# Regiospecific O-alkylation of 4-polyfluoroalkyl-1*H*-pyrimidin-2-ones*

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The alkylation of 4-polyfluoroalkylpyrimidin-2-ones with iodomethane, 4-bromobutyl acetate, and epichlorhydrin occurs regiospecifically to form O-regioisomers.

**Key words:** 4-polyfluoroalkylpyrimidin-2-ones, alkylation, organofluorine compounds, epichlorhydrin.

Guanine derivatives with the 2-hydroxyethoxymethyl fragment and its amino acylated analog, *viz.*, acyclovir and valacyclovir, are highly active against virus of simple herpes.[1] Another non-sugar acyclic analog of nucleosides, *viz.*, 1-(2-hydroxyethoxymethyl)-6-(phenylthio)thymine, possesses activity against human immunodeficiency virus (HIV-1). This discovery marked the use in medicine of non-nucleoside inhibitors of reverse transcriptase, which presently occupy a strong position in the treatment of HIV-1 infection.[1,2]

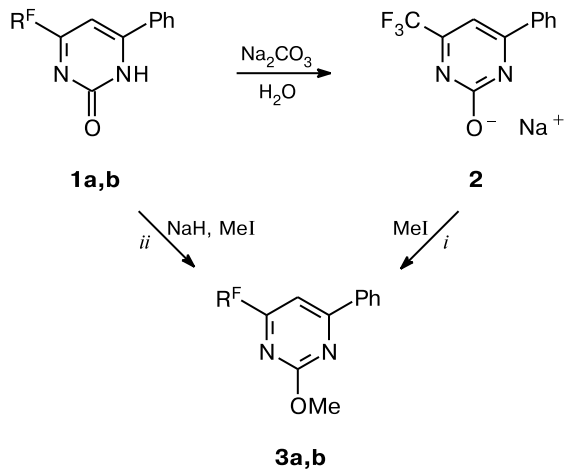
One of the convenient methods for the introduction into the heterocyclic base of a residue containing the terminal hydroxy group is the interaction of metal ($Ag^{2+}$, $Hg^{2+}$, $Na^+$, $K^+$) derivatives of heterocyclic systems with O-protected haloalkanols.[3]

In the present work, we studied the alkylation of structural analogs of uracil, namely, 4-polyfluoroalkyl-6-R-pyrimidin-2-ones **1** (R = Alk, Ar), with 4-bromobutyl acetate and epichlorhydrin.

Compounds **1** have three nonequivalent reaction centers (two endocyclic nitrogen atoms (N(1) and N(3)) and exocyclic oxygen atom) capable of undergoing alkylation (Scheme 1). In order to reveal the most reactive reaction center of pyrimidinones **1**, we studied their reaction with model iodomethane.

Compounds **1** were methylated in the presence of sodium carbonate, sodium hydride, or sodium ethoxide. It turned out that even many-hour heating of pyrimidinones **1** with iodomethane in the presence of sodium ethoxide did not provide their complete conversion. In the case of sodium carbonate or hydride, methylation occurred successfully yielding the desired products **3**. Intermediate sodium salts **2** can be isolated and subjected to the further treatment with iodomethane. It was not necessary to isolate the intermediate salts **2**. The one-step method is most convenient for the synthesis of compounds **3**: stirring of pyrimidinones **1** with iodomethane for ~5 h at room temperature in DMF in the presence of sodium carbonate or in DMSO with sodium hydride provided the formation of the target products in 74—83% yield (Scheme 1).

**Scheme 1**




*i*. DMF, 25 °C; *ii*. DMSO, 25 °C

$R^F$ = $CF_3$ (**1a**, **2**, **3a**), $HCF_2CF_2$ (**1b**, **3b**)

The structure of compound **3a** and, in particular, the position of the methyl group, was proved by the data of $^{13}C$ NMR and 2D heteronuclear $^1H—^{13}C$ HSQC, $^1H—^{13}C$ HMBC, and $^1H—^{15}N$ HMBC experiments. The value of chemical shift of 55.44 ppm is characteristic of the substituent OMe, whereas in the N-methylated products the signals of the methyl group should resonate more than 20 ppm upfield compared to the O-isomers.[4]

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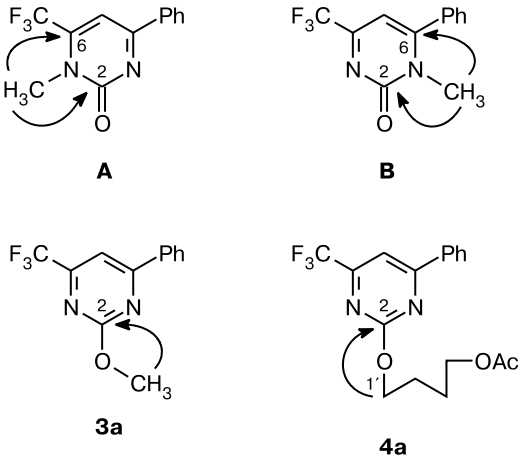



