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Selenium-Ligated Palladium(II) Complexes as Highly Active Catalysts for Carbon–Carbon Coupling Reactions: The Heck Reaction

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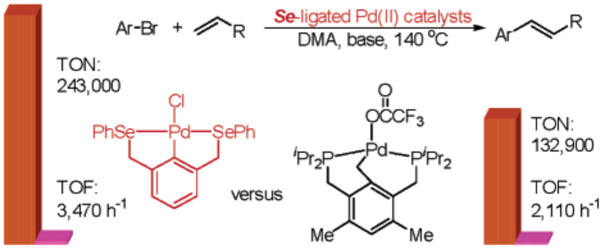
ABSTRACT



Three selenium-ligated Pd(II) complexes were readily synthesized and shown to be extremely active catalysts for the Heck reaction of various aryl bromides, including deactivated and heterocyclic ones. The catalytic activity of the selenide-based Pd(II) complexes not only rivals but vastly outperforms that of the corresponding phosphorus and sulfur analogues. Practical advantages of the selenium-based catalysts include their straightforward synthesis and high activity in the absence of any additives as well as the enhanced stability of the selenide ligands toward air oxidation.

Selenium-containing organic molecules are extremely useful compounds in synthetic organic chemistry.[1] The arylselanyl (ArSe−) and alkylselanyl (RSe−) moieties are two of the most privileged functionalities that are of tremendous synthetic utility by virtue of their versatile and well-behaved transformations. The field is still being enriched by the recent introduction of, among others, polymer-bound selenium reagents,[2] chiral organoselenium compounds,[3] and fluorous selenium reagents.[4] However, one of the most important facets of the electronic properties of selenium, its strong electron-donating ability, has rarely been explored in the field of transition metal catalysis. We report here that organoselenides, when used as ligands in catalytically active species, offer great potential in transition metal-catalyzed C−C bond-forming reactions such as the palladium-mediated Heck reaction.

The Heck reaction is a powerful tool for C−C bond formation in organic synthesis.[5] Outstanding catalyst systems developed to date include those that employ sterically bulky and electron-rich phosphine ligands[6] or phosphine mimics

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(1) Selected monographs: (a) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon: Oxford, 1986. (b) *Organoselenium Chemistry*; Black, T. G., Ed.; Oxford: New York, 1999. (c) *Organoselenium Chemistry*; Wirth, T., Ed.; Springer: Berlin, 2000.

(2) Selected papers: (a) Nicolaou, K. C.; Pastor, J.; Barluenga, S.; Winssinger, N. *Chem. Commun.* **1998**, 1947. (b) Ruhland, T.; Andersen, K.; Pedersen, H. *J. Org. Chem.* **1998**, *63*, 9204. (c) Uehlin, L.; Wirth, T. *Org. Lett.* **2001**, *3*, 2931.

(3) For a recent review, see: Wirth, T. *Tetrahedron* **1999**, *55*, 1.

(4) Crich, D.; Neelamkavil, S.; Sartillo-Piscil, F. *Org. Lett.* **2000**, *2*, 4029 and references therein.

(5) (a) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: London, 1985. (b) Tsuji, J. *Palladium Reagents and Catalysts*; Wiley: Chichester, 1995. (c) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427. (d) Beletskaya, I. P.; Cheprokov, A. *Chem. Rev.* **2000**, *100*, 3009.

(6) Leading examples: (a) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989. (b) Shaughnessy, K. H.; Kim, P.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 2123. (c) Ehrentraut, A.; Zapf, A.; Beller, M. *Synlett* **2000**, 1589.

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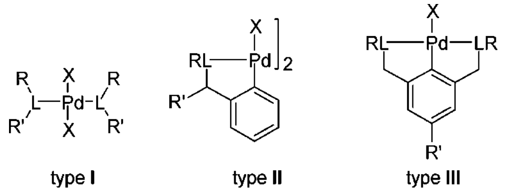


