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*Dedicated to the 70th anniversary of O.N.Chupakhin, Full Member of the Russian Academy of Sciences*

# Fluorine-containing Heterocycles: XI.* 5(6)-Fluoro-6(5)-X-benzofuroxans: Synthesis, Tautomerism, and Transformations

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**Abstract**—Features of 5(6)-fluoro-6(5)-X-benzofuroxans tautomerism were investigated. By $^{1}H$, $^{13}C$, and $^{19}F$ NMR spectroscopy the direction of Boulton–Katritzky rearrangement in nitration, nitrosation, and azo coupling of fluorine-containing furoxanes was determined.

Derivatives of 2,1,3-benzoxadiazole series (benzofuroxans, benzofurazans) form an important class of heterocyclic compounds possessing an exceptional combination of chemical and physical characteristics (easy cycle opening, tautomerism, transformations in reactions both with nucleophiles and electrophiles) and also a wide range of biological (antitumor, antibacterial, and cardiotropic) activity [2–5]. The poorly documented fluorine-containing benzofuroxans are especially interesting for the fluorine incorporation strongly affects their physical and chemical properties, and also increases the ability of organic molecules to penetrate lipid membranes and often intensifies the biological activity [6, 7].

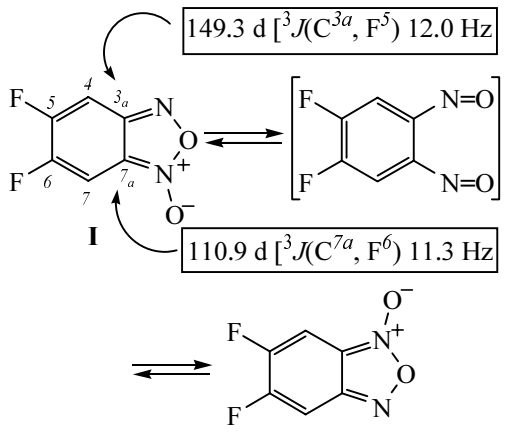
We previously investigated a transformation of the heteroring in fluorine-containing benzofuroxans into quinoxalines [8–10] and a nucleophilic substitution of fluorine in 5,6-difluorobenzofuroxan [11].

In the present communication we discuss the features of tautomerism in the fluorine-containing benzofuroxans and also their involvement into electrophilic substitution reactions accompanied with Boulton–Katritzky rearrangement. As initial objects we selected 5,6-difluorobenzofuroxan (**I**) and 5(6)-fluoro-6(5)-X-benzofuroxans (**II**) containing fragments of cycloalkylimines, dialkylamines, and alcoholates. 5,6-Difluorobenzofuroxan (**I**) was obtained in good yield by thermal decomposition of 2-nitro-4,5-difluorophenyl azide [8]. The synthesis of 5(6)-fluoro-6(5)-X-benzofuroxans (**II**) we had developed before [11].

It is known from the published data that the benzofuroxans easily undergo heterocycle opening, recyclization, and that between 1- and 3-benzofurazan oxides a dynamic equilibrium exists involving an intermediate formation of *ortho*-dinitrosobenzene [12]. For 5,6-difluorobenzofuroxan (**I**) this isomerization is degenerate (Scheme 1).

The kinetic parameters of this equilibrium we derived from the measurement of the temperature dependence

**Scheme 1.**




* For communication IX see [1].

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**Table 1.** $^{1}H$, $^{13}C$ , and $^{19}F$ NMR spectra of 5,6-difluoro-2,1,3-benzoxadiazole 1-oxide (**I**) in acetone-$d_6$ at –20°C

| Fragment | $\delta_C$, ppm | $^{n}J$(C, F), Hz | $\delta_H$ ($\delta_F$), ppm | $^{n}J$(H, F), $^{n}J$(F, F), Hz |
|---|---|---|---|---|
| $C^{3a}$ | 149.31 | $^{3}J(C^{3a}F^{5})$ 12.0 | – | – |
| $C^{4}H$ | 102.70 | $^{2}J(C^{4}, F^{5})$ 23.9 | 7.96 d.d | $^{3}J(H^{4}, F^{5})$ 9.4<br>$^{4}J(H^{4}, F^{6})$ 7.1 |
| $C^{5}F$ | 154.54 | $^{1}J(C^{5}, F^{5})$ 261.2<br>$^{2}J(C^{5}, F^{6})$ 21.0 | (41.16 d.d.d) | $^{3}J(F^{5}, F^{6})$ 14.6<br>$^{3}J(F^{6}, H^{4})$ 9.4<br>$^{4}J(F^{5}, H^{7})$ 7.3 |
| $C^{6}F$ | 151.75 | $^{1}J(C^{6}, F^{6})$ 261.7<br>$^{2}J(C^{6}, F^{5})$ 21.2 | (37.56 d.d.d) | $^{3}J(F^{6}, F^{5})$ 14.6<br>$^{3}J(F^{6}, H^{7})$ 8.0<br>$^{4}J(F^{6}, H^{4})$ 7.1 |
| $C^{7}H$ | 98.45 | $^{2}J(C^{5}, F^{6})$ 24.4<br>$^{3}J(C^{7}, F^{5})$ 1.2 | 7.77 d.d | $^{3}J(H^{7}, F^{6})$ 8.0<br>$^{4}J(H^{7}, F^{5})$ 7.3 |
| $C^{7a}$ | 110.91 | $^{3}J(C^{7a}, F^{6})$ 11.3 | – | – |

