Reaction of 2-methoxy-1,3,2-dioxaphosphorino[4,5-*b*]pyridin-4(4*H*)-one with hexafluoroacetone

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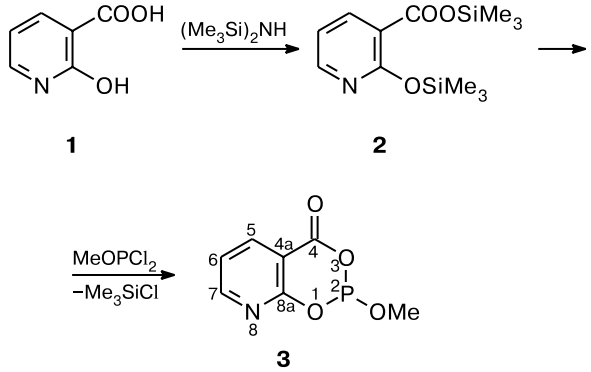
The reaction of the di-*O*-trimethylsilyl derivative of 2-hydroxynicotinic acid with methyl phosphodichloridite afforded 2-methoxy-1,3,2-dioxaphosphorino[4,5-*b*]pyridin-4(4*H*)-one. The NMR spectroscopic data suggest that the reaction of the latter with hexafluoroacetone produces unstable 2-methoxy-2,5-dioxo-4,4-bis(trifluoromethyl)-4,5-dihydro-1,3,2-dioxaphosphepino[4,5-*b*]pyridine, which is readily transformed into 9-methyl-2,5-dioxo-4,4-bis(trifluoromethyl)-4,5-dihydro-1,3,2-dioxaphosphepino[4,5-*b*]pyrid-9-inium-2-oate. The structure of the hydrolysis product of the latter, *viz.*, 1-methyl-3-(2-hydroxy-3,3,3-trifluoro-2-trifluoromethylpropanoyl)pyridin-2-one, was established by X-ray diffraction analysis.

Key words: 2-hydroxynicotinic acid, methyl phosphodichloridite, 2-methoxy-1,3,2-dioxaphosphorino[4,5-*b*]pyridin-4(4*H*)-one, hexafluoroacetone, pyrido-annelated 2,5-dioxo-4,4-bis(trifluoromethyl)-1,3,2-dioxaphosphepine derivatives, pyridin-2-one derivatives.

The phosphorine ring in cyclic phosphorylated derivatives of salicylic acid, *viz.*, 2-R-benzo[*d*]-1,3,2-dioxaphosphorin-4-ones (salicyl phosphites), undergoes expansion under the action of reactive carbonyl compounds, such as hexafluoroacetone,[1,2] ethyl pyruvate,[3] methyl trifluoropyruvate,[4] or nonsymmetrical perfluorinated α-diketones,[5] to give nonsymmetrical functionalized seven-membered heterocycles, *viz.*, benzo[*d*]-1,3,2-dioxaphosphepines. Such compounds derived from hexafluoroacetone can further be used in the synthesis of functionalized fluorinated ketones that are accessible with difficulty.[6] In the present study, we attempted to extend the phosphorine-ring expansion reaction under the action of hexafluoroacetone to more complex compounds, *viz.*, cyclic phosphorylated derivatives of 2-hydroxynicotinic acid (**1**). We saw little reason to use phosphodichloridites for direct phosphorylation of acid **1** because of the possible competition with bases commonly used for scavenging HCl that is eliminated and possible side processes. The readily accessible di-*O*-trimethylsilyl derivative of acid **1** (**2**) is the starting compound of choice for the synthesis of cyclic phosphorylated derivatives of this acid. The reaction of derivative **2** occurs under mild conditions to give the target compound **3** in nearly quantitative yield (Scheme 1). In the ^{31}P NMR spectrum of compound **3**, the signal for the P atom appears as a quartet ($^3J_{P,H}$ = 12.2 Hz) in the characteristic region (δ_P 122.2). Since phosphorine **3** undergoes decomposition during vacuum distillation (0.1 Torr), this was used without additional purification.

Scheme 1



It should be noted that cyclic phosphorylated derivatives of 2-methylaminonicotinic acid methylamide **4** described in the literature cannot undergo ring expansion.

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For example, their reactions with hexafluoroacetone afford λ^5-1,3,2-dioxaphospholane derivatives.[7]

Unlike compounds **4**, phosphite **3** readily reacts with hexafluoroacetone to form phosphepine **5** (Scheme 2). Its ^{31}P NMR spectrum (CH_2Cl_2) contains a singlet at δ_P −12.7. This chemical shift is consistent with those of structurally similar benzo[*d*]-1,3,2-dioxaphosphepines.[1–5] Compound **5** is very unstable both by itself and with respect to atmospheric moisture and is rather rapidly transformed into compounds with chemical shifts δ_{P1} 0.3 and δ_{P2} 2.7 in a ratio varying from 1 : 1 (^{31}P NMR in DMSO) to 1 : 3 (^{31}P NMR in $CDCl_3$) during the reaction (see Experimental). We repeated the experiment with no special protection from atmospheric moisture and demonstrated that the percentage of the compound with δ_{P1} increased. These data are consistent with the ^{19}F NMR spectral patterns for these samples (two br.s at δ_{F2} −74.0 and δ_{F1} −74.14 in DMSO in a ratio of 1 : 1; two br.s at δ_{F2} −73.27 and δ_{F1} −73.21 in $CDCl_3$ in a ratio of 3 : 1). The ^{19}F NMR spectrum in acetone-d_6 (δ_{F1} −73.23 and δ_{F2} −73.26, 1 : 3) is similar to that in $CDCl_3$. The ^1H NMR spectra in various solvents show no signals for the protons of the methoxy substituent at the P atom. The ^1H NMR spectrum (DMSO-d_6) has a singlet for the protons of the Me group at the N atom (δ 3.71). A double set of signals is observed in the region characteristic of the protons of the pyridine ring (Table 1). The IR spectrum of the precipitate that was initially formed in CH_2Cl_2 has the following bands (ν/cm^{-1}): 2500—2700 (N^+Me, POH), 1715—1720 (C=O), 1639, 1635 sh, 1590, 1560 (C=N, C=C), 1300, 1280 sh, 1230—1260, 1160, 1125, 950, 880, 840 (P=O, CF, POC), *i.e.*, the reaction products contain the carbonyl and phosphoryl groups, the ammonium fragment, and the hydroxy group bound to the P atom. Thus, the spectral pattern is consistent with the fact that unstable phosphepine **5** is transformed into two carbonyl-containing phosphorus compounds, one of which bears the methyl group at the N atom. Based on the ^1H and ^{13}C NMR spectroscopic data (see Table 1), structures **6** and **7** were assigned to compounds characterized by the chemical shifts δ_{P1} and δ_{P2} (and, correspondingly, δ_{F1} and δ_{F2}).

