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Dedicated to Full Member of the Russian Academy of Sciences V.A. Tartakovskii on the 75th anniversary of his birth

Synthesis of Fluorine-Containing Analogs of Ellipticine and Other Heterocycles from 2-Nitro- and 2-Amino-4,5-difluoroanilines

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Abstract—2-Nitro- and 2-amino-4,5-difluoroanilines were used as starting materials to synthesize fluorine-containing imidazole, oxazole, and indoloquinoxaline derivatives. The latter may be regarded as ellipticine analogs.

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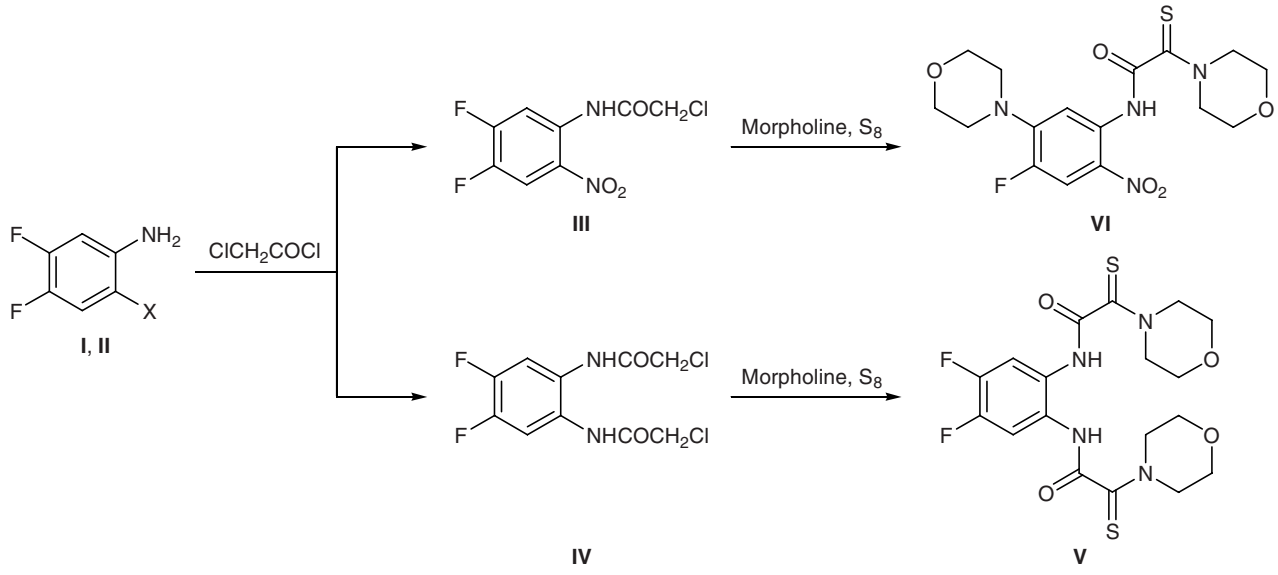
Numerous fluorine-containing heterocycles, e.g., fluoropyrimidines, fluoroindoles, fluorobenzimidazoles, fluoroquinolines, fluoroquinazolines, fluoronaphthyridines, etc., exhibit strong biological activity due to their ability to inhibit specific enzymes, good solubility in lipids, and easy penetration through cell membranes [1–3]. In particular, a broad series of compounds was synthesized on the basis of 4,5-difluorobenzene-1,2-diamine. The latter is an important synthon; the presence of four substituents in its benzene ring provides the possibility for its versatile modification, including preparation of fused heterocyclic structures [4–6].

The goal of the present work was to extend the above studies and synthesize fluorine-containing derivatives of fused imidazoles, oxazoles, and indoloquinoxalines; the latter may be regarded as analogs of natural alkaloids of the pyrido[4,3-*b*]carbazole series which are known to possess antitumor activity [7–10]. The synthetic schemes included mainly acylation of the amino groups in 3,4-difluoroanilines with acid chlorides. The nitro group in difluoroanilines gives rise to additional potential for functionalization via activation of fluorine atom to nucleophilic substitution; moreover, it can be directly involved in heterocyclizations.

