ISSN 1070-4280, Russian Journal of Organic Chemistry, 2010, Vol. 46, No. 7, pp. 1105–1107. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © D.A. Tatarinov, V.F. Mironov, T.A. Baronova, A.A. Kostin, B.I. Buzykin, 2010, published in Zhurnal Organicheskoi Khimii, 2010, Vol. 46, No. 7, pp. 1103–1104.

SHORT COMMUNICATIONS

A Simple Synthetic Approach to Unsymmetrically Substituted (γ-Oxoalkyl)phosphine Oxides

D. A. Tatarinov, V. F. Mironov, T. A. Baronova, A. A. Kostin, and B. I. Buzykin

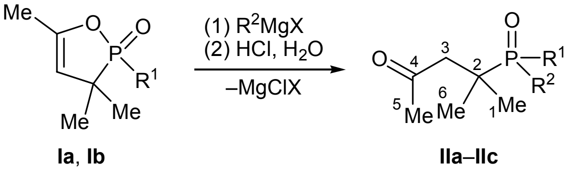
Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center, Russian Academy of Sciences, ul. Arbuzova 8, Kazan, 420088 Tatarstan, Russia
e-mail: mironov@iopc.knc.ru

Received June 25, 2009

DOI: 10.1134/S1070428010070298

Phosphine oxides and phosphines having a chiral phosphorus atom, including optically active compounds, are successfully used as ligands for metal-complex catalysts in organic and asymmetric synthesis [1–3]; some derivatives are known as pesticides and biologically active substances [4]. However, more extensive application of these compounds is seriously limited due to complexity of methods for the preparation of phosphine oxides and phosphines with three different substituents, especially with those containing additional functional groups. Taking into account continuously growing demands for such compounds, development of accessible procedures for their synthesis remains to be important (see, e.g., [3–7]). Most known procedures require the use of expensive reagents and are complex and laborious; isolation of intermediate and final products is often difficult. Either racemates are obtained with subsequent optical resolution or stereoselective syntheses are necessary.

We proposed a new and simple synthetic approach to unsymmetrically substituted phosphine oxides containing an oxo group as additional functional substituent in the γ-position with respect to the phosphorus atom. This approach is based on the reaction of accessible phosphorus-containing heterocycles having two P–C bonds, in particular 2-alkyl(aryl)-3,3,5-trimethyl-2,3-dihydro-1,2λ^5-oxaphosphole 2-oxides like **I** [8–11], with Grignard compounds. Hydrolysis of the reaction mixture gives targeted (1-methyl-4-oxopent-2-yl)phosphine oxides **II** in more than 95% yield. Due to specific structure of the initial dihydrophosphole oxides (they possess one exo- and one endocyclic P–C bond and reactive endocyclic P–O bond), the third P–C bond is formed with high chemoselectivity with no any side process. As a result, the products are formed in high yields and with high purity. The structure of phosphine oxides **II** thus obtained was confirmed by IR, ^{1}H, ^{31}P, and ^{13}C NMR, and mass spectra.



I, R^1 = Me (**a**), Ph (**b**); **II**, R^1 = Me, R^2 = Et (**a**), Pr (**b**); R^1 = Ph, R^2 = $PhCH_2$ (**c**).