Compounds **6** and **7** have cyclic structures, as evidenced by the coupling constants $J_{C,P}$ of the C(5) and C(4) atoms. The position and multiplicity of the signal for the C atom of the methyl group unambiguously indicate that this substituent is bound to the N atom. The signals belonging to the pyridine ring were assigned with account for the chemical shifts, the multiplicities of the signals, the coupling constants $J_{H,C}$, and the literature data.[8,9] Although having similar chemical shifts, the C(8) and C(6) atoms in compound **6** are easily distinguishable due to a larger coupling constant $^1J_{H,C(8)}$. The signal belonging to the C(8) atom has also an additional coupling constant with the protons of the adjacent Me group ($^3J_{H,C(8)}$ = 3.8 Hz). In *N*-alkylated pyridinium salts, the chemical shifts of the α-C nuclei are almost equal to

Scheme 2

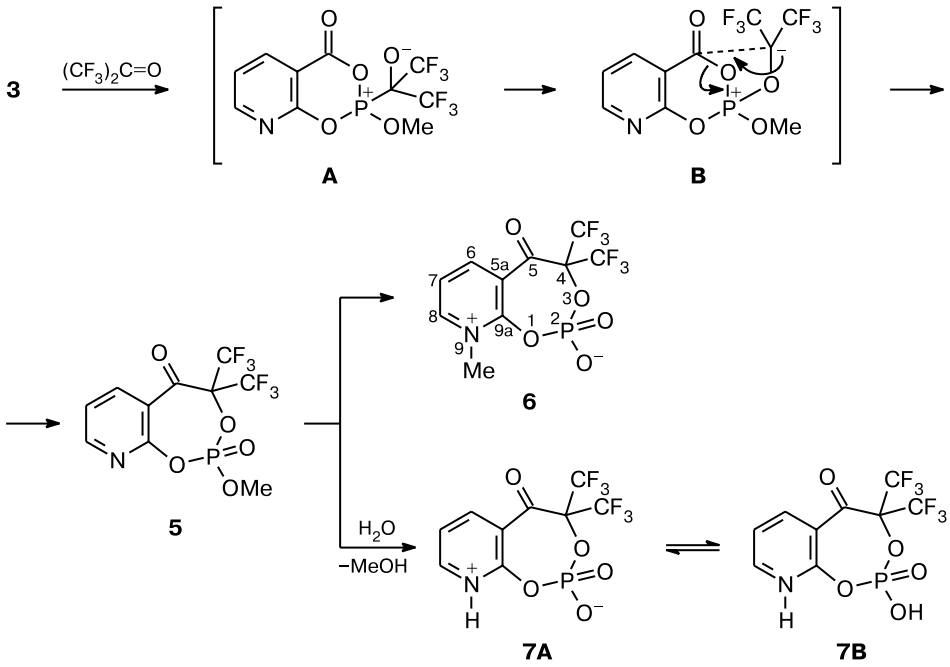


Table 1. ^{1}H, ^{13}C, and $^{13}C\{^{1}H\}$ NMR spectra of compounds **6** and **7** in DMSO-d_6

