First representatives of quinolino-1,3,2-dioxaphosphorinanes*

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Cyclophosphorylation of 7-(1,1,1,3,3,3-hexafluorohydroxyisopropyl)-8-hydroxyquinoline with trivalent phosphorus reagents affords the first representatives of quinolino-1,3,2-dioxaphosphorinanes. The crystal structure of 4,4-bis(trifluoromethyl)-2-diethylamino-2-thio(quinolino-7,8)-1,3,2-dioxaphosphor(v)inane has been studied. A substantial effect of substituents at the P atom on the conformation of the phosphor(v)inane fragment of the molecule has been established.

Key words: 7-(1,1,1,3,3,3-hexafluorohydroxyisopropyl)-8-hydroxyquinoline, phosphorus(III), cyclophosphorylation; quinolino-1,3,2-dioxaphosphorinanes, crystal structure.

Recently, we have obtained the first simplest condensed aromatic 1,3,2-dioxaphosphor(III)inanes.[1] These compounds are promising reagents for fine organic synthesis, for example, for preparation of phosphorylated sterically hindered phenols.[2] The goal of this work is to synthesize quinolino-1,3,2-dioxaphosphor(III)inanes, new condensed heterocycles. Note that these phosphorinanes can be considered as analogs of adenosine (thymidine) cyclic monophosphates.

We have demonstrated the possibility of a smooth cyclophosphorylation of 7-(1,1,1,3,3,3-hexafluoro-2-hydroxyisopropyl)-8-hydroxyquinoline (**1**)[3] under the action of acid chlorides and amides of phosphorous acid (Scheme 1).

2-X-4,4-Bis(trifluoromethyl)-5,6-(quinolino-7,8)-1,3,2-dioxaphosphorinanes **2** have been isolated in crystalline form in high yields. The ^1H and ^{31}P NMR spectra of these compounds contain signals of the corresponding atoms. The signal of the P atom in the ^{31}P NMR spectrum of amidophosphite **2b**, the quadruplet at δ 130, determined by the spatial spin-spin P—F interaction ($J_{P,F}$ = 23.2 Hz) engaged attention. By contrast, in the spectrum of phosphite **2a**, a singlet at δ 109 is observed. Apparently, this difference is determined by a more pronounced flattening of the phosphamide fragment resulting in hanging of one of the CF_3 groups over the P atom. In molecule **2a**, the flattening of the phosphite group is less pronounced, and two CF_3 groups are arranged more symmetrically. On the whole, the structural features resemble those of benzophosphorinanes with two CF_3 groups (*cf.* Ref. 1).

The obtained quinolinophosphorinanes **2** are readily oxidized and add on sulfur to form the corresponding phosphoryl (**3a,b**) and thiophosphoryl (**4**) compounds. We have performed X-ray structural analysis of thionphosphamide **4**. The overall view of molecule **4** is shown in Fig. 1; the bond lengths and bond angles are given in Tables 1 and 2, respectively. In molecule **4**, the endocyclic angles and C—C interatomic distances of the aromatic rings are in the ranges of known values. The

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Scheme 1

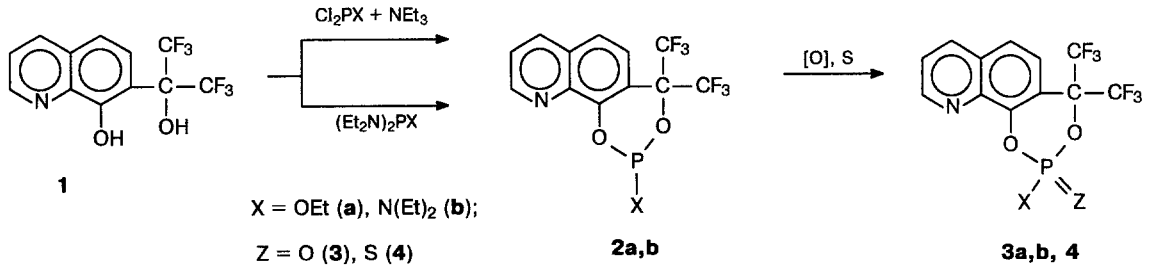

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Table 1. Bond lengths (*d*) in molecule **4**

