Treatment of Polyfluoro-1,1-dihydroalkyl Sulfones with Sodium Cyanate and Triethylamine: A New Method for the Synthesis of 6-(Polyfluoroalkyl)uracils

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Polyfluoro-1,1-dihydroalkyl benzyl sulfones **1** reacted with sodium cyanate in the presence of Et_3N to give triethylammonium salts of uracil derivatives **2**. The structure of **2b** was established by X-ray determination. Acidification of compounds **2** with aqueous HCl gave 5-(benzylsulfonyl)-6-(polyfluoroalkyl)pyrimidine-2,4(1*H*,3*H*)-diones **3**. Alkylation of compounds **3** with CH_3I afforded products methylated at N-2, confirmed by X-ray diffraction. Treatment of **3** with PCl_5 gave dichloropyrimidines **7**. The chlorine atoms in compounds **7** with polyfluoroalkyl substituents of different lengths showed differing reactivities in reactions with ammonia and methanol. The sites of substitution of chlorine atoms in **7** were elucidated by X-ray studies. Direct amination of **3** occurred together with desulfonylation on heating in HMPA, with formation of 6-(polyfluoroalkyl)-substituted 2,4-bis(dimethylamino)pyrimidines **13**.

Introduction

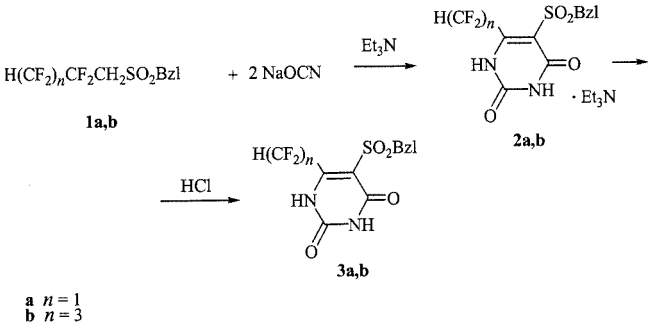
The pyrimidine framework is widespread in nature; there are many biologically and physiologically active compounds that incorporate its nucleus. Pyrimidine derivatives have therefore been extensively studied and great attention paid to the development of methods for their synthesis,[1] especially of uracils − universal synthetic intermediates for the obtainment of various heterocycles with pyrimidine rings.[2] One goal of these investigations focused on the synthesis of pyrimidine compounds with polyfluoroalkyl substituents.[3,4]

The general methods for the synthesis of fluorinated derivatives of pyrimidines consist either of direct polyfluorination of uracils[5−7] or of the use of acyclic fluorine-containing building blocks. The most used building blocks are trifluoromethacrylonitrile,[8] ethyl trifluoroacetate,[9] and fluorinated derivatives of aminocrotonic acid[10] or its structural analogues.[11]

In previous works we have reported on the preparation and properties of polyfluoro-1,1-dihydroalkyl sulfones **1** − new reagents for the synthesis of fluorine-containing compounds. We have described the application of sulfones **1** for the preparation of enamines, imines, and ketones,[12] and of hydrazones, osazones and pyrazoles.[13] In the presence of tertiary amines, sulfones **1** react with sodium azide to give trialkylammonium salts of triazoles.[14] In this paper we report on the treatment of sulfones **1** with sodium cyanate to afford 6-polyfluoroalkyl-substituted uracils, and some chemical properties of the compounds obtained.

Results and Discussion

We have found that treatment of polyfluoro-1,1-dihydroalkyl sulfones with sodium cyanate in the presence of triethylamine affords triethylammonium salts of uracils **2**, which are easily converted into uracils **3** by treatment with hydrochloric acid (Scheme 1). Compounds **3** can also be obtained without isolation of salts **2**, by immediate acidification of the reaction mixture with hydrochloric acid. The optimal molar ratio of reagents for production of uracils **3** in high yields was established to be sulfone **1**/Et_3N/NaOCN = 1:1:2.



Scheme 1. Synthesis of compounds **3a** and **3b**

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The structure of compound **2b** was established by single-crystal X-ray diffraction (Figure 1, Table 1). It was found that, in the solid state, the compound comprises a pyrimidinium anion and an $HNEt_3$ cation, connected by the relatively strong[15] N(4)−H(4)···O(2) hydrogen bond. In turn, two anions are bound in the centrosymmetric dimer by the pair of N(3)−H(3)···O(1′) intermolecular hydrogen bonds. The N(1)C(2)N(3)C(4)C(5)C(6) heterocycle is planar within 0.078 Å, the benzene ring being twisted out of this plane by 21.7°.