Compound	NMR, δ (*J*/Hz)	
	^{1}H	^{13}C
6	3.71 (br.s, 3 H, Me); 6.58 (ddd, 1 H, H(7), $^{3}J_{H(6),H(7)} = 7.5$, $^{3}J_{H(8),H(7)} = 6.5$, $^{6}J_{P,H(7)} = 0.7$); 7.78 (dddq, 1 H, H(8), $^{3}J_{H(7),H(8)} = 6.5$, $^{4}J_{H(6),H(8)} = 2.1$, $^{4}J_{H_{Me},H(8)} = 0.4$, $^{5}J_{P,H(8)} = 0.4$); 8.15 (dddq, 1 H, H(6), $^{3}J_{H(7),H(6)} = 7.5$, $^{4}J_{H(8),H(6)} = 2.1$, $^{5}J_{P,H(6)} \approx 0.3$—$0.4$, $^{6}J_{H_{Me},H(6)} \approx 0.3$—$0.4$)	43.13 (s [qd], Me, $^{1}J_{H,C} = 146.7$, $^{3}J_{H(8),C} \approx 2.0$—$2.5$); 81.69 (sept.d [sept.d], C(4), $^{2}J_{F,C(4)} = 27.9$, $^{2}J_{P,C(4)} = 3.5$); 120.28 (qd [qd], CF_3, $^{1}J_{F,C} = 289.8$, $^{3}J_{P,C} = 5.0$); 120.34 (s [br.dd], C(7), $^{1}J_{H,C(7)} = 180.9$, $^{2}J_{H(8),C(7)} = 2.3$); 124.80 (br.s [br.d], C(5a), $^{3}J_{H(7),C(5a)} = 8.0$); 149.35 (s [dd], C(6), $^{1}J_{H,C(6)} = 173.8$, $^{3}J_{H(8),C(6)} = 7.8$); 149.65 (s [br.dm], C(8), $^{1}J_{H,C(8)} = 194.2$, $^{3}J_{H_{Me},C(8)} = 3.8$); 154.71 (br.s [br.m], C(9a)); 184.62 (d [dd], C(5), $^{3}J_{P,C(5)} \approx 4.4$—$4.5$, $^{3}J_{H(6),C(5)} \approx 4.2$—$4.3$)
7	6.73 (ddd, 1 H, H(7), $^{3}J_{H(6),H(7)} = 7.5$, $^{3}J_{H(8),H(7)} = 6.2$, $^{6}J_{P,H(7)} = 0.8$); 7.80 (br.dd, 1 H, H(8), $^{3}J_{H(7),H(8)} \approx 6.2$—$6.3$, $^{4}J_{H(6),H(8)} = 2.1$); 8.36 (ddd, 1 H, H(6), $^{3}J_{H(7),H(6)} = 7.5$, $^{4}J_{H(8),H(6)} = 2.1$, $^{5}J_{P,H(6)} \approx 0.7$—$0.8$)	81.67 (sept.d [sept.d], C(4), $^{2}J_{F,C(4)} = 28.2$, $^{2}J_{P,C(4)} = 1.5$); 119.24 (s [dd], C(7), $^{1}J_{H,C(7)} = 169.8$, $^{2}J_{H(8),C(7)} = 8.0$); 120.85 (qd [qd], CF_3, $^{1}J_{F,C} = 290.5$, $^{3}J_{P,C} \approx 4.8$—5.0); 124.80 (br.s [br.d], C(5a), $^{3}J_{H(7),C(5a)} = 8.0$); 141.16 (br.s [ddd], C(6), $^{1}J_{H,C(6)} = 166.5$, $^{3}J_{H(8),C(6)} = 6.6$, $^{2}J_{H(7),C(6)} = 1.8$); 153.10 (s [ddd], C(8), $^{1}J_{H,C(8)} = 181.4$, $^{3}J_{H(6),C(8)} = 8.8$, $^{2}J_{H(7),C(8)} = 3.6$); 157.17 (br.s [br.dd], C(9a), $^{3}J_{H(8),C(9a)} = 13.3$, $^{3}J_{H(6),C(9a)} = 8.8$); 180.36 (d [dd], C(5), $^{3}J_{P,C(5)} = 4.4$, $^{3}J_{H(6),C(5)} = 4.4$)

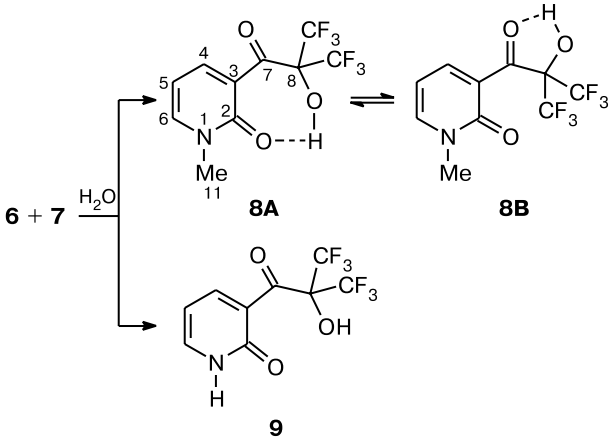
Note. The multiplicity of the signal in the ^{13}C NMR spectrum is given in brackets.

those of the γ-C nuclei.[9] It should be noted that the C(8) and C(6) atoms of the pyridine ring in structure **7**, unlike those in structure **6**, are substantially more nonequivalent. On the whole, the chemical shifts of the C atoms of the pyridine ring in phosphepine **7** and the spin-spin coupling constants $^{1}J_{H,C}$ are in better agreement with uncharged structure **7B** than with zwitterionic structure **7A** and are similar to those in methyl nicotinate.[8,9]

Apparently, the reaction of derivative **3** with hexafluoroacetone starts with a nucleophilic attack of the P atom on the C atom of the carbonyl group to form a bipolar ion with the P—C bond (see Scheme 2, **A**), which undergoes the rearrangement into the ion P^{+}—O—C^{-} (**B**). Subsequent stabilization of betaine **B** involves an intramolecular attack of the carbanionic center on the C atom of the carbonyl group to form product **5**, which undergoes the above-described transformations.

Compounds **6** and **7** are also very sensitive to hydrolysis. A product containing no phosphorus was isolated by crystallization from the mixture obtained in the reaction after its immediate treatment with aqueous acetone. The ^{19}F NMR spectra of this product in acetone-d_6 or $CDCl_3$ show broadened singlets at δ_F −73.26 and −74.99, respectively. Based on the ^{1}H and ^{13}C NMR spectroscopic data (see Experimental), we assigned the structure of 1-methyl-3-(2-hydroxy-3,3,3-trifluoro-2-trifluoromethylpropanoyl)pyridin-2-one (**8**) to the hydrolysis product (Scheme 3). The positions of the signals in the ^{1}H NMR spectrum of pyridinone **8** depend substantially on the solvent. For example, the difference in the chemical shifts of the H(4) and H(6) protons in $CDCl_3$ $\Delta(\delta_{H(4)} - \delta_{H(6)})$ is equal to 0.33, whereas this difference in acetone is 0.07. This may be attributable to a change in hydrogen bonding in the molecule, for example, due to a shift of equilibrium between the forms **8A** and **8B**.

