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Well-Defined N-Heterocyclic Carbenes−Palladium(II) Precatalysts for Cross-Coupling Reactions

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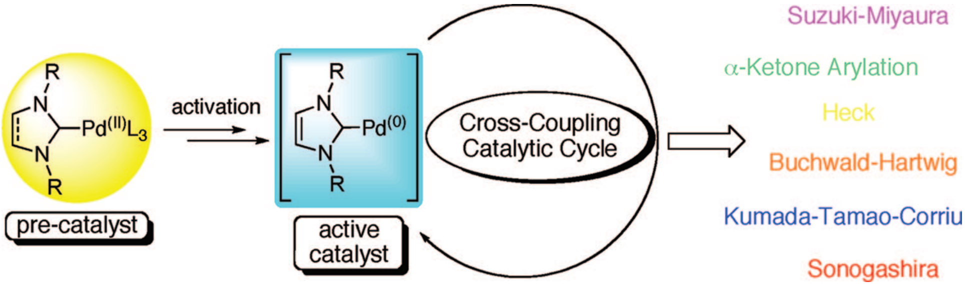
CONSPECTUS



Metal-catalyzed cross-coupling reactions, notably those permitting C−C bond formation, have witnessed a meteoritic development and are now routinely employed as a powerful synthetic tool both in academia and in industry. In this context, palladium is arguably the most studied transition metal, and tertiary phosphines occupy a preponderant place as ancillary ligands. Seriously challenging this situation, the use of N-heterocyclic carbenes (NHCs) as alternative ligands in palladium-catalyzed cross-coupling reactions is rapidly gaining in popularity. These two-electron donor ligands combine strong σ-donating properties with a shielding steric pattern that allows for both stabilization of the metal center and enhancement of its catalytic activity. As a result, the number of well-defined NHC-containing palladium(II) complexes is growing, and their use in coupling reactions is witnessing increasing interest.

In this Account, we highlight the advantages of this family of palladium complexes and review their synthesis and applications in cross-coupling chemistry. They generally exhibit high stability, allowing for indefinite storage and easy handling. The use of well-defined complexes permits a strict control of the Pd/ligand ratio (optimally 1/1), avoiding the use of excess costly ligand that usually requires end-game removal. Furthermore, it partly removes the “black box” character often associated with cross-coupling chemistry and catalyst formation. In the present Account, four main classes of NHC-containing palladium(II) complexes will be presented: palladium dimers with bridging halogens, palladacycles, palladium acetates and acetylacetonates, and finally π-allyl complexes. These additional ligands are best described as a protecting shell that will be discarded going from the palladium(II) precatalyst to the palladium(0) true catalyst. The synthesis of all these precatalysts generally requires simple and short synthetic procedures. Their catalytic activity in different cross-coupling reactions is discussed and put into context. Remarkably, some NHC-containing catalytic systems can achieve extremely challenging coupling reactions such as the formation of tetra-*ortho*-biphenyl compounds and perform reactions at very low loadings of palladium (ppm levels).

The chemistry described here, combining fundamental organometallic, catalysis, and pure organic methodology, remains rich in opportunities considering that only a handful of palladium(II) architectures have been studied. Hence, en route to an “ideal catalyst”, [(NHC)Pd^{II}] compounds exhibit remarkable stability and allow for fine-tuning of the NHC and of surrounding ligands in order to control the activation and the catalytic activity. Finally, unlike [Pd(PPh$_3$)$_4$], [(NHC)Pd^{II}] compounds have so far been examined only in palladium-mediated reactions (most often cross-coupling such as the Suzuki−Miyaura and Heck reactions), leaving a treasure trove of exciting discoveries to come.

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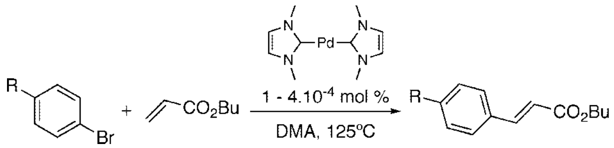
I. Introduction

The impact of the palladium-catalyzed cross-coupling reactions, discovered in the 1970s, has been considerable and continues to be the focus of much organometallic research.[1] It is almost impossible nowadays to find an issue of a journal in the field of organic or organometallic chemistry without a contribution dealing with some aspect of cross-coupling reactions.[2] Due to their wide applicability for C−C bond formation, these reactions belong to the arsenal of synthetic chemists and have clearly changed retrosynthetic analysis.[3] As a consequence of its versatility, the chemical industry has been significantly involved in this area and numerous methods have been patented.[4]

Even though ligandless systems are known,[5] strong σ-donor ligands are necessary to reach a high degree of efficiency.[6] Since the early studies, tertiary phosphines have attracted considerable attention and have allowed for the development of catalytic systems possessing a wide scope. Recently, bulky electron-rich alkylphosphines have enabled the use of extremely low levels of palladium, providing high turnover numbers (TON).[7] To date, N-heterocyclic carbenes (NHCs) are the only class of ligands that has been able to challenge the widely employed tertiary phosphines.[8] Since Herrmann reported that NHC-containing well-defined palladium(0) and palladium(II) complexes efficiently catalyzed the Heck reaction (eq 1),[9] NHCs have been advertised as potential alternatives to phosphines.



