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Fluorocontaining Heterocycles: IX.* Derivatives of Imidazo[2,1-*b*][1,3]benzothiazine

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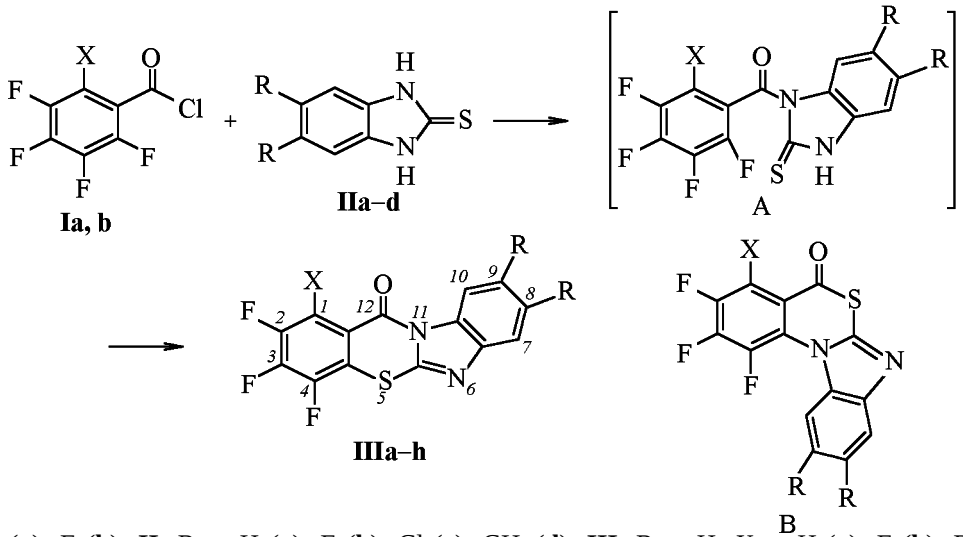
Abstract—The heating of derivatives of benzimidazole-2-thione and imidazolidine-2-thione with tetra(penta)fluorobenzoyl chlorides in toluene or pyridine gave rise to fluorocontaining derivatives of imidazo[2,1-*b*][1,3]benzothiazine. The latter were studied in reactions of nucleophilic substitution of fluorine for amino groups.

Recently polycyclic fluorocontaining derivatives of azaheterocycles are extensively studied due to their versatile biological activity [2–10]. In this connection we were interested in the synthesis and investigation of fluorocontaining derivatives of imidazo[2,1-*b*]-[1,3]benzothiazine. In the literature appeared individual examples of preparation of benzimidazothiazinone derivatives from benzothiazine-2-thione and aromatic diamines [11], benzimidazole-2-thione and derivatives of 2-chlorobenzoic or 2-chloronicotinic acids [12, 13], and also by rearrangement of [3,4-*b*]benzodiazepines [14]. A single publication concerned fluorocontaining fused benzoderivatives of imidazo[2,1-*b*][1,3]benzothiazine prepared from pentafluorobenzoyl chloride and benzimidazole-2-thione under catalysis with bases [15].

In extension of studies on intramolecular cyclization of polyfluorobenzoic acids derivatives containing moieties capable of prototropic tautomerism we investigated acylation of benzimidazole-2-thione (**II**) derivatives with polyfluorobenzoyl chlorides (**I**). We presumed that N-acyl derivatives (A) would be capable of intramolecular cyclization to provide fluorinated benzo[*e*]benzo[4,5]imidazo[2,1-*b*][1,3]-thiazine-12-ones (**III**) (Scheme 1).

Scheme 1.



I, X = H (**a**), F (**b**); **II**, R = H (**a**), F (**b**), Cl (**c**), CH_3 (**d**); **III**, R = H, X = H (**a**), F (**b**), R = F, X = H (**c**), F (**d**), R = Cl, X = H (**e**), F (**f**), R = CH_3, X = H (**g**), F (**h**).

* For communication VIII see [1].

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Table 1. Data of ^{1}H, ^{19}F NMR and mass spectra of compounds **III**

