Phosphinic Acid Induced Reversal of Regioselectivity in Pd-Catalyzed Hydrophosphinylation of Alkynes with $Ph_2P(O)H$**

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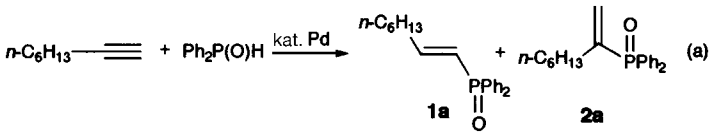
One of the most attractive features of transition metal complex catalyzed addition to carbon–carbon multiple bonds is in the ease of fine-tuning the ligands for better regioselectivities. However, a sharp reversal of the selectivity by fine-tuning the ligand is not always an easy task, since the regioselectivity is usually inherent in the central metal of the catalyst.[1] We recently developed palladium-catalyzed additions of diphenylphosphane oxide to alkynes,[2] which allows efficient preparation of alkenylphosphane oxides of biological and synthetic value.[3] We now report a reversal of the regioselectivity: The selectivity of the addition of $Ph_2P(O)H$ to terminal alkynes, which normally forms (E)-β-adducts selectively,[2] switches in favor of α-adducts simply in the presence of just one drop of $Ph_2P(O)OH$ in the reaction mixture.

As previously reported,[2] when an equimolar mixture of diphenylphosphane oxide and 1-octyne in C_6D_6 was heated at 70 °C for 2 h in the presence of *cis*-$[Me_2Pd(PPhMe_2)_2]$ (5 mol% relative to the substrate), isomeric products **2a** and **1a** were formed in 75% total yield (NMR) in a ratio of 12:88 [Eq. (a)]. Surprisingly the regioselectivity was completely reversed when the same reaction was repeated in the presence of trace diphenylphosphinic acid. Therefore, the reaction in the presence of only 1 mol% of $Ph_2P(O)OH$ (relative to the substrate) resulted in 92% total yield and a **2a**:**1a** ratio of 79:21.[4] The regioselectivity for **2a** was further improved with an increased amount of $Ph_2P(O)OH$ to achieve nearly quantitative formation of the adducts in a ratio of 95:5 in the presence of 5 mol% of $Ph_2P(O)OH$. Besides the phosphinic acid, dibutyl phosphate (92%, **2a**:**1a** = 90:10) and phosphoric acid (89%, **2a**:**1a** = 85:15) also gave **2a** as the major product. However, a similar reversal did not result when hexamethyl phosphoramide (HMPA, 76%, **2a**:**1a** = 13:87), acetic acid (73%, **2a**:**1a** = 20:80), or benzoic acid (76%, **2a**:**1a** = 13:87) was employed.



As Table 1 suggests, the reactions catalyzed by palladium complexes with sterically less demanding and more basic phosphane ligands are more sensitively affected by $Ph_2P(O)OH$. In *cis*-$[PdMe_2(PPh_3)_2]$-catalyzed reactions, for instance, the **2a**:**1a** ratio of 9:91 in the absence of $Ph_2P(O)OH$ increased significantly, but without reversal of the regioselectivity, to 37:63 when 5 mol% of $Ph_2P(O)OH$ was added. On the other hand, as already described, addition of 5 mol% of $Ph_2P(O)OH$ to the *cis*-$[PdMe_2(PPhMe_2)_2]$-catalyzed reaction induced a reversal of the ratio from 12:88 to 95:5. In *cis*-$[PdMe_2(PPh_2Me)_2]$-catalyzed reactions neither decreasing the reaction temperature from 70 to 45 °C nor changing the solvent from benzene to THF affected the regioselectivity.