(1)

In this Account, we will focus on an underdeveloped aspect in Pd-catalyzed cross-coupling: the use of well-defined NHC-containing palladium(II) precatalysts.[10] Besides the inherent advantages associated with NHC ligands (i.e., stability, steric, electronic, tunability),[11] this class of precatalysts exhibits high stability in the solid state and in solution, allowing for indefinite storage and easy handling. Furthermore, the use of well-defined complexes permits a strict control of the Pd/ligand ratio (optimally 1/1),[12] avoiding the use of excess ligand that usually requires removal in workup procedures.[13] Finally, employing well-defined precatalysts ensures the binding mode of the NHC ligand[14] and partly removes the "black box" character often associated with cross-coupling chemistry and catalyst formation. The present Account will focus on an important development effort in our laboratory over the last eight years, and we present here the culmination of studies that were initiated using *in situ* formed catalysts[15] to what we now favor, well-defined species.

II. Palladium Dimers with Bridging Halides

Dinuclear palladium(II) complexes containing one NHC per metal center and two bridging halides ligands are among the most frequently encountered [(NHC)$Pd^{II}X_2$] compounds. This is notably due to their straightforward synthesis, most often from readily available [$Pd(OAc)_2$] and the imidazolium precursor of the NHC. Several protocols have been reported involving the addition of inorganic salts (LiCl, NaBr, NaI, NaOAc) and requiring prolonged heating in polar solvents.[16] The structures of some of these complexes are depicted in Figure 1. Interestingly, the addition of a base is not necessary,[17] and alternative synthetic routes from [MePd(COD)Cl],[18] [(NHC)Pd(allyl)Cl],[19] or [$Pd(PhCN)_2Cl_2$][20] have been described. It should be noted that heating a mixture of [$Pd(OAc)_2$] and imidazolium salt can produce a highly unexpected type of complex [(NHC)(NHC′)$PdCl_2$], where NHC′ is bound by the backbone (C4 or C5) to the palladium center.[21] Therefore, using a [$Pd(OAc)_2$]/imidazolium salt mixture in catalysis can result in a number of catalytic species and varied activities.

In terms of catalysis, the activity of these complexes has been scarcely examined, that is, only in the Heck, the Suzuki−Miyaura, and the Buchwald−Hartwig reactions. Compound **1** was found to catalyze the coupling of 4-bromoacetophenone and butyl acrylate at low catalyst loadings but was only studied for limited examples.[22] On the other hand, **6** showed only poor activity in the Heck reaction, probably because of the lack of steric pressure from the thiazolydene ligand.[17b]

In 2004, Glorius reported the outstanding activity of **2** and **3** in the Suzuki−Miyaura reaction.[16c] These complexes, possessing an NHC of the IBiox family, allowed for the formation of a tetra-*ortho*-substituted biphenyl in high yield. Tested as well in the Suzuki−Miyaura coupling, complex **7** was found to be efficient for the coupling of aryl bromides and chlorides in water,[16e] while **8** coupled only bromides but with a larger scope, involving unactivated and sterically hindered substrates.[16d]

The activity of **2** was further investigated by the Glorius group in the Sonogashira reaction with unactivated secondary alkyl bromides.[23] Under relatively mild reaction conditions, functionalized alkyl bromides could be coupled with

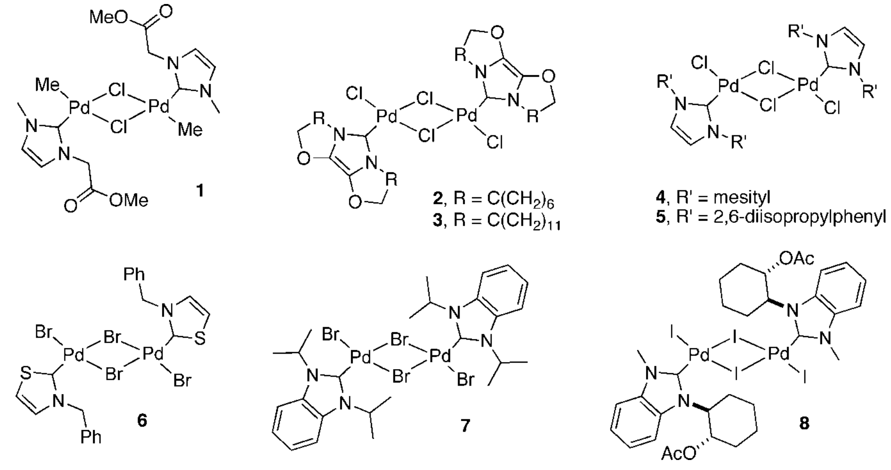
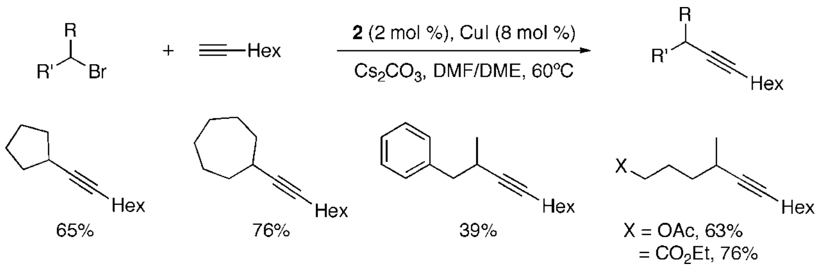
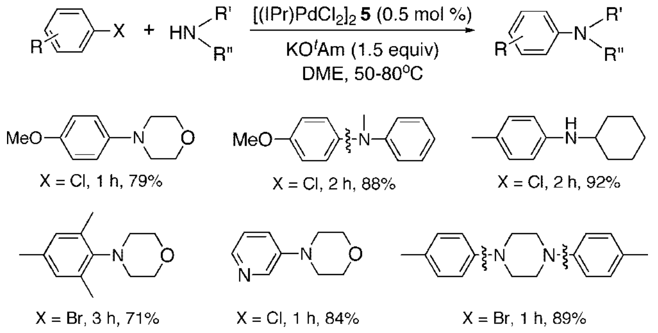


