Novel Palladium-Catalyzed Thiophosphorylation of Alkynes with Phosphorothioate: An Efficient Route to (Z)-1-(Diphenoxyphosphinyl)-2-(phenylthio)alkenes

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Palladium complexes efficiently catalyze the addition of O,O,S-triphenyl phosphorothioate to terminal alkynes to produce (Z)-1-(diphenoxyphosphinyl)-2-(phenylthio)alkenes in high yields with high regio- and stereoselectivity.

Transition metal complex-catalyzed addition of a heteroatom-containing bond to a carbon—carbon unsaturated linkage is generally characterized by its high product yield and selectivity under mild reaction conditions, and hence is particularly attractive from the synthetic viewpoint.[1] Particularly interesting and challenging in this category are those involving the regio- and stereoselective simultaneous introductions of two different heteroatoms as exemplified by Si—Sn and related bond additions, which enable more versatile and elegant synthetic elaboration of the adducts.[2] Herein reported is a new entry to this category; in the presence of a catalytic amount of palladium complexes PhSP(O)(OPh)$_2$ efficiently adds to terminal acetylenes to produce (Z)-1-(diphenoxyphosphinyl)-2-(phenylthio)alkenes in high yields with high regio- and stereoselectivity.[3] The adducts are potentially versatile in organic synthesis, and find applications in the preparation of bidentate ligands having phosphorus and sulfur atoms for transition metal complexes.[4]

In a typical experiment, heating a mixture of PhSP(O)(OPh)$_2$ (2 mmol, 685 mg)[5] and 1-octyne (2.0 mmol, 220 mg) in toluene (2 mL) in the presence of Pd(PPh$_3$)$_4$ (46 mg, 2 mol%) at 100 °C for 5 h resulted in complete disappearance of 1-octyne as confirmed by GC. Purification of the crude products by column chromatography on silica gel (EtOAc/hexane = 1/4) afforded analytically pure (Z)-1-(diphenoxyphosphinyl)-2-(phenylthio)-1-octene (1a) as pale yellow oil in 92% yield (833 mg) (eq 1).[6]

$$n\text{-}C_6H_{13}\text{---}\!\equiv\ +\ (PhO)_2P(O)SPh\ \xrightarrow[\substack{\text{toluene}\\100\ °C}]{\text{cat. Pd}}\ \underset{\mathbf{1a}}{PhS\diagdown\diagup P(OPh)_2}\quad (1)$$
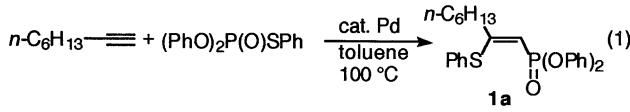
In the absence of the catalyst, the reaction did not proceed at all under the same conditions. In general Pd(0) complexes or readily reducible Pd(II) complexes having less basic ligands are able to efficiently catalyze the reaction. Accordingly, dimethylpalladiums Me$_2$Pd(PR$_3$)$_2$ (PR$_3$ = PPh$_3$, PPh$_2$Me and PPhMe$_2$) and Pd(CH$_2$=CH$_2$)(PPh$_3$)$_2$ also catalyzed the reaction. On the other hand, Pd(II) complexes such as PdMe$_2$(PEt$_3$)$_2$ (cis/trans = 7/1), PdCl$_2$, Pd(OAc)$_2$, PdCl$_2$(PPh$_3$)$_2$ and PdCl$_2$(PhCN)$_2$ were totally inactive because of either the ligand being too basic or the complex not being readily reduced to Pd(0) species. Worth noting is that the in situ generated palladium species by mixing Pd$_2$(dba)$_3$ and PR$_3$ (P/Pd = 1 ~ 2; PR$_3$ = PPh$_3$, Ph$_2$P(CH$_2$)$_3$PPh$_2$) did not show catalytic activity in the addition reaction.