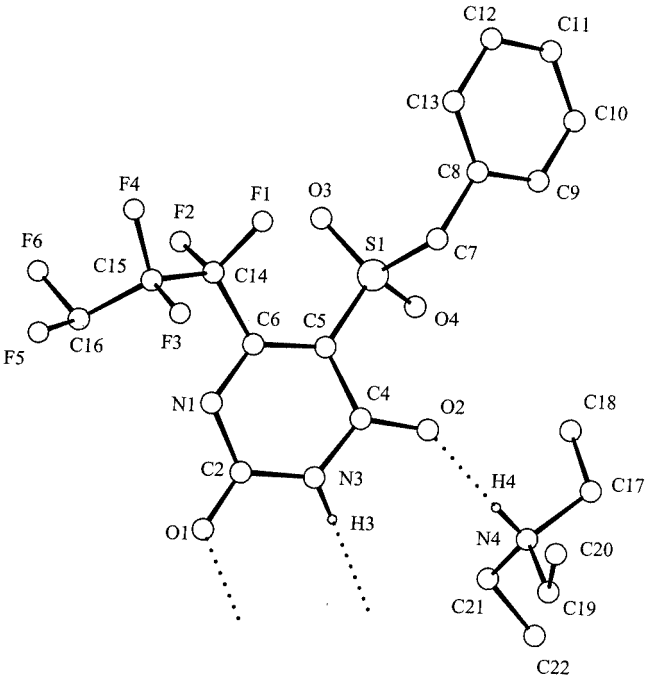


Figure 1. Crystal structure of the salt **2b**; selected interatomic distances [Å] and angles [°]: N(4)···O(2) 2.791(2), H(4)···O(2) 1.93(3) Å, N(4)H(4)O(2) 173(2)°; N(3)···O(1′) 2.776(2), H(3)···O(1′) 1.95(3) Å, N(3)H(3)O(1′) 174(2)° (primed atoms are generated from the asymmetric unit by the inversion center)

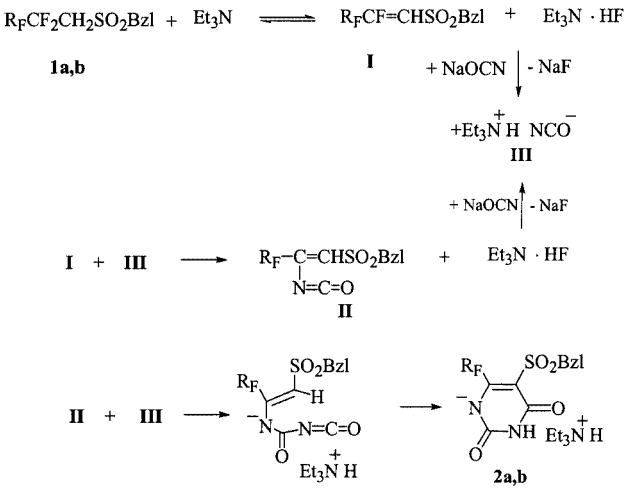
To explain the formation of **2** it should be taken into account that sulfones **1** are dehydrofluorinated with triethylamine to yield vinyl fluorides **I**, which is the first step for all reactions of sulfones **1** that we have studied previously.[12−14] This reaction step is reversible, and removal of either triethylammonium hydrofluoride or vinyl fluoride **I** from the region of the reaction pushes the equilibrium to the right (Scheme 2).

Monitoring of the reactions by ^{19}F NMR spectroscopy showed that only signals of vinyl fluoride **I**,[16] starting sulfone **1** (disappearing in the course of the reaction), and final salt **2** were observed in the reaction mixture, no other intermediate products being detected. Further steps of the reaction should therefore be reasonably rapid. The reaction probably proceeds by nucleophilic substitution of the vinylic fluorine atom in **I** by the isocyanate group, with intermediate formation of vinyl isocyanate **II**. Only triethylammonium cyanate **III**, formed by reaction between sodium cyanate and triethylamine hydrofluoride, can be the source of the isocyanate ion, since isolated vinyl fluorides **I** in the pure state do not react with sodium cyanate under the conditions applied for production of salts **2** (CH_3CN, 70 °C, 6 h). The reaction of triethylammonium cyanate with vinyl isocyanate **II** results in the formation of salt **2**.

Table 1. Comparison of selected bond lengths [Å] and angles [°] in **2b**, **5a**, **8a**, and **9b**

