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Generation of Tertiary Phosphine-Coordinated Pd(0) Species from $Pd(OAc)_2$ in the Catalytic Heck Reaction

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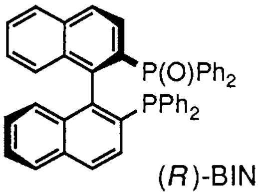
Palladium(II) diacetate reacted with water (1 equiv./Pd) and (*R*)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl ((*R*)-BINAP) (3 equiv./Pd) in benzene in the presence of Et_3N to give the palladium(0) species Pd[(*R*)-BINAP]$_2$ (1 equiv./Pd), (*R*)-BINAP monoxide (1 equiv./Pd), and $Et_3N{\cdot}HOAc$ (2 equiv./Pd). The progress of reaction strongly affected by the content of water in the reaction solution. The reduction of $Pd(OAc)_2$ in the presence of PPh_3 proceeded in a similar process to give $Pd(PPh_3)_4$ and $OPPh_3$.

Palladium(II) diacetate is among the most common precursors of catalyst in palladium-catalyzed organic reactions.[1] It is accepted that $Pd(OAc)_2$ employed in the catalytic systems, generally in combination with tertiary phosphine ligands, is reduced to a catalytically active palladium(0) species. However, little information has been reported so far on the reduction process.[2] We report herein that the reduction process shown in Eq. 1 is operative in the Heck type arylation and alkenylation systems[1-3] where no strong reducing reagents such as metal hydrides, alkylmetals, and metal alkoxides are present.[4,5] This process was observed with PPh_3 and (*R*)-BINAP[6] ligands. The former is the monophosphine ligand most frequently employed in the Heck reaction and the latter is a chiral diphosphine ligand utilized in catalytic asymmetric Heck reaction.[7,8]

$$Pd(OAc)_2 + H_2O + nPR_3 + 2R'_3N \longrightarrow Pd(PR_3)_{n-1} + O{=}PR_3 + 2R'_3N{\cdot}HOAc \qquad (1)$$

Palladium(II) diacetate (0.014 mmol), (*R*)-BINAP (0.044 mmol), and Et_3N (0.72 mmol) were dissolved in benzene (0.4 mL) at room temperature, and the reaction was followed by $^{31}P\{^1H\}$ NMR spectroscopy at 40 °C.[9] At the beginning, two singlets assignable to $Pd(OAc)_2$[(*R*)-BINAP][10] and free (*R*)-BINAP (1 : 2 ratio) appeared at δ 24.7 and −15.7, respectively, indicating a spontaneous complexation of $Pd(OAc)_2$ with (*R*)-BINAP to form $Pd(OAc)_2$[(*R*)-BINAP]. These signals gradually disappeared at 40 °C to be replaced by the signals arising from Pd[(*R*)-BINAP]$_2$[11] (δ 26.0 (s)) and (*R*)-BINAP monoxide[12] ((*R*)-BINAP(O); δ 24.6 (s) and −15.2 (s)). Addition of an excess amount of PMe_3 to the reaction mixture resulted in liberation of the (*R*)-BINAP ligand in Pd[(*R*)-BINAP]$_2$. (*R*)-BINAP and (*R*)-BINAP(O) thus released in the system were isolated in almost quantitative yields by silica gel column chromatography ((*R*)-BINAP, 2.0 equiv./Pd; (*R*)-BINAP(O), 0.94 equiv./Pd). In a separate experiment, $Et_3N{\cdot}HOAc$ was isolated in almost quantitative yield (1.9 equiv./Pd) from the reduction system.

$$Pd(OAc)_2 + H_2O + 3(R)\text{-BINAP} + 2Et_3N \xrightarrow[\text{benzene}]{\Delta} Pd[(R)\text{-BINAP}]_2 + (R)\text{-BINAP(O)} + 2Et_3N\cdot HOAc \qquad (2)$$



(*R*)-BINAP(O)

