Nitroalkyl-substituted tetrahydropyrazines in syntheses of azapolycyclic compounds*

P. A. Slepukhin,[a] N. N. Mochul´skaya,[b] L. P. Sidorova,[b] G. L. Rusinov,[a] M. A. Ezhikova,[a] M. I. Kodess,[a] O. N. Kazheva,[c] A. N. Chekhlov,[c] O. A. D´yachenko,[c] and V. N. Charushin[a]★

[a] *I. Ya. Postovsky Institute of Organic Synthesis, Ural Division of the Russian Academy of Sciences, 22 ul. S. Kovalevskoi, 620219 Ekaterinburg, Russian Federation. Fax: +7 (343) 374 1189. E-mail: charushin@ios.uran.ru*

[b] *Ural State Technical University (UPI), 19 ul. Mira, 620002 Ekaterinburg, Russian Federation. Fax: +7 (343) 374 0458. E-mail: 7708@mail.ur.ru*

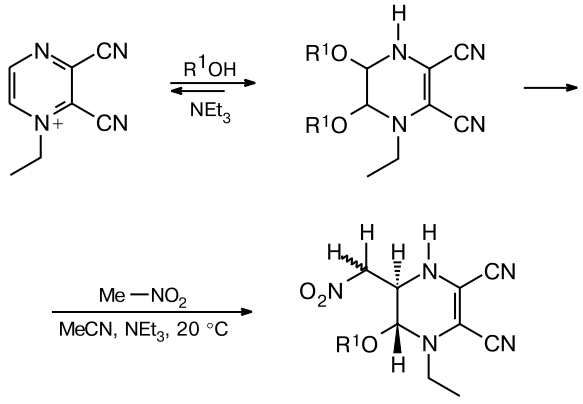
[c] *Institute of Problems of Chemical Physics, Russian Academy of Sciences, 1 prosp. Akad. Semenova, 142432 Chernogolovka, Russian Federation. Fax: +7 (496) 515 5420. E-mail: kon@icp.ac.ru*

Tri- and tetracyclic compounds were synthesized by the cyclization of 6-alkoxy-2,3-dicyano-5-nitromethyl-1,4,5,6-tetrahydropyrazines with 1,2,3-triazinium and quinoxalinium cations.

Key words: 6-alkoxy-5-nitromethyl-1,4,5,6-tetrahydropyrazines, 1,2,4-triazines, quinoxalines, tandem A_N—A_N reactions, azapolycyclic compounds.

Among chemical transformations of azines, their reactions with nucleophilic agents are the most synthetically important. It is known[1—7] that *N*(1)-alkyl-1,4-diazinium cations are prone to add carbo- and heteroatomic nucleophiles to unsubstituted carbon atoms with the consecutive formation of mono- and diadducts, as well as cyclic adducts. Predominantly, σ^H-monoadducts with heteronucleophiles are labile and can be detected only in solutions, while the cyclic monoadducts can be isolated in the crystalline form. It has recently been shown[8] that the reaction of the 2,3-dicyano-*N*(1)-alkylpyrazinium cation with aliphatic alcohols affords unusually stable 5,6-dialkoxy adducts, which can be isolated in the crystalline form. A specific feature of the dialkoxy adducts is their ability to exchange one of the alkoxy groups, under mild conditions, by a C-nucleophilic moiety to form mixed *O*,*C*-diadducts (Scheme 1).

Scheme 1



R^1 = Me, Et

6-Alkoxy-5-nitroalkyl-substituted 1,4,5,6-tetrahydropyrazines are, on the one hand, relatively stable σ^H-adducts of pyrazinium salts with CH-nitroalkanes and, on the other hand, they can be considered as 1,3-dinucleophilic agents and are interesting for subsequent cyclizations with azinium cations.

It has previously been shown[9—11] that the reactions of 1,4-diazinium salts with nitroalkanes afford complex bridged and cage structures (Scheme 2), because methylenic compounds manifest the properties of 1,1-dinucleophilic agents and can bind 1,4-diazinium cations to form complex polycyclic compounds. The adducts of azinium cations with nitroalkanes were assumed to be the key intermediates in cyclizations of this type. However, earlier attempts to isolate them in the free state and to study their properties were unsuccessful.

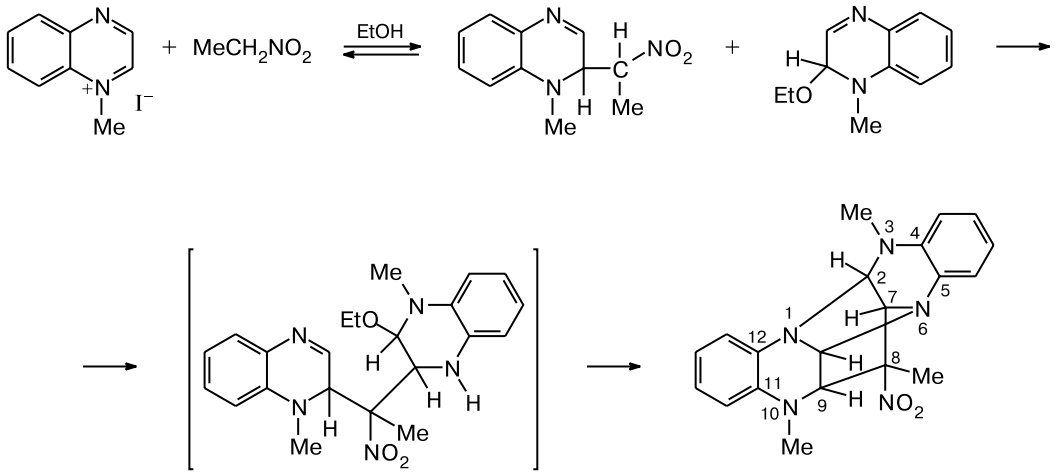
In this work, the reactivity of σ^H-adducts of 1,4-pyrazinium salts with CH-nitroalkanes as N,C-dinucleophiles in the cyclizations with quinoxalinium and 1,2,4-triazinium cations was studied.