	2b	**5a**	**8a**	**9b**[a]
S(1)−O(3)	1.429(2)	1.441(2)	1.435(2)	1.426(8)
S(1)−O(4)	1.431(2)	1.439(2)	1.441(2)	1.424(8)
S(1)−C(5)	1.749(2)	1.745(2)	1.770(2)	1.795(11)
S(1)−C(7)	1.781(2)	1.790(3)	1.788(3)	1.803(13)
N(1)−C(2)	1.364(3)	1.356(4)	1.316(3)	1.299(15)
C(2)−N(3)	1.365(3)	1.384(3)	1.308(3)	1.314(16)
N(3)−C(4)	1.372(3)	1.398(3)	1.354(3)	1.321(14)
C(4)−C(5)	1.435(3)	1.433(4)	1.426(3)	1.374(14)
C(5)−C(6)	1.392(3)	1.392(3)	1.389(3)	1.380(15)
C(6)−N(1)	1.323(3)	1.323(3)	1.340(3)	1.342(14)
C(2)−O(1)	1.235(3)	1.234(3)	1.728(2)[b]	1.347(16)
C(4)−O(2)	1.237(2)	1.228(3)	1.336(3)[c]	1.714(12)[d]
C(6)N(1)C(2)	117.8(2)	119.5(2)	114.6(2)	117.9(11)
N(1)C(2)N(3)	118.4(2)	119.0(2)	129.6(2)	125.2(12)
C(2)N(3)C(4)	125.6(2)	123.5(2)	116.53(2)	116.4(10)
N(3)C(4)C(5)	114.5(2)	114.8(2)	119.6(2)	124.0(10)
C(4)C(5)C(6)	116.5(2)	118.2(2)	116.6(2)	114.2(10)
C(5)C(6)N(1)	125.6(2)	123.9(2)	122.9(2)	121.7(11)

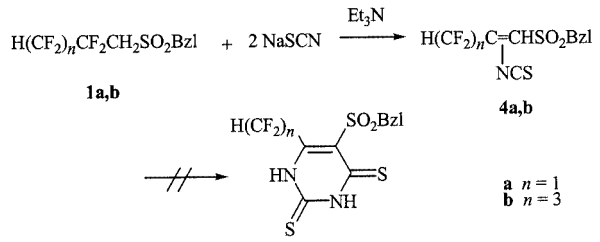
[a] Average values for two independent molecules. [b] C(2)−Cl(1) distance. [c] C(4)−N(4) distance. [d] C(4)−Cl(1) distance.



Scheme 2. Proposed reaction sequence for the formation of salts **2a** and **2b**

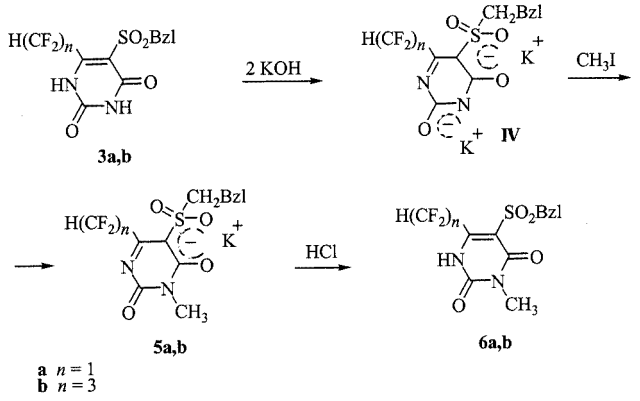
It should be noted that treatment of sulfones **1** with sodium thiocyanate and Et_3N under similar conditions afforded vinyl isothiocyanates **4**. No cyclization to the desired corresponding thiouracil derivatives was observed (Scheme 3). The formation of **4** was confirmed by ^1H NMR and IR spectroscopy, the latter revealing intense absorption bands, attributable to the isothiocyanato group, in the 2050−2100 cm^{-1} region.

The alkylation of the ammonium salts of substituted uracils is well documented.[17] In contrast, triethylammonium salts **2** do not react with alkyl halides or tosylates in boiling acetonitrile. Potassium salts, which can easily be prepared



Scheme 3. Reaction between **1** and sodium thiocyanate

with equimolar amounts of KOH and **3**, have low solubilities in most conventional solvents (in particular in the CH_3CN/CH_3OH mixture used to study the reaction), which makes their use difficult. However, application of 2 equiv. of KOH affords the highly soluble dipotassium salts **IV**, which easily react with methyl iodide at room temperature to provide K salts of monomethylated uracils **5**. No further methylation at the other possible site of **5** was observed even on prolonged boiling of the reaction mixture. After acidification of salts **5** with hydrochloric acid, *N*-methyluracils **6** were obtained (Scheme 4).



Scheme 4. Alkylation of compounds **3a**, **3b** with CH_3I

An X-ray diffraction study of **5a** was used to confirm the formation of the K salt and to establish the site of alkylation. The crystal structure of **5a** is shown in Figure 2, selected bond lengths and angles are listed in Table 1. The N(1)C(2)N(3)C(4)C(5)C(6) heterocycle is planar within 0.061 Å, the benzene ring being twisted out of this plane by 41.2°. The main bond lengths and angles in anion **5a** are quite similar to the corresponding values in **2b**. Some shortening of the S(1)−C(5) bond in **2b** and **5a** in comparison with **8a** and **9b** (see below) and with the standard for $S^{IV}-C(sp^2)$ bond range 1.76−1.78 Å[18,19] is apparently connected with the delocalization of the negative charge not only over the pyrimidine heterocycle, but also towards the SO_2Bzl group.

