Synthesis of regioisomeric N- and O-alkylated 3-polyfluoroalkyl-1,2-dihydroquinoxalin-2-ones*

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3-Polyfluoroalkyl-1,2-dihydroquinoxalin-2-ones react with 4-bromobutyl acetate to furnish 1-(4-acetoxybutyl)quinoxalin-2-ones and 2-(4-acetoxybutoxy)quinoxalines in the ratio 2 : 1. Deacylation of these compounds under acidic conditions gives the corresponding 1-(4-hydroxybutyl)- and 2-(4-hydroxybutoxy)-substituted quinoxalines. The structures of compounds synthesized were established by X-ray crystallography, IR spectroscopy, ^{1}H and ^{19}F NMR spectroscopy, GLC-MS.

Key words: analogs of acyclic nucleosides, 3-polyfluoroalkylquinoxalin-2-ones, alkylation, regioisomers, deacylation.

Successful application of acyclic nucleosides, acyclovir (zovirax)[1] and hancyclovir,[2] in practical medicine as antiviral agents prompts one to the search of new analogs of such compounds modified at both the heterocyclic ring and the acyclic substituent.

We have chosen polyfluoroalkyl-1,2-dihydroquinoxalin-2-ones[3] as heterocyclic bases for the development of analogs of acyclic synthetic nucleosides, since substances possessing antiinflammatory[4] and anticancer[5] activity are found among them, while acyclic derivatives obtained from them (acyclovir analogs), exhibit activity against the hepatitis B virus (HBV).[6] 1-(2,3-Dihydroxypropyl)-6,7-dimethylquinoxalin-2-one[7] inhibits the human immune deficiency virus (HIV-1).

The choice of fluorinated objects as bases for the synthesis of analogs of nonnatural nucleosides is a very promising way for the synthesis of biologically active substances, since a specific behavior of fluorine-containing compounds in biochemical processes is of common knowledge. Due to the high electronegativity of the fluorine atom, its compounds are capable of forming strong intermolecular fluorine—hydrogen bonds. Thus, the presence of fluorine in the molecule can increase its metabolic stability, modulate its physicochemical properties (lipophility, solubility, acidity or basicity), and facilitate transportation through the cell membranes.[8]

In the present work, we studied an introduction of the butyl acetate fragment, simulating an acyclic sugar residue, into the ambident 3-polyfluoroalkyl-1,2-dihydroquinoxalin-2-ones **1a—c** with two nonequivalent centers (the endocyclic nitrogen atom and the exocyclic oxygen atom), which can be alkylated.

It is known[6,9] that nonfluorinated quinoxalin-2-ones react with halogenated acyclic sugar analogs or alkenyl halides in the presence of sodium hydride in DMF giving rise to the mixture of N- and O-isomers.

The following conditions were found to be the most acceptable for the alkylation of fluorine-containing quinoxalinones **1**: reflux in acetone with 4-bromobutyl acetate (**2**) in the presence of anhydrous potassium carbonate (Scheme 1). Such conditions ensure a one-step process with the intermediate formation of potassium salts of quinoxalinones **1**, which react *in situ* with 4-bromobutyl acetate (**2**). It was found that under the reaction conditions, quinoxalin-2-ones **1a—c** form two types of products: **3a—c** and **4a—c** in the ratio 2 : 1 (see Scheme 1), which were isolated from the reaction mixtures by column chromatography.

Earlier,[10] it has been stated that heating nonfluorinated 3-methylquinoxalin-2-one in *tert*-butanol at 60 °C under alkaline conditions (5 *M* NaOH) with ethylene chlorohydrin leads only to *N*-(2-hydroxyethyl)quinoxalin-2-one without its O-regioisomeric analog. However, we have shown that under similar conditions polyfluoroalkyl-substituted quinoxalin-2-one **1b** and 4-bromobutyl acetate (**2**) furnish a mixture of products **3b** and **4b** in the same ratio as upon reflux in acetone in the presence of anhydrous potassium carbonate (see Scheme 1).

