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PROPERTIES OF 8-CYANO-5-PHENYL-7-TRIFLUOROMETHYL-2,3-DIHYDRO-IMIDAZO[1,2-*a*]PYRIDINES

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The alkylation, acylation, halogenation, nitration, oxidation, and hydrolysis reactions of 8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-a]pyridine have been studied. It was found that the 6-halo derivatives add alcohol to give covalent solvates. X-ray analysis has been carried out on one of the solvates (6-chloro-8-cyano-7-ethoxy-5-phenyl-7-trifluoromethyl-1,2,3,7-tetrahydroimidazo[1,2-a]-pyridine) as well as on 8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-a]pyridine trifluoroacetate.

Keywords: 2,3-dihydroimidazo[1,2-*a*]pyridines, covalent solvates, 2,3-dihydroimidazo[1,2-*a*]-pyridinium salts, X-ray analysis.

According to data in [1, 2] 2,3-dihydroimidazo[1,2-*a*]pyridines are a little studied heterocyclic system. This prompted us to study, in more detail, the chemical and physical properties of 8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridine (**1**).

We have previously shown that the imidazo[1,2-*a*]pyridine **1** is readily protonated by acids [3, 4]. With alkylhalides, the imidazopyridine **1**, similarly to other 2,3-dihydroimidazo[1,2-*a*]pyridines [2], gives the 1-alkyl-8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridine salts **2a,b** (Table 1). Up to this time, only in the study [5] there had been reported the acylation of 2,3-dihydroimidazo[1,2-*a*]pyridines (which occurs at the $N_{(1)}$ atom). By refluxing the imidazopyridine **1** in acetyl chloride we obtained the 1-acetylimidazopyridinium chloride (**3a**) as colorless, crystalline needles. Heating the imidazopyridine **1** in acetonitrile with an equimolar amount of benzoyl chloride gave 2-(2-benzoyloxyethylamino)-3-cyano-6-phenyl-4-trifluoromethylpyridine (previously reported by us [3]) in 73% yield. Exchange of acetonitrile for chloroform led to the formation of the 1-benzoylimidazopyridinium salt **3b**.

The imidazopyridine **1** takes part in an electrophilic substitution in the pyridine ring. Hence bromination in DMF and chlorination in dioxane gives the yellow salts **4**, from which the corresponding 6-bromo- and 6-chloroimidazopyridines **5a,b** were obtained by basification. Depending on reaction conditions, the salts **4** can contain a varying amount of complex-bounded bromine and we were able to separate the compound **4c** ($n = 3$). We also obtained the salts **4a,b** by treatment of the imidazopyridines **5a,b** with the corresponding acids (Scheme 1).

In the ^{1}H NMR spectra of the 1-substituted imidazopyridinium salts **2-4** (Table 2) there is a characteristic splitting of the signals of the methylene group protons of the NCH_2NCH_2 into two multiplets. It is apparent that the structure of the compounds **2a,b**, **3a,b**, and the salts **4a,b** is similar to the structure of the

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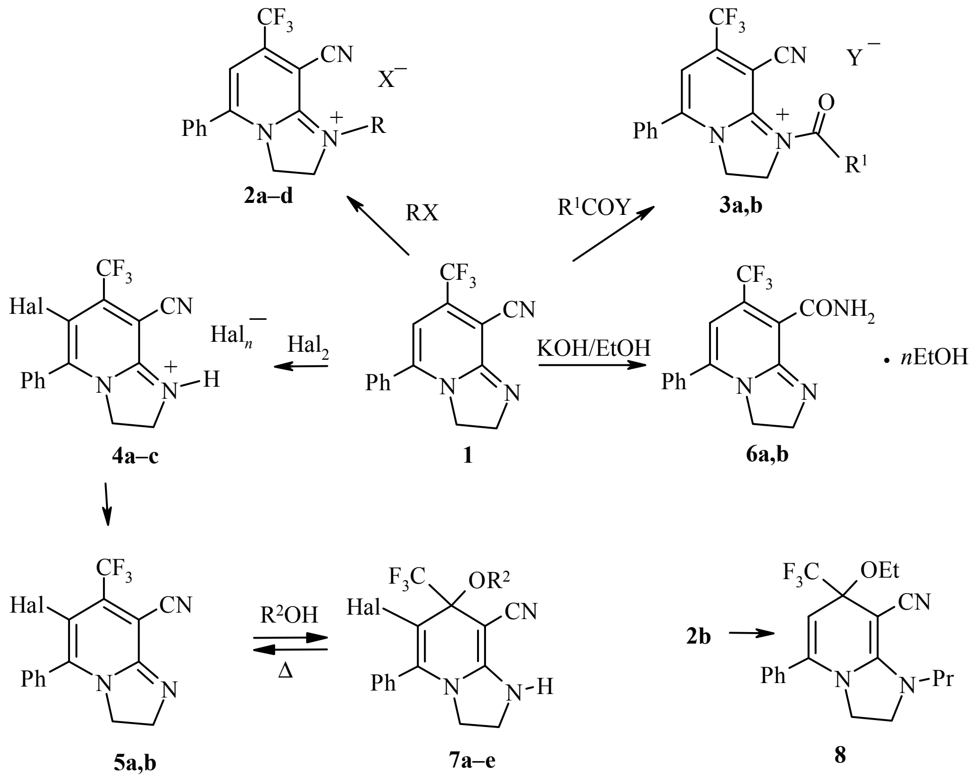
Scheme 1



2 a R = Me, X = I, **b** R = Pr, X = I, **c** R = H, X = CF_3COO [4], **d** R = H, X = $HSeO_3$;
3 a R^1 = Me, Y = Cl, **b** R^1 = Ph, Y = Cl; **4 a** Hal = Cl, *n* = 1, **b** Hal = Br, *n* = 1, **c** Hal = Br, *n* = 3;
5 a Hal = Cl, **b** Hal = Br; **6 a** *n* = 0 [3], **b** *n* = 1; **7 a** Hal = Cl, **b-e** Hal = Br;
a, **c**, R^2 = Et, **b** R^2 = Me, **d** R^2 = Bu, **e** R^2 = Ph

previously reported [3, 4] salt **2** (R = H). For a full identification we used X-ray crystallographic analysis. From all of the imidazopyridinium salts prepared by us [3, 4] we selected for X-ray analysis the 8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium trifluoroacetate (**2c**) which forms stable crystals thanks to a branched system of strong hydrogen bonds. The spatial model for the molecule and the atomic numbering are shown in Fig. 1. The coordinates and equivalent isotropic thermal parameters for the atoms are given in Table 3. Judging by the bond lengths and valence angle values (Tables 4 and 5), the positive charge is localized on the $N_{(1)}$ atom ($N_{(2)}$ in Fig. 1). The investigated molecule has a strong hydrogen bond between the anionic and the cationic parts: $d(H_{(2)} \cdots O_{(2')}) = 1.97$ Å, $\omega\ (N_{(2)}–H_{(2)} \cdots O_{(2')}) = 166°$. Additionally, in the molecule of the salt there is a disturbance of the conjugation of the phenyl substituent and the heterocyclic system; the dihedral angle between the ring planes is 132° and the length of the inter ring bond is 1.484 Å.