In the synthesis of fluorine-containing compounds we used monothiooxamide derivatives of 2-amino- and 2-nitro-4,5-difluoroanilines **I** and **II**. We previously developed a convenient procedure for the preparation of monothiooxamides by reaction of α-chloroacetamides with a preliminarily prepared solution of sulfur in the corresponding amine and showed that these compounds can be converted into various heterocyclic systems [11].

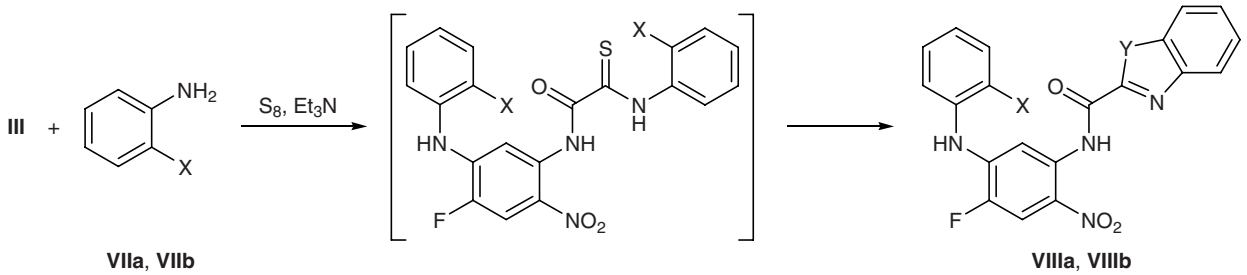
Chloroacetanilide **III** was obtained by acylation of 4,5-difluoro-2-nitroaniline (**I**) with chloroacetyl chloride in dimethylformamide. The reaction of chloroacetyl chloride with 4,5-difluorobenzene-1,2-diamine (**II**) in DMF gave *N*,*N*′-bis(chloroacetyl) derivative **IV** which reacted with a solution of elemental sulfur in morpholine to form the corresponding bis(monothiooxamide) **V** (Scheme 1). Under analogous conditions, the transformation of *N*-(4,5-difluoro-2-nitrophenyl)-2-chloroacetamide (**III**) was accompanied by expected nucleophilic replacement of the fluorine atom in the *para* position relative to the nitro group, yielding compound **VI**. These data demonstrate different behav-

Scheme 1.



I, X = NO_2; **II**, X = NH_2.

Scheme 2.



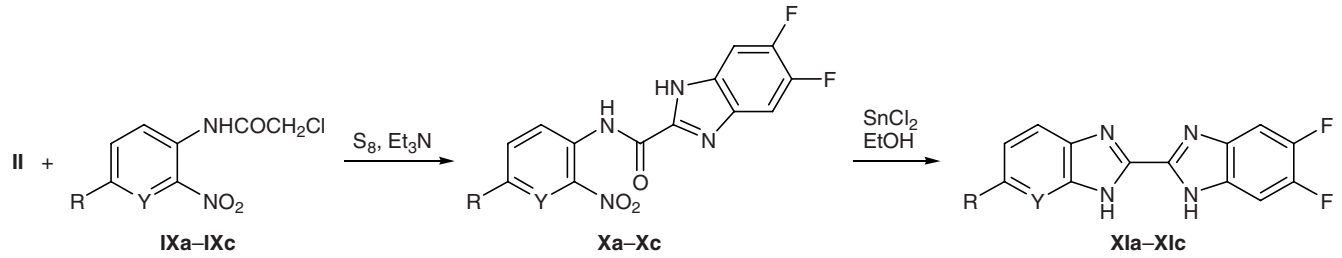
VII, X = NH_2 (**a**), OH (**b**); **VIII**, X = NH_2, Y = NH (**a**); X = OH, Y = O (**b**).

iors of fluoroanilines **I** and **II** and easy modification of fluoroarenes activated due to the presence of a nitro group.

Chloroacetanilide **III** was then used to synthesize fused heterocyclic compounds. Benzimidazole and 1,3-benzoxazole derivatives **VIIIa** and **VIIIb** were obtained by reactions of **III** with *o*-phenylenediamine (**VIIa**) and *o*-aminophenol (**VIIb**), respectively, in the presence of sulfur and triethylamine. The reactions were accompanied by replacement of the fluorine atom in the *para* position with respect to the nitro group by the aromatic acid residue. Presumably, the process involves intermediate formation of monothiooxamide and its subsequent heterocyclization at the thioamide carbonyl group (Scheme 2).

