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Highly Active Pd(II) Catalysts with *trans*-Bidentate Pyridine Ligands for the Heck Reaction

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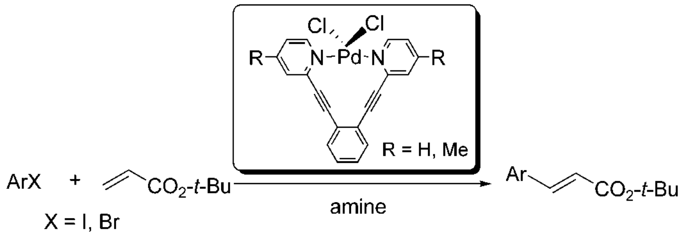
ABSTRACT



The air-, water-, and heat-stable palladium(II) complexes 2a and 2b are prepared by the reaction of palladium(II) salts with the new *trans*-bidentate nitrogen ligands, 1,2-bis(2-pyridylethynyl)benzenes. The structure of complex 2a has been confirmed by X-ray structure analysis. The complexes efficiently catalyze the Heck olefination of aryl iodides and provide a good yield under phosphine-free conditions. The reaction is very sensitive to the nature of the chelating ligand.

The Heck reaction is one of the most widely used palladium-catalyzed carbon−carbon bond-forming reactions in organic synthesis.[1] The reaction is normally carried out in the presence of phosphine ligands and a base under an inert atmosphere. Therefore, the development of the catalyst under phosphine-free conditions would be an important achievement. To date, a number of reports on phosphine-free catalyst systems for the Heck reaction have been made.[2] However, far less attention has been devoted to phosphine-free nitrogen-based catalysts,[3] though nitrogen-based catalysts are also known to show high activity for the palladium-catalyzed Wacker process.[4]

We recently reported that the reaction of copper(I) salts with the nitrogen ligands, 1,2-bis(2-pyridylethynyl)benzenes, gave rise to the formation of *trans*-chelated copper(I) complexes in good yields.[5] The coordination of the ligands with palladium(II) salts is expected to yield a *trans*-chelated palladium(II) complex exclusively as a result of the rigidity of the ligand. In this paper, we report the synthesis of palladium(II) complexes from 1,2-bis(2-pyridylethynyl)-benzene ligands and their catalytic activity for the Heck olefination of aryl halides. The investigation of the reactivity

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(1) For example, see: (a) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: London, 1990. (b) Heck, R. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, New York, 1991; Vol. 4, pp 833−863. (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (d) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1995**, *33*, 2379.

(2) For example, see: (a) Peris, E.; Loch, J. A.; Mata, J.; Crabtree, R. H. *Chem. Commun.* **2001**, 201. (b) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2371. (c) Tulloch, A. A. D.; Danopoulos, A. A.; Tooze, R. P.; Cafferkey, S. M.; Kleinhenz, S.; Hursthouse, M. B. *Chem. Commun.* **2000**, 1247. (d) Ohff, M.; Ohff, A.; Milstein, D. *Chem. Commun.* **1999**, 357. (e) Gruber, A. S.; Zim, D.; Ebeling, G.; Monteiro, A. L.; Dupont, J. *Org. Lett.* **2000**, *2*, 1287. (f) Bergbreiter, D. E.; Osburn, P. L.; Liu, Y.-S. *J. Am. Chem. Soc.* **1999**, *121*, 9531. (g) Reetz, M. T.; Westermann, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 165. (h) Reetz, M. T.; Westermann, E.; Lohmer, R.; Lohmer, G. *Tetrahedron Lett.* **1998**, *39*, 8449. (i) Jeffery, T. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI: London, 1996; Vol. 5, pp 153−260.

(3) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *Synlett* **1992**, 871.

(4) (a) ten Brink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636. (b) Bianchi, D.; Bortolo, R.; D'Aloisio, R.; Ricci, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 706. (c) Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1999**, *64*, 6750.

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of the resulting palladium(II) complexes for the Heck reaction would provide a new catalyst system for the Heck reaction under phosphine-free conditions. Furthermore, the differences in reactivity between *trans*-chelated complexes in this study and a well-known *cis*-chelated palladium(II) complex, dichloro-(2,2′-bipyridine)palladium(II),[6] would be clarified.

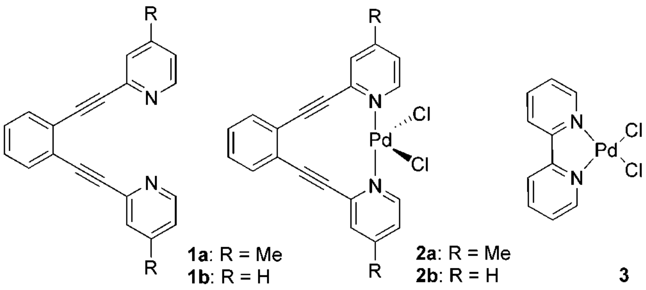

Figure 1. Bidentate nitrogen ligands and their palladium(II) complexes.