Table 1. Pd-catalyzed thiophosphorylation of terminal alkynes[a]

Run	Alkyne	Adduct	Yield/%
1	n-C$_6$H$_{13}$—≡		92
2[b]	t-Bu—≡		65
3	NC〜〜≡		84
4	HO〜〜≡		89
5	Cl〜〜≡		85
6	t-BuCO$_2$〜〜≡		68
7			91
8		R = MeO,	88
9			R = n-Bu$_2$N, 94
10[b]	Me$_3$Si—≡		60
11[c]	≡—(CH$_2$)$_5$—≡		90
12[d]	p-R-C$_6$H$_4$—≡	R = H, 87 (96/4)	
13[d]		R = Cl, 71 (93/7)	
14[d]		R = F, 69 (91/9)	
15[d]		R = Me, 89 (98/2)	

[a]Conditions: an equimolar PhSP(O)(OPh)$_2$ and an alkyne in toluene (0.6 ~ 1 M), 2 ~ 3 mol% Pd(PPh$_3$)$_4$, 100 °C , 3-5 h. Yields refer to isolated yields after PTLC isolation on silica gel and/or preparative GPC isolation. In some cases, consumption of the starting materials was not complete, resulting in lower yields of the adducts. [b]100 °C, 15 h. [c]2.1 equiv of PhSP(O)(OPh)$_2$ was used. [d]THF, 80 °C, 12~16 h. Ratios in parentheses refer to Z/E isomer ratios of the adducts.

As demonstrated in Table 1, the palladium-catalyzed thiophosphorylation could be readily applied to other terminal alkynes, yielding the corresponding (Z)-1-(diphenoxyphosphinyl)-2-(phenylthio)alkenes in good yields. The regio- and stereoselectivity was excellent for aliphatic alkynes. Besides 1-octyne, functionalized aliphatic alkynes such as those having cyano, hydroxyl, chloro, acyloxy, and amino groups also proceeded efficiently affording the adducts in high yields. Multiple phosphoryl and thio groups could be easily introduced regio- and stereoselectively to alkynes having more than one C—C triple bonds. For example, the thiophosphorylation of 1,8-nonadiyne using 2.1 equiv of PhSP(O)(OPh)2 gave the corresponding product in 90% yield. Alkenes were inert toward the reaction. Consequently, only an adduct through the addition to the triple bond was obtained from 1-ethynylcyclohexene.

In contrast to aliphatic alkynes, phenylacetylene gave an E/Z mixture of the adducts under similar reaction conditions (eq 2).[7] Interestingly, the reaction run in THF resulted in a better stereoselectivity. The product could be obtained in 91% yield with an isomer ratio as high as 96/4 by heating an equimolar mixture of the reagents in THF at 80 °C for 16 h. Other aromatic alkynes such as 1-chloro-4-ethynylbenzene and 4-ethynyltoluene behaved similarly.

$$\text{Ph}\!-\!\!\equiv\ +\ (PhO)_2P(O)SPh\ \xrightarrow[\text{Pd(PPh}_3)_4]{\text{2 mol\%}}\ \underset{\mathbf{1b}}{\overset{Ph}{\underset{PhS}{\diagup}}\!\!=\!\!\overset{}{\underset{O}{\diagdown P(OPh)_2}}}\quad (2)$$
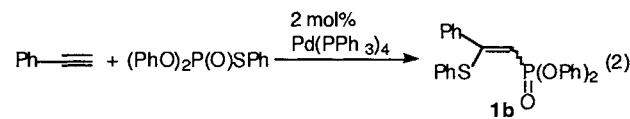
(1) toluene, 100 °C, 5 h, 92% (E/Z = 10/90)
(2) toluene, 80 °C, 5 h, 60% (E/Z = 12/88)
(3) THF, 67 °C, 14 h, 50% (E/Z = 2/98)
(4) THF, 80 °C, 16 h, 91% (E/Z = 4/96)

Despite our effort, PhSP(O)(OPh)2 was totally unreactive towards internal alkynes such as 4-octyne, diphenylacetylene, and dimethyl acetylenedicarboxylate.