* Dedicated to Academician A. L. Buchachenko on the occasion of his 70th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 9, pp. 2132—2137, September, 2005.

1066-5285/05/5409-2197

Scheme 2



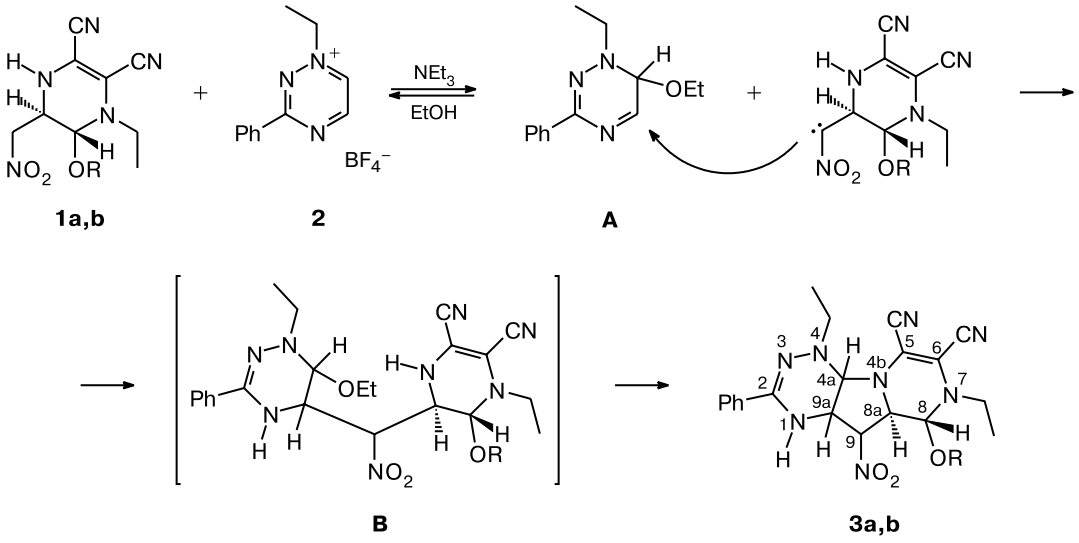
Results and Discussion

The cyclization of 6-alkoxy-2,3-dicyano-5-nitromethyl-1,4,5,6-tetrahydropyrazines **1a,b** with 3-phenyl-1,2,4-triazinium tetrafluoroborate **2** in anhydrous ethanol in the presence of triethylamine affords polycyclic compounds **3a,b** (Scheme 3).

The structures of compounds **3a,b** were determined on the basis of elemental analysis, ^{1}H and ^{13}C NMR, including 2D COSY, NOESY, HSQC, and HMBC spectroscopy, and mass spectra that manifest peaks of molecular ions (M^+).

An analysis of the ^{1}H NMR spectrum of compound **3b** shows that the compound consists of the *N*-ethyltetrahydro-1,2,4-triazine and *N*-ethyltetrahydropyrazine moieties: the spectrum contains multiplets of five protons of the benzene ring, signals of protons of two *N*-ethyl groups, and a singlet of the methoxy group at 3.42 ppm (see Experimental). Two nonequivalent protons of one of the methylene groups at the diastereomeric nitrogen atom appear as double quartets at δ 2.77 and 3.10. The downfield spectral region (δ 7.60) contains a signal from the N(1)H proton, which disappears upon the addition of deuterated acid CD_3COOD due to exchange processes. Two doublet signals at 4.14 and 4.30 ppm were assigned to the resonance of the H(4a) and H(8) protons, respectively. The signal of the H(9) proton appears at δ 5.13 as a doublet of doublets due to the interaction with the H(9a) and H(8a)

Scheme 3



R = Me (**a**), Et (**b**)

protons. The signal of H(9a) in the ^{1}H NMR spectrum is more complex due to the spin-spin interaction with the H(9), H(4a), and N(1)H protons of the tetrahydro-1,2,4-triazine cycle. Remarkably, when acid CD_3COOD is added, the multiplicity of the H(9a) signal simplifies, and the signal becomes a doublet of doublets. This fact is one of the arguments in favor of the orientation of the tetrahydro-1,2,4-triazine cycle relative to the pyrrolopyrazine bicyclic cage, which is presented in Scheme 3.

The data of ^{1}H—^{1}H COSY NMR correlation spectroscopy for compound **3b** make it possible to determine the interacting atoms (groups of atoms), and the doublet of the N(1)H proton (δ 7.60, J = 5.9 Hz) can be used as a reference signal. The scheme of vicinal interactions (Fig. 1) enables one to unambiguously assign signals of all methine protons of compound **3b** and to exclude an alternative regioisomeric structure.

The ^{13}C NMR data are also consistent with the structure proposed. For instance, the signals of the methine carbon atoms are identified by cross-peaks with the corresponding protons in the 2D HSQC spectra. The signals of the quaternary carbon atoms were assigned on the basis of spin-spin coupling (SSC) constants $^2J_{CH}$ and $^3J_{CH}$ observed in 2D HMBC experiments. The assignment of the signals from C(6) (δ 112.74) and C(5) (δ 104.55) is confirmed by the cross-peaks with the N(7)—CH_2 and H(4a) protons, respectively. Among the two signals with chemical shifts δ 47.24 and 41.64 corresponding to the NCH_2 groups, the more downfield signal can be attributed to the N(4)—C carbon atom, because it interacts with the H(4a) proton. In addition, the protons bonded with this carbon atom give the cross-peak with the H(4a) proton in the 2D NOESY spectrum.