Compd. no.	The chemical shifts of aromatic protons, δ, ppm, in ^{1}HNMR spectra in DMSO-d_6; coupling constants, J, Hz		Chemical shifts, δ_F, ppm, in ^{19}F NMR spectra in DMSO-d_6; coupling constants, J, Hz				Mass spectrum, m/z (I_{rel}, %)
	H^1	H^7–H^{10}	F^1	F^2	F^3	F^4	
IIIa	8.34 d.d.d ^3J 10.7, ^4J 7.3, ^5J 1.2	7.50 m (2H, H^8, H^9), 7.76 m (1H, H^{10}), 8.48 m (1H, H^7)	–	134.17 d.d.d ^3J 22.6, ^3J 10.7, ^4J 5.6	150.22 d.d.d ^3J 22.5, ^3J 20.9, ^4J 7.3	133.35 d.d.d ^3J 20.8, ^4J 5.6, ^5J 1.5	306 (100) [M^+], 274 (10), 190 (13), 162 (9)
IIIb	–	7.53 m (2H, H^8, H^9), 7.75 m (1H, H^{10}), 8.41 m (1H, H^7)	145.84 d.d ^3J 21.5, ^4J 11.4	138.39 d.d.d ^3J 21.5, ^3J 22.7, ^4J 9.2	156.46 d.d.d ^3J 22.7, ^3J 21.7, ^4J 11.4	135.26 d.d ^3J 21.7, ^4J 9.2	324 (100) [M^+], 292 (9), 208 (13), 148 (9), 162 (10)
IIIc[a]	8.38 d.d.d ^3J 10.6, ^4J 7.4, ^5J 1.5	7.95 d.d (1H, H^{10}, ^3J 10.4, ^4J 7.3), 8.40 d.d (1H, H^7, ^3J 10.4, ^4J 7.6)	–	134.40 d.d.d ^3J 22.6, ^3J 10.6, ^4J 5.8	149.56 d.d.d ^3J 22.5, ^3J 21.2, ^4J 7.4	133.13 d.d.d ^3J 21.0, ^4J 5.7, ^5J 1.5	342 (100) [M^+], 310 (18), 236 (11), 174 (12)
IIId[b]	–	7.93 d.d (1H, H^{10}, ^3J 10.7, ^4J 7.3), 8.39 d.d (1H, H^7, ^3J 10.4, ^4J 7.6)	145.19 d.d ^3J 21.6, ^4J 11.4	138.10 d.d.d ^3J 21.6, ^3J 22.8, ^4J 9.6	156.03 d.d.d ^3J 22.8, ^3J 21.1, ^4J 11.4	135.11 d.d ^3J 21.1, ^4J 9.6	360 (100) [M^+], 332 (10), 328 (18), 208 (10), 192 (13), 180 (17), 148 (10)
IIIe	8.44 m	8.15 s (1H, H^{10}), 8.62 s (1H, H^7)	–	134.15 d.d.d ^3J 22.6, ^3J 10.5, ^4J 5.9	149.31 d.d.d ^3J 22.3, ^3J 21.2, ^4J 7.2	132.97 d.d.d ^3J 21.0, ^4J 6.0, ^5J 2.1	376 (69), 374 (100) [M^+], 339 (12), 342 (8), 190 (18)
IIIf	–	8.12 s (1H, H^{10}), 8.58 s (1H, H^7)	144.87 d.d ^3J 21.7, ^4J 11.4	137.90 d.d.d ^3J 21.9, ^3J 22.8, ^4J 8.8	155.70 d.d.d ^3J 22.4, ^3J 21.8, ^4J 11.4	134.96 d.d ^3J 21.3, ^4J 8.8	394 (68), 392 (100) [M^+], 360 (8), 357 (14), 208 (19), 180 (11), 148 (11)
IIIg[c]	7.59 m	7.59 s (1H, H^{10}), 9.34 s (1H, H^7)	–	134.15 d.d.d ^3J 22.8, ^3J 10.7, ^4J 5.5	150.47 d.d.d ^3J 22.4, ^3J 21.3, ^4J 7.8	133.46 d.d.d ^3J 21.0, ^4J 5.8, ^5J 2.2	334 (100) [M^+], 335 (21), 333 (39), 319 (45), 305 (4), 302 (2), 190 (5), 167 (7)
IIIh[d]	–	7.48 s (1H, H^{10}), 9.34 s (1H, H^7)	146.35 d.d ^3J 21.5, ^4J 11.6	138.50 d.d.d ^3J 21.5, ^3J 22.6, ^4J 9.6	156.03 d.d.d ^3J 22.6, ^3J 21.4, ^4J 11.6	135.44 d.d ^3J 21.4, ^4J 9.6	352 (100) [M^+], 351 (35), 337 (45), 323 (4), 320 (2), 176 (11)

Chemical shifts of F^8 and F^9:

[a] 140.63 d.d.d (1F, ^3J 21.8, ^3J 10.4, ^4J 7.4); 139.11 d.d.d (1F, ^3J 21.8, ^3J 10.6, ^4J 7.6).

[b] 140.43 d.d.d (1F, ^3J 21.8, ^3J 10.4, ^4J 7.4); 139.04 d.d.d (1F, ^3J 21.8, ^3J 10.6, ^4J 7.6).

[c] Chemical shifts of groups CH_3: 2.29 s (6H, $2CH_3$).

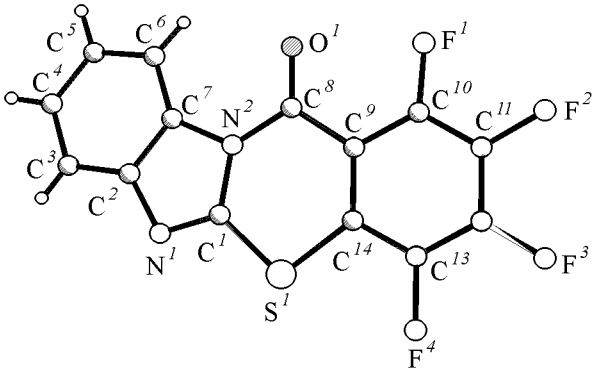
[d] 2.40 s (3H, CH_3), 2.42 s (3H, CH_3).

Actually the heating of acyl chlorides **I** with thiones **IIa–d** for 2–3 h afforded tetracyclic derivatives **III** in 67–94% yield; therewith under these conditions we failed to isolate the intermediate N-acylated benzimidazolethiones (**A**).

For establishing the structure of compounds **III** we studied their ^{1}H and ^{19}F NMR and mass spectra (Table 1).

In the ^{1}H NMR spectra of compounds **III** the protons of the benzimidazole moiety appear as multiplets (**IIIa, b**), doublets (**IIIc, d**), or singlets (**IIIe–h**). As to the fluoroarene moiety, in the spectra of derivatives **IIIa, c, e, g** the proton signal from H^1 is observed as doublet of doublet of doublets (**IIIa, c**) or multiplet (**IIIe, g**) in the 7.6–8.4 ppm region. No signals from NH groups appear in the ^{1}H NMR spectra of compounds **IIIa–h**, and the number of signals in the ^{19}F NMR spectra is equal to the number of fluorine atoms in the respective molecules (Table 1) in agreement with their structure. It should be noted that the maximal abundance of molecular ions M^+ (100%) in the mass spectra of compounds **IIIa–h** corresponds to their aromatic nature. Besides the molecular ions in the mass spectra of compounds **III** are present peaks $[M–S]^+$, and in the spectra of compounds **IIIg, h** also peaks originating from methyl group rupture from M^+ (Table 1).

Since we synthesized tetracyclic compounds **III** under other conditions than described in [15] it was necessary to establish whether they have linear structure **III** or angular (B). The alternative structure (B) that might arise as a result of S-acylation of the ambidental benzimidazole-2-thiones was rejected basing on the data of the X-ray diffraction study. According to these data (see figure) compound **IIIb** is a linear tetracyclic system build up by fusion along the $C^{1}–N^{2}$ bond of benzimidazole and benzothiazine fragments; therewith all the atoms lie actually in the same plane (mean deviation is 0.02 Å). Coordinates of atoms are listed in Table 2.

