Phosphorylation of 1,4-bis(hydroxymethyl)benzene

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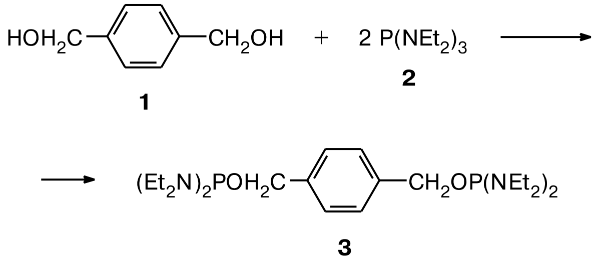
1,4-Bis(hydroxymethyl)benzene undergoes bisphosphorylation with $P(NEt_2)_3$ at room temperature. The reaction produces no cyclic structures.

Key words: 1,4-bis(hydroxymethyl)benzene, bisphosphorylation, sulfurization, X-ray diffraction study.

Earlier,[1—5] we have synthesized a series of phosphamacrocyclic compounds based on aromatic diols and phosphorous acid triamides by molecular assembly, direct synthesis, and dismutation of bis(dialkylphosphoramidites) of aromatic diols. The aim of the present study was to synthesize this class of compounds based on the simplest aromatic glycol, *viz.*, 1,4-bis(hydroxymethyl)benzene (**1**), by the reaction of the latter with $P(NEt_2)_3$ (**2**).

Phenols are known[6,7] to react with phosphorous acid triamides at room temperature, whereas the reactions of aliphatic alcohols occur only at elevated temperature.[8] Data on analogous reactions with aromatic glycols are lacking. However, benzyl alcohol is phosphorylated with hexaethylphosphorous triamide (**2**) on heating.[9] We demonstrated that diol **1** is phosphorylated with amide **2** in acetonitrile or dioxane at room temperature within 30 h without removal of diethylamine that formed during the reaction (Scheme 1).

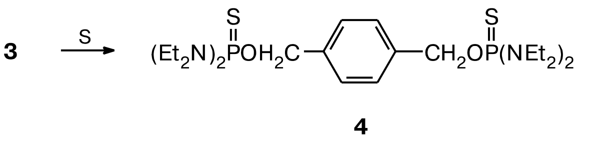
Scheme 1



Bis(phosphorodiamidite) **3** is a colorless viscous oil readily soluble in organic solvents. The ^{31}P NMR spectrum of compound **3** has one singlet at δ 135.3. Sulfurization of product **3** also occurs at room temperature within 4 days to give bis(phosphorothioate) **4** (Scheme 2).

The ^{31}P NMR spectrum of product **4** has a singlet at δ 79.4.

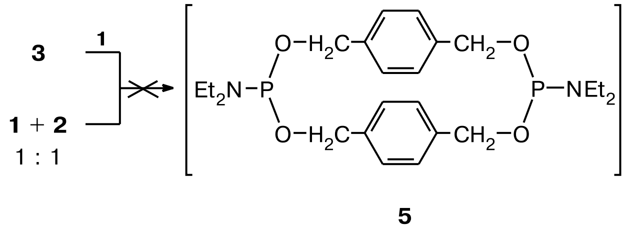
Scheme 2



X-ray diffraction study of compound **4** demonstrated that it has a *trans* configuration and is completely symmetrical (Fig. 1). The molecular packing of **4** in the crystal structure is shown in Fig. 2. The adjacent molecules are shifted with respect to each other by 9.411 Å. The planes of the aromatic rings are parallel to each other and the distance between them is 0.6 Å. The molecules of the next row are arranged in the opposite direction. The P(1)—P(1) and N(2)—N(2) distances between the nearest atoms are 7.909 and 7.377 Å, respectively. The average distance between the planes passing through the aromatic rings of two adjacent rows is 6.69 Å, and the angle between these planes is 7.3°. This molecular packing differs from that observed in the crystals of similar aromatic derivatives, which are packed in stacks.[1,2,4,10]

An attempt to construct cyclic form **5** by molecular assembly, which proved to be efficient in the synthesis of analogous compounds,[1—5] failed (Scheme 3).

Scheme 3



The ^{31}P NMR spectrum of an equimolar mixture of the starting diol **1** and bis(phosphoramidite) **3** recorded after 24 h shows a signal at δ 147 characteristic of aliphatic monoamidoesters. After 30 h, the formation of a transparent oily precipitate started. This precipitate is insoluble

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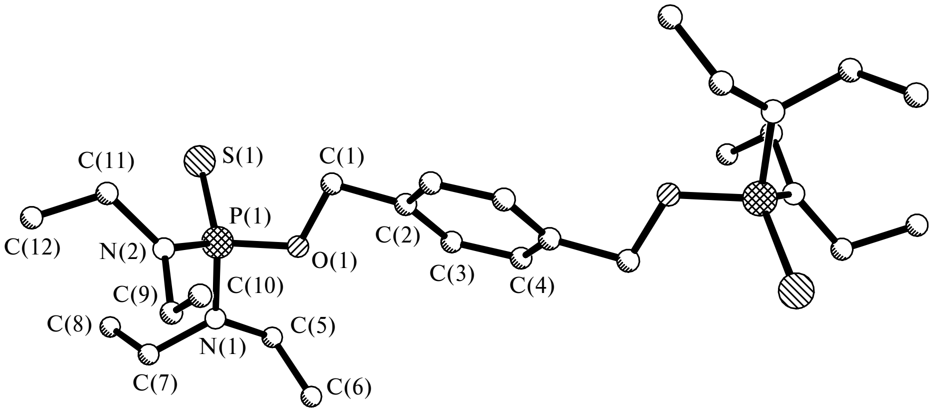