The 2D $^{1}H—^{13}C$ HMBC spectrum contains only one cross-peak between the protons of the $CH_3$ group and the C(2) carbon atom, which agrees with the structure of O-alkylated pyrimidinols, whereas in the case of *N*-methyl-substituted pyrimidin-2-ones (regioisomers **A** and **B**) the HMBC spectrum should exhibit two cross-peaks between the protons of the $N—CH_3$ group and the carbon atoms C(2) and C(6) (see Ref. 4). Another evidence in favor of the proposed structure are chemical shifts $\delta_N$ 239.7 and 254.4 of the nitrogen atoms N(1) and N(3) obtained from the 2D $^{1}H—^{15}N$ HMBC experiment (Fig. 1), whose values correspond to the shifts of the imine nitrogen atoms (in regioisomeric structures **A** and **B** the signal of the substituted amide nitrogen atoms should be observed in a substantially higher field). The IR spectra of compounds **3a,b** contain no band in the region of absorption of the carbonyl lactam group at 1660—1685 $cm^{-1}$, unlike the spectra of the starting pyrimidinones **1**.

Attempted introduction of the acetoxybutyl substituent into pyrimidinones **1a—c** (Scheme 2) with 4-bromobutyl acetate in the presence of $K_2CO_3$ in DMF did not occur at

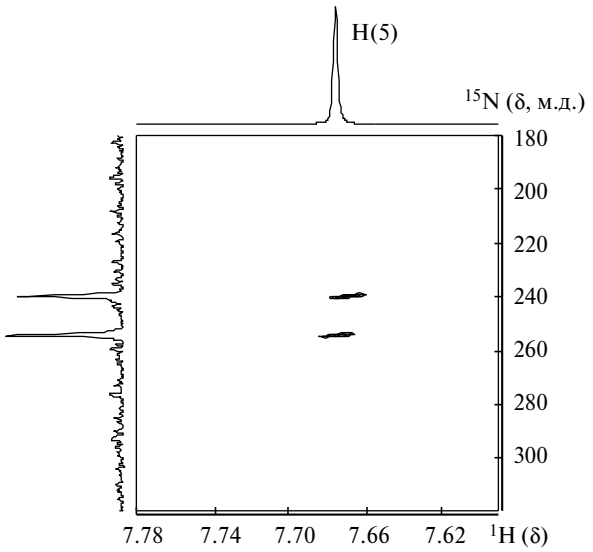
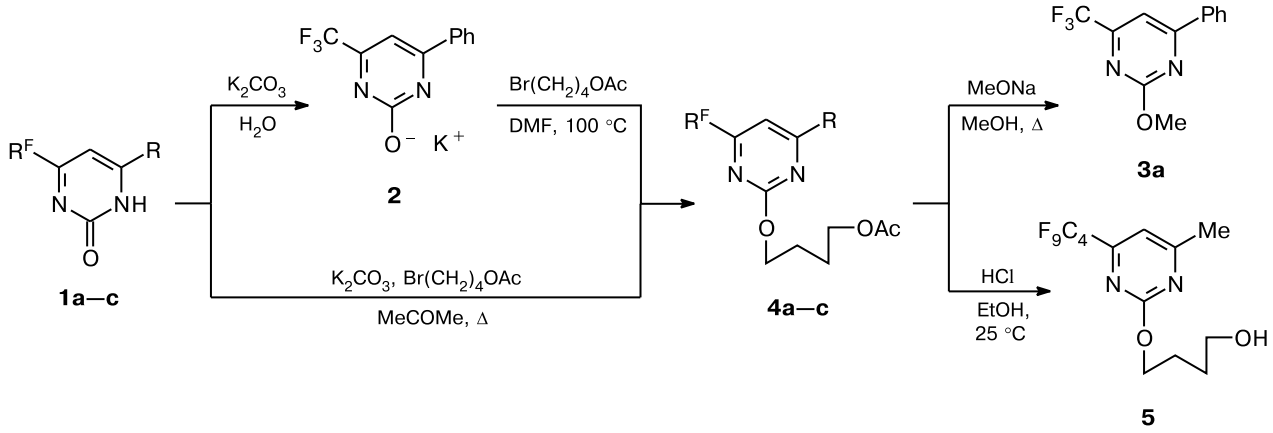



**Fig. 1.** Fragment of the 2D $^{1}H—^{15}N$ HMBC spectrum of compound **3a** (500 MHz, $CDCl_3$).

room temperature. It was found that the following conditions are most appropriate for the synthesis of products **4**: either the stepwise addition of aqueous potassium carbonate for the formation of salt **2** followed by its heating in DMF at 100 °C with 4-bromobutyl acetate, or reflux of pyrimidinone **1** in acetone with 4-bromobutyl acetate in the presence of potassium carbonate.