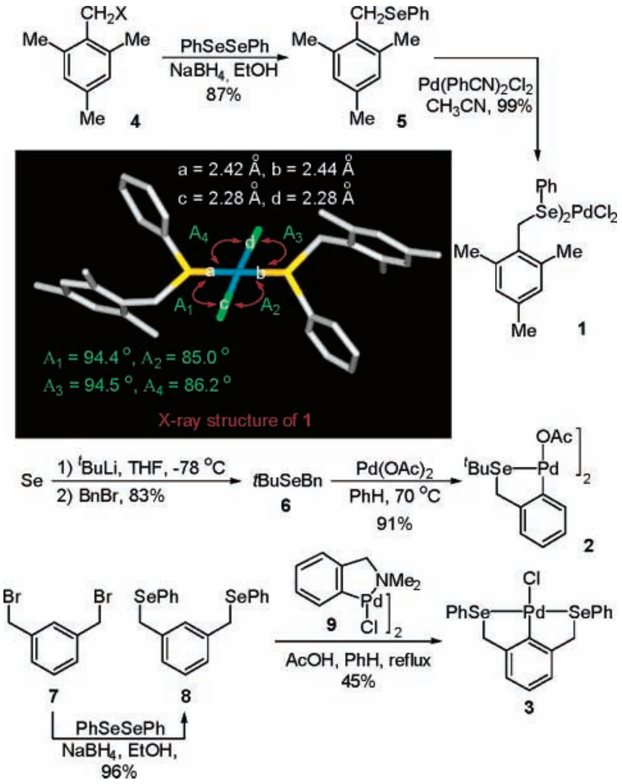
1 (type **I**, L = Se; R = Ph; R′ = (2,4,6-trimethyl)benzyl; X = Cl)
2 (type **II**, L = Se; R = ^{t}Bu; R′ = H; X = OAc)
3 (type **III**, L = Se; R = Ph; R′ = H; X = Cl)

Figure 1. Palladium(II) complexes for Heck reaction.

such as N-heterocyclic nucleophilic carbenes (NHCs).[7] Phosphorus-, nitrogen-, and sulfur-containing palladacycles have also emerged recently as powerful catalysts for this reaction.[8] In view of the strong donating properties of organoselenides but an obvious lack of any precedents in their utilization in the Heck reaction, we synthesized a number of selenide-based Pd complexes including structures **1**−**3** (Figure 1). Each of these complexes represents one of the three major types of Pd(II) catalysts[5b−d,8] (types I−III, respectively, with L being broadly defined as the ligating atom) that have been used in the Heck chemistry. These complexes, which proved to be remarkably stable toward air and moisture, were readily synthesized as described in Scheme 1 and isolated by standard means. Their structures were fully characterized by various NMR techniques and elemental analysis, and in the case of complex **1**, by X-ray crystallographic determination. Complex **1** adopts a distorted square planar geometry at the metal center with the selenide ligands disposed trans relative to each other.

To test their activity in the Heck reaction, we initially examined the reaction of bromobenzene (PhBr) with *n*-butyl acrylate in *N*,*N*-dimethylacetamide (DMA) in the presence of the "pincer" complex **3**. We were pleased to find that the reaction proceeded smoothly with only 0.05 mol % **3** when Na$_2$CO$_3$ was used as the base. Thus, after 22 h at 140 °C, the product *n*-butyl *trans*-cinnamate was isolated in 71% yield, corresponding to a turnover number (TON) of 1420. This is especially interesting since a sulfur analogue of **3** (type **III**: L = S, R = Ph, X = Cl, R′ = NHAc) has previously been shown to be completely inactive for the Heck coupling of aryl bromides under similar conditions.[8i] Other bases, including NaOAc, K$_2$CO$_3$, and KOAc, gave much lower yield (39% with NaOAc, 16% with K$_2$CO$_3$ and 19% with KOAc). No coupling product was isolated when NEt$_3$ was used as the base. Aryl chlorides were found to be inactive under these conditions. The Heck coupling of a variety of aryl bromides including activated, deactivated, and heterocyclic ones with *n*-butyl arylate was subsequently examined using these complexes (Table 1).

Scheme 1. Synthesis of Selenium-Ligated Palladium Complexes



As can be readily seen from the data in Table 1, all three selenium-ligated Pd complexes show excellent catalytic activity, giving rise to extremely high TONs, with complex **3** exhibiting the highest activity. It is noteworthy that the simple bis(selenide)−Pd(II) complex **1** can act as an excellent catalyst for the Heck reaction (TON up to 223 000 for PhBr) and is significantly more reactive than the analogous palladium complex derived from organosulfide, PdCl$_2$(SEt$_2$)$_2$,[9] which gives much lower TON even in the presence of nBu$_4$NBr as an additive.[10] Similarly, the *Se*-palladacycle **2**, which gave a TON of up to 120 000 for PhBr (entry 8) and 1.7 x 10^6 for 4-bromobenzaldehyde (entry 18), outperforms its sulfur analog[8h] (type II: L = S, R = *t*Bu, R′ = Me, X = Cl) (maximum TON up to 33 000 for 4-bromobenzaldehyde in the presence of nBu$_4$NBr). Furthermore, **2** is even more reactive than its phosphine analogues, including Herrmann's *P*-palladacycle[8e] and Gibson's *P*-palladacycle (type II: L = P, R = Ph$_2$, R′ = H, X = Br)[8f] for similar Heck