The ligands **1a** and **1b** were easily prepared in good yields by the cross-coupling reaction of 1,2-bis(ethynyl)benzene[7] with the corresponding 2-bromopyridine derivatives in amine solvent in the presence of tetrakis(triphenylphosphine)-palladium(0) at 100 °C. The new palladium(II) complex **2a** was obtained as yellow-orange crystals in quantitative yield by the reaction of $PdCl_2(CH_3CN)_2$ with **1a** in dichloromethane at room temperature. The palladium(II) complex **2b**[8] was obtained as orange crystals in 82% yield by treatment of $PdCl_2(CH_3CN)_2$ with **1b** in dichloromethane at 50 °C, whereas at room temperature **2b** was isolated in only 56% yield. Obviously, the difference in reactivity between these two metal complexations can be attributed to the electron-donating ability of the substituent of the pyridine ring. Palladium(II) complex **3**, in which 2,2′-bipyridine (bpy) coordinates palladium(II) ion in a *cis*-chelating mode, was prepared as yellow crystals in 88% yield by the reaction of $PdCl_2(cod)$[9] with bpy in dichloromethane at room temperature. Complexes **2a**, **2b**, and **3** have been fully characterized by spectroscopy (^{1}H NMR, FAB mass) and by elemental analysis. Moreover, the structure of **2a** was confirmed by X-ray crystallography. The crystal structure of complex **2a** is similar to that of complex **2b**.[10] Complexes **2a** and **2b** were found to be thermally stable, and no degradation was observed at temperatures up to at least 140 °C as a result of the stabilizing chelate effect. In addition, these complexes were not sensitive to oxygen or moisture; no change in their efficiencies was observed even if the Heck coupling reactions were carried out under aerobic conditions.

The results of the catalytic Heck olefination of aryl iodides and bromides using palladium(II) complexes **2a**, **2b**, and **3** are summarized in Table 1.

Table 1. Heck Couplings of Aryl Halides with *tert*-Butyl Acrylate Using Bidentate Nitrogen Catalysts **2a**, **2b**, and **3**[a]

entry	catalyst, mol %	ArX	solvent	time (h)	yield (%)[b]	TON[c]
1	**2a**, 1.0	PhI	Et_3N	17	96	96
2	**2a**, 0.1	PhI	Et_3N	17	98	981
3	**2a**, 0.01	PhI	Et_3N	17	95	9501
4	**2a**, 0.001	PhI	Et_3N	17	72	71900
5	**2a**, 0.001	PhI	Et_3N	48	80	79630
6	**2b**, 0.01	PhI	Et_3N	17	86	8594
7	**3**, 1.0	PhI	Et_3N	17	82	82
8	**2a**, 1.0	4-Me-C_6H_4I	Et_3N	17	83	83
9	**2a**, 0.01	4-Me-C_6H_4I	Et_3N	17	91	9074
10	**3**, 1.0	4-Me-C_6H_4I	Et_3N	17	88	88
11	**2a**, 1.0	1-$C_{10}H_7I$[d]	Et_3N	17	90	90
12	**2a**, 0.01	1-$C_{10}H_7I$[d]	Et_3N	17	73	7345
13	**3**, 1.0	1-$C_{10}H_7I$[d]	Et_3N	17	85	85
14	**2a**, 1.0	PhBr	Et_3N	72	1	1
15	**2a**, 1.0	PhBr	*n*-Bu_3N	72	4	4
16	**3**, 1.0	PhBr	Et_3N	72	0.6	0.6
17	**2a**, 1.0	4-Me-C_6H_4Br	Et_3N	72	2.1	2.1
18	**2a**, 1.0	4-Me-C_6H_4Br	*n*-Bu_3N	72	3.5	3.5
19	**3**, 1.0	4-Me-C_6H_4Br	Et_3N	72	0.9	0.9
20	**2a**, 1.0	1-$C_{10}H_7Br$[e]	Et_3N	72	2.5	2.5
21	**2a**, 1.0	1-$C_{10}H_7Br$[e]	*n*-Bu_3N	72	55	55
22	**3**, 1.0	1-$C_{10}H_7Br$[e]	*n*-Bu_3N	72	0	0
23	**2a**, 1.0	4-NO_2-C_6H_4Br	*n*-Bu_3N	7	100	100
24	**3**, 1.0	4-NO_2-C_6H_4Br	*n*-Bu_3N	7	18	18

[a] Reaction conditions: aryl halide (20 mmol), *tert*-butyl acrylate (25 mmol), amine solvent (25 mmol), 100 °C. [b] Isolated yield. [c] TON: turnover number (mol product/mol catalyst). [d] 1-$C_{10}H_7I$: 1-iodonaphthalene. [e] 1-$C_{10}H_7Br$: 1-bromonaphthalene.

