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LETTERS TO THE EDITOR

Reactions of Trimethylsilyl Esters of Trivalent Phosphorus Acids with 3,5-Di-*tert*-butyl-4-hydroxybenzoyl Chloride

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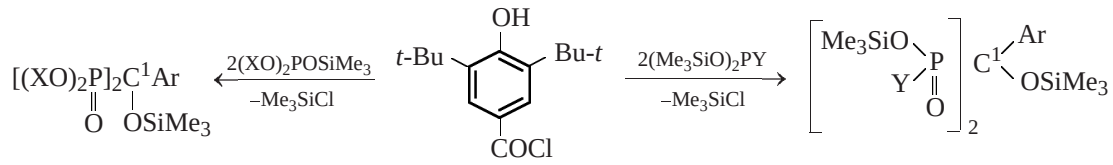
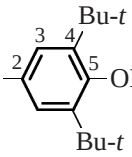
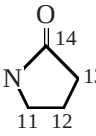
Various derivatives of substituted hydroxymethylenediphosphonic acids are good complexones and are widely used in medicine [1]. In this study we showed that the reactions of trimethylsilyl esters of trivalent phosphorus acids with readily avaliable 3,5-di-*tert*-butyl-4-hydroxybenzoyl chloride **A** [2] yield new diphosphorylated hydroxymethylene derivatives containing a sterically hindered phenolic fragment. Such compounds are of interest as promising complexones and antioxidants. For example, trimethylsilyl phosphites and functionalized trimethylsilyl phosphonites taken in excess readily react with acid chloride **A** in methylene chloride to form diphosphonates **I** and **II**, or diphosphinates **III** and **IV**, respectively, in high yields. The sterically shielded hydroxy group in acid chloride **A** does not enter into trimethylsilylation with excess trimethylsilyl phosphite or trimethylsilyl phosphonite, which was noted in our previous study of related transformations [3].



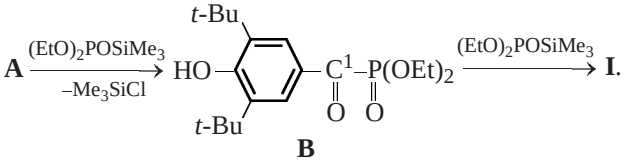
I, II **A** **III, IV**

Ar = 

, X = Et (**I**), Me_3Si (**II**); Y = $C^6H_2C^7H_2$  (**III**), $C^9H_2C^{10}H_2N$ 

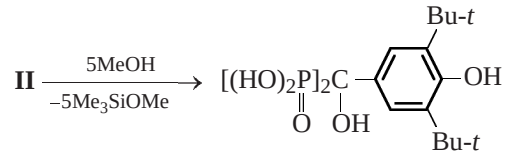
(**IV**).

An NMR monitoring of the reaction of diethyl trimethylsilyl phosphite with acid chloride **A** in 1 : 1 ratio revealed formation of intermediate keto phosphonate **B** [δ_P 0.05 ppm; δ_C (C^1) 196.6 ppm, d, $^1J_{PC}$ 171 Hz]. Thus, the reaction of excess trimethylsilyl phosphite with acid chloride **A** involves two steps: Arbuzov reaction followed by addition of trimethylsilyl phosphite to the carbonyl group of keto phosphonate **B** (cf. [4]).

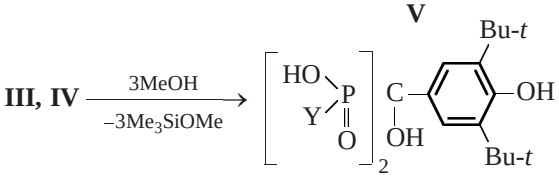


B

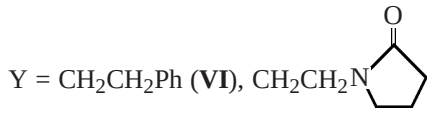
In the reactions of diphosphonate **II** and of diphosphinates **III** and **IV** with excess methanol, we obtained hydroxymethylenediphosphonic (or -diphosphinic) acids **V**–**VII** as white hygroscopic crystals.



V



VI, VII



Acids **V**–**VII** decompose on heating above 120–130°C and do not have clear melting points. The NMR spectra of **I**–**VII** contain characteristic signals of methylenediphosphonic (-diphosphinic) fragments PC^1P, and also signals of substituted aromatic fragments and pyrrolidone moiety. The methylene proton signals of **III**, **IV**, **VI**, and **VII** are partially overlapping multiplets.

