

LETTERS TO THE EDITOR

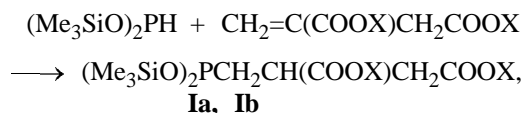
Synthesis of Phosphorus-Substituted Derivatives of Methylsuccinic Acid

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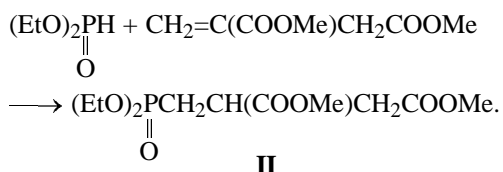
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Trimethylsilyl esters of various phosphonous acids obtained by the addition of bis(trimethylsiloxy)phosphine to esters of unsaturated carboxylic acids are convenient starting compounds for preparing functionalized phosphinates containing carboxy groups [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 (methylene-succinates) to give phosphonites **I** containing fragments of methylsuccinic acid (cf. [2]).



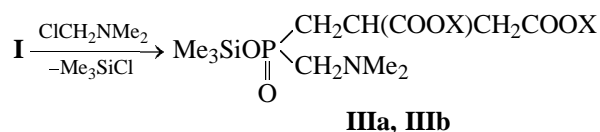
X = Me (**a**), Me₃Si (**b**).

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.



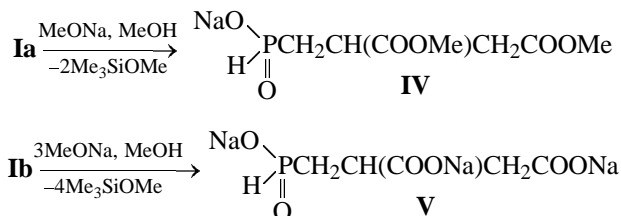
Phosphonites **I** readily react with (chloromethyl)-dimethylamine to give phosphinates **III** containing aminomethyl fragments together with the fragments of methylsuccinic acid.

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



X = Me (**a**), Me₃Si (**b**).

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



Salts **IV** and **V** are white hygroscopic crystals. The NMR spectra of **I–V** contain characteristic signals of the PC¹H₂C²H(C⁵=O)C³H₂C⁴=O and PC⁶H₂NC⁷H₃ 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 ³¹P 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-

tained, bp 126°C (1 mm). ^{13}C NMR spectrum, δ_{C} , ppm: 42.28 d (C^1 , $^1J_{\text{PC}}$ 30.2 Hz), 35.00 d (C^2 , $^2J_{\text{PC}}$ 11.3 Hz), 36.21 d (C^3 , $^3J_{\text{PC}}$ 6.5 Hz), 171.50 s (C^4), 174.65 d (C^5 , $^3J_{\text{PC}}$ 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 , $^1J_{\text{PC}}$ 30.3 Hz), 36.82 d (C^2 , $^2J_{\text{PC}}$ 11.6 Hz), 38.19 d (C^3 , $^3J_{\text{PC}}$ 7.2 Hz), 171.90 s (C^4), 175.07 d (C^5 , $^3J_{\text{PC}}$ 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 , $^1J_{\text{PC}}$ 141.9 Hz), 35.02 d (C^2 , $^2J_{\text{PC}}$ 4.4 Hz), 34.50 d (C^3 , $^3J_{\text{PC}}$ 6.4 Hz), 170.64 s (C^4), 172.51 d (C^5 , $^3J_{\text{PC}}$ 13.7 Hz). ^{31}P NMR spectrum, δ_{P} , ppm: 25.39 s. Found, %: C 44.47; H 7.03; P 10.57. $\text{C}_{11}\text{H}_{21}\text{O}_7\text{P}$. 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 , $^1J_{\text{PC}}$ 93.4 Hz), 34.73 d (C^2 , $^2J_{\text{PC}}$ 3.8 Hz), 35.22 d (C^3 , $^3J_{\text{PC}}$ 5.1 Hz), 170.83 s (C^4), 172.99 d (C^5 , $^3J_{\text{PC}}$ 5.8 Hz), 58.27 d (C^6 , $^1J_{\text{PC}}$ 115.3 Hz), 51.25 d (C^7 , $^3J_{\text{PC}}$ 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 , $^1J_{\text{PC}}$ 93.2 Hz), 34.98 s (C^2), 35.27 d (C^3 , $^3J_{\text{PC}}$ 5.4 Hz), 170.90 s (C^4), 173.10 d (C^5 , $^3J_{\text{PC}}$ 5.9 Hz), 58.70 d (C^6 , $^1J_{\text{PC}}$ 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 iso-

mer (55% content), ^{13}C NMR spectrum, δ_{C} , ppm: 28.72 d (C^1 , $^1J_{\text{PC}}$ 93.4 Hz), 36.40 d (C^2 , $^2J_{\text{PC}}$ 4.2 Hz), 37.14 d (C^3 , $^3J_{\text{PC}}$ 3.9 Hz), 171.49 s (C^4), 173.61 d (C^5 , $^3J_{\text{PC}}$ 4.2 Hz), 59.09 d (C^6 , $^1J_{\text{PC}}$ 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 , $^1J_{\text{PC}}$ 93.6 Hz), 36.58 s (C^2), 37.60 d (C^3 , $^3J_{\text{PC}}$ 4.0 Hz), 171.43 s (C^4), 173.46 d (C^5 , $^3J_{\text{PC}}$ 5.1 Hz), 58.66 d (C^6 , $^1J_{\text{PC}}$ 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, $^1J_{\text{PH}}$ 515.2, $^3J_{\text{HH}}$ 1.8 Hz). ^{13}C NMR spectrum, δ_{C} , ppm: 33.58 d (C^1 , $^1J_{\text{PC}}$ 88.1 Hz), 36.51 s (C^2), 36.99 d (C^3 , $^3J_{\text{PC}}$ 8.3 Hz), 174.86 s (C^4), 177.32 d (C^5 , $^3J_{\text{PC}}$ 9.1 Hz). ^{31}P NMR spectrum, δ_{P} , ppm: 21.81 s. Found, %: C 33.97; H 4.98. $\text{C}_7\text{H}_{12}\text{NaO}_6\text{P}$. 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, $^1J_{\text{PH}}$ 509.2, $^3J_{\text{HH}}$ 1.6 Hz). ^{13}C NMR spectrum, δ_{C} , ppm: 34.95 d (C^1 , $^1J_{\text{PC}}$ 89.3 Hz), 41.04 s (C^2), 42.57 d (C^3 , $^3J_{\text{PC}}$ 11.4 Hz), 181.32 s (C^4), 183.57 d (C^5 , $^3J_{\text{PC}}$ 7.8 Hz). ^{31}P NMR spectrum, δ_{P} , ppm: 25.58 s. Found, %: C 22.68; H 2.26. $\text{C}_5\text{H}_6\text{Na}_3\text{O}_6\text{P}$. 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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