Attempts to prepare a nitro derivative of the imidazopyridine **1** were unsuccessful. Treatment of the imidazopyridine **1** with nitric acid in acetic anhydride at room temperature or nitrating mixture in the cold gave the 8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium nitrate previously reported by us [3]. In order to carry out the nitration we also tried more rigid conditions by heating in nitric acid, a mixture of nitric acid and acetic anhydride, and in nitrating mixture. In none of the examples listed above could the 6-nitro derivative be prepared.

Attempts to prepare the 2,3-dehydro derivative of compound **1** were also unsuccessful. Heating the imidazopyridine **1** with chloranil in dioxane gave the product of cleavage of the imidazole ring, i.e. the previously reported [3] 2-(2-chloroethylamino)-3-cyano-6-phenyl-4-trifluoromethylpyridine. Similarly, attempts to oxidise

TABLE 1. Characteristics for the Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, % (method)
		C	H	N		
2a	$C_{16}H_{13}F_3IN_3$	44.35 44.57	2.90 3.04	9.53 9.75	208-210 (dec.)	87
2b	$C_{18}H_{17}F_3IN_3$	46.90 47.08	4.01 3.73	8.80 9.15	95-97 (dec.)	26
2d	$C_{15}H_{10}F_3N_3 \cdot H_2SeO_3$	42.80 43.08	3.10 2.89	9.89 10.05	103-105 (dec.)	69
3a	$C_{17}H_{13}ClF_3N_3O$	55.63 55.52	3.50 3.56	11.49 11.43	130-132 (dec.)	79
3b	$C_{22}H_{15}ClF_3N_3O$	61.42 61.48	3.38 3.52	9.75 9.78	150-152 (dec.)	67
4a	$C_{15}H_9ClF_3N_3 \cdot HCl$	49.82 50.02	2.93 2.80	11.54 11.67	232-234 (dec.)	48 (A), 90 (B)
4b	$C_{15}H_9BrF_3N_3 \cdot HBr$	40.02 40.12	2.36 2.24	9.10 9.36	253-254 (dec.)	82
4c	$C_{15}H_9BrF_3N_3 \cdot HBr_3$	29.28 29.59	1.15 1.66	6.71 6.90	160-163 (dec.)	48
5a	$C_{15}H_9ClF_3N_3$	55.03 55.66	2.78 2.80	12.79 12.98	158-160	11 (A), 72 (B)
5b	$C_{15}H_9BrF_3N_3$	47.96 48.94	2.51 2.46	11.40 11.40	172-173	20 (A), 72 (B)
6b	$C_{15}H_{12}F_3N_3O \cdot C_2H_5OH$	56.97 57.79	5.13 5.13	11.77 11.89	217-218 (dec.)	61
7a	$C_{17}H_{15}ClF_3N_3O$	55.03 55.22	4.00 4.09	11.19 11.36	146-148 (dec.)	55
7b	$C_{16}H_{13}BrF_3N_3O$	48.35 48.02	3.35 3.27	10.43 10.50	126-128 (dec.)	46
7c	$C_{17}H_{15}BrF_3N_3O$	49.27 49.29	3.50 3.65	10.14 10.14	151-152 (dec.)	53
7d	$C_{19}H_{19}BrF_3N_3O$	51.55 51.60	4.15 4.33	9.50 9.50	179-180 (dec.)	54
7e	$C_{21}H_{15}BrF_3N_3O$	55.32 54.56	3.21 3.27	9.26 9.09	178-180 (dec.)	56
8	$C_{20}H_{22}F_3N_3O$	63.30 63.65	5.66 5.86	11.06 11.13	93-95 (dec.)	50

the imidazopyridine **1** with SeO_2 caused opening of the imidazole ring to give the known [6] 2-cyano-6-phenyl-4-trifluoromethylpyridin-2-one. Milder conditions gave the selenious acid salt **2d**.

According to data in [2], 2,3-dihydroimidazo[1,2-*a*]pyridines react with various nucleophiles and cleavage of the imidazole ring usually occurs to give 2-alkylaminopyridines or 1-alkyl-2-iminopyridines. However, heating the imidazopyridine **1** in ethanolic base solution gives only hydrolysis of the cyano group. The amide **6** formed in the reaction mixture was separated as a solvate with a molecule of ethanol. The solvate **6b** is also formed by recrystallization from ethanol of the amide **6a** which had been prepared by the acid hydrolysis of the nitrile **1** [3]. When heated in vacuo at 100°C, compound **6b** loses the molecule of alcohol.

When studying the reactions of the 2,3-dihydroimidazo[1,2-*a*]pyridines with nucleophiles we observed an unusual effect, i.e. the addition of alcohols to form covalent solvates which are also called pseudo bases. The formation of pseudo bases of this bicyclic system has only been reported once [7] as the addition of water to the $C_{(8a)}=N_{(1)}$ bond though the effect has been well known in other heterocyclic series for a long time. In our example, the addition of the alcohol molecule occurs at the $C_{(7)}=C_{(8)}-C_{(8a)}=N_{(1)}$ conjugated system to give the compounds **7a-e** and **8**. This reaction is reversible and takes place with electron-deficient 2,3-dihydroimidazo[1,2-*a*]-pyridines (the 6-halo derivatives **5a,b** and salt **2b**). Compounds **7a-e** lose the alcohol molecule when heated in

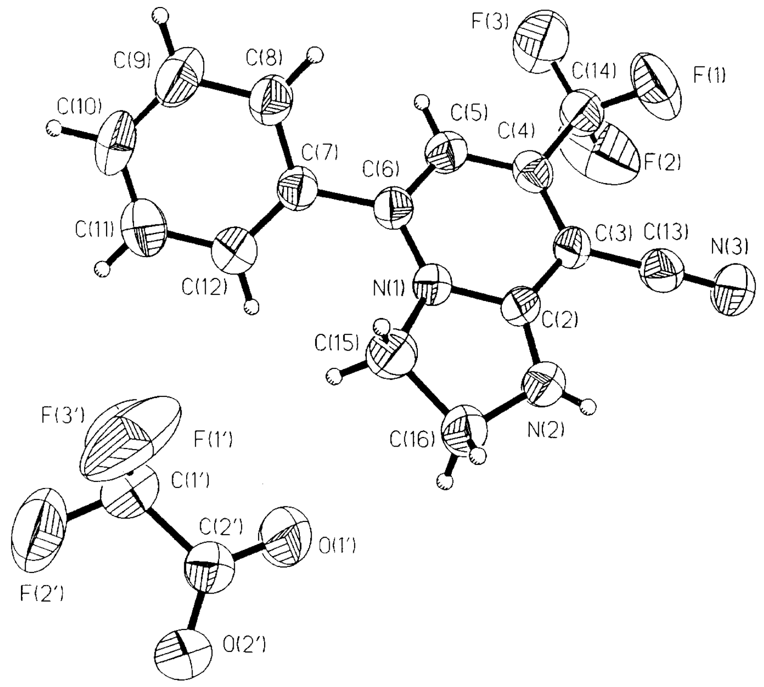


Figure 1. Spatial model for compound **2c**.