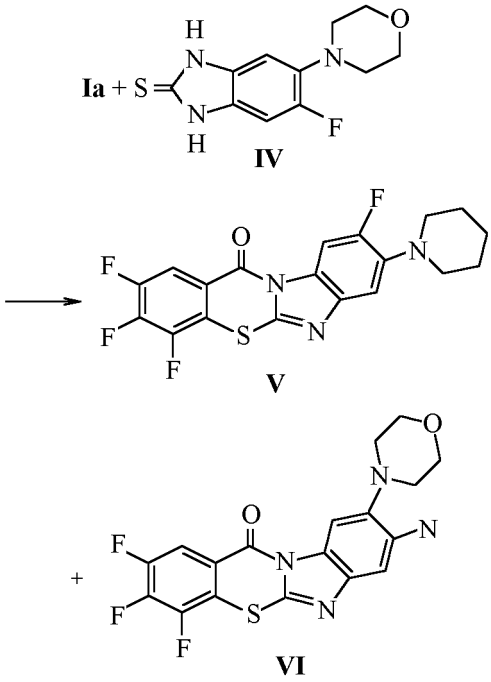


Structure of compound **IIIb**.

Note the readiness of benzothiazine fragment formation through intramolecular substitution of fluorine atom by S-nucleophile (in toluene without addition of base for scavenging HF). Previously under similar conditions were obtained derivatives of 1,3,4-thiadiazino[6,5,4-*i*,*j*]quinoline from 2-(polyfluorobenzoyl)acrylates containing thiosemicarbazide rests in position *3* [5].

We were interested how would behave in this reaction unsymmetrical benzimidazole-2-thiones. To this end we studied the reaction of 5-fluoro-6-(morpholin-4-yl)benzimidazole-2-thione (**IV**) with tetrafluorobenzoyl chloride (**Ia**) in toluene at heating for 2 h (Scheme 2).

Scheme 2.



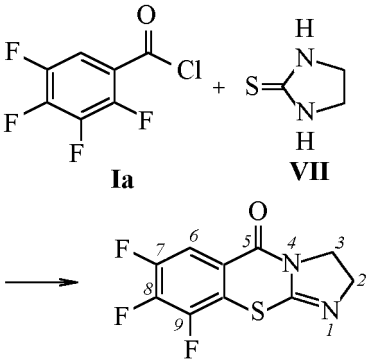
According to ^{1}H NMR data the reaction is nonselective and gives rise to two isomers **V** and **VI** in 7:3 (or 3:7) ratio. We failed to separate the components either by fractional crystallization or by chromatography.

A reaction was also studied between tetrafluorobenzoyl chloride (**I**) and 2-imidazolidinethione (**VII**). The reaction was carried out in pyridine at 80°C for 40 min (Scheme 3). As a result was obtained in 67% yield imidazo[2,1-*b*][1,3]benzothiazin-5-one (**VIII**) whose structure was confirmed by ^{1}H, ^{19}F NMR and mass spectra (see EXPERIMENTAL).

Table 2. Coordinates of atoms ($\times 10^4$) in fractions of unit cell axes in the molecule od compound **IIIb**

Atom	*x*	*y*	*z*
S^1	5249(1)	−3128(1)	−812(1)
F^1	7750(2)	4117(2)	−1625(1)
F^2	6226(2)	3039(3)	−2561(1)
F^3	4308(2)	−812(3)	−2702(1)
F^4	3974(2)	−3586(3)	−1874(1)
O^1	8451(2)	3174(3)	−623(1)
N^1	6436(2)	−2900(3)	201(1)
N^2	7320(2)	81(3)	−266(1)
C^1	6398(2)	−1950(3)	−260(1)
C^2	7453(2)	−1454(4)	538(1)
C^3	7885(3)	−1644(4)	1081(1)
C^4	8864(3)	74(5)	1331(1)
C^5	9403(3)	1934(4)	1053(1)
C^6	9011(3)	2151(4)	511(1)
C^7	8014(2)	418(4)	263(1)
C^8	7566(2)	1503(3)	−692(1)
C^9	6677(2)	821(3)	−1215(1)
C^{10}	6828(3)	2200(4)	−1657(1)
C^{11}	6039(3)	1672(4)	−2149(1)
C^{12}	5072(3)	−288(5)	−2223(1)
C^{13}	4913(3)	−1666(4)	−1799(1)
C^{14}	5682(2)	−1164(3)	−1294(1)

Scheme 3.

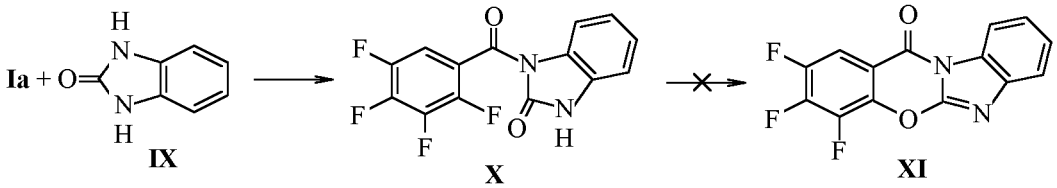


Ia **VII** **VIII**

The reaction of acyl chloride **Ia** with benzimidazolone **IX** in pyridine afforded an N-acyl derivative **X** that unlike its thioanalog was easily isolated and characterized by spectral methods (see EXPERIMENTAL), but we failed to convert it into a fused system **XI** by heating in the presence of various bases (K_2CO_3, KF, LiH, triethylamine, diazabicycloundec-7-ene) (Scheme 4).

