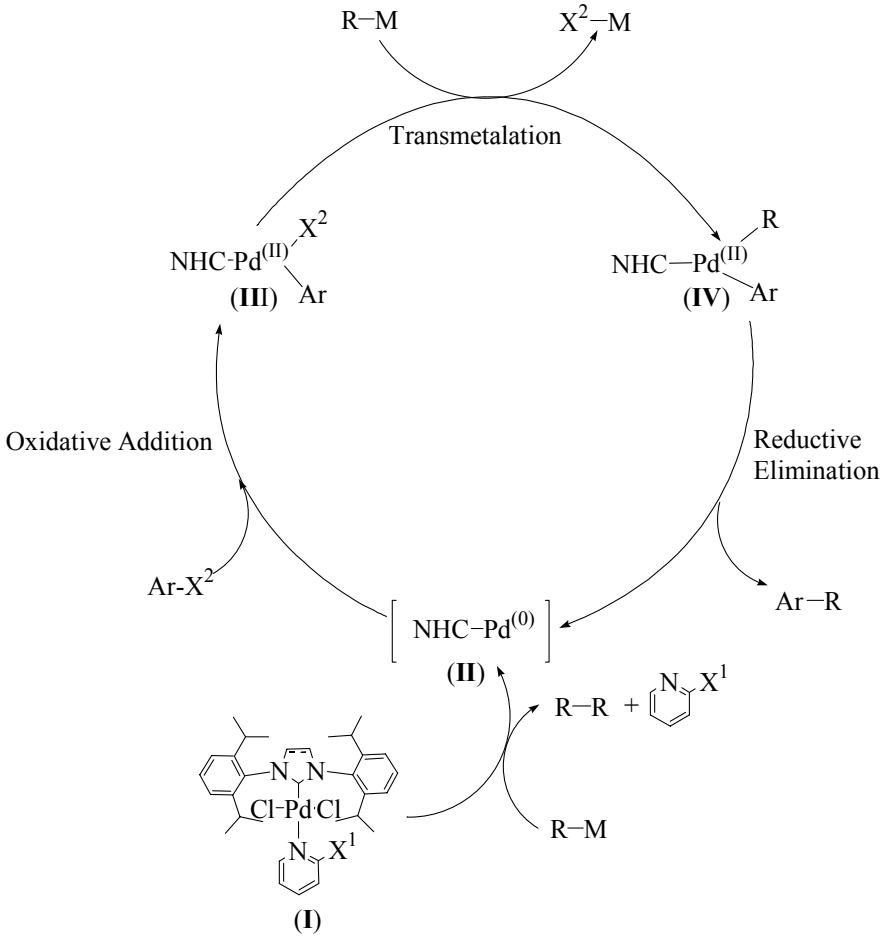


entry	catalyst	temperature	time (h)	yield (%)[a]
1	-	-	-	NR
2	(IPr)Pd(Cl)$_2$(2-chloropyridine)	25	0.25	86[b]
3	(IPr)Pd(Cl)$_2$(2-bromopyridine)	25	3	100
4	(IPr)Pd(Cl)$_2$(pyridine)	25	-	NR
5	(IPr)Pd(Cl)$_2$(pyridine)	60	0.25	80
6	(SIPr)Pd(Cl)$_2$(2-chloropyridine)	25	0.5	80
7	(SIPr)Pd(Cl)$_2$(2-bromopyridine)	25	1	93
8	(SIPr)Pd(Cl)$_2$(2-pyridine)	25	0.5	89

[a]GC yields versus a calibrated internal standard - dodecane (average of two runs). [b]isolated yield.

To arrive at an understanding of comparative catalytic activity, various synthesized complexes were submitted to the coupling of *para*-chlorotoluene and phenylboronic acid (Table 5.4). Not surprisingly, the control reaction in absence of the catalyst did not reveal formation of any coupling product (entry 1, Table 5.4). For screening of the catalysts, the loading was reduced to 1%. All complexes were found to be active in performing the cross-coupling reaction. However, the best result was obtained with $(IPr)Pd(Cl)_2$-(2-chloropyridine) complex. The 4-methyl biphenyl product was isolated in excellent yield.

Scheme 5.5. Proposed Catalytic Cycle



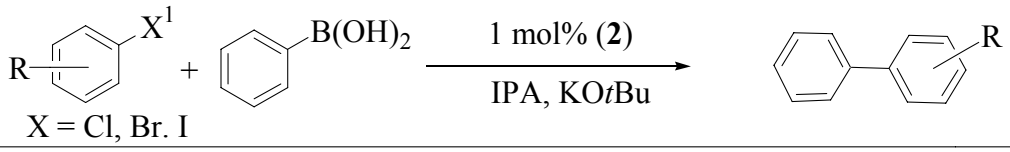
It has been proposed regarding activation of the catalyst that pyridine dissociation is unlikely to initiate activation of the catalyst because these complexes are highly stable.[18] Although we differ from the claim of general stability of these complexes as was revealed by lability demonstrated by complex (**5**) on exposure to air, we agree to the position that dissociation of pyridine is unlikely to be the deciding-factor in determining the rate of the reaction since reaction of the unstable complex (**5**) does not proceed at room temperature and necessitates thermal activation (Scheme 5.5).

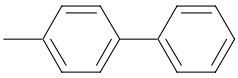
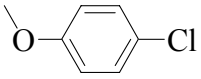
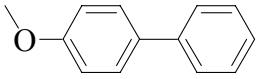
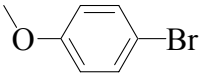
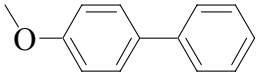
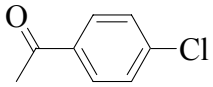
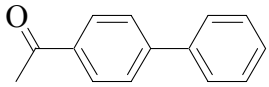
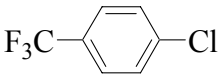
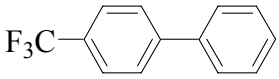
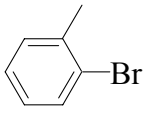
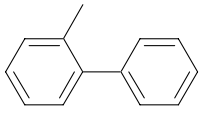
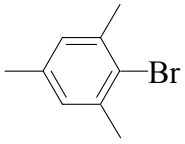
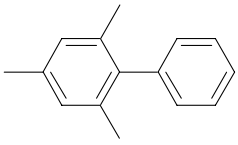
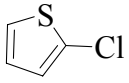
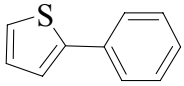
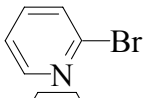
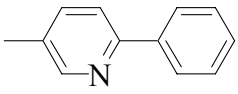
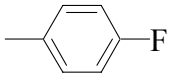
5.2.3 Substrate Screening

Having arrived at an acceptable coupling protocol we turned our attention towards defining the scope and limitation of the process. Towards that end, a study of various functionalities as coupling partners with phenylboronic acid was performed. The substrates were subjected to our alkoxide base – technical grade isopropanol system with 1% catalyst loading and tested for activity (Table 5.5). Not surprisingly, the standard catalyst system for coupling of halides was found to be applicable to iodides without any modifications (entry 1, Table 5.5). Functionalized aryl-halide reagents, including those that bear an alkoxide (entries 2 and 3, Table 5.5) or a trifluoromethyl group (entry 5, Table 5.5), couple with phenylboronic acid in good yields. *para*-Chloroacetophenone was also found to be amiable to the reaction conditions furnishing the product in quantitative yield (entry 4, Table 5.5). However, these reactions required vigorous stirring for longer reaction times as compared to other previously reported

catalyst systems.[15b,40] The efficiency of protocol was also tested with difficult substrates in terms of both sterics (entries 6 and 7, Table 5.5) and electronics (entries 8 and 9, Table 5.5).

Table 5.5. Functional Group Tolerance: Substrate Screening[a]



entry	aryl halide	product	temperature	time (h)	yield (%)[b]
1			25	0.25	92 (82)
2			25	2	93 (90)
3			25	6	100 (97)
4			25	6	100 (95)
5			25	4	100 (98)
6			25	1	85 (83)[c]
7			25	1	79 (76)[c]
8			60	0.25	94 (92)
9			25	12	70 (67)
10		-	60	-	NR

[a]Reaction conditions: 1 mol% of catalyst, 1 mmol of halide, 1.1 mmol of phenylboronic acid, 1.2 mmol of KO*t*Bu, 3 mL of IPA. [b]GC yields versus calibrated internal standard dodecane (isolated yields in parentheses) - average of two runs. [c]Dehalogenation observed.

The catalyst was found to be active in performing the coupling of sterically hindered substrates furnishing mono- and di-ortho substituted coupling products in case of *ortho*-bromotoluene and bromomesitylene respectively. As depicted in the mechanistic cycle (Scheme 5.4), presence of steric bulk in the Pd(II) species (structure (I**V**) in Scheme 5.5) facilitates reductive elimination and the reactions yield the product in rather shorter reaction times. However, in both the reactions formation of dehalogenation side-product was observed. To analyze the activity of heterocyclic substrates, representative examples of both sulphur and nitrogen heterocyclic halides were subjected to the reaction conditions. Both the reactions furnished the desired coupling product. 2-Chlorothiopehene necessitated thermal heating as it did not perform the coupling at room temperature. Despite a few reports detailing C-F bond activation in Suzuki,[41] due to a very strong C-F bond, aryl fluorides had been long considered inert to Suzuki coupling reactions.[42] The present system failed to perform the desired coupling of *para*-fluorotoluene with phenylboronic acid (entry 10, Table 5.5).

5.3 Conclusions

In summary, we realized the potential of (NHC)Pd$(Cl)_2$-dimer species in synthesis and utilized them for achieving a very user-friendly and industrially amenable method to synthesize the targeted (NHC)Pd$(Cl)_2$-(X-pyridine) derivatives. We have established that our new method provides ready access to various such complexes by synthesizing different congeners of the complex. The structures of (**1**), (**4**), (**5**) and (**6**) have been elucidated unambiguously by single crystal diffraction study. Contrary to claimed general stability of similar complexes, we found (IPr)Pd$(Cl)_2$-(pyridine) variant to be sensitive to air and moisture. We have also determined the

scope and limitations of these catalytic species in Suzuki-Miyaura cross-coupling reaction. We found our alkoxide base – technical grade isopropanol Suzuki protocol to be the best system for these reactions. While the catalyst was found to be active for various functionalities on aryl substrates, it required longer reaction times and failed to perform coupling with alkyl chloride. The catalysts appear to possess desirable reactivity profiles with respect to two of the more important facets of coupling reactions relevant to applicability of these systems to medicinal, synthetic and industrial utilization: sterically hindered substrates and heterocyclic substrates. Although claims of steps towards a *universal* catalyst have been made,[19] we believe that the quest for a general one-catalyst-to-couple-them all system is still in its infancy. At this stage, a clearer picture of activation of catalyst is required for further development of these and similar catalyst systems. To that end, the factors governing activation of the catalyst and mechanism at play in coupling reactions are being explored to a greater depth in our laboratories.

5.4 Experimental Section

5.4.1 General considerations

- All aryl halides, alkyl halides and organoboron reagents were used as received (Aldrich, Acros).
- Solids were stored under argon in an MBraun dry-box.
- The solvents for synthesis were distilled from appropriate drying agents or were passed through an alumina column in an MBraun solvent purification system. The solvent for catalysis (technical grade isopropanol) was used as such without any drying.

- The *N*-heterocyclic carbenes (SIPr and IPr) were prepared according to the reported procedures.[43]
- All catalytic reactions were carried out under an atmosphere of argon, in screw-cap vials. ^{1}H- and ^{13}C-NMR spectra were recorded using a Varian-400 MHz spectrometer at ambient temperature in CDCl3 or DMSO-*d6* (Cambridge Isotope Laboratories, Inc.). The solvents for NMR spectroscopy were stored over molecular sieves.
- Flash chromatography was performed on silica gel (230-400 mesh) (Natland International Corporation).

5.4.2 Synthesis of (IPr)Pd(Cl)$_2$(2-chloropyridine) (1)

In a 25 ml flask equipped with a stirring-bar, a solution of 1 mmol (566 mg) of [(IPr)Pd(Cl)$_2$]$_2$ in 5 mL of THF was prepared by stirring for a few minutes at room temperature. Excess (190 μL, 2 mmol) of 2-chloropyridine was then added to the flask with a syringe. The mixture turned clear after allowing to stir for 3 hours at room temperature. Solvent and excess 2-chloropyridine were then removed *in vacuo* and the flask washed with 4 mL of DCM. The volume of DCM was reduced *in vacuo* to ca. 1 mL. Hexanes were added to the flask to precipitate the required complex. The precipitates were allowed to settle and supernatant decanted. The residual product was dried under vacuum to obtain the final product. The procedure furnished the final product, (IPr)Pd(Cl)$_2$(2-chloropyridine) in 81 % (550 mg) yield as light yellow powder. The structure was elucidated unambiguously by X-ray crystallography. The

crystals for single crystal analysis were grown by slow diffusion in a mixture of dichloromethane and hexanes.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.30 (singlet, 1H, py), 7.53 (br singlet, 3H, py), 7.40 (singlet, 4H, aromatic), 7.17-7.06 (multiplet, 2H, 2 x C*H*-imidazole; 2H aromatic), 3.16 (br singlet, 4H, methine), 1.47 (singlet, 12H, 2 x CH(CH_3)$_2$), 1.11 (singlet, 12H, 2 x CH(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.9, 147.8, 139.2, 130.4, 126.4, 125.2, 124.0, 122.9, 29.0, 26.6, 26.4, 23.4. Elemental Analysis Calcd for $C_{32}H_{40}Cl_3N_3Pd$: C – 56.57; H – 5.93; N – 6.18. Found: C – 56.93; H – 6.02; N – 6.36.

5.4.3 Synthesis of (SIPr)Pd(Cl)$_2$(2-chloropyridine) (2)

A procedure similar to procedure for synthesis of (**1**) was followed with 568 mg (1 mmol) of [(SIPr)Pd(Cl)$_2$]$_2$ in place of [(IPr)Pd(Cl)$_2$]$_2$. The reaction mixture became clear in 5 minutes but was allowed to stir for 3 hours at room temperature for maximum conversion. Following the procedure detailed above, the final product, (SIPr)Pd(Cl)$_2$(2-chloropyridine) was obtained in 73 % (497 mg) yield as light brown powder.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.11 (doublet, *J* = 5.2 Hz, 1H, py), 7.47-7.42 (multiplet, 3H, py), 7.34-7.32 (multiplet, 4H, aromatic), 7.14 (multiplet, 1H, aromatic), 7.04 (multiplet, 1H, aromatic), 4.12 (singlet, 4H, 2 x CH_2-imidazole), 3.59-3.56 (multiplet, 4H, methine), 1.54 (doublet, *J* = 4.0 Hz, 12H, 2 x CH(CH_3)$_2$), 1.25 (doublet, *J* = 6.4 Hz, 12H, 2 x CH(CH_3)$_2$). ^{13}C-

NMR (100 MHz, $CDCl_3$): δ = 186.0, 152.4, 151.7, 139.1, 134.7, 129.8, 129.6, 126.3, 124.8, 124.4, 122.8, 53.7, 29.5, 27.2, 26.9, 24.4. Elemental Analysis Calcd for $C_{32}H_{42}Cl_3N_3Pd$: C – 56.40; H – 6.21; N – 6.17. Found: C – 56.58; H – 6.02; N – 6.21.

5.4.4 Synthesis of (IPr)Pd(Cl)$_2$(2-bromopyridine) (3)

In a 25 ml flask equipped with a stirring-bar, a solution of 1 mmol (566 mg) of $[(IPr)Pd(Cl)_2]_2$ in 5 mL of THF was prepared by stirring for a few minutes at room temperature. Excess (190 μL, 2 mmol) of 2-bromopyridine was then added to the flask with a syringe. The mixture was allowed to stir for 12 hours at room temperature. Solvent and excess 2-bromopyridine were then removed *in vacuo* and the flask washed with 4 mL of DCM. The volume of DCM was reduced *in vacuo* to ca. 1 mL. Hexanes were added to the flask to precipitate the required complex. The precipitates were allowed to settle and supernatant decanted. The residual product was dried under vacuum to obtain the final product. The procedure furnished the final product, (IPr)Pd(Cl)$_2$(2-bromopyridine) in 69 % (499 mg) yield as light yellow powder.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.20 (singlet, 1H, py), 7.54 (br singlet, 3H, py), 7.40 (singlet, 4H, aromatic), 7.21-7.14 (multiplet, 2H, 2 x C*H*-imidazole; 2H aromatic), 3.22 (br multiplet, 4H, methine), 1.48 (singlet, 12H, 2 x CH(CH_3)$_2$), 1.12 (singlet, 12H, 2 x CH(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 154.2, 153.4, 147.7, 147.3, 144.4, 140.3, 135.7, 135.2, 131.3, 130.5, 125.5, 124.4, 29.0, 26.8, 23.8, 23.1. Elemental Analysis Calcd for $C_{32}H_{40}BrCl_2N_3Pd$: C – 53.09; H – 5.57; N – 5.80. Found: C – 53.35; H – 6.00; N – 5.36.

5.4.5 Synthesis of (SIPr)Pd(Cl)$_2$(2-bromopyridine) (4)

A procedure similar to procedure for synthesis of (**3**) was followed with 568 mg (1 mmol) of [(SIPr)Pd(Cl)$_2$]$_2$ in place of [(IPr)Pd(Cl)$_2$]$_2$. Following the procedure detailed above, the final product, (SIPr)Pd(Cl)$_2$(2-bromopyridine) was obtained in 65 % (472 mg) yield as light yellow powder. The structure was elucidated unambiguously by X-ray crystallography. The crystals for single crystal analysis were grown by slow diffusion in a mixture of THF and hexanes.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.08 (doublet, *J* = 4.0 Hz, 1H, py), 7.46-7.44 (multiplet, 3H, py), 7.35-7.29 (multiplet, 5H, aromatic), 7.06 (singlet, 1H, aromatic), 4.13 (singlet, 4H, 2 x C*H*$_2$-imidazole) 3.60 (br singlet, 4H, methine), 1.56 (doublet, J = 13.2 Hz, 12H, 2 x CH(C*H*$_3$)$_2$), 1.26 (doublet, J = 7.6 Hz, 12H, 2 x CH(C*H*$_3$)$_2$) ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 186.0, 152.6, 148.9, 143.7, 138.8, 130.2, 129.8, 124.6, 124.4, 123.2, 53.4, 28.2, 27.1, 24.4, 23.8. Elemental Analysis Calcd for $C_{32}H_{42}BrCl_2N_3Pd$: C – 52.95; H – 5.83; N – 5.79. Found: C – 52.94; H – 5.79; N – 5.53.

5.4.6. Synthesis of (IPr)Pd(Cl)$_2$(pyridine) (5)

In a 25 ml flask equipped with a stirring-bar, a solution of 1 mmol (566 mg) of [(IPr)Pd(Cl)$_2$]$_2$ in 5 mL of THF was prepared by stirring for a few minutes at room temperature. Excess (162 μL, 2 mmol) of pyridine was then added to the flask with a syringe. The mixture was allowed to stir for 12 hours at room temperature. Solvent and excess pyridine were then

removed *in vacuo* and the flask washed with 4 mL of DCM. The volume of DCM was reduced *in vacuo* to ca. 1 mL. Hexanes were added to the flask to precipitate the required complex. The precipitates were allowed to settle and supernatant decanted. The residual product was dried under vacuum to obtain the final product. The procedure furnished the final product, (IPr)Pd(Cl)$_2$(pyridine) in 70 % (451 mg) yield as off-white powder. The structure was elucidated unambiguously by X-ray crystallography. The crystals for single crystal analysis were grown by slow diffusion in a mixture of THF and hexanes.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.55 (singlet, 2H, py), 7.58-7.49 (multiplet, 3H, py), 7.36-7.34 (multiplet, 4H, aromatic), 7.12 (singlet, 2H, 2 x C*H*-imidazole), 7.11-7.09 (multiplet, 2H, aromatic), 3.18 (triplet, *J* = 6.8 Hz, 4H, methine), 1.50 (doublet, *J* = 6.8, 12H, 2 x CH(CH_3)$_2$), 1.13 (doublet, *J* = 6.8, 12H, 2 x CH(CH_3)$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.7, 146.9, 137.6, 135.4, 130.5, 125.2, 124.2, 28.9, 26.5, 23.4. Elemental Analysis Calcd for $C_{32}H_{41}Cl_2N_3Pd$: C – 59.59; H – 6.41; N – 6.51. Found: C – 59.73; H – 6.49; N – 6.47.

5.4.7 Synthesis of (SIPr)Pd(Cl)$_2$(pyridine) (6)

A procedure similar to procedure for synthesis of (**5**) was followed with 568 mg (1 mmol) of [(SIPr)Pd(Cl)$_2$]$_2$ in place of [(IPr)Pd(Cl)$_2$]$_2$. Following the procedure detailed above, the final product, (SIPr)Pd(Cl)$_2$(pyridine) was obtained in 65 % (421 mg) yield as off-white powder. The structure was elucidated unambiguously by X-ray crystallography. The crystals for single crystal analysis were grown by slow diffusion in a mixture of THF and hexanes.

^{1}H-NMR (400 MHz, $CDCl_3$): δ = 8.52 (doublet, *J* = 5.2 Hz, 2H, py), 7.52 (multiplet, 1H, py), 7.43-7.39 (multiplet, 2H, py), 7.31-7.29 (multiplet, 4H, aromatic), 7.10-7.06 (multiplet, 2H, aromatic), 4.06 (singlet, 4H, 2 x C*H*$_2$-imidazole) 3.59 (triplet, *J* = 6.8 Hz, 4H, methine), 1.57 (doublet, *J* = 6.8 Hz, 12H, 2 x CH(C*H*$_3$)$_2$), 1.27 (doublet, *J* = 6.8 Hz, 12H, 2 x CH(C*H*$_3$)$_2$) ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 151.3, 147.6, 137.4, 129.5, 124.5, 124.1, 53.9, 28.8, 26.8, 24.3. Elemental Analysis Calcd for $C_{32}H_{43}Cl_2N_3Pd$: C – 59.40; H – 6.70; N – 6.49. Found: C – 59.35; H – 6.38; N – 6.21.

5.4.8 Representative Procedure for Suzuki-Miyaura Coupling

In a dry-box, 1.2 mmol of base was added to a screw-cap vial charged with the specified concentration of (NHC)Pd(Cl)$_2$(X-pyridine) complex. 134 mg (1.1 mmol) of phenylboronic acid was added and the vial sealed with a rubber septum. Outside the drybox, 3 mL of technical grade solvent was injected in the vial with a syringe. 1 mmol of the halide was then added to the vial and the reaction mixture allowed to shake on a Lab-Line Orbit Shaker (set at 25 °C or 60 °C – J-Kem Scientific, Kem-Lab Controller) for the indicated time. The reactions were monitored by Agilent 6890N or Agilent 6890Plus gas chromatographs versus an internal standard - dodecane. After maximum conversion the reaction mixture was quenched with water. The organic layer was extracted with methyl-*tert*-butyl ether. The organic layer extracts were combined and washed with saturated saline solution, and then dried over magnesium sulfate. The solvent was then filtered and evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel (hexanes or 10 % ethyl acetate in hexanes).

5.4.9. Catalyst Screening

In a dry-box, 134 mg (1.2 mmol) of KO*t*Bu was added to a screw-cap vial charged with the 1 % concentration of (NHC)Pd(Cl)$_2$(X-pyridine) complex. 134 mg (1.1 mmol) of phenylboronic acid was added and the vial sealed with a rubber septum. Outside the drybox, 3 mL of technical grade isopropanol was injected in the vial with a syringe. 118 μL (1 mmol) of the *para*-chlorotoluene was then added to the vial and the reaction mixture allowed to shake on a Lab-Line Orbit Shaker (set at 25 °C or 60 °C – J-Kem Scientific, Kem-Lab Controller) for the indicated time. The reactions were monitored by Agilent 6890N or Agilent 6890Plus gas chromatographs versus an internal standard - dodecane. For isolating 4-methyl biphenyl (entry 2, Table 4) the reaction mixture was quenched with water. The organic layer was extracted with methyl-*tert*-butyl ether. The organic layer extracts were combined and washed with saturated saline solution, and then dried over magnesium sulfate. The solvent was then filtered and evaporated *in vacuo*.to obtain the final product in 86% yield (144 mg). The isolated product was spectroscopically analyzed. The ^{1}H- and ^{13}C-NMR spectra of the product was found to be in agreement with previously reported spectroscopic data.

4-Methyl-biphenyl[44] (Table 5.4, entry 2) The procedure afforded 144 mg (86 %) of the isolated product.

5.4.10. Substrate Screening in Suzuki-Miyaura Cross-Coupling Reaction

In a dry-box, 134 mg (1.2 mmol) of KO*t*Bu was added to a screw-cap vial charged with the 1 % concentration (6.8 mg) of (IPr)Pd(Cl)$_2$(2-chloropyridine) complex. 134 mg (1.1 mmol) of phenylboronic acid was added and the vial sealed with a rubber septum. Outside the drybox, 3 mL of technical grade isopropanol was injected in the vial with a syringe. 1 mmol of the halide was then added to the vial and the reaction mixture allowed to shake on a Lab-Line Orbit Shaker (set at 25 °C or 60 °C – J-Kem Scientific, Kem-Lab Controller) for the indicated time. The reactions were monitored by Agilent 6890N or Agilent 6890Plus gas chromatographs versus an internal standard - dodecane. After maximum conversion the reaction mixture was quenched with water. The organic layer was extracted with methyl-*tert*-butyl ether. The organic layer extracts were combined and washed with saturated saline solution, and then dried over magnesium sulfate. The solvent was then filtered and evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel (hexanes or 10 % ethyl acetate in hexanes). All isolated products were spectroscopically analyzed. The ^{1}H- and ^{13}C-NMR spectra for all the coupling products were found to be in agreement with previously reported spectroscopic data.

Isolated Products:

4-Methyl-biphenyl[44] (Table 5.5, entry 1) The procedure afforded 137 mg (82 %) of the isolated product.

4-Methoxy-biphenyl[45] (Table 5.5, entry 2) The procedure afforded 165 mg (90 %) of the isolated product.

4-Methoxy-biphenyl[45] (Table 5.5, entry 3) The procedure afforded 178 mg (97 %) of the isolated product.

1-Biphenyl-4-yl-ethanone[46] (Table 5.5, entry 4) The procedure afforded 186 mg (95 %) of the isolated product.

4-Trifluoromethyl-biphenyl[47] (Table 5.5, entry 5) The procedure afforded 217 mg (98 %) of the isolated product.

2-Methyl-biphenyl[48] (Table 5.5, entry 6) The procedure afforded 139 mg (83 %) of the isolated product.

2,4,6-Trimethyl-biphenyl[49] (Table 5.5, entry 7) The procedure afforded 148 mg (76 %) of the isolated product.

2-Phenyl-thiophene[50] (Table 5.5, entry 8) The procedure afforded 147 mg (92 %) of the isolated product.

2-Phenyl-pyridine[51] (Table 5.5, entry 9) The procedure afforded 103 mg (67 %) of the isolated product.

5.5 Acknowledgement

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5.6 References and Notes

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24. Reaction procedure involved *in situ* deprotonation of NHC salt with a base and required heating the reaction mixture at 80 ^{o}C for 16 hours.

25. The details of the synthetic procedure are presented in the experimental section.

26. Empirical formula = $C_{32}H_{39}Cl_3N_3Pd$, Formula weight = 678.41, Temperature = 297(2) K, Wavelength = 0.71073 A, Crystal system = Monoclinic, Space group = Cc, Unit cell dimensions: a = 34.2738(7) A, alpha = 90 deg, b = 15.5109(3) A, beta = 106.72 deg, c = 12.7275(3) A, gamma = 90 deg, Volume = 6480.1(2) A^3, Z = 8, Calculated density = 1.391 Mg/m^3, Absorption coefficient = 0.845 mm^-1, Reflections collected / unique = 60134 / 11422 [R(int) = 0.0158], Refinement method = Full-matrix least-squares on F^2, Goodness-of-fit on F^2 = 1.080, Final R indices [I>2s(I)] R1 = 0.0240, wR2 = 0.0631, R indices (all data) R1 = 0.0291, wR2 = 0.0664.

27. Empirical formula = $C_{32}H_{42}BrCl_2N_3Pd$, Formula weight = 725.90, Temperature = 295(2) K, Wavelength = 0.71073 Å, Crystal system = Monoclinic, Space group = C2/c, Unit cell dimensions: a = 34.2809(12)Å, alpha = 90 deg, b = 15.5252(5)Å, beta = 107.039(1) deg, c = 12.8182(5)Å, gamma = 90 deg, Volume = 6522.6(4) Å^3, Z = 8, Calculated density = 1.478 Mg/m^3, Absorption coefficient = 1.983 mm^{-1}, F(000) = 2960, Reflections collected / unique = 29159 / 8545 [R(int) = 0.0228], Refinement method = Full-matrix least-squares on F^2, Goodness-of-fit on F^2 = 1.078, Final R indices [I>2sigma(I)] R1 = 0.0550, wR2 = 0.1588, R indices (all data) R1 = 0.0638, wR2 = 0.1686.

28. Empirical formula = $C_{32}H_{41}Cl_2N_3Pd$ 0.25(C_4H_8O), Formula weight = 663.00, Temperature = 568(2) K, Wavelength = 0.71073 Å, Crystal system = Monoclinic, Space

group = $P2_1/n$, Unit cell dimensions: a = 21.4514(14) Å, alpha = 90 deg, b = 14.7266(10) Å, beta = 106.922(1) deg, c = 21.9025(15) Å, gamma = 90 deg, Volume = 6619.5(8) $Å^3$,Z = 8, Calculated density = 1.331 Mg/m^3, Absorption coefficient = 0.748 mm^{-1}, F(000) = 2752, Reflections collected / unique = 44125 / 8516 [R(int) = 0.0313], Refinement method = Full-matrix least-squares on F^2, Goodness-of-fit on F^2 = 1.099, Final R indices [I>2σ(I)] R1 = 0.0863, wR2 = 0.2638 R indices (all data) R1 = 0.0931, wR2 = 0.2658.

29. Empirical formula = $C_{32}H_{43}Cl_2N_3Pd$, Formula weight = 646.99 = Temperature = 295(2) K, Wavelength = 0.71073 Å, Crystal system = Monoclinic, Space group = $P2_1/c$, Unit cell dimensions: a = 15.8956(14) Å, alpha = 90 deg, b = 15.5844(14) Å, beta = 99.144(2)deg, c = 12.8848(11) Å, gamma = 90 deg, Volume = 3151.3(5) $Å^3$, Z = 4, Calculated density = 1.364 Mg/m^3, Absorption coefficient = 0.783 mm^{-1}, F(000) = 1344, q range for data collection = 2.30 to 22.50 deg, Reflections collected / unique = 30038 / 4095 [R(int) = 0.0548], Refinement method = Full-matrix least-squares on F^2, Goodness-of-fit on F^2 = 1.212, Final R indices [I>2sigma(I)] R1 = 0.0450, wR2 = 0.1041, R indices (all data) R1 = 0.0530, wR2 = 0.1101.

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CHAPTER 6

SYNTHESIS OF PHOSPHORUS ESTERS BY TRANSESTERIFICATION MEDIATED BY N-HETEROCYCLIC CARBENES (NHCs)

6.1. Introduction

The versatile nucleophilic organic catalysts *N*-heterocyclic carbenes (NHCs) have been shown to effectively mediate the transesterification of phosphorus esters under mild conditions. User-friendly imidazolium salts can also be employed as precatalysts.

