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Insights into the Heck Reaction with PCP Pincer Palladium(II) Complexes

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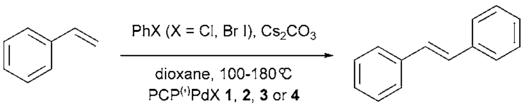
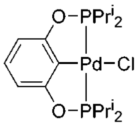
ABSTRACT



The Heck reaction of phenyl halides with styrene using a series of related PCP pincer palladium(II) complexes was studied in order to evaluate the effect of ligand structure and electronics on the catalytic activity and to investigate the nature of the catalyst species. We suggest these pincer complexes are precatalysts for highly active forms of metallic palladium. This conclusion is based on kinetic studies (induction periods, sigmoidal kinetics), Hg drop tests, quantitative poisoning experiments, and NMR studies.

One of the success stories of PCP pincer complexes is their application in the C−C coupling of aryl halides with alkenes in the presence of base, namely, the Heck reaction.[1,2] Milstein et al. first reported the reaction of a series of aryl iodides and bromides with olefin using PCP pincer palladium complexes such as $[\mathrm{PdTFA}\{(\mathrm{C_6H_3})(\mathrm{CH_2})\text{-}1\text{-}(\mathrm{CH_2PPr^{\mathit{i}}_2})_2\text{-}2,6\}]$.[3] Shibasaki et al. obtained extraordinarily high TONs of up to 8 900 000 for the reaction of iodobenzene with *n*-butyl acrylate using bis(phosphito) pincer complex $[\mathrm{PdI}\{(\mathrm{C_6H_3})(\mathrm{OP(OC_6H_4OMe\text{-}4)_2})_2\text{-}2,6\}]$.[4] High activity for forming trisubstituted olefins from acrylates and aryl halides,[5] as well as a unique activity for the conversion of aryl chlorides with styrene to *trans*-stilbenes,[6] was observed with $[\mathrm{PdCl}\{(\mathrm{C_6H_3})(\mathrm{OPPr^{\mathit{i}}_2})_2\text{-}2,6\}]$ **1**.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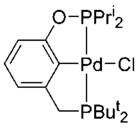
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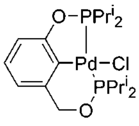
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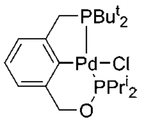
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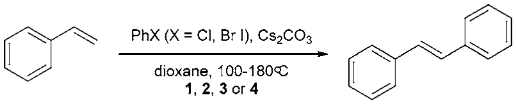
We previously reported on the synthesis of complexes **2**−**4**,[7] as well as compared **1** and **3** in allylic alkylation catalysis.[7a] We found that **3** was more active than **1** and attributed this to electronic effects, as well as a larger P−Pd−P angle compared to **1**. With this in mind, and since complexes **1**−**4** are closely related, we became interested in evaluating the effect of ligand structure and electronics on the activity in the Heck reaction between iodo-, bromo-, and chlorobenzene with styrene and Cs_2CO_3 (eq 1).



(1)

The chemistry of palladacycles and their application in homogeneous catalysis has been reviewed.[8] Several research groups,[9] who have recently investigated palladacycles for C−C coupling reactions, reported that in many cases neither the palladacycles nor the pincer palladium complexes are

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[1] Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.
[2] van der Boom, M. E.; Milstein, D. *Chem. Rev.* **2003**, *103*, 1759.
[3] Ohff, M.; Ohff, A.; van der Boom, M. E.; Milstein, D. *J. Am. Chem. Soc.* **1997**, *119*, 11687.
[4] Miyazaki, F.; Yamaguchi, K.; Shibasaki, M. *Tetrahedron Lett.* **1999**, *40*, 7379.
[5] Morales-Morales, D.; Grause, C.; Kasaoka, K.; Redón, R.; Cramer, R. E.; Jensen, C. M. *Inorg. Chim. Acta* **2000**, *300*−*302*, 958.
[6] Morales-Morales, D.; Redón, R.; Yung, C.; Jensen, C. M. *Chem. Commun.* **2000**, 1619.
[7] (a) Wang, Z.; Eberhard, M. R.; Jensen, C. M.; Matsukawa, S.; Yamamoto, Y. *J. Organomet. Chem.* **2003**, *681*, 189. (b) Eberhard, M. R.; Matsukawa, S.; Yamamoto, Y.; Jensen, C. M. *J. Organomet. Chem.* **2003**, *687*, 185.
[8] (a) Dupont, J.; Pfeffer, M.; Spencer, J. *Eur. J. Inorg. Chem.* **2001**, 1917. (b) Bedford, R. B. *Chem. Commun.* **2003**, 1787.

