ISSN 1070-3632, Russian Journal of General Chemistry, 2007, Vol. 77, No. 9, pp. 1645–1647. © Pleiades Publishing, Ltd., 2007.
Original Russian Text © A.A. Prishchenko, M.V. Livantsov, O.P. Novikova, L.I. Livantsova, 2007, published in Zhurnal Obshchei Khimii, 2007, Vol. 77, No. 9, pp. 1574–1576.

LETTERS TO THE EDITOR

Reaction of Trimethylsilyl Hypophosphite with Aromatic Aldehydes and Azomethines

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Received April 9, 2007

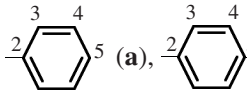
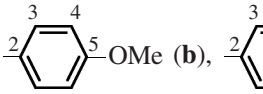
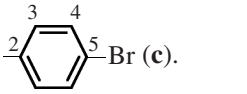
DOI: 10.1134/S1070363207090253

Trimethylsilyl esters of hypophosphorous acid are extensively used in the synthesis of various functional derivatives of organophosphorus acids, which attract interest as perspective ligands and biologically active compounds. Thus, bis(trimethylsiloxy)phosphine is capable of readily adding to aromatic aldehydes and azomethines [1], and trimethylsilyl hypophosphite **A** easily reacts with 2 equiv of *N,N*-diethylvinylsulfonamide [2]. In the present work we have studied the reaction of trimethylsilyl hypophosphite **A** formed from ammonium hypophosphite and chlorotrimethylsilane with aromatic aldehydes and azomethines in methylene chloride. It was found that hypophosphite **A** is capable of easily adding at the carbonyl group of various aromatic aldehydes to form either phosphonites **Ia**–**Ic** or phosphinates **IIa**–**IIc**, depending on the reagent ratio, in quite a high yield (cf. [3]). Phosphonites **I** were isolated by additional treatment of the reaction mixture with bis(trimethylsilyl)amine, and phosphinates **II** were recrystallized from aqueous ethanol.

$$NH_4H_2PO_2 \xrightarrow[-NH_4Cl]{Me_3SiCl} \underset{\mathbf{A}}{Me_3SiOP(O)H_2} \xrightarrow[(2)\ (Me_3Si)_2NH]{(1)\ ArCHO;} \underset{\mathbf{Ia–Ic}}{(Me_3SiO)_2PC^1H(O)(OSiMe_3)Ar},$$

$$\mathbf{A} \xrightarrow[(2)\ EtOH,\ H_2O]{(1)\ ArCHO;} HOP(O)[C^1H(OH)Ar]_2,$$

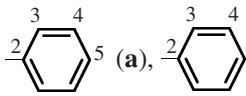
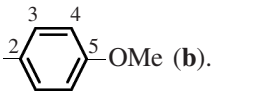
IIa–IIc

Ar =  (**a**),  OMe (**b**),  Br (**c**).

The reaction of hypophosphite **A** with 2 equiv of aromatic azomethines under the same conditions provides aryl-substituted bis(aminomethyl)phosphinates **III** in high yield.

$$\mathbf{A} \xrightarrow[(2)\ EtOH]{(1)\ ArCH{=}NMe;} HOP(O)[C^1H(NHMe)Ar]_2,$$

IIIa, IIIb

Ar =  (**a**),  OMe (**b**).

The NMR spectra of compounds **I**–**III** show characteristic signals of the $PC^1H(OX)Ar$ fragments, whose parameters are presented below. According to the NMR spectra, compounds **II** and **III** are mixtures

of two stereoisomers. The stereoisomer ratios were determined by ^{31}P NMR spectroscopy, and the data for the prevailing isomer are given first. For phosphinates **IIa** and **IIb** only ^{1}H and ^{31}P NMR data are presented because of the minor content of the second isomer.

Bis(trimethylsilyl) [phenyl(trimethylsiloxy)-methyl]phosphonite (Ia). A mixture of 8.3 g of ammonium hypophosphite, 10.6 g of benzaldehyde, and 26 g of chlorotrimethylsilane in 50 ml of methylene chloride was heated under reflux with stirring for 2 h. Ammonium chloride was filtered off, the solvent was distilled off, and 65 g of bis(trimethylsilyl)amine was added to the residue. The mixture was refluxed until ammonia no longer evolved and then distilled to obtain 26.4 g of phosphonite **Ia**, yield 68%, bp 120°C (1.5 mm Hg). ^{1}H NMR spectrum, δ, ppm: –0.10 s, 0.02 s and 0.21 s ($3Me_3Si$), 4.28 s (C^1H), 7.3–7.4 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 0.22 s (Me_3SiOC), 0.80 d and 1.40 d ($2Me_3SiOP$, $^{3}J_{PC}$ 3 Hz), 82.72 d (C^1, $^{1}J_{PC}$ 11 Hz), 139.60 d (C^2, $^{2}J_{PC}$ 13 Hz), 127.45 d (C^3, $^{3}J_{PC}$ 5 Hz), 127.67 s (C^4), 126.85 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 140.47 s.

Phosphonites **Ib** and **Ic** were synthesized by the same method.