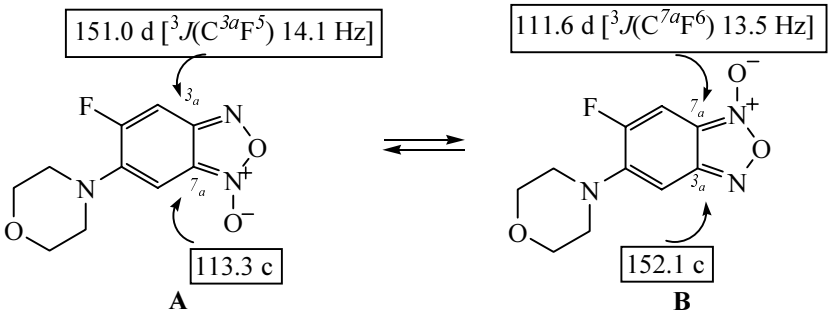
of the $^{1}H$ and $^{19}F$ NMR spectra in the temperature range –30...50°C. At room temperature the protons $H^{4}$ and $H^{7}$ give rise to one broadened signal in the $^{1}H$ NMR spectrum of compound **I,** and in the $^{19}F$ NMR spectrum appear two broadened signals from atoms $F^{5}$ and $F^{6}$. The spectra of the "frozen" structure were observed in the region of slow exchange below –20°C (Table 1). In this case in the $^{1}H$ NMR spectrum appeared two well resolved doublets of doublets with the chemical shift difference $\Delta\delta_H$ 0.19 ppm, and the upfield signal belonged to $H^{7}$ suffering a reverse donor effect of the N-oxide group. Also two well resolved signals with a significantly larger difference in the chemical shifts, $\Delta\delta_F$ 3.6 ppm, were observed in the $^{19}F$. NMR spectrum. The fluorine signals assignment was done basing on the coupling constants $^{n}J$(F, H) with protons $H^{4}$ and $H^{7}$. Note the relatively small value of the vicinal coupling constant $^{3}J(F^{5}, F^{6})$ 14.6 Hz. In the $^{13}C$ NMR spectrum at –30°C quaternary atoms $C^{3a}$ and $C^{7a}$ appeared as doublets at 149.31 and 110.91 ppm with constants of vicinal coupling with fluorine $^{3}J(C^{3a}, F^{5})$ 12.0 θ $^{3}J(C^{7a}, F^{6})$ 11.3 Hz (Scheme 1, Table 1).

On warming the system we observed successive coalescence of signals occurring in proton spectrum at 19°C and in fluorine spectrum at 49°C (near the coalescence points the step in temperature rising was 1 degree). The rate constants of tautomeric transitions in the coalescence point for exchange between two structures of equal occupancy were calculated by the simple Gutowsky–Holm approximation, and the free energy of activation was estimated by Eyring equation [13]. The free energy of activation evaluated for two coalescence temperatures at 59.1 and 57.8 kJ mol$^{-1}$ is well consistent with the barrier values found for transitions in the other benzofuroxan derivatives [12].

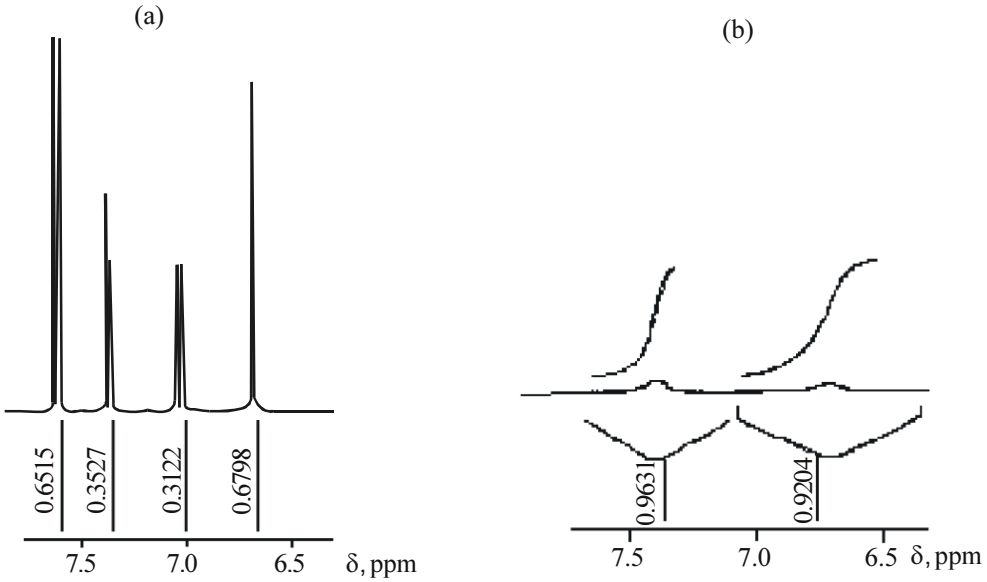
Owing to the presence of fluorine atom in unsymmetrical 5(6)-fluoro-6(5)-X-benzofuroxans (**II**) and to coupling constants $^{n}J(^{19}F, ^{13}C)$ and $^{n}J(^{19}F, ^{1}H)$ we succeeded in unambiguous assignment of signals in the $^{1}H$, $^{19}F$, and $^{13}C$ NMR spectra and in identification of the tautomer forms. The features of the tautomeric equilibrium are considered in detail in this article by an example of 5(6)-fluoro-6(5)-morpholinobenzofuroxan (**IIa**).