Scheme 3



The IR spectrum of compound **8** has intense absorption bands corresponding to vibrations of the C=O, C(O)N, OH, C=C, and CF groups. The presence of an intense and broad band at 2590—2800 cm^{-1} is indicative of strong hydrogen bonding in molecule **8**. The pyridin-2-one structure of this compound is confirmed also by ^{13}C NMR spectroscopy. The low-field region of the spectrum has signals belonging to two types of carbonyl groups, *viz.*, ketone (δ 190.80) and amide (δ 162.52) carbonyl groups. The signals for the C atoms of the pyridinone ring

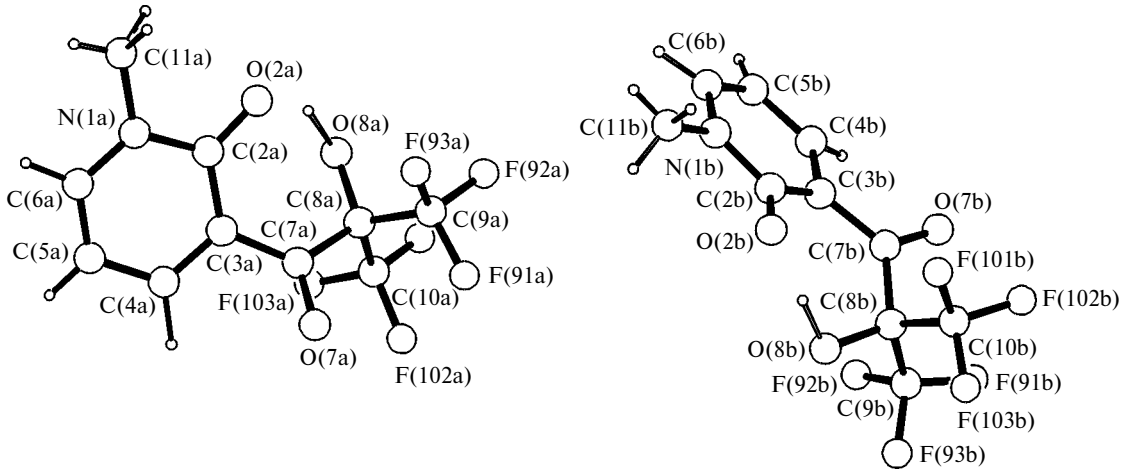


Fig. 1. Molecular geometry of compound **8** in the crystal (independent molecules a and b).

are observed in a substantially broader region compared to the C atoms of the pyridine ring.

The mass spectrum of compound **8** has a peak at m/z 303 corresponding to the molecular ion $[M]^{\bullet+}$. Its low intensity is associated with the presence of two CF_3 groups, which sharply decrease the stability of molecular ions. In the first step of fragmentation of molecule **8** under EI, the F atom is eliminated resulting in the formation of the ion at m/z 284. The latter readily splits the HF molecule off to give the ion at m/z 264. Abstraction of the CF_3 group from the $[M]^{\bullet+}$ ion gives rise to the peak at m/z 234. The appearance of the peak at m/z 218 can be attributable to subsequent elimination of the O atom from the $[M - CF_3]^+$ ion. In the mass spectrum of compound **8**, the most intense peak at m/z 136 is apparently associated with the cleavage of the C(7)—C(8) bond. Another intense peak at m/z 109 belongs to the ion formed due to cleavage of the C(3)—C(7) bond. Other fragment ions in low m/z region in the mass spectrum of compound **8** are apparently attributable to successive fragmentation of the above-mentioned ions under EI.

Fractional crystallization afforded crystals enriched with compound **9**, its content being 70—80%. The positions of the signals in the ^{1}H NMR spectrum of pyridin-2-one **9**, like those in the ^{1}H NMR spectrum of compound **8**, depend on the nature of the solvent and are associated with both the difference in the type of hydrogen bonds and exchange processes.

The structure of compound **8** was also established by X-ray diffraction analysis. The geometry of the molecule in the crystal (two independent molecules a and b) and the atomic numbering scheme are shown in Fig. 1. The selected geometric parameters are given in Table 2.

The main difference in the geometry of two independent molecules (a and b) is the torsion angle about the C(7)—C(8) bond. In the molecule a, the C(3a)—C(7a)—C(8a)—O(8a) torsion angle is −0.1(6)°, (*i.e.*, the molecule adopts a fully eclipsed conformation). In the molecule b, the C(3b)—C(7b)—C(8b)—O(8b) torsion angle is −10.3(6)°. The fragment of the heterocycle is planar (within 0.022(4) and 0.029(4) Å for the molecules a and b, respectively). It should be noted that the C(7a) atom more noticeably deviates from the plane of the heterocycle (0.115(4) and 0.039(4) Å in the molecules a and b, respectively). In spite of a substantial deviation of the O atom of the exocyclic carbonyl group (0.771(3) and 0.474(3) Å in the molecules a and b, respectively), the conformation about the C(3)—C(7) bond is favorable for conjugation (the C(2)—C(3)—C(7)—C(8) torsion angles are 41.1(6) and −26.9(7)° in the molecules a and b, respectively). The bond lengths in compound **8** have standard values.* The exocyclic O(2a)—C(2a)—C(3a) and C(2a)—C(3a)—C(8a) bond angles are slightly larger than the ideal values for the sp^2-hybridized C atom due to steric repulsion between the substituents at positions 2 and 3 of the heterocycle. The O(2a)—C(2a)—N(1a) and C(4a)—C(3a)—C(8a) angles are, correspondingly, slightly decreased.