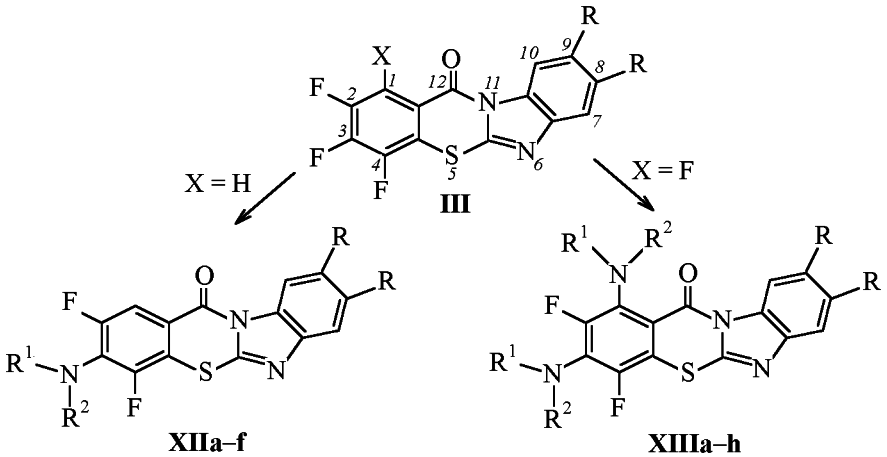
Tetracyclic compounds **III** were subjected to aminodefluorination (Scheme 5)

Scheme 4.



IX **X** **XI**

Scheme 5.



III **XIIa–f** **XIIIa–h**

XII, R = H, NR^1R^2 = pyrrolidin-1-yl (**a**), *N*,*N*-dimethyl-1,3-propanediamin-1-yl (**b**), 4-(morpholin-4-yl)propanamino (**c**), 4-methylpiperidin-1-yl (**d**); R = F, NR^1R^2 = pyrrolidin-1-yl (**e**), 4-(morpholin-4-yl)propanamino (**f**). **XIII**, R = H, NR^1R^2 = 4-(morpholin-4-yl)propanamino (**a**), 4-methylpiperidin-1-yl (**b**), 4-ethoxycarbonylpiperazin-1-yl (**c**), *N*,*N*-dimethyl-1,3-propanediamin-1-yl (**d**), R = F, NR^1R^2 = 4-(morpholin-4-yl)propanamino (**e**); R = Cl, NR^1R^2 = 4-(morpholin-4-yl)propanamino (**f**), *N*,*N*-dimethyl-1,3-propanediamin-1-yl (**g**); R = CH_3, NR^1R^2 = 4-(morpholin-4-yl)propanamino (**h**).

Table 3. Data of ^{1}H NMR and mass spectra of compounds **XII**

Compd. no.	Chemical shifts, δ, ppm, in ^{1}H NMR spectra in DMSO-d_6; coupling constants, J, Hz			Mass spectrum, m/z
	H^1	H^7–H^{10}	NR^1R^2	
XIIa	7.93 d (^3J 14.7)	7.46 m (2H, H^8, H^9), 7.71 m (1H, H^{10}), 8.46 m (1H, H^7)	1.92 m [4H, $(CH_2)_2$], 3.74 m [4H, $N(CH_2)_2$]	$_{357}$ (100) [M^+], 356 (72), 301 (19), 287 (19), 315 (13), 178 (13)
XIIb	7.89 d.d (^3J 12.8, ^5J 1.3)	7.43 m (2H, H^8, H^9), 7.69 m (1H, H^{10}), 8.42 m (1H, H^7)	1.72 m (2H, CH_2), 2.15 s [6H, $N(CH_3)_2$], 2.31 m (2H, CH_2), 3.47 m (2H, CH_2), 7.1 br.s (1H, NH)	388 (9) [M^+], 331 (1), 330 (1), 323 (2), 316 (2), 303 (1), 85 (6), 72 (3), 59 (5), 58 (100)
XIIc	7.89 d.d (^3J 13.0, ^5J 1.2)	7.44 m (2H, H^8, H^9), 7.72 m (1H, H^{10}), 8.44 m (1H, H^7)	1.75 m (2H, CH_2), 2.34 m [4H, $N(CH_2)_2$], 2.39 m (2H, CH_2), 3.49 m (2H, CH_2), 3.57 m [4H, $O(CH_2)_2$], 7.1 br.s (1H, NH)	430 (10) [M^+], 330 (5), 316 (4), 127 (4), 114 (4), 101 (8), 100 (100), 56 (9)
XIId	8.02 d (^3J 12.7	7.49 m (2H, H^8, H^9), 7.78 m (1H, H^{10}), 8.47 m (1H, H^7)	0.97 d (3H, CH_3, ^3J 6.3), 1.2–1.4 m (2H, CH_2), 1.6 m (2H, CH), 1.7 m (2H, CH_2), 3.19 m (2H, NCH_2), 3.55 m (2H, NCH_2)	
XIIe	7.91 d (^3J 12.8	7.80 d.d (1H, H^{10}, ^3J 10.3, ^4J 7.1), 8.40 d.d (1H, H^7, ^3J 10.3, ^4J 7.2)	1.91 m [4H, $(CH_2)_2$], 3.76 m [4H, $N(CH_2)_2$]	393 (100) [M^+], 392 (78), 351 (10), 337 (25), 323 (20), 196 (14)
XIIf	8.20 m	7.7 m (2H)	1.74 m (2H, CH_2), 2.35–2.40 m [6H, CH_2, 2×$N(CH_2)_2$], 3.49 m (2H, CH_2), 3.57 m [4H, 2×$O(CH_2)_2$], 7.13 br.s (1H, NH)	466 (9) [M^+], 366 (3), 352 (3), 127 (3), 114 (4), 101 (8), 100 (100), 57 (5), 56 (10)

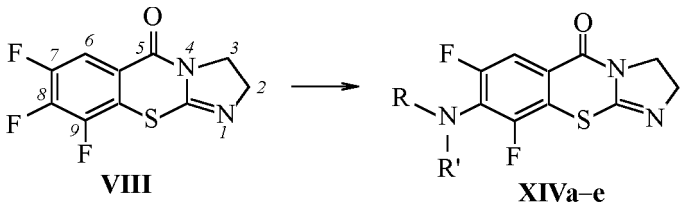
With trifluoro derivatives **III** (X = H) amination was performed in boiling dimethylformamide or pyridine for 4–5 h. Thus were obtained in 56–91% yield the products of fluorine substitution at C^3 **XII** whose structure was confirmed by ^{1}H NMR and mass spectra (Table 3). In the ^{1}H NMR spectra of compounds **XII** the signal of proton H^1 appeared in the region 7.9–8.2 ppm as a doublet of doublets with a *meta*-coupling constant ^3J of 11.5–13 Hz and ^5J of 1.2–1.8 Hz indicating unambiguously the position of remaining fluorine atoms. In the mass spectra of substituted imidazobenzothiazinones **XIIa, c, e**, same as in the spectra of compounds **III**, the peak of maximum intensity is M^+ (Table 3).