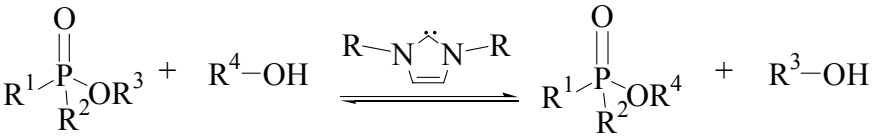
6.2. Results and Discussion

Phosphorus esters are important functional groups in organic synthetic chemistry. They not only play an important role as protective groups in pharmaceuticals[1] but are also used as reagents in organic transformations (e.g. Wadsworth-Emmons reaction)[2] or development of analytical tools.[3] Moreover, on industrial scale, *P*-esters find applications in agrochemicals as fertilizers,[4] pesticides[5] and insecticides.[6] The major means for preparation of *P*-esters involve alkyl dichlorophosphines or the Michaelis-Arbuzov reaction. While the dichlorophosphines are usually expensive, the Michaelis-Arbuzov[7] reaction suffers from low yields when hindered

substrates are used. Gagné has reported the use of alkali metal alkoxide clusters as efficient catalysts for ester interchange reaction leading to phosphorus esters.[8] A method relying on $Ti(OR)_4$/ROH catalyzed transesterification has also been reported but suffers from long reaction times and a lack of reactivity towards phosphonates.[9] An inexpensive, metal-free, catalytic protocol for synthesis of phosphorus esters via transesterification would have a significant impact on the accessibility of this class of compounds.

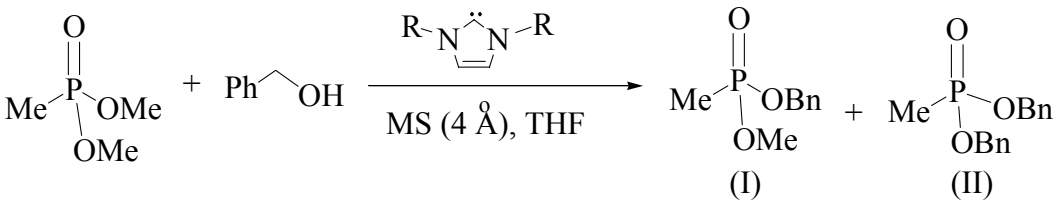
We previously reported on the use of *N*-heterocyclic carbenes (NHCs) as efficient transesterification catalysts for primary and secondary alcohols.[10] We have extended this methodology to now include *P*-esters as substrates achieving excellent yields using mild conditions (Scheme 1). Phosphonate esters, which are usually unreactive using the Michaelis-Arbuzov protocol, underwent transesterification effectively with use of various NHCs as catalysts.

Scheme 6.1. NHC Catalyzed Transesterification of *P*-Esters



Extensive works by Wanzlick[11], Bertrand[12], Arduengo[13] and others[14] have shown that the singlet nucleophilic carbenes are neutral compounds having a divalent carbon atom with two non-bonding electrons. Non-toxicity, non-pyrophoric nature, tunable sterics and electronics have helped establish NHCs as versatile nucleophilic organic catalysts effectively mediating organic transformations.[15-23]

Table 6.1. Screening of *N*-heterocyclic carbenes



entry	catalyst	time (h)	yield (%)	product ratio (I : II)
1	R = Cyclohexyl	2	71	90 :1 0
2	R = Cyclohexyl	8	90	75 : 25
3	R = Adamantyl	2	35	100:0
4	R = *tert*-Butyl	2	32	100:0
5	R = 2,6-Diisopropylphenyl	18	0	-
6	R = 2,4,6-Trimethylphenyl	18	0	-

[a] Reaction conditions: 5 mol% catalyst, 1 mmol of DMMP, 1 mmol of BnOH, 0.5 g of molecular sieves, 1 mL of THF, NMR yields (average of two runs).

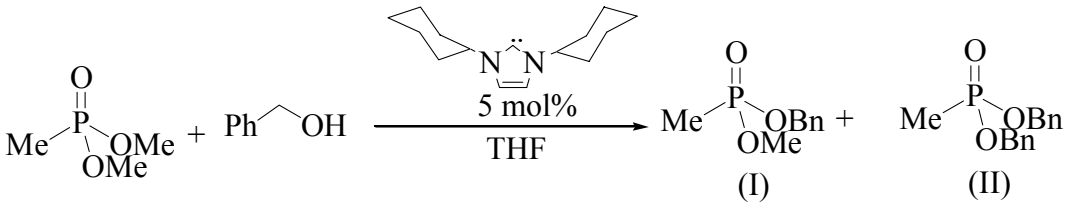
The screening of various NHCs in the reaction of dimethyl methylphosphonate (DMMP) with benzyl alcohol showed the alkyl substituted NHCs, ICy – {1,3-bis(cyclohexyl)-imidazol-2-ylidene}, IAd – {1,3-bis(adamantyl)-imidazol-2-ylidene} and I^{t}Bu – {1,3-bis(*tert*-butyl)-imidazol-2-ylidene} were able to act as mediators in this transesterification reaction. The cyclohexyl substituted NHC, ICy, was found to be the best catalyst giving good yield in only 2 hours (entry 1, Table 6.1). Better yields can be obtained on increasing the reaction time but this allows for an increase in formation of di-esterified product (entry 2, Table 6.1). Sterically demanding, alkyl substituted NHCs, IAd and I^{t}Bu, provide moderate yields. [24] The aryl substituted NHCs, which are less nucleophilic than the alkyl substituted counterparts[14,25] did not show activity in this transformation. Even on increasing the catalyst loading, IPr (1,3-bis(2,6-

diisopropylphenyl)-imidazol-2-ylidene) and IMes (1,3-bis(2,4,6-trimethylphenyl)-imidazol-2-ylidene did not furnish the desired product.[26]

To fully exploit the potential of this reaction, we examined a wide array of conditions. The data presented in Table 6.2 illustrate the effect of various parameters on the efficiency of this protocol. Since transesterification is an equilibrium process, removal of products from the reaction mixture drives the reaction in the forward direction. This is achieved by use of molecular sieves (4 Å) that absorb the methanol formed in the course of the reaction and improve conversion. Initially similar conversions are observed in reactions with and without molecular sieves. However, on allowing the reaction to stir for longer time periods, a significant difference in conversion can be observed (entries 1-4, Table 6.2). Moreover, formation of only mono-esterified product in the absence of molecular sieves is indicative of the reaction being reversible under equilibrium conditoins, rather than undergoing a second esterification.[27]

Not surprisingly, an increase in temperature has a favorable effect on conversion. However, the selectivity suffers in this case and an increase in formation of the di-esterified product is observed (entries 3 and 5, Table 6.2). The effect of excess alcohol was also studied. On conducting the reaction over a longer time period, quantitative conversion with loss of selectivity was observed (entries 7 and 8, Table 6.2). To increase the scope of the reaction, ethyldiphenyl phosphinate was also tested for activity. The reaction proceeded to furnish the product in good yield (entry 9, Table 6.2). Various reactions presented in Table 2 reveal simple and efficient ways to alter the final outcome of the reaction providing flexibility in the protocol.[28]

Table 6.2. Impact of variation of reaction parameters on NHC catalysed transesterification of *P*-esters[a]



(I) (II)

entry	conditions	time (h)	yield (%)	product ratio (I : II)
1	No MS	2	67	100:0
2	No MS	8	70	100:0
3	with MS	2	71	90:10
4	with MS	8	90	75:25
5	T = 40 ^{o}C	2	87	60:40
6	2 equiv Bn-OH	2	75	100:0
7	2 equiv Bn-OH	36	100	45:55
8	2 equiv Bn-OH	120	100	36:64
9	EDPP[b]	6	72	-

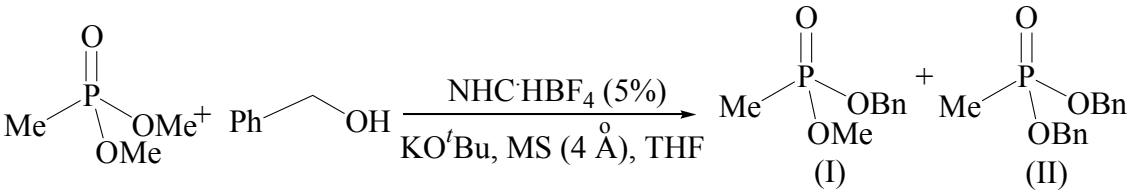
[a] Standard reaction conditions: 5 mol% catalyst, 1 mmol of DMMP, 1 mmol of BnOH, 0.5 g of molecular sieves (4 Å), 1 mL of THF, NMR yields (average of two runs),[b] EDPP = ethyldiphenyl phosphinate: 0.5 g of molecular sieves (5 Å)

To render the protocol more user-friendly, various commercially available, NHC pre-catalysts were also tested for activity. The use of ionic liquid, bmim·HBF_4 (N,N'-butylmethyl imidazol-2-ylidene) is of particular interest since it demonstrated good conversion with preferential formation of mono-esterified product in >80% yield (entry 1, Table 6.3). The imidazolium salts of ICy, IAd and I^{t}Bu also furnished moderate to good yields under similar conditions with ICy·HBF_4 proving to be the best pre-catalyst for this transformation.[29] To

achieve better selectivity from the in situ generated-carbene-protocol, experiments were performed with a slight change in experimental conditions. ICy·HBF_4 was employed in the usual reaction conditions without the presence of molecular sieves (entry 3, Table 6.3). Better selectivity was achieved under these conditions. However, product conversion suffered because of the absence of molecular sieves. The reaction did not proceed further than 55% conversion after 24 hrs. Interestingly, no change in selectivity was observed after allowing the reaction to proceed for 24 hrs.

An additional important use of phosphorus esters is in the manufacture of chemical nerve agents. Chemical weapons such as VX (S-2-(diisopropylamino)ethyl O-ethyl methylphosphonothioate) and GB-Sarin are various forms of *P*-esters. These agents inhibit the control of acetylcholinesterase over the central nervous system by reacting with this enzyme in an irreversible fashion.[6,30] Recent developments have brought attention to chemical weapons, especially methods for their detoxification/decomission. The usual methods of detoxification of the nerve agent VX are incineration and chemical neutralization. However, these methods suffer from limitations making them less acceptable. Chemical detoxification in particular, suffers from release of harmful side products in yields as high as 15%.[31] Moreover, the reagents have to be used in stoichiometric amounts. Metal catalyzed methods for chemical detoxificaion of VX nerve agent have been proposed.[32] The NHC mediated transesterification of *P*-esters could be an attractive alternative to the conventional methods of VX detoxification. Since methyl and ethyl esters are more difficult to cleave compared to benzyl esters,[27] we propose that, using the described methodology, the properties of *P*-esters can be altered to render them innocuous.[33]

Table 6.3. *In-situ* generation of catalyst



entry	catalyst precursor	time(h)	yield (%)	product ratio (I : II)
1	bmim·HBF_4	6	84	81:19
2	ICy·HBF_4	3	71	70:30
3	ICy·HBF_4	3	46[b]	85:15
4	IAd·HBF_4	3	58	63:37
5	I^{t}Bu·HBF_4	12	72	60:40

[a] Reaction conditions: 5 mol% catalyst, 0.9 eq base, 1 mmol of DMMP, 1 mmol of BnOH, 0.5 g of molecular sieves, 1 mL of THF, NMR yields (average of two runs) [b]no molecular sieves

6.3 Conclusions

In summary, an organocatalytic approach for synthesis of phosphorus esters is described. Various parameters affecting the transformation have been examined. Applications of this method can range from synthesis of pharmaceutically important molecules to detoxification of *P*-ester nerve agents. Efforts aimed at expanding the scope of this user-friendly reaction and understanding its mechanism are presently underway.

6.4. Experimental Section

6.4.1. General Consideratons

- All reactions were carried out in an MBraun glovebox containing dry argon or using standard Schlenk techniques under an atmosphere of dry argon.
- Solvents for synthesis of imidazol-2-ylidenes or imidazolium salts were distilled from appropriate drying agents or were passed through an alumina column in an MBraun solvent purification system.
- *N*-heterocyclic carbenes (NHCs) were synthesized according to the literature procedures (although carbenes IAd and I^{t}Bu and imidazolium salts of ICy, IAd and I^{t}Bu are commercially available – see references 24 and 29 in the ms).
- Solvents for NMR spectroscopy were degassed with argon and dried over molecular sieves.
- NMR spectra were collected on 300 MHz or 400 MHz Varian Gemini spectrometers.
- ^{31}P-NMR spectra were recorded with 85 % phosphoric acid as external standard.
- Flash chromatography was performed on silica gel 60 (230-400 mesh) (Natland International Corporation).

6.4.2 Representative Procedure

Under an atmosphere of argon, 1 mmol of *P*-ester was loaded to a screw-cap vial charged with the imidazol-2-ylidene or imidazolium salt (5 mol %). Molecular sieves (4 Å, 0.5 gm /

mmol of alcohol) were then added to the vial. Next, alcohol (1 mmol) and THF (1 mL) were added to the vial. For reactions with carbene generated *insitu*, potassium *tert*-butoxide (0.06 mmol, 6.7 mg) was added to the reaction mixture. The vial was then sealed with cap equipped with a rubber septum. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at indicated temperature (25 ^{o}C for room temperature reactions) – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate at ambient temperature for the indicated time. The reactions were monitored by ^{31}P-NMR of an aliquot in C_6D_6 with 85 % phosphoric acid as external standard. The spectral data of the products was found to be in agreement with the literature values.

Methyl-phosphonic acid benzyl ester methyl ester: ^{31}P-NMR (161.88 MHz, C_6D_6) δ 32.90 ppm. MS (GC) *m/z* 200(M^+)

Methyl-phosphonic acid dibenzyl ester: ^{31}P-NMR (161.88 MHz, C_6D_6) δ 32.33 ppm. MS (GC) *m/z* 276(M^+)

Diphenyl-phosphinic acid benzyl ester: ^{31}P-NMR (161.88 MHz, C_6D_6) δ 32.92 ppm. MS (GC) *m/z* 308(M^+)

6.4.3 Screening of N-Heterocyclic Carbenes

Under an atmosphere of argon, dimethylmethyl phosphonate - DMMP(1 mmol, 109 μl) was loaded to a screw-cap vial charged with the carbene (0.05 mmol). Molecular sieves (4 Å, 0.5

gm) were then added to the vial. Next, benzyl alcohol (1 mmol, 104 μl) and solvent – THF (1 mL) were added to the vial. The vial was then sealed with cap equipped with a rubber septum. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 25 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate at ambient temperature for the indicated time. The reactions were monitored by ^{31}P-NMR of an aliquot in C_6D_6 with 85 % phosphoric acid as external standard.

6.4.4 Screening of Imidazolium Salts as Pre-catalysts

Under an atmosphere of argon, dimethylmethyl phosphonate – DMMP (1 mmol, 109 μl) was loaded to a screw-cap vial charged with the carbene precursor (0.05 mmol). Molecular sieves (4 Å, 0.5 gm) were then added to the vial. Next, potassium *tert*-butoxide (0.9 eq, 5.0 mg) and solvent – THF (1 mL) were added to the vial. The vial was then sealed with a cap equipped with rubber septum. The mixture was stirred for 15 minutes, allowing deprotonation of the imidazolium salt. After 15 minutes, benzyl alcohol (1 mmol, 104 μl) was added. The reaction mixture was allowed to shake on a Lab-Line Orbit Shaker (set at 25 ^{o}C – J-Kem Scientific, Kem-Lab Controller) or stirred over a magnetic plate at ambient temperature for the indicated time. The reactions were monitored by ^{31}P-NMR of an aliquot in C_6D_6 with 85% phosphoric acid as external standard.

6.5 Acknowledgements

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CHAPTER 7

SUMMARY

The principal focus of our research efforts was the development of catalysts and methodologies that would have broader scope and would offer flexibility in order to be acceptable in both laboratorial and industrial applications. Our goal of addressing the challenge of developing effective catalytic systems led us to identifying suitable NHC catalysts and catalyst modifiers. Development of NHCs as both organic catalysts as well as ancillary ligands was recognized as the essential step required towards achieving our goal.[1]

The major functions of an ancillary ligand are to keep the metal in a state of low nuclearity, to stabilize intermediates and to assign a positive effect on the selectivity and reactivity of the system via alteration of steric and electronic factors. NHCs have proven to be very suitable ligands in playing all the above mentioned roles in a variety of different transformations.[2]

Several key aspects of a catalytic system mandate consideration to make it a desirable process. Amongst them more active, inexpensive and highly selective catalyst is a necessity. High activity ensures lower catalyst loadings and hence helps making the process economically more viable. Similarly, achieving prolonged catalytic activity of the catalyst by improving the stability of the ligands also helps in making a positive impact on the economics of the process. Apart from high activity at lower catalyst loadings, better catalyst separation is also an important feature. While this also helps in bringing down the overall cost of the process by circumventing

the expenditure associated with clean-up of the product, the impact of such a system on environment gains much more credence. Easy accessibility is another feature which is imperative for any class of compounds to be widely accepted by the synthetic community. Cognizant of such a need, design and simplified synthesis of NHC-palladium complexes were devised. Simple syntheses of three different classes of NHC-palladium catalysts were achieved in an attempt to make these complexes worthy of acceptance in different methodologies.

Initially our research interests were centered around in situ generated catalysts and we reported considerable advances in utilization of air and moisture stable NHC precursor salts in conjunction with palladium to mediate a number of catalytic coupling reactions. Coupling activity of organotin,[3] organosilane,[4] organomagnesium[5] and organoboron[6] reagents with halides and pseudo-halides was studied and reported upon. Apart from these reactions, Buchwald-Hartwig amination,[7] α-arylation of ketones,[8] arylation of alkynes,[9] Heck coupling,[10] telomerization,[11] dehalogenation of aryl halides[12] and dimerization of alkynes[13] were also studied with NHC-palladium systems. Later reports have mostly carried accounts of well-defined catalysts. Well-defined catalysts allow the possibility of providing an insight into workings of the catalyst if analyzed crystallography.[14]

In the work presented, three different series of NHC-palladium complexes were synthesized via simple procedures. The synthesized NHC-Pd complexes were analyzed for activity in cross-coupling reactions and the scope and limitations of the catalytic systems were analyzed.

NHC-Pd-carboxylate complexes were subjected to Suzuki-Miyaura cross-coupling reaction.[15] The complexes demonstrated exceptional activity as a wide array of difficult

substrates was coupled under mild set of conditions. First examples of activated C(sp^3)-chloride couplings were achieved under very mild reactions.

Similar complexes were utilized for α-arylation of ketones and various reaction parameters were studied.[16] A wide array of functionalized halides were investigated to achieve a better understand of the bearings of electronics and sterics on the reaction pathway.

NHC-Pd-dimers were synthesized and utilized for coupling aryl halides and Grignard reagents in efforts aimed at development of Kumada-Tamao-Corriu methodology.[17] The protocol was demonstrated to be amenable to industrial scale applications by achieving excellent yields in scaled-up process. C-F bond activation of an unactivated aryl fluoride was also achieved.

A series of novel NHC-Pd$(Cl)_2$(X-pyridine) complexes was synthesized.[18] Cognizant of the potent activity of NHC-Pd-dimers, we employed them as synthetic precursors to arrive at a successful protocol extremely simple in its execution. The complexes were studied by crystallography and scope and limitations of the catalysts were determined by analyzing their activity in Suzuki-Miyaura cross-coupling.

Potent nucleophilicity of NHCs was exploited in arriving at a protocol for achieving metal-free transesterification reactions.[19] The scope of the reaction was expanded to include secondary alcohols[20] and phosphorus esters.[21] The environmentally-friendly protocol was proposed to be an alternate method for detoxification of chemical nerve agents such as VX.

In summary, different series of NHC-palladium complexes were synthesized via extremely simplified protocols making them amenable to adoption by industry as well as laboratorial applications. The complexes were analyzed for activity in various cross-coupling reactions such as Suzuki-Miyaura cross-coupling, α-arylation of ketones and Kumada-Tamao-Corriu cross-coupling. NHCs were also utilized as organocatalysts in achieving effective

transesterification of phosphorus esters. Significant developments in these methodologies were achieved promising new platforms for further explorations.[22] Achieving better catalytic systems summon wide adoption of these protocols in both synthetic laboratories and chemical industries.

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APPENDIX

1. Crystal Data and Structure Refinement for $[(SIPr)Pd(Cl)_2]_2$

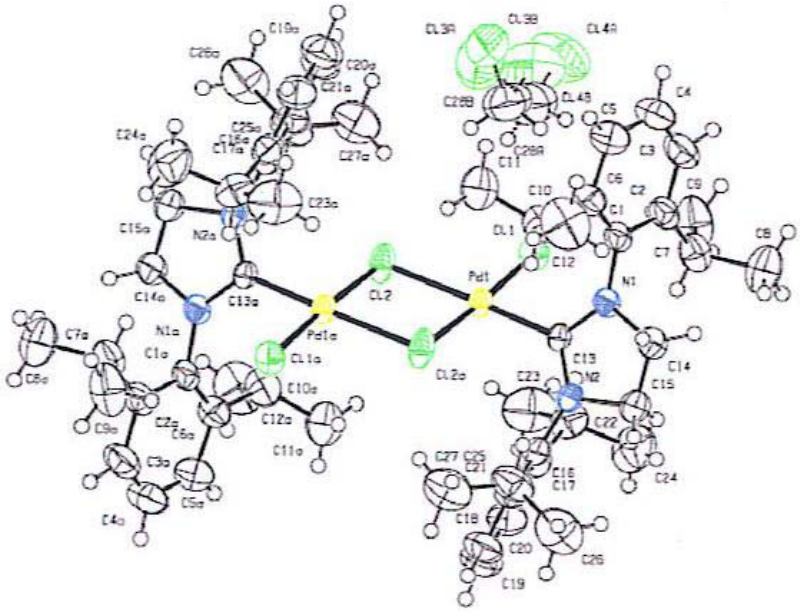

Table 1.1.

Identification code	nol340m
Empirical formula	$C_{56}H_{80}Cl_8N_4Pd_2$
Formula weight	1305.64
Temperature	297(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 14.3993(5) A alpha = 90 deg.
	b = 19.2189(6) A beta = 90 deg.
	c = 23.0287(7) A gamma = 90 deg.
Volume	6372.9(4) A^3
Z, Calculated density	4, 1.361 Mg/m^3
Absorption coefficient	0.936 mm^-1
F(000)	2688
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	1.98 to 22.50 deg.
Limiting indices	-15<=h<=15, -20<=k<=20, -24<=l<=24
Reflections collected / unique	106889 / 4154 [R(int) = 0.0503]
Completeness to theta = 22.50	99.7 %
Absorption correction	Empirical
Max. and min. transmission	0.952218 and 0.813397
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4154 / 312 / 408
Goodness-of-fit on F^2	1.144
Final R indices [I>2sigma(I)]	R1 = 0.0436, wR2 = 0.1098
R indices (all data)	R1 = 0.0657, wR2 = 0.1228
Largest diff. peak and hole	0.701 and -0.642 e.A^-3

Table 1.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for Nol340m. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Pd(1)	5322(1)	866(1)	5006(1)	33(1)
N(1)	6948(4)	1766(3)	5174(2)	37(1)
Cl(1)	4578(1)	1852(1)	5291(1)	45(1)
C(1)	6820(5)	1938(4)	5773(3)	41(2)
Cl(2)	3978(1)	174(1)	5246(1)	52(1)
N(2)	6855(4)	1382(3)	4283(2)	38(1)
C(2)	6555(5)	2631(4)	5906(3)	49(2)
Cl(3A)	4540(20)	1099(14)	7186(19)	140(6)
Cl(3B)	4901(11)	1022(4)	7392(4)	113(3)
C(3)	6559(7)	2819(5)	6488(4)	66(2)
Cl(4A)	3750(30)	2446(19)	7001(14)	144(7)
Cl(4B)	3753(10)	2110(11)	6927(6)	152(4)
C(4)	6817(8)	2365(6)	6912(4)	78(2)
C(5)	7052(8)	1689(6)	6774(4)	72(2)
C(6)	7066(6)	1452(5)	6198(3)	55(2)
C(7)	6290(6)	3155(5)	5449(4)	59(2)
C(8)	7062(6)	3701(5)	5353(5)	83(3)
C(9)	5379(6)	3538(5)	5574(5)	86(3)
C(10)	7349(7)	717(5)	6065(4)	65(2)
C(11)	6716(8)	192(5)	6361(5)	95(3)
C(12)	8364(7)	587(6)	6227(5)	103(4)
C(13)	6447(4)	1395(3)	4802(3)	30(1)
C(14)	7839(6)	1972(6)	4902(4)	56(2)
C(15)	7665(6)	1858(6)	4278(4)	54(2)
C(16)	6500(5)	1138(4)	3736(3)	42(2)
C(17)	5734(5)	1471(4)	3487(3)	48(2)
C(18)	5462(7)	1240(5)	2931(4)	65(2)
C(19)	5928(8)	730(6)	2650(4)	74(2)
C(20)	6667(7)	425(5)	2897(4)	66(2)
C(21)	6980(5)	609(4)	3448(3)	51(2)
C(22)	5239(6)	2087(5)	3764(4)	59(2)
C(23)	4192(7)	2032(7)	3728(5)	100(3)
C(24)	5598(9)	2767(5)	3502(5)	103(4)
C(25)	7838(6)	257(5)	3686(5)	69(2)
C(26)	8716(7)	487(6)	3345(5)	100(4)
C(27)	7773(7)	-538(5)	3687(5)	88(3)
C(28A)	4450(50)	1800(30)	6712(18)	119(7)
C(28B)	4546(14)	1455(13)	6770(6)	103(5)

Table 1.3. Bond Lengths (Å)and Bond Angles (Deg) for Nol340m

Pd(1)-C(13)	1.971(6)
Pd(1)-Cl(1)	2.2736(18)
Pd(1)-Cl(2)#1	2.3127(18)
Pd(1)-Cl(2)	2.4111(18)
N(1)-C(13)	1.325(8)
N(1)-C(1)	1.432(9)
N(1)-C(14)	1.482(9)
C(1)-C(6)	1.398(11)
C(1)-C(2)	1.418(10)
Cl(2)-Pd(1)#1	2.3127(18)
N(2)-C(13)	1.332(8)
N(2)-C(16)	1.439(9)
N(2)-C(15)	1.482(9)
C(2)-C(3)	1.388(12)
C(2)-C(7)	1.506(12)
Cl(3A)-C(28A)	1.733(11)
Cl(3B)-C(28B)	1.733(9)
C(3)-C(4)	1.362(14)
Cl(4A)-C(28A)	1.735(11)
Cl(4B)-C(28B)	1.738(10)
C(4)-C(5)	1.379(15)
C(5)-C(6)	1.401(12)
C(6)-C(10)	1.502(12)
C(7)-C(9)	1.533(11)
C(7)-C(8)	1.545(12)
C(10)-C(11)	1.521(13)
C(10)-C(12)	1.530(13)
C(14)-C(15)	1.477(12)
C(16)-C(21)	1.396(10)
C(16)-C(17)	1.398(10)
C(17)-C(18)	1.409(11)
C(17)-C(22)	1.523(11)
C(18)-C(19)	1.353(13)
C(19)-C(20)	1.341(13)
C(20)-C(21)	1.393(11)
C(21)-C(25)	1.510(12)
C(22)-C(23)	1.513(13)
C(22)-C(24)	1.530(12)
C(25)-C(27)	1.532(14)
C(25)-C(26)	1.554(13)

C(13)-Pd(1)-Cl(1)	91.43(19)
C(13)-Pd(1)-Cl(2)#1	91.62(19)

Cl(1)-Pd(1)-Cl(2)#1	176.58(7)
C(13)-Pd(1)-Cl(2)	177.67(19)
Cl(1)-Pd(1)-Cl(2)	90.89(6)
Cl(2)#1-Pd(1)-Cl(2)	86.05(6)
C(13)-N(1)-C(1)	132.6(6)
C(13)-N(1)-C(14)	110.1(6)
C(1)-N(1)-C(14)	117.1(6)
C(6)-C(1)-C(2)	123.0(7)
C(6)-C(1)-N(1)	119.3(7)
C(2)-C(1)-N(1)	117.3(7)
Pd(1)#1-Cl(2)-Pd(1)	93.95(6)
C(13)-N(2)-C(16)	129.6(5)
C(13)-N(2)-C(15)	110.0(6)
C(16)-N(2)-C(15)	118.2(6)
C(3)-C(2)-C(1)	116.8(8)
C(3)-C(2)-C(7)	120.1(8)
C(1)-C(2)-C(7)	123.1(7)
C(4)-C(3)-C(2)	121.8(9)
C(3)-C(4)-C(5)	120.3(9)
C(4)-C(5)-C(6)	121.9(10)
C(1)-C(6)-C(5)	116.2(9)
C(1)-C(6)-C(10)	123.5(7)
C(5)-C(6)-C(10)	120.2(9)
C(2)-C(7)-C(9)	114.0(8)
C(2)-C(7)-C(8)	111.8(7)
C(9)-C(7)-C(8)	108.4(7)
C(6)-C(10)-C(11)	111.7(8)
C(6)-C(10)-C(12)	111.3(8)
C(11)-C(10)-C(12)	110.7(9)
N(1)-C(13)-N(2)	110.5(5)
N(1)-C(13)-Pd(1)	124.8(5)
N(2)-C(13)-Pd(1)	124.4(5)
C(15)-C(14)-N(1)	102.9(6)
C(14)-C(15)-N(2)	102.6(7)
C(21)-C(16)-C(17)	122.0(7)
C(21)-C(16)-N(2)	118.5(7)
C(17)-C(16)-N(2)	119.4(7)
C(16)-C(17)-C(18)	116.6(8)
C(16)-C(17)-C(22)	123.6(7)
C(18)-C(17)-C(22)	119.7(8)
C(19)-C(18)-C(17)	121.6(9)
C(20)-C(19)-C(18)	120.5(9)
C(19)-C(20)-C(21)	122.1(9)
C(20)-C(21)-C(16)	117.2(8)
C(20)-C(21)-C(25)	118.8(8)
C(16)-C(21)-C(25)	123.9(7)

C(23)-C(22)-C(17)	112.9(8)
C(23)-C(22)-C(24)	112.1(9)
C(17)-C(22)-C(24)	109.9(7)
C(21)-C(25)-C(27)	113.4(8)
C(21)-C(25)-C(26)	110.8(9)
C(27)-C(25)-C(26)	109.5(8)
Cl(3A)-C(28A)-Cl(4A)	111(2)
Cl(3B)-C(28B)-Cl(4B)	111.7(9)

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y,-z+1

Table 1.4. Anisotropic displacement parameters (A^2 x 10^3) for Nol340m.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Pd(1)	25(1)	32(1)	41(1)	0(1)	3(1)	-2(1)
N(1)	26(3)	45(3)	42(3)	-7(2)	0(2)	-8(2)
Cl(1)	36(1)	37(1)	61(1)	-6(1)	7(1)	4(1)
C(1)	30(3)	49(3)	46(3)	-11(3)	0(3)	-11(3)
Cl(2)	31(1)	35(1)	89(1)	-3(1)	20(1)	-3(1)
N(2)	28(3)	46(3)	40(3)	-4(3)	7(2)	-11(2)
C(2)	36(4)	54(4)	57(4)	-17(3)	3(3)	-9(3)
Cl(3A)	144(13)	137(11)	140(15)	21(11)	-21(12)	-33(10)
Cl(3B)	159(8)	100(4)	82(5)	11(3)	1(4)	-37(4)
C(3)	65(5)	67(5)	67(4)	-31(4)	8(4)	-7(4)
Cl(4A)	179(14)	160(17)	94(10)	-15(12)	-47(10)	19(14)
Cl(4B)	148(6)	187(12)	119(6)	-5(7)	6(5)	34(8)
C(4)	91(6)	91(6)	51(5)	-25(4)	6(5)	-14(5)
C(5)	89(6)	81(5)	47(4)	-3(4)	-8(5)	-11(5)
C(6)	56(4)	61(4)	46(4)	-5(3)	-4(4)	-9(4)
C(7)	48(4)	51(4)	77(5)	-13(4)	-2(4)	1(3)
C(8)	59(5)	76(6)	115(8)	14(6)	3(6)	-10(5)
C(9)	51(5)	54(5)	152(9)	-23(6)	3(6)	10(4)
C(10)	75(5)	56(4)	64(5)	1(4)	-14(5)	2(4)
C(11)	133(8)	60(6)	92(7)	5(5)	8(7)	-13(6)
C(12)	88(6)	102(8)	121(9)	1(7)	-33(7)	22(6)
C(13)	22(3)	30(3)	39(3)	1(3)	2(2)	-1(2)
C(14)	38(4)	73(5)	58(4)	-20(4)	13(3)	-23(4)
C(15)	38(4)	70(6)	56(4)	-8(5)	9(4)	-22(4)
C(16)	35(3)	50(4)	40(3)	-2(3)	5(3)	-13(3)

C(17)	49(4)	53(4)	43(4)	9(3)	2(3)	-8(3)
C(18)	73(5)	75(5)	47(4)	4(4)	-11(4)	0(4)
C(19)	90(6)	84(6)	48(5)	-10(4)	-10(4)	-1(5)
C(20)	78(6)	70(6)	50(4)	-21(4)	6(4)	1(4)
C(21)	49(4)	57(4)	47(4)	-9(3)	6(3)	-8(3)
C(22)	58(4)	62(5)	57(5)	9(4)	6(4)	10(4)
C(23)	60(5)	144(10)	95(8)	-3(7)	-2(6)	20(6)
C(24)	129(9)	60(5)	119(9)	17(6)	25(8)	13(6)
C(25)	53(4)	86(5)	68(6)	-28(5)	0(4)	8(4)
C(26)	51(5)	128(8)	122(9)	-49(7)	21(5)	1(6)
C(27)	83(7)	87(5)	94(7)	-20(6)	7(6)	29(5)
C(28A)	119(13)	157(17)	82(13)	8(11)	3(12)	-16(15)
C(28B	105(10)	137(15)	66(8)	7(8)	5(8)	-18(9)

Table 1.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for Nol340m.

	x	y	z	U(eq)
H(3)	6420(70)	3270(50)	6630(40)	90(30)
H(4)	6880(80)	2410(60)	7310(50)	130(40)
H(5)	7220(60)	1350(40)	7010(30)	60(30)
H(7)	6300(50)	2940(40)	5110(30)	40(20)
H(8A)	7184	3939	5712	125
H(8B)	6864	4031	5066	125
H(8C)	7617	3473	5223	125
H(9A)	4892	3205	5637	129
H(9B)	5222	3828	5249	129
H(9C)	5451	3821	5914	129
H(10)	7320(50)	620(40)	5690(30)	50(20)
H(11A)	6804	216	6774	143
H(11B)	6864	-267	6227	143
H(11C)	6081	297	6269	143
H(12A)	8757	891	6006	155
H(12B)	8523	112	6144	155
H(12C)	8450	676	6634	155
H(14A)	8060(50)	2410(40)	4990(30)	50(20)
H(14B)	8280(60)	1660(40)	5030(40)	70(30)
H(15A)	7480(50)	2220(40)	4100(30)	30(20)
H(15B)	8180(50)	1630(40)	4080(30)	50(20)
H(18)	5010(50)	1560(40)	2800(30)	50(20)

H(19)	5830(50)	590(40)	2270(30)	50(20)
H(6)	6990(60)	100(50)	2700(40)	80(30)
H(22)	5360(50)	2090(30)	4190(30)	40(20)
H(23A)	4008	1991	3329	150
H(23B)	3916	2441	3894	150
H(23C)	3989	1629	3939	150
H(24A)	6265	2762	3498	154
H(24B)	5386	3152	3732	154
H(24C)	5370	2815	3112	154
H(25)	7890(40)	350(30)	4060(20)	17(15)
H(26A)	8636	381	2940	150
H(26B)	9248	242	3491	150
H(26C)	8807	978	3391	150
H(27A)	7244	-681	3911	132
H(27B)	8327	-730	3854	132
H(27C)	7707	-702	3295	132
H(28A)	4188	1639	6347	143
H(28B)	5063	1983	6635	143
H(28C)	4264	1125	6505	123
H(28D)	5084	1655	6579	123

Table 1.6. Torsion angles [deg] for Nol340m.