FIGURE 1. Structures of NHC–Pd dimers.

SCHEME 1. Activity of **2** in the Sonogashira Reaction



SCHEME 2. Activity of **5** in the Buchwald–Hartwig Reaction



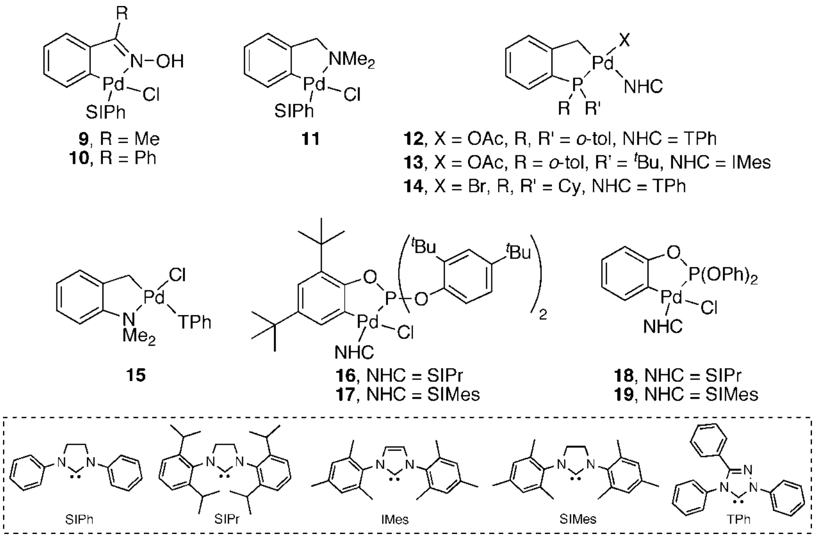
alkyl-substituted terminal alkynes; a representative scope is shown in Scheme 1.

In 2002, we studied the activity of **5** in the *N*-aryl amination reaction.[20] This complex was found to be highly efficient for the coupling of aryl bromides and chlorides. A variety of amines could be coupled with activated, unactivated, encumbered, and heteroaromatic halides in high yields and in short reaction times (Scheme 2). Interestingly, due to the robustness of **5**, reactions could be carried out on the benchtop under aerobic conditions without loss of activity. Recently **5** has been shown as excellent precatalysts in the Suzuki–Miyaura reaction.[20b]

III. Palladacycles

Palladacycles have recently gained importance in catalysis notably because of their flexible framework and robustness.[24] Although promising, the conjugation of a palladacyclic scaffold and an NHC has been scarcely studied. In fact, a limited number of NHC–palladacycles have been synthesized (see Figure 2).

Typically, NHC-containing palladacycles are synthesized in high yields by addition of a nucleophilic carbene to an acetate- or halogen-bridged palladacycle dimer. In 2003, Iyer described the synthesis and applications of palladacyles **9**–**11**.[25] These precatalysts were tested in the Heck reaction where they displayed good to high activity. With aryl bromides, TONs between 40 000 and 90 000 were observed, whereas the use of chlorides was less successful. The activity of compound **10** was further studied in the Suzuki–Miyaura reaction where, as observed in the Heck, aryl bromides were easily coupled and aryl chlorides were found to be more reluctant partners. A large series of NHC-containing phosphapalladacycles, including **12**–**15**, was reported by Herrmann.[26] Their catalytic activity in the Heck reaction was investigated, showing promising results for further improvement. Notably, the use of **15** allowed for the coupling of aryl chlorides with-



9, R = Me
10, R = Ph

11

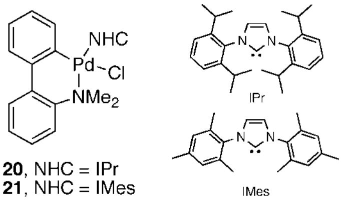
12, X = OAc, R, R' = *o*-tol, NHC = TPh
13, X = OAc, R = *o*-tol, R' = ^{t}Bu, NHC = IMes
14, X = Br, R, R' = Cy, NHC = TPh

15

16, NHC = SIPr
17, NHC = SIMes

18, NHC = SIPr
19, NHC = SIMes

FIGURE 2. Structures of NHC-containing palladacycles.

