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Fluorine-Containing Heterocycles: VII.* Nucleophilic Substitution in 6,7-Difluoroquinoxalines**

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Abstract—For the purpose of biological screening, a number of new quinoxalines have been synthesized via fluorine replacement in 2,3-disubstituted 6,7-difluoroquinoxaline 1,4-dioxides and their deoxygenated derivatives by reactions with dialkylamines, sodium azide, and sodium methoxide.

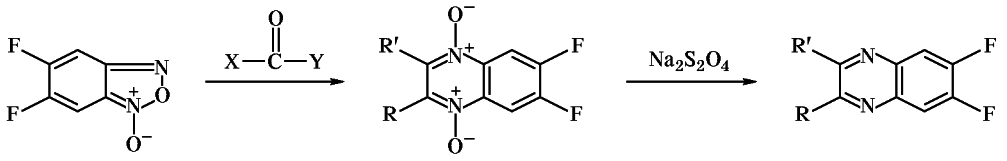
Quinoxalines exhibit a wide spectrum of biological activity, specifically antibacterial, antiphlogistic, antihelminthic, herbicide, fungicide, insecticide, etc. [2–4]. Dioxidin and Quinoxidin [2,3-bis(hydroxymethyl)- and 2,3-bis(acetoxymethyl)quinoxaline 1,4-dioxides], as well as 2,3-dimethylquinoxaline 1,4-dioxide, are efficient antibacterial substances [5, 6]. There are data on prophylactic effect of 2,3-dimethyl- and 6-chloro-2,3-dimethylquinoxaline 1,4-dioxides on exposure to radiation [7]. Tranquilizers [8] and antitumor compounds [9, 10] have been found among this series.

In the recent time, fluorinated derivatives of aza heterocycles attract a specific interest. For example, fluorinated derivatives of oxoquinolinecarboxylic acids constitute a generation of antibacterial drugs with a wide spectrum of activity [11]; an antifungal drug Fluconazole and neuroleptics Fluorophenazin and Triphthazin, as well as other fluorine-containing compounds [12], are successfully used in medical practice. Fluorinated arenes attract attention due to the fact that fluorine atoms therein favor formation of complexes, including those with heterocyclic bases; therefore, interest in fluorinated aza heterocycles increases [13].

We previously described the synthesis of a number of fluorinated quinoxaline derivatives [14–18]. With the goal of obtaining new compounds for biological screening, in the present work we synthesized new 2,3-disubstituted 6,7-difluoroquinoxaline 1,4-dioxides and their deoxygenated analogs and studied fluorine replacement in these compounds.

2,3-Disubstituted 6,7-difluoroquinoxaline 1,4-dioxides **II** and **III** were synthesized by reactions of

Scheme 1.



I **II, III** **IV, V**

II, **IV**, X = CH_2CN, Y = Ph, R = Ph, R′ = CN; **III**, **V**, X = Me, Y = Et, R = R′ = Me.

* For communication VI, see [1].

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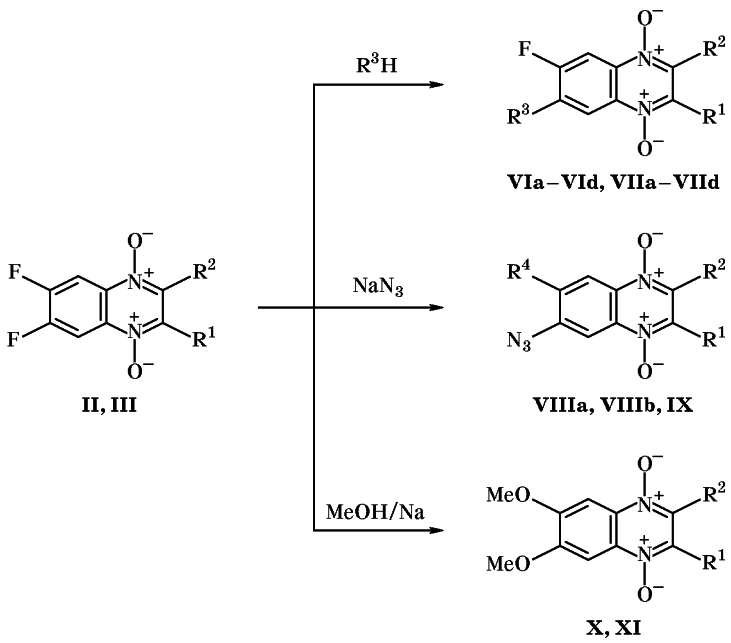
Table 1. ^{1}H NMR and mass spectra of 2,3-disubstituted 6,7-difluoroquinoxalines **II**–**V**