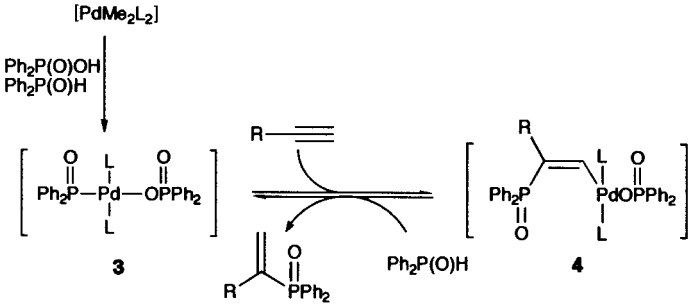
Table 1. Hydrophosphinylation of 1-octyne.[a]

Catalyst	Conditions	Yield [%] with $Ph_2P(O)OH$ (**2a**:**1a**)[b]	Yield [%] without $Ph_2P(O)OH$ (**2a**:**1a**)[b]
$[Pd(PPh_3)_4]$	70 °C, 3 h	89 (33:67)	54 (8:92)
cis-$[PdMe_2(PPh_3)_2]$	70 °C, 3 h	73 (37:63)	43 (9:91)
cis-$[PdMe_2(PPh_2Me)_2]$	70 °C, 3 h	100 (84:16)	56 (10:90)[c]
cis-$[PdMe_2(PPhMe_2)_2]$	70 °C, 2 h	93 (95:5)	75 (12:88)
$[PdMe_2(PEt_3)_2]$[d]	70 °C, 2 h	95 (91:9)	51 (13:87)
$[PdMe_2(dmpe)]$[e]	100 °C, 6 h	93 (92:8)	0

[a] All reactions were conducted in a sealed NMR tube with equimolar amounts of $Ph_2P(O)H$ and 1-octyne (0.25 mmol) dissolved in C_6D_6 (0.5 mL) in the presence of 5 mol% of Pd catalyst. [b] In the presence of 5 mol% of $Ph_2P(O)OH$. The yields for the reactions with and without $Ph_2P(O)OH$ were determined by NMR spectroscopy. [c] Reaction time = 2.5 h. [d] *cis*:*trans* = 1:1. [e] dmpe = 1,2-bis(dimethylphosphino)ethane.

$Ph_2P(O)OH$ also enhances the catalytic activity. For example $[PdMe_2(dmpe)]$, which was nearly inactive in the absence of $Ph_2P(O)OH$, catalyzed the addition at 100 °C. Activities of other palladium–phosphane complexes were also boosted (see Table 1). A seemingly puzzling aspect is that even 1% of $Ph_2P(O)OH$ was sufficient to reverse the regioselectivity, despite a larger quantity (5%) of *cis*-$[Me_2Pd(PPhMe_2)_2]$ in the reaction system (see above). This is presumably due to a new palladium species that is formed upon addition of the phosphinic acid and is more catalytically active.

The present results strongly indicate that the OH group plays a crucial role in inducing the intriguing effect of $Ph_2P(O)OH$ (and related compounds).[5] We believe that the process shown in Scheme 1 is occurring: 1) generation of a new reactive Pd species **3**, 2) insertion of a C≡C unit into the Pd–$P(O)Ph_2$ bond (phosphinylpalladation) with formation of an alkenylpalladium species **4**, and 3) subsequent protonol-



Scheme 1. Proposed mechanism for the Pd-catalyzed hydrophosphinylation (L = PR_3).

