Readily Regenerative and Air-stable Palladium(0) Catalyst with Tris[2-(diphenylphosphino)ethyl]phosphine Tetrasulfide for C–C Coupling Reactions

Sen-ichi Aizawa,* Mitsuyoshi Tamai, Mai Sakuma, and Asari Kubo
Graduate School of Science and Engineering, University of Toyama, 3190 Gofuku, Toyama 930-8555

(Received October 12, 2006; CL-061199; E-mail: saizawa@eng.u-toyama.ac.jp)

The novel air-stable Pd^0 complex, $[Pd(pp_3S_4)(dba)]$ (pp_3S_4 = tris[2-(diphenylphosphino)ethyl]phosphine tetrasulfide, dba = dibenzylideneacetone) was prepared as a C–C coupling catalyst. This is regenerative from the Pd^0 complex with the partially oxidized pp_3S_4 ligand by the chalcogen-atom substitution reaction catalyzed by Pd^0 and applicable to the recyclable Pd^0 catalytic system.

Palladium catalysts are now quite versatile and indispensable in organic synthesis since they can catalyze the formation of various carbon–carbon and carbon–hetero-atom bonds. The catalytic activity in most coupling reactions comes from the ability of Pd^0 species to activate C–X bonds (X = halogens or pseudohalogens) by the oxidative addition that initiates the catalytic cycle.[1] Because phosphines have been regarded as effective ligands to stabilize the zerovalent oxidation state of palladium, phosphine-assisted reactions have been widely employed as the classical and conservative method.[1] However, expensive and toxic phosphines might not be ideal ligands in large-scale applications on industrial and semi-industrial scales considering that they are almost unrecoverable because of their air-sensitivity. On the other hand, phosphine-free catalytic systems have received increasing interest from the environmental and economical reasons. The problem is that the catalytic cycles are blocked by strongly bound ligands of stable phosphine-free complexes to give the low catalytic activity while weakly ligated complexes, which are likely to have high activity, are intrinsically unstable and liable to be decomposed into inactive "palladium black." In these circumstances, we need a new ligand system that can thermodynamically stabilize the Pd^0 center but does not deactivate the catalytic cycle kinetically. It is also desirable that the new catalyst is recoverable and reusable for industrial use.

Recently, some phosphine sulfides have been employed as monodentate or bidentate ligands for some metal ions.[2] The sulfur–phosphorus π bonding orbital is not so stabilized, and consequently the unoccupied π^* orbital is moderately low and can accept electrons from Pd^0 to stabilize the low oxidation state. On the other hand, because the phosphine sulfide group is not a strong σ-donor for Pd^{II}, the formation of the substrate adduct and subsequent catalytic reactions on Pd^{II} are not likely to be blocked. In this paper, we report the isolable Pd^0 complex with tris[2-(diphenylphosphino)ethyl]phosphine tetrasulfide (pp_3S_4) as one of the most promising catalysts, where the four phosphine sulfide groups linked by ethylene chains can stabilize the Pd^0 complex entropically as well as electronically. We also report new catalysis of Pd^0 for substitution reactions of chalcogen atoms of phosphine chalcogenides, which can be utilized for regeneration and reuse of the phosphine sulfide complexes.

The pp_3S_4 ligand was obtained by the reaction of pp_3 with excess sulfur in chloroform followed by the addition of diethyl ether to give colorless crystals.[3] The Pd^0 complex, $[Pd(pp_3S_4)(dba)]$ (dba = dibenzylideneacetone) (**1**), was prepared from $[Pd(dba)_2]$ and pp_3S_4 in chloroform followed by the addition of diethyl ether to give dark brown powder. The coordination of dba and pp_3S_4 and the composition were confirmed by ^{31}P and ^{1}H NMR and elementary analysis.[4] The catalytic activity for Suzuki coupling reaction of **1** was compared with that of $[Pd(PPh_3)_4]$ (**2**) by using iodobenzene and phenylboronic acid as the substrates.[5] The phosphine sulfide complex **1** exhibited almost the same catalytic activity under N_2 and in the air, which was comparable to that for **2** under N_2 (Figure 1). Furthermore, after keeping the completely reacted solution for additional several hours without residual unreacted substrates, the brown solution for **1** maintained the catalytic activity for another addition of the substrates. To the contrary, **2** was gradually decomposed into inactive palladium black to give the almost colorless supernatant in the air especially after consuming the substrates. This fact indicates that the Pd^0 in **1** is stabilized by the phosphine sulfide groups while **2** itself is air-sensitive unless forming the Pd^{II} substrate adduct. We have also prepared the polymer-supported phosphine sulfide Pd^0 complex **3** as a readily recyclable C–C coupling catalyst.[6] **3** used in the air was filtered from the completely reacted solution and then reused in the air. The recycled **3** was not deactivated by repetition of this procedure at least more than four times (Figure 1).

