Polyfluorobenzoyl chlorides and isothiocyanates in reactions with CH-reactive benzimidazoles

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Reactions of 2-benzoylmethylbenzimidazole with tetra- and pentafluorobenzoyl chlorides afford fluorine-containing 6-benzoyl-7*H*-benzimidazo[3,2-*a*]quinolones. 2-Cyanomethyl- or 2-benzoylmethylbenzimidazole reacts with tetra(penta)fluorobenzoyl isothiocyanates to give fluorine-containing 1,3-benzothiazinones, which differently behave in reactions with cycloalkylimines.

Key words: 2-cyanomethylbenzimidazole, 2-benzoylmethylbenzimidazole, polyfluorobenzoyl chlorides, polyfluorobenzoyl isothiocyanates, fluorobenzimidazo[*a*]quinolones, fluorine-containing 1,3-benzothiazinones.

A considerable number of [*a*]-annelated derivatives of fluoroquinolonecarboxylic acids have found to exhibit a high bactericidal activity.[1—9] For construction of such systems, heterocyclic derivatives of acetonitriles and ketones are widely used as CH-reactive reagents.[10—13] For instance, reactions of 2-cyanomethylbenzimidazole with polyfluorobenzoyl chlorides yielded new fluorine-containing benzimidazo[1,2-*a*]quinolones.[14] Benzoyl chlorides are key intermediate products for the synthesis of benzoyl isothiocyanates, which are promising precursors of a variety of azaheterocycles.[15] The presence of a halogen atom in the *ortho*-position of the latter allows not only an attack on the carbonyl group of the intermediate but also a competitive pathway involving intramolecular replacement of the halogen atom to give 2-substituted 1,3-benzothiazinones.[16] Recently, polyfluorobenzoyl isothiocyanates were used to construct new fluorine-containing 1,3-benzothiazinones.[17] Recent studies[18,19] of the cyclocondensation of isocyanates with cyanomethylbenzothiazole and other C,N-dinucleophiles showed that this approach is promising for the synthesis of annelated azaheterocycles.

In continuation of our studies into structural modification of fluoroquinolones,[14,20—23] we synthesized fluorine-containing 6-benzoylbenzimidazo[3,2-*a*]quinolones **3a—d**. Room-temperature reactions of polyfluorobenzoyl chlorides **1a,b** with 2-benzoylmethylbenzimidazole **2a** in methylene dichloride in the presence of triethylamine afforded tetracyclic imidazoquinolines **3a,d** in 73 and 81% yields, respectively (Scheme 1). Intermediates **A**, which are analogous to 2-(1,3-dihydrobenzimidazol-2-ylidene)-3-oxo-3-(polyfluorophenyl)propionitriles,[14] were isolated neither under the above conditions nor upon the reaction of reagents **1a,b** and **2a** in boiling toluene.

The ^{1}H NMR spectra of compounds **3a,d** contain a broadened singlet for the NH group, unsymmetrical multiplets for the H(8)—H(11) protons of the benzimidazole fragment, and signal for the benzoyl protons. The ^{1}H NMR spectrum of quinolone **3a** shows a characteristic signal for H(4) (ddd, ^3J = 9.0 Hz, ^4J = 7.8 Hz, ^5J = 2.2 Hz). The ^{19}F NMR spectrum of compound **3a** contains signals for three fluorine atoms, which indicates the replacement of one F atom in the formation of the cyclic system. The mass spectra of benzimidazoquinolones **3a,d** contain highly intense molecular ion peaks $[M]^+$ and $[M - 1]^+$, which, as with 6-cyano derivatives,[14] suggest a high stability of the aromatic tetracyclic system.