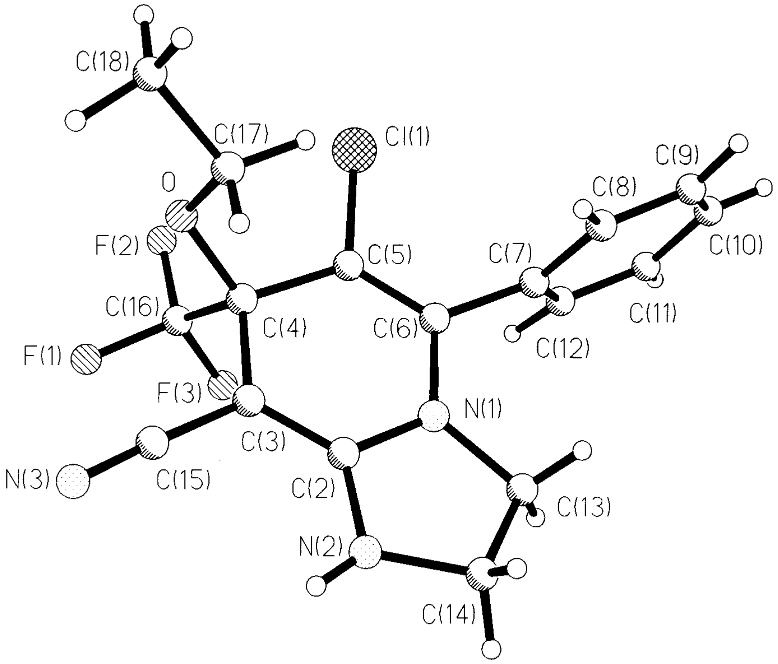


Figure 2. Spatial model for compound **7a**.

TABLE 2. Spectroscopic Parameters for the Compounds Synthesized

Compound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm, *J*, Hz*
2a	3030, 2938, 2238, 1634, 1580	3.64 (3H, s, CH_3); 4.40 (2H, t, *J* = 6, CH_2); 4.69 (2H, t, *J* = 6, CH_2); 6.89 (1H, s, –CH=); 7.33 (3H, m, C_6H_5); 7.78 (2H, m, C_6H_5)
2b	3030, 2971, 2171, 1646 1556	0.98 (3H, t, *J* = 6, CH_3); 1.81 (2H, sextet, *J* = 6, CH_2); 3.89 (2H, t, *J* = 6, CH_2); 4.12 (2H, m, CH_2); 4.61 (2H, m, CH_2); 7.52 (1H, s, –CH=); 7.74 (5H, m, C_6H_5)
2d	3323, 2222, 1639, 1540	3.74-4.32 (4H, m, $2CH_2$); 6.09 (1H, s, –CH=); 7.16 (2H, br. s, NH, $HSeO_3$); 7.65 (5H, m, C_6H_5)
3a	3079, 2235, 1678, 1596, 1552	2.16 (3H, s, CH_3); 3.83 (2H, t, *J* = 6, CH_2); 4.29 (2H, t, *J* = 6, CH_2); 7.58 (3H, m, C_6H_5); 8.05 (3H, m, C_6H_5, –CH=)
3b	3070, 2968, 2231, 1668, 1634, 1596, 1576, 1554	4.07 (2H, t, *J* = 6, CH_2); 4.52 (2H, t, *J* = 6, CH_2); 7.45 (5H, m, C_6H_5); 7.69 (3H, m, C_6H_5); 8.36 (2H, m, C_6H_5); 8.47 (1H, s, –CH=)
4a	2550, 2226, 1654, 1580	4.01 (2H, m, CH_2); 4.43 (2H, m, CH_2); 7.65 (5H, m, C_6H_5); 8.02 (1H, br. s, NH)
4b	3483, 3063, 2239, 1632, 1570, 1524	3.87 (2H, m, CH_2); 4.29 (2H, m, CH_2); 7.44 (2H, m, C_6H_5); 7.64 (3H, m, C_6H_5); 9.07 (1H, br. s, NH)
4c	3521, 3241, 3175-2830, 2229, 1647, 1571, 1533	2.91-3.56 (4H, m, CH_2CH_2); 5.89 (5H, m, C_6H_5); 8.60 (1H, br. s, NH)
5a	2892, 2220, 1639, 1543, 1517	3.87 (4H, m, CH_2CH_2); 7.24 (2H, m, C_6H_5); 7.47 (3H, m, C_6H_5)
5b	3054, 2926, 2230, 1632, 1544, 1518	3.71 (4H, m, CH_2CH_2); 7.53 (5H, m, C_6H_5)
6b	3250, 3120, 2976, 1691, 1641, 1585, 1557	1.07 (3H, t, *J* = 7, CH_3); 3.74 (2H, q, *J* = 7, CH_2); 3.85 (4H, m, $2CH_2$); 4.36 (1H, br. s, OH); 5.61 (1H, s, –CH=); 7.56 (5H, m, C_6H_5); 8.01 (2H, br. s, NH_2)
7a	3284, 2980, 2936, 2900, 2188, 1657, 1607, 1593	1.21 (3H, t, *J* = 7, CH_3); 3.41-3.76 (6H, m, CH_2, NCH_2CH_2N); 7.36 (2H, m, C_6H_5); 7.49 (3H, m, C_6H_5); 7.81 (1H, s, NH)
7b	3270, 2930, 2900, 2190, 1651, 1605, 1589	3.20 (3H, s, CH_3); 3.40 (4H, m, CH_2CH_2); 7.23 (2H, m, C_6H_5); 7.58 (3H, m, C_6H_5); 7.83 (1H, s, NH)
7c	3283, 2965, 2883, 2171, 1653, 1605, 1589, 1541	1.23 (3H, t, *J* = 7, CH_3); 3.38-3.72 (6H, m, CH_2, NCH_2CH_2N); 7.29 (2H, m, C_6H_5); 7.49 (3H, m, C_6H_5); 7.78 (1H, s, NH)
7d	3275, 2959, 2875, 2187, 1652, 1604, 1588, 1560	0.89 (3H, t, *J* = 7, CH_3); 1.23-1.69 (4H, m, CH_2CH_2); 3.43 (6H, m, CH_2, NCH_2CH_2N); 7.34 (2H, m, C_6H_5); 7.52 (3H, m, C_6H_5); 7.78 (1H, s, NH)
7e	3282, 2223, 1632, 1602, 1588, 1542, 1524	3.76 (4H, m, CH_2CH_2); 6.81 (3H, m, C_6H_5); 7.21 (2H, m, C_6H_5); 7.54 (5H, m, C_6H_5); 9.32 (1H, s, NH)
8	3084, 2968, 2880, 2180, 1646, 1556, 1466	0.89 (3H, t, *J* = 6, CH_3); 1.21 (3H, t, *J* = 7, CH_3); 1.65 (2H, sextet, *J* = 6, CH_2); 2.87-3.74 (8H, m, $4CH_2$); 5.16 (1H, s, =CH–); 7.41 (5H, m, C_6H_5)

