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LETTERS TO THE EDITOR

Synthesis of Bis(trimethylsilyl) Pyrid-3-yl(trimethylsiloxy)-methylphosphonite and Its Derivatives

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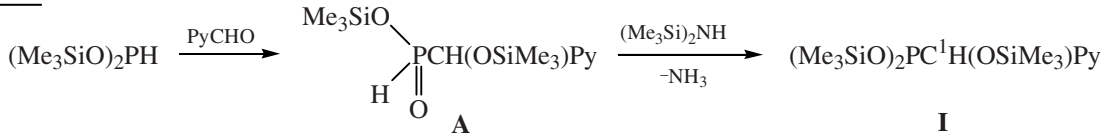
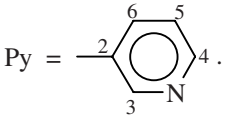
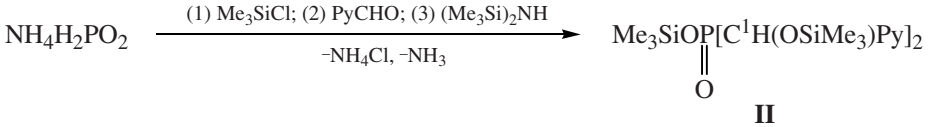
The aryl-substituted trimethylsilyl methylphosphonites that we have prepared earlier [1] are key compounds in the synthesis of various functionalized hydroxymethylphosphinates, which are of interest as potential ligands and biologically active substances [2]. In the present work we developed a convenient method of synthesis of pyrid-3-yl-substituted trimethylsiloxymethylphosphonite (**I**) and its derivatives including pyridine fragments along with hydroxylmethyl groups. Thus, phosphonite **I** was obtained in high yield in a reaction of bis(trimethylsiloxy) phosphine with pyridine-3-carbaldehyde followed by reaction of adduct **A** with bis(trimethylsilyl)amine (cf. [1]).



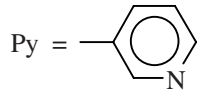
A **I**



Note that we failed to obtain phosphonite (**I**) by method [3] directly from ammonium hypophosphite and pyridine-3-carbaldehyde taken in the ratio 1:1. In this case only phosphinate (**II**) formed in a good yield.