Analysis of intermolecular interactions, which was carried out using the PLATON program,[11] demonstrated that the molecular packing in the crystal is determined by intermolecular nonclassical C—H...O and C—H...F hydrogen bonds and intramolecular O—H...O hydrogen bonds. The chain of intermolecular C—H...F hydrogen bonds linking the molecules a along the 0x axis is shown in Fig. 2. The parameters of the C(4a)—H(4a)...F(93a) hydrogen bond $(-1/2 + x, 3/2 - y, z)$ are as follows: C(4a)—H(4a), 1.15 Å; H(4a)...F(93a), 2.35 Å; C(4a)...F(93a), 3.338(5) Å; C(4a)—H(4a)...F(93a), 142°.

The molecules b are arranged as branches at the main chain consisting of the molecules a (Fig. 3) and are linked

* Compound **8** is structurally similar to 1-bis(hydroxyimino)propyl-3-methylpyridin-2-one.[10]

Table 2. Selected bond lengths (*d*), bond angles (ω), and torsion angles (τ) in molecule **8**

Bond	*d*/Å	Angle	ω/deg	Angle	τ/deg
O(2a)—C(2a)	1.242(5)	C(2a)—N(1a)—C(6a)	123.0(3)	H(8a)—O(8a)—C(8a)—C(7a)	−49
O(7a)—C(7a)	1.215(5)	C(2a)—N(1a)—C(11a)	116.3(3)	H(8a)—O(8a)—C(8a)—C(10a)	−167
O(2b)—C(2b)	1.257(5)	C(6a)—N(1a)—C(11a)	120.7(3)	H(8b)—O(8b)—C(8b)—C(7b)	−50
O(7b)—C(7b)	1.216(6)	C(2b)—N(1b)—C(6b)	121.8(4)	H(8b)—O(8b)—C(8b)—C(10b)	−73
O(8a)—C(8a)	1.395(5)	C(2b)—N(1b)—C(11b)	117.2(4)	C(2a)—C(3a)—C(7a)—C(8a)	41.1(6)
O(8a)—H(8a)	1.223(3)	C(6b)—N(1b)—C(11b)	121.0(4)	C(4a)—C(3a)—C(7a)—C(8a)	−144.9(4)
O(8b)—C(8b)	1.384(5)	O(2a)—C(2a)—N(1a)	118.8(4)	C(2b)—C(3b)—C(7b)—O(7b)	155.0(4)
O(8b)—H(8b)	1.139(3)	O(2a)—C(2a)—C(3a)	125.0(4)	C(2a)—C(3a)—C(7a)—O(7a)	141.6(5)
N(1a)—C(2a)	1.378(6)	N(1a)—C(2a)—C(3a)	116.1(4)	C(2b)—C(3b)—C(7b)—C(8b)	−26.9(7)
N(1a)—C(6a)	1.352(6)	O(2b)—C(2b)—N(1b)	116.0(4)	C(4a)—C(3a)—C(7a)—O(7a)	32.4(6)
N(1a)—C(11a)	1.467(6)	O(2b)—C(2b)—C(3b)	126.8(4)	C(4b)—C(3b)—C(7b)—O(7b)	−20.3(6)
N(1b)—C(2b)	1.384(5)	N(1b)—C(2b)—C(3b)	117.2(4)	C(4b)—C(3b)—C(7b)—C(8b)	157.8(4)
N(1b)—C(11b)	1.435(6)	C(2a)—C(3a)—C(4a)	120.0(4)	C(3a)—C(7a)—C(8a)—O(8a)	−0.1(6)
C(2a)—C(3a)	1.442(6)	C(2a)—C(3a)—C(7a)	124.1(4)	C(3a)—C(7a)—C(8a)—C(9a)	−122.8(4)
C(2b)—C(3b)	1.426(6)	C(4a)—C(3a)—C(7a)	115.7(4)	C(3a)—C(7a)—C(8a)—C(10a)	115.5(4)
N(1b)—C(6b)	1.355(6)	C(2b)—C(3b)—C(4b)	118.4(4)	O(7a)—C(7a)—C(8a)—O(8a)	177.5(4)
C(3a)—C(4a)	1.375(6)	C(2b)—C(3b)—C(7b)	126.2(4)	O(7a)—C(7a)—C(8a)—C(9a)	59.7(5)
C(3a)—C(7a)	1.476(6)	C(4b)—C(3b)—C(7b)	115.3(4)	O(7a)—C(7a)—C(8a)—C(10a)	−61.9(5)
C(3b)—C(4b)	1.381(7)	C(3a)—C(4a)—C(5a)	120.5(4)	O(7b)—C(7b)—C(8b)—O(8b)	167.9(4)
C(3b)—C(7b)	1.483(6)	C(3b)—C(4b)—C(5b)	122.2(4)	O(7b)—C(7b)—C(8b)—C(9b)	51.9(5)
C(4a)—C(5a)	1.405(7)	C(4a)—C(5a)—C(6a)	118.7(4)	O(7b)—C(7b)—C(8b)—C(10b)	−69.6(5)
C(5a)—C(6a)	1.351(6)	C(4b)—C(5b)—C(6b)	118.2(5)	C(3b)—C(7b)—C(8b)—O(8b)	−10.3(6)
C(5b)—C(6b)	1.344(7)	O(7b)—C(7b)—C(3b)	120.1(4)	C(3b)—C(7b)—C(8b)—C(9b)	−126.3(4)
C(7a)—C(8a)	1.566(6)	O(7b)—C(7b)—C(8b)	115.9(4)	C(3b)—C(7b)—C(8b)—C(10b)	112.2(4)
C(7b)—C(8b)	1.560(6)	O(7a)—C(7a)—C(3a)	120.6(4)	O(8b)—C(8b)—C(9b)—F(91b)	167.9(4)
C(8b)—C(9b)	1.518(6)	C(3a)—C(7a)—C(8a)	123.3(4)	O(8b)—C(8b)—C(10b)—F(103b)	−178.1(3)
C(8b)—C(10b)	1.519(7)	N(1a)—C(6a)—C(5a)	121.6(4)	O(8a)—C(8a)—C(9a)—F(91a)	171.1(3)
C(8a)—C(9a)	1.514(7)	O(7a)—C(7a)—C(8a)	116.0(4)		
C(8a)—C(10a)	1.520(6)	C(3b)—C(7b)—C(8b)	124.0(4)		
C(4b)—C(5b)	1.378(7)	O(8b)—C(8b)—C(7b)	115.3(4)		
		O(8b)—C(8b)—C(9b)	104.4(3)		
		O(8b)—C(8b)—C(10b)	108.6(3)		
		C(7b)—C(8b)—C(9b)	107.5(3)		
		C(7b)—C(8b)—C(10b)	109.2(4)		
		C(9b)—C(8b)—C(10b)	111.9(4)		
		O(8a)—C(8a)—C(7a)	113.9(3)		
		O(8a)—C(8a)—C(9a)	109.3(3)		
		O(8a)—C(8a)—C(10a)	104.6(3)		
		C(7a)—C(8a)—C(9a)	109.5(4)		
		C(7a)—C(8a)—C(10a)	107.8(3)		