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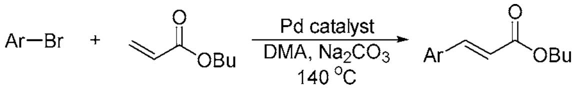
(7) For selected recent reviews, see: (a) Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, C. B. *Chem. Rev.* **2000**, *100*, 39. (b) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290.

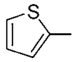
(8) Leading reviews: (a) Albrecht, M.; van Koten, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 3750. (b) Dupont, J.; Pfeffer, M. Spencer, M. *Eur. J. Inorg. Chem.* **2001**, 1917. (c) Bedford, R. B. *Chem. Commun.* **2003**, 1787. (d) van der Boom M. E.; Milstein, D. *Chem. Rev.* **2003,** *103*, 1759. Selected recent examples: (e) Herrmann, W. A.; Brossmer, C.; Reisinger, C.-P.; Priermeier, T. H.; Öfele, K.; Beller, M. *Chem. Eur. J.* **1997**, *3*, 1357. (f) Gibson, S.; Foster, D. F.; Eastam, G. R.; Tooze, R. P.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 779. (g) Ohff, M.; Ohff, A.; van der Boom, M. E.; Milstein, D. *J. Am. Chem. Soc.* **1997**, *119*, 11687. (h) Gruber, A. S.; Zim, D. Z.; Ebeling, G.; Monteriro, A. L.; Dupont, J. *Org. Lett.* **2000**, *2*, 1287. (i) Bergbreiter, D. E.; Osburn, P. L.; Wilson, A.; Sink, E. *J. Am. Chem. Soc*. **2000**, *122*, 9058.

(9) Gruber, A. S.; Pozebon, D.; Monteriro, A. L.; Dupont, J. *Tetrahedron Lett.* **2001**, *42*, 7345.

(10) See Supporting Information for a detailed comparison in activity between catalysts **1**−**3** and their sulfur and phosphorus analogues.

Table 1. Heck Reaction of Aryl Bromides and *n*-Butyl Acrylate Using Pd Complexes **1**−**3**[a]

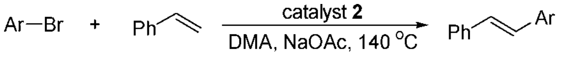


entry	ArBr (mmol)	catalyst (mol % Pd)	time (h)	% yield[b](TON)
1	PhBr (5.0)	**1** (7.0 x 10^{-4})	24	34 (49,000)
2	PhBr (5.0)	**1** (7.0 x 10^{-4})	48	73[c] (100,000)
3	PhBr (5.0)	**1** (3.5 x 10^{-4})	48	52[c] (150,000)
4	PhBr (5.0)	**1** (3.5 x 10^{-4})	70	78[c] (220,000)
5	PhBr (5.0)	**2** (1.35 x 10^{-3})	24	71 (53,000)
6	PhBr (5.0)	**2** (1.35 x 10^{-3})	48	86 (64,000)
7	PhBr (5.0)	**2** (7.5 x 10^{-4})	48	66 (88,000)
8	PhBr (5.0)	**2** (7.5 x 10^{-4})	70	89 (120,000)
9	PhBr (5.0)	**3** (7 x 10^{-4})	24	50 (71,000)
10	PhBr (5.0)	**3** (7 x 10^{-4})	48	80 (110,000)
11	PhBr (5.0)	**3** (3.5 x 10^{-4})	48	61 (170,000)
12	PhBr (5.0)	**3** (3.5 x 10^{-4})	70	85 (240,000)
13	4-Me-PhBr (5.0)	**2** (1.35 x 10^{-3})	24	38 (28,000)
14	4-Me-PhBr (5.0)	**3** (7.0 x 10^{-4})	24	28 (40,000)
15	4-MeO-PhBr (5.0)	**2** (1.35 x 10^{-3})	24	48 (36,000)
16	4-MeO-PhBr (5.0)	**3** (7.0 x 10^{-4})	24	29[c] (41,000)
17	4-OHC-PhBr (5.0)	**2** (1.35 x 10^{-3})	24	91 (67,000)
18[d]	4-OHC-PhBr (15.0)	**2** (4.0 x 10^{-5})	70	68 (1,700,000)
19	4-OHC-PhBr (5.0)	**3** (7.0 x 10^{-4})	24	91 (130,000)
20	4-NC-PhBr (2.0)	**2** (3.9 x 10^{-3})	21	94 (24,000)
21[d]	4-NC-PhBr (2.0)	**2** (9.0 x 10^{-4})	24	88 (98,000)
22	4-CF_3-PhBr (2.0)	**2** (3.9 x 10^{-3})	22	93 (24,000)
23	3-BrPyr (2.0)	**2** (3.9 x 10^{-2})	48	93 (2,400)
24	 Br (2.0)	**2** (3.9 x 10^{-3})	21	79[c] (2,000)