10.1021/ol049430a CCC: $27.50

the true catalysts but instead palladium nanoparticles or low-ligated palladium species. Nowotny et al. presented kinetic-based evidence that cyclopalladated imine catalysts were thermally labile generating finely divided metallic palladium, which was active in the Heck coupling of iodobenzene with styrene.[9a] Fluorous imine palladacycles synthesized by Rocaboy and Gladysz were found to be precursors for highly active Heck and Suzuki catalysts.[9b] On the basis of kinetics and TEM, these palladacycles release catalytically highly active soluble colloidal palladium nanoparticles. A series of NC-palladacycles were reported by Beletskaya et al. as very effective cheap precursors for the phosphine-free Heck reaction.[9c] The authors proposed a noncatalytic Heck reaction that leads to the release of catalytically active low-ligated palladium(0). Dupont et al. showed that chloropalladated propargylamine was a simple and efficient catalyst precursor for the Heck reaction.[9d] Although the authors were not able to characterize the proposed catalytically active palladium nanoparticles by TEM, they used the Hg drop test as a means to support their hypothesis. Bedford et al. found that imine-based palladacycles liberate Pd(0) species that are active in the Suzuki reaction.[9e] This was supported by a mechanistic study using GC-MS analysis. Most recently, de Vries et al. presented kinetic- and MS-based evidence showing that the Herrmann−Beller palladacycle behaves similarly to ligand-free $Pd(OAc)_2$ in Heck catalysis.[9f] They came to the conclusion that the palladacycle merely serves as a source of ligand-free monomeric palladium in Heck reactions of aryl bromides.

We would now like to report our results regarding the structure−activity study, as well as present observations that complexes **1**−**4** may be sources for catalytically active metallic palladium based on kinetic studies (induction periods, sigmoidal kinetics), Hg drop tests, quantitative poisoning experiments, and NMR studies.

Figure 1 shows the result for the iodobenzene/styrene systems, with complex **3** giving 55% conversion and complex **1** yielding 26% product after 4 h at 100 °C, while complexes **2** and **4** achieved 54 and 25% conversion after 4 h at 150 °C, respectively. At 100 °C, systems with complexes **2** and **4** showed little activity. Experiments with **1**, **2**, and **4** exhibit sigmoidal-shaped kinetics with induction periods between 15 and 45 min.

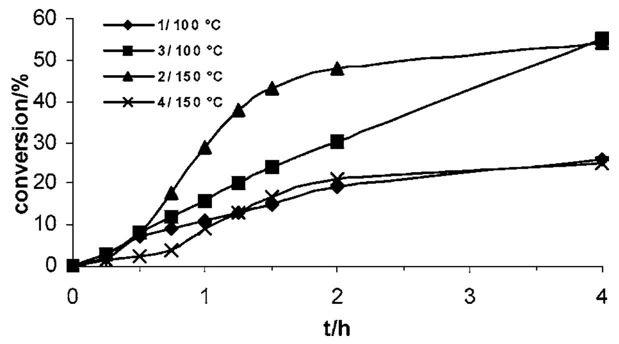

Figure 1. Conversion vs time: $PhI/styrene/Cs_2CO_3$ with complexes **1**−**4** in anhydrous dioxane under argon.

After 6 h at 100 °C, complex **1** gave 72% and **3** gave 61% conversion for bromobenzene/styrene (Figure 2). Systems with complexes **2** and **4** show low activity (8 and 5% yields, respectively). We observe again an induction period of 15 min for systems using **1** and **3** and S-shaped kinetic curves.

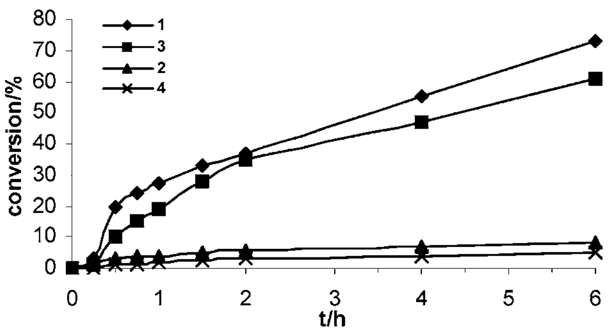

Figure 2. Conversion vs time: $PhBr/styrene/Cs_2CO_3$ at 100 °C with complexes **1**−**4** in anhydrous dioxane under argon.

