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LETTERS TO THE EDITOR

Synthesis of Phosphorus-Substituted Propargyl Alcohol Derivatives

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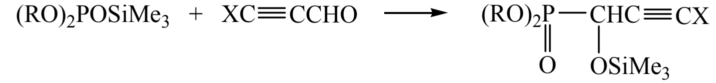
The highly reactive trimethylsilyl esters of the trivalent phosphorus acids add readily to the carbonyl group of aldehydes and ketones to form a variety of the functionalized hydroxymethyl organophosphorus compounds. The latter are of interest as potential ligands and biologically active substances [1]. In this work we describe a convenient method of the synthesis of a number of the phosphorus-substituted derivatives of propargyl alcohols using trimethylsilyl esters of the trivalent phosphorus acids and the appropriate aldehydes. Thus, silylphosphites A add readily to the carbonyl groups of propynal and phenylpropynal in a methylene chloride medium to give phosphonates **I–IV** in high yields [2].

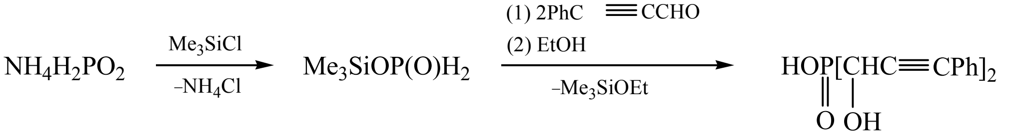


$$\underset{\textbf{A}}{(RO)_2POSiMe_3} + XC{\equiv}CCHO \longrightarrow \underset{\textbf{I–IV}}{(RO)_2\underset{\displaystyle O}{\underset{\|}{P}}{-}\underset{\displaystyle OSiMe_3}{\underset{|}{C}}HC{\equiv}CX}$$

A **I–IV**

R = Et (**I, III**), Me_3Si (**II, IV**); X = H (**I, II**), Ph (**III, IV**).

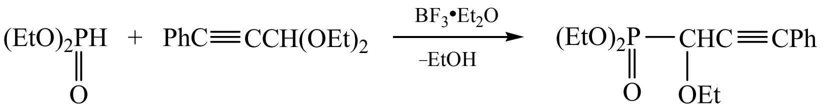
The reaction of trimethylsilylhypophosphite **B** formed from ammonium hypophosphite and trimethylchlorosilane with two equivalents of phenylpropynal in the methylene chloride medium under similar conditions followed by treating the reaction mixture with ethanol results in phosphinic acid **V** [3].



$$NH_4H_2PO_2 \xrightarrow[-NH_4Cl]{Me_3SiCl} Me_3SiOP(O)H_2 \xrightarrow[-Me_3SiOEt]{(1)\ 2PhC\equiv CCHO\quad (2)\ EtOH} HO\underset{\displaystyle O}{\underset{\|}{P}}[\underset{\displaystyle OH}{\underset{|}{C}}HC{\equiv}CPh]_2$$

B **V**

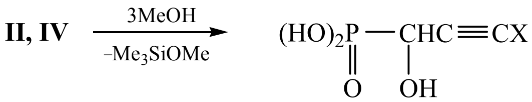
The reaction of phenylnylpropynal diethylacetal with diethyl phosphite proceeds only under heating to 170°C in the presence of boron trifluoride etherate as a catalyst to give phosphonate **VI** in 68% yield [4].



$$(EtO)_2\underset{\displaystyle O}{\underset{\|}{P}}H + PhC{\equiv}CCH(OEt)_2 \xrightarrow[-EtOH]{BF_3{\bullet}Et_2O} (EtO)_2\underset{\displaystyle O}{\underset{\|}{P}}{-}\underset{\displaystyle OEt}{\underset{|}{C}}HC{\equiv}CPh$$

VI

The reaction of phosphonates **II** or **IV** with an excess of methanol gives rise to new phosphonic acids **VII** or **VIII**, respectively, including the propargyl fragments.



$$\mathbf{II, IV} \xrightarrow[-Me_3SiOMe]{3MeOH} (HO)_2P(=O)-CH(OH)C\equiv CX$$

VII, VIII

X = H (**VII**), Ph (**VIII**).

The resulting compounds **I–VIII** contain the terminal and internal acetylene fragments and are promising synthons for generating the new types of the functionalized organophosphorus compounds. The NMR spectra of compounds **I–VIII** contain the characteristic signals of $PC^1H(OR)C^2{\equiv}C^3X$, X = H, C^4 fragments whose parameters are listed below. According to the NMR spectra compound **V** is a mixture of two stereoisomers. The stereoisomers ratio was determined by the ^{31}P NMR spectroscopy. The predominant isomer data are given the first.