2-Cycloalkylimino derivatives **3b,c** were synthesized without isolation of the corresponding 2-fluoroquinolone **3a**. According to ^{1}H NMR data, heating of compounds **1a** and **2a** in toluene for 1 h gave a mixture of 1,3-dihydrobenzimidazol-2-ylidene intermediate **A** and compound **3a** in the 7 : 3 ratio. After the toluene was removed, the residue was refluxed with pyrrolidine or morpholine in DMF for 5 h to give 2-amino derivatives **3b,c**. The replacement of the F(2) atom was concluded from a signal for the H(4) proton (dd, ^3J = 8.5 Hz, ^5J = 1.5 Hz) in the ^{1}H NMR spectra of quinolones **3b,c**. In addition, these spectra contain signals for NH

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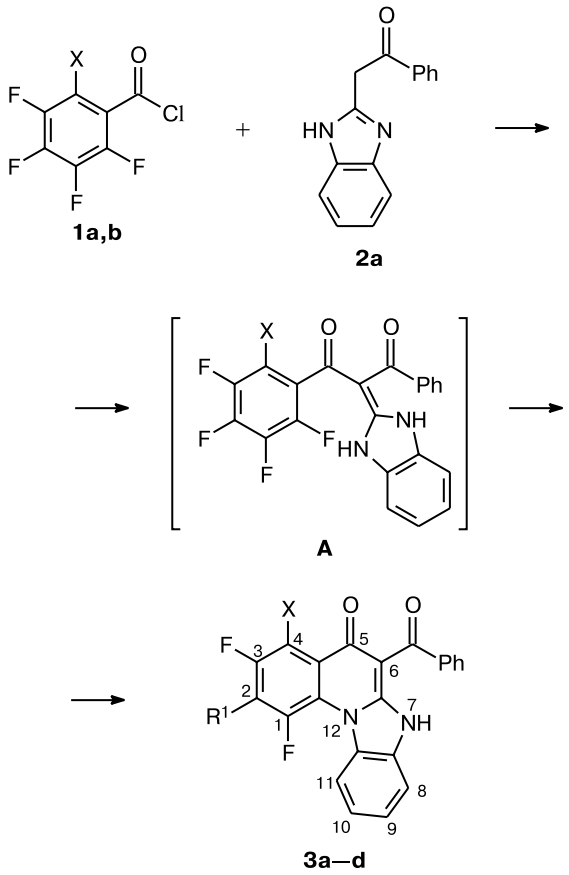
Scheme 1



1: X = H (**a**), F (**b**);

3: X= H, R^1 = F (**a**), N— (**b**), O N— (**c**), X = R^1 = F (**d**)

(δ 12.5—12.6), the amine residue, and the protons of the benzimidazole and benzoyl fragments. In the mass spectrum of compound **3c**, the peak $[M - H]^+$ is most intense. The proposed method for the synthesis of compounds **3b,c** is more convenient than aminodefluorination of compound **3a** (compounds **3b,c** were obtained in higher yields).

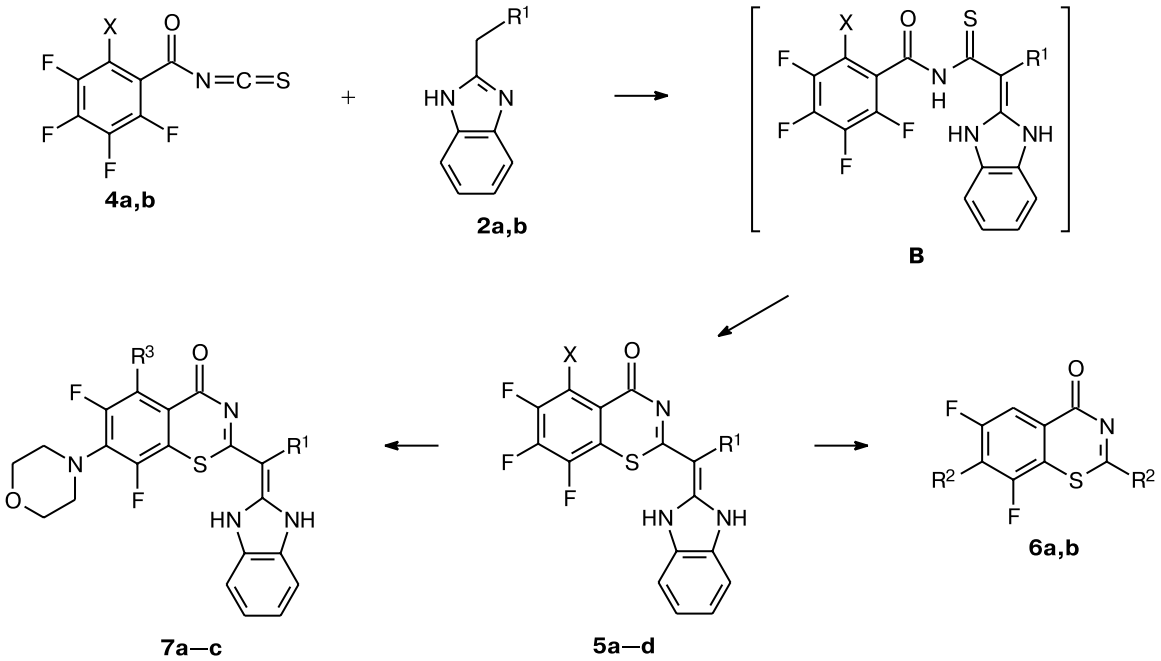
Polyfluorobenzoyl isothiocyanates **4a,b** prepared from the corresponding polyfluorobenzoyl chlorides **1a,b** were studied in reactions with 2-cyanomethyl- and 2-benzoylmethylbenzimidazoles **2a,b**. In the room-temperature reaction between compounds **4a** and **2a** in acetonitrile for 1 h, the methylene fragment of compound **2a** added to the N=C bond of isothiocyanate **4a** and subsequent cyclization gave benzothiazinone **5a** (Scheme 2). However, under the above conditions, product **5a** was obtained only as a mixture with compound **B** (**B** : **5a** = 9 : 10, ^{19}F NMR data). Heating of the mixture with triethylamine in toluene for 3 h afforded individual benzothiazinone **5a** in 72% yield.