Comp. no.	^{1}H NMR spectrum, δ, ppm, *J*, Hz			Mass spectrum, *m*/*z* (I_{rel}, %)
	5-H	8-H	R, R′	
II	8.57 q, ^3J(5-H, 6-F) = 10.7, ^4J(5-H, 7-F) = 7.6	8.64 q, ^3J(8-H, 7-F) = 10.4, ^4J(8-H, 6-F) = 7.6	7.68 m (5H, Ph)	299 (100) M^+, 282 (35), 266 (11), 252 (35), 240 (23), 126 (28), 112 (26)
III	8.37 t[a]		2.49 s (6H, 2Me)	226 (100) M^+, 209 (25), 193 (19), 192 (89), 191 (13), 179 (10), 112 (15)
IV	8.17 q, ^3J(5-H, 6-F) = 10.7, ^4J(5-H, 7-F) = 7.3	8.24 q ^3J(8-H, 7-F) = 10.4, ^4J(8-H, 6-F) = 7.3	7.82 m (5H, Ph)	267 (100) M^+, 240 (20), 215 (22), 112 (22)
V	7.79 t[a]		2.49 s (6H, 2Me)	194 (71) M^+, 153 (100), 112 (43)

[a] The 5-H and 8-H protons are equivalent.

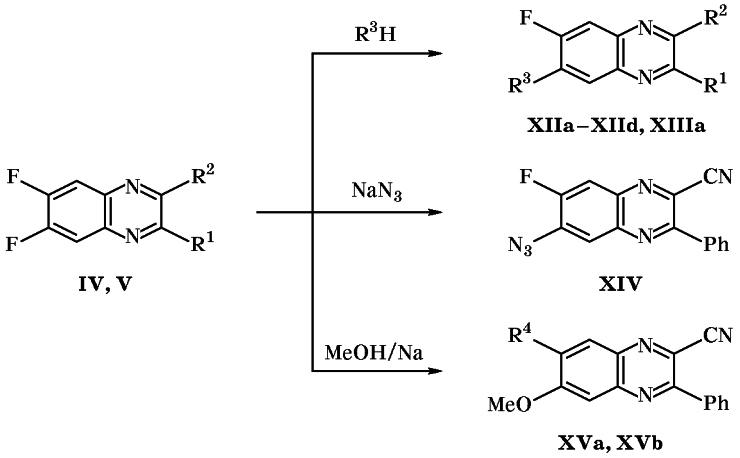
5,6-difluorobenzofuroxan (**I**) [14] with benzoylacetonitrile and methyl ethyl ketone, respectively, and were then reduced to the corresponding quinoxalines **IV** and **V** with $Na_2S_2O_4$ (Scheme 1). The reaction of **I** with benzoylacetonitrile was carried out in anhydrous ethanol at 20–25°C in the presence of triethylamine, and with methyl ethyl ketone, in DMF at 80°C (45 min) in the presence of ammonia. Quinoxaline 1,4-dioxides **II** and **III** were deoxygenated with sodium dithionite by heating in acetonitrile or DMF for 0.5–2.0 h. The ^{1}H NMR spectra of quinoxalines **II**–**V** contain signals from substituents R; the 5-H and 8-H aromatic protons in compounds **II** and **IV** appear as doublets of doublets, and those in the spectra of **III** and **V** are triplets (Table 1). The aromatic proton signals in the spectra of deoxygenated derivatives **IV** and **V** are located ~0.4 ppm upfield relative to the corresponding signals of 1,4-dioxides

Scheme 2.



