# Palladium-Catalyzed Hydrophosphorylation of Alkynes *via* Oxidative Addition of HP(O)(OR)$_2$

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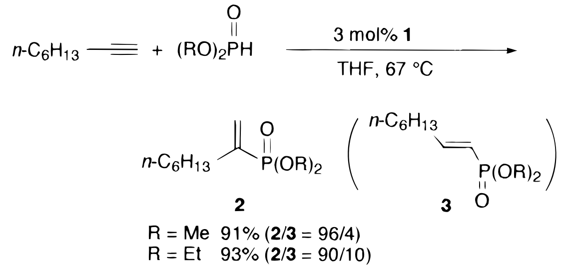
Application of metal complex catalysis to heteroatom chemistry is a research field that will vitally grow in the future. Addition reactions of H−E and E−E′ bonds (E, E′ = a heteroatom or group) across unsaturated carbon linkages in particular are an important class of reactions from a synthetic viewpoint.[1] An exceptional example in this category that has already been experiencing great industrial success is hydrosilylation.[2] Addition reactions of other group 14 element compounds and elemental processes behind the catalysis are also under intense study.[3] To the best of our knowledge, however, the metal-complex-catalyzed addition reaction of the H−P bond appears to have never been explored.[4] Herein are reported (1) the first entry into this category, namely, palladium-catalyzed hydrophosphorylation of acetylenes, and (2) the first example of oxidative addition of HP(O)(OR)$_2$[5] to the Pt(0) complex generating H−Pt−P(O)(OR)$_2$ species. In the new catalysis the H−P bond adds across triple bonds under gentle conditions to afford various alkenylphosphonates in excellent yields. Alkenylphosphonates are both synthetically versatile[6] and biologically active.[7]

Heating a THF solution (1 mL) of 1-octyne (1 mmol) and HP(O)(OR)$_2$ (1 mmol) in the presence of *cis*-PdMe$_2$(PPh$_2$Me)$_2$ (**1**, 3 mol %) at 67 °C for 5 h under argon resulted in a complete disappearance of the starting materials. Simple Kugelrohr distillation afforded the corresponding alkenylphosphonates in high yields (eq 1).



(1)

In the absence of the catalyst, neither **2** nor **3** could be detected by GC under the same reaction conditions. In general, Pd(0) complexes or readily reducible Pd(II) complexes that have less basic ligands are able to efficiently catalyze the reaction. Accordingly, as shown in Table 1, *cis*-PdMe$_2$(PPh$_3$)$_2$, Pd(CH$_2$═CH$_2$)(PPh$_3$)$_2$, and Pd(PPh$_3$)$_4$ 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.[8] Worth noting from a mechanistic viewpoint (*vide infra*) is that some platinum complexes were also able to promote the reaction, albeit sluggishly.

**Table 1.** Palladium-Catalyzed Addition of (EtO)$_2$P(O)H to Acetylenes

| run | catalyst | time (h) | % adduct yield (**2**/**3**)[a] |
|---|---|---|---|
| 1[b,c] | *cis*-PdMe$_2$(PPh$_2$Me)$_2$ | 5 | 93 (90/10) |
| 2[b] | *cis*-PdMe$_2$(PPh$_2$Me)$_2$ | 13 | 92 (89/11) |
| 3[b] | *cis*-PdMe$_2$(PPh$_3$)$_2$ | 17 | 73 (85/15) |
| 4[b,d] | Pd(CH$_2$═CH$_2$)(PPh$_3$)$_2$ | 6 | 93 (91/9) |
| 5[b] | Pd(PPh$_3$)$_4$ | 18 | 89 (86/14) |
| 6[b,c] | Pd(PPh$_3$)$_4$ | 22 | 69 (88/16) |
| 7[e] | Pt(PPh$_3$)$_4$ | 72 | 8 (64/36) |
| 8[e] | Pt(CH$_2$═CH$_2$)(PPh$_3$)$_4$ | 72 | 9 (68/32) |

[a] Determined by GC. [b] 3 mol % Pd catalyst, equimolar 1-octyne and (EtO)$_2$P(O)H in THF (0.2 M), 67 °C. [c] Concentration of the reactants = 1 M. [d] Carried out under 1 atm of ethylene. [e] 5 mol % Pt catalyst, equimolar phenylacetylene and (EtO)$_2$P(O)H in toluene (1 M), 110 °C.