Benzothiazinones **5b—d** were synthesized without isolation of intermediate product **B**. The starting reagents **2a,b** and **4a,b** were kept in acetonitrile at room temperature. The solvent was removed and the residue was refluxed with triethylamine in toluene for 3 h. The structures of benzothiazinone derivatives **5a—d** were confirmed by ^{1}H NMR and mass spectra (for compound **5a**, additionally by ^{19}F NMR data). The ^{1}H NMR spectra of compounds **5a—d** contain the multiplets at δ 7.25—7.36 and 7.47—7.65 for the benzimidazole fragment and the broadened signal at δ 13.3—13.4 for NH. The spectra of trifluoro derivatives **5a,c** show the characteristic signal at δ 7.99—8.03 for the H(5) proton (ddd, ^3J = 9.8—10 Hz, ^4J = 7.5—7.6 Hz, ^5J = 1.8—2.0 Hz). The ylidene structures of compounds **5a—d** agree well with the absence of a singlet for the methine proton from their ^{1}H NMR spectra and with the symmetric signals for the benzimidazole fragment, a signal for two NH groups being broadened. In the mass spectra of compounds **5a—d**, the intensities of the peaks of the molecular ions $[M]^+$ are comparatively low (I < 50%), especially for derivative **5d** (I = 3%). At the same time, the mass spectra of compounds **5a—d** show the characteristic peak of the $[ZCN]^+$ ion (Z is the substituent in position 2); its intensity for benzothiazinones **5a—c** equals 100%. Detachment of ZCN as the major pathway of fragmentation was observed earlier in the mass spectra of 2-aryl, 2-heteryl, and 2-polymethylene imino derivatives of fluorine-containing benzothiazinones.[17] The spectra of compounds **5c,d** containing the benzoyl fragment show the peaks with m/z 77 and 105, which corresponds to detachment of C_6H_5 and C_6H_5CO. The ^{19}F NMR spectrum of benzothiazinone **5a** contains multiplets for three fluorine atoms.

Aminodefluorination reactions of benzothiazinones **5a—d** were also studied. As expected, compounds **5a,b** (R = CN) reacted with morpholine to give compounds **7b,c** through replacement of F(7) for **5a** or F(5) and F(7) for **5b** by the morpholine residue. The ^{1}H NMR spectrum of product **7b** shows the characteristic signal at δ 7.76 for the H(5) proton (dd, ^3J = 12.2 Hz, ^5J = 1.6 Hz) in addition to the signals for the benzimidazole and morpholine residues. The mass spectrum of compound **7b** contains the molecular ion peak with m/z 439 (I = 59%); the peak of ZCN (m/z 182) is most intense, as with the starting reagent **5a**. The structure of compound **7c** was confirmed by ^{1}H and ^{19}F NMR data.