II, **VIa**–**VId**, **VIIIa**, **VIIIb**, **X**, R^1 = Ph, R^2 = CN; **III**, **VIIa**–**VIId**, **IX**, **XI**, R^1 = R^2 = Me; **VIa**, **VIIa**, R^3 = 1-pyrrolidinyl; **VIb**, **VIIb**, R^3 = 4-methyl-1-piperazinyl; **VIc**, **VIIc**, R^3 = morpholino; **VId**, **VIId**, R^3 = thiomorpholino; **VIIIa**, R^4 = F; **VIIIb**, R^4 = N_3; **IX**, R^1 = R^2 = Me, R^4 = N_3.

Scheme 3.



IV, **XIIa**-**XIId**, R^1 = Ph, R^2 = CN; **V**, **XIIIa**, R^1 = R^2 = Me; **XIIa**, R^3 = 1-pyrrolidinyl; **XIIb**, R^3 = 4-methyl-1-piperazinyl; **XIIc**, R^3 = morpholino; **XIId**, R^3 = thiomorpholino; **XIIIa**, R^3 = 1-pyrrolidinyl; **XVa**, R^4 = F; **XVb**, R^4 = OMe.

II and **III**. Compounds **II**–**V** give molecular ion peaks in the mass spectra (Table 1).

We studied the effects of substituents in positions *2* and *3* of compounds **II**–**V**, as well as of the *N*-oxide moieties in the pyrazine ring, on the reactivity of fluorine atoms toward nucleophiles, such as dialkylamines (pyrrolidine, 4-methylpiperazine, morpholine, and thiomorpholine), sodium azide, and sodium methoxide (Schemes 2, 3).

The fluorine atom in position *7* of quinoxaline 1,4-dioxide **II** having electron-acceptor CN group in position *3* is fairly readily replaced by dialkylamino group. Quinoxalines **VIa**–**VId** were obtained in acetonitrile by the action of a 20% excess of amine at 20–25°C for 5–7 h; the yields of the products were 75–80%. Analogous reactions with quinoxaline 1,4-dioxide **III** having two methyl groups in the pyrazine ring required more severe conditions: compounds **VIIa**–**VIId** were formed in 75–85% yield on heating with 2 equiv of amine in acetonitrile containing a catalytic amount of DBU under reflux for 4 h. Fluorine replacement in quinoxalines **IV** and **V** having no *N*-oxide moieties in the pyrazine ring is more difficult, as compared with quinoxaline 1,4-dioxides **IIb** and **III**. Compounds **XIIa**–**XIId** were synthesized in 60–85% yield by heating in boiling ethanol for 1 h with 1.5 equiv of appropriate amine. The fluorine atom in 2,3-dimethylquinoxaline **V** was replaced only in the reaction with the most nucleophilic of the amines used, pyrrolidine. The reaction was carried out in dimethylformamide in the presence of DBU at 120°C (reaction time 5 h) with 2 equiv of pyrrolidine. It should be noted that the reactivity of 2-methyl-6,7-difluoroquinoxaline in an analogous reaction occupies an intermediate place: It reacts with pyrrolidine on heating in boiling acetonitrile in the presence of DBU, yielding a mixture of 2-methyl-7-(1-pyrrolidinyl)-6-fluoroquinoxaline and 2-methyl-6-(1-pyrrolidinyl)-7-fluoroquinoxaline [18]. Our attempts to isolate substitution product in the reactions of 2,3-dimethylquinoxaline (**V**) with the other amines (the reaction time was prolonged to 20 h) were unsuccessful, and the initial compound was recovered. We also failed to effect replacement of both fluorine atoms in 6,7-difluoroquinoxaline 1,4-dioxides **II** and **III**, as well as of the remaining fluorine atom in monoamino derivatives **VIa** and **VIIa**, by dialkylamino groups. In the first case, monosubstitution products **VIa** and **VIIa** were isolated, and in the second, initial compounds.

In the ^{1}H NMR spectra of 7-substituted 6-fluoroquinoxalines **VI**–**VII** and **XII**–**XIII**, signals from the 5-H and 8-H protons appear as doublets with characteristic coupling constants ^3J(5-H, 6-H) = 12.8–14.7 Hz and ^4J(8-H, 6-F) = 8.0–9.5 Hz (Table 2). The electron-donor dialkylamino group introduced in position *7* induces an upfield shift of the 5-H and 8-H signals, the shift of the latter being considerably greater due to conjugation with R^3 ($\Delta\delta$ 0.81–1.30 and 0.45–0.60 ppm for 8-H and 5-H, respectively). The ease of fluorine replacement at the 7-position of compounds **VIa**–**VId** is explained by the activating effect of acceptor cyano group at C^3. A similar effect was observed by us while studying other reactions of 6,7-difluoroquinoxaline 1,4-dioxides [14].