Pd-catalyzed hydrophosphorylation can be easily applied to other alkynes, thus proving to be a new general methodology for the synthesis of alkenylphosphonates, which are not readily accessible by conventional methods.[6,9] As demonstrated in Table 2, both aliphatic and aromatic terminal alkynes reacted efficiently with HP(O)(OMe)$_2$, affording in high yields the corresponding adducts by regioselective attack of the phosphorus at the internal carbon of the triple bond. An exceptional case was the reaction of (trimethylsilyl)acetylene in which only the terminal carbon was phosphorylated, probably owing to steric hindrance at the internal carbon. As exemplified by runs 5 and 6, two phosphoryl groups could be easily introduced to both triple bonds of the diynes. Under similar conditions, the olefinic double bond is totally unreactive to the hydrophosphorylation. Accordingly, 1-ethynylcyclohexene (run 7) underwent the addition reaction selectively at the triple bond.

As compared to terminal alkynes, the hydrophosphorylation of internal alkynes proceeded a little slower. The addition of HP(O)(OEt)$_2$ to 4-octyne produced 23 and 82% yields of the adduct after heating for 15 and 65 h, respectively. The high stereoselectivity is noteworthy; only the *cis* isomer could be observed on $^1$H NMR.

Although the detailed mechanism of the hydrophosphorylation reaction still remains to be clarified, the reaction is envisioned

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[1] (a) Chaloner, P. A. *Handbook of Coordination Catalysis in Organic Chemistry*; Butterworth: London, 1986; Chapter 4. (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Hill Valley, CA, 1987. (c) *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 8, pp 667−792. (d) Parshall, G. W.; Ittel, S. D. *Homogeneous Catalysis*; John Wiley & Sons: New York, 1992; pp 25−50.

[2] *Comprehensive Handbook on Hydrosilylation*; Marciniec, B., Ed.; Pergamon Press: Oxford, U.K., 1992.

[3] For recent reviews, see: (a) Horn, K. A. *Chem. Rev.* **1995**, *95*, 1350. (b) Sharma, H. K.; Pannell, K. H. *Chem. Rev.* **1995**, *95*, 1351. See also: (c) Yamashita, H.; Tanaka, M.; Goto, M. *Organometallics* **1993**, *12*, 988. (d) Hada, M.; Tanaka, Y.; Ito, M.; Murakami, M.; Amii, H.; Ito, Y.; Nakatsuji, H. *J. Am. Chem. Soc.* **1994**, *116*, 8754. (e) Chatani, N.; Amishiro, N.; Morii, T.; Yamashita, T.; Murai, S. *J. Org. Chem.* **1995**, *60*, 1834. (f) Fu, P.-F.; Brard, L.; Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1995**, *117*, 7157. (g) Shimada, S.; Tanaka, M.; Honda, K. *J. Am. Chem. Soc.* **1995**, *117*, 8289. (h) Yamashita, H.; Tanaka, M.; Hond, K. *J. Am. Chem. Soc.* **1995**, *117*, 8873.

[4] For radical and acid- or base-catalyzed addition of H−P, see: (a) *Organic Phosphorus Compounds*; Kosolapoff, G. M., Maier, L., Eds.; Wiley-Interscience: New York, 1972. (b) Goldwhite, H. *Introduction to Phosphorus Chemistry*; Cambridge University Press: Cambridge, 1981.

[5] Hydrogen phosphonates exist in two tautomeric forms, HP(O)(OR)$_2$ and P(OR)$_2$(OH), the former being thermodynamically more favored under ambient conditions. They coordinate, like tertiary phosphines, to transition metals (Pd, Pt, Ir, Rh, etc.) to form complexes which have been used as catalysts in organic reactions: (a) Henbest, H. B.; Mitchell, T. R. B. *J. Chem. Soc. C* **1970**, 785. (b) Roundhill, D. M.; Sperline, R. P; Beaulieu, W. B. *Coord. Chem. Rev.* **1978**, *26*, 263. (c) Bennett, M. A.; Mitchell, T. R. B. *J. Organomet. Chem.* **1985**, *295*, 223.

[6] For a recent review, see: Minami, T.; Motoyoshiya, J. *Synthesis* **1992**, 333.