One path for synthetic application of uracils is their transformation into reactive dichloropyrimidines. Uracils **3** react with PCl_5 to give dichloropyrimidines **7** (Scheme 5).

The chlorine atoms in **7** are not equally reactive in nucleophilic substitution reactions. A chlorine atom should be more active in the position in the heterocycle *para* to the nitrogen atom and *ortho* to the electronegative sulfonyl

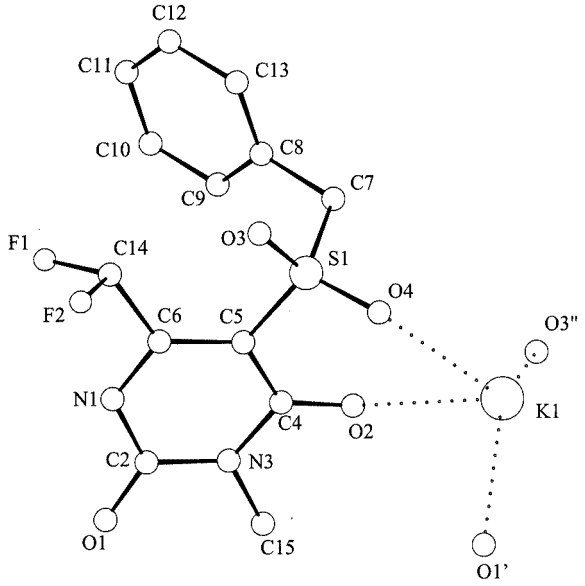
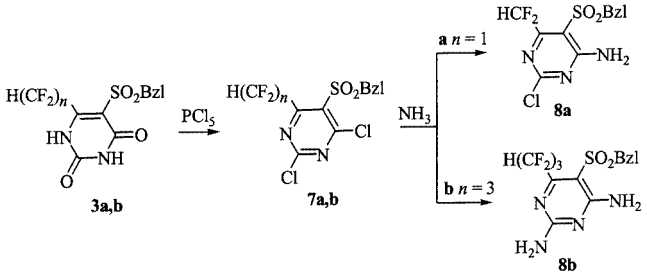


Figure 2. Crystal structure of the salt **5a**; selected interatomic distances [Å] and angles [°]: K(1)···O(2) 2.624(2), K(1)···O(4) 2.885(2), K(1)···O(1′) 2.763(2), K(1)···O(3′′) 2.799(2) Å, O(2)K(1)O(4) 61.4(2)° [primed and double primed atoms are connected with the corresponding atoms in the asymmetric unit by the $(-x + 2, -y, -z + 2)$ and $(x - 3/2, -y - 1/2, z - 1/2)$ operations]; hydrogen atoms are omitted for clarity



Scheme 5. Synthesis of dichlorides **7a** and **7b** and their reactions with ammonia

group.[20] To examine this we studied reactions between dichloropyrimidine **7** and ammonia and methanol.

Treatment of **7a** with 2 equiv. of gaseous ammonia (and also in excess) in diethyl ether afforded as the main reaction product the derivative 4-amino-2-chloropyrimidine (**8a**), which, due to its low solubility, precipitated from the reaction mixture. An X-ray diffraction study confirmed the formation of the 4-amino-substituted pyrimidine (Figure 3, Table 1). The central 6-membered ring N(1)C(2)N(3)C(4)C(5)C(6) is almost planar: deviations from least-square plane do not exceed 0.026 Å. The $N(4)H_2$ amino group is approximately coplanar to this plane (the corresponding dihedral angle being only 8.2°), whereas the C(8)−C(13) benzene ring is twisted out of this plane by 37.1°. The N(4) atom has a trigonal-planar bond configuration [sum of the bond angles 360.0(6)°]. Because of n-π conjugation, the exocyclic N(4)−C(4) bond is at 1.336(3) Å significantly shorter than the standard value for the $N(sp^2)-C(sp^2)$ single bond of 1.45 Å.[21] As an interesting peculiarity of the molecular structure **9a**, one should note

the strong[15] intramolecular H bond N(4)−H(41)···O(4) "assisted by resonance".[22]