In a similar amination reaction of tetrafluorosubstituted derivatives **III** (Y = F) two fluorine atoms F^1 and F^3 are replaced by amino groups. This fact agrees well with the data of our previous studies on substitution of atoms F^8 and F^{10} by amino groups in derivatives of 1,3,4-thiadiazino[1,5,4-*i,j*]quinoline [16], and also with the published data on replacement of both atoms F^5 and F^7 by amino groups in esters of N^1-substituted tetrafluoro-3-quinolonecarboxylic acids [17]. In the ^{1}H NMR spectra of diamino derivatives **XIII** appear signals from two amino groups, and in the ^{19}F NMR spectrum of compound **XIIIb** are present signals from two fluorine atoms as doublets with a coupling constant ^4J 6.4 Hz corresponding to *meta*-location of fluorine atoms. The molecular ions and fragment ions in the mass spectra also are consistent with the assigned structure (Table 4).

At heating of derivative **VIII** with cycloalkylimines in DMF within 4–5 h atom F^8 underwent substitution by the amine rest (Scheme 6). The structures of imidazobenzothiazinones **XIV** obtained were confirmed by ^{1}H and ^{19}F NMR and mass spectra (Table 5).

Thus bringing polyfluorobenzoyl chlorides into reaction with ambidental N,S-nucleophiles resulted

Scheme 6.



VIII **XIVa–e**

XIV, NRR' = pyrrolidin-1-yl (**a**), morpholin-4-yl (**b**), 4-methylpiperidin-1-yl (**c**), 3-methylpiperidin-1-yl (**d**), 4-ethoxycarbonylpiperazin-1-yl (**e**).

Table 4. Data of ^{1}H NMR and mass spectra of compounds **XIII**

Compd. no.	Chemical shifts, δ, ppm, in ^{1}H NMR spectra in DMSO-d_6; coupling constants, J, Hz		Mass spectrum, m/z
	H^7–H^{10}	NR^1R^2	
XIIIa	7.36 m (2H, H^8, H^9), 7.63 m (1H, H^{10}), 8.36 m (1H, H^7)	1.72 m (4H, $2CH_2$), 2.35 m (4H, $2CH_2$), 2.38 m [8H, $2\times N(CH_2)_2$], 3.41 m (4H, $2CH_2$), 3.56 m [8H, $2\times O(CH_2)_2$], 6.8 br.s (1H, NH), 8.7 br.s (1H, NH)	572 (5) [M^+], 552 (3), 472 (3), 446 (5), 128 (15), 127 (100), 100 (100), 112 (34), 120 (10)
XIIIb	7.42 m (2H, H^8, H^9), 7.70 m (1H, H^{10}), 8.44 m (1H, H^7)	0.98 m (6H, $2CH_3$), 1.29 m (4H, $2CH_2$), 1.67 m (8H, $2CH_2$, 2CH), 3.16 m (4H, $2\times NCH_2$), 3.49 m (4H, $2\times NCH_2$)	482 (100) [M^+], 481 (19), 453 (21), 439 (16), 386 (19), 385 (46), 384 (47), 241 (26), 98 (71), 56 (14), 55 (19)
XIIIc	7.42 m (2H, H^8, H^9), 7.70 m (1H, H^{10}), 8.46 m (1H, H^7)	1.2 m (6H, $2CH_3$), 3.25 m [4H, $N(CH_2)_2$], 3.27 m [4H, $N(CH_2)_2$], 3.5 m [8H, $2\times N(CH_2)_2$], 4.1 m (4H, $2\times OCH_2$)	600 (11) [M^+], 499 (30), 498 (100), 472 (18), 56 (39)
XIIId	7.35 m (2H, H^8, H^9), 7.61 m (1H, H^{10}), 8.43 m (1H, H^7)	1.74 m (4H, $2CH_2$), 2.19 s [12H, $2\times N(CH_3)_2$], 2.37 m (4H, $2CH_2$), 3.48 m (4H, $2CH_2$), 6.84 br.s (1H, NH), 8.81 br.s (1H, NH)	488 (5) [M^+], 404 (12), 86 (36), 85 (100), 84 (40), 70 (37), 58 (100)
XIIIe	7.69 d.d (1H, H^{10}, ^3J 10.8, ^4J 7.7), 8.20 d.d (1H, H^7, ^3J 10.7, ^4J 7.9)	1.73 m (4H, $2CH_2$), 2.38 m [12H, $2CH_2$, $2\times N(CH_2)_2$], 3.44 m (4H, $2CH_2$), 3.59 m [8H, $2\times O(CH_2)_2$], 6.9 br.s (1H, NH), 8.6 br.s (1H, NH)	608 (6) [M^+], 588 (3), 578 (2), 577 (3), 558 (2), 508 (1), 387 (2), 127 (90), 112 (32), 100 (100)
XIIIf	7.77 s (1H, H^{10}), 8.40 s (1H, H^7)	1.71 m (4H, $2CH_2$), 2.37 m [12H, $2CH_2$, $2\times N(CH_2)_2$], 3.39 m (4H, $2CH_2$), 3.60 m [8H, $2\times O(CH_2)_2$], $_{6.94}$br.s ($_1$H, NH), $_{8.41}$br.s ($_1$H, NH)	640 (5) [M^+], 622 (2), 620 (2), 611 (2), 609 (3), 540 (2), $_{128}$ (23), 127 (100), 112 (55), 100 (100), 56 (29)
XIIIg	7.78 s(1H, H^{10}), 8.26 s (1H, H^7)	1.71 m (4H, $2CH_2$), 2.16 s [6H, $N(CH_3)_2$], 2.17 s [6H, $N(CH_3)_2$], 2.31 m (4H, $2CH_2$), 3.35 m (4H, $2CH_2$), 6.92 br.s (1H, NH), 8.49 br.s (1H, NH)	558 (15) [M^+], 556 (24), 538 (23), 536 (21), 502 (16), 501 (21), 500 (72), 499 (27), 498 (100), 492 (36), 478 (33), 472 (34), 458 (48), 452 (71), 450 (97), 421 (55), 419 (65), 407 (56)
XIIIh[a]	7.37 s (1H, H^{10}), 8.09 s (1H, H^7)	1.72 m (4H, $2CH_2$), 2.2–2.4 m [16H, $4CH_2$, $2\times N(CH_2)_2$], 3.40 m (4H, $2CH_2$), 3.58 m [8H, $2\times O(CH_2)_2$], 6.8 br.s (1H, NH), 8.7 br.s (1H, NH)	598 (1) [M^+], 580 (2), 500 (3), 475 (3), 474 (9), 423 (2), 128 (13), 127 (89), 112 (98), 100 (100)