C(13)-N(1)-C(1)-C(6)	81.1(10)
C(14)-N(1)-C(1)-C(6)	-92.4(9)
C(13)-N(1)-C(1)-C(2)	-106.5(9)
C(14)-N(1)-C(1)-C(2)	80.0(9)
C(13)-Pd(1)-Cl(2)-Pd(1)#1	-2(5)
Cl(1)-Pd(1)-Cl(2)-Pd(1)#1	-178.46(8)
Cl(2)#1-Pd(1)-Cl(2)-Pd(1)#1	0.0
C(6)-C(1)-C(2)-C(3)	0.8(11)
N(1)-C(1)-C(2)-C(3)	-171.3(7)
C(6)-C(1)-C(2)-C(7)	180.0(7)
N(1)-C(1)-C(2)-C(7)	7.9(10)
C(1)-C(2)-C(3)-C(4)	0.8(13)
C(7)-C(2)-C(3)-C(4)	-178.4(9)
C(2)-C(3)-C(4)-C(5)	-2.3(16)
C(3)-C(4)-C(5)-C(6)	2.2(17)
C(2)-C(1)-C(6)-C(5)	-0.9(12)
N(1)-C(1)-C(6)-C(5)	171.0(7)
C(2)-C(1)-C(6)-C(10)	-180.0(8)
N(1)-C(1)-C(6)-C(10)	-8.0(11)
C(4)-C(5)-C(6)-C(1)	-0.6(14)

C(4)-C(5)-C(6)-C(10)	178.5(10)
C(3)-C(2)-C(7)-C(9)	-50.0(11)
C(1)-C(2)-C(7)-C(9)	130.8(8)
C(3)-C(2)-C(7)-C(8)	73.4(10)
C(1)-C(2)-C(7)-C(8)	-105.8(9)
C(1)-C(6)-C(10)-C(11)	-121.2(9)
C(5)-C(6)-C(10)-C(11)	59.8(12)
C(1)-C(6)-C(10)-C(12)	114.5(10)
C(5)-C(6)-C(10)-C(12)	-64.5(12)
C(1)-N(1)-C(13)-N(2)	180.0(7)
C(14)-N(1)-C(13)-N(2)	-6.2(8)
C(1)-N(1)-C(13)-Pd(1)	-5.4(11)
C(14)-N(1)-C(13)-Pd(1)	168.4(6)
C(16)-N(2)-C(13)-N(1)	-169.5(7)
C(15)-N(2)-C(13)-N(1)	-7.1(9)
C(16)-N(2)-C(13)-Pd(1)	15.8(10)
C(15)-N(2)-C(13)-Pd(1)	178.2(6)
Cl(1)-Pd(1)-C(13)-N(1)	61.5(5)
Cl(2)#1-Pd(1)-C(13)-N(1)	-117.0(5)
Cl(2)-Pd(1)-C(13)-N(1)	-115(5)
Cl(1)-Pd(1)-C(13)-N(2)	-124.6(5)
Cl(2)#1-Pd(1)-C(13)-N(2)	56.9(6)
Cl(2)-Pd(1)-C(13)-N(2)	59(5)
C(13)-N(1)-C(14)-C(15)	16.6(10)
C(1)-N(1)-C(14)-C(15)	-168.5(7)
N(1)-C(14)-C(15)-N(2)	-19.1(10)
C(13)-N(2)-C(15)-C(14)	17.1(10)
C(16)-N(2)-C(15)-C(14)	-178.3(7)
C(13)-N(2)-C(16)-C(21)	-121.4(8)
C(15)-N(2)-C(16)-C(21)	77.4(9)
C(13)-N(2)-C(16)-C(17)	63.4(10)
C(15)-N(2)-C(16)-C(17)	-97.7(9)
C(21)-C(16)-C(17)-C(18)	0.6(11)
N(2)-C(16)-C(17)-C(18)	175.6(7)
C(21)-C(16)-C(17)-C(22)	-175.1(7)
N(2)-C(16)-C(17)-C(22)	-0.1(11)
C(16)-C(17)-C(18)-C(19)	-1.0(13)
C(22)-C(17)-C(18)-C(19)	174.9(9)
C(17)-C(18)-C(19)-C(20)	0.3(16)
C(18)-C(19)-C(20)-C(21)	0.8(16)
C(19)-C(20)-C(21)-C(16)	-1.2(14)
C(19)-C(20)-C(21)-C(25)	-177.9(9)
C(17)-C(16)-C(21)-C(20)	0.4(11)
N(2)-C(16)-C(21)-C(20)	-174.6(7)
C(17)-C(16)-C(21)-C(25)	176.9(8)
N(2)-C(16)-C(21)-C(25)	1.9(11)

C(16)-C(17)-C(22)-C(23)	-136.9(9)
C(18)-C(17)-C(22)-C(23)	47.4(11)
C(16)-C(17)-C(22)-C(24)	97.1(10)
C(18)-C(17)-C(22)-C(24)	-78.5(11)
C(20)-C(21)-C(25)-C(27)	-54.9(12)
C(16)-C(21)-C(25)-C(27)	128.6(9)
C(20)-C(21)-C(25)-C(26)	68.7(11)
C(16)-C(21)-C(25)-C(26)	-107.8(9)

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y,-z+1

2. Crystal Data and Structure Refinement for [(IPr)Pd(Cl)$_2$(2-chloropyridine)]

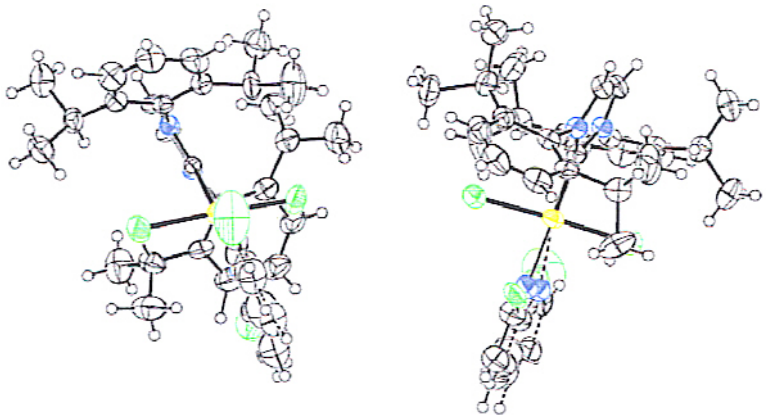

Table 2.1. Crystal data and structure refinement for Nol339.

Identification code	nol339
Empirical formula	$C_{32}H_{39}Cl_3N_3Pd$
Formula weight	678.41
Temperature	297(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, Cc
Unit cell dimensions	a = 34.2738(7) A alpha = 90 deg. b = 15.5109(3) A beta = 106.72 deg. c = 12.7275(3) A gamma = 90 deg.
Volume	6480.1(2) A^3
Z, Calculated density	8, 1.391 Mg/m^3
Absorption coefficient	0.845 mm^-1
F(000)	2792
Crystal size	0.60 x 0.30 x 0.20 mm
Theta range for data collection	2.07 to 25.00 deg.
Limiting indices	-40<=h<=40, -18<=k<=18, -15<=l<=15
Reflections collected / unique	60134 / 11422 [R(int) = 0.0158]
Completeness to theta = 25.00	99.9 %
Absorption correction	Empirical
Max. and min. transmission	0.899229 and 0.768165
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11422 / 1272 / 936
Goodness-of-fit on F^2	1.080
Final R indices [I>2sigma(I)]	R1 = 0.0240, wR2 = 0.0631
R indices (all data)	R1 = 0.0291, wR2 = 0.0664
Absolute structure parameter	0.48(3)
Largest diff. peak and hole	0.586 and -0.422 e.A^-3

Table 2.2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for Nol339. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Pd(1)	7409(1)	6440(1)	5281(1)	37(1)
Cl(1)	6937(1)	6048(2)	6155(2)	62(1)
N(1)	7045(2)	8158(4)	5516(4)	31(1)
C(1)	7261(2)	8259(5)	6666(5)	34(1)
Cl(2)	7886(1)	6775(2)	4396(2)	59(1)
N(2)	6861(2)	7715(3)	3846(4)	30(1)
C(2)	7038(2)	8206(5)	7440(6)	40(2)
Cl(3)	8058(1)	5695(3)	7491(3)	135(2)
C(3)	7264(3)	8377(6)	8550(6)	57(2)
N(3)	7701(2)	5229(4)	5551(6)	59(2)
N(3A)	7703(4)	5296(9)	5879(11)	44(2)
C(4)	7660(4)	8560(6)	8836(9)	64(2)
Cl(4)	7419(3)	4666(6)	3863(6)	122(3)
C(5)	7860(3)	8643(6)	8061(8)	57(2)
C(6)	7666(3)	8496(5)	6964(7)	43(2)
C(7)	6594(2)	8006(6)	7132(7)	50(2)
C(8)	6340(3)	8823(7)	7188(9)	67(2)
C(9)	6495(3)	7303(6)	7874(7)	62(2)
C(10)	7893(2)	8599(5)	6080(8)	58(2)
C(11)	7826(3)	9508(6)	5602(7)	70(2)
C(12)	8364(3)	8402(9)	6565(10)	98(4)
C(13)	7092(2)	7525(4)	4839(6)	28(1)
C(14)	6770(2)	8770(4)	4914(6)	39(2)
C(15)	6658(2)	8502(4)	3901(6)	42(2)
C(16)	6869(2)	7287(5)	2854(6)	36(1)
C(17)	6623(3)	6540(5)	2535(7)	43(2)
C(18)	6640(3)	6159(6)	1570(8)	57(2)
C(19)	6903(4)	6477(5)	951(9)	63(2)
C(20)	7126(3)	7220(6)	1287(7)	56(2)
C(21)	7118(3)	7634(5)	2262(6)	43(2)
C(22)	6336(3)	6218(6)	3104(7)	53(2)
C(23)	5900(3)	6395(7)	2463(7)	79(2)
C(24)	6376(4)	5277(6)	3375(8)	79(3)
C(25)	7385(2)	8429(5)	2598(6)	44(2)
C(26)	7153(3)	9251(6)	2044(8)	70(3)
C(27)	7786(3)	8417(6)	2453(9)	66(2)
C(28)	7957(2)	4943(4)	6484(6)	86(2)
C(28A)	7737(5)	4655(11)	5187(9)	54(3)

C(29)	8119(2)	4111(5)	6585(7)	111(3)
C(29A)	7973(5)	3931(8)	5542(13)	76(4)
C(30A)	8216(5)	3897(10)	6612(14)	83(4)
C(31A)	8201(5)	4573(11)	7320(11)	80(4)
C(32A)	7963(6)	5295(11)	6902(12)	67(3)
C(30)	8007(2)	3580(4)	5695(7)	106(3)
C(31)	7743(2)	3846(4)	4710(6)	91(2)
C(32)	7598(2)	4682(4)	4686(7)	76(2)
Pd(51)	9641(1)	6443(1)	2344(1)	38(1)
Cl(51)	9164(1)	6782(2)	3236(2)	62(1)
N(51)	10181(2)	7737(4)	3783(4)	34(1)
C(51)	10179(2)	7296(5)	4804(6)	36(1)
Cl(52)	10116(1)	6046(2)	1485(2)	61(1)
N(52)	10006(2)	8162(4)	2101(4)	32(1)
C(52)	10419(3)	6587(5)	5144(7)	41(2)
Cl(53)	8999(1)	6109(3)	-45(3)	152(2)
C(53)	10391(3)	6166(6)	6105(7)	54(2)
N(53)	9301(2)	5317(5)	1847(7)	75(2)
N(53A)	9379(6)	5270(30)	1710(30)	75(3)
C(54)	10164(4)	6480(6)	6674(8)	63(2)
Cl(54)	9623(3)	4679(6)	3657(11)	71(3)
C(55)	9930(3)	7193(6)	6331(7)	57(2)
C(56)	9923(2)	7638(5)	5388(6)	42(2)
C(57)	10720(2)	6245(6)	4532(7)	48(2)
C(58)	10663(4)	5253(6)	4302(9)	92(3)
C(59)	11151(3)	6472(8)	5234(10)	100(4)
C(60)	9676(3)	8456(5)	4982(8)	55(2)
C(61)	9892(3)	9236(5)	5592(8)	66(2)
C(62)	9238(3)	8359(7)	5215(10)	73(2)
C(63)	9937(2)	7509(5)	2746(6)	33(1)
C(64)	10399(2)	8471(4)	3764(5)	38(2)
C(65)	10284(2)	8743(5)	2704(6)	39(2)
C(66)	9797(2)	8281(5)	940(6)	36(1)
C(67)	9370(3)	8477(5)	668(7)	44(2)
C(68)	9188(3)	8605(6)	-466(8)	59(2)
C(69)	9402(4)	8573(6)	-1228(8)	63(2)
C(70)	9817(3)	8347(6)	-896(7)	53(2)
C(71)	10012(2)	8197(5)	183(6)	41(2)
C(72)	9144(2)	8613(5)	1492(7)	52(2)
C(73)	9204(4)	9514(7)	2001(11)	99(3)
C(74)	8706(3)	8432(9)	1090(11)	104(4)
C(75)	10472(2)	7986(5)	463(6)	48(2)
C(76)	10557(3)	7269(7)	-260(8)	72(3)
C(77)	10710(3)	8786(7)	421(8)	66(2)
C(78)	9039(2)	5260(5)	799(7)	97(2)
C(79)	8814(2)	4512(6)	459(7)	108(2)

C(80)	8860(3)	3841(6)	1185(8)	111(3)
C(81)	9118(3)	3884(5)	2227(8)	101(2)
C(82)	9333(2)	4653(6)	2514(6)	88(2)
C(82A)	9171(8)	5270(20)	630(30)	77(4)
C(81A)	8928(7)	4580(20)	132(16)	93(5)
C(80A)	8900(10)	3890(20)	780(20)	89(4)
C(79A)	9107(11)	3870(20)	1880(20)	96(4)
C(78A)	9344(6)	4580(30)	2314(16)	87(4)

Table 2.3. Bond lengths (Å) and angles (Deg) for Nol339.

Pd(1)-C(13)	1.994(7)
Pd(1)-N(3A)	2.074(11)
Pd(1)-N(3)	2.109(5)
Pd(1)-Cl(1)	2.293(2)
Pd(1)-Cl(2)	2.296(2)
N(1)-C(13)	1.346(9)
N(1)-C(14)	1.401(8)
N(1)-C(1)	1.446(8)
C(1)-C(6)	1.380(11)
C(1)-C(2)	1.412(10)
N(2)-C(13)	1.317(9)
N(2)-C(15)	1.417(7)
N(2)-C(16)	1.434(9)
C(2)-C(3)	1.428(10)
C(2)-C(7)	1.490(11)
Cl(3)-C(28)	1.694(7)
C(3)-C(4)	1.330(15)
N(3)-C(28)	1.334(6)
N(3)-C(32)	1.354(6)
N(3A)-C(32A)	1.349(7)
N(3A)-C(28A)	1.356(7)
C(4)-C(5)	1.362(15)
Cl(4)-C(28A)	1.724(10)
C(5)-C(6)	1.383(12)
C(6)-C(10)	1.549(11)
C(7)-C(9)	1.543(11)
C(7)-C(8)	1.550(12)
C(10)-C(11)	1.526(13)
C(10)-C(12)	1.584(12)
C(14)-C(15)	1.302(9)
C(16)-C(21)	1.397(11)
C(16)-C(17)	1.422(11)

C(17)-C(18)	1.379(12)
C(17)-C(22)	1.468(13)
C(18)-C(19)	1.446(14)
C(19)-C(20)	1.381(12)
C(20)-C(21)	1.405(11)
C(21)-C(25)	1.521(11)
C(22)-C(24)	1.496(14)
C(22)-C(23)	1.508(13)
C(25)-C(27)	1.441(11)
C(25)-C(26)	1.560(11)
C(28)-C(29)	1.396(6)
C(28A)-C(29A)	1.382(7)
C(29)-C(30)	1.362(6)
C(29A)-C(30A)	1.378(7)
C(30A)-C(31A)	1.394(7)
C(31A)-C(32A)	1.398(7)
C(30)-C(31)	1.382(6)
C(31)-C(32)	1.386(6)
Pd(51)-C(63)	1.930(8)
Pd(51)-N(53A)	2.09(3)
Pd(51)-N(53)	2.094(7)
Pd(51)-Cl(52)	2.291(2)
Pd(51)-Cl(51)	2.305(2)
N(51)-C(64)	1.365(8)
N(51)-C(63)	1.390(9)
N(51)-C(51)	1.471(9)
C(51)-C(52)	1.367(11)
C(51)-C(56)	1.408(10)
N(52)-C(63)	1.366(9)
N(52)-C(65)	1.374(9)
N(52)-C(66)	1.457(8)
C(52)-C(53)	1.414(11)
C(52)-C(57)	1.554(12)
Cl(53)-C(78)	1.680(8)
C(53)-C(54)	1.300(14)
N(53)-C(82)	1.319(6)
N(53)-C(78)	1.380(6)
N(53A)-C(78A)	1.347(7)
N(53A)-C(82A)	1.356(7)
C(54)-C(55)	1.362(13)
Cl(54)-C(78A)	1.709(11)
C(55)-C(56)	1.378(11)
C(56)-C(60)	1.529(11)
C(57)-C(59)	1.531(12)
C(57)-C(58)	1.568(13)
C(60)-C(61)	1.511(12)

C(60)-C(62)	1.619(11)
C(64)-C(65)	1.359(8)
C(66)-C(71)	1.379(11)
C(66)-C(67)	1.436(11)
C(67)-C(68)	1.412(12)
C(67)-C(72)	1.486(12)
C(68)-C(69)	1.376(15)
C(69)-C(70)	1.404(14)
C(70)-C(71)	1.364(11)
C(71)-C(75)	1.546(11)
C(72)-C(74)	1.468(13)
C(72)-C(73)	1.529(14)
C(75)-C(77)	1.495(12)
C(75)-C(76)	1.523(11)
C(78)-C(79)	1.391(5)
C(79)-C(80)	1.371(6)
C(80)-C(81)	1.367(6)
C(81)-C(82)	1.395(6)
C(82A)-C(81A)	1.382(7)
C(81A)-C(80A)	1.377(7)
C(80A)-C(79A)	1.377(7)
C(79A)-C(78A)	1.386(7)

C(13)-Pd(1)-N(3A)	173.3(4)
C(13)-Pd(1)-N(3)	172.6(3)
N(3A)-Pd(1)-N(3)	11.7(5)
C(13)-Pd(1)-Cl(1)	87.61(17)
N(3A)-Pd(1)-Cl(1)	86.0(4)
N(3)-Pd(1)-Cl(1)	92.99(18)
C(13)-Pd(1)-Cl(2)	94.44(17)
N(3A)-Pd(1)-Cl(2)	92.0(4)
N(3)-Pd(1)-Cl(2)	84.84(18)
Cl(1)-Pd(1)-Cl(2)	177.68(10)
C(13)-N(1)-C(14)	109.3(6)
C(13)-N(1)-C(1)	127.3(6)
C(14)-N(1)-C(1)	123.3(6)
C(6)-C(1)-C(2)	121.8(7)
C(6)-C(1)-N(1)	119.3(7)
C(2)-C(1)-N(1)	118.5(6)
C(13)-N(2)-C(15)	108.3(6)
C(13)-N(2)-C(16)	125.7(6)
C(15)-N(2)-C(16)	125.2(6)
C(1)-C(2)-C(3)	115.6(7)
C(1)-C(2)-C(7)	123.0(7)
C(3)-C(2)-C(7)	121.4(8)
C(4)-C(3)-C(2)	122.1(9)

C(28)-N(3)-C(32)	117.8(5)
C(28)-N(3)-Pd(1)	127.0(5)
C(32)-N(3)-Pd(1)	115.2(4)
C(32A)-N(3A)-C(28A)	118.0(7)
C(32A)-N(3A)-Pd(1)	118.1(9)
C(28A)-N(3A)-Pd(1)	120.8(9)
C(3)-C(4)-C(5)	120.7(9)
C(4)-C(5)-C(6)	121.3(9)
C(1)-C(6)-C(5)	118.4(8)
C(1)-C(6)-C(10)	120.2(8)
C(5)-C(6)-C(10)	121.3(8)
C(2)-C(7)-C(9)	112.0(7)
C(2)-C(7)-C(8)	111.2(7)
C(9)-C(7)-C(8)	108.9(7)
C(11)-C(10)-C(6)	109.5(6)
C(11)-C(10)-C(12)	110.7(8)
C(6)-C(10)-C(12)	111.4(8)
N(2)-C(13)-N(1)	107.5(6)
N(2)-C(13)-Pd(1)	126.0(5)
N(1)-C(13)-Pd(1)	126.2(5)
C(15)-C(14)-N(1)	106.6(6)
C(14)-C(15)-N(2)	108.3(6)
C(21)-C(16)-C(17)	124.3(7)
C(21)-C(16)-N(2)	117.7(7)
C(17)-C(16)-N(2)	117.9(7)
C(18)-C(17)-C(16)	15.5(8)
C(18)-C(17)-C(22)	1119.9(8)
C(16)-C(17)-C(22)	124.3(7)
C(17)-C(18)-C(19)	122.1(9)
C(20)-C(19)-C(18)	119.5(9)
C(19)-C(20)-C(21)	120.4(9)
C(16)-C(21)-C(20)	118.1(8)
C(16)-C(21)-C(25)	124.9(7)
C(20)-C(21)-C(25)	117.1(7)
C(17)-C(22)-C(24)	114.5(9)
C(17)-C(22)-C(23)	111.9(8)
C(24)-C(22)-C(23)	108.2(8)
C(27)-C(25)-C(21)	118.2(7)
C(27)-C(25)-C(26)	109.5(7)
C(21)-C(25)-C(26)	110.4(7)
N(3)-C(28)-C(29)	122.1(6)
N(3)-C(28)-Cl(3)	112.5(5)
C(29)-C(28)-Cl(3)	125.3(6)
N(3A)-C(28A)-C(29A)	122.4(7)
N(3A)-C(28A)-Cl(4)	118.6(10)
C(29A)-C(28A)-Cl(4)	118.4(11)

C(30)-C(29)-C(28)	118.3(6)
C(30A)-C(29A)-C(28A)	119.0(6)
C(29A)-C(30A)-C(31A)	119.1(7)
C(30A)-C(31A)-C(32A)	118.9(8)
N(3A)-C(32A)-C(31A)	121.3(8)
C(29)-C(30)-C(31)	121.9(6)
C(30)-C(31)-C(32)	115.8(6)
N(3)-C(32)-C(31)	124.2(6)
C(63)-Pd(51)-N(53A)	169.9(8)
C(63)-Pd(51)-N(53)	177.3(3)
N(53A)-Pd(51)-N(53)	10.1(7)
C(63)-Pd(51)-Cl(52)	88.09(19)
N(53A)-Pd(51)-Cl(52)	82.3(6)
N(53)-Pd(51)-Cl(52)	92.38(16)
C(63)-Pd(51)-Cl(51)	93.84(19)
N(53A)-Pd(51)-Cl(51)	95.9(7)
N(53)-Pd(51)-Cl(51)	85.77(16)
Cl(52)-Pd(51)-Cl(51)	177.47(10)
C(64)-N(51)-C(63)	112.3(6)
C(64)-N(51)-C(51)	123.0(6)
C(63)-N(51)-C(51)	124.5(6)
C(52)-C(51)-C(56)	123.2(7)
C(52)-C(51)-N(51)	119.9(7)
C(56)-C(51)-N(51)	117.0(7)
C(63)-N(52)-C(65)	111.3(6)
C(63)-N(52)-C(66)	125.7(6)
C(65)-N(52)-C(66)	122.9(5)
C(51)-C(52)-C(53)	117.4(8)
C(51)-C(52)-C(57)	122.9(7)
C(53)-C(52)-C(57)	119.7(8)
C(54)-C(53)-C(52)	120.6(9)
C(82)-N(53)-C(78)	118.9(5)
C(82)-N(53)-Pd(51)	121.3(6)
C(78)-N(53)-Pd(51)	119.8(6)
C(78A)-N(53A)-C(82A)	118.2(7)
C(78A)-N(53A)-Pd(51)	125(2)
C(82A)-N(53A)-Pd(51)	116(2)
C(53)-C(54)-C(55)	121.1(8)
C(54)-C(55)-C(56)	123.2(9)
C(55)-C(56)-C(51)	114.3(8)
C(55)-C(56)-C(60)	125.5(8)
C(51)-C(56)-C(60)	120.1(7)
C(59)-C(57)-C(52)	107.3(7)
C(59)-C(57)-C(58)	112.5(8)
C(52)-C(57)-C(58)	111.3(8)
C(61)-C(60)-C(56)	110.5(7)

C(61)-C(60)-C(62)	108.7(7)
C(56)-C(60)-C(62)	108.2(7)
N(52)-C(63)-N(51)	102.7(6)
N(52)-C(63)-Pd(51)	130.1(5)
N(51)-C(63)-Pd(51)	126.6(6)
C(65)-C(64)-N(51)	105.8(6)
C(64)-C(65)-N(52)	107.9(6)
C(71)-C(66)-C(67)	124.4(7)
C(71)-C(66)-N(52)	119.4(6)
C(67)-C(66)-N(52)	116.2(7)
C(68)-C(67)-C(66)	113.4(8)
C(68)-C(67)-C(72)	122.3(8)
C(66)-C(67)-C(72)	124.1(7)
C(69)-C(68)-C(67)	123.1(9)
C(68)-C(69)-C(70)	119.8(9)
C(71)-C(70)-C(69)	120.5(9)
C(70)-C(71)-C(66)	118.7(8)
C(70)-C(71)-C(75)	116.2(7)
C(66)-C(71)-C(75)	125.0(7)
C(74)-C(72)-C(67)	114.6(8)
C(74)-C(72)-C(73)	108.8(9)
C(67)-C(72)-C(73)	113.3(7)
C(77)-C(75)-C(76)	112.5(8)
C(77)-C(75)-C(71)	110.2(7)
C(76)-C(75)-C(71)	112.0(7)
N(53)-C(78)-C(79)	120.2(5)
N(53)-C(78)-Cl(53)	118.6(6)
C(79)-C(78)-Cl(53)	121.2(6)
C(80)-C(79)-C(78)	118.5(6)
C(81)-C(80)-C(79)	122.3(6)
C(80)-C(81)-C(82)	116.2(6)
N(53)-C(82)-C(81)	124.0(6)
N(53A)-C(82A)-C(81A)	122.4(7)
C(80A)-C(81A)-C(82A)	117.9(7)
C(81A)-C(80A)-C(79A)	121.1(7)
C(80A)-C(79A)-C(78A)	117.7(7)
N(53A)-C(78A)-C(79A)	122.7(7)
N(53A)-C(78A)-Cl(54)	113(3)
C(79A)-C(78A)-Cl(54)	125(3)