Diethyl (1-trimethylsiloxyprop-2-yn-1-yl)phosphonate (I). To a solution of 21 g of diethyl(trimethylsilyl) phosphite in 20 ml of methylene chloride was added a solution of 3.8 g of propynal in 25 ml of methylene chloride under stirring and cooling to 10°C. The mixture was stirred for 0.5 h, the solvent was distilled off. The residue was distilled. Yield 2.15 g (82%), bp 112°C (2 mm Hg). ^1H NMR spectrum, δ, ppm: 4.41 d.d (C^1H, $^2J_{PH}$ 18.4, $^4J_{HH}$ 2.4 Hz), 2.51 d.d (C^3H, $^4J_{PH}$ 5.6, $^4J_{HH}$ 2.4 Hz), –0.01 s (Me_3Si), 1.1–1.5 m (2Me), 3.9–4.1 m (CH_2O). ^{13}C NMR spectrum, δ_C, ppm: 59.34 d (C^1, $^1J_{PC}$ 180.4 Hz), 78.57 d (C^2, $^2J_{PC}$ 4.0 Hz), 76.13 d (C^3, $^3J_{PC}$ 10.4 Hz), –0.29 s (Me_3Si), 16.1–16.3 m (Me), 63.4–63.7 m (CH_2O). ^{31}P NMR spectrum: δ_P 15.74 ppm. Found, %: C 45.11; H 7.92. $C_{10}H_{21}O_4PSi$. Calculated, %: C 45.44; H 8.01.

Phosphonates **II–IV** were similarly obtained.

Bis(trimethylsilyl) (1-trimethylsiloxyprop-2-yn-1-yl)phosphonate (II). Yield 84%, bp 104°C (1 mm Hg). ^1H NMR spectrum, δ, ppm: 4.02 d.d (C^1H, $^2J_{PH}$ 19.2, $^4J_{HH}$ 2.4 Hz), 2.67 d.d (C^3H, $^4J_{PH}$ 6.0, $^4J_{HH}$ 2.4 Hz), –0.17 s ($2Me_3SiOP$), –0.21 s (Me_3Si). ^{13}C NMR spectrum, δ_C, ppm: 59.16 d (C^1, $^1J_{PC}$ 187.2 Hz), 78.66 d (C^2, $^2J_{PC}$ 4.7 Hz), 75.93 d (C^3, $^3J_{PC}$ 10.2 Hz), –0.21 (Me_3Si), –0.17 (Me_3SiOP). ^{31}P NMR spectrum: δ_P –1.99 ppm. Found, %: C 40.72; H 8.18. $C_{12}H_{29}O_4PSi_3$. Calculated, %: C 40.88; H 8.29.

Diethyl (1-trimethylsiloxy-3-phenylprop-2-yn-1-yl)phosphonate (III). Yield 87%, bp 157°C (1 mm Hg). ^1H NMR spectrum, δ, ppm: 4.75 d (C^1H, $^2J_{PH}$ 18.8 Hz), 0.11 s (Me_3Si), 1.15–1.25 m (2Me), 4.0–4.2 m ($2CH_2O$), 7.1–7.3 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 60.15 d (C^1, $^1J_{PC}$ 180.4 Hz), 83.96 d (C^2, $^2J_{PC}$ 4.8 Hz), 87.46 d (C^3, $^3J_{PC}$ 10.4 Hz), 122.05 d (C^4, $^4J_{PC}$ 3.2 Hz), 128.19, 128.62 and 131.46 (C_{Ph}), 63.4–64.0 m (CH_2O), 1.20–1.25 m (Me), –0.04 (Me_3Si). ^{31}P NMR spectrum: δ_P 15.86 ppm. Found, %: C 56.12; H 7.29. $C_{16}H_{25}O_4PSi$. Calculated, %: C 56.45; H 7.40.

Bis(trimethylsilyl) (1-trimethylsiloxy-3-phenylprop-2-yn-1-yl)phosphonate (IV). Yield 85%, bp 154°C (1 mm Hg). ^1H NMR spectrum, δ, ppm: 4.63 d (C^1H, $^2J_{PH}$ 19.2 Hz), 0.09 s (Me_3Si), 0.16 s (Me_3SiOP), 7.1–7.3 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 60.72 d (C^1, $^1J_{PC}$ 187.5 Hz), 85.65 d (C^2, $^2J_{PC}$ 4.7 Hz), 87.01 d (C^3, $^3J_{PC}$ 10.4 Hz), 122.30 d (C^4, $^4J_{PC}$ 3.2 Hz), 128.18, 128.44 and 131.35 (C_{Ph}), 0.04 (Me_3Si), 0.84 (Me_3SiOP). ^{31}P NMR spectrum: δ_P –1.48 ppm. Found, %: C 50.26; H 7.69. $C_{18}H_{33}O_4PSi_3$. Calculated, %: C 50.43; H 7.76.