[a] δ(CH_3): 2.54 s (6H).

in the synthesis of a series of new fluorocontaining polycyclic azaheterocycles interesting for biological tests.

EXPERIMENTAL

^{1}H and ^{19}F NMR spectra were registered on spectrometers Bruker WH-250 and DRX-400 at respective operating frequencies 250 MHz for protons and 376 MHz for fluorine, solvent DMSO-d_6, internal references for proton spectra TMS, for fluorine spectra hexafluorobenzene. Mass spectra were obtained on Varian MAT 311A instrument, accelerating voltage 3 kV, emission cathode current 300μA, direct admission of the sample into the ion source.

X-ray diffraction study on a single crystal of compound **IIIb** was performed on an automatic diffractometer "Inraf-Nonius, Cad-4" (λMoK_α radiation, graphite monochromator, omega-scanning, $2\tau_{max}$ 54°, 3920 reflections, among them 2603 with $F^2 >$

Table 5. Spectral characteristics of compounds **XIV**

Compd. no.	Chemical shifts, δ, ppm, in ^{1}H NMR spectra in DMSO-d_6; coupling constants, *J*, Hz			Mass spectrum, *m/z*
	H^6	$^2CH_2$, $^3CH_2$	NR^1R^2	
XIVa[a]	7.53 d.d ^3J 14.7, ^5J 1.8	3.90 m (4H)	1.86 m [4H, $(CH_2)_2$], 3.62 m [4H, $N(CH_2)_2$]	309 (100) [M^+], 308 (93), 267 (13), 253 (19), 68 (23)
XIVb	7.66 d.d ^3J 12.8, ^5J 1.8	3.92 m (4H)	3.29 m [4H, $N(CH_2)_2$], 3.70 m [4H, $O(CH_2)_2$]	325 (100) [M^+], 324 (10), 268 (16), 267 (68), 266 (79), 200 (12), 199 (25), 120 (14), 68 (37)
XIVc	7.62 d.d ^3J 12.8, ^5J 1.8	3.92 m (4H)	0.95 d (3H, CH_3, ^3J 6.4), 1.23 m (2H, CH_2), 1.55 m (1H, CH), 1.67 m (2H, CH_2), 3.12 m (2H, CH_2), 3.39 m (2H, CH_2)	337 (100) [M^+], 336 (98), 282 (15), 268 (21), 266 (26), 68 (20), 55 (15)
XIVd	7.68 d.d ^3J 12.9, ^5J 1.9	3.93 m (4H)	0.95 d (3H, CH_3, ^3J 6.3), 1.2 (1H, CH), 1.6–1.8 m [4H, $(CH_2)_2$], 2.75 m (1H, CH), 3.04 m (1H, CH), 3.49 m (2H, NCH_2)	337 (100) [M^+], 336 (64), 283 (12), 282 (74), 268 (12), 267 (12), 266 (27), 199 (10), 68 (19)
XIVe	7.68 d.d ^3J 12.7, ^5J 1.9	3.93 m (4H)	1.2 m (3H, CH_3), 3.25 m [4H, $N(CH_2)_2$], 3.93 m [4H, $N(CH_2)_2$], 4.07 q (4H, OCH_2)	397 (21) [M^+], 396 (100), 381 (23), 295 (16), 294 (70), 282 (76), 281 (28), 268 (19), 267 (15), 266 (32), 253 (15), 115 (18), 68 (24), 56 (94)

[a] Chemical shifts, δ_F, ppm, in ^{19}F NMR spectra (in DMSO-d_6): 126.58 m (1F), 125.73 m (1F).

2σ(**I**)). The crystals were grown by slow evaporation at room temperature of a solution of compound **IIIb** in toluene saturated at heating. $C_{14}H_4F_4N_2OS$, mononoclinic crystals, *a* 8.1510(16) Å, *b* 5.7770(12) Å, *c* 25.523(5) Å, α 90°, β 97.31(3)°, γ 90°, *V* 1192.1(4) Å^3, d_{calc} 1.807 g/cm^3, *Z* 4, space group P2(1)/*n*. The structure was solved by the direct method and refined by the least-squares procedure with the use of SHELXS-97 and SHELXL-97 software in anisotropic (isotropic for hydrogen atoms) approximation till R 0.0401 (wR2 0.111) for 2603 reflection with $F^2 > 2\sigma(\mathbf{I})$, at the value of fitting factor GOOF 1.056. The final coordinate of atoms are given in Table 2.

Tetra(penta)benzoyl chlorides (**I**) were obtained by treating the corresponding polyfluorinated benzoic acids with thionyl chloride in toluene. Thiones **II** were prepared by thionating benzimidazoles [18] or by reaction of *o*-phenylenediamine derivatives with carbon disulfide [3].