The reaction of benzothiazinone **5c** (R = COPh) with morpholine followed a different pathway: the amine residue replaced not only F(7) but also the group in position 2 to give 2,7-bis(morpholin-4-yl)benzothiazinone (**6a**). The ^{1}H NMR spectrum of product **6a** shows no signals for the protons of the benzimidazole and benzoyl fragments, but it contains signals for the protons of two morpholine residues. The mass spectrum of compound **6a** contains an intense molecular ion peak and the

Scheme 2



2: R^1 = COPh (**a**), CN (**b**); **5**: R^1 = CN, X = H (**a**), F (**b**); R^1 = COPh, X = H (**c**), F (**d**);
6: R^2 = morpholin-4-yl (**a**), 4-ethoxycarbonylpiperazin-1-yl (**b**);
7: R^1 = COPh, R^3 = morpholin-4-yl (**a**); R^1 = CN, R^3 = H (**b**), morpholin-4-yl (**c**)

100%-intensity peak $[M - (morpholin\text{-}4\text{-}yl)CN]^+$ characteristic of benzothiazinone fragmentation. Similarly, benzothiazinone **5c** reacted with 1-ethoxycarbonylpiperazine to give compound **6b**. In the case of 5,6,7,8-tetrafluorobenzothiazinone **5d**, the morpholine residue replaced only the F(5) and F(7) atoms, as with compound **5b**, while the group in position 2 was retained (product **7a**). Obviously, introduction of the electron-donating amine residues lowers the electrophilicity of the C(2) atom, thus impeding nucleophilic substitution for the group in position 2. Structure **7a** was confirmed by ^1H and ^{19}F NMR data.

Thus, we obtained new derivatives of benzimidazo[1,2-*a*]quinolones and fluorinated 1,3-benzothiazinones, which are of interest for biological tests.

Experimental

^1H NMR spectra were recorded on Bruker WM-250 and Bruker DRX-400 spectrometers (250.14 and 400.13 MHz, respectively). ^{19}F NMR spectra were recorded on a Bruker DRX-400 spectrometer (376.45 MHz). Tetramethylsilane (^1H NMR) and hexafluorobenzene (^{19}F NMR) were used as the internal standards. Mass spectra were recorded on a Varian MAT 311A spectrometer (accelerating voltage 3 kV, cathode emission current 300 μA, energy of ionizing electrons 70 eV, direct inlet probe).

2-Benzoylmethylbenzimidazole **2a** was prepared from 2-methylbenzimidazole as described earlier;[13] 2-cyanomethylbenzimidazole **2b** was synthesized by condensation of ethyl cyanoacetate with *o*-phenylenediamine according to a known procedure.[24]

6-Benzoyl-1,2,3-trifluoro-7*H*-benzimidazo[1,2-*a*]quinolin-5-one (3a). A solution of tetrafluorobenzoyl chloride **1a** (0.53 g, 2.5 mmol) in toluene (2 mL) and triethylamine (0.7 mL, 0.51 g, 5 mmol) were added to a suspension of 2-benzoylmethylbenzimidazole **2a** (0.6 g, 2.5 mmol) in dry methylene dichloride (10 mL). The reaction mixture was kept at room temperature for a day and concentrated. The residue was washed with water and recrystallized from DMSO. The yield of compound **3a** was 0.72 g (73%), m.p. > 250 °C. ^1H NMR (DMSO-d_6), δ: 7.41 (m, 3 H, Ph); 7.54 (m, 2 H, Ph); 7.62 (m, 1 H, benzimid.); 7.67 (m, 2 H, benzimid.); 8.19 (ddd, H(4), ^3J = 9.0 Hz, ^4J = 7.8 Hz, ^5J = 2.2 Hz); 8.61 (m, 1 H, benzimid.); 12.6 (br.s, 1 H, NH). ^{19}F NMR (DMSO-d_6), δ_F: 8.40, 21.87, 31.48 (all m, 1 F each). MS, *m/z*: 392 [M^+] (100), 391 (99), 315 (24), 287 (24), 259 (14), 105 (52), 77 (53), 51 (12). Found (%): C, 67.40; H, 2.87; N, 7.08. $C_{22}H_{11}F_3N_2O_2$. Calculated (%): C, 67.35; H, 2.83; N, 7.14.