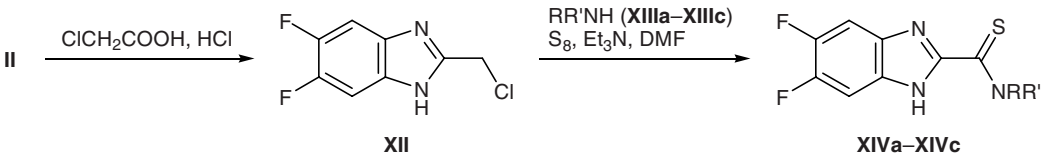
4,5-Difluorobenzene-1,2-diamine (**II**) reacted with chloroacetamides **IXa**–**IXc** of the nitroaniline and nitropyridine series in the presence of elemental sulfur

Scheme 3.



Y = CH, R = H (**a**), Cl (**b**); Y = N, R = H (**c**).

Scheme 4.



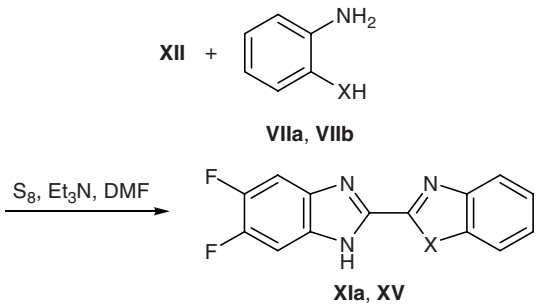
RR′N = morpholino (**a**); R = H, R′ = Ph (**b**), pyridin-2-yl (**c**).

and triethylamine to give benzimidazole derivatives **Xa**–**Xc** (Scheme 3). The reduction of the nitro group in compounds **Xa**–**Xc** was accompanied by intramolecular cyclization which opens a way to fluorinated 2,2′-bibenzimidazoles **XIa**–**XIc**.

We also made an attempt to synthesize 2-chloromethyl-5,6-difluoro-1*H*-benzimidazole (**XII**) which attracts considerable interest from the viewpoint of obtaining thioamides and heterocyclic compounds based thereon. However, we failed to effect cyclization of bis-chloroacetamide **IV** (see above) by thermolysis or heating in polyphosphoric acid. We succeeded in obtaining 2-chloromethyl-5,6-difluoro-1*H*-benzimidazole (**XII**) in good yield by reaction of difluorophenylenediamine **II** with chloroacetic acid on heating in boiling concentrated hydrochloric acid (Scheme 4). Treatment of **XII** with elemental sulfur and amines **XIIIa**–**XIIIc** in the presence of triethylamine in DMF afforded thioamides **XIVa**–**XIVc**.

We also demonstrated the possibility for synthesizing fused heterocycles from thioamides based on 2-chloromethyl-5,6-difluoro-1*H*-benzimidazole (**XII**). Compound **XII** reacted with *o*-phenylenediamine and *o*-aminophenol in the presence of sulfur to give 2-(1*H*-benzimidazol-2-yl)- and 2-(1,3-benzoxazol-2-yl)-substituted 5,6-difluorobenzimidazoles **XIa** and **XV**, respectively (Scheme 5).

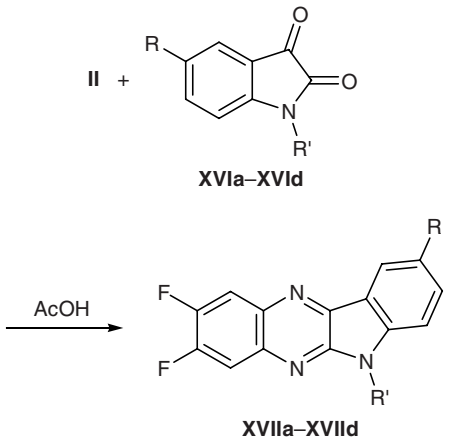
Scheme 5.



VIIa, **XIa**, X = NH; **VIIb**, **XV**, X = O.