One of the most probable mechanisms for the formation of pentaazafluorenes **3a,b** is presented in Scheme 3. This mechanism assumes that, after 1,2,4-triazinium cation **1** was dissolved in anhydrous ethanol in the presence of TEA, the ethanol residue adds to C(6) of the triazine ring to form the corresponding σ^H-adduct **A**. Then the CH-anionic center of 6-alkoxy-2,3-dicyano-5-nitromethyl-1,4,5,6-tetrahydropyrazine **2**, which was generated under the action of triethylamine, attacks the C(5) position, and the resulting intermediate **B** undergoes intramolecular cyclization affording pentaazatricyclodienes **3a,b**.

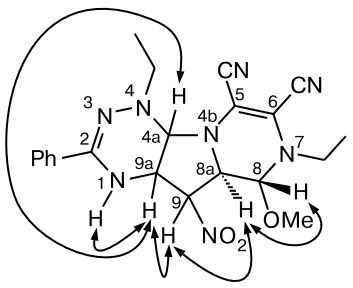
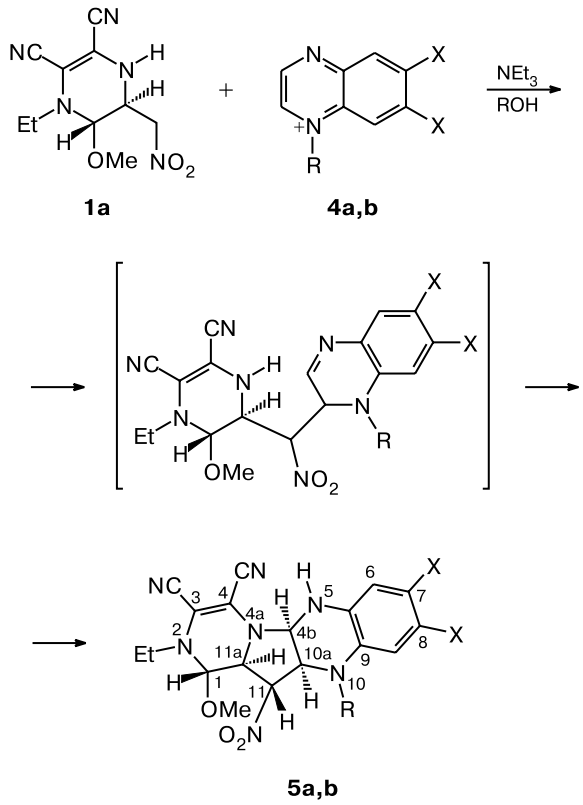


Fig. 1. Vicinal interactions for compound **3b**.

Under the same conditions, the reactions of 6-alkoxy-2,3-dicyano-5-nitromethyl-1,4,5,6-tetrahydropyrazines **1a** with quinoxalinium salts **4a,b** give 10-alkyl-2-ethyl-1-methoxy-11-nitro-1,2,4b,5,10,10a,11,11a-octahydro-2,4a,5,10-tetraazabenzo[*b*]fluorene-3,4-dicarbonitriles **5a,b** (Scheme 4).

Scheme 4



R = Me, X = H (**a**); R = Et, X = F (**b**)

The ^{1}H NMR spectrum of compound **5a** recorded in $(CD_3)_2SO$ is characterized by signals of protons of the benzene ring (multiplet), the methoxy group at δ 3.26 (singlet), and the NMe group at δ 2.86 (singlet). The absorption region of the NCH_2 protons is superimposed on the region of water absorption and, therefore, it is difficult to estimate the multiplicity and spin-spin coupling constants of these signals. However, the protons of the terminal methyl group of the N-ethyl moiety give a distinct signal at δ 1.10 as a triplet with ^3J = 7.2 Hz. The downfield spectral region (δ 6.49) exhibits a signal of the N(5)—H proton (broadened singlet). The doublet at δ 3.88 was assigned to the proton at the C(1) atom bonded to the methoxy group ($^3J_{H(1),H(11a)}$ = 6.9 Hz). The H(11a) proton, in turn, resonates at δ 3.68 and has the couplings with the H(11) proton ($^3J_{H(11a),H(1)}$ = 6.9 Hz, $^3J_{H(11a),H(11)}$ =

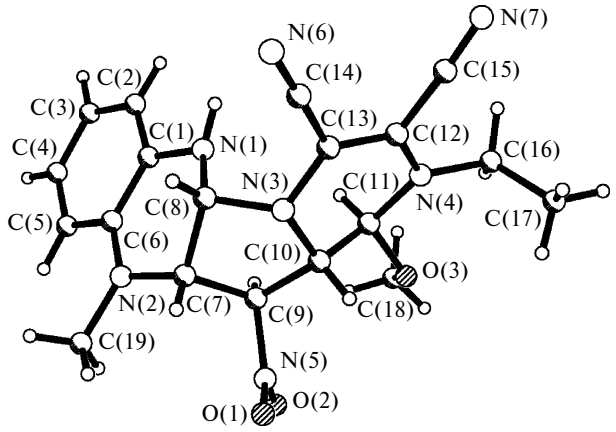


Fig. 2. Geometry of molecule **5a** in crystal.

4.4 Hz). The signals from the H(11) and H(10a) protons are superimposed and appear as a multiplet at δ 4.90. The H(4b) proton gives a broadened doublet at δ 5.00.