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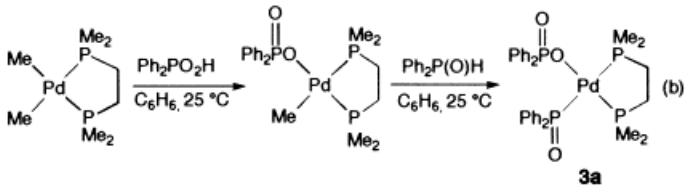
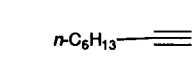
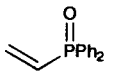
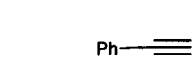
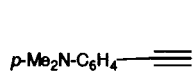
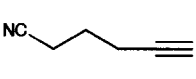
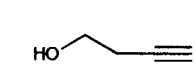
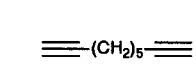
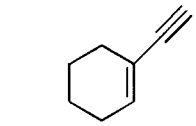
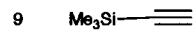
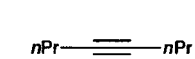
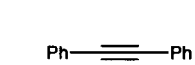
ysis of **4** with $Ph_2P(O)H$[6] leading to the α-adduct with concomitant regeneration of **3**.[7] Protonolysis of a C–Pd bond in the generation of **3** from $[PdMe_2L_2]$ and its regeneration from **4** appears reasonable, since similar protonolyses with various acidic reagents are known.[8] We were able to confirm such reactions with $Ph_2P(O)H$ and $Ph_2P(O)OH$. When $[PdMe_2(PEt_3)_2]$ and $[Ph_2P(O)H]$ (4 equiv) were mixed in C_6D_6 at 25 °C, methane gas immediately evolved, and the colorless solution became pale yellow. The starting material $[PdMe_2(PEt_3)_2]$ disappeared within 0.5 h, and the ^{31}P NMR spectrum displayed signals for a new Pd complex in addition to those for remaining $Ph_2P(O)H$ ($\delta = 17.2$) and free PEt_3 ($\delta = -19.6$). Although the complex could not be isolated, the structure was assigned as $[PdMe\{P(O)Ph_2\}(PPh_2OH)(PEt_3)]$ on the basis of NMR data; the oxygen atoms are linked through an O-H-O hydrogen bond. Likewise, when $Ph_2P(O)OH$ was added to *trans*-$[PdMe_2(PEt_3)_2]$ (1 equiv) in benzene at 25 °C, evolution of methane gas was immediately observed, and a colorless oil of *trans*-$[PdMe\{OP(O)Ph_2\}(PEt_3)_2]$ produced quantitatively.[9] A similar reaction with *cis*-$[PdMe_2(dmpe)]$ allowed isolation of analytically pure *cis*-$[PdMe[OP(O)Ph_2](dmpe)]$ as a white solid. The resulting complex did not react further with excess $Ph_2P(O)OH$, even at 70 °C. Very interestingly, however, protonolysis of the complex with one equivalent of $Ph_2P(O)H$ proceeded readily at room temperature and *cis*-$[Pd\{Ph_2P(O)\}\{OP(O)Ph_2\}(dmpe)]$ (**3a**) was obtained as a white solid in good yield with liberation of another molecule of methane [Eq. (b)].[10] We were unable to detect intermediates formed by insertion of a C≡C unit into the Pd–$P(O)Ph_2$ bond in reactions of **3a** with acetylenes. In strong support of the proposed mechanism shown in Scheme 1, however, **3a** catalyzed the addition of $Ph_2P(O)H$ to 1-octyne at 100 °C in the absence of $Ph_2P(O)OH$; the adducts were obtained in 95% yield (NMR) with a **2a**:**1a** ratio of 90:10 after 10 h, which was in good agreement with the value observed for $[PdMe_2(dmpe)]$-catalyzed addition in the presence of $Ph_2P(O)OH$ (Table 1).



As shown in Table 2, this new recipe for hydrophosphinylation could be generally applied to various aliphatic and aromatic terminal alkynes to afford a variety of 1-alken-2-ylphosphane oxides regioselectively and in good yields. Functionalities such as amino, cyano, and hydroxyl groups were tolerated under the reaction conditions. As exemplified by entry 7, two phosphinyl groups could be efficiently introduced to both C–C triple bonds. Under the reaction conditions an olefinic bond is unreactive with respect to hydrophosphinylation. Accordingly, 1-ethynylcyclohexene (entry 8) underwent selective addition at the triple bond. As for the regioselectivity, the reaction of (trimethylsilyl)acetylene is an exception: Only the terminal carbon atom was phosphinylated, presumably owing to the steric hindrance at the internal carbon atom. Acetylenes with internal C≡C units also reacted, albeit somewhat slowly, to afford the corresponding products selectively. Worth noting from another synthetic viewpoint is that the reaction run in the presence of the phosphinic acid is very clean. On the other hand, reactions carried out without the phosphinic acid resulted in unidentified by-products, in particular at higher temperatures.[2] Applications of the current finding to other transition metal complex catalyzed additions are now under extensive study.