IR spectroscopy has proved efficient in establishing the regioisomeric structure of obtained compounds **3a—c** and **4a—c**. Thus, solid compounds **3a—c** were identified

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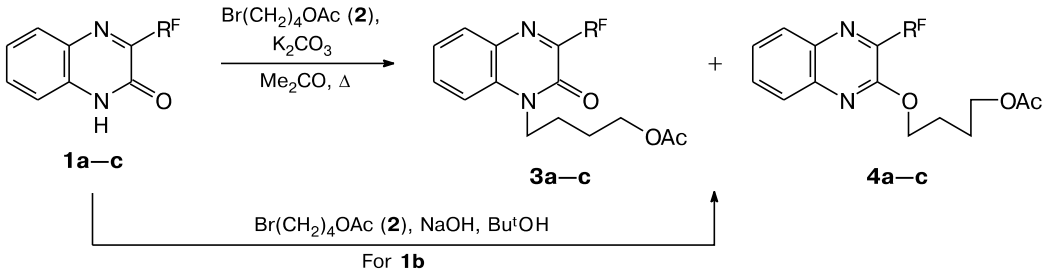
Scheme 1



1, **3**, **4:** R^F = CF_3 (**a**), $(CF_2)_4H$ (**b**), C_4F_9 (**c**)

as N-substituted isomers, since their IR spectra exhibit two absorption bands of the carbonyl groups (the acetate group in the region ~1730—1740 cm^{-1} and lactam group in the region 1665—1675 cm^{-1}). It was found that oily products **4a—c** have the structure of O-substituted isomers, since their IR spectra exhibit only one absorption band of the carbonyl group from the acetate moiety at 1740 cm^{-1}.

The GLC-MS also gives information on regioisomeric structures of products **3** and **4**. We found that all the mass spectra of O-regioisomeric compounds **4**, unlike N-regioisomeric heterocycles **3**, are characterized by the presence of the $[M - OC_4H_7OC{=}OCH_3]^+$ peak.

The ^1H NMR spectra of products **3** and **4** differ in the signals for the methylene protons bound to the quinoxaline heteroatom (N or O). Thus, the NCH_2 group in $CDCl_3$ was found as a triplet signal in the region δ 4.33—4.34 with J = 7.5 Hz, while the OCH_2 group, as a more downfield triplet signal (at δ 4.59—4.62) with J = 6.1—6.2 Hz.

X-ray diffraction study of the crystals of compound **3b** confirmed the structure of this compound as the N-regioisomer, whose carbonyl group remained preserved (the measured C(2)—O(1) bond distance equal to 1.214(2) Å corresponds to the bond distance of a C=O double bond) (Fig. 1). The carbon and nitrogen atoms involved in the formation of quinoxaline heterocycle are virtually placed in one plane. The largest deviation from the mean plane of quinoxaline is observed for the C(3) atom (0.038 Å), whereas the 4-acetoxybutyl and octafluorobutyl substituents are turned to the opposite sides with respect to the plane of heterocycle.

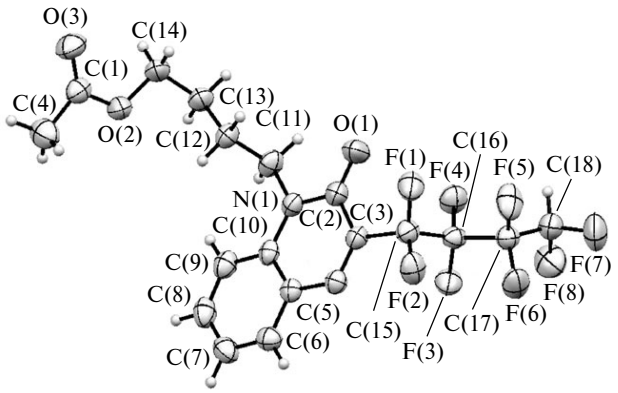
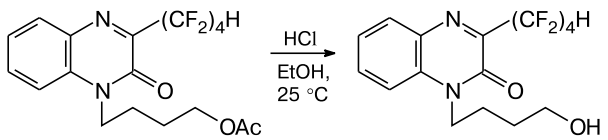


Fig. 1. Molecular structure of 1-(4-acetoxybutyl)-3-(1,1,2,2,3,3,4,4-octafluorobutyl)-1*H*-quinoxalin-2-one (**3b**).

An example of quinoxalin-2-one **3b** shows that the butyl acetate moiety can be deacylated in anhydrous ethanol under acidic conditions upon bubbling gaseous hydrogen chloride to give *N*-(4-hydroxybutyl)quinoxalin-2-one **5** in quantitative yield (Scheme 2).

