Activation and Reactivity of (NHC)Pd(allyl)Cl (NHC = N-Heterocyclic Carbene) Complexes in Cross-Coupling Reactions

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Summary: Mononuclear palladium-allyl complexes bearing one N-heterocyclic carbene (NHC) ligand have been synthesized. These complexes offer a straightforward entryway into a number of catalytic cycles by simple action of a base.

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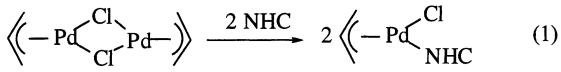
N-Heterocyclic carbenes (NHC) have recently been used as supporting ligands in a variety of transition-metal-catalyzed reactions.[1] Of these, metal-mediated cross-coupling reactions, leading to C−C and C−N bond formation, have most benefited from the use of electron-rich and sterically demanding NHC ligands.[2] In palladium-mediated coupling studies, the NHC−palladium moiety has been generated in situ by the action of a base on the imidazolium salt precursor followed by addition of a palladium source.[3] In these studies, the ratio of ligand to metal was optimized to 1:1. These observations led us to explore synthetic avenues leading to palladium complexes bearing a single NHC ligand per palladium; the number of such complexes is still rather limited.[4] Our recent success in generating Pd(II) complexes of the type $[(NHC)PdCl_2]_2$ and the observed catalytic reactivity of these systems led us to explore the synthesis of monomeric palladium(II) complexes.

Our synthetic approach makes use of a simple palladium(II) source, $[(allyl)PdCl]_2$ (**1**), and the optimal metal-to-ligand ratio.[5] Various (NHC)Pd(allyl)Cl complexes were synthesized in excellent yields using the reaction depicted in eq 1: **2**, NHC = SIPr (*N*,*N*′-bis(2,6-



(1)

diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene); **3**, NHC = IPr (*N*,*N*′-bis(2,6-diisopropylphenyl)imidazol-2-ylidene); **4**, NHC = IMes (*N*,*N*′-bis(2,4,6-trimethylphenyl)imidazol)-2-ylidene); **5**, NHC = I^{t}Bu (*N*,*N*′-bis(2,6-*tert*-butylphenyl)imidazol-2-ylidene). The reaction of most NHC species with **1** can be performed in THF at room temperature in 1 h. The reaction of SIPr and **1** proceeds smoothly at −78 °C in Et_2O, affording **2** in 96% yield. Once the complexes are formed, the workup and recrystallization can be performed in air with no deleterious effect on yield.

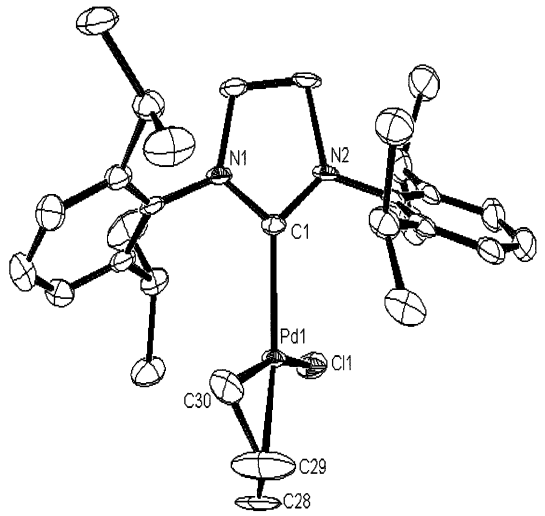


Figure 1. ORTEP diagram of (SIPr)Pd(allyl)Cl (**2**). Selected bond lengths (Å) and angles (deg): Pd−C(1), 2.042(5); Pd−C(30), 2.098(6); Pd−C(29), 2.124(7); Pd−C(28), 2.210(6); Pd−Cl(1), 2.3757(14); C(1)−Pd(1)−C(29), 137.4(2); C(1)−Pd(1)−C(28), 169.0(2); C(30)−Pd(1)−C(28), 68.4(2); C(1)−Pd(1)−Cl(1), 92.36(14); C(29)−Pd(1)−Cl(1), 129.1(2).

To confirm the structure of this family of complexes, a single-crystal X-ray analysis of **2** (formed in Et_2O by slow cooling) was performed (Figure 1). The ORTEP of **2** reveals η^3 coordination of the allyl fragment and a distorted-square-planar coordination around the Pd center.

With the isolation of **2**−**5** now achieved, the question of activation of this system toward catalysis was examined. In the formation of in situ catalysts from Pd(II) sources and imidazolium salts, the exact reaction path-

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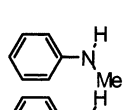
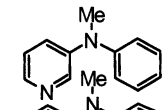
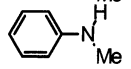
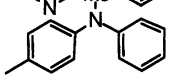
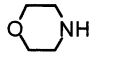
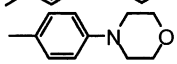
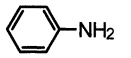
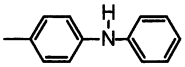
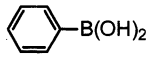
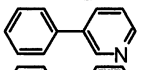
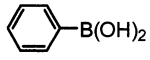
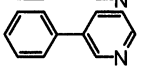
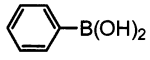
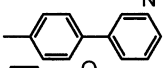
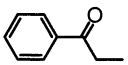
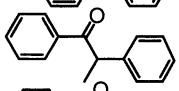
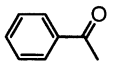
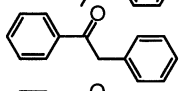
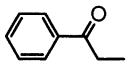
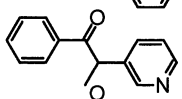
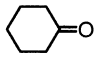
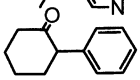
Table 1. Palladium-Mediated Cross-Coupling of Aryl Chlorides and Various Coupling Partners[a]

entry	substrates	product	temp(°C)	time (h)	yield(%)
1			RT	24	88[a]
2			RT	14	96[a]
3			RT	1.3	93[a]
4			50	1	95[a]
5			80	1.5	95[b]
6			80	1.5	97[c]
7			80	1.5	95[c]
8			50	1	91[d]
9			70	1	88[d]
10			80	1	66[d]
11			80	3	72[d]

