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LETTERS TO THE EDITOR

Synthesis of Substituted Hydroxymethylene Diphosphonic Acids and Their Derivatives Containing Unsaturated Fragments

A. A. Prishchenko, M. V. Livantsov, O. P. Novikova, and L. I. Livantsova

Lomonosov Moscow State University, Vorob'evy gory, Moscow, 119991 Russia
e-mail: aprishchenko@yandex.ru

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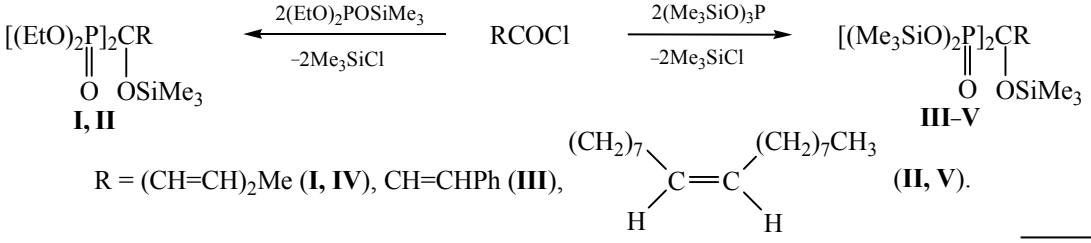
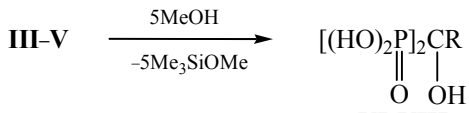
A variety of substituted hydroxymethylene diphosphonic acids derivatives comprises good complexones and the substances widely used in medicine [1]. Compounds containing hydrolytically stable hydroxymethylene diphosphonic fragment PCP are of interest as an unusual organophosphorus analogs of natural pyrophosphates [2]. We found that the reaction of trimethylsilyl esters of trivalent phosphorus with the readily accessible chlorides of unsaturated carboxylic acids affords new hydroxymethylene diphosphonic compounds containing unsaturated fragments. They may be of interest as promising complexones and antioxidants.

An excess of alkylsilylphosphite in methylene chloride solution reacts readily with unsaturated carboxylic acids chlorides to form diphosphonates **I–IV** in a high yield [3].

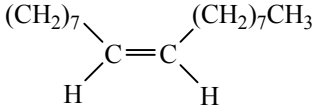


R = $(CH=CH)_2Me$ (**I, IV**), CH=CHPh (**III**), (**II, V**).

The reaction of diphosphonates **III–V** with an excess of methanol gives rise to the substituted hydroxymethylenediphosphonic acids **VI–VIII**, which are thick oils. Note that the mild conditions of the methanolysis of trimethylsilyl esters **III–V** allow retaining unchanged the methylenediphosphonic fragments in the acids **VI–VIII** [3].



R = CH=CHPh (**VI**), $(CH=CH)_2Me$ (**VII**),

 (**VIII**).

Tetraethyl (1,3-pentadien-1-yl)trimethylsiloxymethylene diphosphonate (I). To a solution of 21 g of diethyl(trimethylsilyl)phosphite in 20 ml of methylene chloride with stirring and cooling to 10°C was added a solution of 6 g of sorbinoyl chloride in 10 ml of methylene chloride. The mixture was stirred for 0.5 h and then heated to boiling. The solvent was distilled off in a vacuum; the residue was kept in a vacuum (0.5 mm Hg) for 1 h at 30°C. Yeld 19.5 g, 96%, oil. ^{1}H NMR spectrum, δ_H, ppm: 0.16 s (Me_3Si), 0.9–1.1 m ($4MeCH_2OP$), 1.37 d (C^6H_3, $^3J_{HH}$ 5.6 Hz), 3.6–3.8 m ($4CH_2OP$), 5.2–6.1 m (CH=CH). ^{13}C NMR spectrum, δ_C, ppm: 78.53 t (C^1, $^1J_{PC}$ 155.9 Hz), 132.63 t (C^2, $^2J_{PC}$ 10.1 Hz), 124.26 t (C^3, $^3J_{PC}$ 5.9 Hz), 130.36 (C^4, C^5), 17.37 (C^6). ^{31}P NMR spectrum: δ_P 15.59 ppm. Found, %: C 45.96; H 8.11. $C_{17}H_{36}O_7P_2Si$. Calculated, %: C 46.14; H 8.20.