Scheme 2



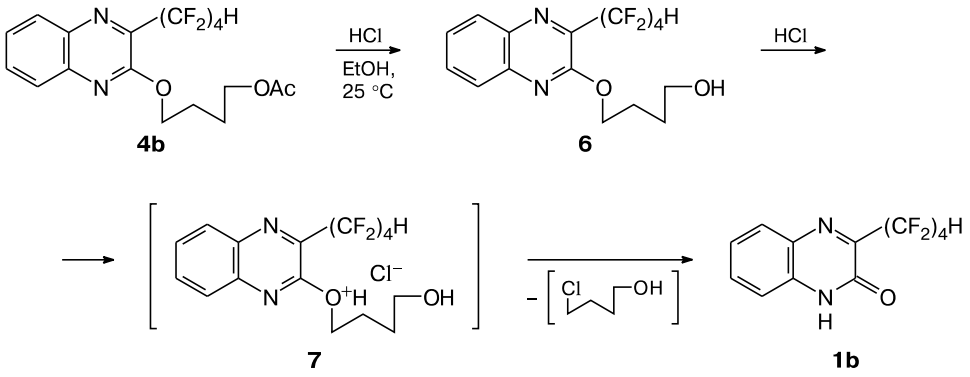
O-Regioisomeric analog **4b** is also deacylated under acidic conditions to form *O*-(4-hydroxybutoxy)quinoxaline **6**. However, in this case after treatment of **4b** with hydrochloric acid, the starting 2-hydroxyquinoxaline **1b** was additionaly isolated from the reaction mixture (the content from the GC-MS data was 7%), which presumably results from the elimination of 4-chlorobutanol from product **6**. Apparently, the reaction proceeds through the intermediate oxonium salts **7** (Scheme 3).[11]

Running the deacylation reaction under basic conditions (upon the action of sodium methoxide) leads to a difficult to separate mixture of products.

The IR spectra of compounds **5** and **6**, unlike of their acylated precursors **3b** and **4b**, do not exhibit absorption band of the acetate group at 1730—1740 cm^{-1}, rather an absorption band of the stretching vibrations of the OH group is observed in the region 3375—3465 cm^{-1}.

In conclusion, we found that the alkylation of fluoroalkyl-containing quinoxalin-2-ones with 4-bromobutyl acetate proceeds as two competing processes: the O- and N-alkylation with predominance of the latter. Deacyla-

Scheme 3



tion the thus formed compounds to *N*-(4-hydroxybutyl)- and *O*-(4-hydroxybutoxy)-substituted quinoxalines occurs under acidic conditions.

Experimental

^{1}H and ^{19}F NMR spectra were recorded on a Bruker DRX-400 spectrometer (400 (^{1}H) and 75 MHz (^{19}F)) relatively to $SiMe_4$ and C_6F_6, respectively. IR spectra were recorded on a Perkin—Elmer Spectrum One IR Fourier-spectrometer in the region 4000—400 cm^{-1} using a diffuse reflectance accessory (DRA) or frustrated total internal reflection (FTIR). Melting points were measured in open capillary tubes using a Stuart SMP30 apparatus. Column chromatography was performed on silica gel 60 (0.063—0.02 mm). Mass spectra were recorded on a Agilent GC 7890A MSD 5975C inert XL EI/CI chromato-mass instrument with an HP5-MS quartz capillary column (dimethylpolysiloxane with 5% of phenyl groups, 30 m × 0.25 mm, the film was 0.25 μm thick) and quadrupole mass-spectrometric detector in the mode of electron ionization (70 eV); helium as a carrier gas; chloroform as a solvent. Elemental analysis (C, H, N) was performed on a Perkin—Elmer PE 2400 series II analyzer.

Synthesis of 1-(4-acetoxybutyl)-3-polyfluoroalkyl-1*H*-quinoxalin-2-ones 3a—c and 2-(4-acetoxybutoxy)-3-polyfluoroalkylquinoxalines 4a—c (general procedure *A*). A mixture of quinoxalinone **1** (2.5 mmol), acetone (10 mL), 4-bromobutyl acetate (0.49 g, 2.5 mmol) and potassium carbonate (0.41 g, 3.0 mmol) was refluxed for 16—20 h. A precipitate was filtered off, the mother liquor was concentrated. The products were separated by column chromatography (eluent chloroform—ethyl acetate, 7 : 1 (**3a** and **4a**); chloroform—ethyl acetate, 9 : 1 (**3b** and **4b**); hexane—ethyl acetate, 1 : 1 (**3c** and **4c**)) collecting two fractions: the first one was 1-(4-acetoxybutyl)-1*H*-quinoxalin-2-one **3**, the second one was 2-(4-acetoxybutoxy)quinoxaline **4**.

1-(4-Acetoxybutyl)-1*H*-quinoxalin-2-one 3b and 2-(4-acetoxybutoxy)quinoxaline 4b. Method *B*. Quinoxaline **1b** (0.8 g, 3 mmol) was dissolved in *tert*-butanol (9 mL), followed by addition of 5 *M* aqueous NaOH (3 mL), 4-bromobutyl acetate (1.17 g, 6 mmol), and the mixture was stirred for 4 h at 60 °C. Then, the reaction mixture was neutralized with acetic acid to pH 7 and diluted with water (10 mL). The water-alcoholic solution was extracted with chloroform. The organic layer was dried with Na_2SO_4, the solvent was evaporated. The products were separated as described above.