The structure of **5a** was unambiguously determined by X-ray diffraction analysis (Fig. 2). The arrangement of the pyrazine cycle relatively to the *N*-alkyl group of annelated quinoxaline in **5a** is opposite to that in compounds **3a,b**, which were formed in the reactions with triazines. This is caused by the fact that *N*-alkylquinoxalinium cation **4** reacts directly with cyanopyrazines **2a,b** instead of the covalent adduct of the quinoxalinium salt with alcohol (this adduct is relatively lowly stable). Structures of the type of **5** were earlier postulated as intermediates leading to tetraazatetracyclo[7.3.1.$0^{2,7}$.$0^{6,13}$]trideca-4,11-dienes.[9] However, direct proves of their participation in the formation of polycyclic compounds were unavailable.

A specific feature of the crystal structure of synthesized compound **5a** is molecular stacking formed by only one of the enantiomers (Figs 3 and 4).

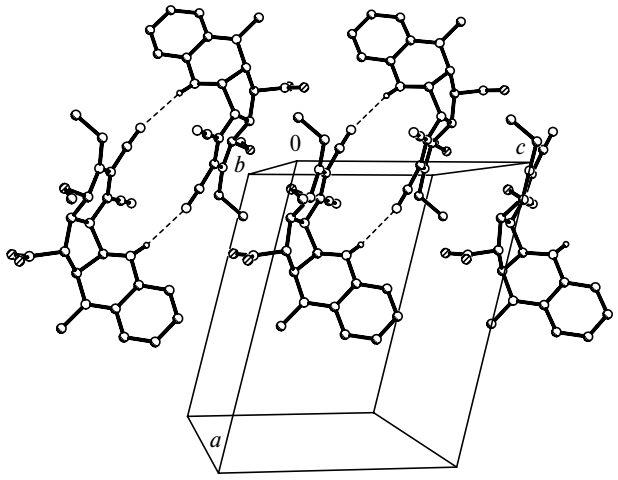


Fig. 3. Stacking of molecule **5a**.

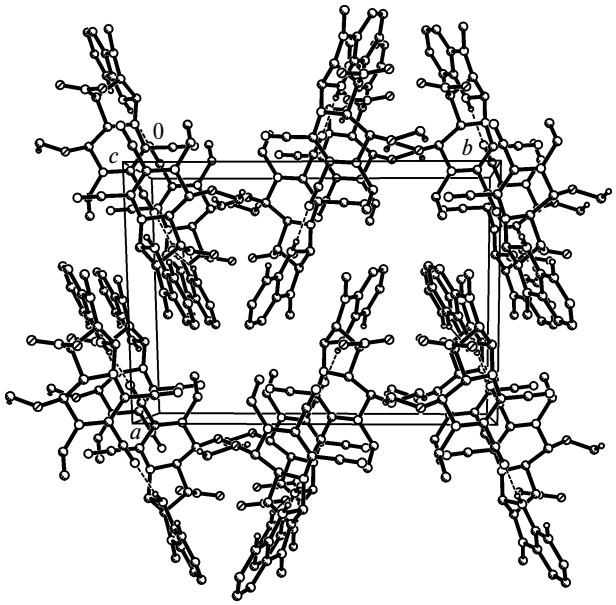


Fig. 4. Fragment of the crystal structure of **5a**.

The studied reactions are very sensitive to spatial factors. For instance, unlike nitromethyl derivatives **1a,b**, 6-alkoxy-2,3-dicyano-1-ethyl-5-nitropropyl- and 6-alkoxy-2,3-dicyano-1-ethyl-5-nitroethyl-1,4,5,6-tetrahydropyrazines do not react with quinoxalinium or 1,2,4-triazinium salts under similar conditions.

It should be noted in conclusion that the adducts of pyrazines with simple nucleophiles, in particular, 6-alkoxy-5-nitroalkyl-substituted pyrazines, are very interesting for subsequent chemical reactions as 1,3-dinucleophilic agents. The studies of the cyclization of nitroalkyl-substituted tetrahydropyrazines with the 1,2,4-triazinium and quinoxalinium cations demonstrate a possibility to synthesize complex tri- and tetracyclic compounds.

Experimental

^{1}H NMR spectra were recorded on a Bruker WP-250 spectrometer with a working frequency of 250.13 MHz using Me_4Si as the internal standard. Mass spectra were obtained on a Varian MAT-311A spectrometer. Detection conditions: accelerating voltage 3 kV, energy of ionizing electrons 70 eV, and direct sample injection into the source. The course of the reaction and purity of products were monitored by TLC on Silufol UV-254 plates using a chloroform—acetone (4 : 1) mixture as the eluent (UV detection).

3-Phenyl-1,2,4-triazinium borofluoride[12] and 6-alkoxy-2,3-dicyano-5-nitromethyl-1,4,5,6-tetrahydropyrazines[8] were synthesized according to an earlier described procedure.

