Synthesis of 1,3,4-oxazaphospholines based on phosphorylated carbamates

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Addition of alcohols to bis(chloromethyl)phosphinoyl isocyanate, as well as the reaction of bis(chloromethyl)phosphinoyl chloride with urethanes or their silylated derivatives, gave the corresponding phosphorylated carbamates which undergo cyclization into 1,3,4-oxazaphospholines under the action of Et_3N.

Key words: bis(chloromethyl)phosphinoyl chloride(isocyanate), phosphorylated carbamates, heterocyclization, 1,3,4-oxazaphospholines.

At present, we are developing methods for the synthesis of polyheterophosphacyclanes with an endocyclic P—C bond. These are based on intramolecular transformations of polyfunctional derivatives of the four-coordinate phosphorus atom.[1] In particular, various saturated and unsaturated phosphacyclanes with the P—C bond can be obtained by combination of a chloromethyl group and urea (thiourea, acylamide, *etc.*) fragments in a molecule. Functionalized chloromethylphosphonates (-phosphinates) can be synthesized by addition of amines, thiols, hydrazines, phosphines, and other protonic nucleophiles to (thio)phosphonoyl(phosphinoyl) iso(thio)cyanates.[1–5] We undertook synthesis of phosphorylated carbamates bearing the chloromethyl groups at the phosphorus atom and attempted to perform their cyclization.

We developed three methods for the synthesis of the target products. Bis(chloromethyl)phosphinoyl isocyanate (**1**) easily adds alcohols to give phosphorylated carbamates (**2, 3**).

$$\underset{\mathbf{1}}{(ClCH_2)_2P(O)NCO} + ROH \longrightarrow \underset{\mathbf{2,\,3}}{(ClCH_2)_2P(O)NHC(O)OR}$$

R = Me (**2**), Et (**3**)

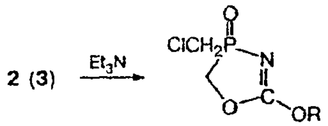
The structures and compositions of compounds **2** and **3** were confirmed by data from NMR and IR spectroscopy and elemental analysis. Taking into account the data obtained by us earlier,[6] we attempted to synthesize compounds **2** and **3** by phosphorylating silylated carbamates. The reaction of bis(chloromethyl)phosphinoyl chloride (**4**) with ethyl *N*-trimethylsilylcarbamates[7] (**5**) easily proceeds with the elimination of chlorotrimethylsilane to give product **3**.

$$\underset{\mathbf{4}}{(ClCH_2)_2P(O)Cl} + \underset{\mathbf{5}}{Me_3SiNHC(O)OEt} \xrightarrow[-Me_3SiCl]{} \mathbf{3}$$

In addition, compound **3** can be obtained by phosphorylation of ethyl carbamate (**6**) with chloride **4** in the absence of a base.

$$\mathbf{4} + \underset{\mathbf{6}}{H_2NCOOEt} \longrightarrow \mathbf{3}$$

In the presence of triethylamine, carbamates **2** and **3** easily split off hydrogen chloride to transform into the corresponding 1,3,4-thiazaphospholines (**7, 8**).



7 (8)

R = Me (**7**), Et (**8**)

The structures and compositions of compounds **7** and **8** were confirmed by data from NMR and IR spectroscopy and elemental analysis. Note that the protons of the endo- and exocyclic methylene groups manifest themselves as one doublet in the ^1H NMR spectra.

Experimental

^{31}P NMR spectra were recorded on a Bruker MSL-400 spectrometer (161.97 MHz) with 85% H_3PO_4 as the external

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standard. ^{1}H NMR spectra were recorded on a Varian T-60 spectrometer (60 MHz) with tetramethylsilane as the internal standard. IR spectra were recorded on a UR-20 spectrometer (thin films or Vaseline oil) in the range 400—3600 cm^{-1}.

Methyl *N*-bis(chloromethyl)phosphinoylcarbamate (2). Isocyanate **1** (2 g, 0.011 mol) was added dropwise with cooling to anhydrous MeOH (3.2 g, 0.1 mol). The crystals that formed were thrice washed with MeOH to give compound **2** (1.53 g, 65.4%), m.p. 160—161 °C. Found (%): C, 21.41; H, 3.47; N, 6.35; P, 13.40. $C_4H_8Cl_2NO_3P$. Calculated (%): C, 21.84; H, 3.66; N, 6.36; P, 14.08. ^{1}H NMR (CD_3CN), δ: 3.63 (s, 3 H, OMe); 3.90 (d, 4 H, CH_2P, *J* = 8 Hz); 10.72 (br.s, 1 H, NH). ^{31}P NMR, δ: 27.26. IR, ν/cm^{-1}: 1190 (P=O); 1720 (C=O); 3100 (NH).