1-(4-Acetoxybutyl)-3-(trifluoromethyl)-1*H*-quinoxalin-2-one (3a). The yield was 54%, m.p. 70—71 °C. IR (FTIR), ν/cm^{-1}: 1740 (MeC=O); 1665 (NC=O); 1470, 1565, 1605 (C=C, C=N); 1145—1185 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.81—1.90 (m, 4 H, CH_2CH_2); 2.06 (s, 3 H, MeCO); 4.15 (t, 2 H, OCH_2, $^3J_{H,H}$ = = 6.1 Hz); 4.34 (t, 2 H, NCH_2, $^3J_{H,H}$ = 7.5 Hz); 7.4 (d, 1 H, C_6H_4, $^3J_{H,H}$ = 8.5 Hz); 7.43—7.47 (m, 1 H, C_6H_4); 7.73 (ddd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 7.4 Hz, $^4J_{H,H}$ = 1.5 Hz); 8.02 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 1.5 Hz). ^{19}F NMR ($CDCl_3$), δ: 91.7 (s, CF_3). MS, *m/z* (I_{rel} (%)): 43 $[C{=}OCH_3]^+$ (25.4), 55 $[C_4H_7]^+$ (9.1), 71 $[C_4H_7O]^+$ (13.7), 129 $[NC_4H_8OC{=}OCH_3]^+$ (10.7), 166 $[M - C_4H_8OC{=}OCH_3 - C{=}O - F]^+$ (16.3), 186 $[M - C_4H_7OC{=}OCH_3 - C{=}O]^+$ (16.8), 199 $[M - NC_4H_8OC{=}OCH_3]^+$ (21.7), 214 $[M - C_4H_7OC{=}OCH_3]^+$ (99.9), 268 $[M - CH_3C{=}OOH]^+$ (15.8), 285 $[M - C{=}OCH_3]^+$ (17.7), 286 $[M - C{=}OCH_2]^+$ (23.3), 328 $[M]^+$ (9.7). Found (%): C, 55.02; H, 4.84; F, 17.6; N, 8.41. $C_{15}H_{15}F_3N_2O_3$. Calculated (%): C, 54.88; H, 4.61; F, 17.36; N, 8.53.

1-(4-Acetoxybutyl)-3-(1,1,2,2,3,3,4,4-octafluorobutyl)-1*H*-quinoxalin-2-one (3b). The yield was 52 (method *A*) and 48% (method *B*), m.p. 76—78 °C. IR (DRA), ν/cm^{-1}: 1730 (MeC=O); 1675 (NC=O); 1470, 1560, 1605 (C=C, C=N); 1055—1165 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.79—1.90 (m, 4 H, CH_2CH_2); 2.05 (s, 3 H, MeCO); 4.15 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.1 Hz); 4.33 (t, 2 H, NCH_2, $^3J_{H,H}$ = 7.5 Hz); 6.33 (tt, 1 H, $H(CF_2)_4$, $^2J_{H,F}$ = = 52.1 Hz, $^3J_{H,F}$ = 5.8 Hz); 7.39 (d, 1 H, C_6H_4, $^3J_{H,H}$ = 8.4 Hz); 7.43—7.47 (m, 1 H, C_6H_4); 7.72—7.76 (m, 1 H, C_6H_4); 8.02 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.1 Hz, $^4J_{H,H}$ = 1.3 Hz). ^{19}F NMR ($CDCl_3$), δ: 24.16—24.38 (m, 2 F, HCF_2, $^2J_{F,H}$ = 52.1 Hz); 31.78—31.88 (m, 2 F, CF_2); 38.71 (t, 2 F, CF_2, $^3J_{F,F}$ = 8.2 Hz); 48.34—48.39 (m, 2 F, CF_2). MS, *m/z* (I_{rel} (%)): 43 $[C{=}OCH_3]^+$ (36.6), 55 $[C_4H_7]^+$ (15.7), 71 $[C_4H_7O]^+$ (21.3), 167 $[M - C_3F_6H - C_4H_7OC{=}OCH_3 - C{=}O]^+$ (12), 180 $[M - C_3F_6 - C_3H_7OC{=}OCH_3 - C{=}O]^+$ (20.1), 195 $[M - C_3F_6H - C_4H_7OC{=}OCH_3]^+$ (97), 326 $[M - F - C_4H_8OC{=}OCH_3]^+$ (9.1), 331 $[M - NC_4H_8OC{=}OCH_3]^+$ (24.4), 346 $[M - C_4H_7OC{=}OCH_3]^+$ (99.9), 371 $[M - CH_3C{=}OOH - C_2H_5]^+$ (10.8), 400 $[M - CH_3C{=}OOH]^+$ (26.5), 417 $[M - C{=}OCH_3]^+$ (24.6), 418 $[M - C{=}OCH_2]^+$ (28.1), 460 $[M]^+$ (11.9). Found (%): C, 46.71; H, 3.4; F, 32.86; N, 6.39. $C_{18}H_{16}F_8N_2O_3$. Calculated (%): C, 46.97; H, 3.5; F, 33.02; N, 6.09.