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* ^{1}H NMR spectra for compounds **2a,b, 3a,b, 5a,b, 8** were recorded in $CDCl_3$; the remainder in DMSO-d_6.

vacuo at 100°C. The formation of pseudo bases with water, malononitrile, isopropanol, and amines under analogous conditions has not been observed. The covalent solvates **7a-e** are less strongly colored than the imidazopyridines **5a,b**. They all melt with decomposition in the range 93-163°C. The IR spectra of compounds **7** show characteristic maxima for C≡N stretching in the range 2171-2190 and N–H stretching at 3270-3284 cm^{-1}.

TABLE 3. Coordinates ($\times10^4$) and Equivalent Isotropic Thermal Parameters ($Å^2\times10^3$) for the Atoms in the Molecule of Compound **2c**

Atom	*x*	*y*	*z*	$U_{(eq)}$
$N_{(1)}$	6663(4)	8719(3)	1735(2)	42(1)
$C_{(2)}$	5913(6)	8630(4)	959(3)	42(1)
$C_{(3)}$	4464(6)	8095(4)	914(3)	43(1)
$C_{(4)}$	3856(6)	7698(4)	1668(3)	43(1)
$C_{(14)}$	2329(7)	7090(5)	1653(4)	56(2)
$F_{(1)}$	1163(4)	7584(3)	1275(3)	94(1)
$F_{(2)}$	2475(5)	6233(3)	1238(4)	127(2)
$F_{(3)}$	1805(5)	6868(4)	2426(3)	112(2)
$C_{(5)}$	4651(6)	7814(4)	2442(3)	46(1)
$C_{(6)}$	6067(6)	8332(4)	2482(3)	44(1)
$C_{(7)}$	6944(6)	8472(4)	3302(3)	44(1)
$C_{(8)}$	6105(7)	8813(4)	4015(3)	54(2)
$C_{(9)}$	6863(8)	8926(5)	4795(4)	71(2)
$C_{(10)}$	8442(9)	8683(6)	4871(4)	81(2)
$C_{(11)}$	9250(8)	8315(6)	4180(4)	80(2)
$C_{(12)}$	8518(7)	8214(5)	3388(4)	65(2)
$N_{(2)}$	6705(5)	9101(4)	348(3)	54(1)
$C_{(13)}$	3690(6)	8008(4)	93(3)	52(1)
$N_{(3)}$	3090(6)	7954(5)	-565(3)	75(2)
$C_{(15)}$	8046(7)	9432(5)	1628(3)	67(2)
$C_{(16)}$	8221(7)	9502(5)	668(3)	61(2)
$O_{(1')}$	8498(6)	9949(5)	-1327(3)	125(2)
$C_{(2')}$	7338(7)	9633(4)	-1678(3)	55(2)
$O_{(2')}$	6067(5)	9346(4)	-1370(2)	78(1)
$C_{(1')}$	7460(8)	9566(5)	-2648(4)	64(2)
$F_{(1')}$	8246(8)	8788(4)	-2924(3)	158(3)
$F_{(2')}$	6038(6)	9458(4)	-3035(2)	119(2)
$F_{(3')}$	7997(6)	10400(4)	-3009(3)	121(2)

In their ^1H NMR spectra the pseudobases **7** are characterized by the appearance of a broad N–H signal at low field in the range 7.78-9.32 ppm. The signal for the methylene protons appears as a multiplet in the range 3.40-3.76 ppm.

TABLE 4. Mean Atomic Distances in the Molecule of Compound **2c**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
$C_{(6)}$–$N_{(1)}$	1.362(6)	$C_{(8)}$–$C_{(7)}$	1.387(7)	$C_{(16)}$–$H_{(16B)}$	0.9700
$C_{(2)}$–$N_{(1)}$	1.367(6)	$C_{(7)}$–$C_{(6)}$	1.484(6)	$C_{(8)}$–$H_{(8)}$	0.9300
$C_{(15)}$–$N_{(1)}$	1.498(7)	$C_{(12)}$–$C_{(7)}$	1.374(7)	$C_{(9)}$–$H_{(9)}$	0.9300
$N_{(2)}$–$C_{(2)}$	1.313(6)	$C_{(9)}$–$C_{(8)}$	1.379(7)	$C_{(10)}$–$H_{(10)}$	0.9300
$C_{(4)}$–$C_{(3)}$	1.381(7)	$C_{(10)}$–$C_{(9)}$	1.371(9)	$C_{(11)}$–$H_{(11)}$	0.9300
$C_{(13)}$–$C_{(3)}$	1.437(7)	$C_{(11)}$–$C_{(10)}$	1.360(9)	$C_{(12)}$–$H_{(12)}$	0.9300
$C_{(5)}$–$C_{(4)}$	1.383(7)	$C_{(12)}$–$C_{(11)}$	1.383(8)	$N_{(2)}$–$H_{(2)}$	0.82(5)
$C_{(3)}$–$C_{(2)}$	1.406(7)	$N_{(2)}$–$C_{(16)}$	1.465(7)	$C_{(2')}$–$O_{(1')}$	1.191(6)
$C_{(14)}$–$C_{(4)}$	1.510(7)	$N_{(3)}$–$C_{(13)}$	1.142(6)	$C_{(2')}$–$O_{(2')}$	1.231(6)
$F_{(1)}$–$C_{(14)}$	1.311(6)	$C_{(15)}$–$C_{(16)}$	1.503(7)	$C_{(2')}$–$C_{(1')}$	1.514(8)
$F_{(2)}$–$C_{(14)}$	1.293(7)	$C_{(15)}$–$H_{(15A)}$	0.9700	$C_{(1')}$–$F_{(1')}$	1.284(7)
$F_{(3)}$–$C_{(14)}$	1.313(6)	$C_{(15)}$–$H_{(15B)}$	0.9700	$C_{(1')}$–$F_{(2')}$	1.346(7)
$C_{(6)}$–$C_{(5)}$	1.371(7)	$C_{(16)}$–$H_{(16A)}$	0.9700	$C_{(1')}$–$F_{(3')}$	1.302(7)