4,7-Diethyl-8-methoxy-9-nitro-2-phenyl-1,4,4a,7,8,8a,9,9a-octahydro-1,3,4,4b,7-pentaazafluorene-5,6-dicarbonitrile (3a). A solution of the anionic form of 2,3-dicyano-1-ethyl-6-methoxy-5-nitromethyl-1,4,5,6-tetrahydropyrazine, which was obtained by the addition of triethylamine (0.07 mL) to a sus-

pension of neutral 1,4,5,6-tetrahydropyrazine **1a** (133 mg, 0.50 mmol) in anhydrous ethanol (2 mL), was added to a suspension of the 1,2,4-triazinium salt **2** (126 mg, 0.50 mmol) in anhydrous ethanol (0.5 mL). The reaction mixture was magnetically stirred for 1 h at room temperature, and a formed precipitate of **3a** was filtered off and recrystallized from anhydrous ethanol The yield was 77 mg (35%), m.p. 189 °C. Found (%): C, 57.79; H, 5.59; N, 25.47. $C_{21}H_{24}N_8O_3$. Calculated (%): C, 57.79; H, 5.54; N, 25.67. Mass spectrum, m/z (I_{rel} (%)): 436 $[M]^+$ (5.1), 251 (23.3), 220 (17.7), 187 (13.8), 186 (15.5), 173 (28.5), 160 (16.8), 159 (18.1), 147 (55.6), 145 (23.2), 131 (35.0), 129 (26), 119 (41.3), 104 (38.2), 103 (100). ^{1}H NMR (DMSO-d_6), δ: 1.14, 1.20 (both t, 6 H each, 2 $NCH_2C\underline{H}_3$); 2.79, 3.10 (both m, 2 H each, $NC\underline{H}_2CH_3$); 3.30—3.50 (m, 5 H, $NC\underline{H}_2CH_3$, OCH_3); 3.66 (dd, 1 H, H(8a), $J_{H(8a),H(8)}$ = 6.6 Hz, $J_{H(8a),H(9)}$ = 7.1 Hz); 4.11 (d, 1 H, H(4a), $J_{H(4a),H(9a)}$ = 4.0 Hz); 4.21 (d, 1 H, H(8), $J_{H(8),H(8a)}$ = 6.6 Hz); 4.60—4.70 (m, 1 H, H(9a)); 5.07 (dd, 1 H, H(9), $J_{H(9),H(8a)}$ = 7.1 Hz, $J_{H(9),H(9a)}$= 7.1 Hz); 7.32 (m, 3 H, Ph); 7.47 (d, 1 H, N(1)H, $J_{N(1)H,H(9a)}$ = 4.8 Hz); 7.60—7.70 (m, 2 H, Ph).

8-Ethoxy-4,7-diethyl-9-nitro-2-phenyl-1,4,4a,7,8,8a,9,9a-octahydro-1,3,4,4b,7-pentaazafluorene-5,6-dicarbonitrile (3b). A solution of the anionic form of 1,4,5,6-tetrahydropyrazine **1b**, which was obtained by the addition of triethylamine (0.07 mL) to a suspension of 2,3-dicyano-6-ethoxy-1-ethyl-5-nitromethyl-1,4,5,6-tetrahydropyrazine (**1b**) (133 mg, 0.5 mmol) in anhydrous ethanol (2.2 mL) and short-term heating of the mixture, was added with stirring to a suspension of the 1,2,4-triazinium salt **2** (137 mg, 0.5 mmol) in anhydrous ethanol (0.7 mL). After the reaction mixture was magnetically stirred for 1 h at room temperature, a formed precipitate of **3b** was filtered off and recrystallized from anhydrous ethanol. The yield was 104 mg (36%), m.p. 171—172 °C. Found (%): C, 58.69; H, 5.84; N, 24.87. $C_{22}H_{26}N_8O_3$. Calculated (%): C, 58.65; H, 5.82; N, 24.87. Mass spectrum, m/z (I_{rel} (%)): 451 $[M + 1]^+$ (13.7), 450 $[M]^+$ (49.2), 358 (46.4), 331 (17.0), 269 (21.8), 265 (14.0), 225 (18.5), 224 (100), 212 (21.9), 200 (51.0), 197 (28.4), 187 (69.2), 186 (82.1), 174 (15.0), 172 (23), 159 (22.9), 158 (35.2), 147 (29.8), 131 (28.3), 119 (17.7), 105 (16.5), 104 (78.8), 103 (32.2). ^{1}H NMR (DMSO-d_6), δ: 1.07 (t, 3 H, $OCH_2C\underline{H}_3$); 1.12 (t, 3 H, $N(7)CH_2C\underline{H}_3$); 1.19 (t, 3 H, $N(4)CH_2C\underline{H}_3$); 2.77, 3.10 (both dq, 2 H each, $N(4)C\underline{H}_2CH_3$, J = 12.5 Hz, J = 7.0 Hz); 3.39 (m, 2 H, $N(7)C\underline{H}_2CH_3$); 3.66 (dd, 1 H, H(8a), $J_{H(8a),H(9a)}$ = 6.6 Hz, $J_{H(8a),H(8)}$ = 6.5 Hz); 3.73 (m, 2 H, $OC\underline{H}_2CH_3$); 4.14 (d, 1 H, H(4a), $J_{H(4a),H(9a)}$ = 4.2 Hz); 4.30 (d, 1 H, H(8), $J_{H(8),H(8a)}$ = 6.5 Hz); 4.69 (ddd, 1 H, H(9a), $J_{H(9a),H(9)}$ = 7.9 Hz, $J_{H(9a),N(1)H}$ = 5.9 Hz, $J_{H(9a),H(4a)}$ = 4.2 Hz); 5.13 (dd, 1 H, H(9), $J_{H(9),H(9a)}$ = 7.9 Hz, $J_{H(9),H(8a)}$ = 6.6 Hz); 7.32 (m, 3 H, Ph); 7.60 (d, 1 H, N(1)H, $J_{N(1)H,H(9a)}$ = 5.9 Hz); 7.60—7.70 (m, 2 H, Ph). ^{13}C NMR (DMSO-d_6), δ: 11.08 (1 C, $N(4)CH_2\underline{C}H_3$); 12.98 (1 C, $N(7)CH_2\underline{C}H_3$); 15.03 (1 C, $OCH_2\underline{C}H_3$); 41.64 (1 C, $N(7)\underline{C}H_2CH_3$); 47.24 (1 C, $N(4)\underline{C}H_2CH_3$); 58.82 (1 C, C(9a)); 59.57 (1 C, C(8a)); 65.62 (1 C, $O\underline{C}H_2CH_3$); 66.41 (1 C, C(4a)); 83.91 (1 C, C(8)); 91.59 (1 C, C(9)); 104.55 (1 C, C(5)); 112.74 (1 C, C(6)); 113.08 (1 C, CN); 113.69 (1 C, CN); 125.16 (2 C, C_o, Ph); 128.13 (2 C, C_m, Ph); 129.01 (1 C, C_p, Ph); 133.07 (1 C, C_i, Ph); 141.99 (1 C, C(2)).