With a view to synthesize fluorine-containing analogs of ellipticine [7–10], we examined reactions of 4,5-difluorobenzene-1,2-diamine (**II**) with isatins **XVIa**–**XVId** in various solvents (dioxane, alcohol, acetic acid). The best yields (60–75%) of 6-substituted 2,3-difluoro-6*H*-indolo[2,3-*b*]quinoxalines **XVIIa**–**XVIId** were obtained when the reactions were carried out in acetic acid (Scheme 6).

Scheme 6.



R = H, R′ = H (**a**), Me (**b**), Bu (**c**); R = Br, R′ = Et (**d**).

To conclude, we have proposed new approaches to the synthesis of fluorine-containing elliptitcne analogs and other fused heterocycles on the basis of difluoroaniline derivatives.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Bruker AC-200 (200 MHz) and WM-250 (250 MHz) spectrometers from solutions in DMSO-d_6; the ^{13}C NMR spectra were measured on a Bruker AC-200 instrument at 50.3 MHz using DMSO-d_6 as solvent. The mass spectra (electron impact, 70 eV) were obtained on a Varian MAT CH-6 mass spectrometer with direct sample admission into the ion source (accelerating voltage 1.75 kV). The melting points were determined on a Boetius hot stage and were not corrected. The reaction mixtures and isolated products were analyzed by TLC on Silica gel 60 F254 (Merck).

Chloroacetamides **III** and **IV** were synthesized according to the procedure described in [12].

2-Chloro-*N*-(4,5-difluoro-2-nitrophenyl)acetamide (III). Yield 97%, mp 84–85°C. ^{1}H NMR spectrum, δ, ppm: 4.41 s (2H), 8.0 m (1H, H_{arom}), 8.35 m (1H, H_{arom}), 10.8 s (1H, NH). Mass spectrum: *m*/*z* 250 $[M]^+$. Found, %: C 38.27; H 2.12; N 11.09. $C_8H_5ClF_2N_2O_3$. Calculated, %: C 38.34; H 2.01; N 11.18.

***N*,*N*′-(4,5-Difluorobenzene-1,2-diyl)bis(2-chloroacetamide) (IV)** was synthesized from 1 mol of diamine **III** and 2.4 mmol of chloroacetyl chloride. Yield 96%, mp 142–143°C. ^{1}H NMR spectrum, δ, ppm: 4.33 s (4H), 7.65 m (2H, H_{arom}), 9.78 s (2H, 2NH). Mass spectrum: *m*/*z* 297 $[M]^+$. Found, %: C 40.32; H 2.63; N 9.57. $C_{10}H_8Cl_2F_2N_2O_2$. Calculated, %: C 40.43; H 2.71; N 9.43.

Monothiooxamides V and VI (*general procedure*). A mixture of 0.045 g (1.4 mmol) of sulfur and 0.94 mmol of morpholine in 1 ml of DMF was kept for 30 min, 0.47 mmol of chloroacetanilide **III** or 0.24 mmol of compound **IV** was added, and the mixture was left to stand for 6 h at room temperature. The mixture was then poured into water, the precipitate was filtered off and dissolved in acetone, the solution was separated from the undissolved material, the solvent was removed under reduced pressure, and the solid residue was recrystallized from ethanol.

***N*,*N*′-(4,5-Difluorobenzene-1,2-diyl)bis(2-morpholino-2-thioxoacetamide) (V).** Yield 52%, mp 280–282°C. ^{1}H NMR spectrum, δ, ppm: 3.7 d (4H, CH_2, J = 4.8 Hz), 3.78 s (8H), 4.12 d (4H, J = 4.65 Hz), 7.75 m (2H, H_{arom}), 10.0 s (2H, 2NH). Mass spectrum: *m*/*z* 458 $[M]^+$. Found, %: C 47.06; H 4.24; N 12.36. $C_{18}H_{20}F_2N_4O_4S_2$. Calculated, %: C 47.15; H 4.40; N 12.22.

***N*-(4-Fluoro-5-morpholino-2-nitrophenyl)-2-morpholino-2-thioxoacetamide (VI).** Yield 78%, mp 169–170°C. ^{1}H NMR spectrum, δ, ppm: 3.75 m (10H), 4.15 m (2H), 4.3 m (2H), 4.55 s (2H), 7.50 d (1H, H_{arom}, J = 8.21 Hz), 7.98 m (1H, H_{arom}), 11.0 s (1H, NH). Mass spectrum: *m*/*z* 398 $[M]^+$. Found, %: C 48.06; H 4.95; N 14.24. $C_{16}H_{19}FN_4O_5S$. Calculated, %: C 48.24; H 4.81; N 14.06.