Compounds **II–V** were obtained similarly.

Tetraethyl (8-heptadecen-1-yl)trimethylsiloxymethylene diphosphonate (II). Yield 97%, oil. ^{1}H

NMR spectrum, δ_H, ppm: –0.06 s (Me_3Si), 0.9–1.1 m ($5CH_3$, $11CH_2$), 1.25–1.40 m (C^2H_2), 1.7–1.8 m ($2CH_2C$=), 3.8–4.0 m ($4CH_2OP$), 5.0–5.1 m (CH=CH). ^{13}C NMR spectrum, δ_C, ppm: 78.66 t (C^1, $^1J_{PC}$ 155.9 Hz), 23.33 t (C^2, $^2J_{PC}$ 5 Hz), 31.58 and 35.03 ($2\underline{C}H_2CH$=), 129.46 (CH=CH). ^{31}P NMR spectrum: δ_P 19.16 ppm. Found, %: C 56.68; H 10.12. $C_{29}H_{62}O_7P_2Si$. Calculated, %: C 56.84; H 10.20.

Tetra(trimethylsilyl) (2-phenylethyl-1-yl)trimethylsiloxymethylene diphosphonate (III). Yield 96%, oil. ^1H NMR spectrum, δ_H, ppm: 0.5–1.0 m (Me_3Si), 6.19 d. t (C^3H, $^4J_{HH}$ 15.8, $^4J_{PH}$ 6.2 Hz), 6.47 d. t (C^2H, $^3J_{HH}$ 15.8, $^4J_{PH}$ 5.2 Hz), 6.8–7.1 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 79.03 t (C^1, $^1J_{PC}$ 162.6 Hz), 130.37 t (C^2, $^2J_{PC}$ 10 Hz), 126.34 t (C^3, $^3J_{PC}$ 5.8 Hz), 136.22 t (C^4, $^4J_{PC}$ < 1 Hz), 128.43 and 126.04 (C^5, C^6), 127.32 (C^7), 2.46 (Me_3SiOC), 0.95 d (Me_3SiOP, $^3J_{PC}$ 5.9 Hz). ^{31}P NMR spectrum ^{31}P: δ_P –2.58 ppm. Found, %: C 43.89; H 7.91. $C_{24}H_{52}O_7P_2Si_5$. Calculated, %: C 44.01; H 8.00.

Tetra(trimethylsilyl) (1,3-pentadien-1-yl)trimethylsiloxymethylene diphosphonate (IV). Yield 96%, oil**.** ^1H NMR spectrum, δ_H, ppm: –0.2–0.3 m (Me_3Si), 1.22 d (C^6H_3, $^3J_{HH}$ 6 Hz), 5.1–5.8 m (CH=CH). ^{13}C NMR spectrum, δ_C, ppm: 78.30 t (C^1, $^1J_{PC}$ 162.6 Hz), 131.01 t (C^2, $^2J_{PC}$ 10.9 Hz), 126.69 t (C^3, $^3J_{PC}$ 5.9 Hz), 130.28 t (C^4, $^3J_{PC}$ < 1 Hz), 129.13 (C^5), 17.55 (C^6), 2.12 ($\underline{Me}_3SiOC$), 0.64 d (Me_3SiOP, $^3J_{PC}$ 5.8 Hz). ^{31}P NMR spectrum: δ_P –2.46 ppm. Found, %: C 40.61; H 8.40. $C_{21}H_{52}O_7P_2Si_5$. Calculated, %: C 40.75; H 8.47.