For the chlorobenzene/styrene system at 180 °C (Figure 3), complex **1** reaches 65% and **3** achieves 43% conversion within the first 30 min. After 6 h, 75 and 63% conversions are obtained, respectively. These highly active systems do not show induction periods. Complex **2** shows an induction period of ca. 15 min and then a gradual increase in

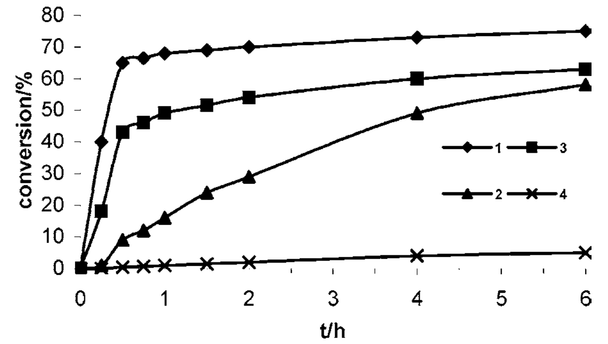

Figure 3. Conversion vs time: $PhCl/styrene/Cs_2CO_3$ at 180 °C with complexes **1**−**4** in anhydrous dioxane under argon.

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(9) (a) Nowotny, M.; Hanefeld, U.; van Koningsveld, H.; Maschmeyer, T. *Chem. Commun.* **2000**, 1877. (b) Rocaboy, C.; Gladysz, J. A. *New J. Chem.* **2003**, *27*, 39. (c) Beletskaya, I. P.; Kashin, A. N.; Karlstedt, N. B.; Mitin, A. V.; Cheprakov, A. V.; Kazankov, G. M. *J. Organomet. Chem.* **2001**, *622*, 89. (d) Consorti, C. S.; Zanini, M. L.; Leal, S.; Ebeling, G.; Dupont, J. *Org. Lett.* **2003**, *5*, 983. (e) Bedford, R. B.; Cazin, C. S. J.; Hursthouse, M. B.; Light, M. E.; Pike, K. J. Wimperis, S. *J. Organomet. Chem.* **2001**, *633*, 173 (f) de Vries, A. H. M.; Mulders, J. M. C. A.; Mommers, J. H. M.; Henderickx, H. J. W.; de Vries, J. G. *Org. Lett.* **2003**, *5*, 3285.

conversion, rising to 58% conversion after 6 h. Complex **4** is inactive toward chlorobenzene (only 5% yield after 6 h). Deactivation occurs for systems with **1** and **3** after 30 min, which is substantiated by the observation of Pd black.

Induction periods, S-shaped kinetic curves, and formation of Pd black suggest that complexes **1**−**4** are precatalysts and that palladium(0), possibly in the form of palladium nanoparticles, may be the active catalytic species. We tested this hypothesis as follows.

First, we subjected all 12 experiments to mercury drop tests.[10] Crabtree[10a] and Whitesides[10b] found that adding an excess of metallic mercury (with respect to the metal complex) to the reaction mixture will lead to the amalgamation of the surface of a heterogeneous metal particle, thus poisoning it, but will not affect a homogeneous catalyst. When we added up to 300 equiv of Hg(0) (relative to the complex used) to the reaction mixtures at $t = 0$ min, no catalytic activity at all was observed in any of the 12 experiments.[11,12] Figure 4 further illustrates these observations for 4 of the 12 systems. Metallic mercury was added to a reaction mixture at a certain time after the reaction had started, and a catalytically active system had formed. For systems with **1** or **3** and PhCl/styrene/Cs_2CO_3/180 °C, we added Hg(0) at 15 min; for systems with **2** or **4** and PhI/styrene/Cs_2CO_3/150 °C, we added Hg(0) at 75 min. All four catalytic reactions were suppressed instantly.

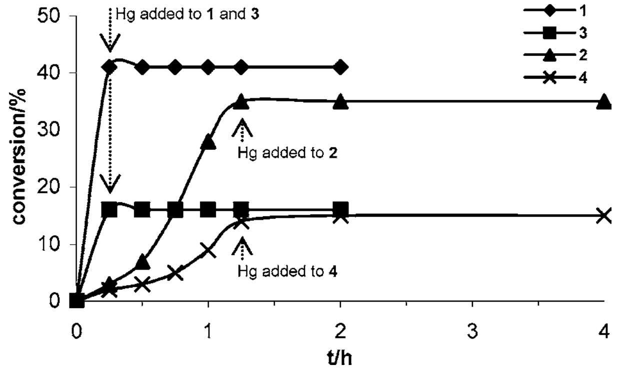

Figure 4. Conversion vs time: (a) PhCl/styrene/Cs_2CO_3/180 °C/**1** or **3**; Hg at 15 min; (b) PhI/styrene/Cs_2CO_3/150 °C/**2** or **4**; Hg at 75 min.