[a] Conditions: (a) 1.5 mmol of NaO^{t}Bu, 4 mL of DME, 1 mol % of **2**; (b) 10 mmol % of NaO^{t}Bu, 1.5 mmol of Cs_2CO_3, 4 mL of dioxane, 0.5 mol % of **4**; (c) 1.5 mmol of NaO^{t}Bu, 4 mL of dioxane, 2 mmol % of **3**; (d) 1.5 mmol of NaO^{t}Bu, 4 mL of THF, 1 mol % of **2**. All yields are isolated and are the average of two runs.

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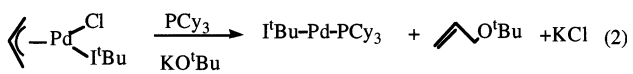
way leading to Pd(0) species has not been investigated. With monomeric compounds in hand, the reduction of Pd(II) to Pd(0) was examined with various bases used under catalytic conditions. The reaction of **5** with NaO^{t}Bu at room temperature led within minutes to a mixture of two allyl-containing species (60/40), as observed by ^{1}H NMR spectroscopy. When this solution was warmed to 40 °C for 1 h, one species was converted to the second species exclusively. The final allylic species is allyl *tert*-butyl ether, whose identity was confirmed by comparison with an authentic sample.[6] In palladium allyl systems, there are precedents for nucleophilic attack by an alkoxide base either at the allyl[7] or at the palladium center.[8] At this point, we adopt the view that both reaction pathways are possible for the (NHC)Pd(allyl)Cl activation. Direct attack leads to allyl ether formation, and attack at palladium leads to a palladium complex, which undergoes reductive elimination at elevated temperatures. Regardless of the activation route, an NHC−Pd^0 complex is formed. The existence of such a complex was confirmed by a trapping experiment carried out in the presence of PCy_3 (eq 2).[9]



(2)

We postulate that the new (NHC)Pd(allyl)X species formed is the (NHC)Pd(allyl)(O^{t}Bu) complex. The formation of this species would be the result of a simple metathesis between (NHC)Pd(allyl)Cl and NaOR. In either alkoxide attack at the allyl position or metathetical alkoxide replacement, a single new NHC−Pd species is formed.

The reductive elimination of ether from a palladium(II) complex can be used to generate catalytically active (NHC)Pd^0 species. Since a palladium(0) species is formed under basic conditions, the catalytic activity of the precatalyst, (NHC)Pd(allyl)Cl, in cross-coupling reactions of aryl chlorides with various substrates was examined. The palladium-mediated aryl amination reaction requires, with few exceptions, the use of a strong base (such as an alkoxide).[10] The aryl amination reactions were performed, under optimized conditions, in DME with NaO^{t}Bu and precatalyst **2**. In most cases, reactions can be conducted at room temperature (or at mild temperatures) (entries 1−4, Table 1). This catalytic

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system is robust enough to tolerate technical grade solvent.

Successful Suzuki−Miyaura reactions have been conducted with NHC−palladium systems.[3c,d,f] The most commonly used bases in this instance are inorganic carbonates, phosphates, or fluorides. In our initial attempts at Suzuki−Miyaura coupling with **2**, the use of Cs_2CO_3, CsF, K_3PO_4, or NaOAc alone led to no product conversion involving aryl chlorides and benzeneboronic acid. These bases simply failed to activate the catalyst. The use of NaO^{t}Bu led to a complete conversion (95% isolated) of the desired product (Table 1, entry 7). The optimum conversions and reaction times were obtained with a two-base system: a catalytic amount of NaO^{t}Bu was used to initiate the Pd(II) complex, and Cs_2CO_3 was used as an operating base in the Suzuki−Miyaura reaction (Table 1, entry 5).

The coupling of simple ketones and aryl halides, despite its great synthetic importance, has been less explored.[11] Strong bases are required to generate carbanions from ketones.[12] NaO^{t}Bu is a convenient base in this system, since it can activate the catalyst and deprotonate the ketone. Ketone arylation competes with condensation of two ketone molecules, due to the presence of substrates with acidic protons and their conjugate bases.[11] This side reaction can be minimized if a rapid oxidative addition of aryl chloride and a fast reductive elimination to the desired product are involved in the catalytic cycle. The size and donating properties of SIPr in **2** were found to be beneficial to this transformation. Aryl chlorides represent good coupling partners in ketone arylation (superior to bromides). In all cases examined (Table 1, entries 8−11), byproducts were formed in less than 5%.

In conclusion, a novel (NHC)Pd(allyl)Cl family of complexes have been synthesized and characterized. The well-defined complexes are air- and moisture-stable. A general and convenient method of activation leading to very active NHC−Pd^0 species has been identified, and this route to (NHC)Pd^0 species has been tested in aryl amination, Suzuki−Miyaura cross-coupling, and ketone arylation. Ongoing efforts are aimed at exploring the scope of this facile activation protocol in a number of cross-coupling and related reactions.

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Supporting Information Available: Text giving experimental details for the synthesis of (NHC)Pd(allyl)Cl complexes, catalysis protocol, and product isolation and tables of X-ray crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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