TABLE 5. Valence Angles in the Molecule of Compound **2c**

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
$C_{(2)}-N_{(1)}-C_{(6)}$	123.4(4)	$C_{(6)}-C_{(7)}-C_{(12)}$	122.2(5)	$H_{(12)}-C_{(12)}-C_{(7)}$	120.3
$N_{(1)}-C_{(2)}-C_{(3)}$	119.0(4)	$C_{(6)}-C_{(7)}-C_{(8)}$	118.2(5)	$H_{(12)}-C_{(12)}-C_{(11)}$	120.3
$N_{(1)}-C_{(2)}-N_{(2)}$	111.4(5)	$C_{(7)}-C_{(8)}-C_{(9)}$	120.1(6)	$H_{(15A)}-C_{(15)}-N_{(1)}$	111.2
$C_{(6)}-N_{(1)}-C_{(15)}$	127.7(4)	$C_{(8)}-C_{(9)}-C_{(10)}$	119.9(6)	$H_{(15A)}-C_{(15)}-C_{(16)}$	111.2
$C_{(2)}-N_{(1)}-C_{(15)}$	108.2(4)	$C_{(9)}-C_{(10)}-C_{(11)}$	120.0(6)	$H_{(15B)}-C_{(15)}-N_{(1)}$	111.2
$C_{(3)}-C_{(2)}-N_{(2)}$	129.6(4)	$C_{(10)}-C_{(11)}-C_{(12)}$	120.9(6)	$H_{(15B)}-C_{(15)}-C_{(16)}$	111.2
$C_{(2)}-C_{(3)}-C_{(4)}$	117.8(4)	$C_{(7)}-C_{(12)}-C_{(11)}$	119.5(6)	$H_{(15A)}-C_{(15)}-H_{(15B)}$	109.1
$C_{(4)}-C_{(3)}-C_{(13)}$	123.8(5)	$C_{(2)}-N_{(2)}-C_{(16)}$	111.4(4)	$H_{(16A)}-C_{(16)}-N_{(2)}$	111.1
$C_{(2)}-C_{(3)}-C_{(13)}$	118.4(5)	$C_{(3)}-C_{(13)}-N_{(3)}$	178.7(6)	$H_{(16A)}-C_{(16)}-C_{(15)}$	111.1
$C_{(3)}-C_{(4)}-C_{(5)}$	121.2(5)	$N_{(1)}-C_{(15)}-C_{(16)}$	103.1(4)	$H_{(16B)}-C_{(16)}-N_{(2)}$	111.1
$C_{(5)}-C_{(4)}-C_{(14)}$	118.8(5)	$C_{(15)}-C_{(16)}-N_{(2)}$	103.2(4)	$H_{(16B)}-C_{(16)}-C_{(15)}$	111.1
$C_{(3)}-C_{(4)}-C_{(14)}$	120.0(4)	$H_{(2)}-N_{(2)}-C_{(2)}$	124(4)	$H_{(16A)}-C_{(16)}-H_{(16B)}$	109.1
$F_{(1)}-C_{(14)}-F_{(2)}$	105.8(5)	$H_{(2)}-N_{(2)}-C_{(16)}$	123(4)	$O_{(2')}-C_{(2')}-O_{(1')}$	129.8(6)
$F_{(2)}-C_{(14)}-F_{(3)}$	107.4(5)	$H_{(5)}-C_{(5)}-C_{(6)}$	119.6	$C_{(1')}-C_{(2')}-O_{(1')}$	114.7(5)
$F_{(1)}-C_{(14)}-F_{(3)}$	105.4(5)	$H_{(5)}-C_{(5)}-C_{(4)}$	119.6	$C_{(1')}-C_{(2')}-O_{(2')}$	115.5(5)
$C_{(4)}-C_{(14)}-F_{(2)}$	112.2(5)	$H_{(8)}-C_{(8)}-C_{(9)}$	120.0	$F_{(3')}-C_{(1')}-F_{(1')}$	109.4(6)
$C_{(4)}-C_{(14)}-F_{(1)}$	112.8(5)	$H_{(8)}-C_{(8)}-C_{(7)}$	120.0	$F_{(2')}-C_{(1')}-F_{(1')}$	103.1(6)
$C_{(4)}-C_{(14)}-F_{(3)}$	112.8(5)	$H_{(9)}-C_{(9)}-C_{(10)}$	120.0	$F_{(2')}-C_{(1')}-F_{(3')}$	101.7(5)
$C_{(4)}-C_{(5)}-C_{(6)}$	120.8(5)	$H_{(9)}-C_{(9)}-C_{(8)}$	120.0	$C_{(2')}-C_{(1')}-F_{(1')}$	114.5(5)
$N_{(1)}-C_{(6)}-C_{(5)}$	117.7(4)	$H_{(10)}-C_{(10)}-C_{(11)}$	120.0	$C_{(2')}-C_{(1')}-F_{(3')}$	113.9(5)
$N_{(1)}-C_{(6)}-C_{(7)}$	120.2(4)	$H_{(10)}-C_{(10)}-C_{(9)}$	120.0	$C_{(2')}-C_{(1')}-F_{(2')}$	112.9(5)
$C_{(5)}-C_{(6)}-C_{(7)}$	122.1(5)	$H_{(11)}-C_{(11)}-C_{(10)}$	119.5		
$C_{(8)}-C_{(7)}-C_{(12)}$	119.6(5)	$H_{(11)}-C_{(11)}-C_{(12)}$	119.5		

TABLE 6. Coordinates ($\times10^4$) and Equivalent Isotropic Thermal Parameters ($Å^2\times10^3$) for the Atoms in the Molecule of Compound **7a**

