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Functional Derivatives of (Bromomethyl)phosphonic Acid

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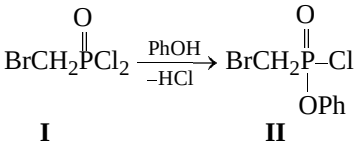
Abstract — Reaction of equimolar amounts of (bromomethyl)phosphonic dichloride and phenol gives phenyl (bromomethyl)chlorophosphonate. Its reactions with heptamethyldisilazane, *N*,*O*-bis(trimethylsilyl)acetamide, and potassium thiocyanate, leading respectively to a silylamidophosphonate, a silyl phosphonate, and an isothiocyanatophosphonate, were studied. (Bromomethyl)(chloromethyl)phosphinoyl isocyanate was synthesized. Chemical properties of the prepared functionalyzed (bromomethyl)phosphonates were investigated.

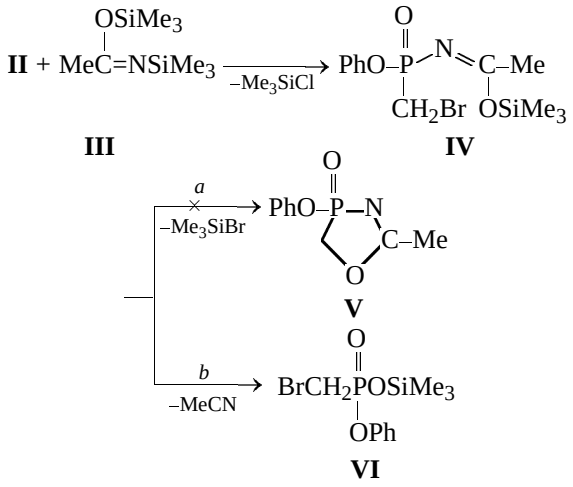
Recently we showed that polyfunctional derivatives of four-coordinate phosphorus, containing a chloromethyl group, can serve as convenient starting materials for preparing saturated and unsaturated polyheterophosphacyclanes [1–3]. Developing this work we have prepared several derivatives of (bromomethyl)phosphonic acid and studied some of their chemical transformations.

Heating of equimolar amounts of (bromomethyl)phosphonic dichloride (**I**) and phenol for some hours leads to formation of phenyl (bromomethyl)chlorophosphonate **II**.



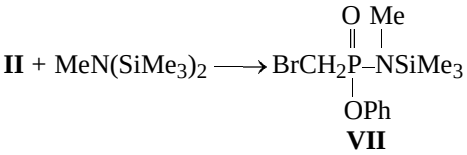
I **II**

Reaction of chlorophosphonate **II** with bis(*N*,*O*-trimethylsilyl)acetamide (**III**) involves liberation of chlorotrimethylsilane and initial formation of amidophosphonate **IV**. Subsequent cyclization of the latter with chlorotrimethylsilane might lead to oxazaphospholine **V**. The reaction between compounds **II** and **III** proceeds easily with heat release, but the final reaction product is silyl phosphonate **VI** (δ_P 7 ppm). Its ^{1}H NMR spectrum contains a singlet of trimethylsilyl protons at 0.33 ppm, a doublet of protons of the methylene group at phosphorus at 3.36 ppm ($^2J_{HP}$ 10 Hz), and a broadened singlet of phenyl protons. Evidently, the subsequent transformation of the initial phosphorylation product **IV** includes its β-cleavage with liberation of acetonitrile and formation of silyl phosphonate **VI**. The same result was obtained when the reaction was carried out in ether at 0°C.



III **IV** **V** **VI**

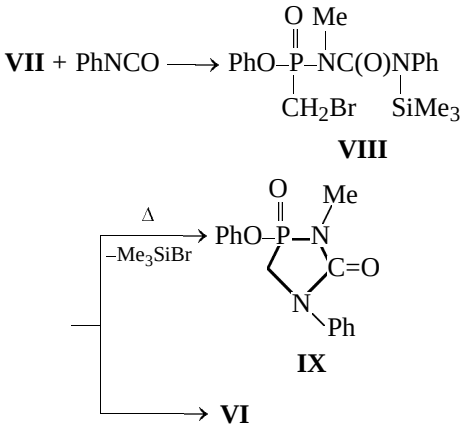
Reaction of chlorophosphonate **II** with heptamethyldisilazane is accompanied by cleavage of one of the Si–N bonds of the latter and gives rise to silylamidophosphonate **VII**.



VII

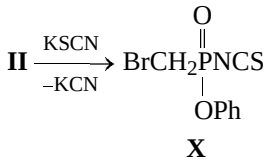
Compound **VII** easily adds to phenyl isothiocyanate to form silylurea **VIII** which undergoes cyclization to 3-methyl-1-phenyl-4-phenoxy-1,3,4λ^5-diazaphospholidin-2-one 4-oxide (**IX**) (δ_P 23.4 ppm) with trimethylbromosilane liberation.