The position of the acetoxybutyl substituent in compounds **4** was established by spectral methods. It was found that the 2D $^{1}H—^{13}C$ HMBC spectrum of compound **4a** contains one cross-peak between the protons of the $C(1')H_2$ group of the acetoxybutyl substituent and the carbon nucleus C(2) (Scheme 2), whereas in the $^{13}C$ NMR spectrum the signal at 67.81 ppm is characteristic of the carbon atom of the $O—CH_2$ fragment of the acetoxybutyl

**Scheme 2**



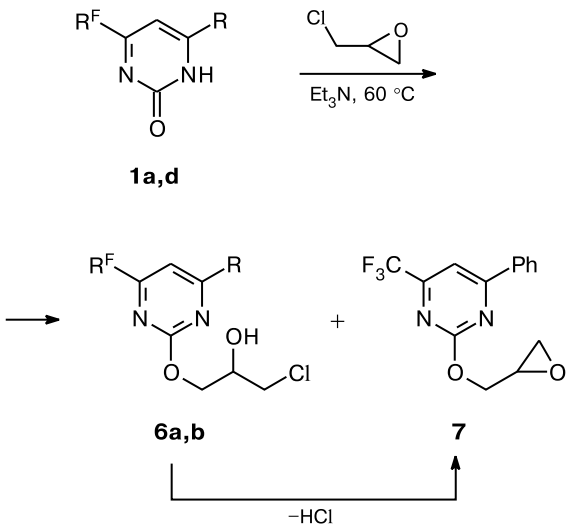

**1, 4:** $R^F = CF_3$, R = Ph (**a**); $R^F = HCF_2CF_2$, R = Bu (**b**); $R^F = C_4F_9$, R = Me (**c**)

substituent. The IR spectra of compounds **4a—c** contain no absorption bands characteristic of vibrations of the lactam carbonyl groups.

The attempts to deacylate acetate **4a** under basic conditions by the action of sodium methoxide gave methoxylated derivative **3a** due to transalkoxylation (see Scheme 2). However, the deacylation proceeds smoothly under acidic conditions when passing gaseous hydrogen chloride through a solution of pyrimidine **4c** in absolute ethanol at room temperature to give 2-(4-hydroxybutoxy)-substituted pyrimidine **5** in high yield (see Scheme 2). The IR spectrum of this compounds has no absorption band of the acetoxy group at 1740 $cm^{-1}$, as compared to acylated precursor **4c**, but the absorption band of stretching vibrations of the OH group is detected at 3375 $cm^{-1}$.

We studied the transformations of pyrimidinones **1** with epichlorohydrin (Scheme 3). The successful occurrence of these reactions needs heating of pyrimidinones **1a**,**d** with a small excess of epichlorhydrin in the presence of triethylamine. It turned out that the main process in these reactions is the nucleophilic addition of the carbonyl oxygen atom of pyrimidinones **1a**,**d** to the C(3) atom of the epoxide cycle followed by its opening[5] leading to 2-(2-hydroxy-3-chloropropoxy)-containing pyrimidines **6a**,**b** in moderate yields. Apparently, the low yields of the products are caused by side processes, for example, polymerization. In addition, these reactions are very sensitive to the amount of the basic catalyst used, because even a slight increase in the amount of triethylamine in the reaction of pyrimidinone **1a** resulted in the formation of 2-glycidyl-substituted pyrimidine **7** (see Scheme 3), most likely, due to the dehydrochlorination of compound **6a** under basic conditions.

**Scheme 3**




$R^F = CF_3$, R = Ph (**1a**, **6a**); $R^F$ = R = $CF_3$ (**1d**, **6b**)

To assign products **6a**,**b** and **7** to the O-isomeric series, we used the IR spectral data containing no absorption band of the carbonyl group. In addition, in the $^{19}F$ NMR spectrum of derivative **6b**, two $CF_3$ groups appear as one singlet signal because of their equivalence, which is possible only in the case of symmetrical structure **6b**.

Thus, we found that the alkylation of 4-polyfluoroalkylpyrimidin-2-ones with various alkylating agents proceeds regiospecifically to form O-isomers.

Further we are planning to develop methods for the introduction into pyrimidines **1** of other acyclic residues modeling sugar fragments and methods for the synthesis of glycosyl-substituted pyrimidines. In addition, we assume to study the biological activity of the compounds synthesized in this work.

