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LETTERS TO THE EDITOR

Synthesis of N-Substituted Aminomethylenediphosphonites and Their Derivatives

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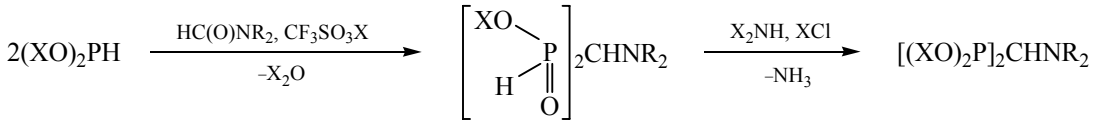
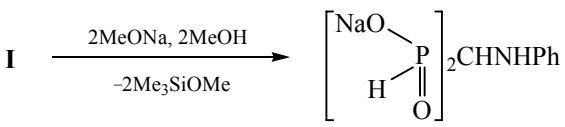
Substituted aminomethylenediphosphonites are of interest as the key materials in the synthesis of functionalized aminomethylenediphosphorus-containing compounds, which are analogs of natural organophosphorus pyrophosphates and amino acids, promising ligands and biologically active substances with diverse properties [1]. Recently, we have prepared two types of the compounds by reacting bis(trimethylsiloxy) phosphine with substituted methyleneimines [2]. To synthesize new types of N-substituted aminomethylenediphosphonites we studied the direct interaction of bis(trimethylsiloxy) phosphine **A** with available N-substituted formamides. Note that the phosphine **A** can be easily attached to the carbonyl groups of various aldehydes and ketones [3], but the analogous reaction with formamide is not described. The reaction of an excess of bis(trimethylsiloxy)phosphine **A** with *N*-substituted formamides proceeds readily in methylene chloride only in the presence of a catalyst (trimethylsilyl trifluoromethanesulfonate) to give the intermediate diphosphonites **B**. The latter react with bis(trimethylsilyl)amine under reflux in the presence of trimethylchlorosilane to afford diphosphonites **I–III** with good yields (cf. [4]).



A **B** **I–III**

X = Me_3Si, NR_2 = NHPh (**I**), NMe_2 (**II**), N⟨CH2CH2⟩O (**III**).

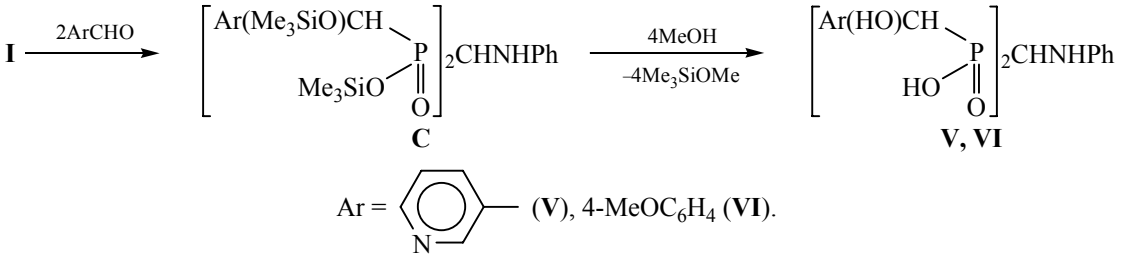
The resulting aminomethylenediphosphonites we used for the synthesis of new types of aminomethylenediphosphorus-containing compounds. Thus, the reaction of diphosphonite **I** with a dilute solution of sodium methylate in methanol results in a stable diphosphonous acid salt **IV**, which is white hygroscopic crystals (cf. [2]).



IV

Diphosphonite **I** containing a highly reactive moiety POSi easily attaches to the carbonyl group of aromatic aldehydes taken in excess in methylene chloride to form the intermediate diphosphinates **C**. The treatment of the reaction mixture with methanol gives rise to new functionalized aminomethylenediphosphinic acids **V**, **VI** in high yields.

The NMR spectra of compounds **I–VI** contain the typical signals of $P_2C^1HNC^2H$ fragments, and in the spectra of compounds **V**, **VI** there are also the signals of $PC^3H(Ar)OH$ moiety, parameters of which are listed below. According to the NMR spectra, compounds **V**,



VI containing four asymmetric atoms are a mixture of three stereoisomers whose ratio was determined by the ^{1}H, ^{31}P NMR spectra. Two diastereotopic phosphoryl groups of the predominant isomer of compounds **V**, **VI** in the ^{31}P NMR spectrum are observed as a typical AB-system.