As might be expected, the mobility of fluorine atoms in quinoxalines **II**–**V** also depends on the

Table 2. ^{1}H NMR spectra of substituted 6-fluoroquinoxalines **VI**, **VII**, and **XII**–**XIII**

Comp. no.	Chemical shifts δ, ppm, and coupling constants *J*, Hz			
	5-H, d, ^3J(5-H, 6-F)	8-H, d, ^4J(8-H, 6-F)	R^1, R^2	R^3
VIa	8.01 (13.1)	7.32 (8.2)	7.62 m (5H, Ph)	2.06 m [4H, $(CH_2)_2$], 3.69 m [4H, $N(CH_2)_2$]
VIb	8.04 (13.1)	7.79 (8.2)	7.62 m (5H, Ph)	2.29 s (3H, NCH_3), 2.54 m [4H, $N(CH_2)_2$], 3.40 m [4H, $N(CH_2)_2$]
VIc	8.14 (12.8)	7.83 (8.2)	7.68 m (5H, Ph)	3.39 m [4H, $N(CH_2)_2$], 3.82 m [4H, $O(CH_2)_2$]
VId	8.12 (12.8)	7.82 (8.0)	7.65 m (5H, Ph)	2.80 m [4H, $N(CH_2)_2$], 3.71 m [4H, $S(CH_2)_2$]
VIIa	7.93 (14.0)	7.39 (8.2)	2.55 s (6H, 2Me)	2.04 m [4H, $(CH_2)_2$], 3.59 m [4H, $N(CH_2)_2$]
VIIb	8.04 (13.1)	7.82 (8.2)	2.58 s (6H, 2Me)	2.28 s (3H, NCH_3), 2.49 m [4H, $N(CH_2)_2$], 3.27 m [4H, $N(CH_2)_2$]
VIIc	8.06 (12.8)	7.81 (8.2)	2.55 s (6H, 2Me)	3.60 m [4H, $N(CH_2)_2$], 3.82 m [4H, $O(CH_2)_2$]
VIId	8.05 (12.8)	7.82 (9.2)	2.59 s (6H, 2Me)	2.82 m [4H, $N(CH_2)_2$], 3.41 m [4H, $S(CH_2)_2$]
XIIa	7.62 (14.4)	6.98 (9.2)	7.71 m (5H, Ph)	2.06 m [4H, $(CH_2)_2$], 3.68 m [4H, $N(CH_2)_2$]
XIIb	7.79 (13.4)	7.74 (9.2)	7.78 m (5H, Ph)	2.29 s (3H, NCH_3), 2.53 m [4H, $N(CH_2)_2$], 3.39 m [4H, $N(CH_2)_2$]
XIIc	7.83 (13.4)	7.50 (8.9)	7.78 m (5H, Ph)	3.38 m [4H, $N(CH_2)_2$], 3.83 m [4H, $O(CH_2)_2$]
XIId	7.80 (13.1)	7.52 (8.6)	7.78 m (5H, Ph)	2.83 m [4H, $N(CH_2)_2$], 3.59 m [4H, $S(CH_2)_2$]
XIIIa	7.39 (14.7)	6.89 (9.5)	2.58 s (6H, 2Me)	2.02 m [4H, $(CH_2)_2$], 3.52 m [4H, $N(CH_2)_2$]

Table 3. ^{1}H NMR and mass spectra of substituted 7-azidoquinoxalines **VIIIa**, **VIIIb**, **IX**, and **XIV**