Detailed quantitative poisoning experiments were conducted for systems with **1** or **3** and chlorobenzene/styrene. This method has been described in detail in a review by Widegren and Finke.[13] The authors state that if a catalyst can be poisoned completely with ≪1 equiv of the added ligand (per metal atom), then this is highly suggestive (kinetic-based) evidence of a heterogeneous catalyst. A heterogeneous catalyst only has a fraction of the metal atoms on the surface; hence, even if every surface atom is active, ≪1 equiv of ligand will be sufficient to poison the catalyst. Ligands suitable for quantitative poisoning experiments are, for example, CS_2, thiophene, or PPh_3.

At $t = 15$ min, catalytic activity of system PhCl/styrene/Cs_2CO_3/180 °C with complex **1** was effectively stopped when any of the following four ligands was added: 0.5 equiv of CS_2, 0.1 or 0.3 equiv of thiophene, or 0.03 equiv of PPh_3 (relative to complex **1**) (Figure 5a−d, respectively).[14] Similarly, for the system PhCl/styrene/Cs_2CO_3/180 °C with complex **3**, 0.03 equiv of PPh_3 only (relative to complex **3**) added at $t = 15$ min was sufficient to suppress the catalytic activity (Figure 5e).

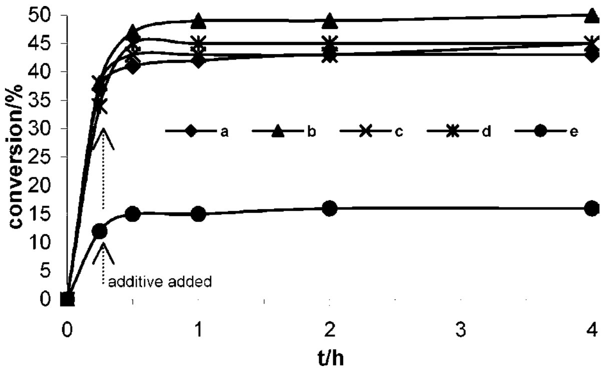

Figure 5. Conversion vs time: PhCl/styrene/Cs_2CO_3 at 180 °C with complex **1** (a−d) and **3** (e): (a) 0.5 equiv of CS_2 at 15 min; (b) 0.1 equiv of thiophene at 15 min; (c) 0.3 equiv of thiophene at 15 min; (d) 0.03 equiv of PPh_3 at 15 min; (e) 0.03 equiv of PPh_3 at 15 min.

When 0.03, 0.5, 1, 2, or 4 equiv of PPh_3, respectively, were added at $t = 0$ min to PhCl/styrene/Cs_2CO_3/180 °C with complex **1**, only 10, 7, 5, 3, and 2% conversions to *trans*-stilbene were observed, respectively. $^{31}P\{^1H\}$ NMR spectroscopy also showed the formation of Ph_3PO.

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[10] (a) Anton, D. R.; Crabtree, R. H. *Organometallics* **1983**, *2*, 855. (b) Foley, P.; DiCosimo, R.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 6713

[11] It is interesting to note in this context that Crabtree reported that the Hg(0) drop test is negative for pincer CNC (C = carbene) palladium complexes used in Heck catalysis. The stability of the catalyst was attributed to the great strength of the carbene−palladium bond. Peris, E.; Loch, J. A.; Mata, J.; Crabtree, R. H. *Chem. Commun*. **2001**, 201.

[12] In most cases, Hg(0) will not affect a homogeneous catalyst but forms an amalgam with a heterogeneous catalyst thereby poisoning it. However, it cannot be completely excluded that Hg(0) interferes with catalysis in a way other than killing the true heterogeneous catalyst. Hg(0) would possibly also react with a PCP Pd(0) pincer complex (which to the best of our knowledge is not known yet).

[13] Widegren, J. A.; Finke, R. G. *J. Mol. Catal. A* **2003**, *198*, 317. See also: Lin, Y.; Finke, R. G. *Inorg. Chem*. **1994**, *33*, 4891. Weddle, K. S.; Aiken, J. D., III; Finke, R. G. *J. Am. Chem. Soc.* **1998**, *120*, 5653.