Table 2. Hydrophosphinylation of alkynes.[a]

Entry	Alkyne	Adduct	Yield [%] (**2**:**1**)[b]
1			92 (95/5)
2	HC≡CH [c]		54
3			78 (98/2)
4			86 (97/3)
5			90 (94/6)
6			93 (93/7)
7			85 [d]
8			89 (98/2)
9			63 [e, f]
10			81 [g]
11			94 [h]

[a] Conditions: equimolar amounts of $Ph_2P(O)H$ and alkyne in benzene (≈ 0.5 M), 3–4 mol% of *cis*-$[PdMe_2(PPhMe_2)_2]$, ≈ 5 mol% of $Ph_2P(O)OH$, 70 °C, 2–4 h. [b] Yields refer to isolated amounts after column chromatography or preparative gel permeation chromatography (GPC). The ratios of isomers were determined by ^1H NMR spectroscopy of the crude reaction mixture. [c] 1 atm CH≡CH, 70 °C, 5 h. [d] Amount of $Ph_2P(O)H$ used = 2.2 equiv. Regioselectivity > 95%. [e] *cis*-$[PdMe_2(PPh_2Me)_2]$ was used as the catalyst. [f] Only the *trans* isomer was formed. [g] Heated for 36 h. [h] Heated for 12 h.

Experimental Section

Catalytic additions of $Ph_2P(O)H$: Diphenylphosphane oxide (202 mg, 1.0 mmol), 1-octyne (110 mg, 1.0 mmol), diphenylphosphinic acid (11 mg, 5 mol%), and *cis*-[$PdMe_2(PPhMe_2)_2$] (12 mg, 3 mol%) were dissolved in dry benzene (2 mL) under argon. The solution was heated at 70 °C for 4 h and evaporated in vacuo to leave a pale yellow oil, which was purified by column chromatography (SiO_2, EtOAc/hexane 1/1) to give the adducts as a colorless oil in 92% combined yield (287 mg, 0.92 mmol, **2a**:**1a** = 95:5). The two regioisomers (**2a** and **1a**) could be isolated by preparative thin layer chromatography (PTLC; silica gel, hexane/EtOAc 2/3; **2a**: 250 mg, 80% yield; **1a**: 11 mg, 4% yield).

2a: Colorless oil. ^{1}H NMR (300 MHz, C_6D_6): δ = 7.77 – 7.83 (m, 4H), 7.05 – 7.16 (m, 6H), 5.60 (d, 1H, J(H,P) = 42.1 Hz), 5.55 (d, 1H, J(H,P) = 20.4 Hz), 2.30 – 2.38 (m, 2H), 1.39 – 1.49 (m, 2H), 1.01 – 1.21 (m, 6H), 0.80 (t, 3H, J = 6.8 Hz); ^{13}C NMR (C_6D_6, 75.5 MHz): δ = 145.8 (J(C,P) = 90.8 Hz), 133.4 (J(C,P) = 99.8 Hz), 132.2 (J(C,P) = 9.3 Hz), 131.5 (J(C,P) = 2.7 Hz), 128.5 (J(C,P) = 11.6 Hz), 127.8 (J(C,P) = 9.6 Hz), 32.6 (J(C,P) = 15.0 Hz), 31.9, 29.2, 28.7 (J(C,P) = 4.9 Hz), 22.9, 14.2; ^{31}P NMR (C_6D_6, 121.5 MHz): δ = 27.9; IR (neat/NaCl): $\tilde{\nu}$ = 3058, 2930, 2860, 1437, 1191, 1120, 940, 727, 696 cm^{-1}. HRMS calcd for $C_{20}H_{25}OP$: 312.1642, found: 312.1624.