$^{1}H$, $^{13}C$, and $^{19}F$ NMR spectra registered in the temperature range –20...20°C showed that compound **IIa** in solution in acetone-$d_6$ existed as an equilibrium mixture of two isomers: 6-morpholino-5-fluorobenzofuroxan **A** and 5-morpholino-6-fluorobenzofuroxan **B** (Scheme 2). In the $^{1}H$ NMR spectrum of compound **IIa** at –20°C two groups of doublets were observed corresponding to the respective $H^{4}$ and $H^{7}$ protons of isomers **A** and **B** with characteristic coupling constants: $^{3}J(H^{4}, F^{5})$ 12.2, $^{4}J(H^{7}, F^{5})$ 7.8 Hz (for isomer **A**) and $^{3}J(H^{7}, F^{6})$ 11.0, $^{4}J(H^{4}, F^{6})$ 7.6 Hz (for isomer **B**) (Table 2, figure). The ratio of isomers **A** and **B** was 7 : 3. On rising the temperature to 0°C the signals of protons $H^{4}$ and $H^{7}$

**Scheme 2.**




**IIa**




$^1$H NMR spectra of compound **IIa** in $(CD_3)_2CO$ at –20 (a) and 20°C (b).

broadened, and at 20°C their coalescence occurred. The pattern of $^{19}$F NMR spectrum of compound **IIa** in the temperature range –20...20°C changed in a similar way, and the isomers ratio was the same. The most characteristic signals in the $^{13}$C NMR spectrum of compound **IIa** suitable for tautomers identification are the signals of nodal carbons. Thus in the spectrum registered at–20°C two groups of signals from $C^{3a}$ and $C^{7a}$ carbon atoms were observed belonging to isomers **A** and **B**. In the spectrum of isomer **A** quaternary atom $C^{3a}$ gave rise to a doublet at $\delta_C$ 151.0 ppm with a vicinal coupling constant $^3J(C^{3a}, F^5)$ 14.1 Hz, whereas the resonance of $C^{7a}$ appeared as a singlet at $\delta_C$ 113.31 ppm. In the spectrum of isomer **B** the doublet from $C^{7a}$ was observed at $\delta_C$ 111.60 ppm with a coupling constant $^3J(C^{7a}, F^6)$ 13.5 Hz, and singlet from $C^{3a}$ appeared at $\delta_C$ 152.12 ppm (Table 2).

As seen from the $^1$H NMR spectra of furoxan **IIa** the difference in resonance frequencies for protons $H^4$ (**A**) and $H^7$ (**B**) is 89.7 Hz, and these signals coalesce at 20°C. The corresponding difference for protons $H^7$ (**A**) and $H^4$ (**B**) equals to 146.1 Hz, and their coalescence occurs at 25°C. The rate constants of the reciprocal transitions were calculated with the use of an approximate method for

**Table 2.** $^1$H, $^{13}$C, and $^{19}$F NMR spectra of tautomers **A** and **B** of 6(5)-morpholino-5(6)-fluoro-2,1,3-benzoxadiazole 1(3)-oxide **IIa** in acetone-$d_6$ at –20°C

| **A** | | | | | **B** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Fragment | $\delta_C$, ppm | $^nJ$(C, F), Hz | $\delta_H$ ($\delta_F$), ppm | $^nJ$(H, F), $^nJ$(F, F), Hz | Fragment | $\delta_C$, ppm | $^nJ$(C, F), Hz | $\delta_H$ ($\delta_F$), ppm | $^nJ$(H, F), $^nJ$(F, F), Hz |
| $C^{3a}$ | 151.01 | $^3J(C^{3a}, F^5)$ 14.1 | – | – | $C^{3a}$ | 152.12 | – | – | – |
| $C^4H$ | 102.29 | $^2J(C^4, F^5)$ 28.3 | 7.60 d | $^3J(H^4, F^5)$ 12.2 | $C^4H$ | 101.48 | $^3J(C^4, F^6)$ 3.4 | 7.03 d | $^4J(H^4, F^6)$ 7.6 |
| $C^5F$ | 161.43 | $^1J(C^5, F^5)$ 262.7 | (55.48 d.d) | $^3J(F^5, H^4)$ 12.2<br>$^4J(F^5, H^7)$ 7.8 | $C^5$ | 148.23 | $^2J(C^5, F^6)$ 15.5 | – | – |
| $C^6$ | 145.47 | $^2J(C^6, F^5)$ 16.2 | – | – | $C^6F$ | 158.78 | $^1J(C^6, F^6)$ 262.7 | (52.30 d.d) | $^3J(F^6, H^7)$ 10.8<br>$^4J(F^6, H^4)$ 7.6 |
| $C^7H$ | 96.55 | $^3J(C^7, F^5)$ 4.0 | 6.68 d | $^4J(H^7, F^5)$ 7.7 | $C^7H$ | 97.77 | $^2J(C^7, F^6)$ 31.0 | 7.37 d | $^3J(H^7, F^6)$ 11.0 |
| $C^{7a}$ | 113.31 | – | – | – | $C^{7a}$ | 111.60 | $^3J(C^{7a}, F^6)$ 13.5 | – | – |
| $OCH_2$ | 66.80 | – | 3.83 m | – | $OCH_2$ | 66.38 | – | 3.83 m | – |
| $NCH_2$ | 51.54 | 4.7 | 3.22 m | – | $NCH_2$ | 51.47 | 4.7 | 3.22 m | – |

the case of unequal occupancy developed by Shanan-Atidi and Bar-Eli [14, 15]. The free energy of activation estimated by Eyring equation amounted to 62.2 kJ mol$^{-1}$ for transition from **A** to **B** and 59.1 kJ mol$^{-1}$ for the reverse process