Substituted benzimidazole- and 1,3-benzoxazole-2-carboxamides VIIIa and VIIIb (*general procedure*). A mixture of 0.3 mmol of sulfur, 0.2 mmol of amine **VIIa** or **VIIb**, and 0.2 mmol of triethylamine in 1 ml of DMF was kept for 30 min, 0.1 mmol of chloroacetanilide **III** was added, and the mixture was stirred for 4 h at room temperature. The mixture was poured into water, the precipitate was filtered off, dried, and dissolved in acetone, the acetone solution was separated from the undissolved material, the solvent was evaporated under reduced pressure, and the residue was purified by thin-layer chromatography using petroleum ether–ethyl acetate (3:1) as eluent.

***N*-{5-[(2-Aminophenyl)amino]-4-fluoro-2-nitrophenyl}-1*H*-benzimidazole-2-carboxamide (VIIIa).** Yield 38%, mp 197–199°C. ^{1}H NMR spectrum, δ, ppm: 4.6 s (2H, NH_2), 6.9 m (2H, H_{arom}), 7.02 m (1H, H_{arom}), 7.1 m (1H, H_{arom}), 7.3 d (2H, H_{arom}, J = 7.4 Hz), 7.4 d (2H, H_{arom}, J = 7.3 Hz), 7.9 m (1H, H_{arom}), 8.1 m (1H, H_{arom}), 9.6 s (1H, NH), 10.2 s (1H, NH), 10.95 s (1H, NH). Mass spectrum: *m*/*z* 406 $[M]^+$. Found, %: C 59.23; H 3.76; N 20.54. $C_{20}H_{15}FN_6O_3$. Calculated, %: C 59.11; H 3.72; N 20.68.

***N*-{5-[(2-Hydroxyphenyl)amino]-4-fluoro-2-nitrophenyl}-1,3-benzoxazole-2-carboxamide (VIIIb).** Yield 41%, mp 162–164°C. ^{1}H NMR spectrum, δ, ppm: 7.0 m (2H, H_{arom}), 7.15 m (2H, H_{arom}), 7.2 m (1H, H_{arom}), 7.4 m (2H, H_{arom}), 7.55 m (1H, H_{arom}, J = 7.3 Hz), 7.9 m (2H, H_{arom}), 9.4 s (1H, NH), 9.8 s (1H, NH), 10.6 s (1H, OH). Mass spectrum: *m*/*z*: 408 $[M]^+$. Found, %: C 58.89; H 3.17; N 13.79. $C_{20}H_{13}FN_4O_5$. Calculated, %: C 58.83; H 3.21; N 13.72.

5,6-Difluoro-1*H*-benzimidazole-2-carboxamides Xa–Xc (*general procedure*). A suspension of 3 mmol of sulfur, 1.8 mmol of 4,5-difluorobenezene-1,2-diamine (**II**), and 2.2 mmol of triethylamine in 3 ml of DMF was kept for 25 min, 0.9 mmol of chloroacetanilide **IXa**–**IXc** was added, and the mixture was stirred for 5 h at room temperature. The mixture was poured into water, the precipitate was filtered off, dried, and dissolved in acetone, the solution was separated from the undissolved material, the solvent was evaporated under reduced pressure, and the solid residue was recrystallized from ethanol.

5,6-Difluoro-*N*-(2-nitrophenyl)-1*H*-benzimidazole-2-carboxamide (Xa). Yield 70%, mp 181–183°C. ^{1}H NMR spectrum, δ, ppm: 7.2 m (1H, H_{arom}), 7.5 m (1H, H_{arom}), 7.85 m (2H, H_{arom}), 8.15 m (1H, H_{arom}), 8.45 m (1H, H_{arom}), 11.7 s (1H, NH), 13.85 s (1H, NH). Mass spectrum: *m*/*z* 318 $[M]^+$. Found, %: C 52.89; H 2.50; N 17.51. $C_{14}H_8F_2N_4O_3$. Calculated, %: C 52.84; H 2.53; N 17.61.