Bis(trimethylsilyl) [(4-methoxyphenyl)(trimethylsiloxy)methyl]phosphonite (Ib). Yield 59%, bp 115°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: –0.16 s, –0.06 s and 0.14 s ($3Me_3Si$), 4.15 s (C^1H), 6.74 d (C^3H, $^{3}J_{HH}$ 8 Hz), 7.10 d (C^4H, $^{3}J_{HH}$ 8 Hz), 3.64 s (MeO). ^{13}C NMR spectrum, δ_C, ppm: 0.18 s, 0.77 s and 1.32 s ($3Me_3Si$), 82.18 d (C^1, $^{1}J_{PC}$ 9 Hz), 131.72 d (C^2, $^{2}J_{PC}$ 13 Hz), 128.51 d (C^3, $^{3}J_{PC}$ 5 Hz), 113.13 s (C^4), 158.77 s (C^5), 54.89 s (MeO). ^{31}P NMR spectrum, δ_P, ppm: 140.07 s.

Bis(trimethylsilyl) [(4-bromophenyl)(trimethylsiloxy)methyl]phosphonite (Ic). Yield 64%, bp 159°C (1 mm Hg), mp 62°C. ^{1}H NMR spectrum, δ_H, ppm: –0.12 s, –0.04 s and 0.12 s ($3Me_3Si$), 4.19 s (C^1H), 7.06 d (C^3H, $^{3}J_{HH}$ 8 Hz), 7.32 d (C^4H, $^{3}J_{HH}$ 8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 0.16 s (Me_3SiOC), 0.90 d and 1.35 d($2\ Me_3SiOP$, $^{3}J_{PC}$ 3 Hz), 81.77 d (C^1, $^{1}J_{PC}$ 14 Hz), 138.60 d (C^2, $^{2}J_{PC}$ 11 Hz), 128.89 d (C^3, $^{3}J_{PC}$ 4 Hz), 130.60 s (C^4), 120.50 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 139.22.

Bis[hydroxy(phenyl)methyl]phosphinic acid (IIa). A mixture of 8.3 g of ammonium hypophosphite, 22.4 g of benzaldehyde, and 40 g of chlorotrimethylsilane in 60 ml of methylene chloride was heated under reflux with stirring for 2 h. Ammonium chloride was filtered off, the solvent was distilled off, and 60 ml of ethanol was added to the residue. The mixture was heated to boil, ethanol was distilled off, and the residue was recrystallized from 70% aqueous ethanol. The white crystals that formed were kept in a vacuum (1 mm Hg) for 1 h to obtain compound **IIa**. Yield 21.7 g (78%), mp 187°C. Major isomer (90%). ^{1}H NMR spectrum, δ, ppm: 5.17 d (C^1H, $^{2}J_{PH}$ 8 Hz), 7.3–7.5 m ($2C_6H_5$). ^{13}C NMR spectrum, δ_C, ppm: 68.96 d (C^1, $^{1}J_{PC}$ 106 Hz), 139.06 d (C^2, $^{2}J_{PC}$ 3 Hz), 128.14 d (C^3, $^{3}J_{PC}$ 5 Hz), 128.00 s (C^4), 127.35 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 39.31 s. Minor isomer. ^{1}H NMR spectrum, δ, ppm: 4.86 d (C^1H, $^{2}J_{PH}$ 8 Hz), 7.3–7.5 m ($2C_6H_5$). ^{31}P NMR spectrum, δ_P, ppm: 37.05 s. Found, %: C 60.09; H 5.49. $C_{14}H_{15}O_4P$. Calculated, %: C 60.43; H 5.43.

Compounds **IIb** and **IIc** were prepared by the same method.

Bis[hydroxy(4-phenoxyphenyl)methyl]phosphinic acid (IIb). Yield 72% yield, mp 165°C. Major isomer (86%). ^{1}H NMR spectrum, δ, ppm: 5.07 d (C^1H, $^{2}J_{PH}$ 8 Hz), 6.90 d (C^3H, $^{3}J_{HH}$ 8 Hz), 7.35 d (C^4H, $^{3}J_{HH}$ 8 Hz), 3.74 s (MeO). ^{13}C NMR spectrum, δ_C, ppm: 68.50 d (C^1, $^{1}J_{PC}$ 107 Hz), 130.93 d (C^2, $^{2}J_{PC}$ 4 Hz), 129.36 d (C^3, $^{2}J_{PC}$ 4 Hz), 113.56 s (C^4), 158.95 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 38.88 s. Minor isomer. ^{1}H NMR spectrum, δ_H, ppm: 4.75 d (C^1H, $^{2}J_{PH}$ 8 Hz), 7.14 d (C^3H, $^{3}J_{HH}$ 8 Hz), 7.89 d (C^4H, $^{3}J_{HH}$ 8 Hz), 3.74 s (MeO). ^{31}P NMR spectrum, δ_P, ppm: 36.96 s. Found, %: C 56.69; H 5.72. $C_{16}H_{19}\cdot O_6P$. Calculated, %: C 56.81; H 5.66.