4-[Ethyl(methyl)phosphoryl]-4-methylpentan-2-one (IIa). Compound **Ia**, 5.7 g (35.6 mmol), was added dropwise to the Grignard compound prepared according to standard procedure from 1.3 g (54.2 mmol) of magnesium and 4.1 ml (5.9 g, 54.2 mmol) of ethyl bromide in 100 ml of diethyl ether. When the addition was complete, the mixture was heated to the boiling point under vigorous stirring over a period of 1 h, cooled to 20°C, and neutralized under vigorous stirring at the boiling point by adding in succession 30 ml of water and 5 ml of hydrochloric acid. The organic phase was separated, the aqueous phase was extracted with methylene chloride (2× 100 ml), the extracts were combined with the organic phase, the solvent was distilled off, and the residue was dried under reduced pressure (12 mm) at 100°C. Yield 6.6 g (98%), light brown oily substance. IR spectrum, cm^{-1}: 3416, 2972, 2940, 2920, 2881, 2351, 2303, 1713, 1555, 1466, 1420, 1383, 1363, 1298, 1267, 1240, 1172, 1144, 1032, 1014, 944, 878, 780, 718, 700, 658, 626, 585, 564, 526, 482, 460. ^{1}H NMR spectrum, δ, ppm: 1.17 d (3H, CH_3, $^3J_{PH}$ = 16.0 Hz), 1.22 d (3H, CH_3, $^3J_{PH}$ = 15.9 Hz), 1.54 d (3H, CH_3, $^3J_{PH}$ = 11.4 Hz), 1.7–2.0 m (2H, PCH_2, *AB* part of *ABM*$_3$*X* spin system), 2.12 s (3H, CH_3), 2.78 d (2H, CH_2, $^3J_{PH}$ = 10.2 Hz). ^{13}C NMR spectrum, δ_C, ppm (hereinafter the multiplicity of signal in the proton-decoupled spectrum is given in parentheses: 5.90 q.d (d), ($\mathbf{C}H_3CH_2$, $^1J_{CH}$ = 129.1–129.7, $^2J_{CP}$ = 5.4 Hz), 8.95 q.d (d) (PCH_3, $^1J_{CP}$ = 63.7, $^1J_{CH}$ = 129.2 Hz), 17.75 t.d.m (d), (PCH_2, $^1J_{CP}$ = 65.5, $^1J_{CH}$ = 128.0 Hz), 21.08 q.m (d), (C^1, C^6, $^2J_{CP}$ = 10.2, $^1J_{CH}$ = 129.0–129.5 Hz), 32.46 q (s) (C^5, $^1J_{CH}$ = 128.0 Hz), 34.07 d.m (d) (C^2, $^1J_{CP}$ = 67.2 Hz), 47.79 br.t (s) (C^3, $^1J_{CH}$ = 125.0 Hz), 206.99 d.m (d) (C^4, $^3J_{CP}$ = 12.01 Hz). ^{31}P–{^{1}H} NMR spectrum: δ_P 56.3 ppm. Mass spectrum: *m*/*z* 191 [*M* + H]$^{+\cdot}$. Found, %: C 56.75; H 10.15; P 16.28. $C_9H_{19}O_2P$. Calculated, %: C 56.83; H 10.07; P 16.28.

Compounds **IIb** and **IIc** were synthesized in a similar way.

4-Methyl-4-[methyl(propyl)phosphoryl]pentan-2-one (IIb) was synthesized from compound **Ia** and propylmagnesium bromide. Yield 95%, light yellow thick oily substance. IR spectrum, cm^{-1}: 3040, 2966, 2936, 2876, 1713, 1466, 1421, 1383, 1363, 1298, 1170, 1144, 1076, 946, 907, 875, 833, 769, 730, 626, 565, 526, 463, 445. ^{1}H NMR spectrum, δ, ppm: 1.17 d (3H, CH_3, $^3J_{PH}$ = 16.0 Hz), 1.22 d (3H, CH_3, $^3J_{PH}$ = 15.9 Hz), 1.50 d (3H, CH_3, $^3J_{PH}$ = 11.8 Hz), 1.7–1.8 m (2H, PCH_2, *AB* part of *ABM*$_2$*X* spin system), 2.01 s (3H, CH_3), 2.64 d (2H, CH_2, $^3J_{PH}$ = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 8.39 br.q.d (d) (PCH_3, $^1J_{CH}$ = 130.6, $^1J_{CP}$ = 62.1 Hz), 14.78 br.t.m (br.s) ($CH_3\mathbf{C}H_2$, $^1J_{CH}$ = 128.0 Hz), 15.05 br.q.m (d) ($\mathbf{C}H_3CH_2$, $^1J_{CH}$ = 125.1, $^3J_{CP}$ = 12.0 Hz), 20.41 br.q.m (s) (C^1, C^6, $^1J_{CH}$ = 128.7 Hz), 25.50 br.t.d.m (d) (PCH_2, $^1J_{CH}$ = 128.0, $^1J_{CP}$ = 62.4 Hz), 31.63 q (s) (C^2, $^1J_{CH}$ = 127.4 Hz), 33.63 br.d.m (d) (C^5, $^1J_{CP}$ = 64.7 Hz), 47.01 br.t (s) (C^3, $^1J_{CH}$ = 126.1 Hz), 205.80 m (d) (C^4, $^3J_{CP}$ = 12.0, $^2J_{CH}$ = 5.5–5.7, 5.5–5.7 Hz). ^{31}P–{^{1}H} NMR spectrum: δ_P 55.3 ppm. Mass spectrum: *m*/*z* 205 [*M* + H]$^{+\cdot}$. Found, %: C 59.0; H 10.16; P 15.31. $C_{10}H_{21}O_2P$. Calculated, %: C 58.80; H 10.36; P 15.16.