## Experimental

NMR spectra were measured in $CDCl_3$ on Bruker DRX-400 ($^1H$: 400 MHz, relative to $SiMe_4$; $^{19}F$: 376 MHz, relative to $C_6F_6$) and Avance 500 ($^{13}C$: 126 MHz, relative to the signal from $CDCl_3$ 77 ppm; $^{15}N$: relative to external liquid ammonia) spectrometers. The signals of $^1H$ and $^{13}C$ were assigned on the basis of 2D $^1H$—$^{13}C$ HSQC and HMBC experiments. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer in the range 4000—400 $cm^{-1}$ using a diffuse reflectance attachment (DRA) or frustrated total internal reflection (FTIR) technique. Melting points were measured in open capillaries on a Stuart SMP30 apparatus for melting point determination. Column chromatography was carried out on silica gel 60 (0.063—0.02 mm, Merck). Mass spectra were recorded on an Agilent GC 7890A MSD 5975C inert XL EI/CI GC/MS chromatograph with a quartz capillary column HP5-MS (dimethylpolysiloxane with 5% phenyl groups, 30 m×0.25 mm, film thickness 0.25 μm) and a quadrupole mass spectrometric detector in the electron ionization mode (70 eV) using helium as a carrier gas and chloroform as a solvent. Elemental analysis (C, H, N) was carried out on a Perkin—Elmer PE 2400 series II analyzer.

Starting pyrimidinones **1** were synthesized by the condensation of fluoroalkyl-containing 1,3-diketones with urea.[6]

**Alkylation of pyrimidinones 1a,b with iodomethane.** ***A.*** A suspension of pyrimidinone **1a** (0.84 g, 3.5 mmol) in a 17% aqueous solution of $Na_2CO_3$ (2.5 mL) was stirred at room temperature for 30 min. Sodium salt **2** was filtered off, dried, and dissolved in DMF (4 mL), iodomethane (0.57 g, 4 mmol) was added, and the mixture was stirred at room temperature for 5 h. Water (30 mL) was added, and the suspension was extracted with ethyl acetate. The organic layer was separated and concentrated. The product was purified by column chromatography using chloroform as an eluent.

***B.*** A suspension of 60% sodium hydride in mineral oil (0.14 g) in DMSO (2 mL) was added to pyrimidinone **1a,b** (3.5 mmol), and the reaction mixture was stirred at room temperature for 30 min, then iodomethane (0.57 g, 4 mmol) was added dropwise, and the mixture was stirred for more 10 h. The product was precipitated from DMSO with water, filtered off, and dried.

**2-Methoxy-6-phenyl-4-trifluoromethylpyrimidine (3a).** The yield by method ***A*** was 83%, and the yield by method ***B*** was 75%, m.p. 47—49 °C. IR (DRA), ν/$cm^{-1}$: 1480, 1550, 1585, 1600

(C=C, C=N); 1120—1255 (C—F). $^1$H NMR, δ: 4.16 (s, 3 H, OMe); 7.51—7.59 (m, 3 H, $H_m$, $H_p$); 7.68 (s, 1 H, H(5)); 8.15 (dd, 2 H, $H_o$, $J$ = 8.1 Hz, $J$ = 1.5 Hz). $^{19}$F NMR ($CDCl_3$), δ: 91.58 (s, $CF_3$). $^{13}$C NMR, δ: 55.44 (OMe); 106.12 (q, C(5), $^3J_{C,F}$ = 2.8 Hz); 120.43 (q, $CF_3$, $^1J_{C,F}$ = 275.1 Hz); 127.47 ($C_o$); 129.06 ($C_m$); 132.08 ($C_p$); 135.35 ($C_{ipso}$); 158.24 (q, C(4), $^2J_{C,F}$ = = 35.8 Hz); 166.18 (C(2)); 169.23 (C(6)). $^{15}$N NMR, δ: 239.7, 254.4. Found (%): C, 56.74; H, 3.46; F, 22.2; N, 10.76. $C_{12}H_9F_3N_2O$. Calculated (%): C, 56.7; H, 3.57; F, 22.42; N, 11.02.

Compound **3a** was also obtained during attempted deacetylation of derivative **4a**. 2-(4-Acetoxybutoxy)pyrimidine **4a** (0.47 g, 1.3 mmol) was added to a solution of sodium methoxide prepared from metallic sodium (32 mg, 1.4 mmol) and absolute methanol (10 mL). The reaction mixture was refluxed for 1 h, cooled, neutralized with acetic acid, and concentrated *in vacuo*. Product **3a** was isolated from the obtained residue by column chromatography using chloroform as an eluent. The yield was 76%.