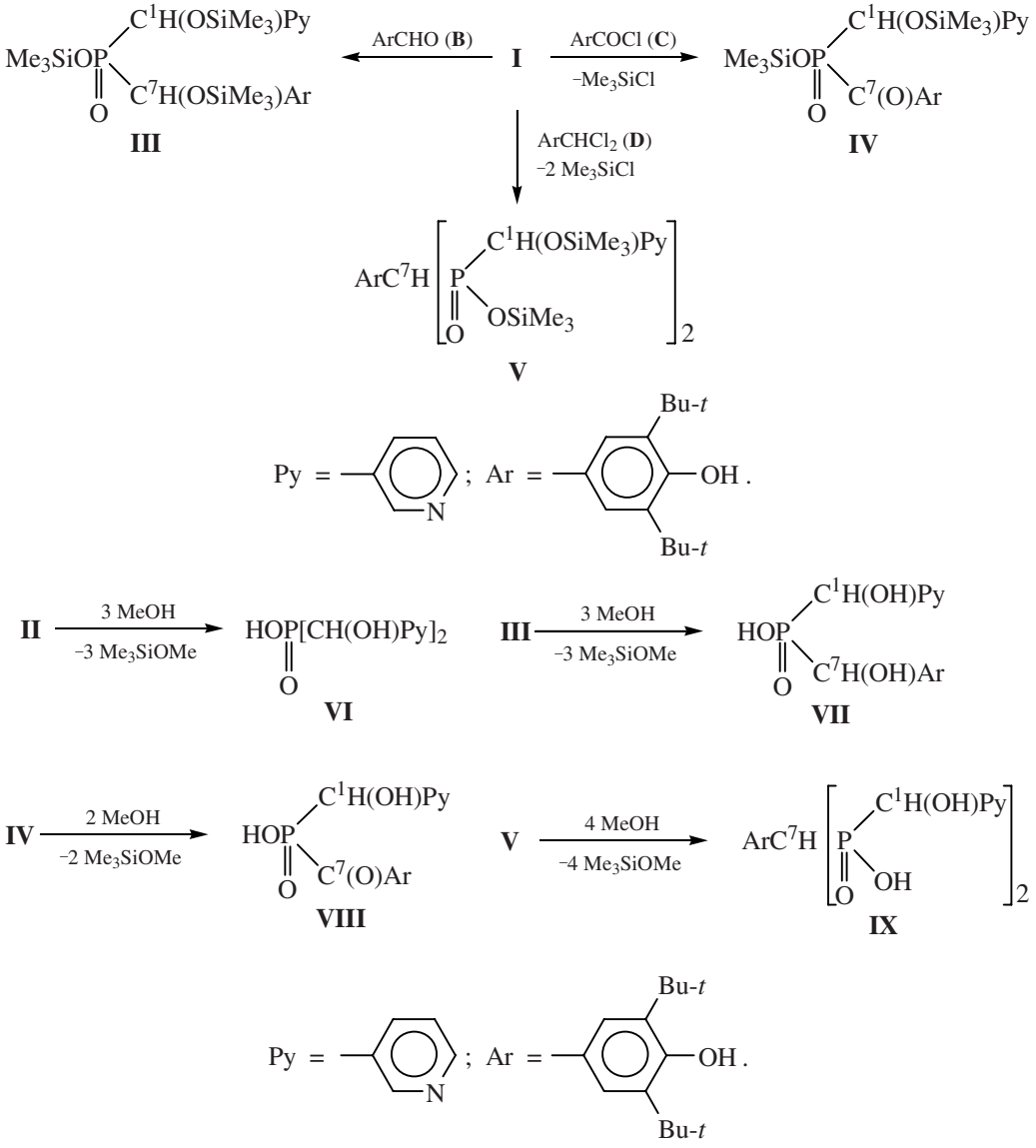
II



Phosphonite **I** is a suitable synton for a series of pyridine-containing hydroxymethylphosphinates including 2,6-di-*tert*-butyl-4-methylphenol fragments. Thus, phosphonite **I** added readily to the carbonyl group of aldehyde **B** and reacts smoothly with chloroanhydride **C** and benzalchloride **D** along the scheme of Arbuzov reaction in methylene chloride medium to form phosphinates **III, IV,** and diphosphinate **V**.

Reaction of phosphinates **II–IV** and diphosphinate **V** with methanol excess gives rise to new types of hydroxymethylphosphinic acids containing pyridine and 2,6-di-*tert*-butyl-4-methylphenol (**VI–IX**) fragments.

The functionalized phosphinic acids **VI-IX** obtained are promising antioxidants and effective ligands for complexes of various structure using both pyridine fragments and phosphoryl groups.



The NMR spectra of compounds **I–IX** contain characteristic signals of $PC^1H(OX)$ fragments whose parameters are given below. In accordance with the NMR spectra compounds **II–VII** and **IX** are the mixtures of two stereoisomers whose ratio was determined from ^{31}P NMR spectra. Data on the prevailing isomer are given first.

Bis(trimethylsilyl) pyrid-3-yl(trimethylsiloxy)-methylphosphonite (I). To a solution of 30 g of bis-(trimethylsiloxy)phosphine in 60 ml of methylene chloride was added dropwise a solution of 10.7 g of pyridin-3-carbaldehyde in 25 ml of methylene chloride at cooling to 10°C and stirring. The mixture was stirred for 0.5 h and then heated to boiling. After the solvent removal to the residue was added 20 g of bis (trimethylsilyl)amine. The mixture was refluxed at stirring until the ammonia liberation ceased, and then it was distilled. Yield 87% (33.9 g), bp 118°C (1 mm Hg). ^1H NMR spectrum, δ, ppm: –0.25 s, –0.18 s and –0.06 s (Me_3Si), 4.13 d (C^1H, $^2J_{PC}$ 4 Hz), 6.9–7.0 m and 7.3–7.4 m (C^5H and C^6H), 8.2–8.25 m (C^3H and C^4H). ^{13}C NMR spectrum, δ, ppm: –0.12 s (Me_3SiOC), 0.74 d ($^3J_{PC}$ 3 Hz) and 1.08 d (Me_3SiOP, $^3J_{PC}$ 2 Hz), 79.56 d (C^1, $^1J_{PC}$ 14 Hz), 134.59 d (C^2, $^2J_{PC}$ 9 Hz), 148.57 d (C^3, $^3J_{PC}$ 4 Hz), 147.83 s (C^4), 122.34 s (C^5), 134.18 d (C^6, $^3J_{PC}$ 4 Hz). ^{31}P NMR spectrum, δ, ppm: 137.91 s.