Treatment of a benzene solution of $Pd(OAc)_2$ and PPh_3 (5 equiv./Pd) with an excess amount of Et_3N (50 equiv./Pd) at 40 °C for 2 days gave $Pd(PPh_3)_4$ (δ 19.3) and triphenylphosphine oxide (δ 24.0) in a 1 : 1 ratio,[9] which were identified by $^{31}P\{^1H\}$ NMR spectroscopy. Silica gel column chromatography of the reaction solution, after addition of an excess amount of PMe_3, gave PPh_3 (3.9 equiv./Pd) and $OPPh_3$ (0.82 equiv./Pd). Thus, the similar process to the BINAP system proceeds in the reduction of $Pd(OAc)_2$ in the presence of PPh_3.

The experiments described above were carried out under the conditions usually employed in the catalytic organic reactions in our group.[9] On the other hand, the following experiments performed with particular care on the content of water in the system clearly showed that the presence of water is essential for the reduction to proceed (Fig. 1).[13]

In the reaction carried out with proton sponge[14] as the base in carefully dried benzene which contains 0.12 equivalents of water to palladium,[15] the reduction stopped at about 10% conversion of $Pd(OAc)_2[(R)\text{-BINAP}]$ into $Pd[(R)\text{-BINAP}]_2$ (entry a), demonstrating that 1 equivalent of water is required for the reduction of the palladium(II) species. Saturation of the benzene/proton sponge solution with water (0.81 equiv./Pd) effectively enhanced the rate of reduction and the conversion of $Pd(OAc)_2[(R)\text{-BINAP}]$ (entry b).[16] The conversion further increased with increasing the content of water in the solution by employment of aliphatic amines (entries c and d). Particularly, the reduction was completed in 9 h in a benzene/Et_3N solution saturated with water, which contains an excess amount of water to palladium (5.7 equiv./Pd) (entry d).

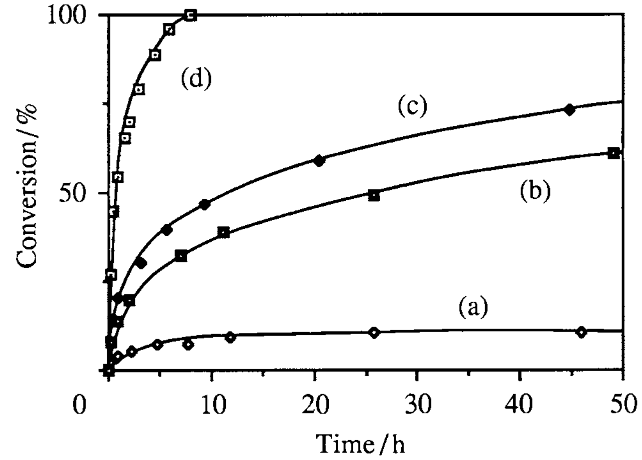


Fig. 1. Time-conversion curves for the reduction of $Pd(OAc)_2[(R)\text{-BINAP}]$ to give $Pd[(R)\text{-BINAP}]_2$.

Entry	Initial conditions [a]	
	Amine (equiv./Pd)	H_2O (equiv./Pd) [b]
a	proton sponge (10) [c]	0.12
b	proton sponge (10) [c]	0.81
c	*i*-Pr_2NEt (50)	1.6
d	Et_3N (50)	5.7

a) The reaction was carried out in an NMR sample tube using $Pd(OAc)_2$ (0.015 mmol) and (*R*)-BINAP (0.045 mmol) at 40 °C in a benzene/amine solution (0.5 mL). Entries b–d were run in a solution saturated with water, and entry a was examined without added water. b) The amount was measured by Karl Fisher method using Mitsubishi Moisturemeter Model CA-02. c) Proton sponge: 1,8-bis(dimethylamino)naphthalene.