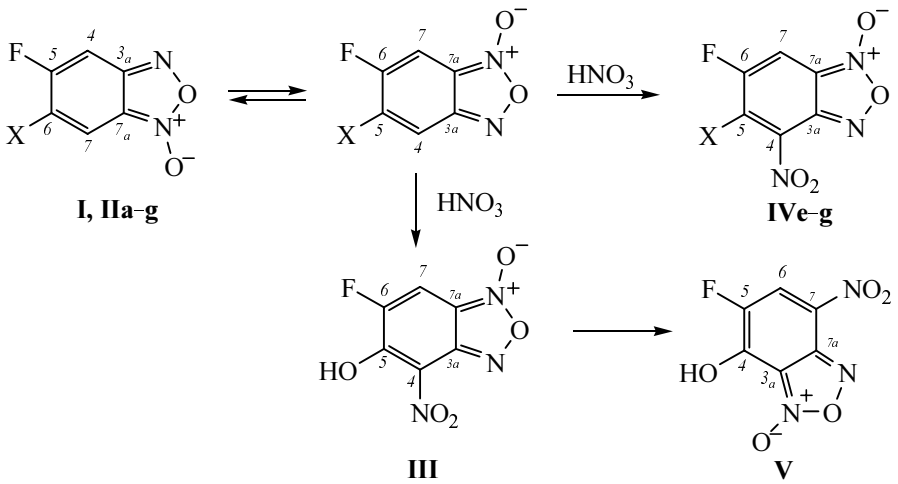
The benzene ring of benzofuroxans is known to be able to undergo electrophilic substitution, and when the nitration occurs into a position adjacent to the heterocycle the arising nitro derivative suffers Boulton–Katritzky rearrangement [2, 16, 17]. It was also noted that the presence of a fluorine in the position *5* of the 4-nitrobenzofuroxan prevents the rearrangement [2].

This study established that fluorine-containing benzofuroxans underwent nitration with relative ease, and not all nitration products suffered theBoulton–Katrizky rearrangement (Scheme 3). The nitration of 5,6-difluorobenzofuroxan (**I**) was performed with $HNO_3$ (*d* 1.54) in sulfuric acid at cooling. The reaction product on the strength of elemental analysis, $^1$H NMR and mass spectrum was identified as 4-nitro-6-fluoro-2,1,3-benzoxadiazol-5-ol 1-oxide (**III**). Inasmuch as the electrophilic attack into the *ortho*-position with respect to fluorine atom is inhibited we presume that under the reaction conditions first occurs hydrolysis of one of fluorine atoms and then the nitration of 6-fluoro-2,1,3-benzoxadiazol-5-ol 1-oxide takes place in the *ortho*-position with respect to electron-donor hydroxy group. Actually, in the $^1$H NMR spectrum of compound **III** in $CDCl_3$ the characteristic doublet of proton $H^7$ is observed at 7.48 ppm with the *ortho*-constant of coupling with fluorine $^3J(H^7, F^6)$ 6.4 Hz.

At dissolution of compound **III** in DMSO-$d_6$ the color of the solution changed from yellow to red, and the TLC reveals an additional red spot. In the $^1$H NMR spectrum appeared doublet signals of protons belonging to two substances, **III** and **V**, at 7.19 ppm with $^3J(H^7, F^6)$ 7.6 Hz and 12.97 ppm with $^3J(H^5, F^6)$ 14.4 Hz respectively, and also the common hydroxy group signal at 7.73 ppm. The intensity ration of the CH signals was just after the dissolution 69:31, and in 12 h it reached the value 56:44 that did not change further. A similar pattern was observed in the $^{19}$F NMR spectra in $CDCl_3$ and DMSO-$d_6$ (Table 3). For instance, in the $^{13}$C NMR spectrum in DMSO-$d_6$ two groups of signals from atoms $C^{3a}$ and $C^{7a}$ characteristic of two furoxans **III** and **V** were observed. In the spectrum of compound **III** quaternary atom $C^{3a}$ appeared as a doublet at $\delta_C$ 148.99 ppm with a coupling constant to atom $F^6$ $^4J(C^{3a}, F^6)$ 0.6 Hz, and the resonance of atom $C^{7a}$ was observed as a doublet at $\delta_C$ 108.00 ppm coupled to $F^6$ with a constant $^3J(C^{7a}, F^6)$ 14.1 Hz. In the spectrum of the rearranged product **V** the signal of atom $C^{3a}$ was a doubet at $\delta_C$ 147.74 ppm with a coupling constant to $F^6$ $^4J(C^{3a}, F^6)$ 1.5 Hz, whereas the signal from atom $C^{7a}$ appeared as a doublet at $\delta_C$ 110.62 ppm with a coupling constant to $F^6$ $^3J(C^{7a}, F^6)$ 12.3 Hz (Table 3). From these data we made a conclusion that in polar solvents 4-nitro-6-fluoro-2,1,3-benzoxadiazol-5-ol 1-oxide (**III**) partially transformed by Boulton–Katritzky rearrangement into 7-nitro-5-fluoro-2,1,3-benzoxadiazol-4-ol 3-oxide (**V**).