Fig. 1. Overall view of molecule **4** and the atomic numbering scheme (X-ray diffraction data).

but swells in such solvents as DMF and DMSO. After drying, a colorless elastic film was obtained; the melting point of the film is 281—310 °C. The tendency of the compound to swelling and a diffuse melting point range are indicative of an oligomeric nature of this product. The EI mass spectrum showed fragmentation of oligomeric products containing from three to six 1,4-bis(hydroxymethyl)benzene fragments with *m/z* 730—2900.

Analogous results were obtained in the reaction of equimolar amounts of compounds **1** and **2** (this method was used to prepare cyclobis(phosphoramidites) based on aromatic diols[1—5]). We believe that this is apparently associated with the structural features of both the bisphosphorylated product and the starting diol **1**.

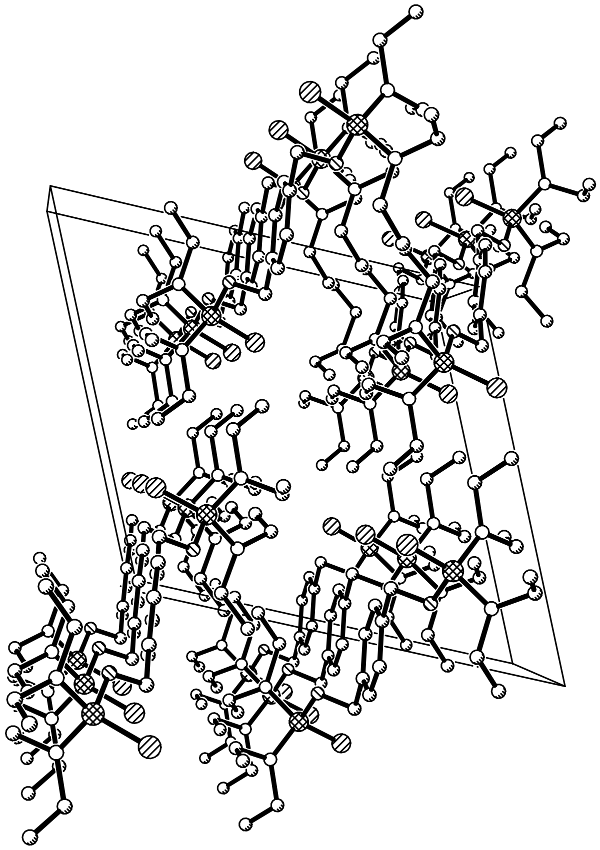

Fig. 2. Molecular packing in the crystal structure of compound **4**.

The addition of sulfur to the reaction mixture in different steps with the aim of identifying the products did not give satisfactory results. An oily substance precipitated from the solution followed by its transformation into a glassy state upon storage. The latter substance is insoluble and does not swell in organic solvents.

Earlier, we have demonstrated[1,2,5,11] that diamidoesters of phosphorous acid are prone to dismutation upon storage in solution, *i.e.*, diamidoesters are spontaneously transformed into monoamidoesters with elimination of triamides. Compound **3** does not undergo this transformation even upon prolonged heating to 80 °C. This is apparently associated with both the absence of conjugation between the aromatic and phosphorous functions due to the presence of the methylene fragments and the steric factor. In the study of dismutation of bis(phosphorodiamidites) of aromatic diols,[11] we have concluded that the molecules of bisphosphorylated derivatives initially approach each other due to stacking interactions between the aromatic fragments. However, X-ray diffraction study demonstrated that this is impossible because of steric hindrance.

To summarize, we found that fatty aromatic alcohols are phosphorylated with phosphorous acid triamides at room temperature. However, this reaction proceeds much more slowly than the analogous reactions of aromatic dihydric alcohols.[1—5] In addition, fatty aromatic alcohols do not form cyclobis(phosphoramidites) because of their structural features.

Experimental

The ^1H NMR spectrum was recorded in $CDCl_3$ on a Bruker AC-200 instrument (200 MHz) with Me_4Si as the internal standard. The ^{31}P NMR spectra were measured in dioxane, MeCN, and CH_2Cl_2 on a Bruker instrument (32.4 MHz) relative to 85% H_3PO_4. Column chromatography was carried out on silica gel L 100/150. The TLC analysis was performed on Silufol plates; visualization was carried out by burning the plates in a burner flame. Hexaethylphosphorous triamide (**2**) was prepared according to a procedure described earlier.[12]

1,4-Bis(tetraethyldiaminophosphinoxymethyl)benzene (3). A solution of 1,4-bis(hydroxymethyl)benzene (**1**) (0.839 g, 6 mmol) in dioxane (10 mL) was added with stirring to hexaethylphosphorous triamide (**2**) (0.3 g, 12 mmol) at ~20 °C. After 30 h, the solvent was removed and compound **3** was obtained as a viscous colorless oil, R_f 0.60 (hexane—dioxane, 5 : 1). ^{31}P NMR, δ: 135.3.