to the main chain also through nonclassical C—H...O and C—H...F hydrogen bonds to form dimers with the molecules a. The parameters of the C(6b)—H(6b)...O(7a′) hydrogen bond (x, y, $1 + z$) are as follows: C(6b)—H(6b), 1.04 Å; H(6b)...O(7a′), 2.47 Å; C(6b)...O(7a′), 3.289(6) Å; C(6b)—H(6b)...O(7a′), 134°. The parameters of the C(5b)—H(5b)...F(102a) hydrogen bond (x, y, $1 + z$) are as follows: C(5b)—H(5b), 1.01 Å; H(5b)...F(102a), 2.45 Å; C(5b)...F(102a), 3.394(5) Å; C(5b)—H(5b)...F(102a), 154°.

In both molecules, there are also classical intramolecular O—H...O hydrogen bonds giving rise to seven-membered rings. These rings adopt slightly distorted boat conformations containing two planar fragments in the molecule a (O(2a)C(2a)C(3a)C(7a) and C(3a)C(7a)C(8a)O(8a)) and one planar fragment in the molecule b (O(2b)C(2b)C(3b)C(7b)). The C(8), O(8), and H(8) atoms deviate from the O(2)C(2)C(3)C(7) plane in the same direction (by −0.794(4), −1.537(3), and −0.89 Å in the molecule a and by −0.530(4), −1.241(3), and −0.63 Å in the molecule b). The parameters of this hydrogen bond in the molecule a are as follows: O(8a)—H(8a), 1.22 Å; H(8a)...O(2a), 1.41 Å; O(8a)...O(2a), 2.531 Å; O(2a)...H(8a)—O(8a), 149°. The parameters of the corresponding hydrogen bond in the molecule b are as follows: O(8b)—H(8b), 1.14 Å; H(8b)...O(2b), 1.40 Å; O(8b)...O(2b), 2.494 Å; O(2b)...H(8b)—O(8b), 158°.

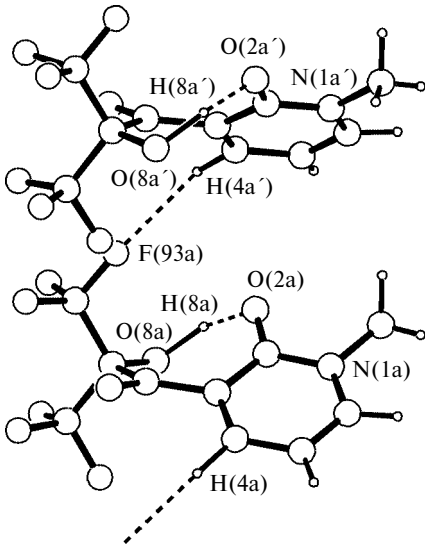


Fig. 2. Fragment of the chain of intermolecular hydrogen bonds formed by molecules **8**a.

Therefore, the use of derivatives based on 2-hydroxynicotinic acid demonstrates that the modification of cyclic phosphorylated hydroxy carboxylic acid with hexafluoroacetone holds promise for extension of this approach to more complex acids of the heterocyclic series.

Experimental

The NMR spectra were recorded on Varian Unity-300 (300 MHz for ^{1}H, 282.4 MHz for ^{19}F, and 121.42 MHz for ^{31}P) and Bruker MSL-400 (162.0 MHz for ^{31}P and 100.6 MHz for ^{13}C) instruments with HMDS as the internal standard (^{1}H and ^{13}C NMR spectra). The ^{19}F NMR spectra were measured in the presence of 10% C_6F_6 in a solution of the sample; the chemical shifts of the F nuclei were recalculated relative to $CFCl_3$. The ^{31}P NMR spectra were recorded with H_3PO_4 as the external standard. The IR spectra were measured on a Specord M-80 instrument in thin films or Nujol mulls between KBr plates. The mass spectra (EI) were obtained on a Finnigan MAT TRACE MS instrument with direct inlet of the sample into the ion source; the energy of ionizing electrons was 70 eV; the temperature of the ion source was 200 °C. The evaporator tube was heated in programmed mode from 35 to 150 °C with a step of 35 °C min^{-1}. The mass-spectrometric data were processed using the Xcalibur program.