Likewise behave 5(6)-fluoro-6(5)-amino-substituted benzofuroxans **IIa–d** where the amino group was easily

**Scheme 3.**




**I**, X = F; **II,IV**, X = morpholino (**a**), thiomorpholin-4-yl (**b**), pyrrolidin-1-yl (**c**), $N(CH_3)_2$ (**d**), $OCH_3$ (**e**), $OC_2H_5$ (**f**), tetrahydrofuran-2-ylmethoxy (**g**).

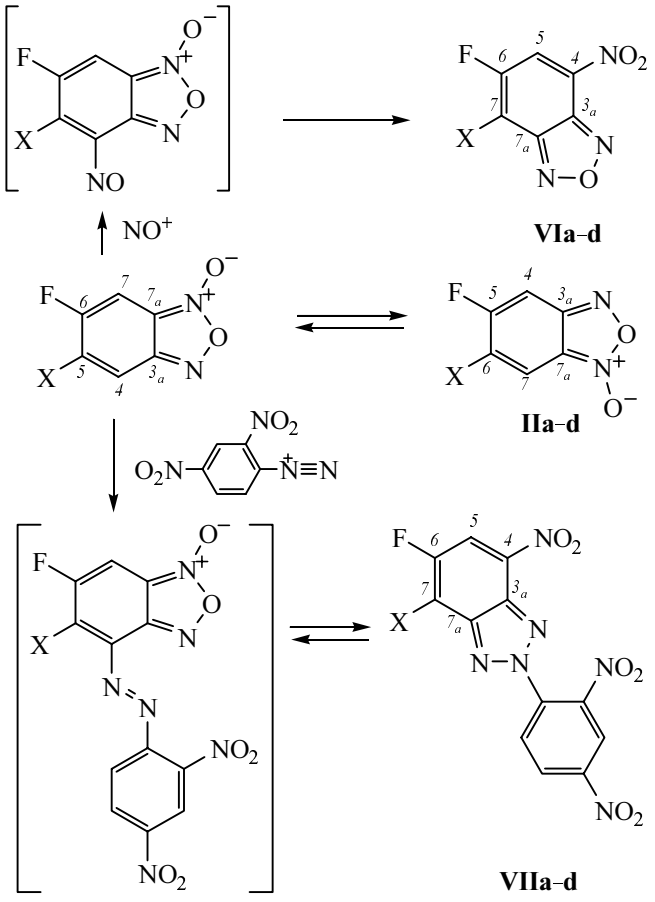
**Table 3.** $^{1}H$, $^{13}C$, and $^{19}F$ NMR spectra of 4-nitro-6-fluoro-2,1,3-benzoxadiazol-5-ol 1-oxide (**III**) and 7-nitro-5-fluoro-2,1,3-benzoxadiazol-4-ol 3-oxide (**V**)

| Fragment | $CDCl_3$ | | | | DMSO-$d_6$ | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **III** | | | | **III** | | | | **V** | | | |
| | $\delta_C$, ppm | $^{n}J$(C, F), Hz | $\delta_H$ ($\delta_F$), ppm | $^{n}J$(H, F), $^{n}J$(F, F), Hz | $\delta_C$, ppm | $^{n}J$(C, F), Hz | $\delta_H$ ($\delta_F$), ppm | $^{n}J$(H, F), Hz | $\delta_C$, ppm | $^{n}J$(C, F), Hz | $\delta_H$ ($\delta_F$), ppm | $^{n}J$(H, F), $^{n}J$(F, F), Hz |
| $C^{3a}$ | 142.70 | – | – | – | 148.99 | $^{4}J(C^{3a}, F^{6})$ 0.6 | – | – | 110.62 | $^{3}J(C^{7a}, F^{6})$ 12.3 | – | – |
| $C^{4}$ | 119.81 | – | – | – | | – | – | – | 121.12 | $^{2}J(C^{7}, F^{6})$ 23.9 | 7.73 br.s (OH) | – |
| $C^{5}$ | 156.59 | $^{2}J(C^{5}, F^{6})$ 20.5 | 13.08 br.s (OH) | – | 163.17 | $^{2}J(C^{5}, F^{6})$22.4 | 6.23 br.s (OH) | $^{3}J(F^{6}, H^{7})$ 7.9 | 144.61 | $^{1}J(C^{6}, F^{6})$ 235.6 | (8.42 d) | $^{3}J(H^{6}, F^{5})$ 13.8 |
| $C^{6}$ | 152.18 | $^{1}J(C^{6}, F^{6})$ 269.9 | (42.04 d) | $^{3}J(F^{6}, H^{7})$ 6.4 | 158.36 | $^{1}J(C^{6}, F^{6})$ 264.4 | (49.02 d) | – | 159.92 | $^{2}J(C^{5}, F^{6})$22.4 | 12.97 d | $^{3}J(F^{6}, H^{5})$14.4 |
| $C^{7}$ | 105.48 | $^{2}J(C^{7}, F^{6})$ 25.4 | 7.48 d | $^{3}J(H^{7}, F^{6})$ 6.4 | 98.11 | $^{2}J(C^{7}, F^{6})$ 29.1 | 7.19 d | $^{3}J(H^{7}, F^{6})$ 7.6 | – | – | – | – |
| $C^{7a}$ | 109.22 | $^{3}J(C^{7a}, F^{6})$ 10.07 | – | – | 108.00 | $^{3}J(C^{7a}, F^{6})$ 14.1 | – | – | 147.74 | $^{4}J(C^{3a}, F^{6})$ 1.5 | – | – |
| C–$NO_2$ | – | – | – | – | 116.16 | 4.6 | – | – | 107.78 | 7.7 | – | – |