Ethyl *N*-bis(chloromethyl)phosphinoylcarbamate (3). ***A.*** By analogy, compound **3** was obtained from isocyanate **1** (2 g, 0.011 mol) and anhydrous EtOH (4.6 g, 0.1 mol). Yield 1.40 g (56.2%), m.p. 126—128 °C. Found (%): C, 24.83; H, 4.16; N, 5.74; P, 13.18. $C_5H_{10}Cl_2NO_3P$. Calculated (%): C, 25.65; H, 4.30; N, 5.98; P, 13.23. ^{1}H NMR (CD_3CN), δ: 1.03 (t, 3 H, MeC, *J* = 7 Hz); 3.77 (d, 4 H, CH_2P, *J* = 8 Hz); 3.90 (m, 2 H, OCH_2); 10.76 (br.s, 1 H, NH). ^{31}P NMR (C_6H_6), δ: 28.34. IR, ν/cm^{-1}: 1190 (P=O); 1725 (C=O); 3100 (NH).

B. A mixture of silylcarbamate **5** (1.61 g, 0.01 mol) and chloride **4** (1.81 g, 0.01 mol) was heated at 100 °C for 1 h. The crystals that formed were recrystallized from benzene to give compound **3** (1.05 g, 43%), m.p. 126—127 °C. ^{31}P NMR (C_6H_6), δ: 28.34. IR, ν/cm^{-1}: 1190 (P=O); 1725 (C=O); 3100 (NH).

C. A mixture of chloride **4** (2.9 g, 0.016 mol) and ethyl carbamate **6** (1.42 g, 0.016 mol) in 10 mL of anhydrous benzene was heated at 80 °C for 10 h. The crystals that formed were washed with benzene and hexane to give compound **3** (1.7 g, 46.3%), m.p. 126—127 °C. Found (%): Cl, 30.24; P, 13.43. $C_5H_{10}Cl_2NO_3P$. Calculated (%): Cl, 30.32; P, 13.23. ^{31}P NMR (Me_2SO), δ: 28.34.

4-Chloromethyl-2-methoxy-4-oxo-1,3,4-oxazaphosphol-2-ine (7). A solution of carbamate **2** (1 g, 4.5 mmol) and Et_3N (0.46 g, 4.5 mmol) in 10 mL of anhydrous benzene was kept at 20 °C for 1 day. Triethylamine hydrochloride was separated, the filtrate was concentrated, and the crystalline product that formed was washed thrice with hexane to give compound **7** (0.4 g, 39%), m.p. 136—137 °C. Found (%): C, 25.83; H, 4.05; Cl, 18.94, N, 8.06; P, 16.49. $C_4H_7ClNO_3P$. Calculated (%): C, 26.17; H, 3.84; Cl, 19.32, N, 7.63; P, 16.87. ^{1}H NMR (CD_3CN), δ: 3.63 (s, 3 H, Me); 3.92 (d, 4 H, CH_2P, *J* = 8 Hz). ^{31}P NMR (C_6H_6), δ: 59.60. IR, ν/cm^{-1}: 1625 (C=N).

4-Chloromethyl-2-ethoxy-4-oxo-1,3,4-oxazaphosphol-2-ine (8). By analogy, compound **8** was obtained from carbamate **3** (1 g, 4.3 mmol) and Et_3N (0.43 g, 4.3 mmol) in 15 mL of anhydrous benzene. Yield 0.65 g (77.3%), m.p. 147 °C. Found (%): C, 31.09; H, 5.04; N, 6.88; P, 14.97. $C_5H_9ClNO_3P$. Calculated (%): C, 30.39; H, 4.59; N, 7.09; P, 15.69. ^{1}H NMR ($CDCl_3$), δ: 1.60 (t, 3 H, MeC, *J* = 7 Hz); 3.92 (m, 2 H, OCH_2); 4.00 (d, 4 H, CH_2P, *J* = 8 Hz). ^{31}P NMR (C_6H_6), δ: 60.23. IR, ν/cm^{-1}: 1630 (C=N).

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