While phosphines are known to be susceptible to oxidation in the air, we found in this work that the oxidation is catalyzed by Pd^0. As shown in Figure 2, PPh_3 was completely oxidized by dissolved oxygen in 2 h in the DMF solution of **2** though only ca. 15% of free PPh_3 was oxidized for 4 days under the same

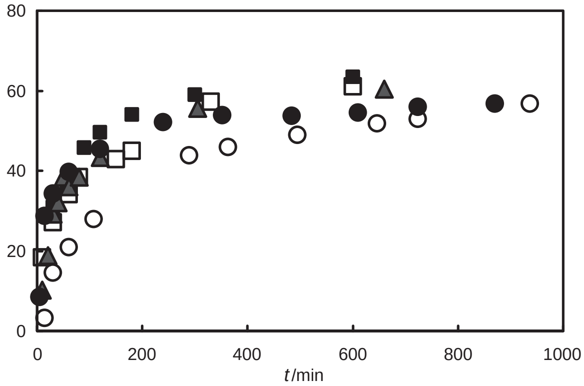

Figure 1. Change in the yield of biphenyl with time in Suzuki coupling reaction catalyzed by **1** (■, in the air; □, under N_2), **2** (▲, under N_2), and **3** (●, freshly prepared; ○, recycled four times; in the air).

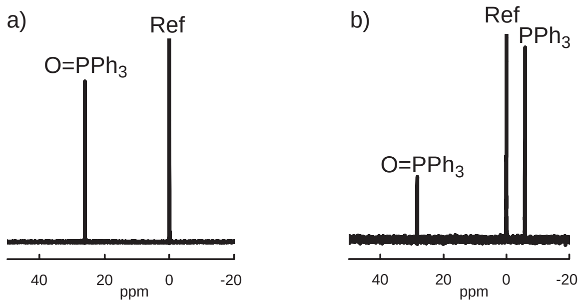

Figure 2. ^{31}P NMR spectra of DMF solutions of **2** (0.043 mol kg^{-1}) (a) and PPh_3 (0.171 mol kg^{-1}) (b) allowed to stand at room temperature for 2 h and 4 days, respectively. Ref denotes the signal for D_3PO_4 in the outer D_2O.

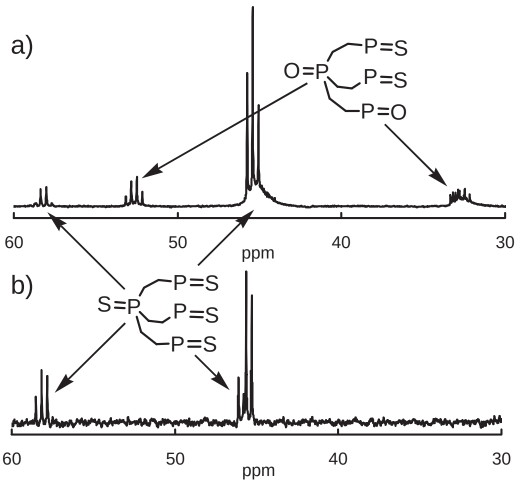

Figure 3. ^{31}P NMR spectra for DMF solution (1.5 cm^3) of **1** (0.029 mmol) allowed to stand at room temperature for 13 days (a) and the solution after subsequent reaction with excess sulfur (29 mmol) at 125 °C for 2 h (b).

conditions. This catalysis leads to a serious problem in the phosphine-assisted palladium-catalyzed reactions. Furthermore, chalcogen-atom substitution reactions on phosphine chalcogenides were also revealed to be catalyzed by Pd^0. For example, the sulfur atoms in free pp_3S_4, are hardly replaced by oxygen atoms at room temperature, but those in **1** were partially replaced to give some phosphine oxide groups by standing for a long time (Figure 3a). Such a substitution reaction of phosphine sulfide groups is possible during the prolonged or repeated catalytic reaction using **1** or **3**. However, pp_3S_4 was readily regenerated from the partially oxidized ligand in **1** by the reaction with excess sulfur in DMF at 125 °C for 2 h (Figure 3b) though the transformation from phosphine oxide into phosphine sulfide does not proceed at all without Pd^0 even by reflux in DMF. The regenerative phosphine sulfide Pd^0 complex can be applied to the recyclable catalytic system.

A few chalcogen-transfer reactions from phosphine chalcogenides to phosphines were reported[7] and a nucleophilic attack of the phosphine to the phosphine chalcogenide P atom was proposed.[8] However, there is no phosphine initially in the present system of the chalcogen-atom substitution. In order to clarify the reaction mechanism, **1** was reacted with relatively labile $[PtCl_2(NCC_6H_5)_2]$ in DMF at 95 °C for several hours, and the ^{31}P NMR signal for phosphine coordinated to Pt^{II} was observed, which was confirmed by a strong coupling between ^{31}P and ^{195}Pt ($^1J = 3800$ Hz).[9] Such a P=S bond cleavage was not observed for a DMF solution containing pp_3S_4 and $[PtCl_2(NCC_6H_5)_2]$ without Pd^0. Considering that oxidation of phosphine, that is, phosphine chalcogenide formation was also promoted by Pd^0 as mentioned above, the chalcogen-atom substitution of phosphine chalcogenides results from the catalytic P=Y (Y = chalcogen atom) bond cleavage and formation by Pd^0. The π-back donation from Pd^0 to π^* orbital on doubly bonded chalcogen atom can activate the P=Y bond and the π-back donation to the phosphine P atom may promote the oxidative chalcogenide formation.