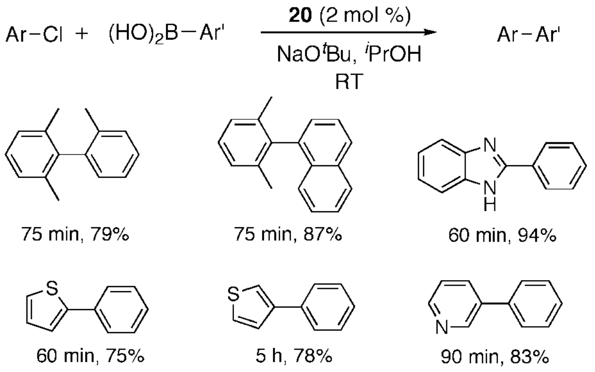


20, NHC = IPr
21, NHC = IMes

Buchwald-Hartwig	**α-Ketone Arylation**	**Dehalogenation**
1 mol % of **20**	0.25 mol % of **20**	1 mol % of **20**
1.1 equiv of NaO^{t}Bu	1.1 equiv of NaO^{t}Bu	1.1 equiv of KO^{t}Bu
dioxane, 70°C	THF, 60°C	^{i}PrOH, RT

FIGURE 3. Structures and activity of **20** and **21**.

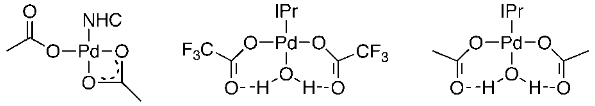
SCHEME 3. Activity of Palladacycle **20** in the Suzuki–Miyaura Reaction



out the need for additives. Bedford and co-workers reported the formation of phosphite palladacycles **16–19** and studied their activity in the Suzuki–Miyaura reaction.[27] Overall, these catalysts performed quite poorly (**17** being the most efficient) and could only couple unhindered and activated aryl bromides.[28]

Along these lines, we reported, as early as 2003, the synthesis of amino-palladacycles **20** and **21** (Figure 3).[29] Since then, the activity of the most efficient one, the IPr-containing **20**, has been investigated in the Buchwald–Hartwig, the α-ketone arylation, the reductive dehalogenation, and the Suzuki–Miyaura reactions. It was proposed, based on NMR studies, that in the presence of isopropanol, a Pd-hydride could be formed, enabling the reductive elimination of the aminobiphenyl shell and producing the active [(IPr)Pd^0] species. Reactions could be performed at low catalyst loadings (1–0.05 mol %) and under mild conditions (rt to 65 °C). Precatalyst **20** proved to be quite versatile and displayed a wide scope in numerous cross-coupling reactions. Aryl chlorides, bromides, and triflates, including heteroaromatics, reacted efficiently with a wide array of nucleophilic partners. In the Buchwald–Hartwig amination, primary and secondary alkyl and aryl amines were coupled in high yields.[29] Similarly, in the α-ketone arylation, aryl and alkyl ketones reacted well.[30] Additionally, reactions could be carried out under microwave heating without loss of yield, allowing for extremely short reaction times (i.e., 2 min). Compound **20** was further found to catalyze the dehalogenation of aryl chlorides, a relevant process for environmental issues keeping in mind the toxicity of polychlorinated compounds.[31] Again, as a testimony to the high activity of **20**, reactions occurred at room temperature in isopropanol, serving both as solvent and hydride donor.[30]

Adding to the high activity and versatility of **20** described above, its most impressive performance was observed in the Suzuki–Miyaura reaction. Biphenyls were produced smoothly at room temperature and in short reaction times in technical grade isopropanol; a representative scope is given in Scheme 3.[32] It was proposed that isopropoxide, formed *in situ* from isopropanol, would form, upon addition onto boronic acid, a tetravalent boronate species, facilitating the transmetalation



22, NHC = IPr
23, NHC = IMes
24
25

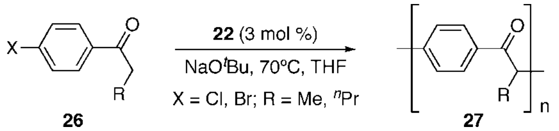
FIGURE 4. Carboxylate-containing NHC−palladium complexes.

step in the catalytic cycle. This method notably allowed for the straightforward synthesis of tri-*ortho*-subsituted and heteroaromatic biaryls from aryl chlorides or triflates.[30,32] It should be noted that, despite its high activity, tetra-*ortho*-substituted biaryls could not be produced with this catalytic system.[33]

IV. Palladium Acetate and Acetylacetonate Complexes

Palladium Acetate Derivatives. Among the multiple sources of simple palladium(II) salts available for carrying out cross-coupling reactions in conjunction with external ligands, [Pd(OAc)$_2$] is one of the most employed. It is therefore surprising that only a handful of well-defined NHC-containing palladium acetate complexes have been reported and studied in catalysis.