Table 2.4. Anisotropic displacement parameters (A^2 x 10^3) for Nol339. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Pd(1)	38(1)	33(1)	41(1)	8(1)	12(1)	10(1)
Cl(1)	64(2)	44(1)	90(2)	19(1)	41(1)	4(1)
N(1)	26(3)	30(3)	34(2)	2(2)	6(2)	3(2)
C(1)	39(3)	31(3)	30(3)	-2(3)	9(2)	-1(3)
Cl(2)	62(1)	54(1)	76(2)	19(1)	42(1)	21(1)
N(2)	30(3)	26(2)	31(2)	0(2)	5(2)	6(2)
C(2)	43(3)	43(4)	33(3)	-2(3)	10(3)	-3(3)
Cl(3)	82(2)	242(5)	71(2)	50(2)	4(1)	26(2)
C(3)	70(4)	74(5)	25(3)	-1(3)	10(3)	-7(4)
N(3)	64(4)	41(3)	92(4)	38(3)	53(3)	26(3)
N(3A)	50(5)	45(5)	57(5)	28(4)	50(4)	18(4)
C(4)	61(4)	82(6)	38(4)	-10(4)	-1(3)	-8(4)
Cl(4)	130(6)	148(7)	81(3)	-31(4)	20(4)	-2(5)
C(5)	39(4)	66(5)	55(4)	-10(4)	-6(3)	-12(3)
C(6)	38(3)	45(4)	46(3)	-5(3)	14(3)	-3(3)
C(7)	47(3)	67(4)	43(4)	-10(3)	24(3)	-10(3)
C(8)	52(5)	86(5)	68(6)	17(5)	23(4)	9(4)
C(9)	57(5)	70(5)	59(5)	-4(4)	17(4)	-18(4)
C(10)	35(3)	71(5)	77(4)	2(3)	32(3)	-1(3)
C(11)	78(5)	76(5)	62(4)	-3(4)	32(3)	-10(4)
C(12)	35(4)	166(10)	87(7)	13(6)	10(4)	9(5)
C(13)	24(3)	24(2)	35(3)	0(2)	9(2)	-1(2)
C(14)	45(4)	25(3)	42(3)	3(3)	5(3)	10(3)
C(15)	45(4)	30(3)	49(4)	8(3)	9(3)	20(3)
C(16)	38(3)	36(3)	33(3)	2(2)	7(2)	10(2)
C(17)	51(4)	35(3)	39(3)	-12(2)	7(3)	1(2)
C(18)	69(5)	49(4)	57(4)	-8(3)	21(3)	-2(4)
C(19)	86(6)	58(5)	49(5)	-8(3)	26(4)	5(4)
C(20)	76(5)	53(4)	46(4)	-3(3)	31(4)	5(3)
C(21)	56(4)	39(3)	35(3)	5(3)	13(3)	8(3)
C(22)	63(4)	46(3)	47(4)	-7(4)	14(3)	-16(4)
C(23)	72(4)	116(6)	50(4)	-6(4)	17(3)	-6(4)
C(24)	109(7)	52(4)	77(6)	-5(4)	26(5)	-11(4)
C(25)	55(4)	48(3)	28(3)	4(2)	13(3)	2(3)
C(26)	78(6)	52(5)	78(6)	20(4)	20(5)	6(4)
C(27)	68(4)	68(5)	68(5)	29(4)	30(4)	9(3)
C(28)	66(4)	84(4)	121(5)	56(3)	47(4)	38(3)
C(28A)	57(6)	33(5)	89(5)	30(5)	49(5)	32(5)
C(29)	85(5)	83(5)	168(6)	76(4)	41(5)	33(4)
C(29A)	70(7)	25(6)	148(7)	43(6)	57(6)	37(6)

C(30A)	59(7)	44(6)	156(8)	59(6)	48(6)	48(6)
C(31A)	65(7)	69(7)	112(7)	56(6)	34(6)	40(6)
C(32A)	64(6)	75(7)	75(6)	51(5)	41(5)	55(6)
C(30)	83(5)	66(5)	182(6)	62(4)	60(5)	39(4)
C(31)	96(5)	45(3)	159(5)	20(4)	77(4)	29(3)
C(32)	86(6)	41(3)	118(6)	21(4)	54(5)	26(4)
Pd(51)	41(1)	35(1)	41(1)	-7(1)	13(1)	-11(1)
Cl(51)	64(1)	57(1)	76(2)	-20(1)	38(1)	-21(1)
N(51)	39(3)	36(3)	27(2)	2(2)	8(2)	-2(2)
C(51)	43(3)	37(3)	25(3)	3(2)	5(2)	-8(2)
Cl(52)	63(1)	50(1)	81(2)	-11(1)	39(1)	-5(1)
N(52)	35(3)	33(3)	28(2)	4(2)	7(2)	-1(2)
C(52)	44(3)	38(3)	35(3)	-6(2)	5(3)	-8(2)
Cl(53)	126(2)	231(3)	79(2)	-35(2)	-2(1)	-53(2)
C(53)	70(5)	45(4)	42(3)	22(3)	8(3)	-4(3)
N(53)	65(3)	69(3)	109(4)	-40(3)	56(3)	-33(3)
N(53A)	57(7)	74(6)	112(6)	-54(5)	51(6)	-30(5)
C(54)	77(5)	71(5)	43(4)	26(3)	21(4)	-12(3)
Cl(54)	59(6)	35(4)	136(7)	15(5)	55(5)	-6(4)
C(55)	59(4)	73(5)	44(4)	-1(3)	22(3)	-10(3)
C(56)	38(3)	50(4)	36(3)	-3(3)	9(3)	-7(3)
C(57)	49(4)	48(4)	39(4)	5(3)	3(3)	3(3)
C(58)	117(8)	54(5)	109(8)	-11(5)	35(7)	28(5)
C(59)	40(4)	163(9)	95(7)	-27(5)	18(4)	-10(4)
C(60)	44(4)	55(4)	70(5)	-7(3)	23(3)	7(3)
C(61)	56(5)	48(4)	95(6)	3(4)	24(4)	12(3)
C(62)	48(4)	92(6)	87(6)	-15(5)	35(4)	5(4)
C(63)	33(3)	38(3)	26(2)	-2(2)	7(2)	0(2)
C(64)	37(4)	48(4)	26(3)	1(2)	5(3)	-6(2)
C(65)	37(3)	44(3)	37(3)	5(3)	14(3)	-9(3)
C(66)	33(3)	36(3)	32(3)	5(3)	-1(2)	-3(3)
C(67)	32(3)	44(4)	47(3)	6(3)	-4(2)	-2(3)
C(68)	38(4)	77(6)	51(4)	8(4)	-4(3)	4(4)
C(69)	60(4)	82(6)	33(4)	3(3)	-6(3)	3(4)
C(70)	47(3)	65(4)	44(3)	4(3)	10(3)	1(3)
C(71)	46(3)	43(4)	32(3)	-1(3)	7(3)	-4(3)
C(72)	42(3)	54(4)	53(3)	27(3)	4(3)	14(3)
C(73)	125(8)	72(6)	134(8)	-3(5)	90(7)	20(5)
C(74)	45(4)	155(10)	121(9)	31(6)	38(5)	3(5)
C(75)	43(3)	62(4)	37(3)	-6(3)	9(3)	2(3)
C(76)	82(6)	86(6)	62(5)	-12(4)	41(5)	11(5)
C(77)	56(5)	85(5)	65(5)	8(5)	29(4)	-10(4)
C(78)	69(4)	108(4)	131(5)	-95(3)	57(4)	-56(3)
C(79)	76(4)	119(5)	139(5)	-72(4)	47(4)	-51(4)
C(80)	83(5)	87(5)	177(7)	-64(5)	59(5)	-30(4)
C(81)	80(4)	78(4)	165(6)	-47(5)	66(5)	-29(4)

C(82)	73(4)	64(4)	144(5)	-36(4)	56(4)	-22(3)
C(82A)	58(7)	94(6)	105(6)	-89(5)	63(6)	-46(6)
C(81A)	60(8)	103(8)	133(8)	-81(6)	56(7)	-50(7)
C(80A)	61(8)	79(7)	154(8)	-81(7)	74(7)	-21(7)
C(79A)	70(7)	74(7)	164(7)	-50(7)	64(7)	-26(6)
C(78A)	69(7)	66(6)	143(7)	-46(6)	58(7)	-24(6)

Table 2.5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for Nol339.

	x	y	z	U(eq)
H(3)	7097(11)	8360(20)	9110(30)	53(10)
H(4)	7801	8633	9573	76
H(5)	8134	8802	8274	69
H(7)	6501(6)	7783(13)	6319(17)	1(5)
H(8A)	6460	9119	7868	101
H(8B)	6066	8658	7147	101
H(8C)	6338	9197	6586	101
H(9A)	6651	6794	7844	93
H(9B)	6210	7169	7624	93
H(9C)	6563	7510	8616	93
H(11A)	7547	9673	5494	104
H(11B)	7887	9519	4912	104
H(11C)	8001	9904	6101	104
H(12A)	8491	8853	7064	146
H(12B)	8488	8373	5978	146
H(12C)	8400	7862	6948	146
H(14)	6706(5)	9248(10)	5274(18)	70(20)
H(15)	6481(4)	8730(12)	3265(15)	50(20)
H(18)	6512(15)	5500(30)	1320(40)	58(16)
H(19)	6923	6183	331	76
H(20)	7282	7448	866	67
H(22)	6389	6533	3799	63
H(23A)	5859	7006	2367	119
H(23B)	5721	6170	2856	119
H(23C)	5841	6121	1758	119
H(24A)	6184(11)	5180(20)	3940(30)	51(10)
H(24B)	6672(12)	5150(30)	3630(30)	50(11)
H(24C)	6255(13)	4940(30)	2660(40)	65(13)
H(26A)	7324	9747	2265	105
H(26B)	6909	9321	2264	105

H(26C)	7082	9190	1261	105
H(27A)	7929	7911	2795	99
H(27B)	7933	8921	2784	99
H(27C)	7765	8410	1684	99
H(29)	8297	3923	7242	133
H(29A)	7968	3473	5066	91
H(30A)	8388	3429	6858	99
H(31A)	8347	4545	8059	96
H(32A)	7984	5785	7336	80
H(30)	8113	3024	5752	127
H(31)	7666	3485	4101	110
H(32)	7420	4880	4035	92
H(58C)	10556(14)	5760(30)	6300(40)	37(12)
H(54)	10193(13)	6220(30)	7360(40)	65(12)
H(55)	9771(10)	7400(20)	6690(30)	39(9)
H(57)	10671(10)	6470(20)	4000(30)	27(8)
H(58A)	10910	5014	4212	139
H(58B)	10444	5161	3645	139
H(58D)	10600	4976	4908	139
H(59A)	11165	7075	5408	150
H(59B)	11342	6341	4835	150
H(59C)	11217	6142	5900	150
H(60)	9639(3)	8524(6)	4230(40)	66
H(61A)	9908	9186	6355	98
H(61B)	9742	9747	5296	98
H(61C)	10161	9271	5512	98
H(62A)	9114	7827	4908	109
H(62B)	9066	8833	4883	109
H(62C)	9276	8361	5992	109
H(64)	10603(10)	8688(19)	4347(17)	50(20)
H(65)	10376(8)	9217(14)	2402(16)	30(15)
H(68)	8975(14)	8730(30)	-610(40)	62(13)
H(69)	9252(14)	8630(30)	-2010(40)	79(14)
H(70)	9958	8299	-1416	63
H(72)	9259(5)	8200(18)	2100(30)	62
H(73A)	9015(15)	9540(30)	2410(40)	84(16)
H(73B)	9144(14)	9960(30)	1430(40)	76(15)
H(73C)	9551(17)	9550(30)	2500(40)	94(18)
H(74A)	8577	8848	542	156
H(74B)	8589	8464	1690	156
H(74C)	8665	7864	777	156
H(75)	10517(5)	7877(12)	860(40)	57
H(76A)	10487	7463	-1007	108
H(76B)	10397	6771	-209	108
H(76C)	10841	7122	-18	108
H(77A)	10629(9)	8960(20)	-290(30)	30(8)

H(77B)	10980(15)	8680(30)	650(40)	69(13)
H(77C)	10647(11)	9290(30)	820(30)	50(11)
H(79)	8637	4468	-246	130
H(80)	8711	3339	962	134
H(81)	9148	3427	2717	122
H(82)	9511	4700	3218	106
H(82A)	9193	5741	200	93
H(81A)	8788	4592	-611	111
H(80A)	8739	3417	463	107
H(79A)	9088	3399	2314	116

Table 2.6. Torsion angles (Deg) for Nol339.

C(13)-N(1)-C(1)-C(6)	71.3(9)
C(14)-N(1)-C(1)-C(6)	-103.2(8)
C(13)-N(1)-C(1)-C(2)	-115.9(7)
C(14)-N(1)-C(1)-C(2)	69.6(8)
C(6)-C(1)-C(2)-C(3)	-2.7(12)
N(1)-C(1)-C(2)-C(3)	-175.4(7)
C(6)-C(1)-C(2)-C(7)	176.0(8)
N(1)-C(1)-C(2)-C(7)	3.4(11)
C(1)-C(2)-C(3)-C(4)	-0.9(13)
C(7)-C(2)-C(3)-C(4)	-179.7(10)
C(13)-Pd(1)-N(3)-C(28)	-171.7(16)
N(3A)-Pd(1)-N(3)-C(28)	-24(2)
Cl(1)-Pd(1)-N(3)-C(28)	-77.3(5)
Cl(2)-Pd(1)-N(3)-C(28)	103.6(5)
C(13)-Pd(1)-N(3)-C(32)	5.2(19)
N(3A)-Pd(1)-N(3)-C(32)	153(3)
Cl(1)-Pd(1)-N(3)-C(32)	99.63(15)
Cl(2)-Pd(1)-N(3)-C(32)	-79.53(15)
C(13)-Pd(1)-N(3A)-C(32A)	-68(5)
N(3)-Pd(1)-N(3A)-C(32A)	148(4)
Cl(1)-Pd(1)-N(3A)-C(32A)	-85.3(13)
Cl(2)-Pd(1)-N(3A)-C(32A)	95.9(13)
C(13)-Pd(1)-N(3A)-C(28A)	133(4)
N(3)-Pd(1)-N(3A)-C(28A)	-12(2)
Cl(1)-Pd(1)-N(3A)-C(28A)	115.0(12)
Cl(2)-Pd(1)-N(3A)-C(28A)	-63.8(12)
C(2)-C(3)-C(4)-C(5)	4.0(15)
C(3)-C(4)-C(5)-C(6)	-3.4(15)
C(2)-C(1)-C(6)-C(5)	3.3(12)

N(1)-C(1)-C(6)-C(5)	175.9(7)
C(2)-C(1)-C(6)-C(10)	-176.3(7)
N(1)-C(1)-C(6)-C(10)	-3.7(11)
C(4)-C(5)-C(6)-C(1)	-0.2(13)
C(4)-C(5)-C(6)-C(10)	179.4(8)
C(1)-C(2)-C(7)-C(9)	132.2(8)
C(3)-C(2)-C(7)-C(9)	-49.1(11)
C(1)-C(2)-C(7)-C(8)	-105.8(9)
C(3)-C(2)-C(7)-C(8)	72.9(10)
C(1)-C(6)-C(10)-C(11)	86.1(9)
C(5)-C(6)-C(10)-C(11)	-93.5(10)
C(1)-C(6)-C(10)-C(12)	-151.1(9)
C(5)-C(6)-C(10)-C(12)	29.3(11)
C(15)-N(2)-C(13)-N(1)	-0.12(16)
C(16)-N(2)-C(13)-N(1)	169.6(6)
C(15)-N(2)-C(13)-Pd(1)	174.1(4)
C(16)-N(2)-C(13)-Pd(1)	-16.2(7)
C(14)-N(1)-C(13)-N(2)	0.14(16)
C(1)-N(1)-C(13)-N(2)	-175.0(6)
C(14)-N(1)-C(13)-Pd(1)	-174.1(4)
C(1)-N(1)-C(13)-Pd(1)	10.7(7)
N(3A)-Pd(1)-C(13)-N(2)	-125(4)
N(3)-Pd(1)-C(13)-N(2)	-12(2)
Cl(1)-Pd(1)-C(13)-N(2)	-106.9(4)
Cl(2)-Pd(1)-C(13)-N(2)	72.0(4)
N(3A)-Pd(1)-C(13)-N(1)	49(4)
N(3)-Pd(1)-C(13)-N(1)	161.1(17)
Cl(1)-Pd(1)-C(13)-N(1)	66.3(4)
Cl(2)-Pd(1)-C(13)-N(1)	-114.8(4)
C(13)-N(1)-C(14)-C(15)	-0.10(14)
C(1)-N(1)-C(14)-C(15)	175.3(6)
N(1)-C(14)-C(15)-N(2)	0.02(12)
C(13)-N(2)-C(15)-C(14)	0.06(14)
C(16)-N(2)-C(15)-C(14)	-169.7(6)
C(13)-N(2)-C(16)-C(21)	-93.2(8)
C(15)-N(2)-C(16)-C(21)	74.8(8)
C(13)-N(2)-C(16)-C(17)	87.0(8)
C(15)-N(2)-C(16)-C(17)	-105.0(7)
C(21)-C(16)-C(17)-C(18)	-0.5(12)
N(2)-C(16)-C(17)-C(18)	179.4(7)
C(21)-C(16)-C(17)-C(22)	-174.5(8)
N(2)-C(16)-C(17)-C(22)	5.4(12)
C(16)-C(17)-C(18)-C(19)	2.7(14)
C(22)-C(17)-C(18)-C(19)	177.0(9)
C(17)-C(18)-C(19)-C(20)	-4.7(15)
C(18)-C(19)-C(20)-C(21)	4.2(15)

C(17)-C(16)-C(21)-C(20)	0.1(12)
N(2)-C(16)-C(21)-C(20)	-179.8(7)
C(17)-C(16)-C(21)-C(25)	-179.5(8)
N(2)-C(16)-C(21)-C(25)	0.6(11)
C(19)-C(20)-C(21)-C(16)	-2.0(13)
C(19)-C(20)-C(21)-C(25)	177.6(8)
C(18)-C(17)-C(22)-C(24)	55.7(11)
C(16)-C(17)-C(22)-C(24)	-130.5(9)
C(18)-C(17)-C(22)-C(23)	-67.9(11)
C(16)-C(17)-C(22)-C(23)	105.9(10)
C(16)-C(21)-C(25)-C(27)	139.2(8)
C(20)-C(21)-C(25)-C(27)	-40.4(11)
C(16)-C(21)-C(25)-C(26)	-93.7(9)
C(20)-C(21)-C(25)-C(26)	86.7(9)
C(32)-N(3)-C(28)-C(29)	0.08(12)
Pd(1)-N(3)-C(28)-C(29)	176.9(5)
C(32)-N(3)-C(28)-Cl(3)	179.95(7)
Pd(1)-N(3)-C(28)-Cl(3)	-3.2(5)
C(32A)-N(3A)-C(28A)-C(29A)	12(2)
Pd(1)-N(3A)-C(28A)-C(29A)	171.7(15)
C(32A)-N(3A)-C(28A)-Cl(4)	-177.8(15)
Pd(1)-N(3A)-C(28A)-Cl(4)	-18.1(18)
N(3)-C(28)-C(29)-C(30)	-0.07(12)
Cl(3)-C(28)-C(29)-C(30)	-179.92(9)
N(3A)-C(28A)-C(29A)-C(30A)	-7.1(18)
Cl(4)-C(28A)-C(29A)-C(30A)	-177.3(7)
C(28A)-C(29A)-C(30A)-C(31A)	3.3(9)
C(29A)-C(30A)-C(31A)-C(32A)	-4.8(12)
C(28A)-N(3A)-C(32A)-C(31A)	-13(3)
Pd(1)-N(3A)-C(32A)-C(31A)	-173.7(12)
C(30A)-C(31A)-C(32A)-N(3A)	10(3)
C(28)-C(29)-C(30)-C(31)	0.01(12)
C(29)-C(30)-C(31)-C(32)	0.03(11)
C(28)-N(3)-C(32)-C(31)	-0.03(12)
Pd(1)-N(3)-C(32)-C(31)	-177.2(5)
C(30)-C(31)-C(32)-N(3)	-0.02(12)
C(64)-N(51)-C(51)-C(52)	-99.7(8)
C(63)-N(51)-C(51)-C(52)	86.6(9)
C(64)-N(51)-C(51)-C(56)	80.4(8)
C(63)-N(51)-C(51)-C(56)	-93.3(8)
C(56)-C(51)-C(52)-C(53)	2.7(12)
N(51)-C(51)-C(52)-C(53)	-177.1(7)
C(56)-C(51)-C(52)-C(57)	-176.4(7)
N(51)-C(51)-C(52)-C(57)	3.8(11)
C(51)-C(52)-C(53)-C(54)	-4.3(13)
C(57)-C(52)-C(53)-C(54)	174.8(9)

C(63)-Pd(51)-N(53)-C(82)	-161(5)
N(53A)-Pd(51)-N(53)-C(82)	101(7)
Cl(52)-Pd(51)-N(53)-C(82)	99.08(18)
Cl(51)-Pd(51)-N(53)-C(82)	-79.20(19)
C(63)-Pd(51)-N(53)-C(78)	20(6)
N(53A)-Pd(51)-N(53)-C(78)	-78(7)
Cl(52)-Pd(51)-N(53)-C(78)	-80.3(3)
Cl(51)-Pd(51)-N(53)-C(78)	101.4(3)
C(63)-Pd(51)-N(53A)-C(78A)	131(5)
N(53)-Pd(51)-N(53A)-C(78A)	-64(7)
Cl(52)-Pd(51)-N(53A)-C(78A)	113.7(16)
Cl(51)-Pd(51)-N(53A)-C(78A)	-64.6(16)
C(63)-Pd(51)-N(53A)-C(82A)	-60(6)
N(53)-Pd(51)-N(53A)-C(82A)	104(7)
Cl(52)-Pd(51)-N(53A)-C(82A)	-77.7(6)
Cl(51)-Pd(51)-N(53A)-C(82A)	104.0(6)
C(52)-C(53)-C(54)-C(55)	3.7(16)
C(53)-C(54)-C(55)-C(56)	-1.4(16)
C(54)-C(55)-C(56)-C(51)	-0.2(13)
C(54)-C(55)-C(56)-C(60)	-178.1(8)
C(52)-C(51)-C(56)-C(55)	-0.5(11)
N(51)-C(51)-C(56)-C(55)	179.3(7)
C(52)-C(51)-C(56)-C(60)	177.4(8)
N(51)-C(51)-C(56)-C(60)	-2.7(10)
C(51)-C(52)-C(57)-C(59)	106.7(9)
C(53)-C(52)-C(57)-C(59)	-72.4(10)
C(51)-C(52)-C(57)-C(58)	-129.8(9)
C(53)-C(52)-C(57)-C(58)	51.1(10)
C(55)-C(56)-C(60)-C(61)	79.9(11)
C(51)-C(56)-C(60)-C(61)	-97.8(9)
C(55)-C(56)-C(60)-C(62)	-39.0(12)
C(51)-C(56)-C(60)-C(62)	143.2(7)
C(65)-N(52)-C(63)-N(51)	1.3(4)
C(66)-N(52)-C(63)-N(51)	-174.4(6)
C(65)-N(52)-C(63)-Pd(51)	-170.6(5)
C(66)-N(52)-C(63)-Pd(51)	13.7(8)
C(64)-N(51)-C(63)-N(52)	-2.1(4)
C(51)-N(51)-C(63)-N(52)	172.2(7)
C(64)-N(51)-C(63)-Pd(51)	170.2(5)
C(51)-N(51)-C(63)-Pd(51)	-15.5(8)
N(53A)-Pd(51)-C(63)-N(52)	47(6)
N(53)-Pd(51)-C(63)-N(52)	-36(6)
Cl(52)-Pd(51)-C(63)-N(52)	63.9(5)
Cl(51)-Pd(51)-C(63)-N(52)	-117.8(5)
N(53A)-Pd(51)-C(63)-N(51)	-123(6)
N(53)-Pd(51)-C(63)-N(51)	154(5)

Cl(52)-Pd(51)-C(63)-N(51)	-106.3(4)
Cl(51)-Pd(51)-C(63)-N(51)	72.1(4)
C(63)-N(51)-C(64)-C(65)	2.1(4)
C(51)-N(51)-C(64)-C(65)	-172.3(6)
N(51)-C(64)-C(65)-N(52)	-1.2(4)
C(63)-N(52)-C(65)-C(64)	-0.1(4)
C(66)-N(52)-C(65)-C(64)	175.7(6)
C(63)-N(52)-C(66)-C(71)	-113.7(7)
C(65)-N(52)-C(66)-C(71)	71.0(9)
C(63)-N(52)-C(66)-C(67)	65.9(9)
C(65)-N(52)-C(66)-C(67)	-109.4(7)
C(71)-C(66)-C(67)-C(68)	-1.8(12)
N(52)-C(66)-C(67)-C(68)	178.6(7)
C(71)-C(66)-C(67)-C(72)	-176.6(8)
N(52)-C(66)-C(67)-C(72)	3.8(11)
C(66)-C(67)-C(68)-C(69)	-2.2(12)
C(72)-C(67)-C(68)-C(69)	172.8(8)
C(67)-C(68)-C(69)-C(70)	4.6(14)
C(68)-C(69)-C(70)-C(71)	-3.0(14)
C(69)-C(70)-C(71)-C(66)	-0.7(13)
C(69)-C(70)-C(71)-C(75)	-177.8(9)
C(67)-C(66)-C(71)-C(70)	3.2(13)
N(52)-C(66)-C(71)-C(70)	-177.2(7)
C(67)-C(66)-C(71)-C(75)	-179.9(8)
N(52)-C(66)-C(71)-C(75)	-0.4(12)
C(68)-C(67)-C(72)-C(74)	31.1(12)
C(66)-C(67)-C(72)-C(74)	-154.5(9)
C(68)-C(67)-C(72)-C(73)	-94.5(11)
C(66)-C(67)-C(72)-C(73)	79.9(10)
C(70)-C(71)-C(75)-C(77)	75.2(9)
C(66)-C(71)-C(75)-C(77)	-101.7(10)
C(70)-C(71)-C(75)-C(76)	-50.9(10)
C(66)-C(71)-C(75)-C(76)	132.2(9)
C(82)-N(53)-C(78)-C(79)	0.07(12)
Pd(51)-N(53)-C(78)-C(79)	179.5(4)
C(82)-N(53)-C(78)-Cl(53)	179.94(8)
Pd(51)-N(53)-C(78)-Cl(53)	-0.7(4)
N(53)-C(78)-C(79)-C(80)	-0.10(11)
Cl(53)-C(78)-C(79)-C(80)	-179.96(8)
C(78)-C(79)-C(80)-C(81)	0.09(12)
C(79)-C(80)-C(81)-C(82)	-0.05(12)
C(78)-N(53)-C(82)-C(81)	-0.03(12)
Pd(51)-N(53)-C(82)-C(81)	-179.4(4)
C(80)-C(81)-C(82)-N(53)	0.02(12)
C(78A)-N(53A)-C(82A)-C(81A)	0.0(2)
Pd(51)-N(53A)-C(82A)-C(81A)	-169.4(15)

N(53A)-C(82A)-C(81A)-C(80A)	0.0(2)
C(82A)-C(81A)-C(80A)-C(79A)	0.0(2)
C(81A)-C(80A)-C(79A)-C(78A)	0.0(2)
C(82A)-N(53A)-C(78A)-C(79A)	0.0(2)
Pd(51)-N(53A)-C(78A)-C(79A)	168.4(17)
C(82A)-N(53A)-C(78A)-Cl(54)	180.00(15)
Pd(51)-N(53A)-C(78A)-Cl(54)	-11.6(17)
C(80A)-C(79A)-C(78A)-N(53A)	0.0(2)
C(80A)-C(79A)-C(78A)-Cl(54)	-179.97(17)

3. Crystal Data and Structure Refinement for [(SIPr)Pd(Cl)$_2$(2-bromopyridine)]

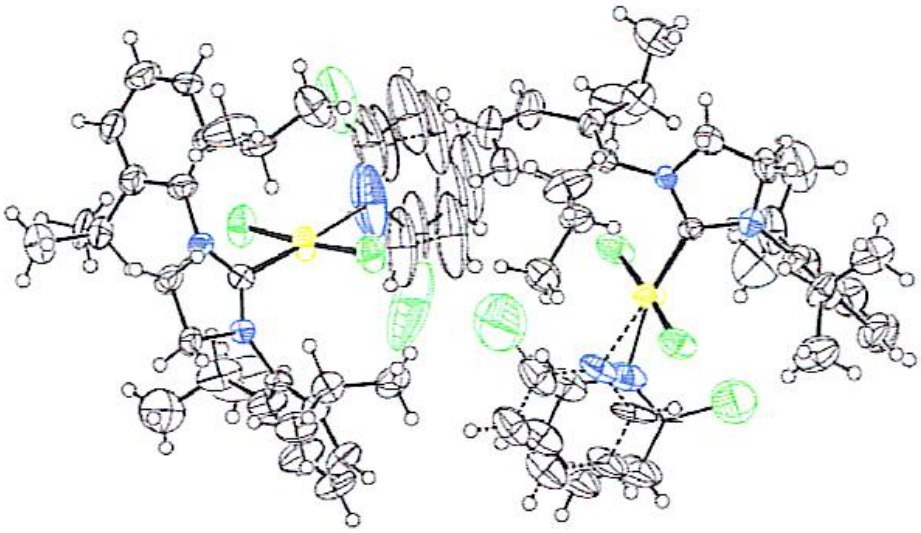

Table 3.1.

