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Chloropalladated Propargyl Amine: A Highly Efficient Phosphine-Free Catalyst Precursor for the Heck Reaction

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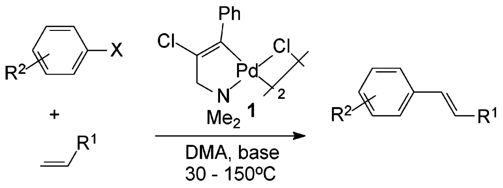
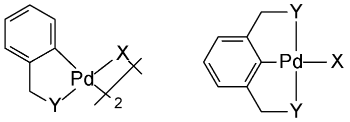
ABSTRACT



The palladacycle {Pd[k^1-*C*, k^1-*N*-C=(C$_6$H$_5$)C(Cl)CH$_2$NMe$_2$](μ-Cl)}$_2$ 1 derived from the chloropalladation of 3-(dimethylamino)-1-phenyl-1-propyne promotes the arylation of olefins under relatively mild reaction conditions. The coupling of iodoarenes and activated bromoarenes with *n*-butylacrylate and styrene occurs at room temperature. Turnover numbers of up to 85 000 have been achieved with deactivated bromoarenes and up to 1000 for activated chloroarenes at higher temperatures (80–150 °C).

Palladacycles are among the most simple and efficient catalyst precursors to promote the arylation of olefins with aryl halides (Heck reaction).[1] Since the first report on the use of a cyclopalladated compound derived from the *ortho*-palladation of tris(*o*-tolyl)phosphine,[2] a plethora of dimeric palladacycles with PC, NC, and SC coordination modes and PCP, NCN, and SCS pincer-type complexes (Figure 1) have been reported to effectively promote the Heck reaction of various bromo- and iodoarenes.[3] However, all palladacycles reported to date only promote the Heck reaction at temperatures above 80 °C even for highly activated iodoarenes. It has been recently proposed that, at least for NC palladacycles, the reaction proceeds through the classical phosphine-free Pd(0)/Pd(II) catalytic cycle.[4]



Y= NR$_2$, =NR, SR, PAr$_2$, P(OR)$_2$, etc.
X= Cl, Br, OAc, OTf, etc.

Figure 1. Example of palladacycles used as catalyst precursors.

The catalytic activity differences observed with these different palladacycle precursors have been rationalized in terms of catalyst preactivation. In these cases, the pallada-

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[1] For recent reviews, see: (a) Dupont, J.; Pfeffer, M.; Spencer, J. *Eur. J. Inorg. Chem.* **2001**, 1917−1927. (b) Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750−3781. (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009−3066.

[2] Herrmann, W. A.; Brossmer, C.; Ofele, K.; Reisinger, C. P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844−1848.

[3] See for example: (a) Ohff, M.; Ohff, A.; Milstein, D. *Chem. Commun.* **1999**, 357−358. (b) Zim, D.; Gruber, A. S.; Ebeling, G.; Dupont, J.; Monteiro, A. L. *Org. Lett.* **2000**, *2*, 2881−2884. (c) Bergbreiter, D. E.; Osburn, P. L.; Wilson, A.; Sink, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 9058−9064. (d) Munoz, M. P.; Martin-Matute, B.; Fernandez-Rivas, C.; Cardenas, D. J.; Echavarren, A. M. *Adv. Synth. Catal.* **2001**, *343*, 338−342. (e) Alonso, D. A.; Najera, C.; Pacheco, M. C. *Adv. Synth. Catal.* **2002**, *344*, 172−183. (f) Morales-Morales, D.; Redon, R.; Yung, C.; Jensen, C. M. *Chem. Commun.* **2000**, 1619−1620. (g) Albisson, D. A.; Bedford, R. B.; Scully, P. N. *Tetrahedron Lett.* **1998**, *39*, 9793−9796.

[4] Beletskaya, I. P.; Kashin, A. N.; Karlstedt, N. B.; Mitin, A. V.; Cheprakov, A. V.; Kazankov, G. M. *J. Organomet. Chem.* **2001**, *622*, 89−96.