[14] It is important to note that quantitative poisoning experiments reported in the literature are usually conducted at temperatures <50 °C, whereas our experiments are conducted at 180 °C. In some reported cases, higher temperatures lead to dissociation of the ligand (poison) from the heterogeneous catalyst (thus regenerating a catalytically active system). However, in our case, the addition of CS_2, PPh_3, and thiophene and conducting the experiment at 180 °C is effective in poisoning the catalytically active system. Catalysis ceases, and the observed conversions are approximately 25−30% lower for **1** and 45% lower for **3** (Figure 5) as compared to an unpoisoned system where the conversion reaches 73% for **1** and 60% for **3** after 4 h (Figure 3). One possible explanation is that in our case, these ligands do not dissociate from the palladium particle even under these forcing conditions or, alternatively, that addition of these ligands accelerates growth of the metal particles, resulting in faster production of inactive Pd black.

Furthermore, when we investigated the residues of all catalysis experiments by $^{31}P\{^1H\}$ NMR spectroscopy, we found that none of the experiments had the original complex or a species related to it present.[15] In all experiments, we observed species that resonate between 45 and 55 ppm, the major species giving a signal at 51.0 ppm. We believe that these species are phosphine oxides. The shift at 51.0 ppm is reminiscent of the reported shift for $Pr^i_2PhP(O)$ at 51.4 ppm in $CDCl_3$.[16] GC-MS of the catalysis samples also shows a species with m/z 210. M^+ for $Pr^i_2PhP(O)$ is 210.[16]

It has been found by other researchers that formation of phosphine oxides is an integral part in the prereduction/-activation stage of the Heck catalysis with Pd(II) and phosphines leading to a Pd(II)/Pd(0) catalytic cycle.[1] The reduction of Pd(II) to Pd(0) occurs with relative ease in the presence of phosphines and oxygenated ligands such as NO_3^-,[17a] AcO^-,[17b] oxide, or OH^-.[17c] It is possible that CO_3^{2-} may act in a similar way, but an alternative explanation is that adventitious traces of H_2O and OH^- decompose the pincer complex.[18]

The pincer complexes **1**−**4** are otherwise stable for prolonged periods of time in solution up to 200 °C; thus, their decomposition must be triggered by one of the reactants. Indeed, experiments show that these complexes are also stable (in dioxane/150−180 °C) in the presence of phenyl halides, styrene, or Hg(0) (or any combination thereof) but decompose in the presence of Cs_2CO_3 (indicated by $^{31}P\{^1H\}$ NMR studies) forming Pd black and a phosphine oxide (similar shift to the species observed in the catalytic residue). Bis(phosphinito) pincer complexes **1** and **3** decompose rapidly, whereas **2** and **4** are more stable and show slower signs of decomposition.

At this point, we cannot completely exclude that the pincer palladium(II) complexes studied here catalyze in part the Heck reaction. However, all observations combined, i.e., induction periods, S-shaped kinetic curves, formation of Pd black, poisoning experiments (Hg drop tests, quantitative poisoning with $\ll$1 equiv of CS_2, thiophene, and PPh_3), and NMR studies, suggest that metallic palladium(0) plays a significant role in this catalysis. The pincer palladium complexes serve as precursors for the true catalytic species. Complexes **1** and **3**, possessing only phosphinito donors, decompose more easily and therefore lead to more active sources of metallic palladium than either complexes **2** or **4**. The introduction of a Bu^t_2P group leads to more stable complexes but less active catalyst precursors.

Acknowledgment. Experiments were carried out by Zhaohui Wang at the University of Hawaii. We thank Dr. Gadi Rothenberg for valuable comments.

Note Added after ASAP. Zhaohui Wang was deleted from the author list of the version posted ASAP on April 24, 2004; a corrected version including a sentence in the Acknowledgment indicating his contribution to the paper was posted on May 21, 2004.

Supporting Information Available: Experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) $^{31}P\{^1H\}$ NMR shifts for complexes **1**−**4** and derivatives are between 150 and 200 ppm for $-OPPr^i_2$ and 70−80 ppm for $-PBu^t_2$.[5,7]

(16) Keglevich, G.; Tamás, A.; Parlagh, G. Töke, L. *Heteroatom Chem.* **2001**, *12*, 38.

(17) (a) Malatesta, L.; Angoletta, M. *J. Chem. Soc*. **1957**, 1186. (b) Amatore, C.; Jutand, A. *Organometallics* **1992**, *11*, 3009. (c) Grushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 1890.

(18) Although every precaution was taken to exclude H_2O from the catalytic systems, traces may still be present.