Russian Journal of General Chemistry, Vol. 74, No. 6, 2004, pp. 963–964. Translated from Zhurnal Obshchei Khimii, Vol. 74, No. 6, 2004, pp. 1043–1044.

LETTERS TO THE EDITOR

HO-Modification of Dialkyl [3-(Dialkylamino)-1-hydroxy-2,2-dimethylpropyl]phosphonates

M. B. Gazizov, R. A. Khairullin, L. R. Bagauva, G. G. Safina, R. F. Karimova, and O. G. Sinyashin

Kazan State Technological University, Kazan, Tatarstan, Russia

Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center, Russian Academy of Sciences, Kazan, Tatarstan, Russia

Received October 22, 2003

We have been the first to effect HO-modification of dialkyl [3-(dialkylamino)-1-hydroxy-2,2-dimethylpropyl]phosphonates **I** by means of acylating and trimethylsilylating agents. Treatment of compound **I** with acyl halides **II** in the presence of triethylamine leads to a smooth formation of *O*-acyl derivatives **III** with a free dialkylamino group.

$$\underset{\textbf{Ia–Ic}}{(R^1O)_2P(O)CH(OH)CMe_2CH_2NR^2_2} + \underset{\textbf{IIa–IIc}}{R^3COCl} + Et_3N \longrightarrow \underset{\textbf{IIIa–IIId}}{(R^1O)_2P(O)CH(OCOR^3)CMe_2CH_2NR^2_2} + Et3N\cdot HCl,$$

I, R^1 = R^2 = Me (a), R^1 = Et, R^2 = Me (**b**), R^1 = Me, R^2 = Et (**c**); **II**, R^3 = Me (**a**), *t*-Bu (**b**), Ph (**c**); **III**, $R^1 = R^2 = R^3$ = Me (**a**), $R^1 = R^2$ = Me, R^3 = *t*-Bu (**b**), R^1 = Et, R^2 = Me, R^3 = *t*-Bu (**c**), R^1 = Me, R^2 = Et, R^3 = Ph (**d**).

O-Trimethylsilyl derivatives **IV** were synthesized by two methods: (a) reaction of compound **I** with hexamethyldisilazane and (b) reaction of compound **I** with chlorotrimethylsilane in the presence of triethylamine.

$$\textbf{Ia, Id} \xrightarrow{Me_3SiCl + Et_3N} \underset{\textbf{IV}}{(R^1O)_2P(O)CH(OSiMe_3)CMe_3CH_2NR^2_2} + Et_3N\cdot HCl,$$

$$\textbf{Ia, Id} \xrightarrow{(Me_3Si)_2NH} \textbf{IV} + Me_3SiNH_2,$$

I, $R^1 = R^2$ = Et (**d**); **IV**, $R^1 = R^2$ = Me (**a**), E (**b**).

Acylation of compound Ib with dimethylpropanoyl chloride (IIb). A solution of 1.44 g of acid chloride **IIb** in 15 ml of absolute ether was added dropwise with stirring at 0°C under dry argon to a solution of 3.21 g of compound **Ib** and 1.21 g of triethylamine in 35 ml of absolute ether. The temperature of reaction mixture was gradually raised to 25°C, the amine salt was filtered off, the solvent was removed, and the residue was distilled in a vacuum to give 1.7 g (61%) of diethyl [3-(diethylamino)-1-(dimethylpropanoyloxy)-2,2-dimethylpropyl]phosphonate (**IIIc**), mp 84°C (0.05 mm), n_D^{20} 1.4442. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.90 s, 0.97 s (6H, CMe_2), 1.12 s (9H, CMe_3), 1.21 t, 1.25 t (6H, $POCH_2\textit{Me}$, $^3J_{HH}$ 7.5 Hz), 2.20 s (6H, NMe_2), 2.12 s, 2.30 s (2H, CH_2N), 3.75–4.20 m (4H, $POCH_2$), 5.21 d (1H, PCH, $^2J_{PH}$ 8.75 Hz). Found, %: N 3.87, P 8.66. $C_{16}H_{34}\cdot NO_5P$. Calculated, %: N 3.98; P 8.81.

Dimethyl [3-(dimethylamino)-1-(dimethylpropanoyloxy)-2,2-dimethylpropyl]phosphonate (IIIb) was obtained in 55% yield from 1.51 g of acid chlo-

1070-3632/04/7406-0963

ride **IIb**, 3 g of compound **Ia**, and 1.27 g of triethylamine. n_D^{20} 1.4487. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.87 s, 0.92 s (6H, CMe_2), 1.12 s (6H, CMe_2), 1.12 s (9H, CMe_3), 2.1 s, 2.2 s (2H, CH_2N), 2.2 s (6H, NMe_3), 3.63 d, 3.60 d (6H, POMe, $^3J_{PH}$ 11.2 Hz), 5.25 d (1H, PCH, $^2J_{PH}$ 9.0 Hz). Found, %: N 4.28, P 9.71. $C_{14}H_{30}NO_5P$. Calculated, %: N 4.33, P 9.60.