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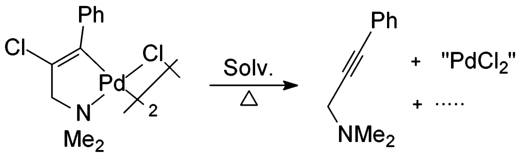
cycle serves as a “reservoir” of Pd catalytic species under the given reaction conditions.[4,5] The key step in these cases is the slow release of a low-ligated active Pd(0) species. Therefore, the most efficient palladacycles will be those where the release of active Pd is neither too fast (typical of poorly thermally stable palladacycles that preferentially result in the formation of inactive metallic palladium) nor too slow (typical of thermally robust palladacycles, which would require higher temperatures to start the reaction in order to maintain a reasonable rate).

We have recently reported that various types of palladacycles can be easily obtained by the chloropalladation of heterosubstituted alkynes.[6] Moreover, we have found that depending upon the reaction conditions, the alkyne can be regenerated together with soluble Pd(II) and Pd(0) species (Scheme 1).[7] Therefore, these chloropalladated alkynes are potentially good candidates for the generation of catalytically active species of Pd(0) for the Heck reaction.

Scheme 1. Retrochloropalladation Reaction



We report herein that indeed the palladacycle $\{\mathrm{Pd}[k^1\text{-}C,k^1\text{-}N\text{-C}{=}(\mathrm{C_6H_5})\mathrm{C(Cl)CH_2NMe_2}](\mu\text{-Cl})\}_2$ **1** derived from the chloropalladation of 3-(dimethylamino)-1-phenyl-1-propyne is among the most effective catalyst precursors for the coupling of haloarenes with alkenes.

The catalyst precursor is easily obtained, in almost quantitative yield, by simple addition of 3-(dimethylamino)-1-phenyl-1-propyne[6] to a methanolic solution of $\mathrm{Li_2PdCl_4}$ at room temperature (see also Supporting Information). This yellow compound is air and water stable in both solid and solution ($\mathrm{CH_2Cl_2}$, acetone, DMSO, etc.) at room temperature. Palladacycle **1** starts to decompose at 172−175 °C in the solid state and in solution (DMSO) at around 80 °C (monitored by variable-temperature ^{1}H NMR).

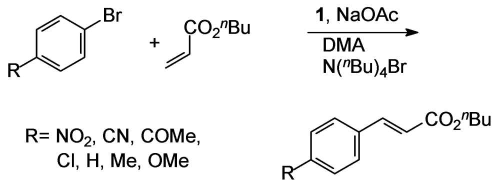
The catalytic performance of **1** in the coupling of haloarenes with *n*-butylacrylate and styrene under different reactions conditions is summarized in Table 1.

The initial experimental protocol was based on our previous results that indicated, for the Heck coupling promoted by sulfur-containing palladacycles, that DMA is the best solvent and NaOAc is the base of choice. The turnover numbers (TON) of 1 000 000 achieved at 150 °C and in the presence of $\mathrm{N(^nBu)_4Br}$ (entry 1, Table 1) are not exceptional since the coupling of iodobenzene with *n*-butylacrylate under the reaction conditions can be promoted by almost any palladium catalyst precursor.[8] However, this coupling can be performed at room temperature (entries 8 and 10, Table 1), and this is an exceptional result since examples of Pd catalyst precursors that catalyze the Heck coupling at room temperature are very rare.[9] Moreover, this coupling reaction can be performed in the absence of $\mathrm{N(^nBu)_4Br}$[10] using $\mathrm{K_3PO_4}$ as the base with minimal reduction in the TON (entry 9, Table 1).

The reaction of bromoarenes substituted with electron-withdrawing groups can also be performed under mild reaction conditions (entries 17 and 27), although better conversions were achieved at higher temperatures (50−80 °C, Table 1, entries 15, 16, and 26). In the case of nonactivated and deactivated bromoarenes, temperatures above 120 °C are necessary to achieve good reaction yields (entries 19 and 23). This is also evident for chloroarenes where only those substituted with electron-withdrawing groups give reasonable yields in coupling products (entries 28−30). Nonactivated and deactivated chloroarenes failed to react with *n*-butylacrylate and styrene under the conditions presented in Table 1.[11]

To gain insight into the mechanism of the reaction, a competitive experiment with seven aryl bromides was performed under pseudo-first-order conditions with respect to *n*-butylacrylate (Scheme 2).