Simple addition of IPr ligand to a toluene solution of [Pd(OAc)$_2$] produced compounds **22** and **23**, where the two acetate molecules are bound differently (Figure 4).[34] Interestingly, as a function of the synthetic route, closely related complexes **24** and **25**, where a molecule of water occupies a coordination site, can be obtained, the latter being extremely active in palladium-catalyzed aerobic oxidation of alcohols.[35] These precatalysts, primarily tested in the hydroarylation of alkynes,[34] were later found to be efficient in the Suzuki−Miyaura[36] and the α-ketone arylation reactions.[37] An interesting application of the activity of **22** in α-ketone arylation using *p*-haloarylketones **26** to produce poly-α-arylketones **27** was reported by Matsubara (eq 2).[38]



26 **27** (2)

Importantly, the authors observed that while **22** was extremely efficient, a combination of [Pd(OAc)$_2$] and IPr·HCl afforded only poor yields. This is not surprising since a mixture of [Pd(OAc)$_2$] and NHC·HCl generally furnishes chloride-bridged palladium dimers (see section II) and not an acetate-containing palladium species. These last observations highlight the advantage of using well-defined complexes in lieu of mixtures of palladium salts and ligands and can be better understood in light of a report on the use of [Pd(OAc)$_2$]/imidazolium salt mixtures in the Heck reaction.[21]

Palladium Acetylacetonate Derivatives. Similarly to [Pd(OAc)$_2$], [Pd(acac)$_2$] (acac = acetylacetonate) has only scarcely been used to form NHC-containing Pd^{II} complexes. Cavell and co-workers reported the first synthesis of [(NHC)Pd(acac)L] (where L = Me) complexes.[39] They were shown to efficiently catalyze the Heck reaction of activated aryl bromides, reaching high TONs (∼100 000). Recently, we described the synthesis of two novel types of NHC-containing Pd(acac) derivatives, [(IPr)Pd(acac)$_2$] (**28**) and [(NHC)Pd(acac)Cl] (**29**, **30**).[40] It was shown that **28**, possessing an η^1-C-bound and a κ^2-O,O-bound acac, was an intermediate en route to **29**, and a one-pot procedure (Scheme 4, bottom path) was successfully developed.

The synthesis of **29** and **30** was further improved and now simply requires heating a mixture of imidazolium salt and [Pd(acac)$_2$] in technical grade dioxane without the need for a base.[41] This improved protocol allowed for the synthesis of a 14 g batch of [(IPr)Pd(acac)Cl], **29**. This compound was found to efficiently catalyze the aryl amination and the α-ketone arylation reactions using aryl chlorides and bromides under relatively mild conditions.[42] The reaction scope of **29** was found to be broad, including sterically hindered and unactivated substrates as well as heteroaromatics for both couplings; a representative scope in α-ketone arylation is presented in Scheme 5.

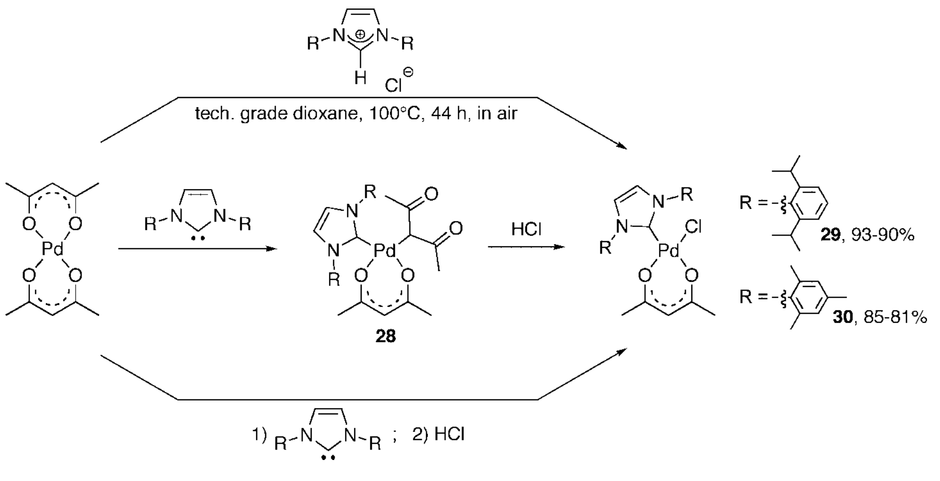
Furthermore, mechanistic studies were conducted to gain insight into the activation pathway involving this palladium(II) precatalyst and on the catalytically active species. The use of inert atmosphere MALDI-TOF techniques to examine mixtures of [(IPr)Pd(acac)Cl] (**29**) and KO^{t}Bu revealed the presence of monoligated [(IPr)Pd^0],[43] supporting the hypothesis of a bare monoligated 12-electron palladium species as true catalyst in cross-coupling reactions.