***N*-(4-Chloro-2-nitrophenyl)-5,6-difluoro-1*H*-benzimidazole-2-carboxamide (Xb).** Yield 76%, mp 167–169°C. ^{1}H NMR spectrum, δ, ppm: 7.0 m

(1H, H_{arom}), 7.2 m (1H, H_{arom}), 7.5 m (2H, H_{arom}), 7.8 m (1H, H_{arom}), 11.3 s (1H, NH), 12.8 s (1H, NH). Mass spectrum: *m*/*z* 353 $[M]^+$. Found, %: C 47.55; H 2.08; N 15.94. $C_{14}H_7ClF_2N_4O_3$. Calculated, %: C 47.68; H 2.00; N 15.89.

5,6-Difluoro-*N*-(2-nitropyridin-3-yl)-1*H*-benzimidazole-2-carboxamide (Xc). Yield 67%, mp 135–137°C. ^{1}H NMR spectrum, δ, ppm: 7.7 m (1H, pyridine), 7.9 m (1H, H_{arom}), 8.0 m (1H, pyridine), 8.65 m (2H, H_{arom}), 11.5 s (1H, NH), 12.9 s (1H, NH). Mass spectrum: *m*/*z* 319 $[M]^+$. Found, %: C 48.74; H 2.13; N 21.99. $C_{13}H_7F_2N_5O_3$. Calculated, %: C 48.91; H 2.21; N 21.94.

5,6-Difluoro-1*H*,1′*H*-2,2′-bibenzimidazoles XIa–XIc (*general procedure*). A mixture of 1 mmol of benzimidazole-2-carboxamide **Xa**–**Xc** and 5 mmol of $SnCl_2 \cdot 2H_2O$ in 5 ml of ethanol was heated for 90 min under reflux. The mixture was cooled to room temperature, the solvent was removed under reduced pressure, 5 ml of water and an aqueous solution of sodium hydroxide were added to the residue, and the mixture was extracted with ethyl acetate. The extract was evaporated, and the residue was purified by recrystallization from ethanol or by thin-layer chromatography on silica gel using ethyl acetate–petroleum ether (1:3) as eluent.

5,6-Difluoro-1*H*,1′*H*-2,2′-bibenzimidazole (XIa). Yield 60%, mp 198–200°C. ^{1}H NMR spectrum, δ, ppm: 7.25 m (2H, H_{arom}), 7.40 m (2H, H_{arom}), 7.5 m (2H, H_{arom}), 11.55 s (1H, NH), 12.3 s (1H, NH). Mass spectrum: *m*/*z* 270 $[M]^+$. Found, %: C 62.27; H 2.91; N 20.79. $C_{14}H_8F_2N_4$. Calculated, %: C 62.22; H 2.98; N 20.73.

6′-Chloro-5,6-difluoro-1*H*,1′*H*-2,2′-bibenzimidazole (XIb). Yield 63%, mp 234–236°C. ^{1}H NMR spectrum, δ, ppm: 7.25 m (1H, H_{arom}), 7.45 m (1H, H_{arom}), 7.5 m (1H, H_{arom}), 7.75 m (2H, H_{arom}), 11.9 s (1H, NH), 12.4 s (1H, NH). Mass spectrum: *m*/*z* 305 $[M]^+$. Found, %: C 55.11; H 2.16; N 18.32. $C_{14}H_7ClF_2N_4$. Calculated, %: C 55.19; H 2.32; N 18.39.

2-(5,6-Difluoro-1*H*-benzimidazol-2-yl)-3*H*-imidazo[4,5-*b*]pyridine (XIc). Yield 60%, mp 246–248°C. ^{1}H NMR spectrum, δ, ppm: 7.8 m, 8.0 m, and 8.15 m (1H each, 4-H, 5-H, 6-H); 8.4 m (2H, H_{arom}); 11.15 s and 12.0 s (1H each, NH). Mass spectrum: *m*/*z* 271 $[M]^+$. Found, %: C 57.51; H 2.71; N 25.88. $C_{13}H_7F_2N_5$. Calculated, %: C 57.57; H 2.60; N 25.82.