Identification code	nol341m
Empirical formula	$C_{32}H_{42}BrCl_2N_3Pd$
Formula weight	725.90
Temperature	295(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	a = 34.2809(12)Å alpha = 90 deg. b = 15.5252(5)Å beta = 107.039(1) deg. c = 12.8182(5)Å gamma = 90 deg.
Volume	6522.6(4) Å^3
Z, Calculated density	8, 1.478 Mg/m^3
Absorption coefficient	1.983 mm^{-1}
F(000)	2960
Crystal size	0.50 x 0.50 x 0.30 mm
Theta range for data collection	1.66 to 22.50 deg.
Limiting indices	$-36 \le h \le 36$, $-16 \le k \le 16$, $-13 \le l \le 13$
Reflections collected / unique	29159 / 8545 [R(int) = 0.0228]
Completeness to theta = 22.50	100.0 %
Absorption correction	Empirical
Max. and min. transmission	0.952153 and 0.866649
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8545 / 1468 / 871

Goodness-of-fit on F^2	1.078
Final R indices [I>2sigma(I)]	R1 = 0.0550, wR2 = 0.1588
R indices (all data)	R1 = 0.0638, wR2 = 0.1686
Absolute structure parameter	0.00
Largest diff. peak and hole	2.344 and -1.145 e.$Å^{-3}$

Table 3.2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2$ $x10^3$) for Nol341m. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Pd(1)	1130(1)	6861(3)	6039(1)	45(1)
Cl(1)	648(1)	7158(3)	6916(3)	62(1)
Br(1)	1139(3)	5056(7)	7581(8)	177(5)
Br(51)	491(1)	4516(4)	8718(3)	241(3)
N(1)	1491(3)	8572(7)	5812(7)	40(2)
C(1)	1261(4)	8705(9)	4695(8)	43(2)
Br(2)	527(1)	6779(3)	3431(3)	151(2)
Cl(2)	1617(1)	6480(3)	5220(3)	58(1)
N(2)	1653(3)	8138(7)	7510(6)	30(2)
C(2)	1482(3)	8630(9)	3887(9)	48(3)
C(3)	1247(4)	8734(11)	2796(9)	65(4)
N(3)	739(2)	5875(6)	5173(7)	69(3)
N(3B)	831(4)	5659(6)	5646(18)	52(4)
C(4)	845(4)	8911(14)	2530(9)	75(3)
C(5)	652(4)	9030(12)	3351(11)	70(3)
C(6)	841(4)	8878(12)	4380(9)	54(3)
C(7)	1930(4)	8435(11)	4187(10)	53(3)
C(8)	2005(5)	7669(13)	3452(13)	84(5)
C(9)	2170(5)	9232(12)	4067(12)	77(4)
C(10)	601(4)	8975(13)	5173(13)	70(3)
C(11)	197(5)	8657(18)	4816(15)	127(7)
C(12)	633(6)	9910(13)	5681(16)	110(6)
C(13)	1433(3)	7906(8)	6465(8)	30(2)
C(14)	1744(4)	9253(9)	6433(9)	51(3)
C(15)	1909(4)	8893(11)	7539(9)	48(3)
C(16)	1650(3)	7708(8)	8490(8)	33(2)
C(17)	1891(4)	6957(10)	8812(9)	46(2)
C(18)	1872(4)	6541(10)	9753(11)	63(3)
C(19)	1630(5)	6872(13)	10369(11)	72(3)
C(20)	1396(4)	7556(10)	10024(11)	62(3)
C(21)	1397(4)	8051(9)	9073(10)	42(2)
C(22)	2177(5)	6621(10)	8268(13)	57(3)

C(23)	2130(6)	5678(9)	7957(13)	78(4)
C(24)	2623(4)	6741(15)	8930(10)	84(5)
C(25)	1147(3)	8858(11)	8728(10)	52(3)
C(26)	718(4)	8713(12)	8773(15)	92(5)
C(27)	1341(5)	9609(12)	9350(14)	76(5)
C(28)	757(3)	5176(7)	5825(8)	68(3)
C(28B)	847(3)	4960(12)	6329(10)	75(5)
C(29)	542(4)	4440(7)	5392(10)	81(4)
C(29B)	622(6)	4222(11)	5942(17)	76(5)
C(30)	313(4)	4420(7)	4315(11)	92(4)
C(30B)	381(8)	4189(11)	4869(19)	86(5)
C(31)	296(4)	5132(7)	3658(8)	91(4)
C(31B)	363(7)	4884(14)	4181(13)	77(5)
C(32)	504(2)	5877(5)	4052(7)	26(2)
C(32B)	587(6)	5617(11)	4566(16)	71(5)
Pd(51)	1134(1)	3921(3)	11045(1)	45(1)
N(51)	1654(3)	2682(7)	12497(7)	36(2)
C(51)	1639(4)	3132(9)	13478(9)	43(2)
Br(52)	1128(3)	5773(9)	12494(13)	132(4)
N(52)	1485(3)	2240(6)	10811(7)	31(2)
C(52)	1877(4)	3824(10)	13839(9)	48(2)
Cl(53)	645(1)	3616(4)	11918(3)	65(1)
N(53)	812(5)	5103(8)	10730(40)	135(4)
C(53)	1867(4)	4213(8)	14802(10)	58(3)
N(53B)	864(3)	5148(6)	10650(12)	124(3)
Cl(54)	1624(1)	4321(4)	10228(3)	57(1)
C(54)	1644(5)	3908(13)	15402(9)	67(3)
C(55)	1405(4)	3140(9)	15063(9)	60(3)
C(56)	1395(4)	2774(9)	14108(10)	51(3)
C(57)	2187(5)	4171(9)	13208(11)	55(3)
C(58)	2105(8)	5169(12)	13010(17)	114(6)
C(59)	2617(4)	3905(16)	13900(12)	94(5)
C(60)	1133(4)	1958(10)	13752(10)	56(3)
C(61)	690(4)	1966(11)	13888(9)	64(3)
C(62)	1354(5)	1162(12)	14436(12)	71(4)
C(63)	1434(3)	2817(8)	11503(9)	32(2)
C(64)	1926(4)	1909(11)	12536(9)	47(3)
C(65)	1746(4)	1520(8)	11417(8)	44(3)
C(66)	1266(4)	2137(8)	9647(8)	37(2)
C(67)	1473(3)	2170(9)	8905(9)	47(3)
C(68)	1276(4)	1955(11)	7836(9)	58(3)
C(69)	872(4)	1730(13)	7488(9)	70(3)
C(70)	654(3)	1762(14)	8225(10)	74(4)
C(71)	860(4)	1915(14)	9396(9)	56(3)
C(72)	1938(4)	2361(10)	9158(11)	53(3)
C(73)	2029(5)	3053(10)	8449(10)	62(3)

C(74)	2169(4)	1539(10)	9111(11)	68(4)
C(75)	629(4)	1800(15)	10280(12)	68(3)
C(76)	163(4)	2132(17)	9810(14)	124(7)
C(77)	622(6)	829(14)	10539(15)	104(5)
C(78)	602(6)	5024(18)	9630(30)	163(6)
C(78B)	601(4)	5284(7)	9628(11)	183(4)
C(79)	388(7)	5720(30)	9080(20)	188(6)
C(79B)	377(4)	6038(9)	9437(11)	213(5)
C(80)	385(12)	6490(20)	9620(30)	193(6)
C(80B)	422(4)	6629(7)	10270(14)	202(5)
C(81)	596(14)	6568(12)	10710(30)	170(6)
C(81B)	686(4)	6483(7)	11287(12)	171(5)
C(82)	810(11)	5871(14)	11270(20)	144(5)
C(82B)	912(3)	5729(8)	11486(10)	146(4)

Table 3.3. Bond lengths [Å] and angles [deg] for Nol341m.

Pd(1)-C(13)	1.918(11)
Pd(1)-N(3B)	2.119(7)
Pd(1)-N(3)	2.122(7)
Pd(1)-Cl(2)	2.293(3)
Pd(1)-Cl(1)	2.301(4)
Br(1)-C(28B)	1.629(9)
Br(51)-C(78B)	1.632(9)
N(1)-C(13)	1.381(15)
N(1)-C(1)	1.433(13)
N(1)-C(14)	1.448(15)
C(1)-C(6)	1.403(17)
C(1)-C(2)	1.456(16)
Br(2)-C(32)	1.623(8)
N(2)-C(13)	1.379(13)
N(2)-C(16)	1.425(13)
N(2)-C(15)	1.459(17)
C(2)-C(3)	1.403(15)
C(2)-C(7)	1.501(17)
C(3)-C(4)	1.348(19)
N(3)-C(28)	1.362(7)
N(3)-C(32)	1.425(7)
N(3B)-C(28B)	1.385(8)
N(3B)-C(32B)	1.394(8)
C(4)-C(5)	1.409(19)
C(5)-C(6)	1.309(17)

C(6)-C(10)	1.490(18)
C(7)-C(9)	1.52(2)
C(7)-C(8)	1.58(2)
C(10)-C(11)	1.41(2)
C(10)-C(12)	1.58(3)
C(14)-C(15)	1.474(17)
C(16)-C(21)	1.406(16)
C(16)-C(17)	1.418(18)
C(17)-C(18)	1.387(18)
C(17)-C(22)	1.455(19)
C(18)-C(19)	1.40(2)
C(19)-C(20)	1.33(2)
C(20)-C(21)	1.442(18)
C(21)-C(25)	1.510(19)
C(22)-C(24)	1.53(2)
C(22)-C(23)	1.51(2)
C(25)-C(27)	1.46(2)
C(25)-C(26)	1.503(16)
C(28)-C(29)	1.385(8)
C(28B)-C(29B)	1.390(8)
C(29)-C(30)	1.374(7)
C(29B)-C(30B)	1.381(7)
C(30)-C(31)	1.380(7)
C(30B)-C(31B)	1.384(7)
C(31)-C(32)	1.377(7)
C(31B)-C(32B)	1.380(8)
Pd(51)-C(63)	1.996(11)
Pd(51)-N(53B)	2.114(6)
Pd(51)-N(53)	2.118(7)
Pd(51)-Cl(54)	2.311(4)
Pd(51)-Cl(53)	2.321(3)
N(51)-C(63)	1.293(13)
N(51)-C(51)	1.452(14)
N(51)-C(64)	1.512(17)
C(51)-C(52)	1.344(19)
C(51)-C(56)	1.435(18)
Br(52)-C(82)	1.631(9)
N(52)-C(63)	1.308(14)
N(52)-C(66)	1.470(13)
N(52)-C(65)	1.498(13)
C(52)-C(53)	1.384(17)
C(52)-C(57)	1.608(19)
N(53)-C(78)	1.382(9)
N(53)-C(82)	1.383(9)
C(53)-C(54)	1.320(19)
N(53B)-C(78B)	1.372(7)

N(53B)-C(82B)	1.374(8)
C(54)-C(55)	1.44(2)
C(55)-C(56)	1.341(18)
C(56)-C(60)	1.544(19)
C(57)-C(59)	1.54(2)
C(57)-C(58)	1.58(2)
C(60)-C(62)	1.57(2)
C(60)-C(61)	1.576(18)
C(64)-C(65)	1.513(16)
C(66)-C(67)	1.344(16)
C(66)-C(71)	1.377(16)
C(67)-C(68)	1.379(16)
C(67)-C(72)	1.560(17)
C(68)-C(69)	1.372(18)
C(69)-C(70)	1.366(18)
C(70)-C(71)	1.479(16)
C(71)-C(75)	1.572(18)
C(72)-C(73)	1.498(19)
C(72)-C(74)	1.513(19)
C(75)-C(77)	1.54(3)
C(75)-C(76)	1.62(2)
C(78)-C(79)	1.383(8)
C(78B)-C(79B)	1.382(8)
C(79)-C(80)	1.382(7)
C(79B)-C(80B)	1.381(7)
C(80)-C(81)	1.382(7)
C(80B)-C(81B)	1.371(7)
C(81)-C(82)	1.386(8)
C(81B)-C(82B)	1.384(8)

C(13)-Pd(1)-N(3B)	175.9(6)
C(13)-Pd(1)-N(3)	165.0(4)
N(3B)-Pd(1)-N(3)	18.6(6)
C(13)-Pd(1)-Cl(2)	86.7(3)
N(3B)-Pd(1)-Cl(2)	91.7(5)
N(3)-Pd(1)-Cl(2)	90.4(3)
C(13)-Pd(1)-Cl(1)	95.6(3)
N(3B)-Pd(1)-Cl(1)	85.7(5)
N(3)-Pd(1)-Cl(1)	88.0(3)
Cl(2)-Pd(1)-Cl(1)	176.24(15)
C(13)-N(1)-C(1)	125.3(10)
C(13)-N(1)-C(14)	112.5(8)
C(1)-N(1)-C(14)	120.6(10)
C(6)-C(1)-N(1)	122.3(11)
C(6)-C(1)-C(2)	120.9(9)
N(1)-C(1)-C(2)	116.8(10)

C(13)-N(2)-C(16)	126.3(9)
C(13)-N(2)-C(15)	112.8(9)
C(16)-N(2)-C(15)	120.9(9)
C(3)-C(2)-C(1)	115.7(10)
C(3)-C(2)-C(7)	121.6(11)
C(1)-C(2)-C(7)	122.7(9)
C(4)-C(3)-C(2)	121.4(12)
C(28)-N(3)-C(32)	122.1(7)
C(28)-N(3)-Pd(1)	110.3(6)
C(32)-N(3)-Pd(1)	127.5(6)
C(28B)-N(3B)-C(32B)	119.6(9)
C(28B)-N(3B)-Pd(1)	127.8(14)
C(32B)-N(3B)-Pd(1)	112.6(12)
C(3)-C(4)-C(5)	120.4(10)
C(6)-C(5)-C(4)	121.8(12)
C(5)-C(6)-C(1)	119.2(11)
C(5)-C(6)-C(10)	117.4(12)
C(1)-C(6)-C(10)	123.2(10)
C(2)-C(7)-C(9)	110.7(13)
C(2)-C(7)-C(8)	109.4(12)
C(9)-C(7)-C(8)	111.3(11)
C(11)-C(10)-C(6)	115.3(16)
C(11)-C(10)-C(12)	113.3(17)
C(6)-C(10)-C(12)	112.9(16)
N(1)-C(13)-N(2)	105.0(9)
N(1)-C(13)-Pd(1)	128.5(8)
N(2)-C(13)-Pd(1)	126.4(8)
C(15)-C(14)-N(1)	104.5(11)
C(14)-C(15)-N(2)	102.8(9)
C(21)-C(16)-N(2)	117.1(11)
C(21)-C(16)-C(17)	123.7(10)
N(2)-C(16)-C(17)	119.2(10)
C(18)-C(17)-C(16)	117.6(11)
C(18)-C(17)-C(22)	117.4(13)
C(16)-C(17)-C(22)	124.9(13)
C(19)-C(18)-C(17)	120.5(13)
C(20)-C(19)-C(18)	120.4(11)
C(19)-C(20)-C(21)	123.9(12)
C(16)-C(21)-C(20)	113.7(11)
C(16)-C(21)-C(25)	123.1(11)
C(20)-C(21)-C(25)	123.2(12)
C(17)-C(22)-C(24)	113.2(12)
C(17)-C(22)-C(23)	116.0(16)
C(24)-C(22)-C(23)	106.1(14)
C(27)-C(25)-C(21)	111.9(10)
C(27)-C(25)-C(26)	113.3(14)

C(21)-C(25)-C(26) 110.0(14)
N(3)-C(28)-C(29) 119.3(5)
N(3B)-C(28B)-C(29B) 120.3(6)
N(3B)-C(28B)-Br(1) 116.7(16)
C(29B)-C(28B)-Br(1) 123.0(14)
C(30)-C(29)-C(28) 120.1(5)
C(30B)-C(29B)-C(28B) 119.5(5)
C(29)-C(30)-C(31) 120.3(5)
C(29B)-C(30B)-C(31B) 120.6(5)
C(30)-C(31)-C(32) 121.6(5)
C(32B)-C(31B)-C(30B) 119.9(5)
C(31)-C(32)-N(3) 116.6(5)
C(31)-C(32)-Br(2) 129.7(6)
N(3)-C(32)-Br(2) 113.7(6)
C(31B)-C(32B)-N(3B) 120.1(6)
C(63)-Pd(51)-N(53B) 174.7(5)
C(63)-Pd(51)-N(53) 174.1(13)
N(53B)-Pd(51)-N(53) 6.5(11)
C(63)-Pd(51)-Cl(54) 89.0(3)
N(53B)-Pd(51)-Cl(54) 88.5(3)
N(53)-Pd(51)-Cl(54) 95.0(10)
C(63)-Pd(51)-Cl(53) 93.8(3)
N(53B)-Pd(51)-Cl(53) 88.4(3)
N(53)-Pd(51)-Cl(53) 82.0(11)
Cl(54)-Pd(51)-Cl(53) 175.91(16)
C(63)-N(51)-C(51) 128.1(10)
C(63)-N(51)-C(64) 109.7(9)
C(51)-N(51)-C(64) 122.0(9)
C(52)-C(51)-C(56) 120.6(10)
C(52)-C(51)-N(51) 120.8(12)
C(56)-C(51)-N(51) 118.3(11)
C(63)-N(52)-C(66) 129.2(10)
C(63)-N(52)-C(65) 109.8(8)
C(66)-N(52)-C(65) 119.6(9)
C(51)-C(52)-C(53) 119.1(12)
C(51)-C(52)-C(57) 121.2(11)
C(53)-C(52)-C(57) 119.6(12)
C(78)-N(53)-C(82) 120.8(10)
C(78)-N(53)-Pd(51) 102(2)
C(82)-N(53)-Pd(51) 137(2)
C(54)-C(53)-C(52) 122.1(13)
C(78B)-N(53B)-C(82B) 122.6(7)
C(78B)-N(53B)-Pd(51) 119.1(10)
C(82B)-N(53B)-Pd(51) 117.5(9)
C(53)-C(54)-C(55) 119.8(11)
C(56)-C(55)-C(54) 119.2(12)

C(55)-C(56)-C(51)	119.1(12)
C(55)-C(56)-C(60)	118.3(13)
C(51)-C(56)-C(60)	122.5(11)
C(59)-C(57)-C(52)	106.5(12)
C(59)-C(57)-C(58)	116.9(16)
C(52)-C(57)-C(58)	107.2(16)
C(56)-C(60)-C(62)	109.6(11)
C(56)-C(60)-C(61)	117.2(13)
C(62)-C(60)-C(61)	105.5(12)
N(51)-C(63)-N(52)	113.7(10)
N(51)-C(63)-Pd(51)	122.0(9)
N(52)-C(63)-Pd(51)	123.3(8)
N(51)-C(64)-C(65)	102.0(9)
N(52)-C(65)-C(64)	102.1(10)
C(67)-C(66)-C(71)	123.4(10)
C(67)-C(66)-N(52)	119.7(10)
C(71)-C(66)-N(52)	116.5(10)
C(66)-C(67)-C(68)	119.3(11)
C(66)-C(67)-C(72)	125.4(10)
C(68)-C(67)-C(72)	115.2(11)
C(69)-C(68)-C(67)	122.5(11)
C(68)-C(69)-C(70)	118.1(10)
C(69)-C(70)-C(71)	120.8(10)
C(66)-C(71)-C(70)	115.3(11)
C(66)-C(71)-C(75)	123.3(10)
C(70)-C(71)-C(75)	121.4(11)
C(73)-C(72)-C(74)	112.1(12)
C(73)-C(72)-C(67)	113.1(12)
C(74)-C(72)-C(67)	110.2(12)
C(77)-C(75)-C(71)	108.0(16)
C(77)-C(75)-C(76)	108.4(18)
C(71)-C(75)-C(76)	110.3(13)
N(53)-C(78)-C(79)	119.6(7)
N(53B)-C(78B)-C(79B)	118.3(5)
N(53B)-C(78B)-Br(51)	121.3(11)
C(79B)-C(78B)-Br(51)	119.5(10)
C(80)-C(79)-C(78)	119.9(5)
C(80B)-C(79B)-C(78B)	119.7(5)
C(79)-C(80)-C(81)	120.4(5)
C(81B)-C(80B)-C(79B)	121.3(5)
C(80)-C(81)-C(82)	119.9(5)
C(80B)-C(81B)-C(82B)	119.5(5)
N(53)-C(82)-C(81)	119.4(7)
N(53)-C(82)-Br(52)	108(3)
C(81)-C(82)-Br(52)	132(2)
N(53B)-C(82B)-C(81B)	118.6(5)

Table 3.4. Anisotropic displacement parameters ($Å^2$ x10^3) for Nol341m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U11 + ... + 2hka^*b^*U12]$

	U11	U22	U33	U23	U13	U12
Pd(1)	44(1)	45(1)	50(1)	-16(1)	18(1)	-17(1)
Cl(1)	59(2)	51(2)	89(2)	-21(2)	41(2)	-22(2)
Br(1)	186(9)	150(8)	159(7)	26(6)	-4(6)	23(7)
Br(51)	129(2)	412(7)	134(2)	162(3)	-37(2)	-34(3)
N(1)	41(5)	43(5)	35(4)	5(4)	12(3)	0(4)
C(1)	36(4)	54(6)	35(4)	3(5)	5(3)	-6(5)
Br(2)	199(4)	115(2)	98(2)	2(2)	-24(2)	-45(2)
Cl(2)	59(2)	47(2)	78(2)	-17(2)	36(2)	1(2)
N(2)	35(5)	27(4)	30(3)	-1(3)	13(3)	-7(4)
C(2)	48(5)	60(7)	33(4)	8(5)	8(4)	-1(5)
C(3)	72(6)	78(8)	34(4)	9(6)	-3(5)	15(7)
N(3)	70(6)	57(6)	78(6)	-25(4)	21(5)	-23(5)
N(3B)	47(8)	32(6)	86(7)	-21(6)	32(7)	-13(6)
C(4)	70(6)	94(8)	42(5)	12(7)	-15(5)	-4(7)
C(5)	48(6)	77(7)	66(5)	10(7)	-13(4)	-3(7)
C(6)	41(5)	57(6)	58(5)	13(6)	6(4)	6(6)
C(7)	54(6)	78(7)	34(6)	5(6)	22(5)	14(6)
C(8)	83(11)	102(10)	73(9)	-18(9)	29(8)	24(9)
C(9)	58(8)	116(11)	69(8)	-17(9)	37(7)	-19(8)
C(10)	43(5)	76(7)	94(7)	44(7)	26(5)	30(7)
C(11)	47(7)	212(18)	125(13)	0(14)	29(8)	1(11)
C(12)	141(13)	87(9)	141(14)	27(9)	100(11)	30(10)
C(13)	30(5)	31(4)	29(4)	-3(3)	9(4)	3(4)
C(14)	49(6)	47(6)	55(5)	14(5)	12(5)	-11(5)
C(15)	39(6)	47(6)	52(5)	-3(5)	5(5)	-22(5)
C(16)	36(5)	32(5)	29(4)	-2(4)	7(4)	-11(4)
C(17)	47(5)	41(6)	46(5)	-2(4)	8(4)	-3(5)
C(18)	71(7)	54(7)	64(7)	19(5)	20(5)	7(6)
C(19)	85(8)	75(8)	62(7)	28(7)	30(6)	0(7)
C(20)	66(7)	73(7)	60(6)	16(6)	41(6)	0(6)
C(21)	39(5)	52(5)	35(5)	2(4)	14(4)	-3(4)
C(22)	68(6)	43(6)	58(7)	-9(6)	15(5)	16(6)
C(23)	113(11)	44(7)	76(9)	0(6)	27(8)	28(7)
C(24)	67(6)	125(12)	60(8)	-28(9)	16(6)	14(8)
C(25)	34(5)	68(6)	57(6)	1(6)	17(5)	6(5)
C(26)	39(6)	101(12)	155(13)	-38(10)	57(8)	11(6)

C(27)	57(8)	57(8)	113(12)	-7(8)	23(8)	6(7)
C(28)	63(7)	51(6)	98(7)	-16(5)	37(6)	-5(6)
C(28B)	73(9)	51(8)	115(8)	0(7)	50(8)	-11(8)
C(29)	77(7)	55(6)	111(8)	-10(6)	27(7)	-20(6)
C(29B)	80(9)	50(8)	114(9)	3(8)	53(9)	-5(8)
C(30)	87(8)	58(7)	119(9)	-19(7)	10(8)	-29(7)
C(30B)	83(10)	54(8)	120(10)	-5(8)	29(9)	-14(9)
C(31)	90(8)	62(6)	102(8)	-27(6)	-2(7)	-25(7)
C(31B)	73(8)	47(7)	98(8)	-18(7)	4(8)	-27(7)
C(32)	21(4)	30(4)	34(4)	-33(3)	20(3)	-19(3)
C(32B)	65(8)	51(7)	90(8)	-49(7)	12(8)	-29(7)
Pd(51)	43(1)	43(1)	53(1)	16(1)	17(1)	13(1)
N(51)	42(5)	35(5)	29(3)	0(3)	6(3)	6(4)
C(51)	48(6)	42(6)	36(4)	-4(4)	9(4)	8(4)
Br(52)	123(8)	108(9)	225(9)	61(8)	142(7)	51(7)
N(52)	27(4)	33(4)	32(3)	0(3)	7(3)	2(4)
C(52)	61(6)	42(6)	36(5)	-6(4)	6(4)	10(5)
Cl(53)	68(2)	67(3)	74(2)	24(2)	44(2)	25(2)
N(53)	93(9)	118(7)	223(9)	124(7)	94(8)	76(7)
C(53)	98(8)	34(6)	40(5)	-10(5)	17(5)	7(6)
N(53B)	84(7)	112(6)	210(8)	120(5)	94(6)	71(6)
Cl(54)	57(2)	50(2)	73(2)	11(2)	33(2)	4(2)
C(54)	94(9)	65(7)	42(6)	-8(6)	20(5)	20(6)
C(55)	91(8)	54(6)	36(5)	14(5)	23(5)	22(6)
C(56)	68(6)	45(5)	40(5)	6(5)	17(5)	14(5)
C(57)	69(6)	59(7)	34(5)	-22(5)	11(4)	-10(5)
C(58)	168(16)	64(8)	101(13)	6(9)	29(12)	-33(9)
C(59)	54(6)	143(12)	77(9)	-52(10)	8(6)	-12(8)
C(60)	81(7)	49(6)	44(6)	10(5)	27(5)	1(5)
C(61)	83(7)	73(8)	41(6)	31(6)	28(6)	12(6)
C(62)	72(9)	62(8)	79(9)	18(8)	23(8)	1(7)
C(63)	25(5)	33(4)	38(4)	-1(4)	10(4)	0(4)
C(64)	62(7)	45(6)	32(4)	2(5)	12(5)	20(6)
C(65)	60(7)	36(5)	34(5)	10(4)	13(5)	12(5)
C(66)	39(5)	35(6)	33(4)	-9(4)	6(3)	-8(5)
C(67)	48(5)	52(6)	38(4)	0(5)	12(4)	-3(5)
C(68)	56(5)	83(8)	36(4)	0(6)	15(4)	13(6)
C(69)	65(6)	94(9)	41(5)	-18(6)	0(4)	2(7)
C(70)	43(6)	122(9)	49(5)	-20(7)	0(4)	-12(7)
C(71)	37(5)	80(7)	49(5)	-20(6)	9(4)	-5(6)
C(72)	46(5)	63(7)	51(7)	-3(6)	16(5)	1(5)
C(73)	71(9)	79(8)	47(7)	-8(6)	36(7)	-9(7)
C(74)	61(8)	77(8)	67(8)	-21(7)	22(7)	7(7)
C(75)	37(5)	102(8)	67(6)	-24(8)	19(5)	-2(7)
C(76)	35(7)	208(17)	124(12)	-56(13)	17(7)	15(10)
C(77)	102(11)	111(10)	120(12)	-15(10)	67(10)	-37(10)

C(78)	102(10)	171(9)	227(10)	154(8)	66(9)	65(9)
C(78B)	105(8)	196(8)	251(9)	187(6)	58(7)	66(7)
C(79)	115(11)	186(10)	274(11)	180(8)	70(10)	67(10)
C(79B)	119(9)	219(9)	302(11)	211(7)	65(9)	63(8)
C(80)	117(11)	170(10)	315(12)	184(10)	101(11)	63(10)
C(80B)	121(9)	167(9)	347(12)	191(7)	116(9)	52(8)
C(81)	115(11)	123(9)	313(12)	160(9)	125(10)	72(9)
C(81B)	130(9)	113(8)	318(11)	120(8)	140(9)	65(7)
C(82)	104(9)	101(8)	269(10)	124(7)	121(9)	81(8)
C(82B)	126(8)	89(7)	266(10)	103(7)	125(8)	66(7)

Table 3.5. Hydrogen coordinates (x10^4) and isotropic displacement parameters (Å^2 x10^3) for Nol341m.

	x	y	z	U(eq)
H(3)	1371	8678	2245	79
H(4)	694	8956	1800	90
H(5)	383	9221	3156	84
H(7)	2020	8250	4952	64
H(8A)	1955	7866	2714	127
H(8B)	1824	7201	3470	127
H(8C)	2283	7476	3726	127
H(9A)	2134	9341	3308	116
H(9B)	2454	9142	4434	116
H(9C)	2073	9718	4384	116
H(10)	740	8602	5786	84
H(11A)	41	8993	4208	191
H(11B)	76	8697	5401	191
H(11C)	200	8067	4598	191
H(12A)	879	9957	6274	166
H(12B)	402	10012	5945	166
H(12C)	635	10328	5131	166
H(14A)	1962	9400	6125	61
H(14B)	1583	9765	6445	61
H(15A)	1885	9300	8090	57
H(15B)	2193	8731	7682	57
H(18)	2021	6039	9977	76
H(19)	1633	6611	11025	86
H(20)	1220	7725	10418	74

H(22)	2140(30)	6910(70)	7680(90)	50(30)
H(23A)	2194	5332	8606	116
H(23B)	2312	5535	7539	116
H(23C)	1854	5568	7529	116
H(24A)	2794	6405	8612	127
H(24B)	2660	6555	9667	127
H(24C)	2695	7338	8928	127
H(25)	1131	8965	7963	63
H(26A)	724	8564	9504	139
H(26B)	596	8252	8287	139
H(26C)	562	9229	8555	139
H(27A)	1161	10095	9162	115
H(27B)	1590	9734	9180	115
H(27C)	1401	9492	10116	115
H(28)	912	5192	6554	81
H(29)	552	3958	5831	97
H(29B)	633	3753	6401	92
H(30)	169	3925	4027	111
H(30B)	230	3696	4608	103
H(31)	139	5107	2931	109
H(31B)	201	4857	3460	93
H(32B)	575	6084	4104	85
H(53)	2023	4704	15036	69
H(54)	1641	4189	16040	80
H(55)	1260	2901	15501	71
H(57)	2127	3882	12499	66
H(58A)	1832	5256	12549	170
H(58B)	2295	5404	12664	170
H(58C)	2139	5452	13697	170
H(59A)	2683	4196	14591	141
H(59B)	2812	4060	13526	141
H(59C)	2625	3294	14016	141
H(60)	1080(20)	1890(50)	12880(70)	30(20)
H(61A)	690	1650	14531	95
H(61B)	503	1703	13261	95
H(61C)	608	2550	13954	95
H(62A)	1632	1143	14423	106
H(62B)	1217	641	14126	106
H(62C)	1347	1217	15176	106
H(64A)	2040(30)	1640(60)	13110(80)	40(30)
H(64B)	2210(30)	2350(60)	12560(70)	40(20)
H(65A)	1957	1366	11085	52
H(65B)	1583	1014	11448	52
H(68)	1423	1964	7331	69
H(69)	749	1559	6771	84
H(70)	372	1688	7987	89

H(73)	2030(20)	2590(40)	9950(60)	12(16)
H(73A)	2318	3147	8644	93
H(73B)	1895	3576	8549	93
H(73C)	1932	2878	7698	93
H(74A)	2159	1169	9704	101
H(74B)	2447	1674	9169	101
H(74C)	2046	1251	8431	101
H(75)	750(20)	2110(50)	10920(60)	20(19)
H(76A)	-2	1682	9387	186
H(76B)	154	2628	9357	186
H(76C)	60	2282	10407	186
H(77A)	549	754	11201	156
H(77B)	888	588	10628	156
H(77C)	426	543	9951	156
H(78)	604	4506	9272	196
H(79)	246	5674	8340	226
H(79B)	196	6147	8752	255
H(80)	241	6960	9242	231
H(80B)	270	7135	10138	242
H(81)	593	7087	11072	204
H(81B)	713	6887	11840	206
H(82B)	1092	5619	12171	175

Table 3.6. Torsion angles [Deg] for Nol341m.