V. π-Allyl Palladium Complexes: [(NHC)Pd(allyl)Cl]

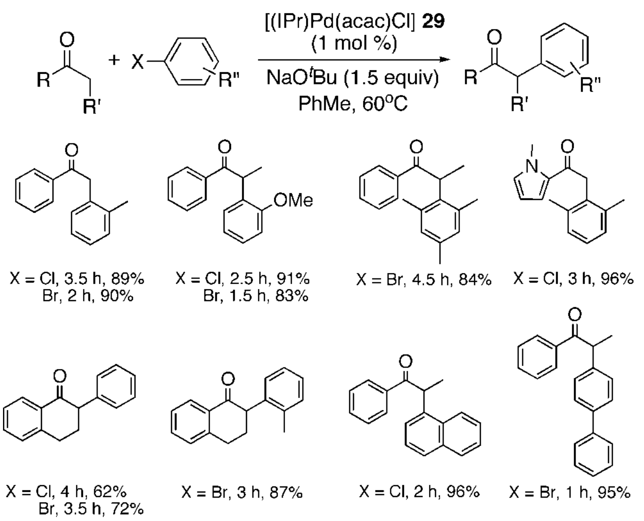
Once again, the main advantages of utilizing mononuclear [(NHC)Pd(allyl)Cl] complexes lie in their very straightforward synthesis and high stability. They are usually produced from [(allyl)PdCl]$_2$ upon addition of 2 equiv of NHC ligand. In 2002, we synthesized a number of [(NHC)Pd(allyl)Cl] (Figure 5, **31**−**37**), which enabled the evaluation of the steric properties of the entire series of NHCs.[44]

These precatalysts are thought to be activated either through a nucleophilic attack at the allyl moiety or through a chloride/alkoxide σ-metathesis followed by reductive elimination, liberating in both cases a [(NHC)Pd^0] species (Scheme 6).

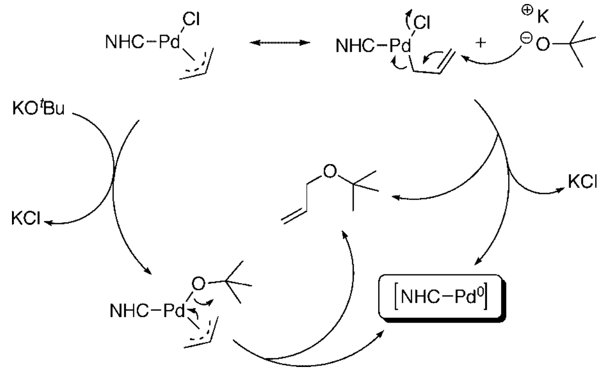
SCHEME 4. Synthetic Routes to [(NHC)Pd(acac)Cl] Complexes



SCHEME 5. Representative Scope of **29** in the α-Ketone Arylation Reaction



SCHEME 6. Postulated Activation Pathways for [(NHC)Pd(allyl)Cl] Complexes



In the course of the comparison of their activity in cross-coupling reactions,[45] optimization of the NHC ligand on the Pd center showed IPr and SIPr to be the most efficient ligands in aryl amination reactions, with a clear advantage for SIPr, which performed best at room temperature. Further investigation showed that **31** and **32** were able to perform a wide array of cross-coupling reactions (Suzuki–Miyaura, Buchwald–Hartwig, dehalogenation, ketone arylation) at low catalyst loading and under mild reactions conditions.[46] These precatalysts, which are both commercially available,[47] can be synthesized in a one-pot procedure from the imidazolium chloride that is deprotonated *in situ*.[48]

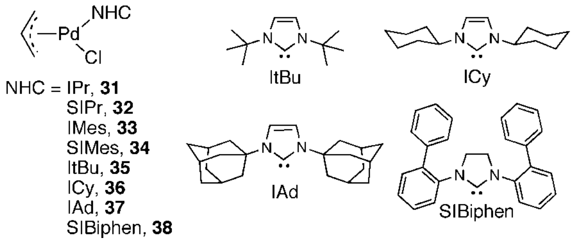
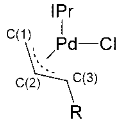


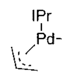
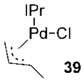
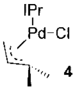
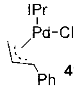
FIGURE 5. Structures of [(NHC)Pd(allyl)Cl] complexes **31**–**38**.

Closely related to cross-coupling reactions, intramolecular direct arylations have been shown to proceed in the presence of several NHC–palladium(II) complexes, including **25**. Thorough screening involving compounds **4**, **5**, **25**, and **31** revealed the superiority of **25** in this particular transformation.[49] Recently, Bellemin–Laponnaz and co-workers reported the synthesis of palladium compound **38**,[50] bearing the SIBiphen carbene ligand, with the purpose of mimicking Buchwald's highly active biphenylphosphine scaffold.[51] Disappointingly, the use of **38** in cross-coupling resulted in very poor yield and rapid catalyst decomposition.