Tetra(trimethylsilyl) (8-heptadecen-1-yl)trimethylsiloxymethylene diphosphonate (V). Yield 97%, oil**.** ^1H NMR spectrum, δ_H, ppm: –0.1–0.0 s (Me_3Si), 0.97 t (CH_3, $^3J_{HH}$ 6.4 Hz), 1.4–1.5 m ($11CH_2$), 1.62–1.72 m (C^2H_2), 2.05–2.15 m ($2CH_2C$=), 5.35–5.45 m (CH=CH). ^{13}C NMR spectrum, δ_C, ppm: 77.89 t (C^1, $^1J_{PC}$ 164.6 Hz), 23.37 t (C^2, $^2J_{PC}$ 5.9 Hz), 129.29 and 129.46 (CH=CH), 31.56 and 35.20 ($2\underline{C}H_2C$=), 22.31–29.91 m ($11CH_2$), 13.73 (CH_3), 2.45 ($\underline{Me}_3SiOC$), 0.96 d (Me_3SiOP, $^3J_{PC}$ 5.1 Hz),). ^{31}P NMR spectrum: δ_P 1.80 ppm. Found, %: C 50.03; H 9.88. $C_{33}H_{78}O_7P_2Si_5$. Calculated, %: C 50.21; H 9.96.

(2-Phenylethyl-1-yl)hydroxymethylene diphosphonic acid (VI). To 30 ml of methanol at 10°C under stirring was added a solution of 11 g of diphosphonate **III** in 10 ml of diethyl ether. The mixture was heated to boiling, the solvent was distilled off, the residue was kept in a vacuum (1 mm Hg) for 1 h. Yield 4.8 g, 98%, oil. ^1H NMR spectrum, δ_H, ppm: 6.95 d.t (C^2H, $^3J_{HH}$ 15.4, $^3J_{PH}$ 4.8 Hz), 6.67 d t (C^3H, $^3J_{HH}$ 15.4, $^4J_{PH}$ < 1 Hz), 7.2–7.5 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 75.79 t (C^1, $^1J_{PC}$ 149.2 Hz), 130.96 t (C^2, $^2J_{PC}$ 10 Hz), 123.47 t (C^3, $^3J_{PC}$ < 1 Hz), 136.57 (C^4), 126.45 and 128.50 (C^5, C^6), 127.69 (C^7). ^{31}P NMR spectrum: δ_P 16.12 ppm. Found, %: C 36.64; H 4.07. $C_9H_{12}O_7P_2$. Calculated, %: C 36.75; H 4.11.

Compound **VII, VIII** were obtained similarly.

(1,3-Pentadien-1-yl)hydroxymethylene diphosphonic acid (VII). Yield 97%, oil. ^1H NMR spectrum, δ_H, ppm: 5.5–6.6 m (CH=CH), 1.75 (C^6H_3). ^{13}C NMR spectrum, δ_C, ppm: 75.25 t (C^1, $^1J_{PC}$ 149.6 Hz), 131.35 t (C^2, $^2J_{PC}$ < 1 Hz), 129.58 t (C^3, $^3J_{PC}$ < 1 Hz), 131.07 (C^4), 124.27 (C^5), 17.41 (C^6). ^{31}P NMR spectrum: δ_P 16.27 ppm. Found, %: C 27.78; H 4.59. $C_6H_{12}O_7P_2$. Calculated, %: C 27.92; H 4.68.

(8-Heptadecen-1-yl)hydroxymethylene diphosphonic acid (VIII). Yield 96%, oil. ^1H NMR spectrum, δ_H, ppm: 5.5–6.6 m (CH=CH), 2.0–2.2 m ($2CH_2C$=), 1.6–1.8 m (C^2H_2), 1.1–1.4 m ($11\ CH_2$), 0.89 t (CH_3, $^3J_{HH}$ 6.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 73.18 t (C^1, $^1J_{PC}$ 147.1 Hz), 23.30 t (C^2, $^2J_{PC}$ < 1 Hz), 129.39 and 129.60 (CH=CH), 30.39 and 31.84 ($2\underline{C}H_2CH$=), 22.53–29.65 m ($11CH_2$), 13.62 (CH_3). ^{31}P NMR spectrum: δ_P 20.35 ppm. Found, %: C 50.26; H 8.86. $C_{18}H_{38}O_7P_2$. Calculated, %: C 50.46; H 8.94.

The NMR spectra were recorded on a Bruker Avance-400 spectrometer in $CDCl_3$ (**I–V**) and CD_3OD (**VI–VIII**), internal reference TMS (^1H, ^{13}C) and external reference 85% phosphoric acid solution in D_2O (^{31}P).

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