1-X-2,3,4-Trifluoro-6*a*,10*a*-dihydro-8-R-9-R-12*H*-benzo[*e*]benzo[4,5]imidazo[2,1-*b*]-[1,3]thiazin-12-ones (III). To 1.2 g (8 mmol) of benzimidazole-2-thione (**IIa**) in 15 ml of anhydrous toluene was added 1.8 ml (2.55 g, 12 mmol) of tetrafluorobenzoyl chloride (**Ia**). The reaction mixture was boiled for 2 h and then cooled. The separated precipitate of compound **IIIa** was filtered off and recrystallized from DMSO. Yield 2.2 g (90%). Compounds **IIIb–h** were obtained in a similar way. Yields, melting points, and elemental analyses of compounds **III** are listed in Table 6.

2,3,4,9-Tetrafluoro-6*a*,10*a*-dihydro-8-(morpholin-4-yl)-12*H*-benzo[*e*]benzo[4,5]imidazo-[2,1-*b*]-[1,3]thiazin-12-one (V) and 2,3,4,8-tetrafluoro-6*a*,10*a*-dihydro-9-(morpholin-4-yl)-12*H*-benzo[*e*]-benzo[4,5]imidazo[2,1-*b*][1,3]thiazin-12-one (VI). To 0.5 g (2 mmol) of 5-fluoro-6-(morpholin-4-yl) benzimidazole-2-thione (**IV**) in 10 ml of anhydrous toluene was added 1 ml (6 mmol) of tetrafluorobenzoyl chloride (**Ia**). The reaction mixture was boiled for 3.5 h and then cooled. The separated bright yellow precipitate was filtered off and recrystallized from DMSO to afford a mixture of compounds **V** and **VI** in 7 : 3 (or 3 : 7) ratio. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.08 m [4H, $N(CH_2)_2$], 3.81 m [4H, $O(CH_2)_2$], 7.4 d [H^{10} (**VI**) or H^7 (**V**), ^4J 7.9], 7.6 d [H^{10} (V) or H^7 (**VI**), ^3J 12.5], 8.1 d [H^7 (V) or H^{10} (**VI**), ^4J 7.9], 8.2 d [H^7 (**VI**) or H^{10} (**V**), ^3J 12.5], 8.4 m [H^1 (**V** and **VI**)].

7,8,9-Trifluoro-2,3-dihydro-5*H*-benzo[4,5]-imidazo[2,1-*b*][1,3]thiazin-5-one (VIII). To 0.8 g

Table 6. Yields, melting points, and elemental analyses of compounds synthesized

Compd. no.	mp, °C (solvent for crystallization)	Yield, %	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIIa	224–226 (DMSO)	90	55.00	1.30	9.19	$C_{14}H_5F_3N_2OS$	54.91	1.65	9.15
IIIb	174–176 (DMSO)	88	51.86	1.54	8.70	$C_{14}H_4F_4N_2OS$	51.86	1.24	8.64
IIIc	209–211 (DMSO)	84	49.34		8.36	$C_{14}H_3F_5N_2OS$	49.13	0.88	8.18
IIId	205–207 (DMSO)	84	46.85		8.04	$C_{14}H_2F_6N_2OS$	46.68	0.56	7.78
IIIe	264–266 (DMSO)	94	44.83		7.40	$C_{14}Cl_2H_3F_3N_2OS$	44.82	0.80	7.47
IIIf	210–212 (DMSO)	82	42.95		7.16	$C_{14}Cl_2H_2F_4N_2OS$	42.76	0.51	7.12
IIIg	270–272 (DMSO)	82	57.61	2.52	8.19	$C_{16}H_9F_3N_2OS$	57.48	2.71	8.38
IIIh	206–208 ($CHCl_3$)	67	54.76	2.19	7.91	$C_{16}H_8F_4N_2OS$	54.55	2.29	7.95
VIII	135–137 (ethanol)	67	46.69	2.08	10.71	$C_{10}H_5F_3N_2OS$	46.51	1.95	10.85
X	233–235 (ethanol)	62	54.35	2.12	8.86	$C_{14}H_6F_4N_2O_2$	54.21	1.95	9.03
XIIa	248–250 (DMSO)	91	60.33	4.19	11.84	$C_{18}H_{13}F_2N_3OS$	60.50	3.67	11.76
XIIb	140–142 (ethanol)	79	58.69	5.10	14.50	$C_{19}H_{18}F_2N_4OS$	58.75	4.67	14.42
XIIc	178–180 (DMSO)	65	58.48	4.66	13.20	$C_{21}H_{20}F_2N_4O_2S$	58.59	4.68	13.02
XIId	176–178 (DMSO)	56	62.54	4.28	10.76	$C_{20}H_{17}F_2N_3OS$	62.33	4.44	10.90
XIIe	278–280 (DMSO)	85	54.78	2.72	10.77	$C_{18}H_{11}F_4N_3OS$	54.96	2.82	10.68
XIIf	201–203 (DMSO)	67	53.88	4.05	11.91	$C_{21}H_{18}F_4N_4O_2S$	54.07	3.89	12.01
XIIIa	153–155 (DMSO)	67	58.62	5.64	14.81	$C_{28}H_{34}F_2N_6O_3S$	58.73	5.98	14.67
XIIIb	193–195 (DMSO)	92	64.55	5.69	11.78	$C_{26}H_{28}F_2N_4OS$	64.71	5.85	11.61
XIIIc	188–190 (DMSO)	59	54.12	4.89	14.13	$C_{28}H_{30}F_2N_6O_5S$	55.99	5.03	13.99
XIIId	106–108 (DMSO)	61	59.18	6.02	17.33	$C_{24}H_{30}F_2N_6OS$	59.00	6.19	17.20
XIIIe	184–186 (DMSO)	78	55.42	5.17	14.03	$C_{28}H_{32}F_4N_6O_3S$	55.25	5.30	13.81
XIIIf	149–151 (DMSO)	89	52.71	4.92	13.02	$C_{28}H_{30}Cl_2F_2N_6O_3S$	52.58	4.73	13.14
XIIIg	144–146 (DMSO)	52	51.55	5.21	14.89	$C_{24}H_{28}Cl_2F_2N_6OS$	51.71	5.06	15.07
XIIIh	101–103 (DMSO)	90	60.31	5.87	14.15	$C_{30}H_{36}F_2N_6O_3S$	60.18	6.06	14.04
XIVa	160–162 (ethanol)	97	54.51	4.42	13.39	$C_{14}H_{13}F_2N_3OS$	54.36	4.23	13.58
XIVb	159–160 (ethanol)	80	51.81	3.88	13.06	$C_{14}H_{13}F_2N_3O_2S$	51.69	4.03	12.92
XIVc	103–104 (ethanol)	74	57.11	4.89	12.61	$C_{16}H_{17}F_2N_3OS$	56.96	5.08	12.45
XIVd	112–114 (ethanol)	51	56.81	5.19	12.29	$C_{16}H_{17}F_2N_3OS$	56.96	5.08	12.45
XIVe	168–170 (ethanol)	77	51.58	4.72	13.99	$C_{17}H_{18}F_2N_4O_3S$	51.42	4.57	14.11