C(13)-N(1)-C(1)-C(6)	63.3(19)
C(14)-N(1)-C(1)-C(6)	-101.5(16)
C(13)-N(1)-C(1)-C(2)	-115.0(13)
C(14)-N(1)-C(1)-C(2)	80.2(15)
C(6)-C(1)-C(2)-C(3)	0(2)
N(1)-C(1)-C(2)-C(3)	177.9(12)
C(6)-C(1)-C(2)-C(7)	-179.2(15)
N(1)-C(1)-C(2)-C(7)	-1(2)
C(1)-C(2)-C(3)-C(4)	1(2)
C(7)-C(2)-C(3)-C(4)	-179.8(17)
C(13)-Pd(1)-N(3)-C(28)	179(40)
N(3B)-Pd(1)-N(3)-C(28)	5.9(19)
Cl(2)-Pd(1)-N(3)-C(28)	100.1(2)
Cl(1)-Pd(1)-N(3)-C(28)	-76.5(2)
C(13)-Pd(1)-N(3)-C(32)	3(2)
N(3B)-Pd(1)-N(3)-C(32)	-170(2)
Cl(2)-Pd(1)-N(3)-C(32)	-75.8(6)
Cl(1)-Pd(1)-N(3)-C(32)	107.6(6)

C(13)-Pd(1)-N(3B)-C(28B)	34(10)
N(3)-Pd(1)-N(3B)-C(28B)	-171(3)
Cl(2)-Pd(1)-N(3B)-C(28B)	102.3(12)
Cl(1)-Pd(1)-N(3B)-C(28B)	-74.9(12)
C(13)-Pd(1)-N(3B)-C(32B)	-147(9)
N(3)-Pd(1)-N(3B)-C(32B)	7.0(18)
Cl(2)-Pd(1)-N(3B)-C(32B)	-79.2(4)
Cl(1)-Pd(1)-N(3B)-C(32B)	103.6(4)
C(2)-C(3)-C(4)-C(5)	2(3)
C(3)-C(4)-C(5)-C(6)	-8(3)
C(4)-C(5)-C(6)-C(1)	9(3)
C(4)-C(5)-C(6)-C(10)	-176.5(19)
N(1)-C(1)-C(6)-C(5)	177.1(15)
C(2)-C(1)-C(6)-C(5)	-5(2)
N(1)-C(1)-C(6)-C(10)	3(3)
C(2)-C(1)-C(6)-C(10)	-179.1(16)
C(3)-C(2)-C(7)-C(9)	74.7(17)
C(1)-C(2)-C(7)-C(9)	-106.6(15)
C(3)-C(2)-C(7)-C(8)	-48.3(19)
C(1)-C(2)-C(7)-C(8)	130.4(14)
C(5)-C(6)-C(10)-C(11)	41(3)
C(1)-C(6)-C(10)-C(11)	-144.8(19)
C(5)-C(6)-C(10)-C(12)	-92(2)
C(1)-C(6)-C(10)-C(12)	83(2)
C(1)-N(1)-C(13)-N(2)	-167.0(11)
C(14)-N(1)-C(13)-N(2)	-1.2(14)
C(1)-N(1)-C(13)-Pd(1)	14.8(17)
C(14)-N(1)-C(13)-Pd(1)	-179.4(8)
C(16)-N(2)-C(13)-N(1)	172.1(10)
C(15)-N(2)-C(13)-N(1)	-9.0(13)
C(16)-N(2)-C(13)-Pd(1)	-9.7(17)
C(15)-N(2)-C(13)-Pd(1)	169.3(9)
N(3B)-Pd(1)-C(13)-N(1)	136(9)
N(3)-Pd(1)-C(13)-N(1)	-12(2)
Cl(2)-Pd(1)-C(13)-N(1)	67.2(10)
Cl(1)-Pd(1)-C(13)-N(1)	-115.7(10)
N(3B)-Pd(1)-C(13)-N(2)	-42(10)
N(3)-Pd(1)-C(13)-N(2)	170.0(11)
Cl(2)-Pd(1)-C(13)-N(2)	-110.6(10)
Cl(1)-Pd(1)-C(13)-N(2)	66.5(10)
C(13)-N(1)-C(14)-C(15)	10.3(15)
C(1)-N(1)-C(14)-C(15)	176.9(11)
N(1)-C(14)-C(15)-N(2)	-14.3(14)
C(13)-N(2)-C(15)-C(14)	15.0(14)
C(16)-N(2)-C(15)-C(14)	-166.0(11)
C(13)-N(2)-C(16)-C(21)	-98.0(14)

C(15)-N(2)-C(16)-C(21)	83.1(14)
C(13)-N(2)-C(16)-C(17)	80.6(15)
C(15)-N(2)-C(16)-C(17)	-98.3(13)
C(21)-C(16)-C(17)-C(18)	0.3(18)
N(2)-C(16)-C(17)-C(18)	-178.2(11)
C(21)-C(16)-C(17)-C(22)	-175.5(13)
N(2)-C(16)-C(17)-C(22)	6.0(18)
C(16)-C(17)-C(18)-C(19)	-2(2)
C(22)-C(17)-C(18)-C(19)	174.6(15)
C(17)-C(18)-C(19)-C(20)	4(3)
C(18)-C(19)-C(20)-C(21)	-6(3)
N(2)-C(16)-C(21)-C(20)	177.0(11)
C(17)-C(16)-C(21)-C(20)	-1.5(18)
N(2)-C(16)-C(21)-C(25)	-2.3(17)
C(17)-C(16)-C(21)-C(25)	179.2(11)
C(19)-C(20)-C(21)-C(16)	4(2)
C(19)-C(20)-C(21)-C(25)	-176.3(15)
C(18)-C(17)-C(22)-C(24)	-67.4(19)
C(16)-C(17)-C(22)-C(24)	108.4(16)
C(18)-C(17)-C(22)-C(23)	55.6(19)
C(16)-C(17)-C(22)-C(23)	-128.6(15)
C(16)-C(21)-C(25)-C(27)	-100.0(16)
C(20)-C(21)-C(25)-C(27)	80.8(17)
C(16)-C(21)-C(25)-C(26)	133.1(13)
C(20)-C(21)-C(25)-C(26)	-46.1(18)
C(32)-N(3)-C(28)-C(29)	0.02(5)
Pd(1)-N(3)-C(28)-C(29)	-176.1(7)
C(32B)-N(3B)-C(28B)-C(29B)	-0.01(5)
Pd(1)-N(3B)-C(28B)-C(29B)	178.4(15)
C(32B)-N(3B)-C(28B)-Br(1)	180.00(3)
Pd(1)-N(3B)-C(28B)-Br(1)	-1.6(15)
N(3)-C(28)-C(29)-C(30)	-0.02(5)
N(3B)-C(28B)-C(29B)-C(30B)	0.01(5)
Br(1)-C(28B)-C(29B)-C(30B)	180.00(4)
C(28)-C(29)-C(30)-C(31)	0.01(5)
C(28B)-C(29B)-C(30B)-C(31B)	0.00(5)
C(29)-C(30)-C(31)-C(32)	-0.01(5)
C(29B)-C(30B)-C(31B)-C(32B)	0.00(5)
C(30)-C(31)-C(32)-N(3)	0.02(5)
C(30)-C(31)-C(32)-Br(2)	179.98(4)
C(28)-N(3)-C(32)-C(31)	-0.02(5)
Pd(1)-N(3)-C(32)-C(31)	175.4(8)
C(28)-N(3)-C(32)-Br(2)	180.00(3)
Pd(1)-N(3)-C(32)-Br(2)	-4.6(8)
C(30B)-C(31B)-C(32B)-N(3B)	0.00(5)
C(28B)-N(3B)-C(32B)-C(31B)	0.00(5)

Pd(1)-N(3B)-C(32B)-C(31B)	-178.6(13)
C(63)-N(51)-C(51)-C(52)	-91.0(16)
C(64)-N(51)-C(51)-C(52)	93.5(15)
C(63)-N(51)-C(51)-C(56)	94.8(16)
C(64)-N(51)-C(51)-C(56)	-80.7(15)
C(56)-C(51)-C(52)-C(53)	-3(2)
N(51)-C(51)-C(52)-C(53)	-177.2(12)
C(56)-C(51)-C(52)-C(57)	173.4(12)
N(51)-C(51)-C(52)-C(57)	-0.7(19)
C(63)-Pd(51)-N(53)-C(78)	-151(5)
N(53B)-Pd(51)-N(53)-C(78)	79(10)
Cl(54)-Pd(51)-N(53)-C(78)	76.8(9)
Cl(53)-Pd(51)-N(53)-C(78)	-105.9(9)
C(63)-Pd(51)-N(53)-C(82)	38(6)
N(53B)-Pd(51)-N(53)-C(82)	-91(9)
Cl(54)-Pd(51)-N(53)-C(82)	-93.7(13)
Cl(53)-Pd(51)-N(53)-C(82)	83.5(13)
C(51)-C(52)-C(53)-C(54)	3(2)
C(57)-C(52)-C(53)-C(54)	-174.0(14)
C(63)-Pd(51)-N(53B)-C(78B)	146(5)
N(53)-Pd(51)-N(53B)-C(78B)	-94(10)
Cl(54)-Pd(51)-N(53B)-C(78B)	83.4(4)
Cl(53)-Pd(51)-N(53B)-C(78B)	-99.3(4)
C(63)-Pd(51)-N(53B)-C(82B)	-44(6)
N(53)-Pd(51)-N(53B)-C(82B)	76(10)
Cl(54)-Pd(51)-N(53B)-C(82B)	-106.5(5)
Cl(53)-Pd(51)-N(53B)-C(82B)	70.9(5)
C(52)-C(53)-C(54)-C(55)	1(2)
C(53)-C(54)-C(55)-C(56)	-4(2)
C(54)-C(55)-C(56)-C(51)	3(2)
C(54)-C(55)-C(56)-C(60)	-179.2(12)
C(52)-C(51)-C(56)-C(55)	0(2)
N(51)-C(51)-C(56)-C(55)	174.4(12)
C(52)-C(51)-C(56)-C(60)	-177.2(12)
N(51)-C(51)-C(56)-C(60)	-3.0(18)
C(51)-C(52)-C(57)-C(59)	-105.4(14)
C(53)-C(52)-C(57)-C(59)	71.1(17)
C(51)-C(52)-C(57)-C(58)	128.8(15)
C(53)-C(52)-C(57)-C(58)	-54.7(18)
C(55)-C(56)-C(60)-C(62)	-75.0(16)
C(51)-C(56)-C(60)-C(62)	102.4(15)
C(55)-C(56)-C(60)-C(61)	45.2(17)
C(51)-C(56)-C(60)-C(61)	-137.4(12)
C(51)-N(51)-C(63)-N(52)	-172.5(11)
C(64)-N(51)-C(63)-N(52)	3.5(14)
C(51)-N(51)-C(63)-Pd(51)	18.7(18)

C(64)-N(51)-C(63)-Pd(51)	-165.3(8)
C(66)-N(52)-C(63)-N(51)	174.0(11)
C(65)-N(52)-C(63)-N(51)	7.7(14)
C(66)-N(52)-C(63)-Pd(51)	-17.3(17)
C(65)-N(52)-C(63)-Pd(51)	176.3(7)
N(53B)-Pd(51)-C(63)-N(51)	42(6)
N(53)-Pd(51)-C(63)-N(51)	-28(6)
Cl(54)-Pd(51)-C(63)-N(51)	104.2(9)
Cl(53)-Pd(51)-C(63)-N(51)	-72.8(10)
N(53B)-Pd(51)-C(63)-N(52)	-126(5)
N(53)-Pd(51)-C(63)-N(52)	164(6)
Cl(54)-Pd(51)-C(63)-N(52)	-63.5(9)
Cl(53)-Pd(51)-C(63)-N(52)	119.5(9)
C(63)-N(51)-C(64)-C(65)	-12.6(14)
C(51)-N(51)-C(64)-C(65)	163.6(11)
C(63)-N(52)-C(65)-C(64)	-15.0(13)
C(66)-N(52)-C(65)-C(64)	177.1(10)
N(51)-C(64)-C(65)-N(52)	15.5(12)
C(63)-N(52)-C(66)-C(67)	120.8(14)
C(65)-N(52)-C(66)-C(67)	-74.0(14)
C(63)-N(52)-C(66)-C(71)	-66.2(18)
C(65)-N(52)-C(66)-C(71)	98.9(15)
C(71)-C(66)-C(67)-C(68)	-1(2)
N(52)-C(66)-C(67)-C(68)	171.1(13)
C(71)-C(66)-C(67)-C(72)	-175.9(16)
N(52)-C(66)-C(67)-C(72)	-3(2)
C(66)-C(67)-C(68)-C(69)	2(2)
C(72)-C(67)-C(68)-C(69)	176.9(15)
C(67)-C(68)-C(69)-C(70)	3(3)
C(68)-C(69)-C(70)-C(71)	-9(3)
C(67)-C(66)-C(71)-C(70)	-4(3)
N(52)-C(66)-C(71)-C(70)	-176.4(14)
C(67)-C(66)-C(71)-C(75)	174.6(16)
N(52)-C(66)-C(71)-C(75)	2(2)
C(69)-C(70)-C(71)-C(66)	9(3)
C(69)-C(70)-C(71)-C(75)	-170(2)
C(66)-C(67)-C(72)-C(73)	-129.5(14)
C(68)-C(67)-C(72)-C(73)	55.7(17)
C(66)-C(67)-C(72)-C(74)	104.1(16)
C(68)-C(67)-C(72)-C(74)	-70.7(17)
C(66)-C(71)-C(75)-C(77)	-97(2)
C(70)-C(71)-C(75)-C(77)	81(2)
C(66)-C(71)-C(75)-C(76)	144.3(19)
C(70)-C(71)-C(75)-C(76)	-38(3)
C(82)-N(53)-C(78)-C(79)	0.00(5)
Pd(51)-N(53)-C(78)-C(79)	-172.5(15)

C(82B)-N(53B)-C(78B)-C(79B)	0.01(5)
Pd(51)-N(53B)-C(78B)-C(79B)	169.6(7)
C(82B)-N(53B)-C(78B)-Br(51)	-169.1(9)
Pd(51)-N(53B)-C(78B)-Br(51)	0.5(7)
N(53)-C(78)-C(79)-C(80)	0.02(5)
N(53B)-C(78B)-C(79B)-C(80B)	0.00(5)
Br(51)-C(78B)-C(79B)-C(80B)	169.3(9)
C(78)-C(79)-C(80)-C(81)	-0.02(5)
C(78B)-C(79B)-C(80B)-C(81B)	0.01(5)
C(79)-C(80)-C(81)-C(82)	0.00(5)
C(79B)-C(80B)-C(81B)-C(82B)	-0.03(5)
C(78)-N(53)-C(82)-C(81)	-0.02(5)
Pd(51)-N(53)-C(82)-C(81)	169(2)
C(78)-N(53)-C(82)-Br(52)	-173(2)
Pd(51)-N(53)-C(82)-Br(52)	-4.1(16)
C(80)-C(81)-C(82)-N(53)	0.02(5)
C(80)-C(81)-C(82)-Br(52)	171(3)
C(78B)-N(53B)-C(82B)-C(81B)	-0.02(5)
Pd(51)-N(53B)-C(82B)-C(81B)	-169.8(7)
C(80B)-C(81B)-C(82B)-N(53B)	0.03(5)

4. Crystal Data and Structure Refinement for [(IPr)Pd(Cl)$_2$(pyridine)]

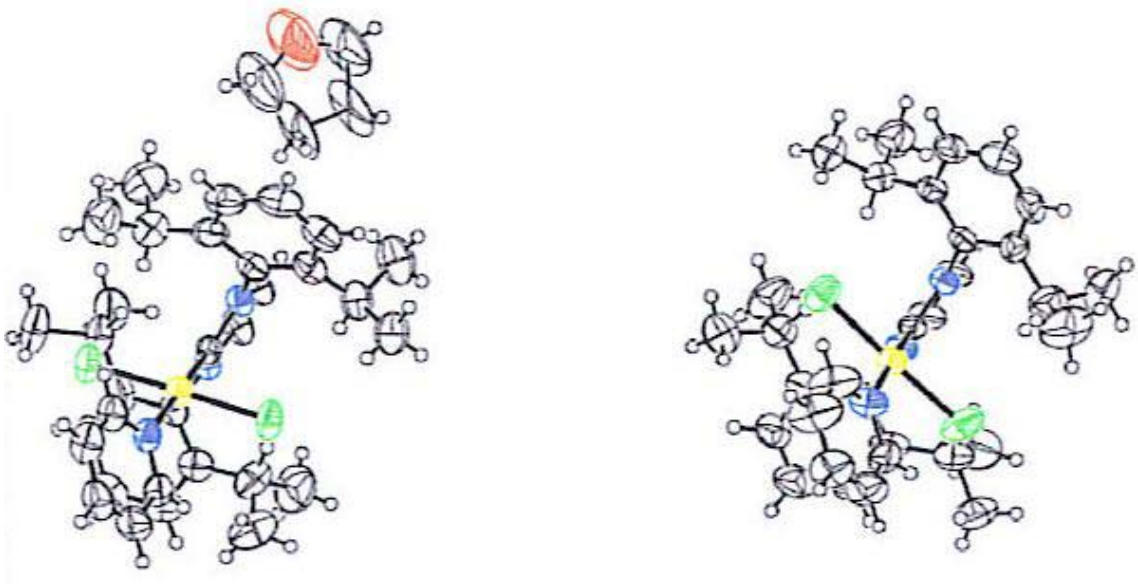

Table 4.1.

Identification code	nol344m
Empirical formula	$C_{32}H_{41}Cl_2N_3Pd$ 0.25(C_4H_8O)
Formula weight	663.00
Temperature	568(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/n$
Unit cell dimensions	a = 21.4514(14) Å α = 90 deg.
	b = 14.7266(10) Å β = 106.922(1) deg.
	c = 21.9025(15) Å γ = 90 deg.
Volume	6619.5(8) Å^3
Z, Calculated density	8, 1.331 Mg/m^3
Absorption coefficient	0.748 mm^{-1}
F(000)	2752
Crystal size	0.50 x 0.40 x 0.20 mm
Theta range for data collection	1.17 to 22.50 deg.
Limiting indices	-23<=h<=23, -15<=k<=15, -23<=l<=23
Reflections collected / unique	44125 / 8516 [R(int) = 0.0313]
Completeness to theta = 22.50	98.5 %
Absorption correction	Empirical
Max. and min. transmission	0.937611 and 0.820100

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8516 / 694 / 747
Goodness-of-fit on F^2	1.099
Final R indices [I>2σ(I)]	R1 = 0.0863, wR2 = 0.2638
R indices (all data)	R1 = 0.0931, wR2 = 0.2658
Extinction coefficient	0.0017(2)
Largest diff. peak and hole	2.263 and -0.838 e.Å^{-3}

Table 4.2. Atomic coordinates (x10^4) and equivalent isotropic displacement parameters (Å^2 x10^3) for Nol344m. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Pd(1)	3536(1)	2117(1)	1615(1)	41(1)
Cl(1)	2977(2)	1141(2)	2087(2)	64(1)
N(1)	3829(5)	3541(7)	2630(5)	46(2)
C(1)	4506(7)	3263(10)	2906(7)	55(3)
Cl(2)	4065(2)	3088(3)	1121(2)	67(1)
N(2)	2830(5)	3594(7)	2067(5)	43(2)
C(2)	4643(8)	2515(11)	3311(7)	67(3)
N(3)	3693(5)	1051(7)	1046(5)	51(2)
C(3)	5301(9)	2308(13)	3577(8)	81(4)
C(4)	5777(9)	2818(14)	3445(8)	82(4)
C(5)	5641(8)	3562(12)	3061(8)	77(4)
C(6)	4992(7)	3818(11)	2782(7)	61(3)
C(7)	4106(10)	1985(13)	3480(9)	87(4)
C(8)	4248(12)	947(15)	3578(12)	131(7)
C(9)	3981(13)	2300(20)	4076(10)	133(7)
C(10)	4848(7)	4671(11)	2387(8)	70(3)
C(11)	4998(9)	5514(13)	2841(11)	99(6)
C(12)	5237(8)	4705(14)	1900(9)	86(5)
C(13)	3387(6)	3109(8)	2134(6)	42(2)
C(14)	3553(7)	4271(10)	2839(7)	59(3)
C(15)	2932(7)	4310(9)	2496(7)	57(3)
C(16)	2190(6)	3355(9)	1650(7)	49(3)
C(17)	1761(7)	2898(10)	1943(8)	60(3)
C(18)	1138(8)	2733(11)	1558(9)	75(4)
C(19)	958(9)	2930(14)	914(10)	90(5)
C(20)	1384(8)	3406(13)	643(8)	77(4)
C(21)	2018(7)	3614(10)	1006(7)	60(3)
C(22)	1946(8)	2675(10)	2635(8)	65(3)
C(23)	1675(9)	3359(12)	3002(9)	84(5)
C(24)	1733(10)	1686(11)	2774(10)	90(5)

C(25)	2441(9)	4146(13)	724(9)	82(4)
C(26)	2469(11)	3796(17)	102(9)	111(6)
C(27)	2179(12)	5186(14)	649(12)	120(7)
C(28)	3929(7)	271(9)	1286(8)	59(3)
C(29)	3990(8)	-470(11)	921(8)	72(4)
C(30)	3768(8)	-383(11)	264(9)	73(4)
C(31)	3523(8)	422(12)	11(8)	73(4)
C(32)	3494(7)	1125(10)	413(7)	57(3)
O(33)	5190(30)	4740(60)	5520(30)	206(15)
C(34)	4920(30)	4130(40)	5070(50)	207(17)
C(35)	4790(30)	4700(50)	4510(40)	192(17)
C(36)	5010(40)	5610(50)	4710(40)	184(16)
C(37)	5270(30)	5610(60)	5400(40)	197(17)
Pd(51)	7678(1)	11486(1)	901(1)	42(1)
Cl(51)	7781(2)	10473(3)	1724(2)	70(1)
N(51)	7720(5)	12961(7)	1846(5)	42(2)
C(51)	8394(6)	12846(9)	2213(6)	46(2)
Cl(52)	7584(2)	12552(3)	118(2)	78(1)
N(52)	6749(5)	12757(7)	1242(5)	45(2)
C(52)	8517(6)	12437(9)	2815(6)	48(3)
N(53)	7965(6)	10473(8)	346(5)	58(3)
C(53)	9154(8)	12374(12)	3183(8)	74(4)
C(54)	9656(8)	12707(13)	2946(8)	78(4)
C(55)	9508(8)	13156(12)	2388(9)	80(5)
C(56)	8880(7)	13273(10)	2010(7)	57(3)
C(57)	7984(8)	12094(11)	3092(7)	65(3)
C(58)	7881(10)	12736(13)	3575(8)	88(5)
C(59)	8125(10)	11125(12)	3376(8)	87(5)
C(60)	8734(9)	13713(14)	1350(8)	79(4)
C(61)	9183(10)	13410(20)	952(10)	130(7)
C(62)	8820(12)	14733(15)	1464(10)	120(7)
C(63)	7367(5)	12445(9)	1368(5)	38(2)
C(64)	7332(7)	13610(10)	2007(6)	57(3)
C(65)	6732(7)	13478(10)	1625(6)	55(3)
C(66)	6161(6)	12414(11)	787(6)	54(3)
C(67)	5844(6)	11642(11)	992(7)	58(3)
C(68)	5265(7)	11385(13)	567(8)	71(4)
C(69)	4989(8)	11786(15)	6(9)	88(5)
C(70)	5295(7)	12548(14)	-154(8)	78(4)
C(71)	5889(7)	12862(12)	241(6)	62(3)
C(72)	6114(8)	11214(11)	1619(7)	65(3)
C(73)	5787(12)	11597(14)	2089(9)	103(6)
C(74)	6027(9)	10172(13)	1623(10)	91(5)
C(75)	6180(8)	13713(13)	31(8)	75(4)
C(76)	6196(10)	13738(15)	-691(8)	96(5)
C(77)	5824(11)	14580(15)	176(11)	113(6)

C(78)	8210(10)	9678(13)	549(8)	94(6)
C(79)	8313(12)	9007(14)	171(9)	109(6)
C(80)	8177(9)	9117(13)	-490(8)	85(5)
C(81)	7925(9)	9930(13)	-701(8)	80(4)
C(82)	7836(8)	10581(11)	-296(7)	62(3)

Table 4.3. Bond lengths [Å] and angles [Deg] for Nol344m.

Pd(1)-C(13)	1.934(12)
Pd(1)-N(3)	2.091(11)
Pd(1)-Cl(2)	2.284(4)
Pd(1)-Cl(1)	2.301(3)
N(1)-C(14)	1.369(17)
N(1)-C(13)	1.372(16)
N(1)-C(1)	1.460(17)
C(1)-C(2)	1.39(2)
C(1)-C(6)	1.41(2)
N(2)-C(13)	1.363(16)
N(2)-C(15)	1.386(16)
N(2)-C(16)	1.452(16)
C(2)-C(3)	1.39(2)
C(2)-C(7)	1.52(2)
N(3)-C(28)	1.303(18)
N(3)-C(32)	1.332(17)
C(3)-C(4)	1.37(3)
C(4)-C(5)	1.36(3)
C(5)-C(6)	1.40(2)
C(6)-C(10)	1.50(2)
C(7)-C(9)	1.48(3)
C(7)-C(8)	1.56(3)
C(10)-C(12)	1.54(2)
C(10)-C(11)	1.56(2)
C(14)-C(15)	1.326(19)
C(16)-C(21)	1.40(2)
C(16)-C(17)	1.43(2)
C(17)-C(18)	1.38(2)
C(17)-C(22)	1.49(2)
C(18)-C(19)	1.38(3)
C(19)-C(20)	1.41(3)
C(20)-C(21)	1.40(2)
C(21)-C(25)	1.46(2)
C(22)-C(23)	1.51(2)
C(22)-C(24)	1.58(2)

C(25)-C(26)	1.47(3)
C(25)-C(27)	1.62(3)
C(28)-C(29)	1.38(2)
C(29)-C(30)	1.38(2)
C(30)-C(31)	1.35(2)
C(31)-C(32)	1.37(2)
O(33)-C(36)#1	0.75(4)
O(33)-C(35)#1	0.84(6)
O(33)-C(37)	1.34(5)
O(33)-C(34)	1.34(4)
C(34)-C(35)	1.44(3)
C(35)-C(36)	1.44(3)
C(36)-C(37)	1.44(3)
Pd(51)-C(63)	1.970(12)
Pd(51)-N(53)	2.126(11)
Pd(51)-Cl(52)	2.290(4)
Pd(51)-Cl(51)	2.300(4)
N(51)-C(63)	1.337(15)
N(51)-C(64)	1.378(17)
N(51)-C(51)	1.445(15)
C(51)-C(56)	1.396(19)
C(51)-C(52)	1.403(18)
N(52)-C(63)	1.354(15)
N(52)-C(65)	1.360(17)
N(52)-C(66)	1.451(16)
C(52)-C(53)	1.373(19)
C(52)-C(57)	1.53(2)
N(53)-C(78)	1.31(2)
N(53)-C(82)	1.362(18)
C(53)-C(54)	1.41(2)
C(54)-C(55)	1.34(2)
C(55)-C(56)	1.37(2)
C(56)-C(60)	1.53(2)
C(57)-C(58)	1.48(2)
C(57)-C(59)	1.55(2)
C(60)-C(62)	1.52(3)
C(60)-C(61)	1.54(3)
C(64)-C(65)	1.330(18)
C(66)-C(71)	1.34(2)
C(66)-C(67)	1.46(2)
C(67)-C(68)	1.37(2)
C(67)-C(72)	1.47(2)
C(68)-C(69)	1.34(2)
C(69)-C(70)	1.39(3)
C(70)-C(71)	1.39(2)
C(71)-C(75)	1.53(2)

C(72)-C(73)	1.51(2)
C(72)-C(74)	1.55(2)
C(75)-C(77)	1.57(3)
C(75)-C(76)	1.59(2)
C(78)-C(79)	1.35(2)
C(79)-C(80)	1.40(2)
C(80)-C(81)	1.34(2)
C(81)-C(82)	1.36(2)
C(13)-Pd(1)-N(3)	179.5(5)
C(13)-Pd(1)-Cl(2)	89.8(4)
N(3)-Pd(1)-Cl(2)	89.9(3)
C(13)-Pd(1)-Cl(1)	90.6(4)
N(3)-Pd(1)-Cl(1)	89.7(3)
Cl(2)-Pd(1)-Cl(1)	178.36(17)
C(14)-N(1)-C(13)	111.2(11)
C(14)-N(1)-C(1)	123.8(11)
C(13)-N(1)-C(1)	125.0(10)
C(2)-C(1)-C(6)	123.4(14)
C(2)-C(1)-N(1)	119.1(13)
C(6)-C(1)-N(1)	117.4(13)
C(13)-N(2)-C(15)	111.4(11)
C(13)-N(2)-C(16)	125.4(10)
C(15)-N(2)-C(16)	123.0(10)
C(1)-C(2)-C(3)	116.2(16)
C(1)-C(2)-C(7)	121.7(15)
C(3)-C(2)-C(7)	122.0(16)
C(28)-N(3)-C(32)	117.4(12)
C(28)-N(3)-Pd(1)	122.3(10)
C(32)-N(3)-Pd(1)	120.0(10)
C(4)-C(3)-C(2)	121.2(18)
C(5)-C(4)-C(3)	122.4(17)
C(4)-C(5)-C(6)	119.5(18)
C(5)-C(6)-C(1)	117.2(16)
C(5)-C(6)-C(10)	119.2(15)
C(1)-C(6)-C(10)	123.6(13)
C(9)-C(7)-C(2)	113.2(17)
C(9)-C(7)-C(8)	105.4(19)
C(2)-C(7)-C(8)	113.9(18)
C(6)-C(10)-C(12)	111.4(14)
C(6)-C(10)-C(11)	109.1(15)
C(12)-C(10)-C(11)	111.2(14)
N(2)-C(13)-N(1)	103.0(10)
N(2)-C(13)-Pd(1)	128.4(9)
N(1)-C(13)-Pd(1)	128.4(9)
C(15)-C(14)-N(1)	107.8(12)
C(14)-C(15)-N(2)	106.6(12)

C(21)-C(16)-C(17)	124.2(13)
C(21)-C(16)-N(2)	119.3(12)
C(17)-C(16)-N(2)	116.5(12)
C(18)-C(17)-C(16)	116.4(15)
C(18)-C(17)-C(22)	120.6(14)
C(16)-C(17)-C(22)	122.9(13)
C(17)-C(18)-C(19)	121.4(16)
C(18)-C(19)-C(20)	120.7(16)
C(21)-C(20)-C(19)	120.9(16)
C(20)-C(21)-C(16)	116.1(15)
C(20)-C(21)-C(25)	119.9(15)
C(16)-C(21)-C(25)	123.8(14)
C(17)-C(22)-C(23)	111.4(14)
C(17)-C(22)-C(24)	113.2(14)
C(23)-C(22)-C(24)	109.5(13)
C(21)-C(25)-C(26)	113.6(18)
C(21)-C(25)-C(27)	108.0(16)
C(26)-C(25)-C(27)	110.0(17)
N(3)-C(28)-C(29)	123.8(15)
C(28)-C(29)-C(30)	117.8(16)
C(31)-C(30)-C(29)	118.8(15)
C(30)-C(31)-C(32)	119.1(16)
N(3)-C(32)-C(31)	123.0(15)
C(36)#1-O(33)-C(35)#1	129(10)
C(36)#1-O(33)-C(37)	125(10)
C(35)#1-O(33)-C(37)	9(7)
C(36)#1-O(33)-C(34)	9(8)
C(35)#1-O(33)-C(34)	128(8)
C(37)-O(33)-C(34)	123(7)
O(33)-C(34)-C(35)	100(5)
C(34)-C(35)-C(36)	108(5)
C(37)-C(36)-C(35)	109(5)
O(33)-C(37)-C(36)	100(5)
C(63)-Pd(51)-N(53)	176.4(4)
C(63)-Pd(51)-Cl(52)	85.9(4)
N(53)-Pd(51)-Cl(52)	91.7(4)
C(63)-Pd(51)-Cl(51)	91.6(4)
N(53)-Pd(51)-Cl(51)	90.8(4)
Cl(52)-Pd(51)-Cl(51)	177.14(15)
C(63)-N(51)-C(64)	110.4(10)
C(63)-N(51)-C(51)	128.0(10)
C(64)-N(51)-C(51)	121.3(10)
C(56)-C(51)-C(52)	122.6(12)
C(56)-C(51)-N(51)	119.3(12)
C(52)-C(51)-N(51)	117.2(12)
C(63)-N(52)-C(65)	109.8(10)