6-Benzoyl-1,2,3,4-tetrafluoro-7*H*-benzimidazo[1,2-*a*]quinolin-5-one (3d) was obtained analogously in 81% yield, m.p. > 250 °C. ^1H NMR (DMSO-d_6), δ: 7.33 (m, 3 H, Ph); 7.34 (m, 2 H, Ph); 7.36 (m, 1 H, benzimid.); 7.37 (m, 2 H, benzimid.); 8.59 (m, 1 H, benzimid.); 12.5 (br.s, 1 H, NH). MS, *m/z*: 410 [M^+] (100), 409 (87), 391 (13), 390 (18), 333 (25), 305 (19), 277 (17), 105 (59), 102 (16), 77 (64), 76 (11), 51 (14). Found (%): C, 64.35; H, 2.42; N, 6.87. $C_{22}H_{10}F_4N_2O_2$. Calculated (%): C, 64.40; H, 2.46; N, 6.83.

6-Benzoyl-1,3-difluoro-2-pyrrolidino-7*H*-benzimidazo[1,2-*a*]quinolin-5-one (3b). A solution of tetrafluorobenzoyl

chloride **1a** (0.74 g, 3.5 mmol) in toluene (3 mL) was added to a suspension of 2-benzoylmethylbenzimidazole **2a** (0.6 g, 2.5 mmol) in dry toluene (15 mL). The reaction mixture was refluxed for 1 h and filtered hot and the filtrate was concentrated. Dimethylformamide (5 mL) and pyrrolidine (0.5 mL, 0.43 g, 6 mmol) were added and the mixture was refluxed for 4 h and then cooled. Water (15 mL) was added and the precipitate of compound **3b** was filtered off, washed with ethanol, and recrystallized from DMSO. The yield of compound **3b** was 0.69 g (62%), m.p. > 250 °C. ^{1}H NMR (DMSO-d_6), δ: 1.97 (m, 4 H, $(CH_2)_2$); 3.75 (m, 4 H, $N(CH_2)_2$); 7.13, 7.25—7.35 (both m, 2 H each); 7.42 (dd, 1 H, H(4), ^3J = 8.5 Hz, ^5J = 1.5 Hz); 7.40—7.50 (m, 5 H); 12.5 (br.s, 1 H, NH). MS, *m/z*: 442 $[M - H]^+$ (100), 372 (23), 354 (26), 257 (23), 193 (24), 190 (26), 78 (32), 63 (36), 55 (21). Found (%): C, 70.49; H, 4.38; N, 9.43. $C_{26}H_{19}F_2N_3O_2$. Calculated (%): C, 70.42; H, 4.32; N, 9.48.

An analogous reaction with morpholine gave 6-benzoyl-1,3-difluoro-2-morpholino-7*H*-benzimidazo[1,2-*a*]quinolin-5-one (**3c**) in 58% yield, m.p. 275—277 °C. ^{1}H NMR (DMSO-d_6), δ: 3.11 (m, 4 H, $N(CH_2)_2$); 3.40, 3.80 (both m, 2 H each, OCH_2); 7.20—7.45 (m, 5 H, Ph); 7.47 (m, 2 H, benzimid.); 7.60 (m, 1 H, benzimid.); 7.78 (dd, 1 H, H(4), ^3J = 8.5 Hz, ^5J = 1.5 Hz); 7.86 (m, 1 H, benzimid.); 12.6 (br.s, 1 H, NH). Found (%): C, 67.91; H, 4.10; N, 9.21. $C_{26}H_{19}F_2N_3O_3$. Calculated (%): C, 67.97; H, 4.17; N, 9.15.