**2-Methoxy-6-phenyl-4-(1,1,2,2-tetrafluoroethyl)pyrimidine (3b).** The yield was 74%, m.p. 48—49 °C. IR (DRA), ν/cm$^{-1}$: 1555, 1580, 1600 (C=C, C=N); 1080—1150 (C—F). $^1$H NMR (DMSO-$d_6$), δ: 4.08 (s, 3 H, OMe); 6.98 (tt, 1 H, H($CF_2$)$_2$, $^2J_{H,F}$ = = 51.7 Hz, $^3J_{H,F}$ = 5.5 Hz); 7.56—7.66 (m, 3 H, $H_m$, $H_p$); 8.11 (s, 1 H, H(5)); 8.32 (dd, 2 H, $H_o$, $J$ = 8.2 Hz, $J$ = 1.5 Hz). $^{19}$F NMR (DMSO-$d_6$), δ: 24.12 (dt, 2 F, $HCF_2$, $^2J_{F,H}$ = 51.8 Hz, $^3J_{F,F}$ = = 8.1 Hz); 42.47 (td, 2 F, $CF_2$, $J$ = 8.1 Hz, $J$ = 5.5 Hz). Found (%): C, 54.7; H, 3.48; F, 26.26; N, 9.76. $C_{13}H_{10}F_4N_2O$. Calculated (%): C, 54.55; H, 3.52; F, 26.55; N, 9.79.

**Alkylation of pyrimidinones 1a—c with 4-bromobutyl acetate.** ***A.*** A suspension of pyrimidinone **1a** (0.96 g, 4 mmol) in a 17% aqueous solution of $K_2CO_3$ (3.5 mL) was stirred for 30 min at room temperature. Potassium salt **2** was filtered off, dried and dissolved in DMF (5 mL). 4-Bromobutyl acetate (0.78 g, 4 mmol) was added to the reaction mixture, and the mixture was heated at 100 °C for 5 h. Water (30 mL) was added to the cooled reaction mixture. The suspension was extracted with ethyl acetate. The organic layer was separated and concentrated. The product was purified with column chromatography using a dichloromethane—hexane (2 : 1) mixture as an eluent.

***B.*** A mixture of pyrimidinone **1a—c** (2.5 mL), acetone (10 mL), 4-bromobutyl acetate (0.49 g, 2.5 mmol), and potassium carbonate (0.3 g, 3.0 mmol) was refluxed for 8—10 h. The precipitate was filtered off, and the mother liquor was concentrated. The product was purified with column chromatography using a hexane—ethyl acetate (5 : 1) mixture as an eluent.

**2-(4-Acetoxybutoxy)-6-phenyl-4-trifluoromethylpyrimidine (4a).** The yields were 73% (method ***A***) and 82% (method ***B***), m.p. 48—49 °C. IR (DRA), ν/cm$^{-1}$: 1735 (C=O); 1555, 1600 (C=C, C=N); 1120—1250 (C—F). $^1$H NMR, δ: 1.88 (m, 2 H, $CH_2$); 1.97 (m, 2 H, $CH_2$); 2.06 (s, 3 H, MeCO), 4.16 (t, 2 H, H(4′), $^3J_{H,H}$ = 6.3 Hz); 4.56 (t, 2 H, H(1′), $^3J_{H,H}$ = 6.3 Hz); 7.51—7.60 (m, 3 H, $H_m$, $H_p$); 7.67 (s, 1 H, H(5)); 8.13 (dd, 2 H, $H_o$, $J$ = 8.2 Hz, 1.5 Hz). $^{19}$F NMR, δ: 91.56 (s, $CF_3$). $^{13}$C NMR ($CDCl_3$), δ: 20.88 (CO<u>Me</u>); 25.23, 25.41 (C(2′), C(3′)); 63.95 (C(4′); 67.81 (C(1′)); 106.14 (q, C(5), $^3J_{C,F}$ = 2.8 Hz); 120.41 (q, $CF_3$, $^1J_{C,F}$ = 275.1 Hz); 127.47 ($C_o$); 129.05 ($C_m$); 132.06 ($C_p$); 135.38 ($C_{ipso}$); 158.23 (q, C(4), $^2J_{C,F}$ = 35.8 Hz); 165.75 (q, C(2), $^4J_{C,F}$ = 0.8 Hz); 169.27 (C(6)); 171.08 (<u>C</u>OMe). Found (%): C, 57.36; H, 4.84; F, 16.08; N, 7.64. $C_{17}H_{17}F_3N_2O_3$. Calculated (%): C, 57.63; H, 4.84; F, 16.09; N, 7.91.