A black solid, presumably palladium black, precipitated from the reaction mixture when 1.00 mol % of complexes **2a**, **2b**, and **3** was used. The use of every complex for the Heck olefination of aryl iodides gives rise to the formation of *trans*-acrylic acid esters exclusively in good yield (entry 1−13). When 0.001 mol % of **2a** was used, a turnover number (TON) of 79630 was achieved (entry 5). No marked difference in the reactivity between **2a** and **2b** was observed (entries 3 and 6). We have found that complexes **2a** and **2b** are more effective catalysts than classical palladium(II) salts because palladium(II) chloride alone is an active catalyst for the Heck reactions when aryl iodides are used. As seen in entry 5 of Table 1, for example, when 0.001 mol % of **2a** was used, a TON of 79630 was achieved; however, $PdCl_2(PhCN)_2$ had a TON of only 4790 under similar experimental conditions. On the other hand, complexes **2a** and **2b** were not effective for the Heck olefination of less reactive aryl bromides (entry 14−22). Among them, more reactive 1-bromo-4-nitrobenzene only led to the formation of the desired product in a quantitative yield (entry 23). The reactivity for aryl iodides and bromides indicates that the oxidative addition process is involved in the rate-determining

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(7) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627.

(8) (a) Hu, Y.-Z.; Chamchoumis, C.; Grebowicz, J. S.; Thummel, R. P. *Inorg. Chem*. **2002**, *41*, 2296. (b) Bosch, E.; Barnes, C. L. *Inorg. Chem*. **2001**, *40*, 3097.

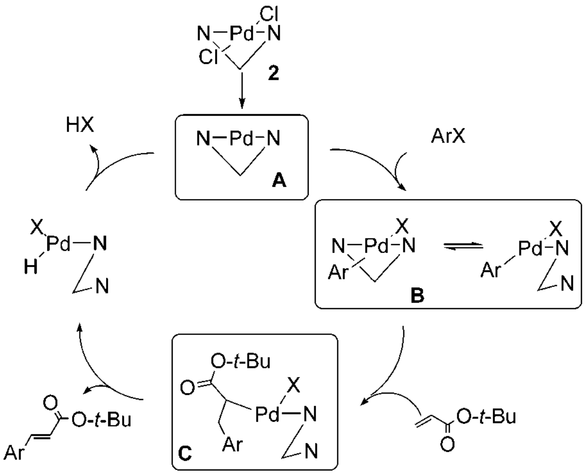
(9) Drew, D.; Doyle, J. R. *Inorg. Synth*. **1990**, *28*, 348.

(10) See Supporting Information for full details.

step for the Heck reaction in this study. It is remarkable that, for the Heck olefination of aryl bromides, complex **2a** has a better catalytic activity than complex **3** (especially entries 21 and 22).

Scheme 1 shows a plausible mechanism in our system with *trans*-bidentate nitrogen complex **2**. Oxidative addition of aryl halide probably involves a palladium(0) complex, which is most likely obtained by the preactivation of complex **2**. This intermediate might be the *trans*-chelated complex **A**. Oxidative addition to **A** affords the complex **B**, which is also coordinated by the ligand in a *trans*-configuration. Migratory insertion of olefin associated with the chelate opening in **B** will allow production of the complex **C**. This **B**-to-**C** process might be essential for determining the trend of reactivity for complexes **2** and **3**, because complex **3** with a *cis*-chelation mode is a stronger chelated complex than complex **2** with a *trans*-chelation mode. In addition, it is worth noting that the rigidity of the ligand structure makes *trans*-to-*cis* isomerization of complex **B** impossible. β-H elimination followed by reductive elimination and chelate closure completes the catalytic cycle.

Scheme 1. Plausible Mechanism



In conclusion, we have demonstrated that new palladium(II) complexes derived from bidentate nitrogen ligands, 1,2-bis(2-pyridylethynyl)benzenes, are effective catalysts for the Heck reactions of aryl iodides under phosphine-free conditions. The new catalyst system is air-, water-, and heat-stable. Further studies aimed at the improvement of the catalytic activity of our nitrogen catalysts are in progress.

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Supporting Information Available: Characterization data and crystal data (CIF) for complex **2a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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