2-Ethyl-1-methoxy-10-methyl-11-nitro-1,2,4b,5,10,10a,11,11a-octahydro-2,4a,5,10-tetraazabenzo[*b*]fluorene-3,4-dicarbonitrile (5a). Triethylamine (56 μL) was added to a suspension of 2,3-dicyano-6-methoxy-5-nitromethyl-1,4,5,6-tetrahydropyrazine **1a** (100 mg, 0.40 mmol) and 1-methylquinoxalinium iodide **4a** (104 mg, 0.40 mmol) in MeOH (2 mL). After 6 h, the resulting crystals were filtered off and recrystallized from a MeOH—butanone (1 : 1) mixture. The yield of compound **5a** was 79 mg (51%), m.p. 163—164 °C. Found (%): C, 57.70; H, 5.38; N, 24.86. $C_{19}H_{21}N_7O_3$. Calculated (%): C, 57.71; H, 5.35; N, 24.79. Mass spectrum, m/z (I_{rel} (%)): 395 $[M]^+$ (15.38), 251 (1.14), 146 (100.00), 131 (39.21). ^{1}H NMR (DMSO-d_6), δ: 1.10 (t, 3 H, CH_3, ^3J = 7.2 Hz); 2.86 (s, 3 H, $N(2)CH_2C\underline{H}_3$); 3.26 (s, 3 H, OCH_3); 3.35 (m, 2 H, $N(2)C\underline{H}_2CH_3$); 3.68 (dd, 1 H, H(11a), $J_{H(11a),H(1)}$ = 6.9 Hz, $J_{H(11),H(11a)}$ = 4.4 Hz); 3.88 (d, 1 H, H(1), $J_{H(1),H(11a)}$ = 6.9 Hz); 4.90 (m, 2 H, H(10a), H(11)); 5.00 (d, 1 H, H(4b), $J_{H(4b),H(10a)}$ = 4.6 Hz); 6.49 (s, 1 H, N(5)H); 6.62 (m, 4 H, Ar).

X-ray diffraction analysis was carried out on an Enraf-Nonius CAD-4 diffractometer. The crystals of **5a** ($C_{19}H_{21}N_7O_3$) are monoclinic, space group $P2_1/c$, unit cell parameters: a = 12.426(3) Å, b = 17.140(4) Å, c = 9.419(2) Å, β = 104.22(2)°. The structure was solved by the direct method using the SHELXS-97 program and refined by the SHELXL-97 program[13] in the anisotropic (isotropic for H atoms) approximation to

Table 1. Bond lengths (d) in the structure of **5a**

Bond	d/Å	Bond	d/Å	Bond	d/Å	Bond	d/Å
O(1)—N(5)	1.222(2)	N(3)—C(8)	1.462(2)	C(9)—C(10)	1.532(2)	C(17)—H(13)	1.00(3)
O(2)—N(5)	1.198(2)	N(4)—C(12)	1.370(2)	C(17)—H(15)	0.97(4)	C(17)—H(14)	1.02(4)
O(1′)—N(5)	1.22(1)	N(4)—C(11)	1.458(2)	C(18)—H(16)	1.01(3)	C(16)—H(11)	0.99(2)
O(2′)—N(5)	1.195(9)	N(4)—C(16)	1.465(2)	C(18)—H(17)	0.94(3)	C(16)—H(12)	0.99(2)
O(3)—C(11)	1.405(2)	N(5)—C(9)	1.496(2)	C(18)—H(18)	0.97(3)	C(10)—C(11)	1.532(2)
O(3)—C(18)	1.420(3)	C(3)—H(3)	0.98(3)	C(19)—H(19)	1.02(3)	C(10)—H(9)	0.97(2)
N(1)—C(1)	1.404(2)	C(4)—C(5)	1.382(3)	C(19)—H(20)	0.96(3)	C(11)—H(10)	1.00(2)
N(1)—C(8)	1.438(2)	C(4)—H(4)	0.99(2)	C(19)—H(21)	0.96(3)	C(1)—C(2)	1.376(2)
N(1)—H(1)	0.88(1)	C(5)—C(6)	1.393(2)	C(9)—H(8)	0.96(1)	C(1)—C(6)	1.408(2)
N(2)—C(6)	1.393(2)	C(5)—H(5)	0.97(2)	C(12)—C(13)	1.358(2)	C(2)—H(2)	0.94(2)
N(2)—C(7)	1.431(2)	C(7)—C(8)	1.520(2)	C(12)—C(15)	1.443(2)	C(3)—C(4)	1.370(3)
N(2)—C(19)	1.445(2)	C(7)—C(9)	1.542(2)	C(13)—C(14)	1.427(3)	N(6)—C(14)	1.141(2)
N(3)—C(13)	1.397(2)	C(7)—H(6)	0.98(2)	C(16)—C(17)	1.487(3)	N(7)—C(15)	1.141(2)
N(3)—C(10)	1.456(2)	C(8)—H(7)	0.96(2)	C(2)—C(3)	1.380(3)		