Scheme 2



A solution containing 1.0×10^{-5} mmol of catalyst precursor **1**, 0.14 mmol of each of the aryl bromides, 10 mmol of *n*-butylacrylate, 0.2 mmol of $\mathrm{N(^nBu)_4Br}$, and 1.4 mmol of NaOAc was heated at 150 °C with stirring in 5 mL of DMA. The concentrations of the various coupling products were determined by GC using methyl benzoate as an internal standard.[12] The resulting Hammett plot is exhibited in Figure 2.

The use of σ_p constants results in a good fit, and correlation yields a value of $r = 2.7$. This electronic effect is not

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(5) Biffis, A.; Zecca, M.; Basato, M. *Eur. J. Inorg. Chem.* **2001**, 1131−1133.

(6) (a) Dupont, J.; Basso, N. R.; Meneghetti, M. R. *Polyhedron* **1996**, *15*, 2299−2302. (b) Dupont, J.; Basso, N. R.; Meneghetti, M. R.; Konrath, R. A.; Burrow, R.; Horner, M. *Organometallics* **1997**, *16*, 2386−2391. (c) Ebeling, G.; Meneghetti, M. R.; Rominger, F.; Dupont, J. *Organometallics* **2002**, *21*, 3221−3227.

(7) Zanini, M. L.; Ebeling, G.; Livotto, P. R.; Marken. F.; Meneghetti, M. R.; Dupont, J. *Polyhedron* **2003**, accepted for publication.

(8) Gruber, A. S.; Pozebon, D.; Monteiro, A. L.; Dupont, J. *Tetrahedron Lett.* **2001**, *42*, 7345−7348.

(9) (a) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989−7000. (b) Deshmukh, R. R.; Rajagopal, R.; Srinivasan, K. V. *Chem. Commun.* **2001**, 1544−1545.

(10) For a review about the use of molten salts in catalysis, see: Dupont, J.; deSouza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667−3692.

(11) For a recent review of Pd-catalyzed coupling reactions of chloroarenes, see: Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176−4211.

(12) Experiment was validated by determining the relative initial reaction rate of experiments performed separately (activated from deactivated bromoarenes).

Table 1. Heck Reaction between Alkenes and Aryl Halides Catalyzed by Palladacycle **1**[a]