Tetraethyl (3,5-di-*tert*-butyl-4-hydroxyphenyl)-trimethylsilyloxymethylenediphosphonate I. A mixture of 3.8 g of 3,5-di-*tert*-butyl-4-hydroxybenzoic acid, 10 ml of hexane, and 8 ml of thionyl chloride was refluxed for 0.5 h, the solvent was distilled off in a vacuum, and the residue was kept in a vacuum (0.5 mm Hg) for 0.5 h. To a solution of thus obtained acid chloride **A** in 15 ml of methylene chloride, a solution of 8 g of diethyl trimethylsilyl phosphite in 20 ml of methylene chloride was added with stirring and cooling to 10°C. The mixture was stirred for 0.5 h and heated to reflux, after which the solvent was distilled off, 25 ml of hexane was added to the residue, and the mixture was cooled to 0°C. The precipitated white crystals were filtered off and kept in a vacuum (0.5 mm Hg) for 1 h. Phosphonate **I** was obtained; yield 8 g (91%), mp 127°C. ^{1}H NMR spectrum, δ, ppm: 0.21 s (Me_3Si), 1.09 t and 1.24 t (CH_3CH_2O, $^3J_{HH}$ 6 Hz), 1.40 s (Me_3C), 3.8–4.3 m (CH_2O), 5.80 br.s (OH), 7.63 s (C_6H_2). ^{13}C NMR spectrum, δ_C, ppm: 3.15 s (Me_3Si), 15.83 m and 16.04 m (CH_3CH_2O), 30.35 s (Me_3C), 34.43 s (Me_3C), 63.60–64.50 m (CH_2O), 80.57 t (C^1, $^1J_{PC}$ 152 Hz), 123.05 t (C^3, $^3J_{PC}$ 7 Hz), 126.75 s (C^2), 136.38 s (C^4), 153.52 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 16.60 s. Found, %: C 53.59; H 8.57. $C_{26}H_{50}O_8P_2Si$. Calculated, %: C 53.78; H 8.68.

Compounds **II**–**IV** were prepared similarly.

Tetrakis(trimethylsilyl) (3,5-di-*tert*-butyl-4-hydroxyphenyl)trimethylsilyloxymethylenediphosphonate II. Yield 90%, mp 146°C. ^{1}H NMR spectrum, δ, ppm: 0.04 s and 0.06 s (Me_3SiOP), 0.26 s (Me_3SiOC), 1.37 s (Me_3C), 5.05 br.s (OH), 7.55 s (C_6H_2). ^{13}C NMR spectrum, δ_C, ppm: 0.96 s (Me_3SiOP), 2.99 s (Me_3SiOC), 30.27 s (Me_3C), 34.44 s (Me_3C), 79.82 t (C^1, $^1J_{PC}$ 161 Hz), 124.05 s (C^3), 127.67 s (C^2), 134.46 s (C^4), 153.10 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: –0.90 s.

Bis(trimethylsilyl) (3,5-di-*tert*-butyl-4-hydroxyphenyl)trimethylsilyloxymethylenebis(2-phenylethylphosphinate) III. Yield 92%, mp 111°C. ^{1}H NMR spectrum, δ, ppm: –0.17 s (Me_3SiOP), 0.34 s (Me_3SiOC), 1.45 s (Me_3C), 5.35 br.s (OH), 7.0–7.5 m (C_6H_2, $2C_6H_5$). ^{13}C NMR spectrum, δ_C, ppm: 1.34 s (Me_3SiOP), 3.50 s (Me_3SiOC), 30.47 s (Me_3C), 34.67 s (Me_3C), 83.07 t (C^1, $^1J_{PC}$ 97 Hz), 124.11 s (C^3), 126.08 s (C^2), 135.42 s (C^4), 153.71 s (C^5), 28.74 d (C^6, $^1J_{PC}$ 97 Hz), 28.16 s (C^7), 141.41 d (C^8, $^3J_{PC}$ 8 Hz) and 141.49 d (C^8, $^3J_{PC}$ 8 Hz). ^{31}P NMR spectrum, δ, ppm: 39.16 s.