hydrolyzed to hydroxy group under nitrating conditions giving as a result 4-nitro-6-fluoro-2,1,3-benzoxadiazol-5-ol 1-oxide (**III**). The nitration of 5(6)-fluoro-6(5)-alkoxybenzofuroxans **IIe–g** afforded 5-alkoxy-4-nitro-6-fluoro-2,1,3-benzoxadiazole 1-oxides (**IVe–g**). In this reaction the electrophilic attack was also directed on atom $C^{4}$ in the *ortho*-position with respect to the electron-donor substituent and remote from the N-oxide group. However the products of the Boulton–Katritzky rearrangement were not formed in this case. In the $^{1}H$ NMR spectra of compounds **IVe–g** both in $CDCl_3$ and in DMSO-$d_6$ clear-cut doublets of $H^{7}$ protons were observed with vicinal coupling constants $^{3}J$ ($H^{7}$, $F^{6}$) 7.9–9.2 Hz (Table 4).

Due to lower reactivity of nitrosonium cation we failed to perform nitrosation of 5,6-difluorobenzofuroxan (**I**) and 6(5)-fluoro-5(6)-alkoxybenzofuroxans (**IIe–h**) (only initial compounds were recovered) whereas the nitrosation of 5(6)-fluoro-6(5)-amino derivatives of benzofuroxans (**IIa–d**) proceeded readily (Scheme 4). Although we did not succeed to isolate the product of the primary electrophilic attack because of rapid and irreversible Boulton–Katritzky rearrangement, the final reaction products were reliably identified as 4-nitro-6-fluoro-7-X-2,1,3-benzoxadiazoles (**VIa–d**). In the $^{1}H$ NMR spectra of compounds **VIa–d** appear doublets of protons $H^{5}$ with constant of vicinal coupling with atom $F^{6}$ $^{3}J(H^{5}, F^{6})$ 14.7– 15.8 Hz, and also the signals of substituents attached to position *7* in the region $\delta_H$ 2.88–4.20 ppm. The mass spectra of nitrofurazans **VIa–d** contain molecular ion peaks (Table 4). A similar pattern

**Scheme 4.**



**VI, VII**, X = morpholino (**a**), thiomorpholin-4-yl (**b**), pyrrolidin-1-yl (**c**), $N(CH_3)_2$ (**d**)

**Table 4.** $^1$H NMR spectra (DMSO-$d_6$) and mass spectra of 5-alkoxy-4-nitro-6-fluoro-2,1,3-benzoxadiazole 1-oxides (**IVe–g**), 4-nitro-6-fluoro-7-X-2,1,3-benzoxadiazoles (**VIa–d**), and 2-(2,4-dinitrophenyl)-4-nitro-6-fluoro-7-X-benzotriazoles (**VIIa–d**)