In conclusion, by introducing the phosphine sulfide as a new ligand for the Pd^0 catalyst, we have been able to provide the readily regenerative and air-stable Pd^0 catalyst offering a prospect of the industrial application as a novel recyclable Pd^0 catalytic system.

References and Notes

1 J. Tsuji, in *Palladium Reagents and Catalysts*, Wiley, Chichester, **1995**; R. F. Heck, in *Palladium Reagents in Organic Synthesis*, VCH, Weinheim, **1996**; A. Suzuki, *J. Organomet. Chem.* **1999**, *576*, 147; I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009.

2 T. Y. H. Wong, S. J. Rettig, B. R. Jamws, *Inorg. Chem.* **1999**, *38*, 2143; H. Liu, N. A. G. Bandeira, M. J. Calhorda, M. G. B. Drew, V. Félix, J. Novosad, F. F. de Biani, P. Zanwllo, *J. Organomet. Chem.* **2004**, *689*, 2808; N. Zúñiga-Villarreal, J. M. Germán-Acacio, A. A. Lemus-Santana, M. Reyes-Lezama, R. A. Toscano, *J. Organomet. Chem.* **2004**, *689*, 2827; A. N. Skvortsov, A. N. Reznikov, D. A. de Vekki, A. I. Stash, V. K. Belsky, V. N. Spevak, N. K. Skvortsov, *Inorg. Chim. Acta* **2006**, *359*, 1031; D. K. Dutta, P. Chutia, J. D. Woollins, A. M. Z. Slawin, *Inorg. Chim. Acta* **2006**, *359*, 877; P. Sekar, J. A. Ibers, *Inorg. Chim. Acta* **2006**, *359*, 2751.

3 Yield 94%. Anal. Found: C, 63.08; H, 5.30; N, 0.00%. Calcd for $C_{42}H_{42}P_4S_4$: C, 63.14; H, 5.30; N, 0.00%. ^{31}P{^{1}H} NMR ($CHCl_3$): δ (relative to D_3PO_4 in external D_2O) 44.1 (d, terminal), 54.5 (q, center); $^3J_{P\text{-}P} = 56$ Hz.

4 Yield 44%. Anal. Found: C, 44.64; H, 3.80; N, 0.00%. Calcd for $C_{59}H_{56}OP_4PdS_4 \cdot 5CHCl_3 \cdot C_4H_{10}O$: C, 45.11; H, 3.95; N, 0.00%. ^{31}P{^{1}H} NMR ($CHCl_3$): δ (relative to D_3PO_4 in external D_2O) 44.2 (d, terminal), 54.6 (q, center); $^3J_{P\text{-}P} = 56$ Hz. ^{1}H NMR ($CDCl_3$): δ 1.21 (t, CH_3 of diethyl ether), 2.11–2.17 and 2.55–2.65 (m, CH_2CH_2 of pp_3S_4), 3.48 (q, CH_2 of diethyl ether), 7.10 (d, Ph-CH=C*H* of dba), 7.26 (s, $CHCl_3$), 7.41–7.54 and 7.81–7.87 (m, Ph of pp_3S_4), 7.61–7.64 (m, Ph of dba), 7.75 (d, Ph-C*H*=CH of dba). The ^{31}P NMR broadening behavior suggested that less than four sulfide groups are fluxionally coordinated in solution.

5 Reactions of iodobenzene (27.4 mmol) with phenylboronic acid (32.8 mmol) in DMF (3 cm^3) were carried out in the air and under N_2 at 125 °C in the presence of the Pd^0 catalyst (0.011 mmol) and K_2CO_3 (25.5 mmol) as a base. The yields were calculated by the ^{1}H NMR intensity of the ortho protons of biphenyl formed on the basis of the intensity of the ethylene protons of bis(2-butoxyethyl) ether contained as an internal reference and followed as a function of time.

6 **3** was prepared from polymer-supported triphenylphosphine (Aldrich) and $[Pd(dba)_2]$. Anal. Found: C, 73.61; H, 5.35; N, 0.00; S, 6.80; Pd, 4.71%. Calcd for $C_{20}H_{17}PS_{0.7}Pd_{0.15}$: C, 73.52; H, 5.24; N, 0.00; S, 6.87; Pd, 4.88%.

7 L. D. Field, M. P. Wilkinson, *Tetrahedron Lett.* **1997**, *38*, 2779; M. Bollmark, J. Stawinski, *J. Chem. Soc., Chem. Commun.* **2001**, 771.

8 M. Kullberg, J. Stawinsky, *J. Organomet. Chem.* **2005**, *690*, 2571.

9 S. Aizawa, K Saito, T. Kawamoto, E. Matsumoto, *Inorg. Chem.* **2006**, *45*, 4859.

Published on the web (Advance View) December 9, 2006; doi:10.1246/cl.2007.130