2-Chloromethyl-5,6-difluoro-1*H*-benzimidazole (XII). A mixture of 0.5 mmol of 4,5-difluorobenzene-1,2-diamine and 0.74 mmol of chloroacetic acid in 0.7 ml of concentrated hydrochloric acid was heated for 5 h under reflux. The mixture was cooled to 0°C and carefully neutralized to pH 7 by adding aqueous ammonia, and the precipitate was filtered off and washed with a small amount of ice water (3×0.5 ml). Yield 60%, mp 166–168°C. ^{1}H NMR spectrum, δ, ppm: 4.9 s (2H, CH_2), 7.62 t (2H, H_{arom}, J = 9.12 Hz), 10.0 s (1H, NH). Mass spectrum: *m*/*z* 202 $[M]^+$. Found, %: C 47.34; H 2.58; N 13.71. $C_8H_5ClF_2N_2$. Calculated, %: C 47.43; H 2.49; N 13.83.

5,6-Difluoro-1*H*-benzimidazole-2-carbothioamides XIVa–XIVc, XIa, and XV (*general procedure*). A mixture of 1.4 mmol of sulfur and 0.94 mmol of amine **XIIIa**–**XIIIc**, **VIIa**, or **VIIb**, in 1 ml of DMF was kept for 30 min, 0.2 mmol of compound **XII** was added, and the mixture was left to stand for 3 h at room temperature and poured into water. The precipitate was filtered off, washed with water, and dissolved in acetone, the solution was separated from the undissolved material, the solvent was removed under reduced pressure, and the solid residue was recrystallized from ethyl acetate or ethanol.

5,6-Difluoro-2-(morpholinocarbonothioyl)-1*H*-benzimidazole (XIVa). Yield 63%, mp 243–245°C. ^{1}H NMR spectrum, δ, ppm: 3.72 t (2H, J = 4.66 Hz), 3.83 t (2H, J = 4.84 Hz), 4.20 t (2H, J = 4.64 Hz), 4.35 t (2H, J = 4.77 Hz), 7.55 m (1H, H_{arom}), 7.75 m (1H, H_{arom}), 13.10 s (1H, NH). Mass spectrum: *m*/*z* 283 $[M]^+$. Found, %: C 50.96; H 3.78; N 14.72. $C_{12}H_{11}F_2N_3OS$. Calculated, %: C 50.88; H 3.91; N 14.83.

5,6-Difluoro-*N*-phenyl-1*H*-benzimidazole-2-carbothioamide (XIVb). Yield 60%, mp 103–105°C. ^{1}H NMR spectrum, δ, ppm: 7.35–7.94 m (7H, H_{arom}), 12.33 s (1H, NH), 13.2 s (1H, NH). Mass spectrum: *m*/*z* 289 $[M]^+$. Found, %: C 58.03; H 3.30; N 14.65. $C_{14}H_9F_2N_3S$. Calculated, %: C 58.12; H 3.14; N 14.52.

5,6-Difluoro-*N*-(pyridin-2-yl)-1*H*-benzimidazole-2-carbothioamide (XIVc). Yield 58%, mp 249–251°C. ^{1}H NMR spectrum, δ, ppm: 7.1 m, 7.75 m, 7.8 m, and 7.9 m (1H each, pyridine); 8.2 m (2H, H_{arom}); 9.4 s and 10.2 s (1H each, NH). Mass spectrum: *m*/*z* 290 $[M]^+$. Found, %: C 53.88; H 2.64; N 19.42. $C_{13}H_8F_2N_4S$. Calculated, %: C 53.79; H 2.78; N 19.30.

5,6-Difluoro-1*H*,1′*H*-2,2′-bibenzimidazole (XIa). Yield 65%, mp 197–199°C. ^{1}H NMR spectrum, δ, ppm: 7.25 m (2H, H_{arom}), 7.4 m (2H, H_{arom}), 7.5 m (2H, H_{arom}), 11.55 s (1H, NH), 12.3 s (1H, NH). Mass spectrum: *m*/*z* 270 $[M]^+$. Found, %: C 62.27; H 2.82; N 20.61. $C_{14}H_8F_2N_4$. Calculated, %: C 62.22; H 2.98; N 20.73.