Further developments for this family of catalysts led us to the synthesis of unsymmetrically substituted allyl complexes **39**–**42**, **42** being the SIPr-analogue of **41**.[52] As shown in Table 1, terminal substitution on the allyl moiety resulted in an elongation of the Pd–C(3) bond, destabilizing the allyl and making it more prone to activation (regardless of the mecha-

TABLE 1. Selected Bond Distances in [(NHC)Pd(R-allyl)Cl] **31** and **39**−**41**



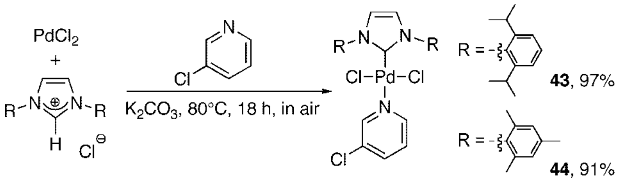
(Å)	 **31**	 **39**	 **40**	 **41**
Pd-C(1)	2.098(6)	2.147(18)	2.095(4)	2.082(9)
Pd-C(2)	2.124(7)	2.122(18)	2.137(5)	2.136(10)
Pd-C(3)	2.210(6)	2.209(16)	2.252(5)	2.284(9)

nistic activation pathway used: either nucleophilic attack or reductive elimination, see Scheme 6).[44,45]

This was confirmed experimentally, the modified allyl compounds **39**−**42** being much more active at room temperature than the unsubstituted allyl **31**. We examined the scope of [(IPr)Pd(cinnamyl)Cl] **41** and [(SIPr)Pd(cinnamyl)Cl] **42** in Suzuki−Miyaura and Buchwald−Hartwig reactions, respectively. A wide array of aryl bromides and chlorides could be coupled at room temperature in short reaction times, notably unactivated and sterically encumbered ones. These second-generation allyl complexes also permitted the coupling of nitrogen-containing heteroaromatics in high yields.[53] Most interestingly, **41** and **42** proved to be long-lived catalysts, allowing catalyst loadings as low as 10 parts-per-million (ppm) when the temperature was increased to 80 °C. A representative scope of these very low palladium level reactions is presented in Scheme 7. It is worth noting that catalytic systems employing such low levels of palladium in aryl amination and in the Suzuki−Miyaura reaction are extremely rare.[54] Remarkably, in the case of **41** and **42**, no loss of activity was observed, and hindered substrates, reluctant aryl chlorides, and heteroaromatics were coupled efficiently.

VI. Pyridine-Containing Palladium Complexes

Surprisingly, while chelating bidentate pyridine−NHC ligands are well-known, pyridine adducts of monodentate NHC-containing palladium(II) compounds are scarce and have only recently been recognized as efficient precatalysts for coupling reactions. Hence, Organ and co-workers, capitalizing on the development of third-generation Grubbs catalyst,[55] recently reported the synthesis of complexes of general formulas [(NHC)PdCl$_2$(pyr)]. Prolonged heating of IPr·HCl with palladium(II) dichloride in the presence of excess base in neat 3-chloropyridine led to compound **43** in high yield (eq 3).[56]



43, 97%

44, 91%

(3)

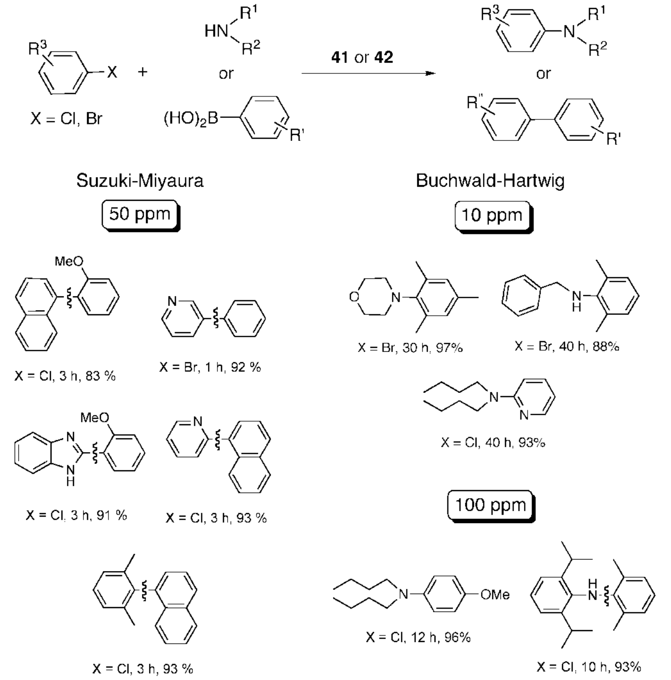
These pyridine adducts, and especially the IPr-containing **43**, showed good activity in the Suzuki−Miyaura reaction, enabling the coupling of heteroaromatics and the formation of tri-*ortho*-substituted biaryls under mild conditions. The same group further investigated the catalytic activity of **43** in the Negishi coupling. Remarkably, this precatalyst allowed for sp^3−sp^3, sp^2−sp^2, and both types of sp^2−sp^3 couplings of zinc reagents with halide derivatives.[57] As a tentative mechanism for the activation of the pyridine palladium(II), the authors proposed a double transmetalation between **43** and the organometallic nucleophile leading, upon reductive elimination, to homocoupling of the boron or zinc reagent and to a [(NHC)Pd^0] species, the remaining pyridine acting as a throw-away ligand. Following up on these initial studies, they reported the use of **43** in the Kumada−Tamao−Corriu reaction.[58] The scope of the catalytic system proved to be wide and tolerant to heteroaromatics including thiophenes, pyridines, pyrazoles, and benzothiazoles.