1-(4-Acetoxybutyl)-3-(nonafluorobutyl)-1*H*-quinoxalin-2-one (3c). The yield was 50%, oil. IR (FTIR), ν/cm^{-1}: 1740 (MeC=O); 1675 (NC=O); 1470, 1560, 1610 (C=C, C=N); 1135—1235 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.78—1.92 (m, 4 H,

CH_2CH_2); 2.05 (s, 3 H, MeCO); 4.15 (t, 2 H, OCH_2, $^3J_{H,H}$ = = 6.1 Hz); 4.34 (t, 2 H, NCH_2, $^3J_{H,H}$ = 7.5 Hz); 7.4 (d, 1 H, C_6H_4, $^3J_{H,H}$ = 8.5 Hz); 7.43—7.47 (m, 1 H, C_6H_4); 7.72—7.77 (m, 1 H, C_6H_4); 8.02 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.1 Hz, $^4J_{H,H}$ = = 1.4 Hz). ^{19}F NMR ($CDCl_3$), δ: 36.49—36.61, 40.94—41.04, 48.65—48.73 (all m, 2 F each, 3 CF_2); 80.91—80.97 (tt, 3 F, CF_3, $^3J_{F,F}$ = 9.9 Hz, $^4J_{F,F}$ = 2.3 Hz). MS, *m/z* (I_{rel} (%)): 43 $[C{=}OCH_3]^+$ (37), 55 $[C_4H_7]^+$ (16.7), 71 $[C_4H_7O]^+$ (21.7), 77 $[C_6H_5]^+$ (9.4), 114 $[C_4H_7OC{=}OCH_3]^+$ (9.8), 129 $[NC_4H_8OC{=}OCH_3]^+$ (7.5), 167 [M – C_3F_7 – $C_4H_7OC{=}OCH_3$ – C=O]$^+$ (13.4), 180 [M – – C_3F_7 – $C_3H_5OC{=}OCH_3$ – C=O]$^+$ (20.7), 195 [M – C_3F_7 – – $C_4H_7OC{=}OCH_3]^+$ (99.9), 209 [M – C_3F_7 – $C_3H_5OC{=}OCH_3]^+$ (9.8), 349 [M – $NC_4H_8OC{=}OCH_3]^+$ (26.2), 364 [M – – $C_4H_7OC{=}OCH_3]^+$ (99.4), 365 [M – $C_4H_7OC{=}OCH_2]^+$ (31.9), 389 [M – $CH_3C{=}OOH$ – $C_2H_5]^+$ (12.2), 418 [M – – $CH_3C{=}OOH]^+$ (27.9), 435 [M – $C{=}OCH_3]^+$ (25.6), 436 [M – $C{=}OCH_2]^+$ (29.9), 478 $[M]^+$ (11.6). Found (%): C, 45.49; H, 3.18; F, 35.97; N, 5.70. $C_{18}H_{15}F_9N_2O_3$. Calculated (%): C, 45.2; H, 3.16; F, 35.75; N, 5.86.

2-(4-Acetoxybutoxy)-3-(trifluoromethyl)quinoxaline (4a). The yield was 22%, oil. IR (FTIR), ν/cm^{-1}: 1740 (MeC=O); 1585, 1615 (C=C, C=N); 1135—1250 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.84—1.91 (m, 2 H, CH_2); 1.94—2.01 (m, 2 H, CH_2); 2.06 (s, 3 H, MeCO); 4.17 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.4 Hz); 4.62 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.2 Hz); 7.63—7.67 (m, 1 H, C_6H_4); 7.77—7.82 (m, 1 H, C_6H_4); 7.88 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = = 0.8 Hz); 8.11 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.2 Hz, $^4J_{H,H}$ = 0.6 Hz). ^{19}F NMR ($CDCl_3$), δ: 93.61 (s, CF_3). MS, *m/z* (I_{rel} (%)): 43 $[C{=}OCH_3]^+$ (50), 55 $[C_4H_7]^+$ (31.5), 71 $[C_4H_7O]^+$ (12.8), 115 $[C_4H_8OC{=}OCH_3]^+$ (16.2), 166 [M – $C_4H_7OC{=}OCH_3$ – C=O – – HF]$^+$ (18.4), 186 [M – $C_4H_7OC{=}OCH_3$ – C=O]$^+$ (16), 198 [M – $OC_4H_7OC{=}OCH_3]^+$ (14.6), 199 [M – $OC_4H_7OC{=}OCH_2]^+$ (12.1), 214 [M – $C_4H_7OC{=}OCH_3]^+$ (99.9), 227 [M – $C_2F_4H]^+$ (12.6), 328 $[M]^+$ (2.3). Found (%): C, 54.69; H, 4.68; F, 17.17; N, 8.50. $C_{15}H_{15}F_3N_2O_3$. Calculated (%): C, 54.88; H, 4.61; F, 17.36; N, 8.53.