Atom	*x*	*y*	*z*	$U_{(eq)}$
$Cl_{(1)}$	506(1)	2342(1)	3629(1)	62(1)
O	805(1)	-466(2)	3453(1)	45(1)
$F_{(1)}$	1431(1)	-350(2)	2089(1)	62(1)
$F_{(2)}$	8489(1)	1097(2)	1866(1)	63(1)
$F_{(3)}$	1637(1)	1601(2)	2536(1)	67(1)
$N_{(1)}$	1889(1)	1631(2)	5494(2)	40(1)
$N_{(2)}$	2465(1)	68(3)	5828(2)	50(1)
$N_{(3)}$	1989(1)	-2464(3)	3938(2)	67(1)
$C_{(2)}$	2015(1)	445(3)	5197(2)	38(1)
$C_{(3)}$	1717(1)	-168(3)	4314(2)	40(1)
$C_{(4)}$	1223(1)	421(3)	3652(2)	41(1)
$C_{(5)}$	1105(1)	1661(3)	4166(2)	42(1)
$C_{(6)}$	1415(1)	2205(3)	5019(2)	38(1)
$C_{(7)}$	1284(1)	3398(3)	5534(2)	40(1)
$C_{(8)}$	1049(1)	3320(4)	6352(3)	59(1)
$C_{(9)}$	907(2)	4418(4)	6807(3)	77(1)
$C_{(10)}$	1000(2)	5598(4)	6453(4)	78(1)
$C_{(11)}$	1244(2)	5696(4)	5666(5)	97(2)
$C_{(12)}$	1384(2)	4603(3)	5193(3)	75(1)
$C_{(13)}$	2284(1)	2109(3)	6400(3)	47(1)
$C_{(14)}$	2624(2)	923(4)	6722(3)	61(1)
$C_{(15)}$	1861(1)	-1435(3)	4091(2)	48(1)
$C_{(16)}$	1282(1)	692(3)	2529(2)	45(1)
$C_{(17)}$	645(2)	-881(4)	4371(3)	59(1)
$C_{(18)}$	209(2)	-1791(7)	4011(4)	97(1)

TABLE 7. Mean Atomic Distances in the Molecule of Compound **7a**

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
$Cl_{(10)}$–$C_{(5)}$	1.727(3)	$C_{(3)}$–$C_{(15)}$	1.417(4)	$C_{(11)}$–$C_{(12)}$	1.385(6)
O–$C_{(4)}$	1.419(3)	$C_{(3)}$–$C_{(4)}$	1.514(4)	$C_{(11)}$–$H_{(11)}$	0.91(4)
O–$C_{(17)}$	1.436(4)	$C_{(4)}$–$C_{(5)}$	1.518(4)	$C_{(12)}$–$H_{(12)}$	1.00(4)
$F_{(1)}$–$C_{(16)}$	1.330(3)	$C_{(4)}$–$C_{(16)}$	1.541(4)	$C_{(13)}$–$C_{(14)}$	1.521(5)
$F_{(2)}$–$C_{(16)}$	1.330(3)	$C_{(5)}$–$C_{(6)}$	1.339(4)	$C_{(13)}$–$H_{(13A)}$	0.93(3)
$F_{(3)}$–$C_{(16)}$	1.333(3)	$C_{(6)}$–$C_{(7)}$	1.488(4)	$C_{(13)}$–$H_{(13B)}$	0.91(3)
$N_{(1)}$–$C_{(2)}$	1.364(3)	$C_{(7)}$–$C_{(8)}$	1.370(4)	$C_{(14)}$–$H_{(14A)}$	0.95(3)
$N_{(1)}$–$C_{(6)}$	1.395(3)	$C_{(7)}$–$C_{(12)}$	1.373(4)	$C_{(14)}$–$H_{(14B)}$	0.92(4)
$N_{(1)}$–$C_{(13)}$	1.465(3)	$C_{(8)}$–$C_{(9)}$	1.380(5)	$C_{(17)}$–$C_{(18)}$	1.478(6)
$N_{(2)}$–$C_{(2)}$	1.345(3)	$C_{(8)}$–$H_{(8)}$	0.91(3)	$C_{(17)}$–$H_{(17A)}$	1.02(4)
$N_{(2)}$–$C_{(14)}$	1.445(4)	$C_{(9)}$–$C_{(10)}$	1.351(6)	$C_{(17)}$–$H_{(17B)}$	0.92(3)
$N_{(2)}$–$H_{(2)}$	0.85(3)	$C_{(9)}$–$H_{(9)}$	0.95(4)	$C_{(18)}$–$H_{(18A)}$	0.94(4)
$N_{(3)}$–$C_{(15)}$	1.151(4)	$C_{(10)}$–$C_{(11)}$	1.353(6)	$C_{(18)}$–$H_{(18B)}$	1.05(4)
$C_{(2)}$–$C_{(3)}$	1.369(4)	$C_{(10)}$–$H_{(10)}$	0.94(4)	$C_{(18)}$–$H_{(18C)}$	0.95(6)

In order to determine the crystalline molecular structure of the covalent solvates we carried out an X-ray analysis of compound **7a** (Fig. 2). The coordinates and equivalent isotropic thermal parameters for the atoms are given in Table 6 and the mean interatomic distances and valence angles in Tables 7 and 8. The dihedral angle between the planes of the phenyl substituent and the heterocyclic system was 96° and the C_6–C_7 bond length 1.488 Å which points to a disturbance of the conjugation between the aromatic ring and the bicyclic system.