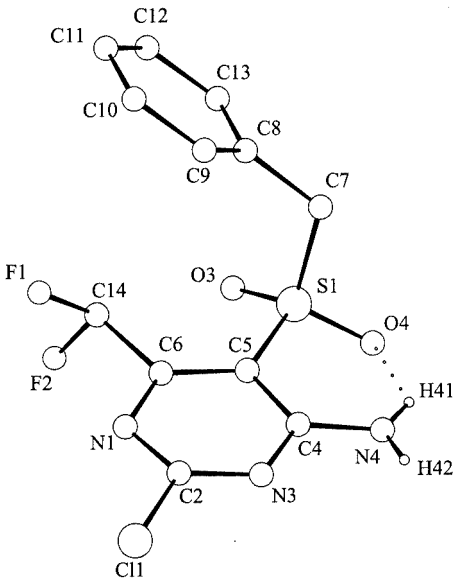
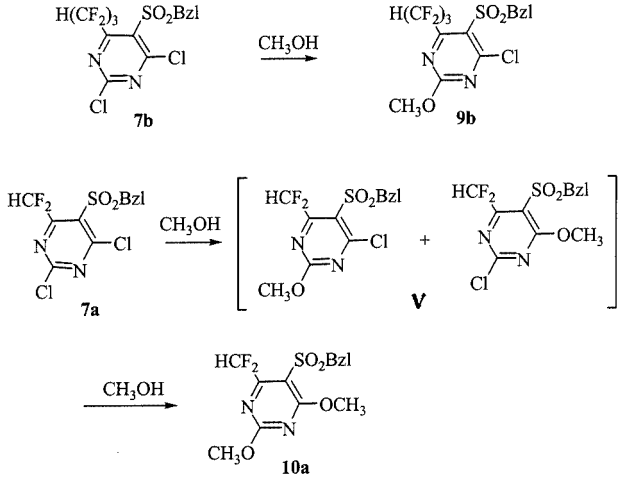


Figure 3. A perspective view and labelling scheme for the molecule **8a**; the main geometrical parameters of the intramolecular H bond: N(4)···O(4) 2.722(3), O(4)···H(41) 2.02(3) A, N(4)H(41)O(4) 135.2(2)°

In the case of compound **7b**, with the more lipophilic hexafluoropropyl substituent, treatment with ammonia proceeded in solution to give at least three products even with only 2 equiv. of ammonia (1 equiv. as reagent and 1 equiv. as base), as deduced from ^{19}F NMR observations. Nevertheless, an excess of ammonia afforded diaminopyrimidine **8b** in high yield.

In contrast, treatment of **7b** with methanol in diethyl ether in the absence of HCl acceptor afforded the product **9b**, monomethoxy-substituted at C-2, in high yield (Scheme 6).



Scheme 6. Reactions of dichlorides **7a** and **7b** with methanol

The substitution at C-2 was confirmed by a single-crystal X-ray diffraction study of the compound **9b** (Figure 4, Table 1). It was found that the asymmetric unit of **9b** contains two independent molecules (A and B). The N(1)C(2)N(3)C(4)C(5)C(6) cyclic systems in these molecules are planar within 0.056 and 0.036 Å, respectively, the benzene rings being almost coplanar with these planes (the corresponding dihedral angles being only 2.5° in molecule A and 14.8° in molecule B). All the bond lengths and angles in **9b** are unexceptional.[18,19]

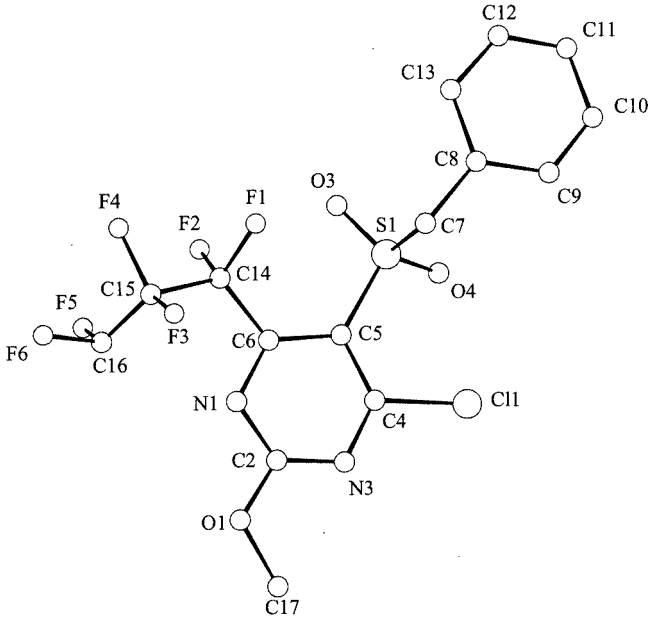


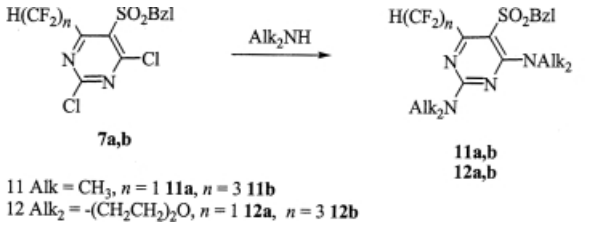
Figure 4. A perspective view and labelling scheme for the independent molecule A of the compound **9b**; hydrogen atoms are omitted for clarity

Comparison of the main geometric parameters of the N(1)C(2)N(3)C(4)C(5)C(6) ring in anions **2b** and **5a** on one hand, and in neutral molecules **8a** and **9b** on the other (Table 1), shows that the N(1)−C(2), C(2)−N(3), and N(3)−C(4) bonds are noticeably longer in the former structures, whereas the C(6)−N(1) bond is slightly shorter. In this regard, one could suppose somewhat different types of electron density delocalization in these two types of heterocyclic systems.