Trimethylsilyl bis[pyrid-3-yl(trimethylsiloxy)-methyl]phosphinate (II). A mixture of 8.3 g of ammonium hypophosphite, 10.7 g of pyridine-3-carbaldehyde and 26 g of trimethylchlorosilane in 50 ml of

methylene chloride was refluxed at stirring for 2 h. Then ammonium chloride was filtered off and the solvent was removed. To the residue was added 65 g of bis(trimethylsilyl)amine. The mixture was refluxed at stirring until the ammonia liberation ceased, and then it was distilled. Yield 78% (19.4 g), bp 167°C (1 mm Hg), mp 69°C. The first isomer (content 60%), ^{1}H NMR spectrum, δ, ppm: –0.10 to 0.55 m (Me_3Si), 4.37 d (C^1H, $^2J_{PH}$ 12 Hz), 6.5–8.0 m (C_5H_4N). ^{13}C NMR spectrum, δ, ppm: –0.8 to –0.5 m (Me_3Si), 69.45 d (C^1, $^1J_{PC}$ 115 Hz), 122.2-149.5 m (C_5H_4N). ^{31}P NMR spectrum, δ, ppm: 30.23 s. The second isomer, ^{1}H NMR spectrum, δ, ppm: –0.10 to 0.55 m (Me_3Si), 4.60 d and 4.71 d (C^1H, $^2J_{PH}$ 8 Hz), 6.5–8.0 m (C_5H_4N). ^{13}C NMR spectrum, δ, ppm: –0.8 to –0.5 m (Me_3Si), 68.47 d (C^1, $^1J_{PC}$ 119 Hz) and 68.90 d (C^1, $^1J_{PC}$ 112 Hz), 122.2–149.5 m (C_5H_4N). ^{31}P NMR spectrum, δ, ppm: 31.59 s. Found, %: C 50.59; H 7.42. $C_{21}H_{37}N_2O_4PSi_3$. Calculated, %: C 50.78; H 7.51.

Trimethylsilyl [pyrid-3-yl(trimethylsiloxy)methyl][3,5-di-*tert*-butyl-4-hydroxyphenyl-(trimethylsiloxy)-methyl]phosphinate (III). To a solution of 7.8 g of phosphonite **I** in 30 ml of methylene chloride was added 4.7 g of 3,5-di-*tert*-butyl-4-hydroxybenzaldehyde at stirring and cooling to 0°C. The mixture was stirred for 0.5 h. After the solvent removal the residue was kept at 30°C in a vacuum (0.5 mm Hg) for 1 h. Yield 86% (10.7 g), viscous oily liquid. The first isomer (content 55%). ^{1}H NMR spectrum, δ, ppm: –0.25 to –0.14 m (Me_3Si), 1.26 s (Me_3C), 4.83 d (C^1H, $^2J_{PH}$ 10 Hz) 5.19 d (C^7H, $^2J_{PH}$ 8 Hz), 7.0–8.5 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: –0.25 to 0.75 m (Me_3Si), 30.18 s (Me_3C), 30.21 s (Me_3C), 70.71 d ($^1J_{PC}$ 108 Hz) and 71.89 d (C^1, C^7, $^1J_{PC}$ 107 Hz), 122.5–154.5 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 30.99 s. The second isomer. ^{1}H NMR spectrum, δ, ppm: –0.25 to –0.14 m (Me_3Si), 1.31 s (Me_3C), 4.57 d ($^2J_{PH}$ 8 Hz) and 4.94 d ($^2J_{PH}$ 6 Hz, C^1H and C^7H), 7.0-8.5 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: –0.25 to 0.75 m (Me_3Si), 29.95 s (Me_3C), 34.95 s (Me_3C), 68.99 d ($^1J_{PC}$ 110 Hz) and 70.67 d ($^1J_{PC}$ 112 Hz, C^1 and C^7), 122.5–154.5 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 33.12 s. Found, %: C 57.52; H 8.64. $C_{30}H_{54}NO_5PSi_3$. Cal-culated, %: C 57.75; H 8.72.

Phosphinates **IV–V** were similarly prepared.