Bond	*d*/Å	Bond	*d*/Å
P(1)—O(1)	1.599(8)	F(6)—C(12)	1.32(2)
P(1)—N(2)	1.600(10)	C(1)—C(2)	1.39(2)
P(1)—O(2)	1.615(8)	C(2)—C(3)	1.35(2)
P(1)—S(1)	1.903(5)	C(3)—C(4)	1.38(2)
O(1)—C(8)	1.384(13)	C(4)—C(9)	1.40(2)
O(2)—C(10)	1.411(13)	C(4)—C(5)	1.42(2)
N(1)—C(1)	1.32(2)	C(5)—C(6)	1.31(2)
N(1)—C(9)	1.395(14)	C(6)—C(7)	1.43(2)
N(2)—C(15)	1.46(2)	C(7)—C(8)	1.38(2)
N(2)—C(13)	1.49(2)	C(7)—C(10)	1.50(2)
F(1)—C(11)	1.33(2)	C(8)—C(9)	1.41(2)
F(2)—C(11)	1.328(14)	C(10)—C(11)	1.52(2)
F(3)—C(11)	1.324(14)	C(10)—C(12)	1.57(2)
F(4)—C(12)	1.30(2)	C(13)—C(14)	1.51(3)
F(5)—C(12)	1.34(2)	C(15)—C(16)	1.49(3)

fragment of atoms bonded to the aromatic cycle is planar within ±0.002 Å.

The phosphorinane ring has a complex sofa-type conformation; the P and O(2) atoms deviate from the mean plane by 0.946 and 0.42 Å, respectively. This situation is unusual for 1,3,2-dioxaphosphor(V)inanes, which often adopt a chair conformation.[4] The N(2) atom is in an equatorial position; this atom deviates from the mean plane by 0.4186 Å. The S atom occupies an axial position; the deviation from the mean plane is 2.8137 Å. Atomic coordinates for nonhydrogen atoms are given in Table 3 (atomic coordinates for H atoms may be obtained from authors).

We have also studied selected transformations of synthesized phosphates and thionphosphates. Phosphate **3a** appears to be a very unstable compound and is readily hydrolized (Scheme 2); only the aliphatic phosphate function is subjected to hydrolysis. This conclusion was drawn when the ^{31}P NMR spectrum of hydrolysis product **5** was compared with the spectra of related compounds that we have studied previously.[1]

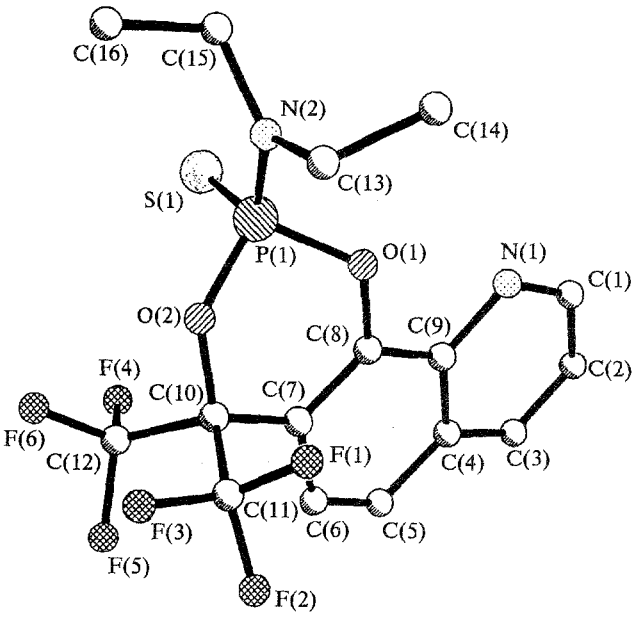

Fig. 1. Overall view of molecule **4**.

Compound **5**, which is a hydrophilic derivative of a sterically hindered phenol, is of interest in regulation of homolytic reactions in a cell.