Dichloride **7a** reacted with an equimolar amount of methanol under analogous conditions to give a mixture of monosubstituted products **V** in a 1:1 ratio, as revealed by ^1H NMR spectroscopy. Further substitution of other chlorine atoms proceeded under more forcing conditions, at reflux with methanol in toluene in the presence of pyridine.

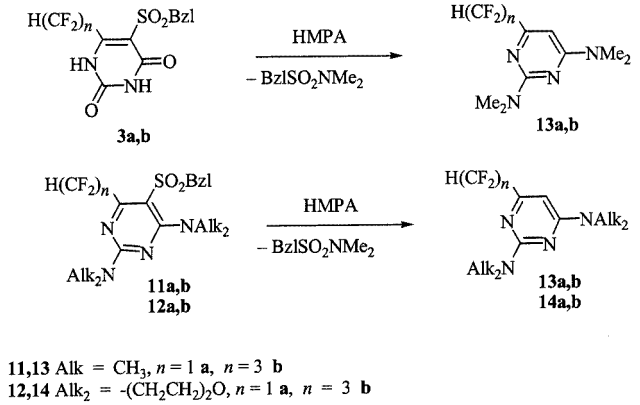
In the reactions between dichloride **7** and stronger nucleophiles and bases − secondary alkylamines − the rates of nucleophilic substitution of the chlorine atoms were equalized and both chlorine atoms were easily substituted to furnish 2,4-bis(dialkylamino)pyrimidines (**11**, **12**) (Scheme 7).

2,4-Bis(dialkylamino)pyrimidines can be obtained by the direct amination of uracils with amides of phosphorous or phosphoric acids.[23] It has also been reported[24] that uracil derivatives with substituents R at the 5-position (specifically R = Cl, Br, CH_2OH) underwent a reductive elimination of R during these amination reactions. Studying the chemical properties of uracils **3**, we found that heating of these com-



Scheme 7. Reactions of dichlorides **7a** and **7b** with secondary amines

pounds with an excess of hexamethylphosphoramide (HMPA) at 215−220 °C resulted in the formation of 2,4-bis(dimethylamino)-6-(polyfluoroalkyl)pyrimidines (**13**) that did not contain benzylsulfonyl groups. *N*,*N*-Dimethylbenzylsulfonamide was isolated from a reaction mixture (Scheme 8). Thus, the replacement of the benzylsulfonyl group by a hydrogen atom had taken place along with amination. It is difficult to offer an acceptable mechanism for this reaction; it is possible only to assume that the sources of protons for the formation of the reduced pyrimidine must be some acid impurity present in HMPA (or their production during high-temperature reactions), because desulfonylation reactions with freshly distilled HMPA were noticeably slowed down.



Scheme 8. Desulfonylation of compounds **3**, **11**, and **12**

We have found that HMPA also acts as a desulfonylation agent for dialkylamino-substituted pyrimidines **11** and **12**, which allowed us to obtain amino-6-(polyfluoroalkyl) derivatives of pyrimidines **13** and **14** not substituted at the 5-positions. Such desulfonylation reactions in the presence of HMPA have not been described previously.

Conclusion

In summary, we have found a new method for the synthesis of 6-(polyfluoroalkyl)uracils, consisting of a ring-closure reaction of fluorovinyl sulfones with 2 equiv. of triethylammonium cyanate, generated by treatment of 1,1-dihydropolyfluoroalkyl sulfones **1** with sodium cyanate and triethylamine. The chlorine atoms in dichloropyrimidines **7** formed from uracils **3**, bearing polyfluoroalkyl substituents of different lengths, displayed differing reactivities in reactions with ammonia and methanol. Uracils **3** underwent amination with simultaneous reductive desulfonylation on treatment with hexamethylphosphoramide.

Experimental Section

General Remarks: All solvents were purified by standard procedures. Melting points were determined with a Boetius heating table and values are uncorrected. NMR spectra were recorded with Varian VXR 300 (299.9 MHz for ^{1}H and 75.4 MHz for ^{13}C) and Varian Gemini 200 (188.1 MHz for ^{19}F) machines. Chemical shifts are given in ppm referenced to residual nondeuterated solvent signals in chloroform (δ = 7.26 for ^{1}H NMR and 77.16 for ^{13}C NMR) and dimethyl sulfoxide (δ = 2.50 for ^{1}H NMR and 39.52 for ^{13}C NMR). For ^{19}F NMR spectra chemical shifts are reported in ppm relative to an internal standard hexafluorobenzene (δ = −162.9). The degree of substitution at the C atoms was determined by APT experiments. The progress of all reactions was monitored by ^{19}F NMR spectroscopy. Elemental analysis was performed in the Analytical Laboratory of the Institute of Organic Chemistry, NAS of Ukraine.