Comp. no.	^{1}H NMR spectrum, δ, ppm, *J*, Hz		Mass spectrum, *m*/*z* (I_{rel}, %)
	5-H, 8-H	R^1, R^2	
VIIIa	8.30 d (1H, 5-H), ^3J(5-H, 6-F) = 10.4, 8.25 d (1H, 8-H), ^4J(8-H, 6-F) = 7.6	7.65 m (5H, Ph)	322 (71) M^+, 306 (20), 296 (44), 280 (50), 250 (36), 249 (58), 127 (48), 115 (27), 103 (52), 85 (31), 77 (100), 69 (30), 57 (78)
VIIIb	8.17 s (1H, 5-H), 8.14 s (1H, 8-H)	7.68 m (5H, Ph)	345 (8) M^+, 329 (7), 301 (2), 289 (3), 273 (11), 259 (12), 248 (18), 232 (32), 220 (19), 153 (32), 127 (49), 115 (18), 103 (100), 91 (47), 77 (95), 63 (26), 51 (55)
IX	8.10 s (2H, 5-H, 8-H)	2.55 s (6H, 2Me)	272 (96) M^+, 246 (110), 218 (6), 200 (8), 182 (9), 171 (7), 143 (8), 130 (9), 118 (12), 104 (47), 92 (44), 79 (42), 66 (24)
XIV	7.92 d (1H, 5-H), ^3J(5-H, 6-F) = 10.4, 7.43 d (1H, 8-H), ^4J(8-H, 6-F) = 7.6	2.55 s (6H, 2Me)	290 (13) M^+, 262 (100), 235 (12), 209 (3), 127 (11), 115 (8), 107 (21), 103 (15), 88 (7), 77 (23), 51 (10)

nucleophile nature. By heating quinoxaline 1,4-dioxide **II** in acetonitrile with an aqueous solution of sodium azide (molar reactant ratio 1 : 1) at the boiling point for 1 h we obtained 63% of monosubstitution product **VIIIa**, whereas with 2 equiv of sodium azide both fluorine atoms were replaced to give diazido derivative **VIIIb** in 60% yield. In the reaction of quinoxaline 1,4-dioxide **III** with sodium azide we failed to isolate product of replacement of only one fluorine atom. Even at an equimolar reactant ratio, only diazido derivative **IX** was isolated together with unchanged initial compound. These findings indicate that the azido group facilitates further replacement of fluorine in position *6*, so that the second fluorine atom is replaced at a higher rate than the first. Disubstituted quinoxaline **IX** was formed on heating of *N*,*N*′-dioxide **III** with 2 equiv of sodium azide in DMF at 100°C for 2 h. Quinoxalines **IV** and **V**, which are not activated by *N*-oxide groups, are difficult to react with sodium azide. When quinoxaline **IV** was

Table 4. Yields, melting points, and elemental analyses of quinoxalines **II**–**XV**