2-(5,6-Difluoro-1*H*-benzimidazol-2-yl)-1,3-benzoxazole (XV). Yield 60%, mp 265–267°C. ^{1}H NMR spectrum, δ, ppm: 6.9 m (1H, H_{arom}), 7.05 m (1H, H_{arom}), 7.15 m (1H, H_{arom}), 7.5 m (1H, H_{arom}), 7.9 m (1H, H_{arom}), 8.8 m (1H, H_{arom}), 10.7 s (1H, NH). Mass spectrum: *m*/*z* 271 $[M]^+$. Found, %: C 62.07; H 2.64; N 15.43. $C_{14}H_7F_2N_3O$. Calculated, %: C 62.00; H 2.60; N 15.49.

Indoloquinoxalines XVIIa–XVIId (*general procedure*). Compound **XVIa**–**XVId**, 1 mmol, was mixed with 1 mmol of diamine **II**, a small amount of acetic acid was added, and the mixture was heated for 30–60 min. The mixture was then poured into water, and the precipitate was filtered off, washed with water, dried, and purified by thin-layer chromatography using petroleum ether–ethyl acetate (3:2) as eluent.

2,3-Difluoro-6*H*-indolo[2,3-*b*]quinoxaline (XVIIa). Yield 60%, mp 198–200°C. ^{1}H NMR spectrum, δ, ppm: 7.38 t (1H, H_{arom}, J = 7.50 Hz), 7.61 d (1H, H_{arom}, J = 8.08 Hz), 7.74 t (1H, H_{arom}, J = 7.70 Hz), 8.08 m (1H, H_{arom}), 8.27 m (1H, H_{arom}), 8.34 d (1H, H_{arom}, J = 7.78 Hz), 12.15 s (1H, NH). Mass spectrum: *m*/*z* 255 $[M]^+$. Found, %: C 65.81; H 2.82; N 16.39. $C_{14}H_7F_2N_3$. Calculated, %: C 65.88; H 2.76; N 16.46.

2,3-Difluoro-6-methyl-6*H*-indolo[2,3-*b*]quinoxaline (XVIIb). Yield 75%, mp 202–203°C. ^{1}H NMR spectrum, δ, ppm: 3.89 s (3H), 7.41 t (1H, H_{arom}, J = 7.35 Hz), 7.72 d (1H, H_{arom}, J = 8.14 Hz), 7.78 t (1H, H_{arom}, J = 7.61 Hz), 8.04 m (1H, H_{arom}), 8.21 m (1H, H_{arom}), 8.32 d (1H, H_{arom}, J = 7.66 Hz). Mass spectrum: *m*/*z* 269 $[M]^+$. Found, %: C 66.97; H 3.27; N 15.70. $C_{15}H_9F_2N_3$. Calculated, %: C 66.91; H 3.37; N 15.61.

6-Butyl-2,3-difluoro-6*H*-indolo[2,3-*b*]quinoxaline (XVIIc). Yield 65%, mp 144–145°C. ^{1}H NMR spectrum, δ, ppm: 0.95 s (3H), 1.35 s (2H), 1.85 s (2H), 4.50 s (2H), 7.43 m (1H, H_{arom}), 7.81 t (2H, H_{arom}, J = 6.54 Hz), 8.11 m (1H, H_{arom}), 8.27 m (1H, H_{arom}), 8.37 d (1H, H_{arom}, J = 7.68 Hz). Mass spectrum: *m*/*z* 311 $[M]^+$. Found, %: C 69.38; H 4.79; N 13.54. $C_{18}H_{15}F_2N_3$. Calculated, %: C 69.44; H 4.86; N 13.50.

9-Bromo-6-ethyl-2,3-difluoro-6*H*-indolo[2,3-*b*]-quinoxaline (XVIId). Yield 60%, mp 216–217°C. ^{1}H NMR spectrum, δ, ppm: 1.43 s (3H), 4.55 s (2H), 7.82 d (1H, H_{arom}, J = 8.68 Hz), 7.93 m (1H, H_{arom}), 8.12 m (1H, H_{arom}), 8.24 m (1H, H_{arom}), 8.45 m (1H, H_{arom}). Mass spectrum: *m*/*z* 362 $[M]^+$. Found, %: C 53.12; H 2.71; N 11.69. $C_{16}H_{10}BrF_2N_3$. Calculated, %: C 53.06; H 2.78; N 11.60.

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