A mixture of (1,3-dihydrobenzimidazol-2-ylidene)(6,7,8-trifluoro-4-oxo-4*H*-benzo[*e*][1,3]thiazin-2-yl)acetonitrile (5a) and *N*-(2,3,4,5-tetrafluorobenzoyl)cyano(1,3-dihydrobenzimidazol-2-ylidene)thioacetamide (B). A solution of NH_4SCN (0.35 g, 4.5 mmol) in dry acetone (5 mL) was added to a solution of tetrafluorobenzoyl chloride **1a** (0.46 g, 4.5 mmol) in toluene (1.7 mL). The reaction mixture was kept at 40 °C for 5 min and NH_4Cl was filtered off. A suspension of 2-cyanomethylbenzimidazole **2b** (0.7 g, 4.5 mmol) in dry acetone (5 mL) was added to the resulting solution of compound **4a**. The reaction mixture was kept at room temperature for 1 h and the precipitate of a mixture of products **5a** and **B** was filtered off. ^{1}H NMR (DMSO-d_6), δ: 7.29 (m, 2 H, benzimid., **5a**); 7.39 (m, 1 H, H(6′), **B**); 7.43, 7.63 (both m, 1 H each, benzimid., **B**); 7.65 (m, 2 H, benzimid., **5a**); 7.95 (m, 2 H, benzimid., **B**); 8.03 (ddd, H(5), ^3J = 9.8 Hz, ^4J = 7.5 Hz, ^5J = 2.0 Hz, **5a**); 13.4 (br.s, 2 H, NH, **5a**); 13.6 (br.s, 2 H, NH, **B**); 15.3 (br.s, 1 H, NH, **B**). ^{19}F NMR (DMSO-d_6), δ_F: 7.80 (m, 1 F, **5a**); 9.47, 12.28 (both m, 1 F each, **B**); 23.65 (m, 1 F, **5a**); 25.53 (m, 1 F, **B**); 26.67 (m, 1 F, **5a**); 27.19 (m, 1 F, **B**). The ratio of compounds **5a** and **B** was 10 : 9.

(1,3-Dihydrobenzimidazol-2-ylidene)(5-X-6,7,8-trifluoro-4-oxo-4*H*-benzo[*e*][1,3]thiazin-2-yl)acetonitriles (5a,b) and 5-X-2-[benzoyl(1,3-dihydrobenzimidazol-2-ylidene)methyl]-6,7,8-trifluoro-4*H*-benzo[*e*][1,3]thiazin-4-ones (5c,d). A solution of NH_4SCN (0.35 g, 4.5 mmol) in dry acetone (5 mL) was added to a solution of tetrafluorobenzoyl chloride **1a** (0.46 g, 4.5 mmol) in toluene (1.7 mL). The reaction mixture was kept at 40 °C for 5 min and NH_4Cl was filtered off. A suspension of 2-cyanomethylbenzimidazole **2b** (0.7 g, 4.5 mmol) in dry acetone (5 mL) was added to the resulting solution of isothiocyanate **4a**. The reaction mixture was kept at ~20 °C for 1 h and the precipitate that formed was filtered off. The precipitate was refluxed with triethylamine (1.35 mL, 9 mmol) in toluene (15 mL) for 3 h. On cooling, the precipitate of (1,3-dihydrobenzimidazol-2-ylidene)(6,7,8-trifluoro-4-oxo-4*H*-benzo[*e*][1,3]thiazin-2-yl)acetonitrile (**5a**) was filtered off, washed with water, and recrystallized from DMSO. The yield of compound **5a** was 1.2 g (72%), m.p. > 310 °C. ^{1}H NMR (DMSO-d_6), δ: 7.29, 7.65 (both m, 2 H each, benzimid.); 8.03 (ddd, H(5), ^3J = 9.8 Hz, ^4J = 7.5 Hz, ^5J = 2.0 Hz); 13.4 (br.s, 2 H, NH). ^{19}F NMR (DMSO-d_6), δ_F: 7.80, 23.65, 26.67 (all m, 1 F each). MS, *m/z*: 372 $[M^+]$ (31), 183 (12), 182 (100), 177(13). Found (%): C, 54.90; H, 1.98; N, 14.97. $C_{17}H_7F_3N_4OS$. Calculated (%): C, 54.84; H, 1.90; N, 15.05.

Compounds **5b**—**d** were obtained analogously.

(1,3-Dihydrobenzimidazol-2-ylidene)(5,6,7,8-tetrafluoro-4-oxo-4*H*-benzo[*e*][1,3]thiazin-2-yl)acetonitrile (5b). The yield was 76%, m.p. > 310 °C. ^{1}H NMR (DMSO-d_6), δ: 7.30, 7.62 (both m, 2 H each, benzimid.); 13.3 (br.s, 2 H, NH). MS, *m/z*: 390 $[M^+]$ (16), 182 (100), 103 (20), 63 (11). Found (%): C, 52.26; N, 14.44. $C_{17}H_6F_4N_4OS$. Calculated (%): C, 52.31; H, 1.54; N, 14.39.