Comp. no.	Yield, %	mp,[a] °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
II	61	220–222	60.53	2.48	14.31	$C_{15}H_7F_2N_3O_2$	60.21	2.36	14.04
III	66	188–109	53.42	3.54	12.80	$C_{10}H_8F_2N_2O_2$	53.10	3.57	12.49
IV	61	220–222	67.62	2.43	15.96	$C_{15}H_7F_2N_3$	67.41	2.64	15.72
V	70	188–189	62.04	4.32	14.40	$C_{10}H_8F_2N_2$	61.85	4.15	14.43
VIa	77	188–190	65.33	4.48	15.97	$C_{19}H_{15}FN_4O_2$	65.13	4.32	15.99
VIb	83	160–161	63.57	4.59	18.23	$C_{20}H_{18}FN_5O_2$	63.31	4.78	18.43
VIc	79	180–182	62.48	4.26	15.40	$C_{19}H_{15}FN_4O_3$	62.29	4.13	15.29
VId	85	182–183	59.62	3.78	14.66	$C_{19}H_{15}FN_4O_2S$	59.67	3.95	14.65
VIIa	79	187–189	60.39	5.78	15.10	$C_{14}H_{16}FN_3O_2$	60.64	5.82	15.15
VIIb	77	155–157	58.49	6.04	18.43	$C_{15}H_{19}FN_4O_2$	58.81	6.25	18.29
VIIc	83	168–170	57.76	5.47	14.10	$C_{14}H_{16}FN_3O_3$	57.39	5.50	14.33
VIId	84	182–184	54.56	5.42	13.74	$C_{14}H_{16}FN_3O_2S$	54.35	5.21	13.58
VIIIa	58	139–141	55.83	2.46	26.32	$C_{15}H_7FN_6O_2$	55.90	2.19	26.08
VIIIb	61	174–176	52.20	2.16	36.23	$C_{15}H_7N_9O_2$	52.18	2.04	36.51
IX	48	259–260	44.16	3.20	41.12	$C_{10}H_8N_8O_2$	44.12	2.96	41.16
X	81	256–258	63.29	4.12	12.31	$C_{17}H_{13}N_3O_4$	63.15	4.05	12.00
XI	43	196–198	57.89	5.43	11.08	$C_{12}H_{14}N_2O_4$	57.59	5.64	11.20
XIIa	81	135–137	71.81	4.59	17.30	$C_{19}H_{15}FN_4$	71.68	4.75	17.60
XIIb	67	162–163	68.94	5.51	20.20	$C_{20}H_{18}FN_5$	69.15	5.22	20.16
XIIc	58	141–143	68.34	4.29	16.51	$C_{19}H_{15}FN_4O$	68.25	4.52	16.76
XIId	86	184–186	64.91	4.63	16.06	$C_{19}H_{15}FN_4S$	65.07	4.40	15.98
XIIIa	83	104–106	68.50	6.50	17.21	$C_{14}H_{16}FN_3$	68.55	6.58	17.13
XIV	85	186–188	62.16	2.32	28.80	$C_{15}H_7FN_6$	62.07	2.43	28.95
XVa	78	184–186	68.60	3.40	15.12	$C_{16}H_{10}FN_3O$	68.81	3.61	15.05
XVb	44	176–178	70.34	4.71	14.28	$C_{17}H_{13}N_3O_2$	70.09	4.50	14.43

[a] Compounds **III** and **IX** were recrystallized from DMF; compounds **VIb**, **VIc**, **VIIc**, **X**, **XIIc**, **XIIIa**, **XVa**, and **XVb** were recrystallized from ethanol; and the others, from acetonitrile.

heated with 2 equiv of NaN_3 in acetonitrile for 2 h, 7-azido-6-fluoroquinoxaline **XIV** was obtained, and no product of substitution of two fluorine atoms in **IV** was detected. All our attempts to replace fluorine atom in **V** by azido group were unsuccessful.

In the ^{1}H NMR spectra of monosubstitution products **VIIIa** and **XIV**, signals from the 5-H and 8-H protons are doublets, and those in the spectra of disubstitution products **VIIIb** and **IX** are singlets (Table 3). The mass spectra of the azido derivatives contain the molecular ion peaks (Table 3).

6,7-Difluoroquinoxaline 1,4-dioxides **II** and **III** very readily react with sodium methoxide in methanol at 20–25°C, resulting in replacement of both fluorine atoms by methoxy groups. In an analogous reaction with quinoxaline **IV** monosubstitution product **XVa** was obtained, while on heating both fluorine atoms were replaced to give 6,7-dimethoxy derivative **XVb**. Quinoxaline **V** failed to react with sodium methoxide even at elevated temperature.

Disubstitution products **X**, **XI**, and **XVb** show in the ^{1}H NMR spectra singlet signals from the 5-H and 8-H protons; the corresponding signals in the spectrum of monomethoxy derivative **XVa** appear as distinct doublets.

Thus, the reactivity of 6,7-difluoroquinoxaline 1,4-dioxides toward nucleophiles is much higher than the reactivity of their deoxygenated derivatives. It also depends on the electronic effects of substituents in the pyrazine ring and nucleophile nature.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker WH-250 spectrometer operating at 250 MHz; tetramethylsilane was used as internal reference. The mass

spectra were run on a Varian-Mat 311A instrument. The yields, melting points, and elemental analyses of compounds **II**–**XV** are given in Table 4.

3-Cyano-6,7-difluoro-2-phenylquinoxaline 1,4-dioxide (II). Triethylamine, 2.4 ml (25 mmol), was added dropwise to a solution of benzofuroxan **I**, 3.0 g (17.5 mmol), in 50 ml of anhydrous ethanol. Benzoylacetonitrile, 2.5 g (20 mmol), was then added, and the mixture was stirred for 2.5 h at 20–25°C. The mixture was cooled, and the precipitate was filtered off, dried, and recrystallized from acetonitrile. Yield 2.5 g.