| Compd. no. | $^1$H NMR spectrum, δ, ppm | | Mass spectrum, *m/z* ($I_{rel}$, %) |
|---|---|---|---|
| | $H^{5(7)}$, δ [$^3J(H^{5(7)}, F^6)$, Hz] | X | |
| **IVe** | 7.32 [7.9] | 4.22 s (3H, $OCH_3$) | 229 (97) [*M*]$^{+\cdot}$, 169 (36), 153 (17), 123 (14), 96 (14), 95 (14), 93 (100), 83 (18), 80 (13), 75 (15) |
| **IVf** | 7.95 [8.8] | 1.46 t (3H, $OCH_2\underline{CH_3}$), 4.47 q (2H, $O\underline{CH_2}CH_3$) | 243 (32) [*M*]$^{+\cdot}$, 215 (100), 199 (23), 185 (10), 139 (20), 125 (22), 110 (11), 109 (44), 98 (30), 97 (111), 93 (13), 82 (17), 81 (12), 80 (19), 69 (15) |
| **IVg** | 7.96 [9.3] | 1.87 m (4H, $2CH_2$), 3.72 m (2H, $CH_2$), 4.35 m (3H, $OCH_2$, CH) | 299 (13) [*M*]$^{+\cdot}$, 85 (100), 71 (49), 67 (24) |
| **VIa** | 8.49 [14.8] | 2.88 m (4H, $NCH_2$), 4.20 m (4H, $OCH_2$) | 268 (100) [*M*]$^{+\cdot}$, 210 (57), 134 (18), 82 (23), 57 (14) |
| **VIb** | 8.48 [14.7] | 3.84 m (4H, $NCH_2$), 4.01 m (4H, $SCH_2$) | 284 (100) [*M*]$^{+\cdot}$, 210 (59), 134 (14), 82 (19), 74 (17), 61 (14), 60 (10), 57 (21), 56 (11) |
| **VIc** | 8.45 [15.1] | 3.84 m [4H, $(CH_2)_2$], 4.01 m (4H, $NCH_2$) | 252 (100) [*M*]$^{+\cdot}$, 197 (11), 176 (23), 175 (55), 164 (20), 155 (28), 150 (14), 148 (25), 147 (11), 136 (12), 134 (10), 121 (15), 82 (10), 57 (10) |
| **VId** | 8.42 [15.8] | 3.63 C [6H, $N(CH_3)_2$] | 226 (100) [*M*]$^{+\cdot}$, 165 (11), 150 (26), 149 (70), 135( 31), 129 (30), 123 (14), 108 (16), 82 (14) |
| **VIIa** | 8.27 [15.2] | 2.74 m (4H, $NCH_2$), 3.86 m (4H, $OCH_2$), 8.71–8.79 m (3H, H arom) | 433 (100) [*M*]$^{+\cdot}$, 417 (12), 416 (44), 386 (15), 38 (17), 329 (12), 328 (18), 79 (11), 75 (11), 57 (17) |
| **VIIb** | 8.31 [14.8] | 3.74 m (4H, $NCH_2$), 3.98 m (4H, $SCH_2$), 8.72–8.81 m (3H, H arom) | 449 (100) [*M*]$^{+\cdot}$, 421 (24), 420 (19), 389 (47), 259 (64), 244 (12), 243 (27), 87 (53), 74 (37), 51 (16) |
| **VIIc** | 8.12 [14.9] | 3.72 m [4H, $(CH_2)_2$], 3.97 m (4H, $NCH_2$), 8.67–8.82 m (3H, H arom) | 417 (100) [*M*]$^{+\cdot}$, 401 (24), 400 (53), 370 (15), 369 (11), 342 (19), 313 (29), 312 (14), 91 (50), 79 (13), 74 (10), 57 (10) |
| **VIId** | 8.38 [15.8] | 3.55, s [6H, N $(CH_3)_2$], 8.68–8.75 m (3H, H arom) | 391 (51) [*M*]$^{+\cdot}$, 374 (23), 344 (33), 298 (17), 153 (12), 149 (16), 137 (11), 122 (12), 107 (13), 92 (12), 91 (47), 90 (13), 79 (13), 76 (13), 75 (17) |

was observed in the azo coupling reaction of furoxans (**IIa–d**) with 2,4-dinitrobenzenediazonium sulfate in sulfuric acid at 45–50°C. As a result of the electrophilic attack and rearrangement compounds **VIIa–d** were isolated that basing on $^1$H NMR and mass spectra and also on elemental analysis data were assigned a structure of 2-(2,4-dinitrophenyl)-4-nitro-6-fluoro-7-X-benzotriazoles. The $^1$H NMR spectra of triazoles **VIIa–d** contain characteristic doublets of $H^5$ protons with vicinal coupling constants $^3J(H^5, F^6)$ 14.8–15.8 Hz, and also the signals of substituents attached to position *7* in the region $\delta_H$ 2.94–3.98 ppm and of protons from the 2,4-dinitrophenyl substituent at 8.68–8.82 ppm.

Hence in the 5(6)-fluoro-6(5)-substituted benzofuroxans only one of the existing equilibrium tautomeric forms is involved into electrophilic substitution. Therewith the attack occurs in the *ortho*-position with respect to an electron-donor substituent that at the same time is remote from the N-oxide group of the heterocycle. As a rule the electrophilic substitution is followed by the Boulton–Katritzky rearrangement providing new possibilities for the synthesis of previously inaccessible fluorinated heterocycles: nitro derivatives of 2,1,3-benzoxadiazoles and 1,2,3-benzotriazoles.

## EXPERIMENTAL

$^1$H NMR spectra in acetone-$d_6$ and DMSO-$d_6$ were registered on spectrometer Bruker WH-250 at operating frequency 250.135 MHz. $^{13}$C NMR spectra and low-temperature $^1$H and $^{19}$F NMR spectra in acetone-$d_6$, deuterochloroform, and DMSO-$d_6$ were recorded on spectrometer Bruker DRX-400 (at operating frequencies 100, 400, and 376 MHz for $^{13}$C, $^1$H, and $^{19}$F nuclei respectively). All spectral data are presented in the δ scale, ppm, with respect to TMS ($^1$H and $^{13}$C) or hexafluorobenzene ($^{19}$F). Mass spectra were measured on Varian 311A instrument under the following conditions: accelerating voltage 3 kV, ionizing electrons energy 70 eV, direct sample admission into the ion source.