Further insight into the reduction process was gained by labeling experiments using $^{18}OH_2$ (Table 1). The reaction carried out in a benzene/Et_3N solution saturated with $^{18}OH_2$ formed ^{18}O-labeled and unlabeled (*R*)-BINAP monoxides ((*R*)-BINAP(^{18}O) and (*R*)-BINAP(^{16}O), respectively).[17] Interestingly, the ratio of (*R*)-BINAP(^{18}O) increased with the progress of reduction. Since the acetate group in $Pd(OAc)_2$ is the only source of ^{16}O in the labeling system, it is strongly suggested that the acetate group is the source of oxygen in (*R*)-BINAP(O). (*R*)-BINAP(^{18}O) may be formed by the reaction of Pd(II)-BINAP species with ^{18}O-labeled acetate generated by exchange of oxygen between acetate and $^{18}OH_2$ in the reaction system.

Table 1. Labeling Experiments Using $^{18}OH_2$ for the Reduction of $Pd(OAc)_2$[(*R*)-BINAP][a)]

Conversion/%[b)]	(*R*)-BINAP(^{18}O)/(*R*)-BINAP(^{16}O)[c)]
26	51/49
52	67/33
97	84/16

a) The reaction was carried out in an NMR sample tube using $Pd(OAc)_2$ (0.015 mmol) and (*R*)-BINAP (0.045 mmol) at 40 °C in a benzene solution (0.5 mL) containing Et_3N (0.75 mmol) saturated with $^{18}OH_2$ (95% isotopic purity). b) Determiend by $^{31}P\{^1H\}$ NMR specrtoscopy. c) Determined by FD mass spectrometry.

We elucidated, for the first time, the reduction process of palladium(II) diacetate in the Heck reaction system. It is noted that 1 equivalent of phosphine ligand is consumed as phosphine oxide during the reduction.[18] This is an important information for designing an efficient catalytic system, because the selectivity and reactivity of catalytic reaction are sometimes strongly affected by amount of phosphine ligand. Furthermore, the reduction forms 2 equiv./Pd of acetate anion in the system, which possibly causes significant effects on the catalytic reactions. We found such an example in the asymmetric Heck reaction of 2,3-dihydrofuran with phenyl triflate.[7d] Further studies on the mechanism of the reduction process are in progress.

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2) a) R. F. Heck, *Org. React.*, **27**, 345 (1982); b) R. F. Heck and J. P. Nolley, Jr., *J. Org. Chem.*, **37**, 2320 (1972); c) J. P. Collman, L. S. Hegedus, J. R. Norton, and R. G. Finke, "Principles and Applications of Organotransition Metal Chemistry," University Science Books, Mill Valley, CA (1987), p. 725; d) R. McCrindle, G. Ferguson, G. J. Arsenault, A. J. McAlees, and D. K. Stephenson, *J. Chem. Res. Synop.*, **1984**, 360.

3) G. D. Daves, Jr. and A. Hallberg, *Chem. Rev.*, **89**, 1433 (1989).

4) Heck suggested the reduction of $Pd(OAc)_2$ by olefin.[2a,b] In the present study, however, no acceleration of the reduction by olefins including 2,3-dihydrofuran, cyclohexene, and methyl acrylate was observed.

5) It is known that triethylamine reduces palladium(II) salts such as $Pd(OAc)_2$ and Li_2PdCl_4.[2c,d] This reaction

was observed in the absence of tertiary phosphine ligands.[2d)] In the present systems containing tertiary phosphine ligands, the reduction of $Pd(OAc)_2$ did take place even in the absence of triethylamine, though the reaction was slower (ca. 1/4) than that in the presence of triethylamine.