6,7-Difluoro-2,3-dimethylquinoxaline 1,4-dioxide (III). Benzofuroxan **I**, 1.7 g (10.0 mmol), was dissolved on heating in 15 ml of DMF, and 2.5 ml (35 mmol) of methyl ethyl ketone and 2.5 ml (7 mmol) of NH_4OH were added dropwise. The mixture was stirred for 45 min at 80°C and cooled, and the precipitate was filtered off, dried, and recrystallized from 1:2 acetonitrile–DMF. Yield 1.2 g.

3-Cyano-6,7-difluoro-2-phenylquinoxaline (IV). A solution of sodium dithionite ($Na_2S_2O_4$), 2.1 g (12 mmol), in 15 ml of water, was added in portions to a hot solution of 0.89 g (3 mmol) quinoxaline dioxide **II** in 45 ml of acetonitrile. The mixture was heated for 2 h on a water bath and poured into cold water (50 ml). A flaky solid separated and was filtered off, dried, and recrystallized from EtOH. Yield 0.6 g.

6,7-Difluoro-2,3-dimethylquinoxaline (V). A solution of sodium dithionite ($Na_2S_2O_4$), 4.1 g (16 mmol), in 10 ml of water was added in portions to a solution of 1.1 g (4 mmol) of quinoxaline dioxide **III** in 20 ml of DMF. The mixture was heated for 0.5 h on a boiling water bath and poured into cold water (50 ml). The precipitate was filtered off, dried, and recrystallized from acetonitrile. Yield 0.7 g.

7-Substituted 3-cyano-6-fluoro-2-phenylquinoxaline 1,4-dioxides VIa–VId. Compound **II**, 0.3 g (1 mmol), was dissolved in 5 ml of anhydrous ethanol, and 1.2 mmol of appropriate secondary amine was added. The mixture was stirred for 3–5 h and cooled, and the precipitate was filtered off, dried, and recrystallized from acetonitrile.

7-Substituted 6-fluoro-2,3-dimethylquinoxaline 1,4-dioxides VIIa and VIIc. Appropriate secondary amine, 2 mmol, was added to a suspension of 0.23 g (1 mmol) of quinoxaline dioxide **III** in 5 ml of acetonitrile. The mixture was refluxed for 1.5 h (**VIIa**) or 5 h (**VIIc**) and cooled, and the precipitate was filtered off, dried, and recrystallized from acetonitrile.

7-Substituted 6-fluoro-2,3-dimethylquinoxaline 1,4-dioxides VIIb and VIId. Appropriate dialkylamine, 2 mmol, and DBU, 0.15 ml (1 mmol), were added to a suspension of 0.23 g (1 mmol) of quinoxaline dioxide **III** in 5 ml of acetonitrile. The mixture was refluxed for 4 h and cooled, and the precipitate was filtered off and recrystallized from acetonitrile.

7-Azido-3-cyano-6-fluoro-2-phenylquinoxaline 1,4-dioxide (VIIIa). A solution of 0.07 g (1 mmol) of sodium azide in 1 ml of water was added to a solution of 0.30 g (1 mmol) of quinoxaline dioxide **II** in 3 ml of acetonitrile. The mixture was refluxed for 1 h and cooled, and the precipitate was filtered off, washed with water on a filter, dried, and recrystallized from acetonitrile. Yield 0.2 g.

6,7-Diazido-3-cyano-2-phenylquinoxaline 1,4-dioxide (VIIIb). A solution of 0.14 g (2 mmol) of sodium azide in 1 ml of water was added to a solution of 0.3 g (1 mmol) of quinoxaline dioxide **II** in 3 ml of acetonitrile. The mixture was refluxed for 2 h and cooled, and the precipitate was filtered off, washed with water on a filter, dried, and recrystallized from ethanol. Yield 0.2 g.