Trimethylsilyl [pyrid-3-yl(trimethylsiloxy)methyl]-3,5-di-*tert*-butyl-4-hydroxybenzoyl-phosphinate (IV). Yield 88%, mp 108°C. The first isomer (content 60%), ^{1}H NMR spectrum, δ, ppm: –0.18 to –0.16 m (Me_3Si), 1.44 s (Me_3C), 5.35 d (C^1H, $^2J_{PH}$ 8 Hz), 6.15 br.s (OH), 7.25–8.65 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: –0.5 to 1.8 m (Me_3Si), 29.93 s (Me_3C), 34.39 s (Me_3C), 70.63 d (C^1, $^1J_{PC}$ 109 Hz), 160.48 s (COH), 200.03 d (C^7, $^1J_{PC}$ 104 Hz), 122.9-149.1 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 14.43 s. The second isomer, ^{1}H NMR spectrum, δ, ppm: –0.18 to –0.16 m (Me_3Si), 1.44 s (Me_3C), 5.24 d (C^1H, $^2J_{PH}$ 6 Hz), 6.15 br. s (OH), 7.25–8.65 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: –0.5 to 1.8 m (Me_3Si), 29.93 s (Me_3C), 34.39 s (Me_3C), 69.36 d (C^1, $^1J_{PC}$ 120 Hz), 160.30 s (COH), 199.61 d (C^7, $^1J_{PC}$ 106 Hz), 122.9–149.1 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 15.79 s. Found, %: C 58.81; H 8.01. $C_{27}H_{44}NO_5PSi_2$. Calculated, %: C 58.99; H 8.07.

Bis(trimethylsilyl) 3,5-di-*tert*-butyl-4-hydroxyphenylmethylenebis[pyrid-3-yl(trimethylsiloxy)methylphosphinate] (V). Yield 89 %, mp 78°C. The first isomer (content 60%), ^{1}H NMR spectrum, δ, ppm: –0.2 to 0.2 m (Me_3Si), 1.36 s (Me_3C), 3.75 t (C^7H, $^2J_{PH}$ 18 Hz), 4.81 d (C^1H, $^2J_{PH}$ 12 Hz), 7.0–8.6 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: –0.15 to 1.85 m (Me_3Si), 29.99 s (Me_3C), 34.41 s (Me_3C), 42.31 t (C^7, $^1J_{PC}$ 78 Hz), 72.36 d (C^1, $^1J_{PC}$ 115 Hz), 153.72 s (COH), 122.9–149.6 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 30.93 s. The second isomer, ^{1}H NMR spectrum, δ, ppm: –0.2 to 0.2 m (Me_3Si), 1.37 s (Me_3C), 3.49 t (C^7H, $^2J_{PH}$ 18 Hz), 4.88 d (C^1H, $^2J_{PH}$ 8 Hz), 7.0-8.6 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: –0.15 to 1.85 m (Me_3Si), 30.42 s (Me_3C), 34.28 s (Me_3C), 43.31 t (C^7, $^1J_{PC}$ 80 Hz), 71.91 d (C^1, $^1J_{PC}$ 113 Hz), 153.72 s (COH), 122.9–149.6 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 30.49 s. Found, %: C 54.89; H 7.94. $C_{39}H_{68}N_2O_7P_2Si_4$. Calculated, %: C 55.03; H 8.05.

Bis[pyrid-3-yl(hydroxy)methyl]phosphinic acid (VI). A mixture of 19.4 g of phosphinate **II** and 50 ml of methanol was heated to boiling. After the solvent removal white crystals were kept in a vacuum (1 mm Hg) for 1 h. Yield 94% (10.3 g), mp 204°C. The first isomer (content 75%), ^{1}H NMR spectrum, δ, ppm: 5.56 d (C^1H, $^2J_{PH}$ 8 Hz), 7.95–8.95 m (C_5H_4N). ^{13}C NMR spectrum, δ, ppm: 70.92 d (C^1, $^1J_{PC}$ 98 Hz), 127.8-145.8 m (C_5H_4N). ^{31}P NMR spectrum, δ, ppm: 29.42 s. The second isomer, ^{1}H NMR spectrum, δ, ppm: 5.61 d (C^1H, $^2J_{PH}$ 8 Hz), 7.95–8.95 m (C_5H_4N). ^{13}C NMR spectrum, δ, ppm: 71.08 d (C^1, $^1J_{PC}$ 98 Hz), 127.8–145.8 m (C_5H_4N). ^{31}P NMR spectrum, δ, ppm: 30.80 s. Found, %: C 51.26; H 4.72. $C_{12}H_{13}N_2O_4P$. Calculated, %: C 51.44; H 4.68.