TABLE 8. Valence Angles in the Molecule of Compound **7a**

Angle	ω, deg.	Angle	ω, deg.	Angle	ω, deg.
$C_{(4)}$–O–$C_{(17)}$	115.0(2)	$C_{(8)}$–$C_{(7)}$–$C_{(6)}$	120.6(3)	$N_{(2)}$–$C_{(14)}$–$C_{(13)}$	103.6(3)
$C_{(2)}$–$N_{(1)}$–$C_{(6)}$	120.9(2)	$C_{(12)}$–$C_{(7)}$–$C_{(6)}$	121.4(3)	$N_{(2)}$–$C_{(14)}$–$H_{(14A)}$	107.4(19)
$C_{(2)}$–$N_{(1)}$–$C_{(13)}$	111.5(2)	$C_{(7)}$–$C_{(8)}$–$C_{(9)}$	121.1(4)	$C_{(13)}$–$C_{(14)}$–$H_{(14A)}$	113.3(19)
$C_{(6)}$–$N_{(1)}$–$C_{(13)}$	127.5(2)	$C_{(7)}$–$C_{(8)}$–$H_{(8)}$	118(2)	$N_{(2)}$–$C_{(14)}$–$H_{(14B)}$	113(3)
$C_{(2)}$–$N_{(2)}$–$C_{(14)}$	111.8(3)	$C_{(9)}$–$C_{(8)}$–$H_{(8)}$	121(2)	$C_{(13)}$–$C_{(14)}$–$H_{(14B)}$	112(3)
$C_{(2)}$–$N_{(2)}$–$H_{(2)}$	120(2)	$C_{(10)}$–$C_{(9)}$–$C_{(8)}$	120.2(4)	$H_{(14A)}$–$C_{(14)}$–$H_{(14B)}$	107(3)
$C_{(14)}$–$N_{(2)}$–$H_{(2)}$	126(2)	$C_{(10)}$–$C_{(9)}$–$H_{(9)}$	118(3)	$N_{(3)}$–$C_{(15)}$–$C_{(3)}$	178.0(3)
$N_{(2)}$–$C_{(2)}$–$N_{(1)}$	108.6(2)	$C_{(8)}$–$C_{(9)}$–$H_{(9)}$	121(3)	$F_{(2)}$–$C_{(16)}$–$F_{(1)}$	106.2(2)
$N_{(2)}$–$C_{(2)}$–$C_{(3)}$	129.3(3)	$C_{(9)}$–$C_{(10)}$–$C_{(11)}$	119.5(4)	$F_{(2)}$–$C_{(16)}$–$F_{(3)}$	106.5(2)
$N_{(1)}$–$C_{(2)}$–$C_{(3)}$	122.1(2)	$C_{(9)}$–$C_{(10)}$–$H_{(10)}$	123(2)	$F_{(1)}$–$C_{(16)}$–$F_{(3)}$	106.7(2)
$C_{(2)}$–$C_{(3)}$–$C_{(15)}$	117.9(2)	$C_{(11)}$–$C_{(10)}$–$H_{(10)}$	118(2)	$F_{(2)}$–$C_{(16)}$–$C_{(4)}$	113.8(2)
$C_{(2)}$–$C_{(3)}$–$C_{(4)}$	122.1(2)	$C_{(10)}$–$C_{(11)}$–$C_{(12)}$	120.8(4)	$F_{(1)}$–$C_{(16)}$–$C_{(4)}$	112.2(2)
$C_{(15)}$–$C_{(3)}$–$C_{(4)}$	119.8(2)	$C_{(10)}$–$C_{(11)}$–$H_{(11)}$	123(3)	$F_{(3)}$–$C_{(16)}$–$C_{(4)}$	111.1(2)
O–$C_{(4)}$–$C_{(3)}$	112.2(2)	$C_{(12)}$–$C_{(11)}$–$H_{(11)}$	116(3)	O–$C_{(17)}$–$C_{(18)}$	107.2(3)
O–$C_{(4)}$–$C_{(5)}$	112.9(2)	$C_{(7)}$–$C_{(12)}$–$C_{(11)}$	120.2(4)	O–$C_{(17)}$–$H_{(17A)}$	108(2)
$C_{(3)}$–$C_{(4)}$–$C_{(5)}$	109.5(2)	$C_{(7)}$–$C_{(12)}$–$H_{(12)}$	117(2)	$C_{(18)}$–$C_{(17)}$–$H_{(17A)}$	113(2)
O–$C_{(4)}$–$C_{(16)}$	101.7(2)	$C_{(11)}$–$C_{(12)}$–$H_{(12)}$	122(2)	O–$C_{(17)}$–$H_{(17B)}$	111(2)
$C_{(3)}$–$C_{(4)}$–$C_{(16)}$	109.9(2)	$N_{(1)}$–$C_{(13)}$–$C_{(14)}$	102.2(2)	$C_{(18)}$–$C_{(17)}$–$H_{(17B)}$	112(2)
$C_{(5)}$–$C_{(4)}$–$C_{(16)}$	110.5(2)	$N_{(1)}$–$C_{(13)}$–$H_{(13A)}$	108.9(18)	$H_{(17A)}$–$C_{(17)}$–$H_{(17B)}$	106(3)
$C_{(6)}$–$C_{(5)}$–$C_{(4)}$	124.9(2)	$C_{(14)}$–$C_{(13)}$–$H_{(13A)}$	113.7(17)	$C_{(17)}$–$C_{(18)}$–$H_{(18A)}$	106(2)
$C_{(6)}$–$C_{(5)}$–$Cl_{(1)}$	119.1(2)	$N_{(1)}$–$C_{(13)}$–$H_{(13B)}$	109(2)	$C_{(17)}$–$C_{(18)}$–$H_{(18B)}$	101(2)
$C_{(4)}$–$C_{(5)}$–$Cl_{(1)}$	115.9(19)	$C_{(14)}$–$C_{(13)}$–$H_{(13B)}$	115(2)	$H_{(18A)}$–$C_{(18)}$–$H_{(18B)}$	109(3)
$C_{(5)}$–$C_{(6)}$–$N_{(1)}$	119.8(2)	$C_{(14)}$–$C_{(13)}$–$H_{(13A)}$	113.7(17)	$C_{(17)}$–$C_{(18)}$–$H_{(18C)}$	115(4)
$C_{(5)}$–$C_{(6)}$–$C_{(7)}$	124.1(2)	$N_{(1)}$–$C_{(13)}$–$H_{(13B)}$	109(2)	$H_{(18A)}$–$C_{(18)}$–$H_{(18C)}$	107(4)
$N_{(1)}$–$C_{(6)}$–$C_{(7)}$	116.1(2)	$C_{(14)}$–$C_{(13)}$–$H_{(13B)}$	115(2)	$H_{(18B)}$–$C_{(18)}$–$H_{(18C)}$	119(5)
$C_{(8)}$–$C_{(7)}$–$C_{(12)}$	118.1(3)	$H_{(13A)}$–$C_{(13)}$–$H_{(13B)}$	108(3)		

EXPERIMENTAL

IR spectra were taken on a Specord IR-75 instrument in paraffin oil (NaCl prism, 1500-1800 cm^{-1} region) or hexachlorobutadiene (LiF prism, 2000-3600 cm^{-1} region). ^{1}H NMR spectra were recorded on a Bruker WH-90/DS spectrometer (90 MHz) using TMS or HMDS internal standards. Monitoring of the reaction course and the purity of the compounds obtained was carried out using TLC on Silufol UV-254 plates in the system ethanol–chloroform (1:9). The unit cell parameters and intensities of the reflections were measured on a Syntex P2$_1$ automatic diffractometer using monochromatic molybdenum irradiation (graphite monochromator) and the ω-scanning method. The structure was solved by a direct method [8] and refined by the least squares method in a full matrix, anisotropic approximation. All calculations were carried out using the program package [9].

Data for the synthesized compound is collated in Tables 1 and 2.

8-Cyano-1-methyl-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium Iodide (2a). Methyl iodide (0.04 ml) was added to a solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) in chloroform (5 ml). The reaction mixture was held at room temperature for 24 h. Solvent was distilled off in vacuo and the oil produced was recrystallized from diethyl ether.