[7] (a) Engel, R. *Chem. Rev.* **1977**, *77*, 349. (b) Harnden, M. R.; Parkin, A.; Parratt, M. J.; Perkins, R. M. *J. Med. Chem.* **1993**, *36*, 1345. (c) Breaker, R. R.; Gough, G. R.; Gilham, P. T. *Biochemistry* **1993**, *32*, 9125.

[8] Some of these Pd(II) complexes appeared to react with the phosphonate since a distinct color change of the solution was observed upon mixing these two components.

[9] Examples of sp$^2$-carbon to phosphorus bond-forming reactions are rare: (a) Hirao, T.; Masunaga, T.; Yamada, N.; Oshiro, Y.; Agawa, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 909. (b) Xu, Y.; Li, Z.; Xia, J.; Guo, H.; Huang, Y. *Synthesis* **1983**, 377. (c) Holt, D. A.; Erb, J. M. *Tetrahedron Lett.* **1989**, *30*, 5393.

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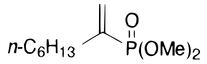
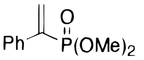
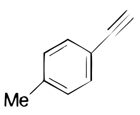
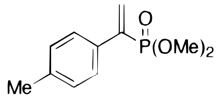
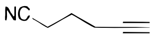
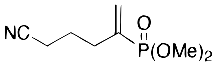
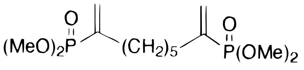
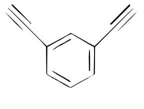
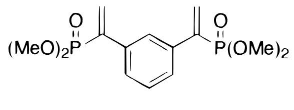
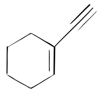
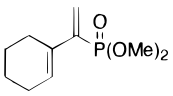
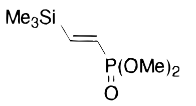
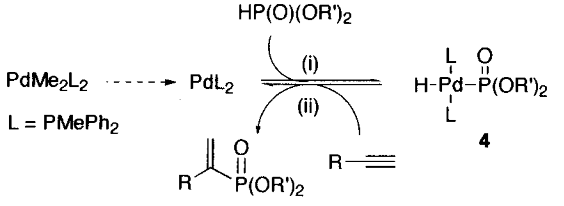
**Table 2.** Hydrophosphorylation of Terminal Alkynes[a]

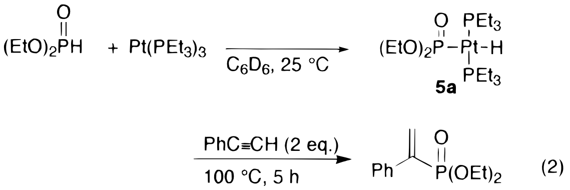
| run | alkyne | adduct | % yield |
|---|---|---|---|
| 1 | $n$-$C_6H_{13}$—≡ |  | 95[b] |
| 2 | Ph—≡ |  | 93[c] |
| 3 |  |  | 90[c] |
| 4 |  |  | 94[b] |
| 5 | ≡—$(CH_2)_5$—≡ |  | 83[b,d] |
| 6 |  |  | 87[c,d] |
| 7 |  |  | 89[e] |
| 8 | $Me_3Si$—≡ |  | 41[f,g] |

[a] Conditions: equimolar $(MeO)_2P(O)H$ and the alkyne in THF (0.2 M), 3 mol % *cis*-$PdMe_2(PPh_2Me)_2$, 67 °C, 15−20 h. Yields refer to isolated yields after Kugelrohr distillation and/or preparative HPLC isolation. [b] Regioselectivity > 95/5. [c] Regioselectivity > 92/8. [d] 2.2 equiv of $(MeO)_2P(O)H$ was used. [e] Regioselectivity = 96/4. [f] 2 equiv of $Me_2SiC{\equiv}CH$ was used. [g] *Trans* isomer only.