(8 mmol) of imidazolidine-2-thione (**VII**) in 7 ml of anhydrous pyridine was added at cooling 2.3 ml (14 mmol) of tetrafluorobenzoyl chloride (**Ia**). The reaction mixture was heated to 80°C for 40 min, and on cooling the solution was diluted with water (35 ml), the separated precipitate of compound **VIII** was filtered off and recrystallized from ethanol. Yield 1.4 g (67%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.95 m (4H, $^2CH_2$, $^3CH_2$), 7.99 d.d.d (1H, H^6, ^3J 10.8, ^4J 7.7, ^5J 2.2). ^{19}F NMR spectrum (DMSO-d_6), δ_F, ppm: 155.11 d.d.d (1F, F^8, $^3J_{FF}$ 22.3, $^3J_{FF}$ 21.2, $^4J_{HF}$ 7.4), 136.18 d.d.d (1F, F^7, $^3J_{FF}$ 22.3, $^3J_{HF}$ 10.7, $^4J_{FF}$ 5.1), 133.99 d.d.d (1F, F^9, $^3J_{FF}$ 21.2, $^4J_{FF}$ 5.1, $^5J_{HF}$ 2.2). Mass spectrum, *m/z*: 258 (M^+, 98%), 257 (100), 190 (37), 175 (16), 162 (21).

1,3-Dihydro-1-(tetrafluorobenzoyl)-2*H*-benzimidazol-2-one (X). To 0.8 g (6 mmol) of benzimidazolone in 7 ml of anhydrous pyridine was added at cooling 1.5 ml (11.8 mmol) of tetrafluorobenzoyl chloride (**Ia**). The reaction mixture was heated to 80°C for 3 h, and on cooling the solution was diluted with water (30 ml), the separated precipitate of compound **X** was filtered off and recrystallized from ethanol. Yield 1.4 g (67%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.1–7.3 m (3H, H$^{5'}$–H$^{7'}$), 7.8 m (1H, H$^{6'}$), 8.0 m (1H, H^4), 11.5 br.s (1H, NH).

2,4-Difluoro-3-NR^{1}R^2-6*a*,10*a*-dihydro-8-R-9-R-12*H*-benzo[*e*]benzo[4,5]imidazo[2,1-*b*]-[1,3]thiazin-12-ones (XII). (a) To 0.7 g (2.3 mmol) of compound **IIIa** in 7 ml of anhydrous pyridine was added 0.7 ml (9.2 mmol) of pyrrolidine. The reaction mixture was heated to boiling for 5 h, and on cooling the separated precipitate of compound **XIIa** was filtered off and recrystallized from DMSO. Yield 0.8 g (91%). In the same way was prepared compound **XIIe**.

(b) To 0.5 g (1.6 mmol) of compound **IIIa** in 7 ml of anhydrous dimethylformamide was added 0.9 g (6.4 mmol) 3-(4-morpholino)-1-propanamine. The reaction mixture was boiled for 5 h, then cooled. The separated precipitate of compound **XIIc** was filtered off and recrystallized from DMSO. Yield 0.45 g (65%). Similarly were prepared compounds **XIIb, d, f**. Yields, melting points, and elemental analyses of compounds **XII** are given in Table 6.

1-NR^{1}R^2-2,4-Difluoro-3-NR^{1}R^2-6*a*,10*a*-dihydro-8-R-9-R-12*H*-benzo[*e*]benzo[4,5]imidazo-[2,1-*b*][1,3]thiazin-12-ones (XIII). To 0.7 g (2.1 mmol) of compound **IIIb** in 5 ml of anhydrous dimethylformamide was added 1.4 ml (10.2 mmol) of 3-(4-morpholino)-1-propanamine. The reaction mixture was boiled for 5 h, then cooled. The separated precipitate of compound **XIIIa** was filtered off and recrystallized from DMSO. Yield 0.8 g (67%). Similarly were prepared compounds **XIIIb–h**. ^{19}F NMR spectrum of compound **XIIIc** (DMSO-d_6), δ_F, ppm: 129.12 d (1F, $^4J_{FF}$ 6.4), 127.11 d (1F, $^4J_{FF}$ 6.4). Yields, melting points, and elemental analyses of compounds **XIII** are given in Table 6.

7,9-Difluoro-8-NR^{1}R^2-2,3-dihydro-5*H*-benzo-[4,5]imidazo[2,1-*b*][1,3]thiazin-5-ones (XIV). To 0.6 g (2.3 mmol) of compound **VIII** in 7 ml of anhydrous dimethylformamide was added 0.7 ml (8.2 mmol) of pyrrolidine. The reaction mixture was boiled for 4 h, then cooled and diluted with water (25 ml). The separated precipitate was filtered off and recrystallized from ethanol Yield 0.7 g (97%). Compounds **XIVb–e** were obtained in the similar way. Yields, melting points, and elemental analyses of compounds **XIV** are given in Table 6.

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