Bis(1-hydroxy-3-phenylprop-2-yn-1-yl)phosphinic acid (V). A mixture of 2.9 g of ammonium hypophosphite, 9.2 g of phenylpropynal, 10 g of trimethylchlorosilane in 30 ml of methylene chloride was boiled with stirring for 1 h. Then ammonium chloride was filtered off, the solvent was distilled off. To the residue was added 30 ml of ethanol. After the mixture was heated to reflux, ethanol was removed. The residue was washed with 10 ml of diethyl ether and kept in a vacuum of 1 mm Hg for 1 h. Yield 8.4 g (74%), viscous oil. The first isomer, content 70%. ^1H NMR spectrum, δ, ppm: 4.77 d (C^1H, $^2J_{PH}$ 14.0 Hz), 7.3–7.5 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 61.23 d (C^1, $^1J_{PC}$ 111.7 Hz), 85.25 d (C^2, $^2J_{PC} < 1$ Hz), 87.63 d (C^3, $^3J_{PC}$ 8.8 Hz), 126.63 d (C^4, $^4J_{PC} < 1$ Hz), 128.93, 129.39 and 131.78 (C_{Ph}). ^{31}P NMR spectrum: δ_P 24.98 ppm. The second isomer. ^1H NMR spectrum, δ, ppm: 5.13 d (C^1H, $^2J_{PH}$ 10.4 Hz), 7.3–7.5 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 69.18 d (C^1, $^1J_{PC}$ 111.0 Hz), 85.15 d (C^2, $^2J_{PC} < 1$ Hz), 87.28 d (C^3, $^3J_{PC}$ 7.9 Hz), 127.38 d (C^4, $^4J_{PC} < 1$ Hz), 128.87, 129.13 and 131.86 (C_{Ph}). ^{31}P NMR spectrum: δ_P 26.87 ppm. Found, %: C 65.98; H 4.57. $C_{18}H_{15}O_4P$. CAlculated, %: C 66.26; H 4.63.

Diethyl (1-ethoxy-3-phenylprop-2-yn-1-yl)phosphonate (VI). A mixture of 8.3 g of diethyl phosphate, 4.1 g of phenylpropynal diethylacetal and 0.6 g of boron trifluoride etherate was heated at 160–170°C with ethanol distilling off. After removing ethanol, the residue was distilled. Yield 4 g (68%), bp 159°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 4.57 d (C^1H, $^2J_{PH}$ 19.2 Hz), 1.12 t (Me, $^3J_{HH}$ 7.2 Hz), 1.19–1.24 s ($\underline{Me}CH_2OP$), 4.0–4.3 m (CH_2O, CH_2OP), 7.1–7.3 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 65.91 d (C^1, $^1J_{PC}$ 174.8 Hz), 81.69 d (C^2, $^2J_{PC}$ 4.0 Hz), 87.93 d (C^3, $^3J_{PC}$ 9.6 Hz), 121.53 d (C^4, $^4J_{PC}$ 2.3 Hz), 14.3–14.5 m (Me), 15.8–16.0 m ($\underline{Me}CH_2OP$), 63.0–63.3 m (CH_2OP), 65.64 d (CH_2O, $^3J_{PC}$ 11.9 Hz), 127.93, 128.40 and 131.20 (C_{Ph}). ^{31}P NMR spectrum: δ_P 14.79 ppm. Found, %: C 60.64; H 7.02. $C_{15}H_{21}O_4P$. Calculated, %: C 60.80; H 7.14.

(1-Hydroxyprop-2-yn-1-yl)phosphonic acid (VII). A mixture of 10 g of phosphonate **II** and 50 ml of methanol was heated to reflux. Then the solvent was removed, and the residue was kept in a vacuum of 1 mm Hg for 1 h. Yield 95% (3.7 g), viscous oil. ^{1}H NMR spectrum, δ, ppm: 4.54 d.d (C^1H, $^2J_{PH}$ 17.6, $^4J_{HH}$ 2.6 Hz), 2.97 d.d (C^3H, $^4J_{PH}$ 5.2, $^4J_{HH}$ 2.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 58.12 d (C^1, $^1J_{PC}$ 168.5 Hz), 78.77 d (C^2, $^2J_{PC}$ 3.1 Hz), 76.21 d (C^3, $^3J_{PC}$ 9.6 Hz). ^{31}P NMR spectrum: δ_P 16.50 ppm. Found, %: C 26.28; H 3.65. $C_3H_5O_4P$. Calculated, %: C 26.48; H 3.71.

Acid **VIII** was obtained similarly.

(1-Hydroxy-3-phenylprop-2-yn-1-yl)phosphonic acid (VIII). Yield 97%, viscous oil. ^{1}H NMR spectrum, δ, ppm: 4.63 d (C^1H, $^2J_{PH}$ 17.2 Hz), 7.2–7.5 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 59.39 d (C^1, $^1J_{PC}$ 169.3 Hz), 84.69 d (C^2, $^2J_{PC}$ 3.2 Hz), 86.53 d (C^3, $^3J_{PC}$ 9.6 Hz), 122.41 d (C^4, $^4J_{PC} < 1$ Hz), 128.25, 128.58 and 131.52 (C_{Ph}). ^{31}P NMR spectrum: δ_P 17.03 ppm. Found, %: C 50.78; H 4.22. $C_9H_9O_4P$. Calculated, %: C 50.96; H 4.28.

The NMR spectra were taken on a Bruker Avance 400 spectrometer using $CDCl_3$ (**I–IV, VI**), $(CD_3)_2SO$ (**V**) or CD_3OD (**VII, VIII**) as a solvent and TMS (^{1}H, ^{13}C) or 85% H_3PO_4 in D_2O (^{31}P) as a reference.

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