Very recently, Lee disclosed the synthesis of compounds **45**−**47** (Figure 6) and studied their behavior in the Suzuki−Miyaura reaction.[59] In the coupling of aryl bromides and phenyl boronic acid, **45** was found more efficient than **46**. Furthermore, relying on their comparative studies, the authors nicely demonstrated that monodentate NHCs perform better than chelating bidentates for cross-coupling reactions, supporting the concept of a bare monoligated palladium(0) as the true active species.[12,43] Pyridine-free palladium complex **48** (Figure 6), reported as early as 2001 by Batey and co-workers, is clearly related to compounds **43**−**47**. Interestingly, its synthesis from [Pd(OAc)$_2$] is unique and involves release of *N*-methylimidazole from a second equivalent of the NHC precursor.[60] The good activity of **48** in the Sonogashira reaction allowed for the coupling of aryl iodides and terminal alkynes at room temperature. Aryl bromides were found to be reluctant and required elevated temperature, while aryl chlorides could not be coupled.

VII. Outlook

The impressive explosion of interest in N-heterocyclic carbenes as ligands was triggered only 17 years ago by the isolation of a stable NHC by Arduengo.[61] Since then, they have evolved from laboratory curiosities to "phosphine mimics" and are now

SCHEME 7. Low Catalyst Loading Cross-Coupling Reactions Catalyzed by **41** and **42**



considered as a very special class of ligands. Following this progression, well-defined NHC-containing palladium(II) precatalysts, resulting from early in situ generated catalytic studies, are now coming to the forefront as they can already, despite being in their infancy, match late-generation tertiary phosphines in terms of catalytic activity in cross-coupling reactions.

This area of chemistry, combining fundamental organometallic, catalysis, and pure organic methodology, remains rich in opportunities considering that only a few palladium(II) architectures have been studied. Hence, en route to an "ideal catalyst", [(NHC)Pd^{II}] compounds exhibit remarkable stability and allow for fine-tuning of the NHC and of the surrounding ligands in order to control the activation and the catalytic activity. The only restraint in the structure of the palladium(II) precatalyst is that, despite its stability, it must be easily activated (i.e., reduced to Pd^0) under the reaction conditions. Additionally, the control of the ligand/Pd ratio can be very advantageous in the context of mechanistic studies and is of economic relevance considering the higher cost of late-generation ligands when compared with palladium sources.

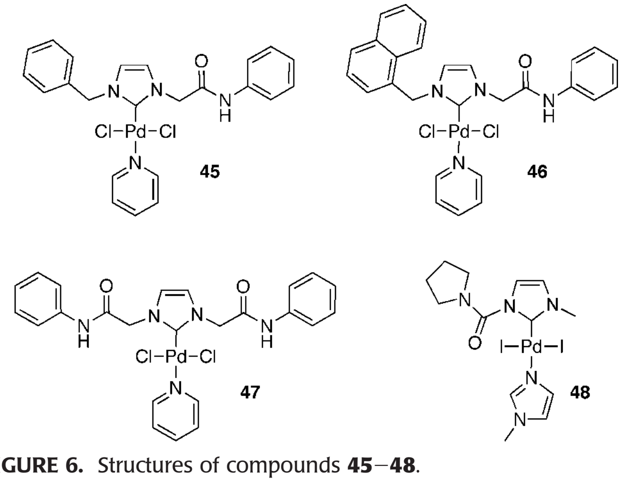


FIGURE 6. Structures of compounds **45**–**48**.

Moreover, whereas popular catalytic systems such as [Pd(PPh$_3$)$_4$] or [Pd$_2$(dba)$_3$]/P^{t}Bu$_3$ have been thoroughly investigated, the efficient [(NHC)Pd^{II}] compounds have so far been examined only in a few cross-coupling reactions (most often Suzuki–Miyaura, Heck, and Buchwald–Hartwig), leaving most of the spectrum of cross-coupling unexplored. Finally, mechanistic studies focusing on precatalyst activation and on the catalytic cycle involving NHCs could enhance our understanding of the particular character of NHCs; such studies are still limited in number.[62] Considering all of the above and the fact that many of these well-defined complexes are now commercially available, we strongly believe that this area will continue to grow in the near future and will bring numerous surprises as it is now clear that NHCs are more than tertiary phosphine mimics.

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Note Added after ASAP. There was an incorrect reference citation in Section III of the version published on September 6, 2008; the corrected version was published on September 11, 2008.

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Nicolas Marion received his M.Sc. in organic chemistry from the Université Pierre et Marie Curie (UPMC) in Paris where he worked under the supervision of Professors Louis Fensterbank and Max Malacria. He obtained his Ph.D. in 2008 under the supervision of Professor Steven P. Nolan at the ICIQ in Tarragona. He is currently pursuing post-doctoral studies at MIT with Professor Gregory C. Fu.

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FOOTNOTES

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