4-[Benzyl(phenyl)phosphoryl]-4-methylpentan-2-one (IIc) was synthesized from compound **Ib** and benzylmagnesium chloride. Yield 96%, mp 114°C. IR spectrum, cm^{-1}: 2953, 2924, 2854, 1705, 1602, 1495, 1463, 1437, 1377, 1355, 1307, 1240, 1200, 1177, 1154, 1137, 1109, 1073, 1032, 942, 824, 770, 747, 698, 675, 600, 557, 505, 486, 460. ^{1}H NMR spectrum, δ, ppm: 1.23 d (3H, CH_3, $^3J_{PH}$ = 15.8 Hz), 1.40 d (3H, CH_3, $^3J_{PH}$ = 15.6 Hz), 2.08 s (3H, CH_3,), 2.51 d.d (1H, PCH_2, part *A* of *ABX* spin system, $^2J_{AB}$ = 16.0, $^2J_{PH}$ = 8.9 Hz), 2.7 d.d (1H, PCH_2, part *B* of *ABX* spin system, $^2J_{AB}$ = 16.0, $^2J_{PH}$ = 7.9 Hz), 3.43 d.d (1H, CH_2, part *A* of *ABX* spin system, $^2J_{AB}$ = 14.9, $^3J_{PH}$ = 9.2 Hz), 3.57 d.d (1H, CH_2, part *B* of *ABX* spin system, $^2J_{AB}$ = 14.9, $^3J_{PH}$ = 14.9 Hz), 7.12 m (1H, 3-H, $^3J_{HH}$ = 7.5–7.3 Hz), 7.17 m (2H, 2-H, $^3J_{HH}$ = 7.5–7.8, 7.3–7.5 Hz), 7.25 m (2H, 1-H, $^3J_{HH}$ = 7.5–7.8 Hz), 7.42 m (2H, 5-H, $^5J_{PH}$ = 2.5, $^3J_{HH}$ = 8.5, 7.4 Hz), 7.47 m (1H, 6-H, $^3J_{HH}$ = 7.4, ^4J = 1.2 Hz), 7.71 m (2H, 4-H, $^3J_{PH}$ = 9.8, $^3J_{HH}$ = 8.5, $^4J_{HH}$ = 1.3 Hz). ^{31}P–{^{1}H} NMR spectrum: δ_P 51.3 ppm. Mass spectrum: *m*/*z* 314 [*M*]$^{+\cdot}$. Found, %: C 72.59; H 7.37; P 9.85. $C_{19}H_{23}O_2P$. Calculated, %: C 72.59; H 7.37; P 9.85.

The IR spectra were measured on a Bruker Vector-22 instrument from samples dispersed in mineral oil or from films between KBr plates. The NMR spectra were recorded on Bruker Avance-600 (600 MHz for ^{1}H and 150.9 MHz for ^{13}C; internal reference HMDS or solvent signal) and Bruker CXP-100 (^{31}P, 36.48 MHz; external reference H_3PO_4) using $CDCl_3$ as solvent. The mass spectra (electron impact, 70 eV) were obtained on a TRACE MS Finnigan MAT mass spectrometer (ion source temperature 200°C; batch inlet probe temperature programming from 35 to 150°C at a rate of 35 deg/min); the data were processed using Xcalibur program.

This study was performed under financial support by the Russian Foundation for Basic Research and ANT (project no. 09-03-97007-r_povolzh'e_a).

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