General Procedure for the Preparation of Triethylammonium Salts 2a and 2b and 5-(Benzylsulfonyl)-6-(polyfluoroalkyl)pyrimidine-2,4(1*H*,3*H*)-diones (3a and 3b): Et_3N (1.1 mL, 7.8 mmol) was added to a solution of sulfone **1** (7.4 mmol) in 15 mL of acetonitrile, the mixture was stirred for 5 min and powdered NaOCN (1.0 g, 15.4 mmol) was added. The suspension was stirred at 70 °C for 4−6 h (monitoring by ^{19}F NMR), and the hot mixture was filtered through a layer of Celite®. After cooling, a quantity of triethylammonium salt **2** precipitated, and was taken for analysis. The warm solution of salt **2** in acetonitrile was acidified with conc. HCl (5 mL) and, after this had stood for 12 h, precipitated crystals were filtered off, washed with water, dried, and recrystallized from ethanol.

Salt 2a: M.p. 230−232 °C (decomp.). ^{1}H NMR ([D$_6$]DMSO): δ = 10.43 (broad s, 1 H, NH), 7.30 (m, 3 H, ArH), 7.20 (m, 2 H, ArH), 6.70 (t, $^2J_{H,F}$ = 55.2 Hz, 1 H, CHF_2), 4.56 (s, 2 H, CH_2SO_2), 3.39 (broad, NH + H_2O), 3.07 (q, 6 H, NCH_2), 1.16 (t, 9 H, CH_3). ^{19}F NMR (CH_3CN): δ = −120.10 (d, $^2J_{H,F}$ = 55.2 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 163.19 (s, C4), 161.29 (t, $^2J_{C,F}$ = 21.1 Hz, C6), 158.77 (s, C2), 130.50 (s, ArC-*ortho*), 129.97 (s, ArC-*para*), 128.07 (s, ArC-*meta*), 127.97 (s, ArC-*ipso*), 108.31 (t, $^1J_{C,F}$ = 240.0 Hz, CF_2H), 103.07 (s, C5), 59.55 (s, CH_2SO_2), 45.75 (s, CH_2N), 8.55 (s, CH_3). $C_{18}H_{25}F_2N_3O_4S$ (417.464): calcd. C 51.79, H 6.04, N 10.07, S 7.68; found C 51.62, H 6.00, N 10.14, S 7.34.

Salt 2b: M.p. 228−230 °C (decomp.). ^{1}H NMR ([D$_6$]DMSO): δ = 10.64 (s, 1 H, NH), 7.29 (m, 3 H, ArH), 7.24 (m, 2 H, ArH), 7.06 (tt, $^2J_{H,F}$ = 54.6, $^3J_{H,F}$ = 6.0 Hz, 1 H, CHF_2), 4.59 (s, 2 H, CH_2SO_2), 3.37 (broad, NH + H_2O), 3.04 (q, 6 H, NCH_2), 1.15 (t, 9 H, CH_3). ^{19}F NMR (CH_3CN): δ = −104.64 (m, 2 F, CF_2), −128.65 (m, 2 F, CF_2), −135.87 (dm, $^2J_{H,F}$ = 54.6 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 163.72 (s, C4), 158.00 (t, $^2J_{C,F}$ = 29.8 Hz, C6), 156.86 (t, $^4J_{C,F}$ = 2.8 Hz, C2), 130.80 (s, ArC-*ortho*), 129.96 (s, ArC-*para*), 128.02 (s, ArC-*meta*), 127.89 (s, ArC-*ipso*), 114.15 (tt, $J_{C,F}$ = 265.8, $^2J_{C,F}$ = 25.6 Hz, $CF_2CF_2CF_2H$), 111.98 (tm, $^1J_{C,F}$ = 265.8 Hz, $CF_2CF_2CF_2H$), 108.48 (tt, $^1J_{C,F}$ = 252.0, $^2J_{C,F}$ = 27.6 Hz, CF_2H), 103.94 (s, C5), 60.14 (s, CH_2SO_2), 45.83 (s, CH_2N), 8.69 (s, CH_3). $C_{20}H_{25}F_6N_3O_4S$ (517.484): calcd. C 46.42, H 4.87, N 8.12, S 6.20; found C 45.87, H 4.85, N 8.15, S 6.58.