Acids **VII–IX** were similarly prepared.

Pyrid-3-yl(hydroxy)methyl[3,5-di-*tert*-butyl-4-hydroxyphenyl(hydroxy)methyl]phosphinic acid (VII). Yield 96%, mp 208°C. The first isomer (content 55%), ^{1}H NMR spectrum, δ, ppm: 1.40 s (Me_3C), 5.09 d ($^2J_{PH}$ 7 Hz) and 5.48 d ($^2J_{PH}$ 10 Hz, C^1H and C^7H), 7.2–8.9 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: 29.51 s (Me_3C), 34.24 s (Me_3C), 67.84 d ($^1J_{PC}$ 97 Hz) and 70.56 d ($^1J_{PC}$ 112 Hz, C^1 and C^7), 122.5–153.5 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 33.23 s. The second isomer, ^{1}H NMR spectrum, δ, ppm: 1.45 s (Me_3C), 4.93 d ($^2J_{PH}$ 8 Hz) and 5.27 d ($^2J_{PH}$ 9 Hz, C^1H and C^7H), 7.2–8.9 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: 29.45 s (Me_3C), 34.24 s (Me_3C), 70.38 d ($^1J_{PC}$ 95 Hz) and 72.66 d ($^1J_{PC}$ 110 Hz, C^1 and C^7), 122.5–153.5 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 30.15 s. Found, %: C 61.59; H 7.56. $C_{21}H_{31}NO_5P$. Calculated, %: C 61.75; H 7.65.

Pyrid-3-yl(hydroxy)methyl(3,5-di-*tert*-butyl-4-hydroxybenzoyl)phosphinic acid (VIII). Yield 95%, mp 165°C. ^{1}H NMR spectrum, δ, ppm: 1.47 s (Me_3C), 5.78 d, (C^1H, $^2J_{PH}$ 8 Hz), 7.7–9.1 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: 29.26 s (Me_3C), 34.18 s (Me_3C), 69.05 d (C^1, $^1J_{PC}$ 102 Hz), 126.0–145.3 m (C_5H_4N, C_6H_2), 160.0 s ($C_{Ar}OH$), 205.86 d (C^7, $^1J_{PC}$ 115 Hz). ^{31}P NMR spectrum, δ, ppm: 18.78 s. Found, %: C 61.98; H 7.03. $C_{21}H_{28}NO_5P$. Calculated, %: C 62.21; H 6.96.

3**,5-Di-*tert*-butyl-4-hydroxyphenylmethylenebis-[pyrid-3-yl(hydroxy)methylphosphinic] acid (IX).** Yield 97%, mp 235°C. The first isomer (content 70%). ^{1}H NMR spectrum, δ, ppm: 1.40 s (Me_3C), 4.32 t (C^7H, $^2J_{PH}$ 20 Hz), 5.38 d (C^1H, $^2J_{PH}$ 8 Hz), 7.3–9.0 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: 29.66 s (Me_3C), 34.13 s (Me_3C), 51.38 t (C^7, $^1J_{PC}$ 84 Hz), 69.95 d (C^1, $^1J_{PC}$ 100 Hz), 153.05 s ($C_{Ar}OH$), 121.5-145.5 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 31.22 s. The second isomer, ^{1}H NMR spectrum, δ, ppm: 1.40 s (Me_3C), 4.32 t (C^7H, $^2J_{PH}$ 20 Hz), 5.59 d (C^1H, $^2J_{PH}$ 8 Hz), 7.3–9.0 m (C_5H_4N, C_6H_2). ^{13}C NMR spectrum, δ, ppm: 29.66 s (Me_3C), 34.13 s (Me_3C), 51.38 t (C^7, $^1J_{PC}$ 84 Hz), 70.30 d (C^1, $^1J_{PC}$ 100 Hz), 153.05 s ($C_{Ar}OH$), 121.5–145.5 m (C_5H_4N, C_6H_2). ^{31}P NMR spectrum, δ, ppm: 31.78 s. Found, %: C 57.52; H 6.49. $C_{27}H_{36}N_2O_7P_2$. Calculated, %: C 57.65; H 6.45.

The NMR spectra were obtained on a Bruker Avance-400 device using $CDCl_3$ (**I–V**), CD_3OD (**VII**) and CD_3COOD (**VI, VIII, IX**) as solvents and TMS (^{1}H, ^{13}C) and 85% H_3PO_4 in D_2O solution (^{31}P) as references.

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