Scheme 2

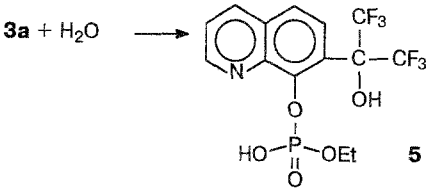

Table 2. Bond angles (ω) in molecule **4**

Angle	ω/deg	Angle	ω/deg	Angle	ω/deg
O(1)—P(1)—N(2)	103.6(5)	C(3)—C(4)—C(5)	124.4(12)	C(11)—C(10)—C(12)	110.1(11)
O(1)—P(1)—O(2)	98.6(4)	C(6)—C(5)—C(4)	120.9(12)	F(3)—C(11)—F(1)	108.1(11)
N(2)—P(1)—O(2)	105.4(5)	C(5)—C(6)—C(7)	123.5(13)	F(3)—C(11)—F(2)	108.0(10)
O(1)—P(1)—S(1)	115.5(4)	C(8)—C(7)—C(6)	116.1(11)	F(1)—C(11)—F(2)	106.3(11)
N(2)—P(1)—S(1)	116.9(4)	C(8)—C(7)—C(10)	120.6(10)	F(3)—C(11)—C(10)	112.4(11)
O(2)—P(1)—S(1)	114.7(4)	C(6)—C(7)—C(10)	122.9(10)	F(1)—C(11)—C(10)	109.2(10)
C(8)—O(1)—P(1)	116.1(7)	O(1)—C(8)—C(7)	120.8(9)	F(2)—C(11)—C(10)	112.5(11)
C(10)—O(2)—P(1)	123.8(7)	O(1)—C(8)—C(9)	117.9(9)	F(4)—C(12)—F(6)	108.3(13)
C(1)—N(1)—C(9)	114.4(11)	C(7)—C(8)—C(9)	121.3(10)	F4)—C(12)—F(5)	107.5(13)
C(15)—N(2)—C(13)	116.0(12)	C(4)—C(9)—N(1)	123.1(10)	F(6)—C(12)—F(5)	105.9(11)
C(15)—N(2)—P(1)	123.0(10)	C(4)—C(9)—C(8)	120.2(10)	F(4)—C(12)—C(10)	112.4(11)
C(13)—N(2)—P(1)	120.7(9)	N(1)—C(9)—C(8)	116.7(10)	F(6)—C(2)—C(10)	111.4(12)
N(1)—C(1)—C(2)	126.1(13)	O(2)—C(10)—C(7)	113.9(9)	F(5)—C(12)—C(10)	110.9(12)
C(3)—C(2)—C(1)	117.9(14)	O(2)—C(10)—C(11)	105.1(10)	N(2)—C(13)—C(14)	111(2)
C(2)—C(3)—C(4)	120.5(14)	C(7)—C(10)—C(11)	111.4(10)	N(2)—C(15)—C(16)	112(2)
C(9)—C(4)—C(3)	117.9(12)	O(2)—C(10)—C(12)	104.9(9)		
C(9)—C(4)—C(5)	117.6(11)	C(7)—C(10)—C(12)	111.1(11)		

Table 3. Atomic coordinates of nonhydrogen atoms ($\times 10^4$) and equivalent temperature factors ($U_{eq} \times 10^3$) in the structure of **4**

Atom	*x*	*y*	*z*	U_{eq}/Å^2
P(1)	4331(5)	9066(2)	2771(2)	49(1)
S(1)	1738(6)	9074(2)	2703(3)	74(1)
O(1)	4129(13)	8222(4)	2304(5)	51(2)
O(2)	6220(12)	9166(4)	3759(5)	54(2)
N(1)	1444(17)	6740(6)	1213(6)	60(3)
N(2)	5462(16)	9722(6)	2371(6)	56(3)
F(1)	9087(13)	8548(6)	3953(6)	92(3)
F(2)	8829(14)	7953(5)	4945(5)	90(3)
F(3)	10001(13)	9257(5)	5208(5)	93(3)
F(4)	3733(18)	8510(6)	4676(6)	99(3)
F(5)	6612(17)	8398(5)	5616(5)	97(3)
F(6)	6735(18)	9539(5)	5308(6)	103(3)
C(1)	86(26)	6001(8)	710(10)	67(4)
C(2)	−566(25)	5309(10)	1007(10)	80(4)
C(3)	347(22)	5380(9)	1892(10)	64(4)
C(4)	1813(19)	6124(7)	2475(8)	55(3)
C(5)	2815(22)	6261(8)	3415(8)	60(3)
C(6)	4204(243)	6987(8)	3928(10)	70(4)
C(7)	4659(18)	7699(7)	3601(7)	49(3)
C(8)	3721(17)	7576(6)	2688(7)	43(3)
C(9)	2288(17)	6797(7)	2121(7)	46(3)
C(10)	6265(19)	8524(7)	4195(7)	50(3)
C(11)	8587(21)	8376(7)	4591(9)	60(3)
C(12)	5798(29)	8746(9)	4953(9)	73(4)
C(13)	7388(27)	9718(12)	2326(11)	79(4)
C(14)	6801(42)	9384(17)	1390(16)	115(8)
C(15)	4818(28)	10394(8)	2107(10)	72(4)
C(16)	6155(64)	11156(14)	2832(18)	132(10)