2-[Benzoyl(1,3-dihydrobenzimidazol-2-ylidene)methyl]-6,7,8-trifluoro-4*H*-benzo[*e*][1,3]thiazin-4-one (5c). The yield was 81%, m.p. 307—309 °C. ^{1}H NMR (DMSO-d_6), δ: 7.19 (m, 2 H, Ph); 7.36 (m, 2 H, benzimid.); 7.49 (m, 3 H, Ph); 7.63 (m, 2 H, benzimid.); 7.99 (ddd, H(5), ^3J = 10.0 Hz, ^4J = 7.6 Hz, ^5J = 1.8 Hz); 13.3 (br.s, 2 H, NH). MS, *m/z*: 451 $[M^+]$ (46), 423 (13), 422 (43), 260 (100), 206 (23), 184 (14), 105 (36), 77 (57). Found (%): C, 61.27; H, 2.74; N, 9.25. $C_{23}H_{12}F_3N_3O_2S$. Calculated (%): C, 61.20; H, 2.68; N, 9.31.

2-[Benzoyl(1,3-dihydrobenzimidazol-2-ylidene)methyl]-5,6,7,8-tetrafluoro-4*H*-benzo[*e*][1,3]thiazin-4-one (5d). The yield was 79%, m.p. 268—270 °C. ^{1}H NMR (DMSO-d_6), δ: 7.25 (m, 2 H, benzimid.); 7.34 (m, 2 H, Ph); 7.47 (m, 2 H, benzimid.); 7.55 (m, 3 H, Ph); 13.3 (br.s, 2 H, NH). MS, *m/z*: 469 $[M^+]$ (3), 261 (54), 260 (80), 206 (11), 156 (12), 105 (54), 77 (100), 51 (11). Found (%): C, 58.92; H, 2.41; N, 8.89. $C_{23}H_{11}F_4N_3O_2S$. Calculated (%): C, 58.85; H, 2.36; N, 8.95.

6,8-Difluoro-2,7-dimorpholinobenzo[*e*][1,3]thiazin-4-one (6a). Morpholine (0.35 mL, 0.35 g, 4 mmol) was added to a solution of benzothiazinone **5c** (0.4 g, 0.89 mmol) in DMF (5 mL). The reaction mixture was refluxed for 5 h, cooled, and diluted with water. The precipitate of compound **6a** was filtered off and recrystallized from DMSO. The yield of compound **6a** was 0.25 g (77%), m.p. > 250 °C. ^{1}H NMR (DMSO-d_6), δ: 3.27 (m, 4 H, $N(CH_2)_2$); 3.72 (m, 8 H, $N(CH_2)_2$, $O(CH_2)_2$); 3.83 (m, 4 H, $O(CH_2)_2$); 7.70 (dd, H(5), ^3J = 12.5 Hz, ^5J = 1.8 Hz). MS, *m/z*: 369 $[M^+]$ (55), 327 (10), 257 (100), 215 (10), 199 (55). Found (%): C, 51.94; H, 4.58; N, 11.44. $C_{16}H_{17}F_2N_3O_3S$. Calculated (%): C, 52.03; H, 4.64; N, 11.38.

2,7-Bis(4-ethoxycarbonylpiperazin-1-yl)-6,8-difluorobenzo[*e*][1,3]thiazin-4-one (6b) was obtained analogously from compound **5c** and 1-ethoxycarbonylpiperazine. The yield of compound **6b** was 67%, m.p. 245—247 °C. ^{1}H NMR (DMSO-d_6), δ: 1.23, 1.25 (both t, 3 H each, Me); 3.28, 3.53, 3.58, 3.87 (all m, 4 H each, $N(CH_2)_2$); 4.07, 4.11 (both q, 2 H each, OCH_2); 7.72 (dd, H(5), ^3J = 12.5 Hz, ^5J = 1.8 Hz). MS, *m/z*: 511 $[M^+]$ (35), 398 (14), 397 (24), 396 (43), 384 (15), 383 (71), 328 (21), 313 (14), 308 (17), 226 (18), 214 (21), 213 (17), 199 (22), 141 (17), 128 (16), 115 (15), 84 (12), 70 (14), 57 (11), 56 (100). Found (%): C, 51.72; H, 5.37; N, 13.61. $C_{22}H_{27}F_2N_5O_5S$. Calculated (%): C, 51.66; H, 5.32; N, 13.69.