2-(4-Acetoxybutoxy)-3-(1,1,2,2,3,3,4,4-octafluorobutyl)-quinoxaline (4b). The yield was 26 (method ***A***) and 24% (method ***B***), oil. IR (FTIR), ν/cm^{-1}: 1740 (MeC=O); 1495, 1575, 1615 (C=C, C=N); 1040—1245 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.82—1.89 (m, 2 H, CH_2); 1.92—1.98 (m, 2 H, CH_2); 2.06 (s, 3 H, MeCO); 4.16 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.3 Hz); 4.59 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.1 Hz); 6.25 (tt, 1 H, $H(CF_2)_4$, $^2J_{H,F}$ = 52.4 Hz, $^3J_{H,F}$ = = 5.9 Hz); 7.64—7.67 (m, 1 H, C_6H_4); 7.78—7.82 (m, 1 H, C_6H_4); 7.88 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 1.2 Hz); 8.11 (d, 1 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz). ^{19}F NMR ($CDCl_3$), δ: 24.32—24.54 (m, 2 F, HCF_2, $^2J_{F,H}$ = 52.2 Hz); 32.01—32.12 (m, 2 F, CF_2); 38.75 (t, 2 F, CF_2, $^3J_{F,F}$ = 8.0 Hz); 49.78—49.83 (m, 2 F, CF_2). MS, *m/z* (I_{rel} (%)): 43 $[C{=}OCH_3]^+$ (34.6), 55 $[C_4H_7]^+$ (24.5), 71 $[C_4H_7O]^+$ (12.4), 115 $[C_4H_8OC{=}OCH_3]^+$ (20.9), 167 [M – C_3F_6H – $C_4H_7OC{=}OCH_3$ – C=O]$^+$ (14.5), 195 [M – C_3F_6H – $C_4H_7OC{=}OCH_3]^+$ (84), 259 [M – C_2F_4 – – $C_3H_6OC{=}OCH_3]^+$ (14.9), 326 [M – F – $C_4H_8OC{=}OCH_3]^+$ (11.9), 330 [M – $OC_4H_7OC{=}OCH_3]^+$ (19.5), 331 [M – – $OC_4H_7OC{=}OCH_2]^+$ (25.8), 346 [M – $C_4H_7OC{=}OCH_3]^+$ (99.9), 359 [M – $C_3H_6OC{=}OCH_3]^+$ (25.5), 400 [M – $CH_3C{=}OOH]^+$ (10.7), 401 [M – $OC{=}OCH_3]^+$ (10.3), 460 $[M]^+$ (3.5). Found (%): C, 47.22; H, 3.68; F, 32.78; N, 6.01. $C_{18}H_{16}F_8N_2O_3$. Calculated (%): C, 46.97; H, 3.50; F, 33.02; N, 6.09.