**Table 5.** Yields,melting points, and elemental analyses of compounds I**II, IVe–g, VIa–d**, and **VIIa–d**

| Compd. no. | Yield, % | mp, °C, (solvent) | Found, % | | | Formula | Calculated, % | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | | C | H | N |
| **III** | 74 | 125–126 | 33.61 | 0.82 | 19.42 | $C_6H_2FN_3O_5$ | 33.48 | 0.94 | 19.53 |
| **IVe** | 73 | 72–74 (EtOH) | 36.74 | 1.64 | 18.26 | $C_7H_4FN_3O_5$ | 36.70 | 1.76 | 18.34 |
| **IVf** | 78 | 69–71 (EtOH) | 39.46 | 2.81 | 16.94 | $C_8H_6FN_3O_5$ | 39.52 | 2.49 | 17.28 |
| **IVg** | 84 | 52–54 (EtOH–$H_2O$, 2:1) | 43.97 | 3.39 | 14.23 | $C_{11}H_{10}FN_3O_6$ | 44.15 | 3.37 | 14.04 |
| **VIa** | 64 | 95–97 | 44.93 | 3.52 | 21.14 | $C_{10}H_9FN_4O_4$ | 44.78 | 3.38 | 20.89 |
| **Vib** | 57 | 82–84 | 42.33 | 3.56 | 20.07 | $C_{10}H_9FN_4O_3S$ | 42.25 | 3.19 | 19.71 |
| **Vic** | 58 | 84–85 | 47.21 | 4.01 | 22.24 | $C_{10}H_9FN_4O_3$ | 47.62 | 3.60 | 22.22 |
| **Vid** | 61 | 87–89 | 42.30 | 2.88 | 24.63 | $C_8H_7FN_4O_3$ | 42.48 | 3.12 | 24.77 |
| **VIIa** | 39 | 153–151 | 44.16 | 3.04 | 22.78 | $C_{16}H_{12}FN_7O_7$ | 44.35 | 2.79 | 22.63 |
| **VIIb** | 34 | 157–159 | 42.38 | 2.34 | 22.12 | $C_{16}H_{12}FN_7O_6S$ | 42.76 | 2.69 | 21.82 |
| **VIIc** | 37 | 128–129 | 46.34 | 2.94 | 23.18 | $C_{16}H_{12}FN_7O_6$ | 46.05 | 2.90 | 23.50 |
| **VIId** | 41 | 157–159 | 42.64 | 2.94 | 25.18 | $C_{14}H_{10}FN_7O_6$ | 42.97 | 2.58 | 25.06 |

Spectral characteristics of compounds **IV–VII** are given in Table 4, yields, melting points, and elemental analyses of compounds **III–VII** are compiled in Table 5.

**4-Nitro-6-fluoro-2,1,3-benzoxadiazol-5-ol (III).** (a) To a solution of 3 g (20 mmol) of compound **I** in 10 ml of concn. $H_2SO_4$ at 0–5°C while stirring was added dropwise a solution of 0.09 ml $HNO_3$ (*d* 1.54) in 2 ml of concn. $H_2SO_4$ maintaining the temperature of the reaction mixture below 15°C. The reaction mixture was stirred for 1 h at 60°C, then cooled, and ice water (25–30 ml) was added by portions thereto, the separated precipitate of compound **III** was filtered off, washed with water, dried, and recrystallized from chloroform. Mass spectrum, *m/z* ($I_{rel}$, %) 215 (100) $[M]^{+\cdot}$, 199 (15), 139 (13), 110 (10), 109 (31), 98 (27), 82 (13), 80 (16), 70 (17), 69 (11).

(b) To a solution of 1 mmol of compound **IIa–e** in 5 ml of concn. $H_2SO_4$ cooled to 0–5°C was added dropwise while stirring a solution of 0.05 ml of $HNO_3$ (*d* 1.54) in 1 ml of concn. $H_2SO_4$ maintaining the temperature of the reaction mixture below 15°C. The reaction mixture was stirred for 10–20 min at room temperature, then ice water was added (25–30 ml), the separated precipitate of compound **III** was filtered off, washed with water, dried, and recrystallized from chloroform.

**5-Alkoxy-4-nitro-6-fluoro-2,1,3-benzoxadiazole 1-oxides (IVe–g).** To a solution of 1 mmol of compound **IIa–e** in 5 ml of concn. $H_2SO_4$ cooled to 0–5°C was added dropwise while stirring a solution of 0.05 ml of $HNO_3$ (*d* 1.54) in 1 ml of concn. $H_2SO_4$ maintaining the temperature of the reaction mixture below 15°C. The reaction mixture was stirred for 10–20 min at room temperature, then ice water was added (25–30 ml), the separated precipitate of compound **IVe–g** was filtered off, washed with water, dried, and recrystallized from an appropriate solvent.

**4-Nitro-6-fluoro-7-X-2,1,3-benzoxadiazoles (VIa–d).** A solution of 1 mmol of compound **IIa-d** in 3–4 ml of acetonitrile was cooled to 0°C, and a solution of 0.4 g (5 mmol) of $NaNO_2$ in 1 ml of HCl (38%) was added dropwise. The reaction mixture was stirred for 1.5–2 h at room temperature, diluted with cold water, extracted with chloroform, the extract was dried on $Na_2SO_4$, and the solvent was evaporated. The compound **VIa–d** obtained was purified by column chromatography on silica gel (eluent chloroform).

**2-(2,4-Dinitrophenyl)-4-nitro-6-fluoro-7-X-2*H*-1,2,3-benzotriazoles (VIIa–d).** To a solution of compound **IIa–d** in 5 ml of ethanol was added a solution of 10 mmol of 2,4-dinitrobenzenediazonium sulfate [18] in 10 ml of 20% $H_2SO_4$ maintaining the temperature of the reaction mixture below 50°C. The reaction mixture was stirred for 1.5–2 h at room temperature, the separated precipitate of compound **VIIa–d** was filtered off, washed with water, dried, and purified by column chromatography on silica gel (eluent chloroform).

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