Bis(trimethylsilyl) (3,5-di-*tert*-butyl-4-hydroxyphenyl)trimethylsilyloxymethylenebis[2-(2-oxopyrrolidino)ethylphosphinate] IV. Yield 93%, mp 129°C. ^{1}H NMR spectrum, δ, ppm: –0.07 s (Me_3SiOP), 0.11 s (Me_3SiOC), 1.20 s (Me_3C), 5.35 br.s (OH), 7.45 br.s (C_6H_2). ^{13}C NMR spectrum, δ_C, ppm: 1.08 s (Me_3SiOP), 3.19 s (Me_3SiOC), 30.18 s (Me_3C), 36.29 s (Me_3C), 82.76 t (C^1, $^1J_{PC}$ 100 Hz), 123.97 t (C^3, $^3J_{PC}$ 5 Hz), 127.87 s (C^2), 135.68 s (C^4), 153.64 s (C^5), 26.04 d (C^9, $^1J_{PC}$ 91 Hz), 34.50 s (C^{10}), 46.48 s (C^{11}), 17.55 s (C^{12}), 30.56 s (C^{13}), 174.20 s (C^{14}). ^{31}P NMR spectrum, δ_P, ppm: 36.90 s.

(3,5-Di-*tert*-butyl-4-hydroxyphenyl)hydroxymethylenediphosphonic acid V. Diphosphonate **II** (8.4 g) was added with stirring and cooling (10°C) to 30 ml of methanol. The mixture was heated to reflux, the solvent was distilled off, and the residue was kept in a vacuum (1 mm Hg) for 1 h. Acid **V** was obtained; yield 4.3 g (98%). ^{1}H NMR spectrum, δ, ppm: 1.36 s (Me_3C), 7.62 s (C_6H_2). ^{13}C NMR spectrum, δ_C, ppm: 30.95 s (Me_3C), 35.08 s (Me_3C), 75.73 t (C^1, $^1J_{PC}$ 146 Hz), 123.98 s (C^3), 127.99 s (C^2), 137.53 s (C^4), 152.92 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 16.51 s. Found, %: C 45.28; H 6.68. $C_{15}H_{26}O_8P_2$. Calculated, %: C 45.46; H 6.61.

Acids **VI** and **VII** were prepared similarly.

(3,5-Di-*tert*-butyl-4-hydroxyphenyl)hydroxymethylenebis(2-phenylethylphosphinic) acid VI. Yield 97%. ^{1}H NMR spectrum, δ, ppm: 1.40 s (Me_3C), 7.75 s (C_6H_2), 7.0–7.25 m ($2C_6H_5$). ^{13}C NMR spectrum, δ_C, ppm: 30.95 s (Me_3C), 35.21 s (Me_3C), 78.13 t (C^1, $^1J_{PC}$ 91 Hz), 123.24 (C^3), 126.69 s (C^2), 138.63 s (C^4), 153.58 s (C^5), 28.53 d (C^6, $^1J_{PC}$ 93 Hz), 27.73 s (C^7), 142.33 d (C^8, $^3J_{PC}$ 8 Hz) and 142.41 d (C^8, $^3J_{PC}$ 8 Hz). ^{31}P NMR spectrum, δ_P, ppm: 45.88 s. Found, %: C 64.89; H 7.47. $C_{31}H_{42}O_6P_2$. Calculated, %: C 65.02; H 7.39.

(3,5-Di-*tert*-butyl-4-hydroxyphenyl)hydroxymethylenebis[2-(2-oxopyrrolidino)ethylphosphinic] acid VII. Yield 94%. ^{1}H NMR spectrum, δ, ppm: 1.39 s (Me_3C), 2.13 t ($C^{13}H_2$, $^3J_{HH}$ 8 Hz), 7.61 s (C_6H_2). ^{13}C NMR spectrum, δ_C, ppm: 30.90 s (Me_3C), 36.27 s (Me_3C), 78.18 t (C^1, $^1J_{PC}$ 93 Hz), 123.84 s (C^3), 126.84 s (C^2), 138.48 s (C^4), 153.49 s (C^5), 24.96 d (C^9, $^1J_{PC}$ 92 Hz), 35.17 s (C^{10}), 46.51 s (C^{11}), 17.83 s (C^{12}), 30.84 s (C^{13}), 174.00 s (C^{14}). ^{31}P NMR spectrum, δ_P, ppm: 43.76 s. Found, %: C 54.43; H 7.35. $C_{26}H_{42}N_2O_8P_2$. Calculated, %: C 54.54; H 7.39.

The NMR spectra were recorded on a Bruker Avance 400 spectrometer, solvents $CDCl_3$ for **I**–**IV** and $(CD_3)_2SO$ for **V**–**VII**, references TMS (^{1}H, ^{13}C) and 85% H_3PO_4 in D_2O (^{31}P).

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