1,4-Bis(tetraethyldiaminothiophosphoryloxymethyl)benzene (4). Sulfur (0.16 g, 5 mmol) was added to a solution of phosphorodiamidite **3** (1 g, 2 mmol) in dioxane (10 mL) and the reaction mixture was kept at ~20 °C for 4 days. Then the solution was filtered, the solvent was removed, and the residue was chromatographed on a column (hexane—dioxane, 10 : 1, as the eluent). Compound **4** was isolated in a yield of 0.84 g (73%), m.p. 132—133 °C, R_f 0.65 (hexane—dioxane, 5 : 1), 0.68 ($CHCl_3$). ^{1}H NMR, δ: 1.07 (t, 24 H, Me, $^3J_{H,H}$ = 7.63 Hz); 3.11 (m, 16 H, CH_2N, $^3J_{P,H}$ = 4.67 Hz); 4.96 (d, 4 H, CH_2O, $^3J_{P,H}$ = 8.24 Hz); 7.34 (s, 4 H, H arom.). ^{31}P NMR, δ: 79.4.

X-ray diffraction study. Crystals of compound **4** were prepared by crystallization from hexane. X-ray diffraction data were collected on an automated Enraf-Nonius CAD-4 diffractometer (β filter, λ(Mo-Kα), θ/2θ scanning technique, θ_{max} = 24.88°). The colorless crystals belong to the monoclinic system ($C_{24}H_{48}N_4O_2P_2S_2$, M = 550.72), the crystal dimensions were 0.38×0.32×0.12 mm, space group $P2(1)/c$, a = 13.168(3) Å, b = 9.411(2) Å, c = 14.107(3) Å, α = 90°, β = 114.98(3)°, γ = 90°, V = 1584.7(6) Å^3, Z = 2, d_{calc} = 1.154 g cm^{-3}. A total of 1358 reflections were measured, of which 1290 reflections were independent (R_{int} = 0.0130). The number of the parameters in the refinement was 374, GOOF 1.024, $R_1(F)$ = 0.0447, $wR_2(F^2)$ = 0.1216. The structure was refined by the full-matrix least-squares method against F^2_{hkl} with anisotropic displacement parameters for nonhydrogen atoms. All H atoms were refined isotropically with fixed parameters (were placed in calculated positions). The bond lengths and bond angles are given in Table 1. The complete tables of bond lengths, bond angles, atomic coordinates, and displacement parameters were deposited with the Cambridge Structural Database.

Table 1. Selected bond lengths (d) and bond angles (ω) in molecule **4**

Bond	d/Å	Angle	ω/deg
P(1)—O(1)	1.593(3)	O(1)—P(1)—N(2)	106.9(2)
P(1)—N(2)	1.633(4)	O(1)—P(1)—N(1)	97.35(18)
P(1)—N(1)	1.640(4)	O(1)—P(1)—S(1)	106.3(2)
P(1)—S(1)	1.9354(18)	O(1)—C(1)—C(2)	108.7(3)
O(1)—C(1)	1.442(5)	N(2)—P(1)—N(1)	113.06(14)
N(1)—C(5)	1.470(6)	N(2)—P(1)—S(1)	113.14(16)
N(1)—C(7)	1.480(7)	N(1)—P(1)—S(1)	118.55(17)
N(2)—C(11)	1.466(6)	C(1)—O(1)—P(1)	119.6(3)
N(2)—C(9)	1.476(7)	C(5)—N(1)—C(7)	115.1(4)
C(1)—C(2)	1.495(6)	C(5)—N(1)—P(1)	119.7(3)
C(2)—C(4)$^{\#1}$	1.376(6)	C(7)—N(1)—P(1)	121.2(3)
C(2)—C(3)	1.386(6)	C(11)—N(2)—C(9)	116.4(4)
C(3)—C(4)	1.380(6)	C(4)$^{\#1}$—C(2)—C(3)	118.6(4)
C(4)—C(2)$^{\#1}$	1.376(6)	C(4)$^{\#1}$—C(2)—C(1)	120.4(4)
C(5)—C(6)	1.457(8)	C(3)—C(2)—C(1)	120.9(4)
C(7)—C(8)	1.424(10)	C(4)—C(3)—C(2)	120.1(4)
C(9)—C(10)	1.443(10)	C(2)$^{\#1}$—C(4)—C(3)	121.3(4)
C(11)—C(12)	1.435(10)	C(6)—C(5)—N(1)	113.6(5)
		C(8)—C(7)—N(1)	116.5(6)
		C(10)—C(9)—N(2)	115.1(6)
		C(12)—C(11)—N(2)	113.8(6)

Note. The symmetry code #1 ($-x$, $-y$, $-z$).

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