2-(4-Acetoxybutoxy)-3-(nonafluorobutyl)quinoxaline (4c). The yield was 25%, oil. IR (FTIR), ν/cm^{-1}: 1740 (MeC=O); 1470, 1575 (C=C, C=N); 1135—1235 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.84—1.90 (m, 2 H, CH_2); 1.92—1.97 (m, 2 H, CH_2); 2.06 (s, 3 H, MeCO); 4.17 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.3 Hz); 4.59 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.1 Hz); 7.65 (d, 1 H, C_6H_4, $^3J_{H,H}$ = 8.4 Hz, $^3J_{H,H}$ = 7.0 Hz, $^4J_{H,H}$ = 1.4 Hz); 7.78—7.82 (m, 1 H, C_6H_4); 7.88 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.4 Hz, $^4J_{H,H}$ = 0.9 Hz); 8.12 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = 0.9 Hz). ^{19}F NMR ($CDCl_3$), δ: 36.36—36.47 (m, 2 F, CF_2); 40.49—40.58 (m, 2 F, CF_2); 49.93—50.01 (m, 2 F, CF_2); 80.89 (tt, 3 F, CF_3, $^3J_{F,F}$ = 9.9 Hz, $^4J_{F,F}$ = 2.5 Hz). MS, *m/z* (I_{rel} (%)): 43 $[C{=}OCH_3]^+$ (69.6), 55 $[C_4H_7]^+$ (49), 71 $[C_4H_7O]^+$ (24.2), 115 $[C_4H_8OC{=}OCH_3]^+$ (33.2), 147 [M – C_3F_8 – $C_4H_8OC{=}OCH_3$ – C=O]$^+$ (13.1), 167 [M – C_3F_7 – $C_4H_7OC{=}OCH_3$ – C=O]$^+$ (20), 195 [M – C_3F_7 – – $C_4H_7OC{=}OCH_3]^+$ (99.9), 259 [M – C_2F_5 – $C_3H_5OC{=}OCH_3]^+$ (12.7), 348 [M – $OC_4H_7OC{=}OCH_3]^+$ (24.7), 349 [M – – $OC_4H_7OC{=}OCH_2]^+$ (25.4), 364 [M – $C_4H_7OC{=}OCH_3]^+$ (95.3), 365 [M – $C_4H_7OC{=}OCH_2]^+$ (35.5), 377 [M – – $C_3H_6OC{=}OCH_3]^+$ (22.3), 418 [M – $CH_3C{=}OOH]^+$ (9), 478 $[M]^+$ (2.6). Found (%): C, 44.97; H, 3.07; F, 36.06; N, 6.05. $C_{18}H_{15}F_9N_2O_3$. Calculated (%): C, 45.20; H, 3.16; F, 35.75; N, 5.86.

Deacylation of 1-(4-acetoxybutyl)-1*H*-quinoxalin-2-one 3b and 2-(4-acetoxybutoxy)quinoxaline 4b. Gaseous hydrogen chloride was babbled through a solution of compounds **3b** or **4b** (0.5 mmol) in ethanol (5 mL) over 1 h. The reaction mixture was stirred for 30 min at room temperature and neutralized with $NaHCO_3$. The product was extracted with diethyl ether and dried with Na_2SO_4. The solvent was evaporated, the product **6** was purified by column chromatography (eluent chloroform).

1-(4-Hydroxybutyl)-3-(1,1,2,2,3,3,4,4-octafluorobutyl)-1*H*-quinoxalin-2-one (5). The yield was 92%, m.p. 70—72 °C. IR (FTIR), ν/cm^{-1}: 3465 (OH); 1665 (NC=O); 1465, 1560, 1605 (C=C, C=N); 1040—1175 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.69—1.76 (m, 2 H, CH_2); 1.78 (br.s, 1 H, OH); 1.86—1.94 (m, 2 H, CH_2); 3.76 (t, 2 H, $C\underline{H}_2OH$, $^3J_{H,H}$ = 6.1 Hz); 4.35 (t, 2 H, NCH_2, $^3J_{H,H}$ = 7.7 Hz); 6.33 (tt, 1 H, $H(CF_2)_4$, $^2J_{H,F}$ = = 52.0 Hz, $^3J_{H,F}$ = 5.7 Hz); 7.43—7.46 (m, 2 H, C_6H_4); 7.71—7.75 (m, 1 H, C_6H_4); 8.01 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = 1 Hz). ^{19}F NMR ($CDCl_3$), δ: 24.20—24.38 (m, 2 F, HCF_2, $^2J_{F,H}$ = 52.1 Hz); 31.83—31.88 (m, 2 F, CF_2); 38.76 (t, 2 F, CF_2, $^3J_{F,F}$ = 8.2 Hz); 48.40—48.44 (m, 2 F, CF_2). MS, *m/z* (I_{rel} (%)): 77 $[C_6H_5]^+$ (11.5), 167 [M – C_3F_6H – C_4H_7OH – C=O]$^+$ (15.5), 180 [M – C_3F_6 – C_3H_7OH – C=O]$^+$ (19.4), 195 [M – C_3F_6H – $C_4H_7OH]^+$ (99.9), 209 [M – C_3F_6 – – $C_3H_6OH]^+$ (15.1), 331 [M – $NC_4H_8OH]^+$ (15.7), 346 [M – – $C_4H_7OH]^+$ (53.5), 418 $[M]^+$ (38.5). Found (%): C, 46.11; H, 3.49; F, 36.56; N, 6.43. $C_{16}H_{14}F_8N_2O_2$. Calculated (%): C, 45.94; H, 3.37; F, 36.34; N, 6.70.