Bis[(4-bromophenyl)hydroxymethyl)]phosphinic acid (IIc). Yield 52%, mp 162°C. Major isomer (55%). ^{1}H NMR spectrum, δ, ppm: 4.87 d (C^1H, $^{2}J_{PH}$ 8 Hz), 7.2–7.6 m ($2C_6H_5$). ^{13}C NMR spectrum, δ_C, ppm: 69.64 d (C^1, $^{1}J_{PC}$ 104 Hz), 138.70 s (C^2), 130.14 s (C^3), 130.97 s (C^4), 120.74 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 35.95 s. Minor isomer. ^{1}H NMR spectrum, δ, ppm: 5.15 d (C^1H, $^{2}J_{PH}$ 8 Hz), 7.2–7.6 m ($2C_6H_5$). ^{13}C NMR spectrum, δ_C, ppm: 68.46 d (C^1, $^{1}J_{PC}$ 106 Hz), 138.33 s (C^2), 130.14 s (C^3), 130.97 s (C^4), 120.77 s (C^5). ^{31}P NMR spectrum, δ_P, ppm: 38.10 s.

Bis[(methylamino)phenylmethyl]phosphinic acid (IIIa). A mixture of 8.3 g of ammonium hypophosphite, 25.2 g of benzylidene(methyl)amine, and 17 g of chlorotrimethylsilane in 60 ml of methylene chloride heated under reflux with stirring for 2 h. Ammonium chloride was filtered off, the solvent was removed in a vacuum, and 60 ml of ethanol was added to the residue. The mixture was heated to boil;

the precipitate that formed was filtered off and washed with 20 ml of ethanol and 20 ml of ether. The resulting white fine crystals were kept in a vacuum of 1 mm Hg for 1 h to obtain compound **IIIa**. Yield 28 g (92%), mp 214°C. Major isomer (67%). ^{1}H NMR spectrum, δ, ppm: 4.69 d (C^1H, $^2J_{PH}$ 8 Hz), 2.55 s (MeN), 7.2–7.5 m (2 C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 61.58 d (C^1, $^1J_{PC}$ 95 Hz), 31.89 s (MeN), 128.0–133.0 m ($2C_6H_5$). ^{31}P NMR spectrum, δ_P, ppm: 19.94 s. Minor isomer. ^{1}H NMR spectrum, δ, ppm: 4.64 d (C^1H, $^2J_{PH}$ 8 Hz), 2.55 s (MeN), 7.2–7.5 m (C_6H_5). ^{13}C NMR spectrum, δ_C, ppm: 61.32 d (C^1, $^1J_{PC}$ 94 Hz), 31.95 s (MeN), 128.0–133.0 m ($2C_6H_5$). ^{31}P NMR spectrum, δ_P, ppm: 19.66 s. Found, %: C 62.97; H 7.09. $C_{16}H_{21}N_2O_2P$. Calculated, %: C 63.15; H 6.96.

Compound **IIIb** was prepared by the same procedure.

Bis[(4-methoxyphenyl)(methylamino)methyl]-phosphinic acid (IIIb). Yield 90%, mp 208°C. Major isomer (80%). ^{1}H NMR spectrum, δ, ppm: 4.54 d (C^1H, $^2J_{PH}$ 8 Hz), 6.81 d (C^3H, $^3J_{HH}$ 8 Hz), 7.24 d (C^4H, $^3J_{HH}$ 8 Hz), 2.56 s (MeN), 3.79 s (MeO). ^{13}C NMR spectrum, δ_C, ppm: 60.95 d (C^1, $^1J_{PC}$ 97 Hz), 132.28 s (C^2), 131.57 s (C^3), 114.21 s (C^4), 160.49 s (C^5), 31.60 s (MeN), 54.73 s (MeO). ^{31}P NMR spectrum, δ_P, ppm: 21.00 s. Minor isomer. ^{1}H NMR spectrum, δ, ppm: 4.39 d (C^1H, $^2J_{PH}$ 8 Hz), 6.96 d (C^3H, $^3J_{HH}$ 8 Hz), 7.34 d (C^4H, $^3J_{HH}$ 8 Hz), 2.55 s (MeN), 3.83 s (MeO). ^{13}C NMR spectrum, δ_C, ppm: 60.55 d (C^1, $^1J_{PC}$ 96 Hz), 132.28 s (C^2), 131.52 s (C^3), 114.21 s (C^4), 160.78 s (C^5), 31.66 s (MeN), 54.82 s (MeO). ^{31}P NMR spectrum, δ_P, ppm: 21.52 s. Found, %: C 59.12; H 6.97. $C_{18}H_{25}N_2O_4P$. Calculated, %: C 59.33; H 6.92.

The NMR spectra were recorded on a Bruker Avance 400 spectrometer in $CDCl_3$ (phosphonites **I**), $(CD_3)_2SO$ (phosphinates **II**), and CD_3COOD (phosphinates **III**) against TMS (^{1}H, ^{13}C) or 85% H_3PO_4 in D_2O (^{31}P).

ACKNOWLEDGMENTS

The work was financially supported by the Russian Foundation for Basic Research (project no. 05-03-32 864).

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