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LETTERS TO THE EDITOR

Synthesis of Phosphorus-Substituted Derivatives of Methylsuccinic Acid

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Trimethylsilyl esters of various phosphonous acids obtained by the addition of bis(trimethylsiloxy)phosphine to esters of unsaturated carboxylic acids are convenient starting compounds for preparing functionalized phosphinates containing carboxy groups [1]. In this work we developed synthetic methods for preparing phosphorus-substituted derivatives of methylsuccinic acid. These substances are of interest as polydentate ligands and biologically active compounds. For example, bis(trimethylsiloxy)phosphine exothermally adds to dialkyl itaconates (methylenesuccinates) to give phosphonites **I** containing fragments of methylsuccinic acid (cf. [2]).

$$(Me_3SiO)_2PH + CH_2{=}C(COOX)CH_2COOX \longrightarrow (Me_3SiO)_2PCH_2CH(COOX)CH_2COOX,$$

Ia, Ib

X = Me (**a**), Me_3Si (**b**).

Diethyl hydrogen phosphite adds to dimethyl itaconate only in the presence of sodium diethyl phosphite at elevated temperature to give phosphonate **II** in high yield.

$$(EtO)_2\overset{\overset{O}{\|}}{P}H + CH_2{=}C(COOMe)CH_2COOMe \longrightarrow (EtO)_2\overset{\overset{O}{\|}}{P}CH_2CH(COOMe)CH_2COOMe.$$

II

Phosphonites **I** readily react with (chloromethyl)dimethylamine to give phosphinates **III** containing aminomethyl fragments together with the fragments of methylsuccinic acid.

Treatment of phosphonites **I** with dilute solutions of sodium methylate in methanol yields water-soluble

$$\mathbf{I} \xrightarrow[-Me_3SiCl]{ClCH_2NMe_2} Me_3SiO\overset{\overset{O}{\|}}{P}\begin{matrix}CH_2CH(COOX)CH_2COOX\\ CH_2NMe_2\end{matrix}$$

IIIa, IIIb

X = Me (**a**), Me_3Si (**b**).

sodium salts of phosphonous acids **IV** and **V** containing carboxy groups.

$$\mathbf{Ia} \xrightarrow[-2Me_3SiOMe]{MeONa,\ MeOH} NaO\overset{\overset{O}{\|}}{P}(H)CH_2CH(COOMe)CH_2COOMe$$

IV

$$\mathbf{Ib} \xrightarrow[-4Me_3SiOMe]{3MeONa,\ MeOH} NaO\overset{\overset{O}{\|}}{P}(H)CH_2CH(COONa)CH_2COONa$$

V

Salts **IV** and **V** are white hygroscopic crystals. The NMR spectra of **I**–**V** contain characteristic signals of the $PC^1H_2C^2H(C^5{=}O)C^3H_2C^4{=}O$ and $PC^6H_2NC^7H_3$ fragments. Their parameters are listed below. The ^1H NMR signals of these fragments partially or completely overlap. Phosphinates **III** contain asymmetric carbon and phosphorus atoms, and, according to NMR data, these compounds exist as mixtures of two stereoisomers. The spectral data for the major isomer and its content in the mixture, evaluated from the ^{31}P NMR spectra, are given first.

Bis(trimethylsilyl) 2,3-bis(methoxycarbonyl)propylphosphonite Ia. A solution of 23.7 g of dimethyl itaconate in 30 ml of methylene chloride was added dropwise with stirring at 10°C to a solution of 42 g of bis(trimethylsiloxy)phosphine in 50 ml of methylene chloride. After the completion of heat evolution, the reaction mixture was heated to boil, the solvent was distilled off, and the residue was distilled in a vacuum. Phosphonite **Ia**, 45.8 g (83%), was ob-

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tained, bp 126°C (1 mm). ^{13}C NMR spectrum, δ_C, ppm: 42.28 d (C^1, $^1J_{PC}$ 30.2 Hz), 35.00 d (C^2, $^2J_{PC}$ 11.3 Hz), 36.21 d (C^3, $^3J_{PC}$ 6.5 Hz), 171.50 s (C^4), 174.65 d (C^5, $^3J_{PC}$ 4.8 Hz). ^{31}P NMR spectrum, δ_P, ppm: 155.58 s.

Phosphonite **Ib** was prepared analogously.

Bis(trimethylsilyl) 2,3-bis(trimethylsiloxycarbonyl)propylphosphonite Ib. Yield 81%, bp 133°C (1 mm). ^{13}C NMR spectrum, δ_C, ppm: 42.46 d (C^1, $^1J_{PC}$ 30.3 Hz), 36.82 d (C^2, $^2J_{PC}$ 11.6 Hz), 38.19 d (C^3, $^3J_{PC}$ 7.2 Hz), 171.90 s (C^4), 175.07 d (C^5, $^3J_{PC}$ 5.9 Hz). ^{31}P NMR spectrum, δ_P, ppm: 156.35 s.

Diethyl 2,3-bis(methoxycarbonyl)propylphosphonate II. To a mixture of 22.1 g of diethyl hydrogen phosphite and 15.8 g of dimethyl itaconate, 0.5 g of sodium was added, and the mixture was carefully heated. After the completion of exothermic reaction, the mixture was distilled in a vacuum to give 25.5 g (86%) of phosphonate **II**, bp 139°C (1 mm), n_D^{20} 1.4395. ^{13}C NMR spectrum, δ_C, ppm: 25.86 d (C^1, $^1J_{PC}$ 141.9 Hz), 35.02 d (C^2, $^2J_{PC}$ 4.4 Hz), 34.50 d (C^3, $^3J_{PC}$ 6.4 Hz), 170.64 s (C^4), 172.51 d (C^5, $^3J_{PC}$ 13.7 Hz). ^{31}P NMR spectrum, δ_P, ppm: 25.39 s. Found, %: C 44.47; H 7.03; P 10.57. $C_{11}H_{21}O_7P$. Calculated, %: C 44.60; H 7.15; P 10.45.