C(63)-N(52)-C(66)	128.8(11)
C(65)-N(52)-C(66)	121.4(11)
C(53)-C(52)-C(51)	117.6(14)
C(53)-C(52)-C(57)	118.4(13)
C(51)-C(52)-C(57)	123.9(12)
C(78)-N(53)-C(82)	113.4(13)
C(78)-N(53)-Pd(51)	126.1(11)
C(82)-N(53)-Pd(51)	120.2(10)
C(52)-C(53)-C(54)	119.7(15)
C(55)-C(54)-C(53)	120.1(15)
C(54)-C(55)-C(56)	122.8(16)
C(55)-C(56)-C(51)	116.4(14)
C(55)-C(56)-C(60)	121.2(14)
C(51)-C(56)-C(60)	121.7(13)
C(58)-C(57)-C(52)	110.9(14)
C(58)-C(57)-C(59)	110.6(14)
C(52)-C(57)-C(59)	112.6(14)
C(62)-C(60)-C(56)	106.3(15)
C(62)-C(60)-C(61)	108.1(19)
C(56)-C(60)-C(61)	115.0(16)
N(51)-C(63)-N(52)	105.4(10)
N(51)-C(63)-Pd(51)	127.9(8)
N(52)-C(63)-Pd(51)	126.6(8)
C(65)-C(64)-N(51)	106.5(12)
C(64)-C(65)-N(52)	107.9(12)
C(71)-C(66)-N(52)	120.3(14)
C(71)-C(66)-C(67)	122.5(13)
N(52)-C(66)-C(67)	116.8(12)
C(68)-C(67)-C(66)	114.6(14)
C(68)-C(67)-C(72)	123.4(15)
C(66)-C(67)-C(72)	121.9(12)
C(69)-C(68)-C(67)	125.0(17)
C(68)-C(69)-C(70)	118.2(16)
C(71)-C(70)-C(69)	121.6(16)
C(66)-C(71)-C(70)	118.0(16)
C(66)-C(71)-C(75)	124.2(13)
C(70)-C(71)-C(75)	117.8(14)
C(67)-C(72)-C(73)	109.9(14)
C(67)-C(72)-C(74)	114.5(14)
C(73)-C(72)-C(74)	106.5(15)
C(71)-C(75)-C(77)	109.9(15)
C(71)-C(75)-C(76)	116.5(15)
C(77)-C(75)-C(76)	109.6(15)
N(53)-C(78)-C(79)	124.6(17)
C(78)-C(79)-C(80)	121.9(18)
C(81)-C(80)-C(79)	113.8(16)

C(80)-C(81)-C(82)	121.7(17)
C(81)-C(82)-N(53)	124.6(16)

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1,-z+1

Table 4.4. Anisotropic displacement parameters ($Å^2$ x10^3) for Nol344m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U11 + ... + 2hka^*b^*U12]$

	U11	U22	U33	U23	U13	U12
Pd(1)	50(1)	32(1)	47(1)	-7(1)	25(1)	-1(1)
Cl(1)	94(3)	41(2)	77(2)	-11(2)	57(2)	-18(2)
N(1)	49(4)	41(6)	52(6)	-11(4)	23(4)	-4(4)
C(1)	54(5)	52(7)	54(7)	-11(5)	5(5)	-4(4)
Cl(2)	90(3)	49(2)	83(3)	-5(2)	58(2)	-14(2)
N(2)	47(4)	39(5)	50(5)	-10(4)	27(4)	-2(4)
C(2)	75(6)	67(8)	51(8)	-3(6)	5(6)	1(6)
N(3)	63(7)	40(4)	58(5)	-7(4)	30(5)	-4(5)
C(3)	82(7)	85(11)	62(9)	-1(8)	-2(8)	12(7)
C(4)	65(8)	104(12)	68(10)	-14(7)	4(8)	17(7)
C(5)	53(6)	82(10)	84(11)	-20(7)	3(7)	1(6)
C(6)	46(5)	70(7)	65(8)	-13(5)	12(6)	-6(5)
C(7)	101(9)	83(9)	76(9)	8(8)	23(8)	-10(8)
C(8)	147(18)	86(10)	145(18)	39(12)	19(15)	-8(11)
C(9)	164(19)	160(18)	91(13)	-4(13)	61(12)	-33(16)
C(10)	53(8)	71(8)	92(10)	-1(6)	29(7)	-8(6)
C(11)	90(12)	76(9)	144(15)	-25(10)	52(12)	-9(10)
C(12)	71(10)	95(13)	104(12)	5(9)	45(9)	-13(9)
C(13)	47(5)	31(5)	48(6)	-2(4)	16(4)	-2(4)
C(14)	60(6)	45(7)	74(9)	-26(6)	24(6)	-6(5)
C(15)	56(6)	40(7)	79(9)	-23(6)	28(6)	-1(5)
C(16)	47(5)	40(7)	62(5)	-7(5)	20(4)	0(5)
C(17)	56(6)	45(7)	84(6)	-11(6)	29(5)	-7(6)
C(18)	58(7)	64(10)	108(8)	-8(9)	31(6)	-21(7)
C(19)	70(9)	91(12)	100(8)	-19(10)	12(7)	-13(8)
C(20)	70(7)	92(12)	63(8)	-6(8)	10(6)	13(7)
C(21)	64(6)	55(7)	61(6)	-7(6)	18(5)	11(6)
C(22)	69(8)	50(7)	91(7)	1(7)	47(6)	-8(7)
C(23)	99(12)	73(9)	96(11)	-19(9)	52(10)	-10(9)
C(24)	114(13)	55(7)	130(14)	11(8)	82(12)	-7(9)
C(25)	88(9)	83(10)	77(8)	26(7)	28(8)	11(8)
C(26)	122(15)	137(16)	80(10)	21(10)	41(10)	17(13)
C(27)	131(16)	75(9)	143(17)	31(11)	21(14)	12(11)
C(28)	71(9)	39(6)	76(7)	-7(5)	34(7)	3(6)

C(29)	94(11)	46(7)	94(8)	-9(6)	56(9)	8(7)
C(30)	88(10)	57(7)	92(7)	-30(7)	52(9)	-16(7)
C(31)	87(10)	74(8)	65(8)	-23(6)	33(8)	-11(8)
C(32)	70(8)	54(7)	58(5)	-9(5)	37(7)	-7(6)
O(33)	280(30)	140(40)	200(30)	-90(30)	70(30)	-80(30)
C(34)	280(30)	130(40)	210(30)	-80(30)	60(30)	-100(30)
C(35)	270(30)	100(40)	200(30)	-100(30)	60(30)	-110(30)
C(36)	270(40)	100(40)	180(30)	-120(20)	70(30)	-100(30)
C(37)	280(40)	130(40)	180(30)	-110(30)	70(30)	-90(30)
Pd(51)	43(1)	43(1)	39(1)	-6(1)	9(1)	7(1)
Cl(51)	94(3)	56(2)	68(2)	10(2)	37(2)	16(2)
N(51)	42(4)	36(5)	44(5)	-4(4)	4(4)	5(4)
C(51)	45(4)	40(7)	44(5)	-9(5)	2(4)	-2(5)
Cl(52)	120(4)	66(3)	52(2)	9(2)	35(2)	30(2)
N(52)	41(4)	48(6)	41(5)	-4(4)	3(4)	10(4)
C(52)	52(5)	43(7)	44(6)	-6(5)	4(4)	3(5)
N(53)	59(7)	63(6)	52(5)	-11(5)	14(5)	17(5)
C(53)	65(6)	72(10)	63(8)	9(7)	-17(6)	-8(8)
C(54)	48(6)	97(12)	73(9)	0(7)	-5(6)	10(8)
C(55)	53(6)	78(11)	90(9)	12(8)	-8(6)	-27(8)
C(56)	47(5)	62(8)	62(7)	11(6)	14(5)	-4(6)
C(57)	75(7)	67(8)	50(7)	2(5)	13(6)	-5(7)
C(58)	113(13)	86(10)	73(10)	-6(8)	41(9)	-1(10)
C(59)	110(13)	73(8)	74(11)	13(8)	21(10)	-13(9)
C(60)	73(9)	110(10)	58(7)	8(7)	23(6)	-7(9)
C(61)	90(13)	220(20)	92(12)	18(14)	51(10)	7(14)
C(62)	148(17)	102(9)	100(14)	43(9)	19(12)	-29(12)
C(63)	36(5)	45(6)	32(5)	-5(4)	10(4)	2(4)
C(64)	55(6)	64(8)	44(7)	-15(6)	5(5)	13(6)
C(65)	50(6)	66(8)	46(7)	-11(5)	7(5)	15(6)
C(66)	37(5)	74(8)	45(6)	-11(4)	3(4)	6(5)
C(67)	41(6)	84(8)	52(6)	-17(5)	18(5)	1(5)
C(68)	46(7)	104(11)	67(8)	-12(7)	21(5)	-16(7)
C(69)	50(8)	136(14)	70(8)	-8(8)	4(6)	-14(8)
C(70)	52(8)	115(12)	52(8)	6(8)	-5(6)	6(7)
C(71)	47(6)	92(8)	41(6)	-8(5)	4(5)	11(6)
C(72)	64(8)	76(7)	63(7)	-7(6)	28(6)	-1(7)
C(73)	164(17)	90(12)	77(10)	8(9)	71(11)	21(12)
C(74)	93(12)	78(7)	103(13)	-14(8)	28(10)	-7(9)
C(75)	65(8)	88(9)	62(7)	6(7)	1(7)	14(6)
C(76)	103(13)	112(14)	62(8)	27(9)	8(9)	13(11)
C(77)	110(14)	101(10)	115(14)	-1(12)	10(12)	37(11)
C(78)	126(13)	90(10)	62(8)	-3(6)	21(9)	61(10)
C(79)	163(15)	86(11)	77(8)	-6(8)	34(11)	62(12)
C(80)	107(12)	85(9)	78(7)	-16(8)	46(9)	23(9)
C(81)	106(12)	81(9)	59(8)	-17(6)	35(9)	10(9)

C(82)	88(10)	58(8)	55(6)	-6(5)	41(7)	-2(7)

Table 4.5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2$ $x10^3$) for Nol344m.

	x	y	z	U(eq)
H(3)	5417	1812	3850	98
H(4)	6210	2651	3624	99
H(5)	5978	3898	2983	92
H(7)	3703	2059	3130	105
H(8A)	4475	741	3285	196
H(8B)	3844	622	3502	196
H(8C)	4512	839	4008	196
H(9A)	4361	2199	4431	200
H(9B)	3619	1975	4141	200
H(9C)	3883	2940	4043	200
H(10)	4383	4676	2154	84
H(11A)	5461	5574	3022	149
H(11B)	4799	5433	3177	149
H(11C)	4827	6051	2603	149
H(12A)	5695	4705	2121	129
H(12B)	5128	5248	1649	129
H(12C)	5133	4185	1625	129
H(14)	3763	4669	3163	71
H(15)	2625	4735	2535	68
H(18)	833	2483	1735	90
H(19)	552	2747	656	108
H(20)	1240	3582	217	92
H(22)	2422	2704	2797	78
H(23A)	1812	3958	2923	126
H(23B)	1834	3228	3450	126
H(23C)	1208	3329	2866	126
H(24A)	1997	1490	3187	135
H(24B)	1788	1276	2454	135
H(24C)	1283	1693	2767	135
H(25)	2883	4139	1019	99
H(26A)	2047	3572	-134	166
H(26B)	2782	3313	168	166
H(26C)	2596	4276	-134	166
H(27A)	1721	5192	433	181
H(27B)	2406	5527	406	181
H(27C)	2257	5454	1064	181

H(28)	4064	210	1727	71
H(29)	4173	-1009	1111	86
H(30)	3788	-872	1	88
H(31)	3376	499	-429	88
H(32)	3327	1679	234	68
H(34A)	4521	3873	5122	248
H(34B)	5218	3640	5053	248
H(35A)	4326	4701	4288	230
H(35B)	5019	4470	4220	230
H(36A)	5336	5795	4516	221
H(36B)	4644	6026	4584	221
H(37A)	5730	5778	5529	237
H(37B)	5032	6011	5598	237
H(53)	9255	12112	3587	89
H(54)	10089	12616	3177	93
H(55)	9845	13398	2252	96
H(57)	7578	12067	2742	78
H(58A)	8266	12760	3933	132
H(58B)	7519	12535	3715	132
H(58C)	7790	13330	3390	132
H(59A)	8499	11141	3745	130
H(59B)	8208	10725	3062	130
H(59C)	7754	10910	3495	130
H(60)	8281	13588	1109	95
H(61A)	8967	13513	508	195
H(61B)	9282	12779	1024	195
H(61C)	9579	13759	1078	195
H(62A)	8564	14929	1733	180
H(62B)	8679	15047	1063	180
H(62C)	9271	14866	1667	180
H(64)	7464	14052	2321	68
H(65)	6366	13819	1620	66
H(68)	5047	10894	677	86
H(69)	4604	11563	-271	105
H(70)	5097	12854	-532	93
H(72)	6581	11353	1773	79
H(73A)	5806	12248	2084	154
H(73B)	6007	11379	2510	154
H(73C)	5340	11405	1971	154
H(74A)	5577	10031	1565	137
H(74B)	6286	9931	2024	137
H(74C)	6164	9908	1283	137
H(75)	6634	13752	299	90
H(76A)	6402	13197	-783	144
H(76B)	6438	14260	-756	144
H(76C)	5759	13772	-970	144

H(77A)	5363	14511	-8	170
H(77B)	5971	15103	-5	170
H(77C)	5921	14656	629	170
H(78)	8320	9567	986	113
H(79)	8480	8456	354	131
H(80)	8255	8668	-757	102
H(81)	7807	10051	-1137	96
H(82)	7675	11140	-470	75

Table 4.6. Torsion angles [deg] for Nol344m.

C(14)-N(1)-C(1)-C(2)	103.6(16)
C(13)-N(1)-C(1)-C(2)	-76.1(18)
C(14)-N(1)-C(1)-C(6)	-71.8(18)
C(13)-N(1)-C(1)-C(6)	108.5(15)
C(6)-C(1)-C(2)-C(3)	-3(2)
N(1)-C(1)-C(2)-C(3)	-177.7(13)
C(6)-C(1)-C(2)-C(7)	174.4(15)
N(1)-C(1)-C(2)-C(7)	-1(2)
C(13)-Pd(1)-N(3)-C(28)	-177(100)
Cl(2)-Pd(1)-N(3)-C(28)	131.0(11)
Cl(1)-Pd(1)-N(3)-C(28)	-50.6(11)
C(13)-Pd(1)-N(3)-C(32)	-4(60)
Cl(2)-Pd(1)-N(3)-C(32)	-55.5(10)
Cl(1)-Pd(1)-N(3)-C(32)	122.9(10)
C(1)-C(2)-C(3)-C(4)	0(2)
C(7)-C(2)-C(3)-C(4)	-176.7(17)
C(2)-C(3)-C(4)-C(5)	1(3)
C(3)-C(4)-C(5)-C(6)	-1(3)
C(4)-C(5)-C(6)-C(1)	-2(2)
C(4)-C(5)-C(6)-C(10)	176.7(16)
C(2)-C(1)-C(6)-C(5)	3(2)
N(1)-C(1)-C(6)-C(5)	178.5(13)
C(2)-C(1)-C(6)-C(10)	-175.0(15)
N(1)-C(1)-C(6)-C(10)	0(2)
C(1)-C(2)-C(7)-C(9)	-93(2)
C(3)-C(2)-C(7)-C(9)	83(2)
C(1)-C(2)-C(7)-C(8)	146.4(18)
C(3)-C(2)-C(7)-C(8)	-37(2)
C(5)-C(6)-C(10)-C(12)	48(2)
C(1)-C(6)-C(10)-C(12)	-133.4(16)
C(5)-C(6)-C(10)-C(11)	-74.7(18)
C(1)-C(6)-C(10)-C(11)	103.5(17)
C(15)-N(2)-C(13)-N(1)	1.4(14)

C(16)-N(2)-C(13)-N(1)	-172.6(11)
C(15)-N(2)-C(13)-Pd(1)	-174.2(10)
C(16)-N(2)-C(13)-Pd(1)	11.8(18)
C(14)-N(1)-C(13)-N(2)	-1.7(14)
C(1)-N(1)-C(13)-N(2)	178.0(12)
C(14)-N(1)-C(13)-Pd(1)	173.9(10)
C(1)-N(1)-C(13)-Pd(1)	-6.4(19)
N(3)-Pd(1)-C(13)-N(2)	50(60)
Cl(2)-Pd(1)-C(13)-N(2)	102.1(11)
Cl(1)-Pd(1)-C(13)-N(2)	-76.3(11)
N(3)-Pd(1)-C(13)-N(1)	-124(59)
Cl(2)-Pd(1)-C(13)-N(1)	-72.4(11)
Cl(1)-Pd(1)-C(13)-N(1)	109.2(11)
C(13)-N(1)-C(14)-C(15)	1.4(17)
C(1)-N(1)-C(14)-C(15)	-178.3(13)
N(1)-C(14)-C(15)-N(2)	-0.5(17)
C(13)-N(2)-C(15)-C(14)	-0.6(16)
C(16)-N(2)-C(15)-C(14)	173.5(12)
C(13)-N(2)-C(16)-C(21)	-84.7(16)
C(15)-N(2)-C(16)-C(21)	102.0(15)
C(13)-N(2)-C(16)-C(17)	98.2(15)
C(15)-N(2)-C(16)-C(17)	-75.1(16)
C(21)-C(16)-C(17)-C(18)	-2(2)
N(2)-C(16)-C(17)-C(18)	175.3(13)
C(21)-C(16)-C(17)-C(22)	-176.8(13)
N(2)-C(16)-C(17)-C(22)	0(2)
C(16)-C(17)-C(18)-C(19)	5(2)
C(22)-C(17)-C(18)-C(19)	-179.5(16)
C(17)-C(18)-C(19)-C(20)	-7(3)
C(18)-C(19)-C(20)-C(21)	6(3)
C(19)-C(20)-C(21)-C(16)	-2(2)
C(19)-C(20)-C(21)-C(25)	-177.1(17)
C(17)-C(16)-C(21)-C(20)	0(2)
N(2)-C(16)-C(21)-C(20)	-176.6(13)
C(17)-C(16)-C(21)-C(25)	174.8(15)
N(2)-C(16)-C(21)-C(25)	-2(2)
C(18)-C(17)-C(22)-C(23)	-75.8(19)
C(16)-C(17)-C(22)-C(23)	99.1(17)
C(18)-C(17)-C(22)-C(24)	48(2)
C(16)-C(17)-C(22)-C(24)	-137.0(14)
C(20)-C(21)-C(25)-C(26)	-50(2)
C(16)-C(21)-C(25)-C(26)	135.4(17)
C(20)-C(21)-C(25)-C(27)	72(2)
C(16)-C(21)-C(25)-C(27)	-102.3(18)
C(32)-N(3)-C(28)-C(29)	1(2)
Pd(1)-N(3)-C(28)-C(29)	174.5(11)

N(3)-C(28)-C(29)-C(30)	-2(2)
C(28)-C(29)-C(30)-C(31)	2(2)
C(29)-C(30)-C(31)-C(32)	-1(2)
C(28)-N(3)-C(32)-C(31)	0(2)
Pd(1)-N(3)-C(32)-C(31)	-173.4(12)
C(30)-C(31)-C(32)-N(3)	0(2)
C(36)#1-O(33)-C(34)-C(35)	109(52)
C(35)#1-O(33)-C(34)-C(35)	9(9)
C(37)-O(33)-C(34)-C(35)	0.0(3)
O(33)-C(34)-C(35)-C(36)	0.0(2)
C(34)-C(35)-C(36)-C(37)	0.0(2)
C(36)#1-O(33)-C(37)-C(36)	-10(10)
C(35)#1-O(33)-C(37)-C(36)	-129(41)
C(34)-O(33)-C(37)-C(36)	0.0(3)
C(35)-C(36)-C(37)-O(33)	0.0(2)
C(63)-N(51)-C(51)-C(56)	91.0(17)
C(64)-N(51)-C(51)-C(56)	-95.9(16)
C(63)-N(51)-C(51)-C(52)	-99.8(15)
C(64)-N(51)-C(51)-C(52)	73.3(16)
C(56)-C(51)-C(52)-C(53)	-7(2)
N(51)-C(51)-C(52)-C(53)	-176.2(12)
C(56)-C(51)-C(52)-C(57)	170.3(14)
N(51)-C(51)-C(52)-C(57)	1.4(19)
C(63)-Pd(51)-N(53)-C(78)	-144(8)
Cl(52)-Pd(51)-N(53)-C(78)	168.0(15)
Cl(51)-Pd(51)-N(53)-C(78)	-10.8(16)
C(63)-Pd(51)-N(53)-C(82)	28(9)
Cl(52)-Pd(51)-N(53)-C(82)	-19.2(11)
Cl(51)-Pd(51)-N(53)-C(82)	162.0(11)
C(51)-C(52)-C(53)-C(54)	-1(2)
C(57)-C(52)-C(53)-C(54)	-178.4(15)
C(52)-C(53)-C(54)-C(55)	6(3)
C(53)-C(54)-C(55)-C(56)	-3(3)
C(54)-C(55)-C(56)-C(51)	-4(3)
C(54)-C(55)-C(56)-C(60)	-174.4(18)
C(52)-C(51)-C(56)-C(55)	10(2)
N(51)-C(51)-C(56)-C(55)	178.4(14)
C(52)-C(51)-C(56)-C(60)	179.9(14)
N(51)-C(51)-C(56)-C(60)	-12(2)
C(53)-C(52)-C(57)-C(58)	74.8(18)
C(51)-C(52)-C(57)-C(58)	-102.8(16)
C(53)-C(52)-C(57)-C(59)	-49.7(19)
C(51)-C(52)-C(57)-C(59)	132.6(14)
C(55)-C(56)-C(60)-C(62)	-78(2)
C(51)-C(56)-C(60)-C(62)	112.3(19)
C(55)-C(56)-C(60)-C(61)	42(3)

C(51)-C(56)-C(60)-C(61)	-128.1(19)
C(64)-N(51)-C(63)-N(52)	-1.8(14)
C(51)-N(51)-C(63)-N(52)	171.9(12)
C(64)-N(51)-C(63)-Pd(51)	174.5(10)
C(51)-N(51)-C(63)-Pd(51)	-11.8(19)
C(65)-N(52)-C(63)-N(51)	2.2(15)
C(66)-N(52)-C(63)-N(51)	-176.7(12)
C(65)-N(52)-C(63)-Pd(51)	-174.1(10)
C(66)-N(52)-C(63)-Pd(51)	6.9(19)
N(53)-Pd(51)-C(63)-N(51)	-148(8)
Cl(52)-Pd(51)-C(63)-N(51)	-100.8(11)
Cl(51)-Pd(51)-C(63)-N(51)	77.9(11)
N(53)-Pd(51)-C(63)-N(52)	27(9)
Cl(52)-Pd(51)-C(63)-N(52)	74.8(11)
Cl(51)-Pd(51)-C(63)-N(52)	-106.6(11)
C(63)-N(51)-C(64)-C(65)	0.7(16)
C(51)-N(51)-C(64)-C(65)	-173.5(12)
N(51)-C(64)-C(65)-N(52)	0.7(17)
C(63)-N(52)-C(65)-C(64)	-1.9(17)
C(66)-N(52)-C(65)-C(64)	177.2(13)
C(63)-N(52)-C(66)-C(71)	-105.3(17)
C(65)-N(52)-C(66)-C(71)	75.9(18)
C(63)-N(52)-C(66)-C(67)	82.3(17)
C(65)-N(52)-C(66)-C(67)	-96.5(16)
C(71)-C(66)-C(67)-C(68)	3(2)
N(52)-C(66)-C(67)-C(68)	175.4(12)
C(71)-C(66)-C(67)-C(72)	-173.9(14)
N(52)-C(66)-C(67)-C(72)	-1.7(19)
C(66)-C(67)-C(68)-C(69)	0(2)
C(72)-C(67)-C(68)-C(69)	176.7(17)
C(67)-C(68)-C(69)-C(70)	-3(3)
C(68)-C(69)-C(70)-C(71)	3(3)
N(52)-C(66)-C(71)-C(70)	-174.6(13)
C(67)-C(66)-C(71)-C(70)	-3(2)
N(52)-C(66)-C(71)-C(75)	4(2)
C(67)-C(66)-C(71)-C(75)	175.5(14)
C(69)-C(70)-C(71)-C(66)	-1(3)
C(69)-C(70)-C(71)-C(75)	-179.0(17)
C(68)-C(67)-C(72)-C(73)	-80(2)
C(66)-C(67)-C(72)-C(73)	96.4(18)
C(68)-C(67)-C(72)-C(74)	39(2)
C(66)-C(67)-C(72)-C(74)	-143.7(15)
C(66)-C(71)-C(75)-C(77)	-100.3(18)
C(70)-C(71)-C(75)-C(77)	77.9(19)
C(66)-C(71)-C(75)-C(76)	134.3(16)
C(70)-C(71)-C(75)-C(76)	-47(2)

C(82)-N(53)-C(78)-C(79)	-2(3)
Pd(51)-N(53)-C(78)-C(79)	171.5(18)
N(53)-C(78)-C(79)-C(80)	2(4)
C(78)-C(79)-C(80)-C(81)	-2(3)
C(79)-C(80)-C(81)-C(82)	2(3)
C(80)-C(81)-C(82)-N(53)	-3(3)
C(78)-N(53)-C(82)-C(81)	2(2)
Pd(51)-N(53)-C(82)-C(81)	-171.4(14)

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1,-z+1

5. Crystal Data and Structure Refinement for [(SIPr)Pd(Cl)$_2$(pyridine)]

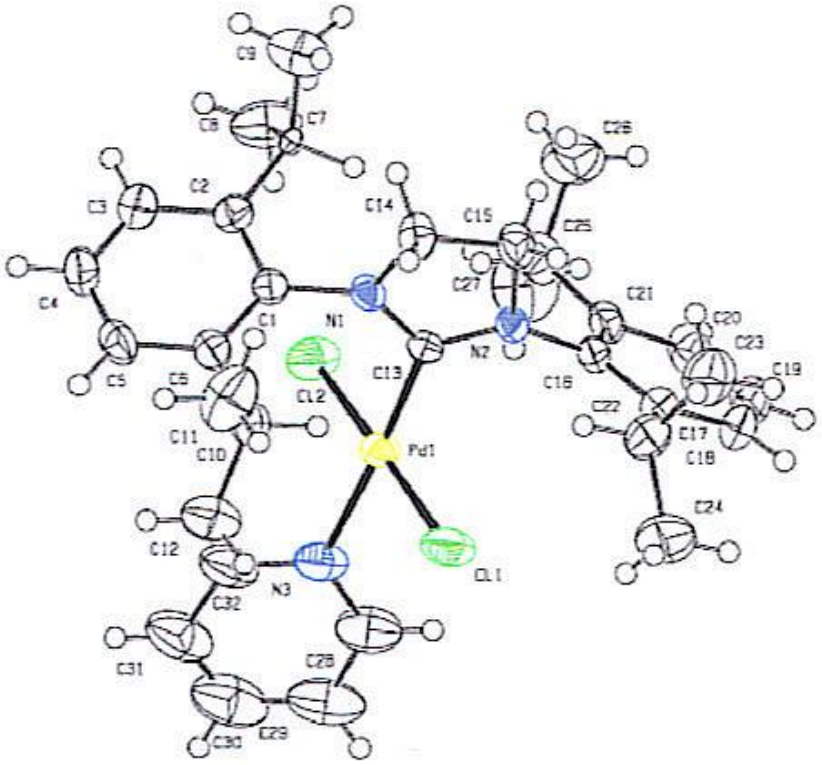

Table 5.1.

Identification code	nol342
Empirical formula	$C_{32}H_{43}Cl_2N_3Pd$
Formula weight	646.99
Temperature	295(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/c$
Unit cell dimensions	a = 15.8956(14) Å alpha = 90 deg. b = 15.5844(14) Å beta = 99.144(2)deg. c = 12.8848(11) Å gamma = 90 deg.
Volume	3151.3(5) $Å^3$
Z, Calculated density	4, 1.364 Mg/m^3
Absorption coefficient	0.783 mm^{-1}
F(000)	1344
Crystal size	0.50 x 0.30 x 0.20 mm
Theta range for data collection	2.30 to 22.50 deg.
Limiting indices	$-17 \le h \le 17$, $-16 \le k \le 16$, $-13 \le l \le 13$
Reflections collected / unique	30038 / 4095 [R(int) = 0.0548]
Completeness to theta = 22.50	99.5 %
Absorption correction	Empirical

Max. and min. transmission	0.914071 and 0.798142
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4095 / 330 / 352
Goodness-of-fit on F^2	1.212
Final R indices [I>2sigma(I)]	R1 = 0.0450, wR2 = 0.1041
R indices (all data)	R1 = 0.0530, wR2 = 0.1101
Extinction coefficient	0.0021(6)
Largest diff. peak and hole	1.130 and -0.722 e.$Å^{-3}$

Table 5.2. Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2$ $x10^3$) for Nol342. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Pd(1)	7196(1)	8939(1)	1666(1)	32(1)
Cl(1)	8136(2)	8585(1)	556(2)	55(1)
N(1)	8257(4)	10239(4)	2852(5)	29(1)
C(1)	8253(5)	9809(5)	3835(6)	30(2)
Cl(2)	6198(2)	9242(2)	2725(2)	51(1)
N(2)	7905(4)	10659(4)	1226(5)	28(1)
C(2)	7772(5)	10168(5)	4552(6)	36(2)
N(3)	6689(5)	7704(5)	1509(6)	50(2)
C(3)	7794(6)	9758(6)	5513(7)	46(2)
C(4)	8256(6)	9012(6)	5727(7)	48(2)
C(5)	8728(6)	8660(6)	5018(7)	42(2)
C(6)	8734(5)	9062(5)	4075(6)	35(2)
C(7)	7338(5)	10981(4)	4368(5)	25(2)
C(8)	6346(6)	10903(7)	4578(10)	69(3)
C(9)	7666(7)	11760(6)	4852(9)	64(3)
C(10)	9325(6)	8712(6)	3348(7)	42(2)
C(11)	10251(7)	8903(9)	3813(9)	72(3)
C(12)	9204(8)	7748(7)	3151(10)	73(3)
C(13)	7791(4)	10039(5)	1919(6)	26(1)
C(14)	8822(6)	10986(5)	2785(7)	41(2)
C(15)	8446(6)	11364(6)	1723(7)	45(2)
C(16)	7405(5)	10776(5)	194(6)	32(2)
C(17)	7807(6)	10718(5)	-681(6)	42(2)
C(18)	7288(7)	10891(6)	-1641(7)	54(2)
C(19)	6452(7)	11084(6)	-1713(8)	57(2)
C(20)	6091(7)	11155(6)	-873(8)	54(2)
C(21)	6538(6)	11017(5)	153(7)	37(2)
C(22)	8743(6)	10507(6)	-636(8)	54(2)
C(23)	9245(7)	11334(8)	-811(9)	69(3)
C(24)	8903(9)	9796(8)	-1396(10)	81(3)

C(25)	6119(6)	11159(6)	1119(8)	51(2)
C(26)	6099(10)	12109(8)	1385(11)	90(4)
C(27)	5216(7)	10792(10)	993(12)	93(4)
C(28)	6345(6)	7360(7)	599(10)	66(2)
C(29)	5972(8)	6538(8)	535(12)	82(3)
C(30)	6031(8)	6079(8)	1484(13)	85(3)
C(31)	6414(8)	6384(7)	2397(12)	79(3)
C(32)	6712(7)	7215(6)	2376(9)	64(2)

Table 5.3. Bond lengths [Å] and angles [Deg] for Nol342.