The IR spectrum of product **IX** contains a band of the carbamide group at 1718 cm^{-1}. The ^{1}H NMR spectrum contains a methyl doublet at 3.02 ppm, $^3J_{HP}$ 7.48 Hz. The methylene group gives two doublets of



doublets (AB part of the ABX system), δ_A 4,03, δ_B 3.96 ppm, $^2J_{AB}$ 13.60, $^2J_{PA}$ 13.76, and $^2J_{PB}$ 16.76 Hz. The signal of the trimethylsilyl group is absent. These data show that in the first stage of the reaction phosphorylation proceeds by the most basic nitrogen atom bound with the methyl group. Along with the main reaction pathway, a minor process takes place, that includes 1,3-N,O migration of the trimethylsilyl group followed by decomposition of the intermediate to silyl phosphonate **VI** (δ_P 7 ppm). Comparative study of the reactions of phenyl isothiocyanate with silylamidophosphonate **VII** and its chloromethyl analog showed that the bromomethyl derivative reacts much faster: The reaction completes within 7 days. According to ^{31}P NMR data, about 50% of the chloromethyl derivative remains unreacted by this time.

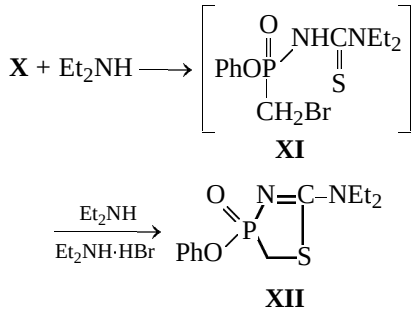
Reaction of chlorophosphonate **II** with potassium thiocyanate in acetonitrile gives (bromomethyl)isothiocyanatophosphonate **X**.



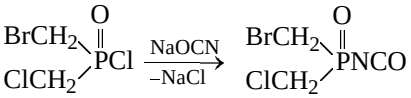
Reaction of isothiocyanate **X** with 2 mol of diethylamine under mild conditions (solvent, 20°C) provides 2-(diethylamino)-4-phenoxy-4,5-dihydro-1,3,4λ^5-thiazaphosphole 4-oxide (**XII**). The IR spectrum of this product contains absorption bands at 925 (P–N), 980–1000, 1190–1200 (POC_6H_5), 1545 (C=N), and 1600 (P=O) cm^{-1}.

The process involved addition of one amine molecule to isothiocyanate **X** with initial formation of phosphorylated thiourea **XI** that, under the action of the second amine molecule, undergoes cyclization to compound **XII**.

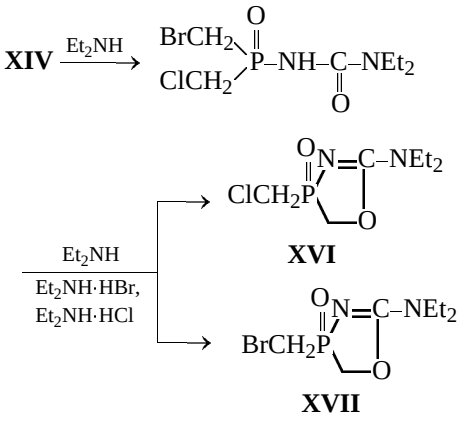
To compare the activities of the halomethyl groups



in the intramolecular alkylation of the thiocarbonyl group of the phosphorylated thiourea, leading to a cyclic structure, we prepared (bromomethyl)(chloromethyl)phosphinoyl isocyanate (**XIV**) from (bromomethyl)(chloromethyl)phosphinoyl chloride (**XIII**) and sodium cyanate.



Addition of one mole of diethylamine to the reaction product gives phosphorylated urea **XV**. We previously showed that prosphorylated ureas containing a chloromethyl group on phosphorus undergo cyclization to 2-amino-4-(chloromethyl)-4,5-dihydro-1,3,4λ^5-oxazaphosphole 4-oxides with liberation of hydrogen chloride or, in the case of N-silylated derivatives, chlorotrimethylsilane [3].



In the case in hand, urea **XV** can cyclize via the chloromethyl or bromomethyl group. Recent theoretical calculations of model compounds showed that the process can involve both these groups with equal probability. The ^{31}P NMR spectrum of the reaction mixture of urea **XV** with diethylamine contains a broadened signal at 60.0 ppm, that provides evidence for the simultaneous formation of two cyclic compounds **XVI** and **XVII**. The same evidence comes

from the elemental analysis. We failed to isolate pure compounds from the reaction mixture.

EXPERIMENTAL

The IR spectra were obtained on a UR-20 spectrometer in the range 400–3600 cm^{-1} in thin films. The ^1H NMR spectra were measured on Bruker WM-250 and Varian T-60 spectrometers against internal TMS. The ^{31}P NMR spectra were recorded an MSL-400 (161.97 MHz) Fourier and KGU-4 (10.2 MHz) NMR spectrometers against external 85% H_3PO_4.