Trimethylsilyl 2-trimethylsilyloxynicotinate (2). A mixture of 2-hydroxynicotinic acid (**1**) (9.73 g, 0.07 mol) and hexamethyldisilazane (28.98 g, 0.18 mol) was heated at 150 °C for 7 h until elimination of ammonia ceased. After removal of an excess of hexamethyldisilazane *in vacuo* (b.p. 62 °C (100 Torr)), ester **2** was obtained as a thick viscous oil in quantitative yield. Found (%): C, 51.03; H, 7.61. $C_{12}H_{21}NO_3Si_2$. Calculated (%): C, 50.88; H, 7.42. IR, ν/cm^{-1}: 1690 (C=O); 1580 (C=C arom.); 1250, 840, 755 ($SiMe_3$); 1080, 1060 (SiOC).

2-Methoxy-1,3,2-dioxaphosphorino[4,5-*b*]pyridin-4(4*H*)-one (3). Methyl phosphodichloridite (10.64 g, 0.08 mol) was added dropwise with stirring to compound **2** (22.64 g, 0.08 mol) at ~20 °C under dry argon (the temperature of the reaction mixture increased from 20 to 50 °C). Trimethylchlorosilane was distilled off under slightly reduced pressure (165—200 Torr) under a stream of argon. Compound **3**, which was prepared as a viscous yellowish oil, was kept *in vacuo* (0.1 Torr) to distill volatile impurities and then was used without additional purification. Found (%): C, 42.39; H, 3.27; P, 15.33. $C_7H_6NO_4P$. Calculated (%): C, 42.21; H, 3.01; P, 15.58. ^{31}P NMR (CH_2Cl_2): δ_P 122.2 (q, $^3J_{P,H}$ = 18.3 Hz).

Reaction of compound 3 with hexafluoroacetone. Hexafluoroacetone (15 g) was condensed in a mixture of phosphorinopyridone **3** (13.9 g, 0.07 mol) and dry CH_2Cl_2 (40 mL) under a stream of dry argon on cooling (−45 °C). The reaction mixture was kept for 6 h until the temperature raised to 20 °C. According to the ^{31}P NMR spectroscopic data (δ_P −12.7), the reaction produced unstable 2-methoxy-2,5-dioxo-4,4-bis(trifluoromethyl)-4,5-dihydro-1,3,2-dioxaphosphepino[4,5-*b*]pyridine (**5**). The reaction mixture was kept at 20 °C for 6 h. The precipitate that formed was filtered off under ambient atmosphere and dried *in vacuo* (12 Torr). A mixture of compound **5**, 9-methyl-2,5-dioxo-4,4-bis(trifluoromethyl)-4,5-dihydro-1,3,2-dioxaphosphepino[4,5-*b*]pyrid-9-inium-2-oate (**6**), and 2-hydroxy-2,5-dioxo-4,4-bis(trifluoromethyl)-4,5-dihydro-1,3,2-dioxaphosphepino[4,5-*b*]pyridine (**7**) was obtained in a total yield of 92%. The precipitate that crystallized from a solution of the mixture in acetone was filtered off and recrystallized from acetone to afford 1-methyl-3-(2-hydroxy-3,3,3-trifluoro-2-tri-

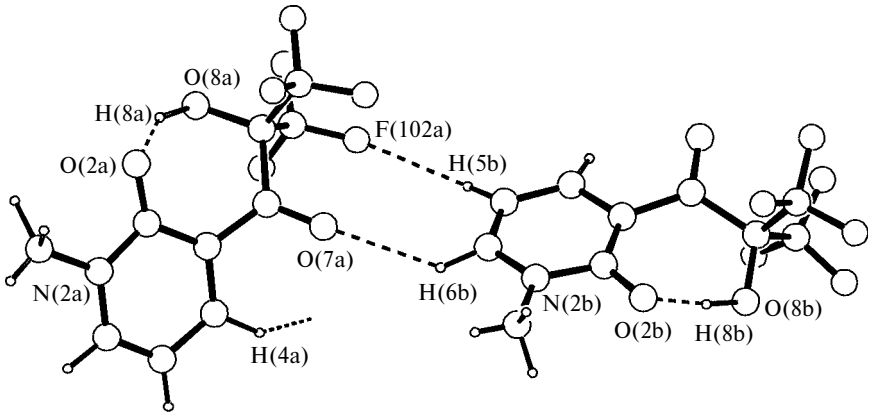


Fig. 3. Intermolecular hydrogen bond network in the dimer formed by molecules **8**a and **8**b.

fluoromethylpropanoyl)pyridin-2-one (**8**). Additional crystallization from the mother liquor gave a mixture of compound **8** and 3-(2-hydroxy-3,3,3-trifluoro-2-trifluoromethylpropanoyl)pyridin-2-one (**9**) in a ratio of ~3 : 7.