6,7-Diazido-2,3-dimethylquinoxaline 1,4-dioxide (IX). A solution of 0.14 g (2.0 mmol) of sodium azide in 1 ml of water was added to a solution of 0.23 g (1 mmol) of quinoxaline dioxide **III** in 3 ml of DMF. The mixture was heated for 2 h on a boiling water bath and cooled, and the precipitate was filtered off, washed with water on a filter, dried, and recrystallized from acetonitrile. Yield 0.15 g.

3-Cyano-6,7-dimethoxy-2-phenylquinoxaline 1,4-dioxide (X). Quinoxaline dioxide **II**, 0.30 g (1 mmol), was added to a solution of 0.05 g (2 mmol) of metallic sodium in 3 ml of methanol. The mixture was stirred for 2 h at 20–25°C and cooled, and the precipitate was filtered off, washed with water on a filter, dried, and recrystallized from acetonitrile. Yield 0.25 g. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.05 s (3H, OCH_3), 4.07 s (3H, OCH_3), 7.69 m (5H, Ph), 7.81 s (2H, 5-H, 8-H).

6,7-Dimethoxy-2,3-dimethylquinoxaline 1,4-dioxide (XI). Quinoxaline dioxide **III**, 0.23 g (1 mmol), was added to a solution of 0.05 g (2 mmol) of metallic sodium in 3 ml of methanol. The mixture was stirred for 8 h at 20–25°C and cooled, and the precipitate was filtered off, washed with water on a filter, and recrystallized from DMF. Yield 0.1 g. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.55 s (6H, 2Me), 4.00 s (6H, 2MeO), 7.74 s (2H, 5-H, 8-H).

7-Substituted 3-cyano-6-fluoro-2-phenylquinoxalines XIIa–XIId. Appropriate secondary amine, 1.5 mmol, was added dropwise to a solution of 0.27 g (1 mmol) of quinoxaline **IV** in 5 ml of anhydrous

ethanol. The mixture was heated for 0.5–1 h on a water bath and cooled, and the precipitate was filtered off, dried, and recrystallized from acetonitrile.

6-Fluoro-2,3-dimethyl-7-(1-pyrrolidinyl)quinoxaline (XIIIa). Pyrrolidine, 0.17 ml (2 mmol), and DBU, 0.15 ml (1 mmol), were added dropwise to a solution of 0.19 g (1 mmol) of quinoxaline **V** in 4 ml of DMF. The mixture was heated for 5 h at 120°C on a glycerol bath, cooled, and poured into cold water (25 ml). The precipitate was filtered off, dried, and recrystallized from ethanol–water (1 : 1). Yield 0.2 g.

7-Azido-3-cyano-6-fluoro-2-phenylquinoxaline (XIV). A solution of 0.07 g (1 mmol) of sodium azide in 1 ml of water was added to a suspension of 0.27 g (1 mmol) of quinoxaline **IV** in 5 ml of acetonitrile. The mixture was heated for 2 h under reflux, cooled, and poured into cold water (30 ml). The precipitate was filtered off, washed with water on a filter, and recrystallized from acetonitrile. Yield 0.3 g.

3-Cyano-6-fluoro-7-methoxy-2-phenylquinoxaline (XVa). Quinoxaline **IV**, 0.27 g (1 mmol), was added to a solution of 0.05 g (2 mmol) of metallic sodium in 6 ml of methanol. The mixture was stirred for 2 h at 20–25°C and cooled, and the precipitate was washed with water on a filter, dried, and recrystallized from acetonitrile. Yield 0.3 g. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.12 s (3H, OCH_3), 7.24 d [1H, 8-H, ^4J(8-H, 6-F) = 8.5 Hz], 7.73 d [1H, 5-H, ^3J(5-H, 6-F) = 12.2 Hz], 7.80 m (5H, Ph).

3-Cyano-6,7-dimethoxy-2-phenylquinoxaline (XVb). Quinoxaline **IV**, 0.27 g (1 mmol), was added to a solution of 0.05 g (2 mmol) of metallic sodium in 6 ml of methanol. The mixture was heated for 2.5 h on a water bath and cooled, and the precipitate was filtered off, washed with water on a filter, dried, and recrystallized from acetonitrile. Yield 0.2 g. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.05 s (6H, 2MeO), 8.28 m (5H, Ph), 7.27 s (2H, 5-H, 8-H).

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