6) (*R*)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl: H. Takaya, K. Mashima, K. Koyano, M. Yagi, H. Kumobayashi, T. Taketomi, S. Akutagawa, and R. Noyori, *J. Org. Chem.*, **51**, 629 (1986).
7) a) F. Ozawa, A. Kubo, and T. Hayashi, *J. Am. Chem. Soc.*, **113**, 1417 (1991); b) F. Ozawa, A. Kubo, and T. Hayashi, *Tetrahedron Lett.*, **33**, 1485 (1992); c) F. Ozawa and T. Hayashi, *J. Organomet. Chem.*, **428**, 267 (1992); d) F. Ozawa, A. Kubo, and T. Hayashi, *Pure Appl. Chem.*, **64**, 421 (1992).
8) Y. Sato, M. Sodeoka, and M. Shibasaki, *J. Org. Chem.*, **54**, 4738 (1989); Y. Sato, M. Sodeoka, and M. Shibasaki, *Chem. Lett.*, **1990**, 1954; K. Kagechika and M. Shibasaki, *J. Org. Chem.*, **56**, 4093 (1991); Y. Sato, S. Watanabe, and M. Shibasaki, *Tetrahedron Lett.*, **33**, 2589 (1992).
9) All reagents were employed without particular care for contamination with water except for benzene, which was dried over sodium benzophenone ketyl.
10) $Pd(OAc)_2$[(*R*)-BINAP] was isolated from the reaction solution and characterized by IR and NMR spectroscopy and elemental analysis. IR (KBr) 1702, 1580, 1372, and 1316 cm^{-1}.
11) Pd[(*R*)-BINAP]$_2$ was independently prepared by thermolysis of $Pd(\eta^3\text{-}C_3H_5)(\eta^5\text{-}C_5H_5)$ in benzene in the presence of 2 equivalents of (*R*)-BINAP. See, M. Hodgson and D. Parker, *J. Organomet. Chem.*, **325**, C27 (1987).
12) (*R*)-BINAP(O): mp 232–235 °C; $[\alpha]_D^{20}$ +94° (*c* 0.82, $CHCl_3$); IR (KBr) 1204 cm^{-1} (ν(P=O)); HRMS (EI) calcd for $C_{44}H_{32}OP_2$ 638.1928, found 638.1914.
13) All reagents employed in the reactions in Fig. 1 were carefully dried according to the following procedures. Palladium(II) diacetate and (*R*)-BINAP were dried under vacuum at 80 °C for 2 days and stored under a nitrogen atmosphere. Benzene, triethylamine, and diisopropylethylamine were dried over $LiAlH_4$, vacuum transferred, and stored under a nitrogen atmosphere. Proton sponge[14)] was dried at room temperature under vacuum for 1 day.
14) Proton sponge: 1,8-bis(dimethylamino)naphthalene.
15) The content of water in the reaction solution of entry a in Fig. 1 was 0.0073 wt %, which was measured by Karl Fisher method using Mitsubishi Moisturemeter Model CA-02. The lowest concentration of water in the reaction solution was achieved with proton sponge as the base. It was hard to minimize the content of water using aliphatic amines such as Et_3N and *i*-Pr_2NEt.
16) Since the reduction of $Pd(OAc)_2$[(*R*)-BINAP] was strongly affected by the content of water in the reaction solution, exact control of the amount of water was required for the reproducibility in Fig. 1. Saturation of the reaction solution with water was the best way to obtain the accurate amount of water in the solution which may vary with amine employed.
17) (*R*)-BINAP(^{18}O): IR (KBr) 1174 cm^{-1} (ν(P=^{18}O)).
18) There are some precedents for the reduction of palladium(II) halides involving formation of phosphine oxide: M. R. Mason and J. G. Verkade, *Organometallics*, **11**, 2212 (1992); R. S. Vinal and L. T. Reynolds, *Inorg. Chem.*, **3**, 1062 (1964); M. Meier, F. Basolo, and R. G. Pearson, *ibid.*, **8**, 795 (1969); M. Meier and F. Basolo, *Inorg. Synth.*, **13**, 112 (1972); A. Sen and J. Halpern, *J. Am. Chem. Soc.*, **99**, 8337 (1977).

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