Table 2. Bond angles (ω) in the structure of **5a**

Angle	ω/deg	Angle	ω/deg	Angle	ω/deg
C(11)—O(3)—C(18)	115.6(2)	C(9)—C(7)—H(6)	108.0(9)	C(17)—C(16)—H(11)	111.8(1)
C(1)—N(1)—C(8)	119.2(1)	N(1)—C(8)—N(3)	111.3(13)	N(4)—C(16)—H(12)	106.5(1)
C(1)—N(1)—H(1)	113.9(1)	N(1)—C(8)—C(7)	109.2(13)	C(17)—C(16)—H(12)	113.0(1)
C(8)—N(1)—H(1)	114.8(1)	N(3)—C(8)—C(7)	100.9(1)	H(11)—C(16)—H(12)	102.3(1)
C(6)—N(2)—C(7)	118.5(1)	N(1)—C(8)—H(7)	113.1(9)	C(11)—N(4)—C(16)	121.0(1)
C(6)—N(2)—C(19)	121.5(2)	N(3)—C(8)—H(7)	109.9(1)	C(5)—C(4)—H(4)	119.8(1)
C(7)—N(2)—C(19)	118.1(2)	C(7)—C(8)—H(7)	111.7(1)	C(4)—C(5)—C(6)	120.9(1)
C(13)—N(3)—C(10)	114.9(1)	N(5)—C(9)—C(10)	110.5(1)	C(4)—C(5)—H(5)	122.0(1)
C(13)—N(3)—C(8)	120.2(1)	N(5)—C(9)—C(7)	111.5(1)	C(6)—C(5)—H(5)	117.0(1)
C(10)—N(3)—C(8)	110.5(1)	C(10)—C(9)—C(7)	105.6(1)	N(2)—C(6)—C(5)	122.6(1)
C(12)—N(4)—C(11)	117.0(1)	N(5)—C(9)—H(8)	106.8(8)	N(2)—C(6)—C(1)	119.2(1)
C(12)—N(4)—C(16)	121.5(1)	C(10)—C(9)—H(8)	111.1(9)	C(5)—C(6)—C(1)	118.1(1)
O(2′)—N(5)—O(2)	46.9(1)	C(7)—C(9)—H(8)	111.4(9)	N(2)—C(7)—C(8)	113.5(1)
O(2′)—N(5)—O(1′)	121.7(1)	N(3)—C(10)—C(9)	103.6(1)	N(2)—C(7)—C(9)	116.5(1)
O(2)—N(5)—O(1′)	102.4(1)	N(3)—C(10)—C(11)	113.9(1)	C(8)—C(7)—C(9)	101.8(1)
O(2′)—N(5)—O(1)	101.3(1)	C(9)—C(10)—C(11)	112.2(1)	C(16)—C(17)—H(13)	111.2(1)
O(2)—N(5)—O(1)	124.0(2)	N(3)—C(10)—H(9)	110.9(9)	C(16)—C(17)—H(14)	115(2)
O(1′)—N(5)—O(1)	50.4(1)	C(9)—C(10)—H(9)	109.7(1)	H(13)—C(17)—H(14)	108(3)
O(2′)—N(5)—C(9)	120.5(9)	C(11)—C(10)—H(9)	106.5(1)	C(16)—C(17)—H(15)	108(2)
O(2)—N(5)—C(9)	119.0(2)	O(3)—C(11)—N(4)	109.1(1)	H(13)—C(17)—H(15)	103(3)
O(1′)—N(5)—C(9)	117.8(9)	O(3)—C(11)—C(10)	107.6(1)	H(14)—C(17)—H(15)	112(3)
O(1)—N(5)—C(9)	116.9(2)	N(4)—C(11)—C(10)	109.8(1)	O(3)—C(18)—H(16)	109.4(1)
C(2)—C(1)—N(1)	120.0(1)	O(3)—C(11)—H(10)	111.2(9)	O(3)—C(18)—H(17)	113.0(1)
C(2)—C(1)—C(6)	119.8(2)	N(4)—C(11)—H(10)	108.6(9)	H(16)—C(18)—H(17)	105(2)
N(1)—C(1)—C(6)	120.1(1)	C(10)—C(11)—H(10)	110.4(9)	O(3)—C(18)—H(18)	108.9(1)
C(1)—C(2)—C(3)	121.2(2)	C(13)—C(12)—N(4)	123.6(1)	H(16)—C(18)—H(18)	111(2)
C(1)—C(2)—H(2)	117.1(1)	C(13)—C(12)—C(15)	118.2(1)	H(17)—C(18)—H(18)	110(2)
C(3)—C(2)—H(2)	121.6(1)	N(4)—C(12)—C(15)	118.1(1)	N(2)—C(19)—H(19)	110.9(1)
C(4)—C(3)—C(2)	119.5(2)	C(12)—C(13)—N(3)	121.9(1)	N(2)—C(19)—H(20)	107.9(1)
C(4)—C(3)—H(3)	122.1(1)	C(12)—C(13)—C(14)	121.1(1)	H(19)—C(19)—H(20)	111(2)
C(2)—C(3)—H(3)	118.5(1)	N(3)—C(13)—C(14)	116.9(1)	N(2)—C(19)—H(21)	112.6(2)
C(3)—C(4)—C(5)	120.3(2)	N(6)—C(14)—C(13)	178.3(2)	H(19)—C(19)—H(21)	106(2)
C(3)—C(4)—H(4)	119.8(1)	N(7)—C(15)—C(12)	177.1(2)	H(20)—C(19)—H(21)	109(2)
N(2)—C(7)—H(6)	108.4(9)	N(4)—C(16)—C(17)	113.9(2)		
C(8)—C(7)—H(6)	108.1(9)	N(4)—C(16)—H(11)	108.6(1)		

$R = 0.034$ ($wR(F^2) = 0.093$) for 2216 reflections with $F_0 > 4\sigma(F_0)$. The bond lengths and bond angles are given in Tables 1 and 2.