[a] Unless otherwise noted, all reactions were performed with 1 equiv of ArBr, 1.2 equiv of *n*-butyl acrylate, and 1.12 equiv of Na_2CO_3. [b] Average of isolated yields of two runs. [c] Single run. [d] Performed with 1.2 equiv of Na_2CO_3.

reactions.[10] The *SeCSe*-pincer complex **3** (TON up to 240 000 for PhBr, entry 12) is also a more powerful catalyst than both the phenyl-containing *SCS*-pincer complex (type **III**: L = S, R = Ph, X = Cl, R′ = NHAc, vide supra)[8i] and an electron-rich *SCS*-type pincer complex (type **III**: L = S, R = *t*Bu, X = Cl, R′ = H),[8h] which were shown to be active only toward aryl iodides. It is interesting to note that **3** (TON up to 243 000 for PhBr, entry 12) is almost twice as reactive as Milstein's *PCP*-pincer complex (TON up to 133 000) for a very similar reaction.[8g] The high reactivity of the *Se*-palladacycle **2** was further established by its excellent performance in the Heck reaction of styrene with various aryl bromides using NaOAc as the base[11] (Table 2).

Table 2. Heck Reaction of Styrene Using Catalyst **2**[a]



entry	ArBr (mmol)	mol % Pd	time (h)	% yield[b] (TON)
1[c]	PhBr (2.0)	3.9×10^{-3}	21	27 (6900)
2[d]	PhBr (2.0)	3.9×10^{-3}	21	4[e] (1000)
3	PhBr (4.0)	2.0×10^{-3}	20	97 (49 000)
4	4-Me-PhBr (2.0)	3.9×10^{-3}	42	56 (14 000)
5	2-Me-PhBr (2.0)	3.9×10^{-2}	90	41 (1000)
6	4-MeO-PhBr (2.0)	3.9×10^{-3}	21	51 (13 000)
7	4-OHC-PhBr (2.0)	3.3×10^{-3}	20	95 (29 000)
8	4-OHC-PhBr (2.0)	9.0×10^{-4}	24	92 (100 000)
9	4-NC-PhBr (2.0)	3.3×10^{-3}	20	99[e] (30 000)
10	4-NC-PhBr (2.0)	9.0×10^{-4}	24	96 (110 000)
11	4-CF_3-PhBr (2.0)	3.9×10^{-3}	21	85 (22 000)
12	4-CF_3-PhBr (2.0)	9.0×10^{-4}	24	77[e] (81 000)
13	3-BrPyr (2.0)	3.9×10^{-3}	43	40 (10 000)

[a] Unless otherwise noted, all reactions were performed with 1 equiv of ArBr, 1.2 equiv of styrene, and 1.2 equiv of NaOAc. [b] Average of isolated yields of two runs. [c] Na_2CO_3 (1.12 equiv) was used as the base. [d] K_3PO_4 (1.2 equiv) was used as the base. [e] Single run.

In conclusion, we have shown that the selenium-ligated Pd(II) complexes **1**−**3** are excellent catalysts for Heck reaction. These catalysts not only rival but, in most cases, outperform each of their respective phosphorus and sulfur analogues for similar Heck reactions of aryl bromides. The high activity of the catalysts reported here introduces a new approach to transition metal catalysis. The repertoire of their application in various coupling reactions and their mechanism of action only remains to be further explored.

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Supporting Information Available: Synthesis and full characterization of **1**−**3**; general procedures for the Heck reactions; tabulated data for reactivity comparison. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Interestingly, other bases such as Na_2CO_3 and K_3PO_4 gave much lower yield for this reaction, cf. entries 1−3, Table 2.