Communications to the Editor

Highly Active Pd(II) PCP-Type Catalysts for the **Heck Reaction**

Manuela Ohff, Andreas Ohff, Milko E. van der Boom, and David Milstein*

Department of Organic Chemistry The Weizmann Institute of Science, 76000 Rehovot, Israel

Received August 25, 1997

The palladium-catalyzed vinylation of aryl halides, also known as the "Heck reaction" (eq 1) is a very useful synthetic

$$Ar - X + R + base - catalyst solvent Ar + base x HX (1)$$

method for the generation of carbon-carbon bonds¹ that has found many applications.² We report here a new type of palladium catalyst for this reaction which shows outstanding activities and yields. These catalysts are exceedingly thermally stable and are not sensitive to oxygen. Our evidence suggests that, contrary to the classical mechanism, in this case Pd(0) may not be involved as the active species. The issue of a possible Pd(II)/Pd(IV) cycle in Heck catalysis is currently under debate.^{3,4} Recently, highly efficient catalysis using cyclopalladated tri-otolylphosphine complexes^{3,5} and palladium carbene complexes⁶ has been reported.

We have reported catalysis of the Heck reaction with aryl chlorides using electron-rich trigonal bisphosphine palladium(0) complexes.7 These reactions exhibit a remarkable chelate effect and enable Heck coupling under reducing conditions in absence of base,^{7c} although at a moderate rate. In recent years, we have studied complexes of tridentate PCP-type ligands in various reactions.⁸ We have now explored the possibility of catalysis of the Heck reaction with such palladium(II) complexes.

The new complexes 1, 2, and 3 were prepared by treatment of $Pd(TFA)_2$ (TFA = OCOCF₃) with the corresponding diphosphines in THF at 80 °C.⁹ Complex 3 was characterized by



(1) (a) Heck, R. F. Palladium Reagents in Organic Synthesis; Academic Press: London, 1985. (b) Heck, R. F. In Comprehensive Organic Synthesis; Trost, B. M., Flemming, I., Eds.; Pergamon Press: Oxford and New York, 1991; Vol. 4, pp 833-863.

(2) Recent reviews: (a) Grushin, V. V.; Alper, H. Chem. Rev. 1994, 94, 1047-1062. (b) de Meijere, A.; Meyer, F. E. Angew. Chem., Int. Ed. Engl. 1994, 33, 2379-2411. (c) Carbri, W.; Candiani, I. Acc. Chem. Res. 1995, 28, 2-7.

(3) (a) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Reisinger, C.-P.; Priermeier, T.; Beller, M.; Fisher, H. Angew. Chem., Int. Ed. Engl. 1995, 34, 1844–1848. (b) Beller, M.; Riermeier, T. H.; Haber, S.; Kleiner, H.-J.; Herrmann, W. A. *Chem. Ber.* **1996**, *129*, 1259–1264.

(4) Louie, J.; Hartwig, J. F. Angew. Chem., Int. Ed. Engl. 1996, 35, 2359-2361.

(5) (a) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Beller, M.; Fisher, H. J. Mol. Catal. A: Chem. 1995, 103, 133–146. (b) Herrmann, W. A.; Reisinger, C.-P.; Öfele, K.; Brossmer, C.; Beller, M.; Fisher, H. J. Mol. Catal. A: Chem. 1996, 108, 51–56.
(6) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. J. Angew. Chem., Int. Ed. Engl. 1995, 34, 2371–2374.



Figure 1. Perspective view (ORTEP) of complex 3. Bond distances (Å) and angles (deg, errors last digits in parentheses): Pd(1)-C(1) =2.046(5); Pd(1)-O(4) = 2.167(4); Pd(1)-P(2) = 2.354(2); Pd(1)-P(3) = 2.381(2); C(1)-C(11) = 1.489(7); C(1)-Pd(1)-O(4) =175.3(2); P(2)-Pd(1)-P(3) = 152.22(5); Pd(1)-C(1)-(C11) = 99.5(3).