2-(4-Hydroxybutoxy)-3-(1,1,2,2,3,3,4,4-octafluorobutyl)-quinoxaline (6). The yield was 81%, m.p. 48—50 °C. IR (FTIR), ν/cm^{-1}: 3375 (OH); 1575, 1615 (C=C, C=N); 1080—1215 (C—F). ^{1}H NMR ($CDCl_3$), δ: 1.76—1.83 (m, 2 H, CH_2); 1.94—2.01 (m, 2 H, CH_2); 2.05 (br.s, 1 H, OH); 3.76 (t, 2 H, $C\underline{H}_2OH$, $^3J_{H,H}$ = 6.4 Hz); 4.60 (t, 2 H, OCH_2, $^3J_{H,H}$ = 6.4 Hz); 6.26 (tt, 1 H, $H(CF_2)_4$, $^2J_{H,F}$ = 52.0 Hz, $^3J_{H,F}$ = 5.6 Hz); 7.64 (ddd, 2 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz, $^3J_{H,H}$ = 7 Hz, $^4J_{H,H}$ = 1 Hz); 7.77—7.81 (m, 1 H, C_6H_4); 7.88 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = = 0.9 Hz); 8.10 (dd, 1 H, C_6H_4, $^3J_{H,H}$ = 8.3 Hz, $^4J_{H,H}$ = 1 Hz). ^{19}F NMR ($CDCl_3$), δ: 24.36—24.59 (m, 2 F, HCF_2, $^2J_{F,H}$ = = 52.0 Hz); 32.09—32.2 (m, 2 F, CF_2); 38.83 (t, 2 F, CF_2, $^3J_{F,F}$ = 8.0 Hz); 49.87—49.92 (m, 2 F, CF_2). MS, *m/z* (I_{rel} (%)):

Table 1. Basic crystallographic data and refinement parameters for compound **3b**

Parameter	Value
Molecular formula	$C_{18}H_{16}F_8N_2O_3$
Molecular weight	460.33
Crystal system	Triclinic
Space group	$P\bar{1}$
a/Å	9.2081(5)
b/Å	10.2100(13)
c/Å	10.8152(12)
α/deg	80.244(10)
β/deg	86.827(7)
γ/deg	71.817(9)
V/Å^3	952.04(17)
Z	2
d_{calc}/g cm^{-3}	1.606
μ/mm^{-1}	0.161
Angle of scanning on θ/deg	2.63—28.28
Total number of reflections	5299
Number of independent reflections	4493
Number of reflections with $I > 2\sigma(I)$	1335
Number of refined parameters	281
R_1/wR_2 ($I > 2\sigma(I)$)	0.0323/0.0622
R_1/wR_2 (on all the reflections)	0.0783/0.0653

167 $[M - C_3F_6H - C_4H_7OH - C{=}O]^+$ (22.3), 180 $[M - C_3F_6 - C_3H_7OH - C{=}O]^+$ (19.4), 195 $[M - C_3F_6H - C_4H_7OH]^+$ (99.9), 217 $[M - C_4F_8H]^+$ (12), 326 $[M - C_4H_8OH - F]^+$ (9.3), 327 $[M - C_4H_7OH - F]^+$ (13.6), 346 $[M - C_4H_7OH]^+$ (79.2), 418 $[M]^+$ (0.5). Found (%): C, 45.76; H, 3.20; F, 36.03; N, 6.75. $C_{16}H_{14}F_8N_2O_2$. Calculated (%): C, 45.94; H, 3.37; F, 36.34; N, 6.70.

X-ray diffraction study. A monocrystal of heterocycle **3b** was obtained by crystallization from ethanol. The X-ray diffraction experiments were performed on an Xcalibur 3 CCD diffractometer (λ(Mo-Kα) = 0.71073 Å, graphite monochromator, ω-scanning, the temperature of 295(2) K). No allowance for absorption was made. The crystal structure was solved by the direct method and subsequent Fourier-synthesis using the SHELXS-97 program.[12] The structure was refined by the least squares method in the anisotropic full-matrix approximation for all the nonhydrogen atoms using the SHELXL-97 program.[13] The hydrogen atoms were placed in the geometrically calculated positions and included in the refinements using the riding model in the isotropic approximation with dependent thermal parameters. The main crystallographic data for product **3b** and some experimental characteristics are given in Table 1. The full set of crystallographic data for compound **3b** was deposited with the Cambridge Structural Database (CCDC No. 809236) and is available at www.ccdc.cam.ac.uk/conts/retrieving.html (CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; e-mail: deposit@ccdc.cam.ac.uk).

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