Pd(1)-C(13)	1.961(7)
Pd(1)-N(3)	2.083(7)
Pd(1)-Cl(1)	2.294(2)
Pd(1)-Cl(2)	2.300(2)
N(1)-C(13)	1.345(9)
N(1)-C(1)	1.434(10)
N(1)-C(14)	1.482(10)
C(1)-C(6)	1.399(11)
C(1)-C(2)	1.406(11)
N(2)-C(13)	1.346(10)
N(2)-C(16)	1.448(10)
N(2)-C(15)	1.477(10)
C(2)-C(3)	1.389(12)
C(2)-C(7)	1.445(11)
N(3)-C(28)	1.326(13)
N(3)-C(32)	1.348(13)
C(3)-C(4)	1.379(13)
C(4)-C(5)	1.384(13)
C(5)-C(6)	1.369(12)
C(6)-C(10)	1.529(13)
C(7)-C(9)	1.425(12)
C(7)-C(8)	1.646(12)
C(10)-C(11)	1.529(14)
C(10)-C(12)	1.530(14)
C(14)-C(15)	1.522(12)
C(16)-C(17)	1.384(12)
C(16)-C(21)	1.420(12)
C(17)-C(18)	1.399(13)
C(17)-C(22)	1.516(13)
C(18)-C(19)	1.352(15)
C(19)-C(20)	1.307(15)
C(20)-C(21)	1.415(13)

C(21)-C(25)	1.519(13)
C(22)-C(24)	1.528(14)
C(22)-C(23)	1.551(15)
C(25)-C(26)	1.521(15)
C(25)-C(27)	1.529(15)
C(28)-C(29)	1.408(16)
C(29)-C(30)	1.41(2)
C(30)-C(31)	1.324(19)
C(31)-C(32)	1.381(15)

C(13)-Pd(1)-N(3)	173.2(3)
C(13)-Pd(1)-Cl(1)	88.2(2)
N(3)-Pd(1)-Cl(1)	89.9(2)
C(13)-Pd(1)-Cl(2)	94.7(2)
N(3)-Pd(1)-Cl(2)	87.4(2)
Cl(1)-Pd(1)-Cl(2)	176.72(9)
C(13)-N(1)-C(1)	127.0(6)
C(13)-N(1)-C(14)	112.5(6)
C(1)-N(1)-C(14)	120.5(6)
C(6)-C(1)-C(2)	121.4(7)
C(6)-C(1)-N(1)	120.4(7)
C(2)-C(1)-N(1)	118.3(7)
C(13)-N(2)-C(16)	125.9(6)
C(13)-N(2)-C(15)	112.1(6)
C(16)-N(2)-C(15)	120.1(6)
C(3)-C(2)-C(1)	117.7(8)
C(3)-C(2)-C(7)	119.6(7)
C(1)-C(2)-C(7)	122.4(7)
C(28)-N(3)-C(32)	117.1(9)
C(28)-N(3)-Pd(1)	123.9(7)
C(32)-N(3)-Pd(1)	118.9(7)
C(4)-C(3)-C(2)	120.2(9)
C(3)-C(4)-C(5)	122.0(8)
C(6)-C(5)-C(4)	119.0(8)
C(5)-C(6)-C(1)	119.8(8)
C(5)-C(6)-C(10)	118.1(7)
C(1)-C(6)-C(10)	121.9(7)
C(9)-C(7)-C(2)	122.8(8)
C(9)-C(7)-C(8)	106.6(7)
C(2)-C(7)-C(8)	110.7(7)
C(11)-C(10)-C(6)	109.7(8)
C(11)-C(10)-C(12)	110.1(9)
C(6)-C(10)-C(12)	112.3(8)
N(1)-C(13)-N(2)	108.3(6)
N(1)-C(13)-Pd(1)	122.2(5)
N(2)-C(13)-Pd(1)	129.0(5)

N(1)-C(14)-C(15)	101.6(6)
N(2)-C(15)-C(14)	102.8(6)
C(17)-C(16)-C(21)	123.9(7)
C(17)-C(16)-N(2)	118.9(7)
C(21)-C(16)-N(2)	117.1(7)
C(16)-C(17)-C(18)	115.1(9)
C(16)-C(17)-C(22)	124.1(8)
C(18)-C(17)-C(22)	120.8(8)
C(19)-C(18)-C(17)	122.6(9)
C(20)-C(19)-C(18)	121.2(9)
C(19)-C(20)-C(21)	122.7(10)
C(20)-C(21)-C(16)	114.5(8)
C(20)-C(21)-C(25)	121.6(9)
C(16)-C(21)-C(25)	123.9(8)
C(17)-C(22)-C(24)	113.3(9)
C(17)-C(22)-C(23)	109.8(8)
C(24)-C(22)-C(23)	111.6(9)
C(21)-C(25)-C(26)	110.8(8)
C(21)-C(25)-C(27)	112.7(9)
C(26)-C(25)-C(27)	109.5(11)
N(3)-C(28)-C(29)	122.1(12)
C(30)-C(29)-C(28)	116.2(12)
C(31)-C(30)-C(29)	123.3(11)
C(30)-C(31)-C(32)	115.4(13)
N(3)-C(32)-C(31)	125.7(12)

Table 5.4. Anisotropic displacement parameters ($Å^2$ x10^3) for Nol342. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U11 + ... + 2hka^*b^*U12]$

	U11	U22	U33	U23	U13	U12
Pd(1)	37(1)	26(1)	34(1)	-4(1)	8(1)	-6(1)
Cl(1)	70(2)	35(1)	69(2)	-10(1)	37(1)	-2(1)
N(1)	32(3)	23(3)	29(3)	2(2)	0(2)	-5(2)
C(1)	34(4)	27(3)	28(3)	-1(3)	0(3)	-6(3)
Cl(2)	52(1)	50(1)	57(1)	-12(1)	24(1)	-12(1)
N(2)	32(3)	25(3)	27(3)	2(2)	5(2)	-5(2)
C(2)	42(4)	34(4)	30(3)	-2(3)	3(3)	-4(3)
N(3)	56(4)	37(3)	63(4)	-13(3)	25(3)	-8(3)
C(3)	58(5)	46(4)	35(4)	4(3)	11(4)	-1(4)
C(4)	65(5)	43(4)	37(4)	14(3)	8(4)	-5(4)
C(5)	47(5)	34(4)	43(4)	12(3)	3(3)	10(4)
C(6)	37(4)	31(4)	33(4)	2(3)	-6(3)	-5(3)

C(7)	44(3)	18(3)	16(3)	2(2)	21(3)	5(2)
C(8)	46(5)	71(7)	92(8)	-31(6)	18(5)	0(4)
C(9)	53(6)	48(5)	89(8)	-11(5)	1(5)	2(4)
C(10)	46(4)	43(4)	35(4)	5(4)	-3(3)	7(4)
C(11)	46(5)	110(9)	57(7)	0(6)	-2(5)	4(5)
C(12)	91(8)	50(5)	79(7)	-10(5)	17(6)	18(5)
C(13)	27(3)	23(3)	30(3)	-1(3)	5(3)	3(3)
C(14)	43(5)	43(4)	34(4)	8(3)	-7(3)	-17(3)
C(15)	57(5)	38(4)	37(4)	6(3)	-2(4)	-16(4)
C(16)	44(4)	25(4)	27(3)	4(3)	2(3)	-3(3)
C(17)	64(4)	33(4)	29(3)	-1(3)	10(3)	3(4)
C(18)	87(5)	47(5)	26(4)	2(4)	5(4)	-1(5)
C(19)	78(5)	49(5)	34(4)	4(4)	-20(4)	-4(4)
C(20)	56(5)	48(5)	50(4)	10(4)	-17(4)	-3(4)
C(21)	42(4)	29(4)	37(4)	8(3)	3(3)	-5(3)
C(22)	68(5)	54(5)	45(5)	0(4)	27(4)	9(4)
C(23)	75(7)	77(6)	63(7)	2(6)	33(6)	-7(5)
C(24)	108(9)	66(6)	80(8)	-7(6)	48(7)	26(6)
C(25)	50(5)	52(5)	56(5)	10(4)	21(4)	1(4)
C(26)	129(10)	67(6)	89(8)	-12(6)	61(8)	8(7)
C(27)	51(6)	123(10)	113(10)	17(8)	31(6)	-12(6)
C(28)	52(5)	55(5)	88(5)	-23(4)	3(5)	-15(4)
C(29)	66(6)	56(5)	123(7)	-34(5)	13(6)	-12(5)
C(30)	68(6)	54(6)	143(8)	-18(5)	45(6)	-20(5)
C(31)	88(7)	43(5)	118(7)	-3(5)	53(6)	-10(5)
C(32)	82(6)	36(4)	86(5)	-6(4)	46(5)	-9(4)

Table 5.5. Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2$ $x10^3$) for Nol342.

	x	y	z	U(eq)
H(3)	7496	9987	6014	55
H(4)	8251	8737	6367	58
H(5)	9036	8157	5179	50
H(7)	7296	11083	3610	29
H(8A)	6060	10458	4142	103
H(8B)	6058	11439	4413	103
H(8C)	6341	10765	5304	103
H(9A)	7707	11710	5601	96
H(9B)	7291	12225	4605	96
H(9C)	8221	11868	4676	96
H(10)	9194	9009	2671	51

H(11A)	10317	9508	3947	108
H(11B)	10616	8730	3325	108
H(11C)	10402	8593	4459	108
H(12A)	9416	7439	3783	110
H(12B)	9512	7575	2602	110
H(12C)	8609	7626	2944	110
H(14A)	9409	10810	2799	49
H(14B)	8794	11391	3350	49
H(15A)	8111	11872	1805	54
H(15B)	8890	11509	1315	54
H(18)	7529	10872	-2253	64
H(19)	6127	11168	-2372	68
H(20)	5518	11302	-954	65
H(22)	8956	10303	77	64
H(23A)	9067	11540	-1514	104
H(23B)	9844	11209	-710	104
H(23C)	9135	11765	-318	104
H(24A)	8591	9292	-1260	121
H(24B)	9501	9665	-1299	121
H(24C)	8719	9983	-2105	121
H(25)	6464	10866	1712	61
H(26A)	6665	12301	1653	135
H(26B)	5738	12197	1907	135
H(26C)	5880	12428	763	135
H(27A)	4839	11145	517	140
H(27B)	5028	10781	1665	140
H(27C)	5215	10219	719	140
H(28)	6351	7671	-16	79
H(29)	5702	6312	-99	98
H(30)	5789	5535	1469	102
H(31)	6478	6060	3011	95
H(32)	6949	7458	3015	77

Table 5.6. Torsion angles [Deg] for Nol342.

C(13)-N(1)-C(1)-C(6)	82.1(10)
C(14)-N(1)-C(1)-C(6)	-97.4(9)
C(13)-N(1)-C(1)-C(2)	-99.4(9)
C(14)-N(1)-C(1)-C(2)	81.1(9)
C(6)-C(1)-C(2)-C(3)	0.3(11)
N(1)-C(1)-C(2)-C(3)	-178.2(7)
C(6)-C(1)-C(2)-C(7)	173.9(7)
N(1)-C(1)-C(2)-C(7)	-4.6(11)
C(13)-Pd(1)-N(3)-C(28)	-132(2)

Cl(1)-Pd(1)-N(3)-C(28)	-58.8(8)
Cl(2)-Pd(1)-N(3)-C(28)	119.4(8)
C(13)-Pd(1)-N(3)-C(32)	47(3)
Cl(1)-Pd(1)-N(3)-C(32)	120.7(7)
Cl(2)-Pd(1)-N(3)-C(32)	-61.1(7)
C(1)-C(2)-C(3)-C(4)	-1.8(13)
C(7)-C(2)-C(3)-C(4)	-175.5(8)
C(2)-C(3)-C(4)-C(5)	1.7(14)
C(3)-C(4)-C(5)-C(6)	-0.2(14)
C(4)-C(5)-C(6)-C(1)	-1.3(13)
C(4)-C(5)-C(6)-C(10)	174.2(8)
C(2)-C(1)-C(6)-C(5)	1.2(12)
N(1)-C(1)-C(6)-C(5)	179.7(7)
C(2)-C(1)-C(6)-C(10)	-174.1(7)
N(1)-C(1)-C(6)-C(10)	4.3(11)
C(3)-C(2)-C(7)-C(9)	72.3(12)
C(1)-C(2)-C(7)-C(9)	-101.1(10)
C(3)-C(2)-C(7)-C(8)	-55.0(10)
C(1)-C(2)-C(7)-C(8)	131.6(8)
C(5)-C(6)-C(10)-C(11)	-70.6(11)
C(1)-C(6)-C(10)-C(11)	104.8(9)
C(5)-C(6)-C(10)-C(12)	52.2(11)
C(1)-C(6)-C(10)-C(12)	-132.4(9)
C(1)-N(1)-C(13)-N(2)	172.7(7)
C(14)-N(1)-C(13)-N(2)	-7.9(9)
C(1)-N(1)-C(13)-Pd(1)	-14.5(10)
C(14)-N(1)-C(13)-Pd(1)	165.0(6)
C(16)-N(2)-C(13)-N(1)	-167.9(7)
C(15)-N(2)-C(13)-N(1)	-3.6(9)
C(16)-N(2)-C(13)-Pd(1)	19.9(11)
C(15)-N(2)-C(13)-Pd(1)	-175.7(6)
N(3)-Pd(1)-C(13)-N(1)	-38(3)
Cl(1)-Pd(1)-C(13)-N(1)	-111.5(6)
Cl(2)-Pd(1)-C(13)-N(1)	70.1(6)
N(3)-Pd(1)-C(13)-N(2)	134(2)
Cl(1)-Pd(1)-C(13)-N(2)	59.8(6)
Cl(2)-Pd(1)-C(13)-N(2)	-118.7(6)
C(13)-N(1)-C(14)-C(15)	15.2(9)
C(1)-N(1)-C(14)-C(15)	-165.3(7)
C(13)-N(2)-C(15)-C(14)	12.7(9)
C(16)-N(2)-C(15)-C(14)	178.1(7)
N(1)-C(14)-C(15)-N(2)	-15.5(9)
C(13)-N(2)-C(16)-C(17)	-118.4(8)
C(15)-N(2)-C(16)-C(17)	78.3(10)
C(13)-N(2)-C(16)-C(21)	66.8(10)
C(15)-N(2)-C(16)-C(21)	-96.5(9)

C(21)-C(16)-C(17)-C(18)	-1.8(12)
N(2)-C(16)-C(17)-C(18)	-176.3(7)
C(21)-C(16)-C(17)-C(22)	176.6(8)
N(2)-C(16)-C(17)-C(22)	2.2(12)
C(16)-C(17)-C(18)-C(19)	-1.2(14)
C(22)-C(17)-C(18)-C(19)	-179.8(9)
C(17)-C(18)-C(19)-C(20)	3.0(16)
C(18)-C(19)-C(20)-C(21)	-1.5(15)
C(19)-C(20)-C(21)-C(16)	-1.4(13)
C(19)-C(20)-C(21)-C(25)	176.0(9)
C(17)-C(16)-C(21)-C(20)	3.1(12)
N(2)-C(16)-C(21)-C(20)	177.6(7)
C(17)-C(16)-C(21)-C(25)	-174.2(8)
N(2)-C(16)-C(21)-C(25)	0.3(11)
C(16)-C(17)-C(22)-C(24)	130.4(10)
C(18)-C(17)-C(22)-C(24)	-51.2(12)
C(16)-C(17)-C(22)-C(23)	-104.1(10)
C(18)-C(17)-C(22)-C(23)	74.3(11)
C(20)-C(21)-C(25)-C(26)	-79.3(12)
C(16)-C(21)-C(25)-C(26)	97.9(11)
C(20)-C(21)-C(25)-C(27)	43.8(12)
C(16)-C(21)-C(25)-C(27)	-139.0(10)
C(32)-N(3)-C(28)-C(29)	3.7(15)
Pd(1)-N(3)-C(28)-C(29)	-176.8(8)
N(3)-C(28)-C(29)-C(30)	-3.9(17)
C(28)-C(29)-C(30)-C(31)	-0.2(19)
C(29)-C(30)-C(31)-C(32)	3.9(19)
C(28)-N(3)-C(32)-C(31)	0.5(16)
Pd(1)-N(3)-C(32)-C(31)	-179.0(9)
C(30)-C(31)-C(32)-N(3)	-4.2(18)

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"Easy Synthesis and Analysis of Scope and Limitations of N-Heterocyclic Carbene (NHC) Palladium$(Cl)_2$-Pyridine in Suzuki-Miyaura Cross-Coupling Reaction" Singh, R.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2007**, *submitted for publication.*

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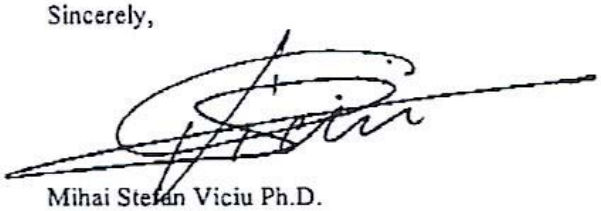

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ORGANIC LETTERS

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Simple (Imidazol-2-ylidene)-Pd-Acetate Complexes as Effective Precatalysts for Sterically Hindered Suzuki–Miyaura Couplings

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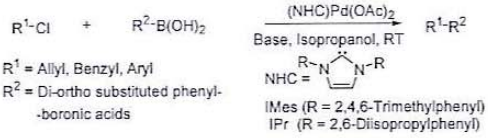
Received March 4, 2005

ABSTRACT

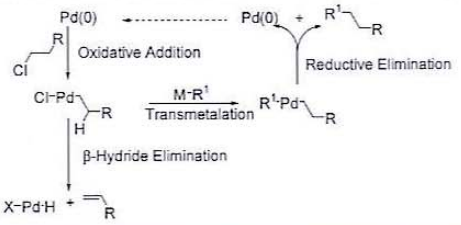


A simplified synthesis of *N*-heterocyclic carbene (NHC)Pd-carboxylate complexes and their activity in Suzuki–Miyaura cross-coupling reactions are described. Coupling of sterically hindered aryl and activated alkyl chlorides bearing β-hydrogens has been successfully achieved.

The versatility of the Suzuki–Miyaura reaction has greatly progressed since its early reports.[1] It serves as one of the most useful cross-coupling tools in synthetic chemistry.[2] Remarkable progress in both volume of work and mechanistic investigations has been achieved in recent years. However, barring a few recent advances, the attempts to use alkyl halides (especially chlorides) as electrophile partners have been largely unsuccessful.[3] Moreover, examples of mild reaction conditions are rare when the desirable coupling products are sterically hindered di-ortho or tri-ortho substituted biaryls.[4,5]

The major impediment in Suzuki–Miyaura coupling of alkyl halides is the presence of a facile β-hydride elimination pathway (Scheme 1). This undesired side reaction competes with the transmetalation step, hindering a productive coupling process.

Scheme 1. Competing Pathways in Suzuki–Miyaura Coupling



Extensive studies by a number of groups have helped this area take new strides.[6] Elegant work by Fu has helped expand

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An efficient and mild protocol for the α-arylation of ketones mediated by an (imidazol-2-ylidene)palladium(acetate) system

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Abstract

The activity of well-defined *N*-heterocyclic carbene (NHC)-palladium acetate complexes has been studied in the α-arylation of ketones. The enolate was generated in situ via use of slight excess of sodium *tert*-butoxide as base. The results showed a high activity, allowing for the coupling of non-activated chlorides. The use of hindered substrates provided an avenue for convenient synthesis of various ketone derivatives. The first examples of α-arylation of ketones at room temperature mediated by an NHC-ligated catalyst are also presented.

Keywords: Arylation; Ketones; Arylchlorides; *N*-heterocyclic carbenes; Palladium

1. Introduction

Transition metal catalyzed cross-coupling reactions are a popular means of adding a variety of carbon nucleophiles to aryl halides [1]. Development of efficient and selective catalytic reactions for C–C bond formation has been a subject of paramount interest in organic and organometallic chemistry. Catalytic conversion of C–H bond to a C–C bond is an important subgrouping of such transformations. During the past years, numerous reactions involving C–H bond transformations have been developed [2]. Among these, palladium-catalyzed conversion of C–H bonds to form C–C bonds via coupling of aryl halides or pseudo aryl halides with carbon nucleophiles is one of the most widely employed transition metal catalyzed reaction [3]. Finding an efficient and reliable catalytic method to form a bond between an arene and carbon α to a carbonyl group is a challenging problem [4]. The use of aryl halides for direct arylation of ketones at the carbon α to the carbonyl group has proven to be a transformation of great utility in pharmaceutical, agrochemical and organic synthesis [5]. It has also found an increasing interest in the synthesis of fine chemicals [6].

The increased acidity of a proton on a carbon α to a carbonyl group helps in its abstraction and generation of an enolate. The simplicity in methodology offered by in situ generation of an enolate via deprotonation is an added advantage of this approach. Initially, the metal mediated coupling of enolates was achieved by use of stoichiometric amounts of metal complexes [7]. Moreover some of the procedures involved use of less readily available carbonyl alternatives [8]. However, in concurrent work, Buchwald [9], Hartwig [10] and Miura [11] reported the first examples of direct, catalytic, α-arylations of ketones in 1997. Since then, a myriad of reports from these and other groups have helped establish the catalytic α-arylation of ketones as an indispensable synthetic tool [12–15].

Since the discovery of stable *N*-heterocyclic carbenes (NHCs), a number of groups have utilized these in catalysis [16]. In the past several years, a number of NHC-metal complexes serving as efficient catalysts for a

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Simple Synthesis of *N*-Heterocyclic Carbene $[(NHC)\text{-}Pd(Cl)_2]_2$ Complexes and Their Use in Kumada-Tamao-Corriu Cross-Coupling Reactions

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Abstract

The activity of well-defined N-heterocyclic carbene $[(NHC)Pd(Cl)_2]_2$ complexes has been studied in the Kumada-Tamao-Corriu (KTC) coupling of Grignard reagents with various halides. The results show a high activity profile, allowing for the coupling of various halides with low catalyst loadings. The use of hindered and heterocyclic substrates provides an avenue for convenient synthesis for motifs frequently encountered in organic synthetic chemistry. The scalability of the reaction and the optimum conditions for KTC coupling of fluoride substrates are also discussed.

Easy Synthesis and Analysis of Scope and Limitations of *N*-Heterocyclic Carbene(NHC)Palladium(Cl)$_2$-Pyridine Derivatives in Suzuki-Miyaura Cross-Coupling Reaction

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ABSTRACT

N-Heterocyclic(NHC)-palladium(Cl)$_2$-pyridine derivative complexes (NHC)Pd(Cl)$_2$-(X-pyridine) (X = Cl, Br, H) have been synthesized and characterized. It is established that these complexes serve as catalysts for coupling reactions. The complexes have been screened for activity in Suzuki-Miyaura cross coupling reaction. The efficiency of the catalytic species, in presence of various functionalities has been evaluated. This study also documents the impact of change of various parameters on the coupling reaction. The scope and limitations of the catalysts are discussed.

Synthesis of phosphorus esters by transesterification mediated by *N*-heterocyclic carbenes (NHCs)†

Rohit Singh and Steven P. Nolan*

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The versatile nucleophilic organic catalysts *N*-heterocyclic carbenes (NHCs) have been shown to effectively mediate the transesterification of phosphorus esters under mild conditions; user-friendly imidazolium salts can also be employed as pre-catalysts.

Phosphorus esters are important functional groups in organic synthetic chemistry. They not only play an important role as protective groups in pharmaceuticals[1] but are also used as reagents in organic transformations (*e.g.* Wadsworth–Emmons reaction)[2] or in the development of analytical tools.[3] Moreover, on the industrial scale, *P*-esters find applications in agrochemicals as fertilizers,[4] pesticides[5] and insecticides.[6] The major means of preparation of *P*-esters involve alkyl dichlorophosphines or the Michaelis–Arbuzov reaction. While the dichlorophosphines are usually expensive, the Michaelis–Arbuzov[7] reaction suffers from low yields when hindered substrates are used. Gagné has reported on the use of alkali metal alkoxide clusters as efficient catalysts for the ester interchange reaction leading to phosphorus esters.[8] A method relying on $Ti(OR)_4$/ROH catalyzed transesterification has also been reported but suffers from long reaction times and a lack of reactivity towards phosphonates.[9] An inexpensive, metal-free, catalytic protocol for the synthesis of phosphorus esters *via* transesterification would have a significant impact on the accessibility of this class of compounds.

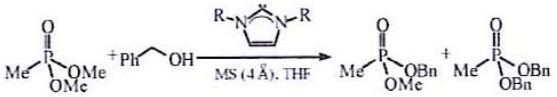
We previously reported on the use of *N*-heterocyclic carbenes (NHCs) as efficient transesterification catalysts for primary and secondary alcohols.[10] We have extended this methodology to now include *P*-esters as substrates, achieving excellent yields using mild conditions (Scheme 1). Phosphonate esters, which are usually unreactive using the Michaelis–Arbuzov protocol, undergo transesterification effectively with the use of various NHCs as catalysts.

Extensive works by Wanzlick,[11] Bertrand,[12] Arduengo[13] and others[14] have shown that the singlet nucleophilic carbenes are neutral compounds having a divalent carbon atom with two non-bonding electrons. Non-toxicity, a non-pyrophoric nature and tunable sterics and electronics have helped establish NHCs as versatile nucleophilic organic catalysts effectively mediating organic transformations.[15–23] The screening of various NHCs in the reaction involving dimethyl methylphosphonate (DMMP) with benzyl alcohol showed the alkyl substituted NHCs, ICy {1,3-bis(cyclohexyl)imidazol-2-ylidene}, IAd {1,3-bis(adamantyl)-imidazol-2-ylidene} and I'Bu {1,3-bis(*tert*-butyl)imidazol-2-ylidene} are capable mediators in this transesterification reaction. The cyclohexyl substituted NHC, ICy, was found to be the best catalyst giving a good yield in only 2 hours (entry 1, Table 1). Better yields can be obtained on increasing the reaction time but this allows for an increase in formation of diesterified product (entry 2, Table 1). Sterically demanding, alkyl substituted NHCs, IAd and I'Bu, provide moderate yields.[24] The aryl substituted NHCs, which are less nucleophilic than the alkyl substituted counterparts,[14,25] did not show activity in this transformation. Even on increasing the catalyst loading, IPr {1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene} and IMes {1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene} did not furnish the desired product.[26]

To fully exploit the potential of this reaction, we examined a wide array of conditions. The data presented in Table 2 illustrate the effect of various parameters on the efficiency of this protocol. Since transesterification is an equilibrium process, removal of products from the reaction mixture drives the reaction in the forward direction. This is achieved by use of molecular sieves (4 Å) that absorb the methanol formed in the course of the reaction and improve conversion. Initially similar conversions are observed in

Scheme 1 NHC catalyzed transesterification of *P*-esters.

Table 1 Screening of *N*-heterocyclic carbenes[a]



Entry	Catalyst	Time (h)	Yield (%)	Product ratio (I:II)
1	R = Cyclohexyl	2	71	90:10
2	R = Cyclohexyl	8	90	75:25
3	R = Adamantyl	2	35	100:0
4	R = *tert*-Butyl	2	32	100:0
5	R = 2,6-Diisopropylphenyl	18	0	—
6	R = 2,4,6-Trimethylphenyl	18	0	—

[a] Reaction conditions: 5 mol% catalyst, 1 mmol of DMMP, 1 mmol of BnOH, 0.5 g of molecular sieves, 1 mL of THF, NMR yields (average of two runs).

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† Electronic supplementary information (ESI) available: Experimental details. See http://dx.doi.org/10.1039/b509783e

JOC*Note*

Transesterification/Acylation of Secondary Alcohols Mediated by *N*-Heterocyclic Carbene Catalysts

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Abstract: *N*-Heterocyclic carbenes (NHC) are efficient catalysts for transesterification/acylation reactions involving secondary alcohols. The catalytic transformations are carried out employing low catalyst loadings in convenient reaction times at room temperature.

The ester moiety is a common functional group in polymers, drugs, and biologically relevant compounds. In addition, the ester functionality serves as a protecting group for alcohols.[1] Preparation of esters may be achieved through reactions of alcohols with carboxylic acids or more effectively by ester interchange[2] or by transesterification,[3] where generally a methyl ester reacts with an alcohol to form a new ester and methanol.

Lewis acidic or basic catalysts have been used as either catalysts or promoters to mediate this reaction. However, Lewis acid catalysts[2] exhibit low substrate selectivity and can cleave sensitive functional groups such as acetals, dienes, and epoxides. They may also lead to formation of side products and deterioration of primary products during the prolonged reaction times.[4] Utilizing strongly basic catalysts such as sodium hydride and potassium *tert*-butoxide leads to high conversions, but the use of such species is problematic for base-sensitive substrates,[2,3] while the weaker tertiary phosphine bases are toxic and expensive. Therefore, with either acidic or basic conditions, such transesterification reactions do not prove to proceed efficiently under mild reaction conditions.[5] Organometallic catalysts such as $Cp^*_2Sm(thf)_2$[6] and distannoxanes,[7] or the basic iminophosphoranes[8] require high catalyst loadings and long reaction times to achieve this transformation. There have been continued efforts to find efficient metal-free catalysts to mediate this transformation in order to provide an environmentally friendly solution that could be carried out under mild reaction conditions.

The *N*-heterocyclic carbenes (NHC) have been shown to act as excellent phosphine mimics.[9] Not only do they possess comparable or better donating properties[9,12c] than most phosphines, but NHCs are neither toxic nor pyrophoric. NHCs were first discovered by Wanzlick[10] in the 1960s, while the isolation and utilization of stable NHCs by Arduengo occurred some 20 years later.[11] In terms of reactivity, NHCs behave as nucleophiles owing to their lone electron pair.[12] The versatility of NHCs has been established in reports demonstrating their role as efficient catalysts in the ring-opening polymerization of lactones,[13] in mediating the benzoin condensation,[14] and in multicomponent reactions.[15] Recent work has established the vast scope of NHCs and their derivatives in terms of their stabilizing effect in organometallic systems.[16]

We and the Hedrick group, simultaneously, reported the use of various alkyl- and aryl-substituted imidazol-2-ylidene carbenes as efficient transesterification/acylation reaction catalysts.[17] Here, we wish to report the use of the same imidazolium-based system for the transesterification/acylation of a variety of secondary alcohols, further establishing the versatility and utility of NHCs for such transformations.

The acylation of commercially available alcohols with varied electronic and steric properties was carried out using a simple protocol (Table 1). All entries in Table 1 reached completion in 1 h, and reported isolated yields are for reactions reaching complete conversion. The reaction of 2-propanol with methyl acetate yields the

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N-Heterocyclic carbenes: Advances in transition metal and organic catalysis

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The use of *N*-heterocyclic carbenes (NHCs) in organic and transition metal chemistry is reviewed. This report presents the developments that have occurred in the last 12 months, describing the use of carbenes as ligands in transition metal chemistry and the catalytic uses of such transition metal complexes. Furthermore, NHCs can act as catalysts in their own right, and recent developments in this growing area of catalysis are described.

1. Introduction

The first reports underlining the existence of carbenic species were provided by Wanzlick in 1960's.[1] Initially the carbenes were found to be unstable and prone to dimerization. In 1968, Ofele reported complexation of *N*-heterocyclic carbenes (NHCs) with transition metals,[2] and subsequently Lappert reviewed the behavior of NHCs in organometallic chemistry.[3]

Major advances were achieved in separate works by Bertrand[4] and Arduengo[5] some 20 years later. Arduengo reported the synthesis of *N*,*N*′-bis(adamantyl)imidazol-2-ylidene in an elegant one step synthetic procedure. Since then a myriad of reports underscoring the effect of NHCs has appeared. Initially branded as "phosphine mimics," the carbenes have overcome the label with their advantages as compared to phosphines. Specifically, better sigma-donating properties, higher thermal stability and better stabilizing effects are noteworthy.[6]

In this report we underscore the major advancements in the utilization of *N*-heterocyclic carbenes as efficient ligands with transition metals. We also discuss latest reports in organic catalysis, with NHCs behaving as effective mediators in various transformations. Some of the commonly used *N*-heterocyclic carbenes are presented in Scheme 1.

Ever since the initial breakthroughs in this area, there have been constant efforts aimed at improving the synthetic pathways leading to NHCs and their complexes with transition metals.[7] Amongst the most recent advances, reports from Arduengo[8] and Crabtree[9] are noteworthy.

Arduengo has synthesized and characterized the first bimetallic ruthenium-palladium complex containing a cyclopentadienyl-annulated imidazol-2-ylidene ligand. The synthesis follows a simple procedure (Scheme 2). The cyclopentadienyl fused imidazolium salt was treated with Meerwein's salt affording an imidazolium tetrafluoroborate (**1**) in 95% yield. Reaction of (**1**) with pentamethylcyclopentadienylrutheniumtris(acetonitrile) triflate in the presence of 4 Å molecular sieves leads

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