***O,O,O,O*-Tetra(trimethylsilyl) *N*-anilinomethylenediphosphonite (I).** To a solution of 18 g of bis(trimethylsiloxy)phosphine and 2.4 g of formanilide in 10 ml of methylene chloride was added with stirring 1 ml of trimethylsilyl trifluoromethanesulfonate. The mixture was heated at 20° C for 4 h. Then the solvent was distilled off, and to the residue was added 20 g of bis(trimethylsilyl)amine and 2 ml of trimethylchlorosilane. The mixture was refluxed for 1 h, then distilled. Yield 7.7 g (74%), bp 152°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 3.2–3.3 m (C^{1}H), 4.44 d (NH, $^3J_{HH}$ 8.0 Hz), 6.68 d (2CH$_{Ph}$, $^3J_{HH}$ 8.0 Hz), 7.07 t (2CH$_{Ph}$, $^3J_{HH}$ 8.0 Hz), 6.60 t (2CH$_{Ph}$, $^3J_{HH}$ 8.0 Hz), 0.1–0.2 m (12 CH$_3$). ^{13}C NMR spectrum, δ_C, ppm: 71.78 t (C^1, $^1J_{PC}$ 38.5 Hz), 151.03 (C^2), 128.53, 115.67 and 112.56 (C$_{Ph}$), 1.31 (CH$_3$). ^{31}P NMR spectrum: δ_P 155.78 ppm.

Diphosphonites **II**, **III** were obtained similarly.

***O,O,O,O*-Tetra(trimethylsilyl) dimethylaminomethylenediphosphonite (II)**. Yield 52%, bp 119°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 2.11 t (C^{1}H, $^2J_{PH}$ 5.6 Hz), 2.67 s (2C^{2}H$_3$N), 0.15 c (4Me$_3$Si). ^{13}C NMR spectrum, δ_C, ppm: 82.37 t (C^1, $^1J_{PC}$ 41.6 Hz), 45.19 t (C^2, $^3J_{PC}$ 7.2 Hz), 1.39 s (Me$_3$Si). ^{31}P NMR spectrum: δ_P 166.82 ppm.

***O,O,O,O*-Tetra(trimethylsilyl) *N*-morpholinomethylenediposphonite (III)**. Yield 72%, bp 144°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 2.08 t (C^{1}H, $^2J_{PH}$ 6.2 Hz), 3.0–3.1 m (2C^{2}H$_2$), 3.4–3.5 m (2CH$_2$O), 0.17 s (4Me$_3$Si). ^{13}C NMR spectrum, δ_C, ppm: 82.34 t (C^1, $^1J_{PC}$ 42.8 Hz), 53.11 t (C^2, $^3J_{PC}$ 6.8 Hz), 67.73 s (CH$_2$O), 1.35 s (Me$_3$Si). ^{31}P NMR spectrum: δ_P 165.33 ppm.

Disodium salt of *N*-anilinomethylenediphosphonous acid (IV). To a solution of 0.93 g of sodium methylate in 30 ml of methanol under cooling to 10°C and stirring was added 4.5 g of diphosphonite **I** in 20 ml of diethyl ether. Then the solvent was distilled off, and the white crystals were kept in a vacuum of 1 mm Hg for 1 h. Yield 2.3 g (95%). ^{1}H NMR, δ, ppm: 3.64 t (C^{1}H, $^2J_{PH}$ 16.0 Hz), 6.77 d (2C^{1}H$_{Ph}$, $^3J_{HH}$ 8.0 Hz), 7.16 t (2CH$_{Ph}$, $^3J_{HH}$ 8.0 Hz), 6.70 t (C^{1}H$_{Ph}$, $^3J_{HH}$ 8.0 Hz), 7.04 d (2PH, $^1J_{PH}$ 532.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 56.24 t (C^1, $^1J_{PC}$ 85.7 Hz), 147.80 s (C^2), 129.52, 118.13 and 113.72 (C$_{Ph}$). ^{31}P NMR spectrum: δ_P 20.10 ppm. Found, %: C 29.90; H 3.26. $C_7H_9NNa_2O_4P_2$. Calculated, %: C 30.13; H 3.25.