Although mechanistic aspects remain to be elucidated, we propose that the reaction is triggered by oxidative addition of the P—S bond. Thus, treatment of Pd(PPh3)4 with PhSP(O)-(OPh)2 at 100 °C generated a dark red solution, which displayed new signals at δ 110.5 (J_{P-P} = 37.3 Hz) and 62.5 (J_{P-P} = 37.3 Hz) assignable to S—Pd—P(O) species in ^{31}P NMR spectroscopy.[2f] PhSP(O)(OPh)2 reacted with Pd(PEt3)4 even at 25 °C to give bright yellow trans-Pd(SPh)[P(O)(OPh)2](PEt3)2 in 87% yield.[8] However, the resulting complex was, as anticipated from the lack of the catalytic activity of Me2Pd(PEt3)2, unreactive toward 1-octyne.

In summary, we have successfully demonstrated the first palladium complexes-catalyzed addition of P—S bonds of phosphorothioate PhSP(O)(OPh)2 to carbon—carbon triple bonds to give (Z)-1-(diphenoxyphosphinyl)-2-(phenylthio)-alkenes in high yields with high regio- and stereoselectivity. Synthetic applications of the adducts as well as detailed mechanistic study on the addition reaction are now in progress.

References and Notes

1   a) J. P. Collman, L. S. Hegedus, J. R. Norton, and R. G. Finke, "Principles and Applications of Organotransition Metal Chemistry,"

University Science Books, Hill Valley (1987). b) G. W. Parshall and S. D. Ittel, "Homogeneous Catalysis", John Wiley & Sons, New York (1992), pp 25-50. c) "Comprehensive Handbook on Hydrosilylation," ed by B. Marciniec, Pergamon Press, Oxford (1992). d) L.-B. Han and M. Tanaka, *Chem. Commun.*, **1999**, 395.

2   Representative E—E' additions (E, E' = heteroatom): Si—Sn: a) T. N. Mitchell and U. Schneider, *J. Organomet. Chem.*, **407**, 319 (1991) and references cited therein. B—S: b) T. Ishiyama, K. Nishijima, N. Miyaura, and A. Suzuki, *J. Am. Chem. Soc.*, **115**, 7219 (1993). Si—S (Si—Se, Ge—S, Ge—Se): c) T. Tsumuraya and W. Ando, *Organometallics*, **8**, 2286 (1989). d) A. Ogawa, H. Kuniyasu, M. Takeba, T. Ikeda, N. Sonoda, and T. Hirao, *J. Organomet. Chem.*, **564**, 1 (1998). e) L.-B. Han and M. Tanaka, *J. Am. Chem. Soc.*, **120**, 8249 (1998). P—Se: f) L.-B. Han, N. Choi, and M. Tanaka, *J. Am. Chem. Soc.*, **118**, 7000 (1996). B—Sn: g) S.-y. Onozawa, Y. Hatanaka, N. Choi, and M. Tanaka, *Organometallics*, **16**, 5389 (1997). B—Si: h) S.-y. Onozawa, Y. Hatanaka, and M. Tanaka, *Chem. Commun.*, **1997**, 1229. i) M. Suginome, H. Nakamura, and Y. Ito, *Angew. Chem., Int. Ed. Engl.*, **36**, 2516 (1997). For other relevant study, see: j) T. Ishiyama, N. Matsuda, M. Murata, F. Ozawa, A. Suzuki, and N. Miyaura, *Organometallics*, **15**, 713 (1996) and references cited therein.

3   For other palladium-catalyzed additions of phosphorous-containing bond: a) L.-B. Han and M. Tanaka, *J. Am. Chem. Soc.*, **118**, 1571 (1996). b) L.-B. Han, N. Choi, and M. Tanaka, *Organometallics*, **15**, 3259 (1996). c) L.-B. Han, R. Hua, and M. Tanaka, *Angew. Chem., Int. Ed.*, **37**, 94 (1998).

4   a) P. Magnus and D. Quagliato, *J. Org. Chem.*, **50**, 1621(1985). b) T. Minami and J. Motoyoshiya, *Synthesis*, **1992**, 333.