entry	ArX	alkene	[ArX]/[Pd]	T (°C)	t (h)[b]	yield (%)[c]	TON[d]
1	PhI	n-butylacrylate	1 000 000	150	24	100 (92)	1 000 000
2	PhI	styrene	1 000 000	150	48	68	680 000
3	$4\text{-MeOC}_6\text{H}_4\text{I}$	n-butylacrylate	1 000 000	150	24	90	900 000
4	$4\text{-MeOC}_6\text{H}_4\text{I}$	styrene	1 000 000	150	48	57	570 000
5	PhI	n-butylacrylate	10 000	80	24	100	10 000
6	PhI	n-butylacrylate	1000	50	24	100 (95)	1000
7	PhI	n-butylacrylate	1000	30	120	50	500
8	PhI	n-butylacrylate	100	30	24	100	100
9[e]	PhI	n-butylacrylate	100	30	48	76	76
10	$4\text{-MeOC}_6\text{H}_4\text{I}$	n-butylacrylate	100	30	72	93	93
11	$4\text{-MeOC}_6\text{H}_4\text{I}$	n-butylacrylate	1000	30	160	40	400
12	$4\text{-MeOC}_6\text{H}_4\text{I}$	n-butylacrylate	10 000	80	24	95 (90)	9 500
13	$4\text{-CF}_3\text{C}_6\text{H}_4\text{Br}$	n-butylacrylate	100 000	150	24	100	100 000
14	$4\text{-CNC}_6\text{H}_4\text{Br}$	n-butylacrylate	10 000	120	24	100	10 000
15	$4\text{-CNC}_6\text{H}_4\text{Br}$	n-butylacrylate	1000	80	24	100	1000
16	$4\text{-CNC}_6\text{H}_4\text{Br}$	n-butylacrylate	100	50	24	100	100
17	$4\text{-CNC}_6\text{H}_4\text{Br}$	n-butylacrylate	100	30	48	50	50
18	$4\text{-CNC}_6\text{H}_4\text{Br}$	n-butylacrylate	100 000	150	24	100 (93)	100 000
19	$4\text{-MeC}_6\text{H}_4\text{Br}$	n-butylacrylate	100 000	150	24	80	80 000
20[e]	$4\text{-MeC}_6\text{H}_4\text{Br}$	n-butylacrylate	100 000	150	24	85	85 000
21	$4\text{-MeCOC}_6\text{H}_4\text{Br}$	n-butylacrylate	100 000	150	24	100 (97)	100 000
22	$4\text{-MeCOC}_6\text{H}_4\text{Br}$	n-butylacrylate	1 000 000	150	24	80	800 000
23	$4\text{-MeOC}_6\text{H}_4\text{Br}$	n-butylacrylate	10 000	150	24	72	7200
24	$4\text{-MeOC}_6\text{H}_4\text{Br}$	styrene	10 000	150	24	65	6500
25	$4\text{-NO}_2\text{C}_6\text{H}_4\text{Br}$	n-butylacrylate	100 000	150	24	100 (99)	100 000
26	$4\text{-NO}_2\text{C}_6\text{H}_4\text{Br}$	n-butylacrylate	100	50	24	100 (99)	100
27	$4\text{-NO}_2\text{C}_6\text{H}_4\text{Br}$	n-butylacrylate	100	30	48	80	80
28	$4\text{-CNC}_6\text{H}_4\text{Cl}$	n-butylacrylate	1000	150	24	60	600
29	$4\text{-MeCOC}_6\text{H}_4\text{Cl}$	n-butylacrylate	1000	150	24	33	330
30	$4\text{-NO}_2\text{C}_6\text{H}_4\text{Cl}$	n-butylacrylate	1000	150	24	100 (91)	1000
31	$4\text{-MeC}_6\text{H}_4\text{Cl}$	n-butylacrylate	100	150	24	traces	

[a] Reaction conditions: DMA (5 mL), NaOAc (1.4 mmol), alkene (1.2 mmol) ArX (1 mmol), and N(^{n}Bu)$_4$Br (0.2 mmol). [b] This is the time after which the reaction was analyzed. The reaction might have been over at an earlier stage. [c] GC yield in *trans*-*n*-butylcinnamates and *trans*-stilbenes (using methyl benzoate as an internal standard); isolated yields are shown in parentheses. [d] TON (mol of product/mol of Pd). [e] K$_3$PO$_4$ as the base and in the absence of N^{n}Bu$_4$Br.

surprising, since electron-withdrawing substituents are expected to accelerate the Ar−Br oxidative addition step. The r value is between those observed for oxidative addition of aryl chlorides to electron-rich Pd(0) complexes ($r = 5.2$)[13] and those obtained for the Heck reaction of aryl iodides involving Pd pincer complexes ($r = 1.34$).[14] Moreover, similar r values have been estimated for the coupling of aryl bromides with methyl acrylate catalyzed by sulfur-containing palladacycles.[15] This result strongly suggests that the rate-determining step is oxidative addition of the aryl bromide to Pd(0) species.[16]

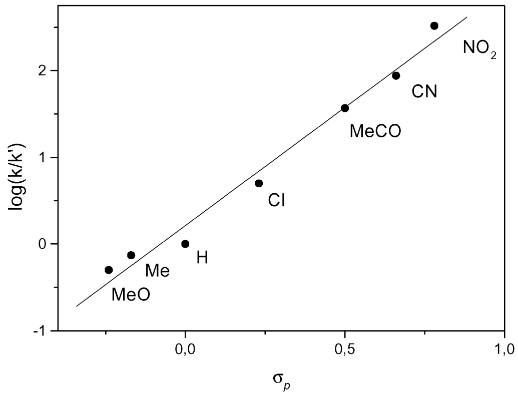

Figure 2. Hammett correlation of the competitive reaction of p-substituted aryl bromides with n-butylacrylate at 150 °C in DMA promoted by palladacycle **1** using σ_p constants.