It is interesting that amidophosphite **3b** is more stable with respect to water, while thioamidophosphate **4** is so stable that it undergoes no hydrolysis either in acidic and alkaline media.

Experimental

All experiments with the P^{III} derivatives were carried out under a dry inert gas atmosphere; anhydrous solvents were used. The ^{31}P NMR spectra were recorded on an Bruker WP-80 instrument (operating at 32.4 MHz) in benzene; chemical shifts were measured relative to an 85 % H_3PO_4 solution at 30 °C with full proton decoupling. The ^1H NMR spectra were recorded on a Bruker AM-400 instrument in $CDCl_3$ and C_6D_6; chemical shifts were measured relative to HMDS.

4,4-Bis(trifluoromethyl)-2-ethoxy-5,6-(quinolino-7,8)-1,3,2-dioxaphosphor(III)inane (2a). Triethylamine (0.9 g, 0.0064 mol) was added to a solution of compound **1** (1 g) in benzene; then a solution of ethylphosphonic dichloride (0.46 g, 0.0032 mol) in benzene was added with stirring. The reaction mixture was stirred for 1.5 h. The precipitate was filtered off, the solvent was evaporated *in vacuo*, and compound **2a** was obtained by distillation of the residue. The yield of **2a** was 78 %, b.p. 140 °C (10^{-4} Torr). ^1H NMR, δ: 1.1 (t, Me); 3.2 (q, OCH_2); 6.7 (t), 6.9 (d), 7.3 (d), 7.6 (d), and 8.7 (d) (Ar). ^{31}P NMR, δ: 109 (s). Found (%): C, 43.7; H, 2.6; P, 8.1. $C_{14}H_{10}F_6NO_3P$. Calculated (%): C, 43.6; H, 2.6; P, 8.0.

4,4-Bis(trifluoromethyl)-2-ethylamino-5,6-(quinolino-7,8)-1,3,2-dioxaphosphor(III)inane (2b). *A.* Triethylamine (0.45 mL, 0.0032 mol) was added to a solution of hydroxyquinoline **1** (0.5 g, 0.0016 mol) in benzene, and then a solution of diethylaminophosphonic dichloride (0.28 g, 0.0016 mol) in benzene was added with stirring. The reaction mixture was stirred for 1 h. The precipitate was filtered off, and the solvent was partially evaporated *in vacuo*. Crystals of compound **2b** were formed on cooling. The yield of **2b** was 82 %, m.p. 68—69 °C. ^1H NMR, δ: 0.9 (t, Me); 2.9 (m, NCH_2); 6.7 (t), 6.9 (d), 7.3 (d), 7.6 (d), and 8.7 (d) (Ar). ^{31}P NMR, δ: 130 (q). Found (%): C, 45.42; H, 3.51; P, 7.49. $C_{16}H_{15}F_6N_2O_2P$. Calculated (%): C, 46.60; H, 3.64; P, 7.52.

B. Hexaethyltriamide of phosphorous acid (0.36 g) was added to compound **1** (0.45 g). The mixture was heated in a distillation flask at 110—120 °C until formation of diethylamine (0.2 g) was completed. The reaction mixture was dissolved in a minimum amount of benzene. Colorless crystals of compound **2b** were formed on cooling. The yield was 66 %.