2-[Benzoyl(1,3-dihydrobenzimidazol-2-ylidene)methyl]-6,8-difluoro-5,7-dimorpholin-4-yl-4*H*-benzo[*e*][1,3]thiazin-4-one (7a). Morpholine (0.42 mL, 0.42 g, 4.8 mmol) was added to a

solution of compound **5d** (0.56 g, 1.19 mmol) in DMF (5 mL). The reaction mixture was refluxed for 5 h, cooled, and diluted with water. The precipitate of compound **7a** was filtered off and recrystallized from ethanol. The yield of compound **7a** was 0.47 g (65%), m.p. > 250 °C. ^{1}H NMR (DMSO-d_6), δ: 3.19, 3.39 (both m, 4 H each, $N(CH_2)_2$); 3.48, 3.71 (both m, 4 H each, $O(CH_2)_2$); 7.15 (m, 2 H, benzimid.); 7.45 (m, 3 H, Ph); 7.54 (m, 2 H, Ph); 7.78 (m, 2 H, benzimid.); 12.9 (br.s, 2 H, NH). ^{19}F NMR (DMSO-d_6), δ_F: 32.28, 33.35 (both m, 1 F each). Found (%): C, 61.75; H, 4.54; N, 11.53. $C_{31}H_{27}F_2N_5O_4S$. Calculated (%): C, 61.69; H, 4.48; N, 11.61.

(1,3-Dihydrobenzimidazol-2-ylidene)(6,8-difluoro-7-morpholin-4-yl-4-oxo-4*H*-benzo[*e*][1,3]thiazin-2-yl]acetonitrile (7b). Morpholine (0.47 mL, 0.47 g, 5.4 mmol) was added to a solution of compound **5a** (0.5 g, 1.34 mmol) in DMF (5 mL). The reaction mixture was refluxed for 5 h, cooled, and diluted with water. The precipitate of compound **7b** was filtered off and recrystallized from DMSO. The yield of compound **7b** was 0.4 g (68%), m.p. > 250 °C. ^{1}H NMR (DMSO-d_6), δ: 3.41 (m, 4 H, $N(CH_2)_2$); 3.56 (m, 4 H, $O(CH_2)_2$); 7.34, 7.63 (both m, 2 H each, benzimid.); 7.76 (dd, H(5), ^3J = 12.2 Hz, ^5J = 1.6 Hz); 13.2 (br.s, 2 H, NH). MS, *m/z*: 439 [M^+] (59), 338 (52), 337 (20), 324 (15), 322 (27), 258 (63), 257 (82), 215 (23), 199 (70), 182 (100), 103 (23), 91 (24), 84 (25), 77 (24). Found (%): C, 57.29; H, 3.38; N, 16.01. $C_{21}H_{15}F_2N_5O_2S$. Calculated (%): C, 57.35; H, 3.41; N, 15.93.

(1,3-Dihydrobenzimidazol-2-ylidene)(6,8-difluoro-5,7-dimorpholin-4-yl-4-oxo-4*H*-benzo[*e*][1,3]thiazin-2-yl)acetonitrile (7c). Morpholine (0.42 mL, 0.42 g, 4.8 mmol) was added to a solution of compound **5b** (0.45 g, 1.15 mmol) in DMF (5 mL). The reaction mixture was refluxed for 5 h, cooled, and diluted with water. The precipitate of compound **7c** was filtered off and recrystallized from DMSO. The yield of compound **7c** was 0.37 g (62%), m.p. > 250 °C. ^{1}H NMR (DMSO-d_6), δ: 3.14, 3.28 (both m, 4 H each, $N(CH_2)_2$); 3.70 (m, 8 H, $2\times O(CH_2)_2$); 7.29, 7.62 (both m, 2 H each, benzimid.); 13.2 (br.s, 2 H, NH). ^{19}F NMR (DMSO-d_6), δ_F: 33.41, 33.51 (both m, 1 F each). Found (%): C, 57.29; H, 4.27; N, 15.95. $C_{25}H_{22}F_2N_6O_3S$. Calculated (%): C, 57.25; H, 4.20; N, 16.03.

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