X-ray analysis (Figure 1).¹⁰ Complexes 1-3 show exceptionally high activity in the catalytic arylation of olefins with aryl iodides and bromides (Table 1). Because of the stabilizing tridentate PCP ligand system, the complexes are extraordinarily thermally stable and no decomposition is observed at temperatures up to 180 °C. These complexes are also not sensitive to oxygen and moisture, and the reactions can be carried out in air, with no change in efficiencies or yield. There is no noticeable catalyst degradation even after heating complexes 1 and 2 for more than 300 h at 140 °C under the reaction conditions. The catalyst remains highly active after the reaction is complete, and upon addition of more substrates, catalysis is resumed, leading to the coupling product in quantitative yield at essentially the same rate. The only change observed at the end of the catalysis is substitution of the trifluoroacetate ligand to give the corresponding palladium halide complex, as shown by ³¹P NMR spectroscopy.

While very high turnover numbers (TONs) and yields are observed for all catalysts, complex 2 exhibits higher turnover rates. Most experiments were performed with complexes 1 and 2.

In a typical experiment a slight excess of the olefin is added to a solution of the aryl halide in freshly distilled N-methylpyrrolidone (NMP), followed by addition of an equimolar amount of sodium carbonate. Pure solvent and starting materials should be used in the highly catalytic reactions. The catalyst

^{(7) (}a) Ben-David, Y.; Portnoy, M.; Gozin, M.; Milstein, D. Organometallics 1992, 11, 1995-1996. (b) Portnoy, M.; Ben-David, Y.; Rousso, I.; Milstein, D. Organometallics 1994, 13, 3465-3479. (c) Portnoy, M.; Ben-David, Y.; Milstein, D. Organometallics 1993, 12, 4734-4735

 ⁽⁸⁾ For example: (a) Rybtchinski, B.; Vigalok, A.; Ben-David, Y.;
 Milstein, D. J. Am. Chem. Soc. 1996, 118, 12406-12415. (b) Van der Boom,
 M. E.; Kraatz, H.-B.; Ben-David, Y.; Milstein, D. Chem. Commun. 1996,
 2167-2168.

⁽⁹⁾ Complexes 1-3, 5, and 6 have been fully characterized by a combination of ¹H, ³¹P{¹H}, and ¹³C{¹H} NMR, FD-MS, elemental analysis, and X-ray analysis. See the Supporting Information for details.

⁽¹⁰⁾ Crystal data for **3**: C₂₉H₄₉O₂P₂F₃Pd-1.5C₆D₆, FW = 772.18, yellow, prism, 0.3 × 0.3 × 0.3 mm³, triclinic, P1 (no. 2), a = 11.738(2) Å, b = 12.183(2) Å, c = 15.259(3) Å, $\alpha = 107.90(3)^{\circ}$, $\beta = 109.15(3)^{\circ}$, $\gamma = 95.55(3)^{\circ}$ from 25 reflections, T = 110 K, V = 1913.6(6) Å³, Z = 2, $D_c = 1.340$ Mg/m³, $\mu = 0.614$ mm⁻¹, Mo K α , 7026 independent reflections, $R_{int} = 0.0119$ final $R_c = 0.0645$ = 0.0119, final $R_1 = 0.0645$.

	ArX	R	arene/ olefin (mmol/ mmol)	catalyst (mmol) $\times 10^{-5}$		time/ temp (h)/(°C)	TON	yield (%) ^a
1	PhI	COOMe	5/6	3.5	1	60/40	142 900	100
2			50/60	17.5	1	253/140	267 600	94
3			50/60	8.75	1	350/140	520 500	91
4			5/6	3.5	2	20/140	142 900	100
5			5/6	1.75	2	40/140	277 700	97
6			50/60	9.0	2	40/140	528 700	95
7			5/6	3.5	3	40/140	142 900	100
8	PhI	COOBu	5/6	3.5	1	40/140	5 650	4
9			5/6	3.5	1	88/160	108 000	77
10			5/6	3.5	2	64/140	142 900	100
11			5/6	3.5	2	14/160	142 900	100
12	PhI	C(O)Me	1.34/1.5	3.5	1	40/140	11 500	30
13	PhI	Ph	5/6	3.5	2	60/140	133 000	93 ^b
14	p-MeOPhI	COOMe	5/6	3.5	2	16/140	142 900	100
15	PhBr	COOMe	5/6	3.5	2	63/140	132 900	93
16	$p ext{-OCHPhBr}$	COOMe	5/6	3.5	2	63/140	113 300	79

^{*a*} Determined by GC, based on haloarene and product (PhCHCH-COOMe). ^{*b*} Product mixture of two isomers (E/Z = 7/1).

is added and the mixture is stirred at 140 °C while the course of the reaction is followed by NMR spectroscopy and gas chromatography. Selected results are listed in Table 1.