1a: White solid, m.p. 68 – 69 °C. ^{1}H NMR (300 MHz, C_6D_6): δ = 7.78 – 7.85 (m, 4H), 7.05 – 7.08 (m, 6H), 6.87 – 7.01 (m, 1H), 6.11 (dd, 1H, J = 16.9, J(H,P) = 25.1 Hz), 1.87 – 1.91 (m, 2H), 1.09 – 1.21 (m, 8H), 0.82 (t, 3H, J = 6.8 Hz); ^{13}C NMR (C_6D_6, 75.5 MHz): δ = 152.2 (J(C,P) = 1.7 Hz), 135.4 (J(C,P) = 92.9 Hz), 131.6 (J(C,P) = 9.5 Hz), 131.3 (J(C,P) = 2.7 Hz), 128.5 (J(C,P) = 11.7 Hz), 123.1 (J(C,P) = 101.8 Hz), 34.6 (J(C,P) = 16.6 Hz), 31.8, 29.1, 28.1, 22.9, 14.2; ^{31}P NMR (C_6D_6, 121.5 MHz): δ = 18.9; IR (KBr): $\tilde{\nu}$ = 2962, 2928, 2856, 1632, 1439, 1185, 1122, 1002, 814, 745 cm^{-1}. HRMS calcd for $C_{20}H_{25}OP$: 312.1642, found: 312.1603.

cis-[PdMe[OP(O)Ph_2](dmpe)]: To a solution of *cis*-[$PdMe_2$(dmpe)] (17.2 mg, 0.06 mmol) in toluene/CH_2Cl_2 (1/1, 6 mL) was added $Ph_2P(O)OH$ (13 mg, 0.06 mmol) at room temperature under nitrogen. As the solid $Ph_2P(O)OH$ gradually dissolved, gas evolution from the solution was observed. A transparent colorless solution was obtained after 1 h at room temperature. Concentration of the solution to about half its volume in vacuo afforded a white precipitate of *cis*-[PdMe[OP(O)Ph_2](dmpe)] (28.6 mg, 0.058 mmol, 97% yield); m.p. 164 °C (decomp). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 – 7.94 (m, 10H), 1.74 (br s, 2H), 1.48 – 1.55 (m, 14H), 0.55 (dd, 3H, J(H,P) = 2.2, 8.2 Hz); ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ = 37.2 (d, J(P,P) = 23.0 Hz), 22.6 (s), 21.4 (d, J(P,P) = 23.0 Hz); elemental analysis calcd for $C_{19}H_{29}O_2P_3Pd$: C 46.69, H 5.98; found: C 46.63, H 5.97.

3a: To a solution of *cis*-[$PdMe_2$(dmpe)] (116.4 mg, 0.406 mmol) in benzene (4 mL) was added $Ph_2P(O)OH$ (88.6 mg, 0.406 mmol) at room temperature under nitrogen. Gas evolution was observed immediately. After the mixture was stirred for 6 h at room temperature, a solution of $Ph_2P(O)H$ (82.1 mg, 0.406 mmol) in benzene (3 mL) was slowly added. The reaction mixture was stirred overnight to afford analytically pure **3a** as a white solid (255.1 mg, 0.378 mmol, 93%); m.p. 198 °C (decomp). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.16 – 7.80 (m, 20H), 1.80 (dd, 6H, J(H,P) = 1.8, 12.0 Hz), 1.71 – 1.83 (m, 4H), 1.56 (dd, 6H, J(H,P) = 3.5, 10.2 Hz); ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ = 66.8 (d, J(P,P) = 467.8 Hz), 42.7 (d, J(P,P) = 33.4 Hz), 26.1 (d, J(P,P) = 9.2 Hz), 20.6 (ddd, J(P,P) = 9.2, 33.4, 467.8 Hz); elemental analysis calcd for $C_{30}H_{36}O_3P_4Pd$: C 53.39, H 5.38; found: C 53.57, H 5.68.

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[1] For partial reversal of the regioselectivity in hydrosilylation, see a) K. H. Pannell, J. Rozell, J. Lii, S.-Y. Tien-Mayr, *Organometallics* **1988**, *7*, 2524; b) M. Rivera-Claudio, J. Rozell, J. E. Ramirez-Oliva, J. Cervantes, K. H. Pannell, *J. Organomet. Chem.* **1996**, *521*, 267.