Compound 8. The yield was 57%, m.p. 58—60 °C. Found (%): C, 39.38; H, 2.64. $C_{10}H_7F_6NO_3$. Calculated (%): C, 39.60; H, 2.31. MS, *m/z* (I_{rel} (%))*: 303 $[M]^{\cdot+}$ (1.0), 284 $[M - F]^+$ (0.31), 264 $[M - F - HF]^+$ (0.42), 234 $[M - CF_3]^+$ (0.80), 218 $[M - CF_3 - O]^+$ (1.5), 136 (100.0), 109 (38.3), 81 (7.0), 80 (12.0), 79 (3.4), 78 (12.9), 69 (8.2), 53 (11.3), 42 (12.5), 39 (15.7). IR, ν/cm^{-1}: 3104, 3048, 2928, 2880, 2792, 2640, 2576, 2104, 2088, 1956, 1920, 1824, 1710, 1668, 1600, 1464, 1392, 1376, 1352, 1232, 1188, 1160, 1092, 1060, 1016, 948, 900, 880, 832, 808, 788, 760. ^{1}H NMR ($CDCl_3$), δ: 3.69 (br.s, 3 H, Me); 6.58 (dd, 1 H, H(5), $^3J_{H(4),H(5)}$ = 7.5 Hz, $^3J_{H(6),H(5)}$ = 6.5 Hz); 7.81 (dd, 1 H, H(6), $^3J_{H(5),H(6)}$ = 6.5 Hz, $^4J_{H(4),H(6)}$ = 2.0 Hz); 8.14 (dd, 1 H, H(4), $^3J_{H(5),H(4)}$ = 7.5 Hz, $^4J_{H(6),H(4)}$ = 2.0 Hz); 11.10 (br, 1 H, OH). ^{1}H NMR (acetone-d_6), δ: 3.75 (s, 3 H, Me); 6.75 (dd, 1 H, H(5), $^3J_{H(4),H(5)}$ = 7.5 Hz, $^3J_{H(6),H(5)}$ = 6.4 Hz); 8.24 (dd, 1 H, H(4), $^3J_{H(5),H(4)}$ = 7.5 Hz, $^4J_{H(6),H(4)}$ = 2.1 Hz); 8.31 (dd, 1 H, H(6), $^3J_{H(5),H(6)}$ = 6.4 Hz, $^4J_{H(4),H(6)}$ = 2.1 Hz); 11.73 (br, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ:** 39.24 (s [qd], C(11) (NMe), $^1J_{H,C(11)}$ = 143.0 Hz, $^3J_{H(6),C(11)}$ = 3.6 Hz); 81.56 (sept [sept], C(8), $^2J_{F,C(8)}$ = 28.6 Hz); 109.46 (s [dd], C(5), $^1J_{H,C(5)}$ = 174.8 Hz, $^2J_{H(6),C(5)}$ = 2.4 Hz); 121.62 (qq [qq], C(9), C(10), $^1J_{F,C}$ = 279.6 Hz, $^3J_{F,C}$ = 1.8 Hz); 128.38 (s [d], C(3), $^3J_{H(5),C(3)}$ = 6.0 Hz); 144.84 (s [dm], C(6), $^1J_{H,C(6)}$ = 181.2 Hz, $^3J_{H(4),C(6)}$ = 8.4 Hz, $^2J_{H(5),C(6)}$ = 5.2 Hz, $^3J_{H(11),C(6)}$ = 3.7 Hz); 147.97 (s [dd], C(4), $^1J_{H,C(4)}$ = 165.8 Hz, $^3J_{H(6),C(4)}$ = 8.0 Hz); 162.52 (s [m], C(2), $^3J_{H(6),C(2)}$ = 7.2 Hz, $^3J_{H(4),C(2)}$ = 7.8 Hz, $^3J_{H(11),C(2)}$ = 3.3 Hz); 190.80 (s [d], C(7), $^3J_{H(4),C(7)}$ = 4.7 Hz).

Compound 9. ^{1}H NMR (acetone-d_6), δ: 6.71 (dd, 1 H, H(5), $^3J_{H(4),H(5)}$ = 7.6 Hz, $^3J_{H(6),H(5)}$ = 6.1 Hz); 8.00 (dd, 1 H, H(6), $^3J_{H(5),H(6)}$ = 6.1 Hz, $^4J_{H(4),H(6)}$ = 2.1 Hz); 8.27 (dd, 1 H, H(4), $^3J_{H(5),H(4)}$ = 7.6 Hz, $^4J_{H(6),H(4)}$ = 2.1 Hz); 9.61 (br, 1 H, OH). ^{1}H NMR ($CDCl_3$), δ: 6.69 (dd, 1 H, H(5), $^3J_{H(4),H(5)}$ = 7.5 Hz, $^3J_{H(6),H(5)}$ = 6.2 Hz); 7.81 (dd, 1 H, H(6), $^3J_{H(5),H(6)}$ = 6.2 Hz, $^4J_{H(4),H(6)}$ = 1.9 Hz); 8.30 (dd, 1 H, H(4), $^3J_{H(5),H(4)}$ = 7.5 Hz, $^4J_{H(6),H(4)}$ = 1.9 Hz); 11.90 (br, 1 H, OH). ^{19}F NMR (acetone-d_6): δ_F −73.31 (br.s).

X-ray diffraction analysis of compound 8. Crystals of compound **8** are monoclinic, space group $P2_1/a$, a = 11.125(2) Å, b = 14.337(2) Å, c = 14.768(4) Å, β = 98.87(2)°, V = 2327.2(9) Å^3, Z = 4, d_{calc} = 1.044 g cm^{-3}, $F(000)$ = 728. The intensities of 2760 reflections were measured on an Enraf Nonius CAD-4 diffractometer at 20 °C (λ(Mo-Kα), ω/2θ scanning technique, $2\theta_{max} < 53.8°$), of which 1760 reflections were with $I > 3\sigma$. The intensities of three check reflections showed no decrease in the course of X-ray data collection. Because of a low value of the coefficient (μ(Mo) = 1.70 cm^{-1}), absorption was ignored. The structure was solved by direct methods using the SIR program[12] and refined first isotropically and then anisotropically. All H atoms were revealed from difference electron density syntheses. Their contributions to the structure factors were taken into account in the final step of the refinement with fixed positional and thermal parameters. All calculations were carried out using the MOLEN complex program[13] on an AlphaStation 200 computer. The final reliability factors were R = 0.047, R_w = 0.070 based on 1861 independent reflections with $F^2 \geq 3\sigma$.

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* The ion peaks containing the most abundant isotopes are given.
** The multiplicities of the signals in the ^{13}C NMR spectrum are given in parentheses, and the multiplicities of the signals in the $^{13}C\{^1H\}$ NMR spectrum are outside parentheses.