

## LETTERS TO THE EDITOR

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

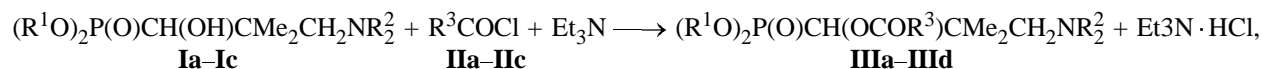
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We have been the first to effect HO-modification of dialkyl [3-(dialkylamino)-1-hydroxy-2,2-dimethylpropyl]phosphonates **I** by means of acylating and tri-

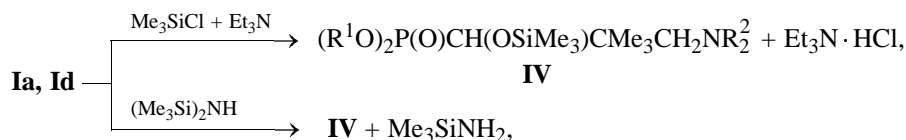
methylsilylating agents. Treatment of compound **I** with acyl halides **II** in the presence of triethylamine leads to a smooth formation of *O*-acyl derivatives **III** with a free dialkylamino group.



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

*O*-Trimethylsilyl derivatives **IV** were synthesized by two methods: (a) reaction of compound **I** with hexa-

methyldisilazane and (b) reaction of compound **I** with chlorotrimethylsilane in the presence of triethylamine.



**I**,  $R^1 = R^2 = \text{Et}$  (**d**); **IV**,  $R^1 = R^2 = \text{Me}$  (**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.  $^1\text{H}$  NMR spectrum (acetone- $d_6$ ),  $\delta$ , ppm: 0.90 s, 0.97 s (6H,  $\text{CMe}_2$ ), 1.12 s (9H,  $\text{CMe}_3$ ), 1.21 t, 1.25 t (6H,  $\text{POCH}_2\text{Me}$ ,  $^3J_{\text{HH}}$  7.5 Hz), 2.20 s (6H,  $\text{NMe}_2$ ), 2.12 s, 2.30 s (2H,  $\text{CH}_2\text{N}$ ), 3.75–4.20 m (4H,  $\text{POCH}_2$ ), 5.21 d (1H,  $\text{PCH}$ ,  $^2J_{\text{PH}}$  8.75 Hz). Found, %: N 3.87, P 8.66.  $\text{C}_{16}\text{H}_{34}\text{NO}_5\text{P}$ . 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-

ride **Ib**, 3 g of compound **Ia**, and 1.27 g of triethylamine.  $n_D^{20}$  1.4487.  $^1\text{H}$  NMR spectrum (acetone- $d_6$ ),  $\delta$ , ppm: 0.87 s, 0.92 s (6H,  $\text{CMe}_2$ ), 1.12 s (6H,  $\text{CMe}_2$ ), 1.12 s (9H,  $\text{CMe}_3$ ), 2.1 s, 2.2 s (2H,  $\text{CH}_2\text{N}$ ), 2.2 s (6H,  $\text{NMe}_3$ ), 3.63 d, 3.60 d (6H,  $\text{POMe}$ ,  $^3J_{\text{PH}}$  11.2 Hz), 5.25 d (1H,  $\text{PCH}$ ,  $^2J_{\text{PH}}$  9.0 Hz). Found, %: N 4.28, P 9.71.  $\text{C}_{14}\text{H}_{30}\text{NO}_5\text{P}$ . 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 **Ia**, 1.92 g of compound **Ia** and 0.81 g of triethylamine,  $n_D^{20}$  1.4507.  $^1\text{H}$  NMR spectrum (acetone- $d_6$ ),  $\delta$ , ppm: 0.85 s, 0.90 s (6H,  $\text{CMe}_2$ ), 2.01 s (3H,  $\text{MeCO}$ ), 2.1 s, 2.2 s (2H,  $\text{CH}_2\text{N}$ ), 2.2 s (6H,  $\text{NMe}_2$ ), 3.60 d, 3.63 d (6H,  $\text{POMe}$ ,  $^3J_{\text{PH}}$  11.2 Hz), 5.25 d (1H,  $\text{PCH}$ ,  $^2J_{\text{PH}}$  9.0 Hz). Found, %: N 4.81, P 10.87.  $\text{C}_{11}\text{H}_{24}\text{NO}_5\text{P}$ . 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 **Ib**, 4 g of compound **Ib**, and 1.51 g of triethylamine.  $n_D^{20}$  1.5044.  $^1\text{H}$  NMR spectrum, acetone- $d_6$ ,  $\delta$ , ppm: 0.87 t (6H,  $\text{NCH}_2\text{Me}$ ,  $^3J_{\text{HH}}$  7.0 Hz), 1.00 s, 1.02 s (6H,  $\text{CMe}_2$ ), 2.37 s, 2.45 s (2H,  $\text{CH}_2\text{N}$ ), 2.5 q (4H,  $\text{NCH}_2\text{Me}$ ,  $^3J_{\text{HH}}$  7.0 Hz), 3.60 d, 3.64 d (6H,  $\text{POMe}$ ,  $^3J_{\text{PH}}$  11.2 Hz), 5.4 d (1H,  $\text{PCH}_2$ ,  $^2J_{\text{PH}}$  8.75 Hz), 7.2–8.1 m (5H, Ph). Found, %: N 3.64, P 8.23.  $\text{C}_{18}\text{H}_{30}\text{NO}_5\text{P}$ . 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.  $^1\text{H}$  NMR spectrum (acetone- $d_6$ ),  $\delta$ , ppm: 0.01 s (9H,  $\text{SiMe}_3$ ), 0.85 s (6H,  $\text{CMe}_2$ ), 2.15 s, 2.25 s (2H,  $\text{CH}_2\text{N}$ ), 3.60 d, 3.62 d (6H,  $\text{POMe}$ ,  $^3J_{\text{PH}}$  10.75 Hz), 3.85 d (1H,  $\text{PCH}$ ,  $^2J_{\text{PH}}$  6.25 Hz). Found, %: N 4.83, P 10.91.  $\text{C}_{12}\text{H}_{30}\text{NO}_4\text{PSi}$ . 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.  $^1\text{H}$  NMR spectrum (acetone- $d_6$ ),  $\delta$ , ppm: 0.87 s (6H,  $\text{CMe}_2$ ), 0.91 t (6H,  $\text{NCH}_2\text{Me}$ ,  $^3J_{\text{HH}}$  6.75 Hz), 1.25 t (4H,  $\text{OCH}_2\text{Me}$ ,  $^3J_{\text{HH}}$  7.5 Hz), 2.5 q (4H,  $\text{NCH}_2\text{Me}$ ,  $^3J_{\text{HH}}$  6.75 Hz), 3.75 d (1H,  $\text{PCH}$ ,  $^2J_{\text{PH}}$  6.5 Hz), 4.01 q (4H,  $\text{POCH}_2$ ,  $^3J_{\text{PH}} = ^3J_{\text{HH}}$  7.5 Hz), the signals of  $\text{CH}_2\text{N}$  and  $\text{NCH}_2\text{Me}$  protons overlap, but the total intensity of the signal corresponds to six protons. Found, %: N 3.64, P 8.51.  $\text{C}_{16}\text{H}_{38}\text{NO}_4\text{PSi}$ . Calculated, %: N 3.81, P 8.45.

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