This reaction probably involves the formation of soluble palladium particles[17] as the catalytically active species since

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(13) Portnoy, M.; Milstein, D. *Organometallics* **1993**, *12*, 1665−1673.

(14) Weissman, H.; Milstein, D. *Chem. Commun.* **1999**, 1901−1902.

(15) Gruber, A. S.; Zim, D.; Ebeling, G.; Monteiro, A. L.; Dupont, J. *Org. Lett.* **2000**, *2*, 1287−1290.

(16) For recent studies on the Heck reaction mechanism, see: (a) Amatore, C.; Carré, E.; Jutand, A.; Medjour, Y. *Organometallics* **2002**, *21*, 4540−4545. (b) Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314−321.

(17) See for example: Choudary, B. M.; Madhi, S.; Chowdari, N. S.; Kantam, M. L.; Sreedhar, B. *J. Am. Chem. Soc.* **2002**, *124*, 14127−14136. Reetz, M. T.; Westermann, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 165−168. Note that PdCl$_2$ does not promote the Heck coupling at room temperature (see ref 9).

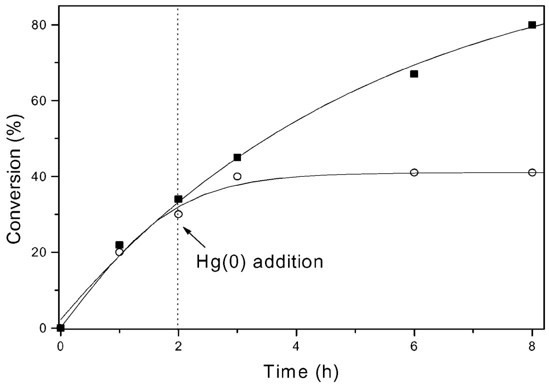
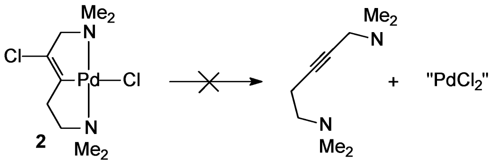


Figure 3. Conversion vs time plot for PhI and *n*-butylacrylate (reaction conditions: DMA (5 mL), NaOAc (1.4 mmol), alkene (1.2 mmol), PhI (1 mmol), **1** (10^{-3}mmol), and $N(^nBu)_4Br$ (0.2 mmol at 80 °C)). (■) Control experiment; (○) Hg(0) (300:1 Hg/Pd) poisoning experiment.

Scheme 3



a Hg test[18] was positive (Figure 3). Attempts to isolate and characterize by transmission electron microscopy (TEM) the species isolated during the catalytic processes have so far met with little success.[19] The formation of Pd(0) species probably follows the same pathway proposed earlier by Beletskaya.[4]

Further indirect evidence that palladacycle **1** serves as a reservoir of catalytically active palladium was obtained through the investigation of the catalytic performance of the analogous pincer palladacycle **2** (Scheme 3). This compound, in opposition to **1**, is much more reluctant to undergo retrochloropalladation under the conditions investigated (up to 120 °C in DMSO). As expected, the pincer palladacycle **2** gave only 7% yield in the coupling of iodo benzene with *n*-butylacrylate at 30 °C after 24 h (PhI/Pd = 100).

In summary, the phosphine-free chloropalladated propargylamine **1** is one of the most simple and efficient catalyst precursors for the arylation of alkenes. The system exhibits unprecedented catalytic activity for the Heck reaction at room temperature. The palladacycle probably acts as a reservoir of soluble catalytically active Pd(0) species. Further investigations on the scope of this class of palladacycles and on the mechanism of the catalytic coupling are currently under investigation in our laboratory.

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Supporting Information Available: Detailed experimental procedure and characterization of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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[18] Hg(0) poisoning was performed according to: Weddle, K. S.; Aiken, J. D.; Finke, R. G. *J. Am. Chem. Soc.* **1998**, *120*, 5653−5666.

[19] After the submission of this manuscript, Gladysz reported the identification of Pd nanoparticles in Heck coupling promoted by palladacycles: Rocaboy, C.; Gladysz, J. A. *New J. Chem.* **2003**, *27*, 39−49.