Phenyl (bromomethyl)chlorophosphonate (II). A mixture of 21 g of phosphonic dichloride **I** and 9 g of phenol was heated for 4 h at 175°C. Fractionation of the reaction mixture gave 19 g (70%) of compound **II**, bp 106°C (0.09 mm Hg). ^{31}P NMR spectrum: δ_P 26 ppm. ^1H NMR spectrum (CCl_4), δ, ppm: 3.83 d (2H, CH_2P, $^3J_{HCP}$ 8 Hz). Found, %: P 11.28. $C_7H_7BrClO_2P$. Calculated, %: P 11.48.

Phenyl trimethylsilyl (bromomethyl)phosphonate (VI). A mixture of 4.05 g of chlorophosphonate **II** and 3.0 g of *N*,*O*-bis(trimethylsilyl)acetamide (**III**) was heated for 1 h at 140°C. Fractionation of the reaction mixture gave 2.8 g (58%) of compound **VI**, bp 116°C (0.08 mm Hg), n_D^{20} 1.5040. ^{31}P NMR spectrum: δ_P 7 ppm. Found, %: P 9.60. $C_{10}H_{16}BrO_3PSi$. Calculated, %: P 9.91.

Phenyl (bromomethyl)[*N*-methyl-*N*(trimethylsilyl)amido]phosphonate (VII). A mixture of 10.8 g of chlorophosphonate **II** and 7.0 g of heptamethyldisilazane was heated for 1 h at 130°C. Fractionation of the reaction mixture gave 7.7 g (57%) of compound **VII**, bp 131°C (0.09 mm Hg), n_D^{20} 1.5235. ^{31}P NMR spectrum: δ_P 24 ppm. ^1H NMR spectrum (CCl_4), δ, ppm: 0.24 s (9H, Me_3Si), 2.61 d (3H, CH_3N, $^3J_{HP}$ 13 Hz), 3.53 d (2H, CH_2P, $^2J_{HCP}$ 9 Hz), 7.1 m (5H, C_6H_5O). Found, %: P 8.96. $C_{11}H_{19}BrNO_2SiP$. Calculated, %: P 9.22.

3-Methyl-1-phenyl-4-phenoxy-1,3,4λ^5-diazaphospholidin-2-one 4-oxide (IX). A mixture of 4 g of phosphonate **III** and 1.4 g of phenyl isocyanate was kept for 1 h at 100°C. The crystals that formed were repeatedly washed with carbon tetrachloride and ether to obtain 2.5 g (69%) of compound **IX**, mp 139°C. ^{31}P NMR spectrum: δ_P 23.4 ppm. Found, %: N 9.50, P 10.62. $C_{15}H_{15}N_2O_3P$. Calculated,%: N 9.27, P 10.26.

Phenyl (bromomethyl)isothiocyanatophosphonate (X). A mixture of 10.8 g of chlorophosphonate **II** and 4 g of potassium thiocyanate in 20 ml of acetonitrile was kept for 24 h at 20°C. Potassium chloride and the solvent were removed and the residue was fractionated to obtain 7 g (60%) of compound **X**, bp 136°C (0.08 ppm), n_D^{20} 1.5962. IR spectrum (KBr), ν, cm^{-1}: 1975 (NCS). ^{31}P NMR spectrum: δ_P 3 ppm. Found, %: P 10.65. $C_8H_7BrNO_2PS$. Calculated, %: P 10.61.

2-(Diethylamino)-4-phenoxy-4,5-dihydro-1,3,4λ^5-thiazaphosphole 4-oxide (XII). To a solution of 2 g of isothiocyanate **X** in 10 ml of benzene, 1 g of diethylamine was added dropwise with stirring. After 12 h, diethylamine hydrochloride was filtered off, the solvent was removed, and the residue was fractionated to give 0.9 g (47%) of crystalline product **XII**, mp 75°C. ^{31}P NMR spectrum: δ_P 62 ppm [1].

(Bromomethyl)(chloromethyl)phosphinoyl isocyanate (XIV). To a suspension of 3.2 g of sodium cyanate in 15 ml of acetonitrile, 11.3 g of phosphinic chloride **XIII** was added with stirring, and the resulting mixture was refluxed for 7 h. The liquid phase was separated, the solvent was removed, and the residue was factionated in a vacuum to obtain 3.5 g (30%) of compound **XIV**, bp 103°C (0.05 mm Hg), n_D^{20} 1.5645. ^{31}P NMR spectrum: δ_P 24 ppm. Found, %: P 12.94. $C_3H_4BrClNO_2P$. Calculated, %: P 13.30.

***N*-[(Bromomethyl)(chloromethyl)phosphinoyl]-*N'*,*N'*-diethylurea (XV).** To a solution of 2.3 g of isocyanate **XIV** in 20 ml of ether, 0.73 g of diethylamine was added. The precipitate that formed was filtered off and washed with ether to obtain 1.9 g (61%) of compound **XV**, mp 93°C. IR spectrum (KBr), ν, cm^{-1}: 1216 (P=O), 1639 (C=O), 3123 (NH). ^{31}P NMR spectrum: δ_P 32.3 ppm. Found, %: C 26.78; H 5.01; N 8.32; P 9.70. $C_8H_7BrNO_2PS$. Calculated, %: C 27.45; H 4.90; N 9.15, P 10.13.

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