**2-(4-Acetoxybutoxy)-6-butyl-4-(1,1,2,2-tetrafluoroethyl)-pyrimidine (4b).** The yield was 69%, oil. IR (FTIR), ν/cm$^{-1}$: 1740 (C=O); 1565, 1595 (C=C, C=N); 1040—1245 (C—F). $^1$H NMR, δ: 0.96 (t, 3 H, Me, $^3J_{H,H}$ = 7.4 Hz), 1.40 (tq, 2 H, $CH_2$, $J$ = 7.4 Hz); 1.74 (m, 2 H, $CH_2$); 1.80—1.96 (m, 4 H, 2 $CH_2$); 2.05 (s, 3 H, MeCO); 2.79 (m, 2 H, $CH_2$); 4.14 (t, 2 H, $OCH_2$, $^3J_{H,H}$ = 6.2 Hz); 4.42 (t, 2 H, $OCH_2$, $^3J_{H,H}$ = 6.2 Hz); 6.31 (tt, 1 H, H($CF_2$)$_2$, $^2J_{H,F}$ = 53.1 Hz, $^3J_{H,F}$ = 5.3 Hz); 7.17 (s, 1 H, H(5)). MS, $m/z$ ($I_{rel}$ (%)): 43 $[C{=}OCH_3]^+$ (21.7), 55 $[C_4H_7]^+$ (14.9), 115 $[C_4H_8OC{=}OCH_3]^+$ (71.7), 210 $[M - C_3H_6 - C_4H_7OC{=}OCH_3]^+$ (99.9), 223 $[M - C_2H_5 - C_4H_7OC{=}OCH_3]^+$ (30.4), 237 $[M - CH_3 - C_4H_7OC{=}OCH_3]^+$ (12.1), 253 $[M - C_4H_7OC{=}OCH_2]^+$ (46.3), 324 $[M - C_3H_6]^+$ (33.1), 366 $[M]^+$ (0.4). Found (%): C, 52.55; H, 5.89; F, 21.08; N, 7.68. $C_{16}H_{22}F_4N_2O_3$. Calculated (%): C, 52.46; H, 6.05; F, 20.74; N, 7.65.

**2-(4-Acetoxybutoxy)-6-methyl-4-nonafluorobutylpyrimidine (4c).** The yield was 70%, oil. IR (FTIR), ν/cm$^{-1}$: 1740 (C=O); 1565, 1595 (C=C, C=N); 1135—1235 (C—F). $^1$H NMR, δ: 1.80—1.95 (m, 4 H, 2 $CH_2$); 2.05 (s, 3 H, MeCO); 2.58 (s, 3 H, Me—C(6)); 4.13 (t, 2 H, H(4′), $^3J_{H,H}$ = 6.2 Hz); 4.43 (t, 2 H, H(1′), $^3J_{H,H}$ = 6.2 Hz); 7.15 (s, 1 H, H(5)). $^{19}$F NMR, δ: 36.15 (m, 2 F, $CF_2$); 39.10 (m, 2 F, $CF_2$); 45.76 (tq, 2 F, $CF_2$, $J$ = 12.9 Hz, $J$ = 2.7 Hz); 80.86 (tt, 3 F, $CF_3$, $J$ = 9.8 Hz, $J$ = 2.7 Hz). MS, $m/z$ ($I_{rel}$ (%)): 43 $[C{=}OCH_3]^+$ (21.6), 54 $[C_4H_6]^+$ (9.3), 71 $[C_4H_7O]^+$ (9.2), 312 $[M - CH_3 - C_4H_8OC{=}OCH_3]^+$ (21.3), 313 $[M - CH_3 - C_4H_7OC{=}OCH_3]^+$ (16.4), 329 $[M - C_4H_7OC{=}OCH_2]^+$ (99.9), 330 $[M - CF_3 - C{=}OCH_3]^+$ (12.0), 355 $[M - C_2H_4OC{=}OCH_3]^+$ (15.4), 383 $[M - OC{=}OCH_3]^+$ (10.9), 442 $[M]^+$ (2.7). Found (%): C, 40.91; H, 3.39; F, 38.51; N, 6.45. $C_{15}H_{15}F_9N_2O_3$. Calculated (%): C, 40.74; H, 3.42; F, 38.66; N, 6.33.