4,4-Bis(trifluoromethyl)-2-oxo-2-ethoxy(quinolino-7,8)-1,3,2-dioxaphosphor(v)inane (3a). Iodosobenzene (0.3 g) was added to a solution of phosphorinane **2a** (0.5 g, 0.0013 mol) in benzene. The mixture was kept at 30 °C for 2 h and purified from iodobenzene by chromatography on Al_2O_3. The solvent was partially evaporated *in vacuo*. Colorless crystals of compound **3a** were formed on cooling. The yield was 54 %, m.p. 126—127 °C (decomp.). ^1H NMR, δ: 1.1 (t, Me); 3.4 (q, OCH_2); 6.8 (t), 7.1 (d), 7.5 (d), 7.8 (d), and 8.9 (d) (Ar). ^{31}P NMR, δ: −17.3 (s). Found (%): C, 41.90; H, 2.50; P, 7.80. $C_{14}H_{10}F_6NO_4P$. Calculated (%): C, 41.89; H, 2.49; P, 7.73.

4,4-Bis(trifluoromethyl)-2-diethylamino-2-oxo(quinolino-7,8)-1,3,2-dioxaphosphor(v)inane (3b). Compound **3b** was prepared from amidophosphite **2b** analogously to compound **3a**. The yield of **3b** was 68 %, m.p. 144—145 °C. ^1H NMR, δ: 1.1 (t, Me); 3.4 (q, NCH_2); 6.6 (t), 6.9 (d), 7.2 (d), 7.5 (d), and 9.0 (d) (Ar). ^{31}P NMR, δ: −3.6 (s). Found (%): C, 44.9; H, 3.5; P, 8.3. $C_{16}H_{15}F_6N_2O_3P$. Calculated (%): C, 44.8; H, 3.5; P, 7.2.

4,4-Bis(trifluoromethyl)-2-diethylamino-2-thio(quinolino-7,8)-1,3,2-dioxaphosphor(v)inane (4). Fine elementary sulfur (0.1 g) was added to a solution of diethylamine **2b** (0.5 g) in benzene. The mixture was kept for 6 h at 80 °C and partially evaporated *in vacuo*. Colorless crystals of compound **4** were formed on cooling. The yield was 86 %, m.p. 103—104 °C. ^1H NMR, δ: 1.3 (t, Me); 3.5 (q, N—CH_2); 6.7 (t), 6.9 (d), 7.4 (d), 7.7 (d), and 8.7 (d) (Ar). ^{31}P NMR, δ: 61.4 (s). Found (%): C, 43.2; H, 3.2; P, 6.9. $C_{16}H_{15}F_6N_2O_2PS$. Calculated (%): C, 43.2; H, 3.4; P, 6.9.

7-(1,1,1,3,3,3-Hexafluoro-2-hydroxyisopropyl)-8-(ethylphosphate)hydroxyquinoline (5). Water (0.1 g) in dioxane was added to a solution of ethyl phosphate **3a** (0.4 g) in dioxane. A precipitate of quinoline **5** was formed after 15 min; the precipitate was recrystallized from methanol. The yield was 91 %, m.p. 310 °C. ^{31}P NMR, δ: −16.4 (s). Found (%): C, 40.1; H, 2.9; P, 7.4. $C_{14}H_{12}F_6NO_5P$. Calculated (%): C, 40.3; H, 3.1; P, 7.5.

X-ray structural analysis of compound 4. Crystals of **4** are triclinic, a = 7.514(1) Å, b = 17.868(4) Å, c = 17.387(4) Å, V = 1915.5(7) Å^3, Z = 4, space group $P\bar{1}$, d_{calc} = 1.541 g cm^{-3}. The unit-cell parameters and intensities of 904 independent reflections with $I > 2\sigma(I)$ were measured on a four-circle automated Syntex P1 diffractometer (without a

monochromator, Mo-Kα radiation, θ/2θ scanning technique, $\sin\theta/\lambda_{max} = 0.539$). The structure was solved by the direct method using the SHELXTL program package and refined by the least-squares method with anisotropic (C, N, O, F, P, and S) and isotropic (H) thermal parameters. Positional and thermal parameters of H atoms were included in the final refinement. The final R factors were as follows: $R = 0.0859$, $R_w = 0.2824$.

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