***N*-Anilinomethylenebis[hydroxy(pyrid-3-yl)methylphosphinic] acid (V).** To a solution of 3.5 g of diphosphonite **I** in 10 ml of methylene chloride under cooling to 10°C and stirring was added a solution of 1.6 g of 3-pyridinecarbaldehyde in 10 ml of methylene chloride. Then the solvent was distilled off, and to the residue was added a mixture of 10 ml of methanol and 20 ml of diethyl ether. The mixture was heated to boiling and cooled. The precipitated crystals were filtered off, washed with diethyl ether, and kept in a vacuum of 1 mm Hg for 1h. Yield 2.7 g (89%), mp > 150°C (decomp.). First isomer, content 50%. ^{1}H NMR spectrum, δ, ppm: 4.14 t (C^{1}H, $^2J_{PH}$ 16.4 Hz), 4.95 d (C^{3}H, $^2J_{PH}$ 12.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 50.24 t (C^1, $^1J_{PC}$ 84.8 Hz), 69.74 d (C^3, $^1J_{PC}$ 104.2 Hz). ^{31}P NMR spectrum, δ_P, ppm: 29.98 d and 31.19 d ($^2J_{PP}$ 20.3 Hz). Second isomer, content 30%. ^{1}H NMR, δ, ppm: 4.31 t (C^{1}H, $^2J_{PH}$ 16.0 Hz), 4.97 d (C^{3}H, $^2J_{PH}$ 12.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 48.51 t (C^1, $^1J_{PC}$ 86.9 Hz), 69.97 d (C^3, $^1J_{PC}$ 106.4 Hz). ^{31}P NMR spectrum: δ_P 30.22 ppm. Third isomer, content 20%. ^{1}H NMR, δ, ppm: 3.92 t (C^{1}H, $^2J_{PH}$ 16.3 Hz), 5.05 d (C^{3}H, $^2J_{PH}$ 12.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 51.89 t (C^1, $^1J_{PC}$ 87.6 Hz), 69.13 d (C^3, $^1J_{PC}$ 97.8 Hz). ^{31}P NMR spectrum: δ_P 30.67 ppm. The signals of aromatic fragments of isomers in the ^{1}H and ^{13}C NMR spectra are in the typical ranges and overlapped.

Found, %: C 50.57; H 4.78. $C_{19}H_{21}N_3O_6P_2$. Calculated, %: C 50.79; H 4.71.

Acid **VI** was obtained similarly.

***N*-Anilinomethylenebis[hydroxy(anisyl)methylphosphinic] acid (VI).** Yield 87%, mp > 150°C (decomp.). First isomer, content 50%. ^{1}H NMR spectrum, δ, ppm: 4.71 t (C^1H, $^2J_{PH}$ 16.2 Hz), 4.89 d (C^3H, $^2J_{PH}$ 16.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 48.39 t (C^1, $^1J_{PC}$ 78.7 Hz), 70.27 d (C^3, $^1J_{PC}$ 103.3 Hz). ^{31}P NMR spectrum, δ_P, ppm: 38.17 d, 39.07 d ($^2J_{PP}$ 24.3 Hz). Second isomer, content 30%. ^{1}H NMR spectrum, δ, ppm: 4.78 t (C^1H, $^2J_{PH}$ 16.0 Hz), 4.89 d (C^3H, $^2J_{PH}$ 16.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 48.59 t (C^1, $^1J_{PC}$ 81.2 Hz), 70.96 d (C^3, $^1J_{PC}$ 105.2 Hz). ^{31}P NMR spectrum: δ_P 39.80 ppm. Third isomer, content 20%. ^{1}H NMR spectrum, δ, ppm: 4.41 t (C^1H, $^2J_{PH}$ 16.2 Hz), 4.89 d (C^3H, $^2J_{PH}$ 16.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 49.64 t (C^1, $^1J_{PC}$ 79.8 Hz), 69.20 d (C^3, $^1J_{PC}$ 106.4 Hz). ^{31}P NMR spectrum: δ_P 39.08 ppm. The signals of methoxy and aromatic fragments of isomers in the ^{1}H and ^{13}C NMR spectra are in the typical ranges and overlapped. Found, %: C 54.26; H 5.28. $C_{23}H_{27}NO_8P_2$. Calculated, %: C 54.44; H 5.36.

The NMR spectra were obtained on a Bruker Avance 400 spectrometer in $CDCl_3$ (**I**–**III**) or D_2O (**IV**–**VI**), internal rference TMS (^{1}H, ^{13}C), external reference 85% H_3PO_4 in D_2O (^{31}P) .

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