**Scheme 1**



to take place *via* the insertion reaction of an alkyne with a HPd-$[P(O)(OR)_2]$ species (**4**) (step ii), as illustrated in Scheme 1. While we have been unable to detect such species by NMR in any reactions of Pd(0) or $PdMe_2(PR'_3)_2$ ($R'_3$ = $Ph_3$, $Ph_2Me$, $Et_3$) with $HP(O)(OR)_2$,[10] we did succeed in isolating Pt analogues (**5**), the first Pt complexes having a H−Pt−$P(O)(OR)_2$ structure.[11] Thus, upon addition of 1 equiv of $HP(O)(OEt)_2$ to $Pt(PEt_3)_3$ in $C_6D_6$ at 25 °C, the color of the solution turned from reddish brown to yellow, and monitoring of the reaction by means of $^1H$ and $^{31}P$ NMR revealed clean conversion of $Pt(PEt_3)_3$ into **5a** in 15 min. Evaporation at 25 °C/~0.5 Torr gave a yellow oil as nearly a sole product which displayed $^1H$ NMR signals centered at −5.23 ppm (H−Pt, dt, $^2J_{H-P(O)}$ = 226 Hz, $^2J_{H-P(Et)}$ = 18 Hz, $^1J_{H-Pt}$ = 737 Hz) and $^{31}P$ NMR signals at 95.1 (t, $J_{P(O)-P(Et)}$ = 33 Hz, $J_{P(O)-Pt}$ = 3288 Hz, P(O)) and 22.3 ppm (d, $J_{P(Et)-Pt}$ = 2630 Hz, P(Et)), indicative of **5a** being *trans*-$HPt[P(O)(OEt)_2](PEt_3)_2$ (eq 2).[12] Analogous complexes **5b** (R = Me)[13] and **5c** (R = Ph) appeared to be generated as well when $Pt(PEt_3)_3$ was treated with 1 equiv of $HP(O)(OMe)_2$ and $HP(O)(OPh)_2$, respectively, in $C_6D_6$, as judged by $^1H$ and $^{31}P$ NMR spectra of the reaction mixture (*i.e.*, in the presence of free phosphine[12]). To substantiate step ii, compound **5a** was heated with 2 equiv of phenylacetylene at 100 °C for 5 h. Compounds **2** and **3** were indeed formed in 63% yield (**2**/**3** ≥ 99/1), indicative of an insertion reaction having taken place.



(2)

In conclusion, this paper, which discloses the cleavage of the H−P bond and addition to acetylenes, clearly demonstrates the power of transition metal catalysis in heteroatom chemistry.

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**Supporting Information Available:** Text describing experimental details and spectral and/or analytical data of alkenylphosphonate products and complexes **5a**−**c** (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(10) When *cis*-$Me_2Pd(PPh_2Me)_2$ was treated with $HP(O)(OMe)_2$ at 25 °C overnight, *trans*-$Pd[P(O)(OMe)_2]_2(PPh_2Me)_2$ was formed; the structure was verified unambiguously by X-ray crystallography. This observation indicates a possible intermediate, $HPd[P(O)(OMe)_2](PPh_2Me)_2$, being quite reactive toward another molecule of $HP(O)(OMe)_2$. Platinum complexes $HPt[P(O)(OR)_2]_2(PEt_3)_2$ also exhibited similar reactivities toward $HP(O)(OR)_2$, but required somewhat severer conditions. Full details will be separately reported.

(11) For Rh and Ir complexes, see: (a) Duncan, J. A. S.; Hedden, D.; Roundhill, D. M.; Stephenson, T. A.; Walkinshaw, M. D. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 452. (b) Bennett, M. A.; Mitchell, T. R. B. *J. Organomet. Chem.* **1985**, *295*, 223. (c) Varshney, A.; Gray, G. M. *J. Organomet. Chem.* **1990**, *391*, 415. See also: Nakazawa, H.; Matsuoka, Y.; Nakagawa, I.; Miyoshi, K. *Organometallics* **1992**, *11*, 1385.

(12) The reaction mixture before evaporation did not exhibit $J_{H-P(Et)}$ and $J_{P(O)-P(Et)}$. This is presumably due to fast exchange of free and coordinating $PEt_3$. Since the boiling point of $PEt_3$ is low (127 °C/760 Torr), evaporation of the reaction mixture gradually strips both the solvent and $PEt_3$, and the foregoing couplings develop to become evident.

(13) When the reaction mixture obtained from $Pt(PEt_3)_3$ and $HP(O)(OMe)_2$ was evaporated for 5 h at 25 °C/~$10^{-4}$ Torr, the $^1H$ NMR signals assignable to H and $P(O)(OMe)_2$ moieties bonding to Pt disappeared, indicative of the reversibility of the oxidative addition reaction.