Trimethylsilyl (dimethylaminomethyl)-2,3-bis(methoxycarbonyl)propylphosphinate IIIa. A solution of 2.8 g of chloromethyldimethylamine in 15 ml of methylene chloride was added dropwise with stirring at 10°C to a solution of 11 g of phosphonite **Ia** in 30 ml of methylene chloride. The mixture was allowed to warm to 20°C and then was refluxed for 15 min, the solvent was distilled off, and the residue was distilled in a vacuum. Phosphinate **IIIa**, 9.4 g (89%) was obtained, bp 141°C (1 mm), n_D^{20} 1.4590. First isomer (60% content), ^{13}C NMR spectrum, δ_C, ppm: 29.04 d (C^1, $^1J_{PC}$ 93.4 Hz), 34.73 d (C^2, $^2J_{PC}$ 3.8 Hz), 35.22 d (C^3, $^3J_{PC}$ 5.1 Hz), 170.83 s (C^4), 172.99 d (C^5, $^3J_{PC}$ 5.8 Hz), 58.27 d (C^6, $^1J_{PC}$ 115.3 Hz), 51.25 d (C^7, $^3J_{PC}$ 4.5 Hz). ^{31}P NMR spectrum, δ_P, ppm: 37.89 s. Second isomer, ^{13}C NMR spectrum, δ_C, ppm: 28.66 d (C^1, $^1J_{PC}$ 93.2 Hz), 34.98 s (C^2), 35.27 d (C^3, $^3J_{PC}$ 5.4 Hz), 170.90 s (C^4), 173.10 d (C^5, $^3J_{PC}$ 5.9 Hz), 58.70 d (C^6, $^1J_{PC}$ 115.1 Hz), 50.74 s (C^7). ^{31}P NMR spectrum, δ_P, ppm: 37.97 s.

Phosphinate **IIIb** was prepared similarly.

Trimethylsilyl (dimethylaminomethyl)-2,3-bis(trimethylsiloxycarbonyl)propylphosphinate IIIb. Yield 81%, bp 157°C (1 mm), n_D^{20} 1.4510. First isomer (55% content), ^{13}C NMR spectrum, δ_C, ppm: 28.72 d (C^1, $^1J_{PC}$ 93.4 Hz), 36.40 d (C^2, $^2J_{PC}$ 4.2 Hz), 37.14 d (C^3, $^3J_{PC}$ 3.9 Hz), 171.49 s (C^4), 173.61 d (C^5, $^3J_{PC}$ 4.2 Hz), 59.09 d (C^6, $^1J_{PC}$ 114.8 Hz), 47.25 s (C^7). ^{31}P NMR spectrum, δ_P, ppm: 38.72 s. Second isomer, ^{13}C NMR spectrum, δ_C, ppm: 29.07 d (C^1, $^1J_{PC}$ 93.6 Hz), 36.58 s (C^2), 37.60 d (C^3, $^3J_{PC}$ 4.0 Hz), 171.43 s (C^4), 173.46 d (C^5, $^3J_{PC}$ 5.1 Hz), 58.66 d (C^6, $^1J_{PC}$ 115.0 Hz), 47.15 s (C^7). ^{31}P NMR spectrum, δ_P, ppm: 38.57 s.

Sodium 2,3-bis(methoxycarbonyl)propylphosphonite IV. A solution of 14.7 g of phosphonite **Ia** in 10 ml of ether was added with stirring at 10°C to a solution of 2.2 g of sodium methylate in 50 ml of methanol. The resulting mixture was heated to boil, the solvent was removed, and the residue was kept in a vacuum at 1 mm for 1 h. Salt **IV**, 9.3 g (94%), was obtained. ^1H NMR spectrum, δ, ppm: 7.0 d.t (PH, $^1J_{PH}$ 515.2, $^3J_{HH}$ 1.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 33.58 d (C^1, $^1J_{PC}$ 88.1 Hz), 36.51 s (C^2), 36.99 d (C^3, $^3J_{PC}$ 8.3 Hz), 174.86 s (C^4), 177.32 d (C^5, $^3J_{PC}$ 9.1 Hz). ^{31}P NMR spectrum, δ_P, ppm: 21.81 s. Found, %: C 33.97; H 4.98. $C_7H_{12}NaO_6P$. Calculated, %: C 34.16; H 4.91.

Salt **V** was prepared similarly.

Trisodium 2,3-bis(carboxy)propylphosphonite V. Yield 96%. ^1H NMR spectrum, δ, ppm: 6.94 d.t (PH, $^1J_{PH}$ 509.2, $^3J_{HH}$ 1.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 34.95 d (C^1, $^1J_{PC}$ 89.3 Hz), 41.04 s (C^2), 42.57 d (C^3, $^3J_{PC}$ 11.4 Hz), 181.32 s (C^4), 183.57 d (C^5, $^3J_{PC}$ 7.8 Hz). ^{31}P NMR spectrum, δ_P, ppm: 25.58 s. Found, %: C 22.68; H 2.26. $C_5H_6Na_3O_6P$. Calculated, %: C 22.92; H 2.31.

The NMR spectra were obtained on a Varian VXR-400 spectrometer in $CDCl_3$ (or D_2O for salts **IV** and **V**) against TMS (^1H, ^{13}C) and 85% solution of H_3PO_4 in D_2O (^{31}P).

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