[2] L.-B. Han, N. Choi, M. Tanaka, *Organometallics* **1996**, *15*, 3259.

[3] a) *Handbook of Organophosphorus Chemistry* (Ed.: R. Engel), Marcel Dekker, New York, **1992**; b) C. R. Johnson, T. Imamoto, *J. Org. Chem.* **1987**, *52*, 2170; c) K. M. Pietrusiewicz, M. Zablocka, W. Wisniewski, *Phosphorus, Sulfur Silicon Relat. Elem.* **1990**, *49-50*, 263; d) K. M. Pietrusiewicz, W. Wisniewski, M. Zablocka, *Tetrahedron* **1989**, *45*, 337; e) K. M. Pietrusiewicz, M. Zablocka, *Tetrahedron Lett.* **1988**, *29*, 1991; f) H. Brunner, S. Limmer, *J. Organomet. Chem.* **1991**, *417*, 173; g) J. Berlan, J.-P. Battioni, K. Koosha, *Tetrahedron Lett.* **1976**, 3351; h) K. M. Pietrusiewicz, M. Zablocka, *ibid.* **1988**, *29*, 937; i) A. Brandi, S. Cicchi, A. Goti, *ibid.* **1991**, *32*, 3265.

[4] In the absence of the catalyst, neither **1a** nor **2a** was obtained under the same conditions.

[5] The possibility of isomerization of **1a** to **2a** catalyzed by $Ph_2P(O)OH$ as the origin of the reversal is readily ruled out, since **1a** did not isomerize to **2a** when heated with $Ph_2P(O)OH$ (13 mol% relative to **1a**) in C_6D_6 at 70 °C for 4 h. Isomerization was also not observed when pure **1a** was added to the solution of the *cis*-[$PdMe_2(PPhMe_2)_2$]-catalyzed reaction of $Ph_2P(O)H$ with 1-octyne in the presence of 5 mol% of $Ph_2P(O)OH$ (Table 1) and reheated at 70 °C for 2 h.

[6] Secondary phosphane oxides exist in two tautomeric forms, P(=O)H and P–OH; the former is dominant in the equilibrium: a) W. J. Bailey, R. B. Fox, *J. Org. Chem.* **1963**, *28*, 531; b) W. J. Bailey, R. B. Fox, *ibid.* **1964**, *29*, 1013; c) L. A. Hamilton, P. S. Landis in *Organic Phosphorus Compounds*, *Vol. 4* (Eds.: G. M. Kosolapoff, L. Maier), Wiley, New York, **1972**, chap. 11.

[7] Hydrophosphinylation of alkynes in the absence of $Ph_2P(O)OH$ proceeds by hydropalladation; see ref. [2].

[8] a) Y.-J. Kim, K. Osakada, A. Takenaka, A. Yamamoto, *J. Am. Chem. Soc.* **1990**, *112*, 1096; b) F. Kawataka, Y. Kayaki, I. Shimizu, A. Yamamoto, *Organometallics* **1994**, *13*, 3517.

[9] The reaction of *cis*-[$PdMe_2(PEt_3)_2$] gave the same product. The complex did not react further with excess $Ph_2P(O)OH$ even upon heating at 70 °C for 2 h.

[10] Complex **3a** was similarly obtained when $Ph_2P(O)H$ was added first to [$PdMe_2$(dmpe)] followed by treatment with $Ph_2P(O)OH$.

Molecular Aluminophosphonate: Model Compound for the Isoelectronic Double-Six-Ring (D6R) Secondary Building Unit of Zeolites**

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Dedicated to Professor Herbert D. Kaesz on the occasion of his 65th birthday

One of the main thrusts in the area of advanced materials has been the synthesis of phosphate materials of Al and Ga,[1–5] which can potentially serve as highly organized matrices of tunable pore size and shape. Since the first successful synthesis of aluminophosphate materials in 1982,[1] several groups have synthesized alumino- and gallophosphate materials by hydrothermal routes in the presence of structure-directing agents.[2–5] To understand the local structures of these complex materials, a few soluble model compounds were prepared which can also serve as secondary building

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