**2-(4-Hydroxybutoxy)-6-methyl-4-nonafluorobutylpyrimidine (5).** Acetoxy derivative **4c** (0.22 g, 0.5 mmol) was dissolved in ethanol (5 mL), and then gaseous hydrogen chloride was bubbled through the solution for 1 h. The reaction mixture was stirred at room temperature for 30 min and neutralized with $NaHCO_3$. The product was extracted with chloroform and dried over $Na_2SO_4$. The solvent was evaporated. Product **5** was purified by column chromatography using chloroform as an eluent. The yield was 84%, oil. IR (FTIR), ν/cm$^{-1}$: 3375 (OH), 1570, 1595 (C=C, C=N); 1135—1235 (C—F). $^1$H NMR, δ: 1.59—2.00 (m, 5 H, 2 $CH_2$, OH); 2.58 (s, 3 H, Me); 3.72 (t, 2 H, H(4′), $^3J_{H,H}$ = 6.4 Hz); 4.44 (t, 2 H, H(1′), $^3J_{H,H}$ = 6.4 Hz); 7.14 (s, 1 H, H(5)). $^{19}$F NMR, δ: 36.17 (m, 2 F, $CF_2$); 39.10 (m, 2 F, $CF_2$); 45.76 (tq, 2 F, $CF_2$, $J$ = 12.8 Hz, $J$ = 2.6 Hz); 80.86 (tt, 3 F, $CF_3$, $J$ = 9.8 Hz, $J$ = 2.6 Hz). MS, $m/z$ ($I_{rel}$ (%)): 71 $[C_4H_7O]^+$ (15.8), 312 $[M - OC_4H_7OH]^+$ (11.4), 329 $[M - C_4H_7O]^+$ (99.9), 330 $[M - HCF_3]^+$ (13.0), 400 $[M]^+$ (1.9). Found (%): C, 38.85; H, 3.2; F, 43.01; N, 7.12. $C_{13}H_{13}F_9N_2O_2$. Calculated (%): C, 39.01; H, 3.27; F, 42.72; N, 7.0.

**Alkylation of pyrimidinones 1a,d with epichlorohydrin.** Epichlorohydrin (0.175 g, 1.9 mmol) and triethylamine (0.16 g, 1.6 mmol) (for compound **1a**) or triethylamine (3 droplets) for compound **1d**) were added dropwise to pyrimidinones **1a,d** (1.6 mmol). The mixture was heated at 60 °C for 8 h. The cooled melt was dissolved in chloroform (5 mL). The solution was placed on the top of a chromatography column packed with silica gel. The products were eluted with a chloroform—ethyl acetate (5 : 1) mixture. Two fractions were collected in the case of the reaction of pyrimidine **1a** with epichlorohydrin: the first fraction contained compound **6a** and the second one was product **7**.

**2-(3-Chloro-2-hydroxypropoxy)-6-phenyl-4-trifluoromethylpyrimidine (6a).** The yield was 45%, m.p. 84—85 °C. IR (DRA), ν/cm$^{-1}$: 3415 (OH); 1560, 1590 (C=C, C=N); 1110—1195 (C—F). $^1$H NMR, δ: 2.85 (br.s, 1 H, OH); 3.78 (dd, 1 H, H(3´b), $^2J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 5.5 Hz); 3.83 (dd, 1 H, H(3´a), $^2J_{H,H}$ = = 11.3 Hz, $^3J_{H,H}$ = 5.3 Hz); 4.34 (q, 1 H, H(2´), *J* = 5.3 Hz); 4.65 (dd, 1 H, H(1´b), $^2J_{H,H}$ = 11.2 Hz, $^3J_{H,H}$ = 5.0 Hz); 4.69 (dd, 1 H, H(1´a), $^2J_{H,H}$ = 11.2, $^3J_{H,H}$ = 5.6 Hz); 7.52—7.61 (m, 3 H, $H_m$, $H_p$); 7.72 (s, 1 H, H(5)); 8.13 (dd, 2 H, $H_o$, *J* = 8.2 Hz, 1.5 Hz). $^{19}$F NMR, δ: 91.63 (s, $CF_3$). MS, *m*/*z* ($I_{rel}$ (%)): 223 [M – – $OCH_2CHOHCH_2Cl]^+$ (10.0), 224 [M – $OCHCHOHCH_2Cl]^+$ (17.8), 241 [M – $CH_2COCH_2Cl]^+$ (99.9), 242 [M – – $CHCOCH_2Cl]^+$ (12.3), 253 [M – $CHOHCH_2Cl]^+$ (15.8), 254 [M – $CHOCH_2Cl]^+$ (10.3), 283 [M – $CH_2Cl]^+$ (26.6), 332 $[M]^+$ (0.1). Found (%): C, 50.66; H, 3.71; F, 17.3; N, 8.48. $C_{14}H_{12}ClF_3N_2O_2$. Calculated (%): C, 50.54; H, 3.64; F, 17.13; N, 8.42.