2,10-Diethyl-7,8-difluoro-1-methoxy-11-nitro-1,2,4b,5,10,10a,11,11a-octahydro-2,4a,5,10-tetraazabenzo[*b*]fluorene-3,4-dicarbonitrile (5b). Compound **5b** was synthesized similarly in 70% yield, m.p. 146—148 °C. Found (%): C, 53.89; H, 4.63; N, 21.93. $C_{20}H_{21}N_7O_3F_2$. Calculated (%): C, 53.93; H, 4.75; N, 22.01. ^{1}H NMR (DMSO-d_6), δ: 1.02 (t, 3 H, CH_3, ^3J = 7.0 Hz); 1.11 (t, 3 H, CH_3, ^3J = 7.2 Hz); 3.38 (s, 3 H, OCH_3); 3.08 (dd, 1 H, NCH_2, ^3J = 7.2 Hz, ^2J = 14.4 Hz); 3.30 (m, 2 H, NCH_2); 3.40 (dd, 1 H, NCH_2, ^3J = 7.2 Hz, ^2J = 14.4 Hz); 3.64 (dd, 1 H, H(11a), $J_{H(11a),H(1)}$ = 6.7 Hz, $J_{H(11a),H(11)}$ = 5.2 Hz); 3.94 (d, 1 H, H(1), $J_{H(1),H(11a)}$ = 6.7 Hz); 4.86, 4.77 (both m, 1 H each, H(10a), H(4b)); 4.96 (dd, 1 H, H(11), $J_{H(11),H(10a)}$ = 7.7 Hz, $J_{H(11),H(11a)}$ = 5.2 Hz); 6.55 (s, 1 H, N(5)H); 6.60 (dd, 1 H, Ar, $^4J_{H,F}$ = 8.2 Hz, $^3J_{H,F}$ = 12.0 Hz); 6.75 (dd, 1 H, Ar, $^4J_{H,F}$ = 7.8 Hz, $^3J_{H,F}$ = 13.1 Hz).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 04-03-96090), the Ministry of the Education and Science of the Russian Federation, and the USA Civilian Research and Development Foundation (CRDF) (Grants REC-005, EK-005-X1, and Y1-C-05-13).

References

1. V. N. Charushin and O.N. Chupakhin, *Pure Appl. Chem.*, 2004, **76**, 1621.
2. V. N. Charushin, O. N. Chupakhin, and H. C. van der Plas, *Adv. Heterocyc. Chem.*, 1988, **43**, 301.
3. V. N. Charushin, I. V. Kazantseva, M. G. Ponizovskii, L. G. Egorova, E. O. Sidorov, and O. N. Chupakhin, *Khim. Geterotsikl. Soedin.*, 1986, **10**, 1380 [*Chem. Heterocycl. Compd.*, 1986, **10** (Engl. Transl.)].
4. V. N. Charushin, M. G. Ponizovskii, O. N. Chupakhin, E. O. Sidorov, and I. M. Sosonkin, *Khim. Geterotsikl. Soedin.*, 1985, 1380 [*Chem. Heterocycl. Compd.*, 1985 (Engl. Transl.)].

5. J. Clark, *J. Chem. Soc. (C)*, 1967, 1543.
6. O. N. Chupakhin, V. N. Charushin, and A. R. Chernyshev, *Progress in Nuclear Magnetic Resonance Spectroscopy*, 1988, **20**, 95.
7. T. J. Batterham, *J. Chem. Soc. (C)*, 1969, 999.
8. P. A. Slepukhin, G. L. Rusinov, V. N. Charushin, V. N. Filyakova, N. S. Karpenko, D. B. Krivolapov, and I. A. Litvinov, *Izv. Akad. Nauk*, *Ser. Khim.*, 2004, 1221 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 1272].
9. O. N. Chupakhin, V. N. Charushin, G. M. Petrova, and G. G. Alexandrov, *Tetrahedron Lett.*, 1985, **26**, 515.
10. V. N. Charushin, G. A. Mokrushina, G. M. Petrova, G. G. Alexandrov, and O. N. Chupakhin, *Mendeleev Commun.*, 1998, 133.
11. V. N. Charushin, G. M. Petrova, O. N. Chupakhin, E. O. Sidorov, G. G. Aleksandrov, A. I. Chernyshev, N. A. Klyuev, and N. N. Sorokin, *Khim. Geterotsikl. Soedin.*, 1986, **3**, 389 [*Chem. Heterocycl. Compd.*, 1985 (Engl. Transl.)].
12. B. V. Rudakov, S. G. Alekseev, V. N. Charushin, O. N. Chupakhin, V. A. Chertkov, G. G. Aleksandrov, and E. S. Klimov, *Zh. Org. Khim.*, 1992, **28**, 589 [*Russ. J. Org. Chem.*, 1992, **28** (Engl. Transl.)].
13. G. M. Sheldrick, *SHELXS-97, SHELXL-97, Programs for Crystal Structure Determination and Refinement*, Göttingen University, Göttingen (Germany), 1997.

Received August 25, 2005