Dimethyl [3-(dimethylamino)-2,2-dimethyl-1-(ethanoyloxy)propyl]phosphonate (IIIa) was prepared in 85% yield from 0.63 g of ethanoyl chloride **IIa**, 1.92 g of compound **Ia** and 0.81 g of triethylamine, n_D^{20} 1.4507. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.85 s, 0.90 s (6H, CMe_2), 2.01 s (3H, MeCO), 2.1 s, 2.2 s (2H, CH_2N), 2.2 s (6H, NMe_2), 3.60 d, 3.63 d (6H, POMe, $^3J_{PH}$ 11.2 Hz), 5.25 d (1H, PCH, $^2J_{PH}$ 9.0 Hz). Found, %: N 4.81, P 10.87. $C_{11}H_{24}NO_5P$. Calculated, %: N 4.98, P 11.03.

Dimethyl [1-(benzenecarbonyloxy)-3-(diethylamino)-2,2-dimethylpropyl]phosphonate (IIId) was obtained in 58% yield from 2.11 g of acid chloride **IIb**, 4 g of compound **Ib**, and 1.51 g of triethylamine. n_D^{20} 1.5044. ^{1}H NMR spectrum, acetone-d_6, δ, ppm: 0.87 t (6H, NCH_2Me, $^3J_{HH}$ 7.0 Hz), 1.00 s, 1.02 s (6H, CMe_2), 2.37 s, 2.45 s (2H, CH_2N), 2.5 q (4H, NCH_2Me, $^3J_{HH}$ 7.0 Hz), 3.60 d, 3.64 d (6H, POMe, $^3J_{PH}$ 11.2 Hz), 5.4 d (1H, PCH_2, $^2J_{PH}$ 8.75 Hz), 7.2–8.1 m (5H, Ph). Found, %: N 3.64, P 8.23. $C_{18}H_{30}NO_5P$. Calculated, %: N 3.77, P 8.35.

O-Trimethylsilylation of compound (Ia). *a*. Chlorotrimethylsilane, 2.87 g, was added dropwise with stirring to a solution of 5.25 g of compound **Ia** and 2.67 g of triethylamine in 35 ml of dry benzene at 10°C under dry nitrogen. The reaction mixture was gradually heated to 50°C and stirred at this temperature for 1 h. The amine salt was filtered off, the benzene was removed, and the residue was distilled in a vacuum to give 4.96 g (80%) of dimethyl [2,2-dimethyl-3-(dimethylamino)-1-(trimethylsiloxy)propyl]-phosphonate (**IVa**), bp 77–78°C (0.05 mm Hg), n_D^{20} 1.4492.

b. A mixture of 4.37 g of compound **Ia** and 3.84 g of hexamethyldisilazane was refluxed for 4 h at the bath temperature 80–90°C. Vacuum distillation gave 3.86 g (67%) of product **IVa**, bp 77°C (0.05 mm Hg), n_D^{20} 1.4487. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.01 s (9H, $SiMe_3$). 0.85 s (6H, CMe_2), 2.15 s, 2.25 s (2H, CH_2N), 3.60 d, 3.62 d (6H, POMe, $^3J_{PH}$ 10.75 Hz), 3.85 d (1H, PCH, $^2J_{PH}$ 6.25 Hz). Found, %: N 4.83. P 10.91. $C_{12}H_{30}NO_4PSi$. Calculated, %: N 4.98, P 11.03.

Diethyl [3-(diethylamino)-2,2-dimethyl-1-(trimethylsiloxy)propyl]phosphonate (IVb). *a*. The compound was prepared in 66% yield from 4.72 g of compound **Id**, 1.74 g of chlorotrimethylsilane, and 1.62 g of triethylamine. bp 83–85°C (0.08 mm Hg), n_D^{20} 1.4487.

b. The compound was prepared in 68% yield from 4 g of compound **Id** and 2.19 g of hexamethyldisilazane. bp 87°C (0.058 mm Hg), n_D^{20} 1.4473. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 0.87 s (6H, CMe_2), 0.91 t (6H, $NCH_2\mathit{Me}$, $^3J_{HH}$ 6.75 Hz), 1.25 t (4H, $OCH_2\mathit{Me}$, $^3J_{HH}$ 7.5 Hz), 2.5 q (4H, $NC\mathit{H}_2Me$, $^3J_{HH}$ 6.75 Hz), 3.75 d (1H, PCH, $^2J_{PH}$ 6.5 Hz), 4.01 q (4H, $PO\mathit{CH}_2$, $^3J_{PH} = {}^3J_{HH}$ 7.5 Hz), the signals of CH_2N and $NC\mathit{H}_2Me$ protons overlap, but the total intensity of the signal corresponds to six protons. Found, %: N 3.64, P 8.51. $C_{16}H_{38}NO_4PSi$. Calculated, %:N 3.81, P 8.45.

The ^{1}H NMR spectra were recorded on Bruker WP-80 (80 MHz) and Tesla BS-567A (100 MHz) spectrometers against internal TMS.