With iodobenzene and methyl acrylate, essentially complete conversions are obtained with exceptionally high TONs of up to 500 000. Lower conversions and yields were realized with aryl bromides, although the observed TON of 132 900 with **2** in the case of bromobenzene is among the highest reported. Chlorobenzene was almost inactive. Thus, we believe that this catalyst is among the most active and stable reported so far.

The new catalysts are of interest also from the mechanistic point of view. While the mechanism has not been studied in detail yet, involvement of a Pd(0) complex as the active species seems unlikely. It was shown that a metalated Pd(II) *o*tolylphosphine complex can be reduced to a Pd(0) complex under conditions of the Heck catalysis via formation of a palladium(II) hydride followed by ring opening by C–H reductive elimination.⁴ The presence of the two strong chelating rings renders opening of the Pd–aryl bond during the reaction unlikely. Nevertheless, to check this possibility, we have studied the reactivity of the hydride complex **4**.¹¹ Significantly, reaction of **4** with *p*-iodoanisole leads exclusively and quantitatively to anisole and to the iodide complex **5** (eq 2),⁹ which was



independently prepared by reaction of the corresponding TFA complex with LiI. Since hydrodehalogenation to the arene is

not observed in our catalysis, a route involving a PCP-Pd(II) hydride such as **4** is unlikely.

Generation of an anionic Pd(0) complex without chelate opening (e.g., by deprotonation of a complex such as **4**) is also unlikely. Such a mechanism would involve nucleophilic attack of the anionic complex on iodobenzene to give the Pd–Ph complex **6**.⁹ However, complex **6**, prepared by reaction of **1** with PhLi, does not lead to any coupling products upon heating with methyl acrylate. Moreover, treating **6** with various aryl iodides results in the quantitative formation of the corresponding palladium iodide complex **7** and biaryls (eq 3).¹² Since biaryl



formation is not observed in our catalysis, such a mechanism can be excluded. Thus, we believe that the traditional mechanism involving a Pd(0) complex may not be involved. A Pd(II)/Pd(IV) cycle based on oxidative addition of the aryl halide to 1-3 is a distinct possibility.

A competitive experiment using *p*-BrPhI, PhI, *p*-MePhI, *p*-MeOPhI, and methyl acrylate (in molar ratio of 5:5:5:5:1) and complex **1** as a catalyst results in a linear correlation with Hammett σ values, yielding $\rho = 1.39$. While this electronic effect is not surprising, since the oxidative addition of the aryl–I bond to the metal is expected to be facilitated by electronwithdrawing substituents on the aromatic ring, the ρ value is too low to fit a rate-determining nucleophilic aromatic substitution.¹³ A subsequent rate-determining step with different electronic requirements, such as olefin insertion, may account for this observation.

The higher efficiency of complex 2 can be attributed to electronic factors, the metal center in 2 being more electron rich than in 1. Complex 3 is less efficient than 2 due to the higher steric bulk of the phosphine ligands.

In summary, the PCP-type palladium(II) complexes show exceedingly high catalytic activity in the Heck reaction, including reactions of nonactivated aryl bromides. The new catalyst system is very thermally and air stable. Our evidence suggests that this catalysis may not involve the classical Pd(0) cycle. Further investigations aimed at clarification of the scope and mechanism of these novel catalysts are in progress.

Acknowledgment. We thank Dr. L. J. W. Shimon for the X-ray analysis of complex 3. This work was supported by The Israel Science Foundation, Jerusalem, Israel. M.O. thanks the Deutsche Forschunggemeinschaft for a fellowship. A.O. thanks the Minerva Foundation, Munich, Germany, for a fellowship. D.M. is the holder of the Israel Matz Professorial Chair of Organic Chemistry.

Supporting Information Available: Spectroscopic characterization of complexes 1-3, 5, and 6, text describing X-ray crystal structure analysis, and tables of crystal data and structure refinement, atomic coordinates, bond lengths and angles, anisotropic displacement parameters, and hydrogen coordinates for complex 3 (9 pages). See any current masthead page for ordering and Internet access instructions.

JA9729692

⁽¹¹⁾ Moulton C. J.; Shaw B. L. J. Chem. Soc., Dalton Trans. 1976, 1020-1024.

⁽¹²⁾ H.-B. Kraatz, M. E. van der Boom, Y. Ben-David, and D. Milstein, unpublished results.

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