8-Cyano-5-phenyl-1-propyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium Iodide (2b). Propyl iodide (0.34 ml, 3.5 mmol) was added to a solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) in acetonitrile (5 ml) and refluxed for 8 h. The reaction mixture was evaporated to dryness in vacuo and water (50 ml) was added to the residue. The precipitate was recrystallized from ethanol and the aqueous filtrate was used in the synthesis of compound **8**.

8-Cyano-5-phenyl-7-trifluoromethyl-2,3-dihydro-(1H)-imidazo[1,2-*a*]pyridinium Hydroselenite (2d). A solution of the imidazopyridine **1** (0.5 g, 1.73 mmol) and selenium dioxide (0.2 g, 1.73 mmol) in tetrahydrofuran (5 ml) was held at room temperature for 7 h. The precipitate was filtered off.

1-Acetyl-8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium Chloride (3a). A solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) in freshly distilled acetyl chloride (5 ml) was refluxed for 4 h. The reaction mixture has poured into crushed ice (50 g) and the precipitate was recrystallzed from ethanol.

1-Benzoyl-8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium Chloride (3b). A solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) and benzoyl chloride (0.1 ml, 0.9 mmol) in chloroform (5 ml) was refluxed for 1 h. The solvent was evaporated off in vacuo and the residue was recrystallized from ethanol.

6-Chloro-8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium Chloride (4a). A. A solution of chlorine (0.06 g, 0.9 mmol) in absolute dioxane (5 ml) was added to a solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) in dioxane (5 ml). The reaction mixture was held at room temperature for 24 h and the precipitate was filtered off. The filtrate was used for the preparation of compound **5a**.

8-Cyano-6-halo-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium halides (4a,b). B. The corresponding acid (0.69 mmol) was added to a solution of the imidazopyridine **5a** or **5b** (0.69 mmol) in tetrahydrofuran (5 ml). The reaction mixture was held at room temperature for 4 h and the crystals formed were filtered off.

6-Bromo-8-cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridinium Tribromide (4c). Bromine (0.04 ml, 0.69 mmol) was added to a solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) in DMF (5 ml). The reaction mixture was held at room temperature for 24 h, the solution was poured into water (50 ml), and the precipitate was filtered off. The filtrate was used for the preparation of compound **5b**.

8-Cyano-6-halo-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridines (5a,b). A. The filtrate obtained in the synthesis of compound **4a** (method A) or **4c** was basified with aqueous ammonia to pH 8-9 and left for 1 h at room temperature. The precipitate was recrystallized from isopropanol.

B. The imidazopyridinium salt (**4a-c**) (0.2 g) was dissolved with heating in water (10 ml). The solution was basified with aqueous ammonia to pH 8-9 and left for 1 h at room temperature. The precipitate was recrystallized from isopropanol.

8-Aminocarbonyl-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]pyridine·EtOH (6b). A solution of the imidazopyridine **1** (0.2 g, 0.69 mmol) and KOH (0.04 g) in ethanol (5 ml) was heated for 4 h. The reaction mixture was cooled to room temperature and the precipitate was filtered off.

7-Alkoxy-8-cyano-6-halo-5-phenyl-7-trifluoromethyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridines (7a-d). A solution of the imidazopyridine **5a,b** (0.2 g) in the corresponding alcohol (5 ml) was heated to reflux and allowed to stand at room temperature for 24 h. The crystals formed were filtered off.

6-Bromo-8-cyano-7-phenoxy-5-phenyl-7-trifluoromethyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine (7e). Phenol (0.05 g, 0.54 mmol) was added to a solution of the imidazopyridine **5b** (0.2 g, 0.54 mmol) in chloroform (5 ml), the product was heated to reflux, and allowed to stand for 24 h at room temperature. The bright red crystals formed were filtered off and washed on the filter with chloroform.

8-Cyano-7-ethoxy-5-phenyl-1-propyl-7-trifluoromethyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine (8). The aqueous filtrate obtained in the synthesis of compound **2b** was basified with aqueous ammonia to pH 8-9 and allowed to stand for 1 h at room temperature. The precipitate formed was recrystallized from ethanol.

X-ray Structural Analysis of 8-Cyano-5-phenyl-7-trifluoromethyl-2,3-dihydroimidazo[1,2-*a*]-pyridinium Trifluoroacetate (2c). Crystals of the investigated compound are monoclinic. Unit cell parameters: $a = 8.421(2)$, $b = 13.005(3)$, $c = 15.546(3)$ Å; $\beta = 90.10(3)°$; $V = 1702.5(7)$ Å^3; $d_{\mathrm{calc}} = 1.573$ mg/m^3; $Z = 4$; space group $P2(1)c$. 2145 Independent reflections were obtained, $2\theta_{\max} = 25.05°$, final R-factor 0.0724.

X-ray Structural Analysis of 6-Chloro-8-cyano-7-ethoxy-5-phenyl-7-trifluoromethyl-1,2,3,7-tetrahydroimidazo[1,2-*a*]pyridine (7a). Crystals of the investigated compound are monoclinic. Unit cell parameters: $a = 26.650(5)$, $b = 10.352(2)$, $c = 13.095(3)$ Å; $\beta = 104.30(3)$; $V = 3500.7(12)$ Å^3; $d_{\mathrm{calc}} = 1.403$ mg/m^3; Z = 8; space group $C2/c$. 2450 Independent reflections were obtained, $2\theta_{\max} = 25.06°$, final R-factor 0.0451.

REFERENCES

1. E. Suloeva, M. Yure, and E. Gudriniece, *Khim. Geterotsikl. Soedin.*, 1299 (1999).
2. E. Suloeva, M. Jure, and E. Gudriniece, *Khim. Geterotsikl. Soedin.*, 1011 (2000).
3. E. Suloyeva, M. Jure, E. Gudriniece, S. Belyakov, M. Petrova, and I. Kalnite, *Khim. Geterotsikl. Soedin.*, 358 (2001).
4. J. Sulojeva, M. Petrova, E. Gudriniece, and M. Jure, *RTU Zinatniskie raksti. Materialzinatne un lietiska kimija*, Vol. 1, Riga (2000), p. 121.
5. T. Kato, and T. Sakamoto, *Yakagaku Zasshi*, **91**, 1174 (1971); *Chem. Abstr.*, **76**, 46141 (1971).
6. S. Portnoy, *J. Org. Chem.*, 3377 (1965).
7. O. Bremer, *Liebigs Ann. Chem.*, **521**, 286 (1936).
8. A. F. Mishnev and S. V. Belyakov, *Kristallografiya*, **33**, 835 (1988).
9. P. Gluzinsky, Ya. Kraevsky, A. Kemme, and A. Mishnev, in: *Precise Structural Investigations of Crystals* [in Russian], Summary Report, Second All Soviet Conference, Riga (1990), p. 30.