5   The starting material PhSP(O)(OPh)2 could be easily prepared via the reaction of PhSLi with an equimolar (PhO)2P(O)Cl in THF (-78 °C, 0.5 h; 25 °C, 3 h). Addition of water to the reaction mixture followed by extraction with Et2O gave almost pure PhSP(O)(OPh)2 in a quantitative yield as confirmed by both ^{1}H and ^{31}P NMR spectroscopy. Minor impurities were removed by distillation (~ 200 °C/0.005 mmHg) or column chromatography on silica gel (EtOAc/hexane = 1/3). The pure PhSP(O)(OPh)2 thus obtained was a colorless oil which slowly solidified on standing at room temperature to afford white solid. In contrast to PhSeP(O)(OPh)2 (ref 2f), the preparation and handling of PhSP(O)(OPh)2 are much easier; the compound is stable towards air and moisture, and more importantly, it does not smell. PhSP(O)(OPh)2: white solid. mp 44—45 °C. ^{1}H NMR (CDCl3) δ 7.49—7.55 (m, 2H), 7.32—7.42 (m, 9H), 7.19—7.22 (m, 4H); ^{13}C NMR (CDCl3) δ 150.4 (J_{C-P} = 9.3 Hz), 135.3 (J_{C-P} = 5.2 Hz), 129.8, 129.6 (J_{C-P} = 3.1 Hz), 129.5 (J_{C-P} = 3.1 Hz), 125.6, 125.1 (J_{C-P} = 7.2 Hz), 120.5 (J_{C-P} = 5.2 Hz); ^{31}P NMR (CDCl3) δ 14.9. This compound is known: S. Masson, J.-F. Saint-Clair, A. Dore, and M. Saquet, *Bull. Soc. Chim. Fr.*, **133**, 951 (1996).

6   1a: HRMS for C26H29O3PS, calcd: 452.1573, found: 452.1577. Anal. Found: C, 69.06; H, 6.72%. Calcd for C26H29O3PS: C, 69.01; H, 6.46%. ^{1}H NMR (CDCl3) δ 7.15—7.41 (m, 15H), 5.81 (d, 1H, J_{H-P} = 17.3 Hz), 2.12 (t, 2H, J = 7.6 Hz), 1.32—1.60 (m, 2H), 1.12—1.24 (m, 2H), 1.4—1.09 (m, 4H), 0.80 (t, 3H, J = 7.0 Hz); ^{13}C NMR (CDCl3) δ 165.3, 150.6 (J_{C-P} = 8.3 Hz), 134.7, 130.9, 129.6, 129.2, 129.1, 124.9, 120.7 (J_{C-P} = 4.1 Hz), 110.6 (J_{C-P} = 197.6 Hz), 38.2 (J_{C-P} = 19.7 Hz), 31.3, 28.5, 28.2, 22.4, 14.0; ^{31}P NMR (CDCl3) δ 8.3; IR (NaCl, neat) 2932, 2860, 1593, 1491, 1272, 1216, 1193, 1164, 1071, 1025, 930, 754 cm^{-1}. NOE experiment: irradiation at the triplet centered at δ 2.12 resulted in a 13% increase of the doublet centered at δ 5.81, indicating the Z-configuration.

7   Heating an E/Z mixture (E/Z = 3/97) of 1b in toluene at 100 °C for 3 h, did not cause detectable change in the E/Z ratio, indicating that the E isomer was not formed via simple thermal isomerization of the Z adduct.

8   trans-Pd(PhS)[P(O)(OPh)2](PEt3)2: bright-yellow solid. mp 114—115 °C. Anal. Found: C, 52.86; H, 6.75%. Calcd for C30H45O3P3PdS: C, 52.60; H, 6.62%. ^{1}H NMR (toluene-d_8) δ 7.67—7.77 (m, 2H), 7.42—7.45 (m, 4H), 6.86—7.13 (m, 9H), 1.99—2.09 (m, 12H), 0.96 (dt, 18H, J = 7.8, J_{H-P} = 16.6 Hz); ^{31}P NMR (toluene-d_8) δ 55.3 (t, J_{P-P} = 16.1 Hz), 19.6 (d, J_{P-P} = 16.1 Hz).