**2-(3-Chloro-2-hydroxypropoxy)-4,6-bis(trifluoromethyl)-pyrimidine (6b).** The yield was 51%, oil. IR (FTIR), ν/cm$^{-1}$: 3420 (OH); 1590 (C=C, C=N); 1120—1225 (C—F). $^1$H NMR, δ: 2.6 (br.d, 1 H, OH, $^3J_{H,H}$ = 5.8 Hz); 3.77 (dd, 1 H, H(3´b), $^2J_{H,H}$ = 11.4 Hz, $^3J_{H,H}$ = 5.5 Hz); 3.81 (dd, 1 H, H(3´a), $^2J_{H,H}$ = = 11.4 Hz, $^3J_{H,H}$ = 5.3 Hz); 4.32 (m, 1 H, H(2´)); 4.62 (dd, 1 H, H(1´b), $^2J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 4.9 Hz); 4.65 (dd, 1 H, H(1´a), $^2J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 5.6 Hz); 7.62 (s, 1 H, H(5)). $^{19}$F NMR, δ: 91.65 (s, $CF_3$). MS, *m*/*z* ($I_{rel}$ (%)): 43 $[HNCO]^+$ (12.8), 69 $[CF_3]^+$ (12.8), 79 $[CHOHCH_2Cl]^+$ (11.2), 147 [M – $OCHCHOHCH_2Cl$ – – $CF_3]^+$ (11.1), 163 [M – $CHCHOHCH_2Cl$ – $CF_3]^+$ (13.7), 177 [M – $CHOCH_2Cl$ – $CF_3]^+$ (12.1), 196 [M – $OCH_2CHOHCH_2Cl$ – – F]$^+$ (11.7), 216 [M – $OCHCHOHCH_2Cl]^+$ (60.5), 217 [M – – $OCH_2COCH_2Cl]^+$ (27.4), 218 [M – $OCHCOCH_2Cl]^+$ (23.2), 233 [M – $CH_2COCH_2Cl]^+$ (66.6), 245 [M – $CHOHCH_2Cl]^+$ (12.3), 246 [M – $CHOCH_2Cl]^+$ (86.2), 249 [M – O=C=CCl]$^+$ (13.7), 275 [M – $CH_2Cl]^+$ (99.9), 325 $[M+H]^+$ (0.3). Found (%): C, 33.16; H, 2.14; F, 35.36; N, 8.74. $C_9H_7ClF_6N_2O_2$. Calculated (%): C, 33.3; H, 2.17; F, 35.12; N, 8.63.

**2-(2,3-Epoxypropoxy)-6-phenyl-4-trifluoromethylpyrimidine (7).** The yield was 19%, m.p. 82—84 °C. IR (DRA), ν/cm$^{-1}$: 1555, 1585 (C=C, C=N); 1115—1200 (C—F). $^1$H NMR, δ: 2.82 (dd, 1 H, H(3´b), $^2J_{H,H}$ = 4.9 Hz, $^3J_{H,H}$ = 2.6 Hz); 2.93 (dd, 1 H, H(3´a), $^2J_{H,H}$ = 4.9 Hz, $^3J_{H,H}$ = 4.2 Hz); 3.47 (dtd, 1 H, H(2´), *J* = 5.8 Hz, *J* = 4.0 Hz, *J* = 2.6 Hz); 4.52 (dd, 1 H, H(1´b), $^2J_{H,H}$ = = 11.8 Hz, $^3J_{H,H}$ = 5.8 Hz); 4.72 (dd, 1 H, H(1´a), $^2J_{H,H}$ = = 11.8 Hz, $^3J_{H,H}$ = 3.9 Hz); 7.51—7.60 (m, 3 H, $H_m$, $H_p$); 7.71 (s, 1 H, H(5)); 8.14 (dd, 2 H, $H_o$, *J* = 8.2 Hz, *J* = 1.5 Hz). $^{19}$F NMR, δ: 91.57 (s, $CF_3$). MS, *m*/*z* ($I_{rel}$ (%)): 77 $[C_6H_5]^+$ (15.3), 128 [M – $NCOCH_2CHOCH_2$ – $CF_3]^+$ (21.9), 197 [M – $NCOCH_2CHOCH_2]^+$ (13.8), 212 [M – $CH_2CHOCH_2$ – – HCN]$^+$ (19.5), 219 [M – $C_6H_5]^+$ (17.5), 223 [M – – $OCH_2CHOCH_2]^+$ (13.1), 224 [M – $OCHCHOCH_2]^+$ (26.1), 227 [M – $CF_3]^+$ (20.1), 238 [M – $CH_3CHOCH_2]^+$ (13.2), 239 [M – $CH_2CHOCH_2]^+$ (45.9), 240 [M – $CHCHOCH_2]^+$ (24.3), 241 [M – $OCH{=}C{=}CH_2]^+$ (40.6), 253 [M – $CHOCH_2]^+$ (47.2), 254 [M – $CHOCH]^+$ (16.5), 265 [M – $CH_2OH]^+$ (99.9), 266 [M – $CH_2O]^+$ (50.4), 267 [M – CHO]$^+$ (20.3), 279 [M – OH]$^+$ (19.1), 295 [M – H]$^+$ (11.6), 296 $[M]^+$ (9.5). Found (%): C, 56.68; H, 3.75; F, 18.97; N, 9.51. $C_{14}H_{11}F_3N_2O_2$. Calculated (%): C, 56.76; H, 3.74; F, 19.24; N, 9.46.

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