5-(Benzylsulfonyl)-6-(difluoromethyl)pyrimidine-2,4(1*H*,3*H*)-dione (3a): Yield 81%, m.p. 257−260 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 12.15 (s, 1 H, NH), 12.4 (s, 1 H, NH), 7.37 (m, 3 H, ArH), 7.30 (m, 2 H, ArH), 7.17 (t, $^2J_{H,F}$ = 52.5 Hz, 1 H, CHF_2), 4.76 (s, 2 H, CH_2), 3.35 (broad, NH + H_2O). ^{19}F NMR (CH_3CN): δ = −120.09 (d, $^2J_{H,F}$ = 52.5 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 160.15 (s, C4), 150.62 (t, $^2J_{C,F}$ = 24.5 Hz, C6), 149.52 (s, C2), 131.04 (s, ArC-*ortho*), 128.83 (s, ArC-*para*), 128.65 (s, ArC-*meta*), 127.92 (s, ArC-*ipso*), 110.76 (t, $^3J_{C,F}$ = 4.1 Hz, C5), 106.65 (t, $^1J_{C,F}$ = 245.3 Hz, CF_2), 60.20 (s, CH_2). $C_{12}H_{10}F_2N_2O_4S$ (316.284): calcd. C 45.57, H 3.19, N 8.86, S 10.14; found C 45.23, H 3.30, N 9.06, S 10.13.

5-(Benzylsulfonyl)-6-(2,2,3,3,4,4-hexafluoropropyl)pyrimidine-2,4(1*H*,3*H*)-dione (3b): Yield 90%, m.p. 253−255 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 11.84 (s, 1 H, NH), 7.34 (m, 3 H, ArH), 7.27 (m, 2 H, ArH), 6.87 (tt, $^2J_{H,F}$ = 51.9, $^3J_{H,F}$ = 5.9 Hz, 1 H, CHF_2), 5.31 (broad, NH + H_2O), 4.74 (s, 2 H, CH_2). ^{19}F NMR (CH_3CN): δ = −101.73 (m, 2 F, CF_2), −122.00 (m, 2 F, CF_2), −138.06 (dm, $^2J_{H,F}$ = 51.4 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 160.94 (s, C4), 150.91 (s, C2), 148.86 (t, $^2J_{C,F}$ = 28.6 Hz, C6,), 131.03 (s, ArC-*ortho*), 128.41 (s, ArC-*para*), 128.26 (s, ArC-*meta*), 128.10 (s, ArC-*ipso*), 113.32 (tm, $^1J_{C,F}$ = 265.1 Hz, $CF_2CF_2CF_2H$), 112.90 (s, C5), 111.82 (tt, $^1J_{C,F}$ = 264.6, $^2J_{C,F}$ = 32.4 Hz, $CF_2CF_2CF_2H$), 108.48 (tt, $^1J_{C,F}$ = 250.8, $^2J_{C,F}$ = 29.6 Hz, CF_2H), 60.96 (s, CH_2). $C_{14}H_{10}F_6N_2O_4S$ (416.304): calcd. C 40.39, H 2.42, N 6.73, S 7.70; found C 40.44, H 2.50, N 6.65, S 7.92.

1-(Benzylsulfonyl)-3,3-difluoro-2-isothiocyanatoprop-1-ene (4a): Dried NaSCN (0.61 g, 7.5 mmol) was added to a solution of sulfone **1a** (1.0 g, 3.7 mmol) and Et_3N (0.52 mL, 3.7 mmol) in 10 mL of acetonitrile. The solution was heated at 70 °C for 4 h and, after cooling, was poured into water. The mixture was then extracted with chloroform (2 × 30 mL), the organic phase was dried with Na_2SO_4, and the solvent was evaporated at reduced pressure. The residue was extracted several times with boiling hexane. Compound **4a** crystallized on cooling of the hexane solution. Yield 70%, m.p. 76−78 °C. IR (film): $\tilde{\nu}$ = 2050 cm^{-1} (NCS). ^{1}H NMR ($CDCl_3$): δ = 7.39 (m, 5 H, ArH), 6.29 (s, 1 H, CH=), 6.01 (t, $^2J_{H,F}$ = 54.3 Hz, 1 H, CHF_2), 4.39 (s, 2 H, CH_2). ^{19}F NMR ($CDCl_3$): δ = −120.91 (d, $^2J_{H,F}$ = 54.3 Hz, 2 F, CF_2H). NMR ^{13}C ($CDCl_3$): δ = 144.75 (s, C=S), 136.05 (t, $^2J_{C,F}$ = 25.8 Hz, HCF_2C), 131.06 (s, ArC-*ortho*), 129.69 (s, ArC-*para*), 129.20 (s, ArC-*meta*), 126.74 (s, ArC-*ipso*), 122.20 (t, $^3J_{C,F}$ = 5.4 Hz, CH=), 109.80 (t, $^1J_{C,F}$ = 249.5 Hz, CF_2H), 62.27 (s, CH_2). $C_{11}H_9F_2NO_2S_2$ (289.304): calcd. C 45.67, H 3.14, N 4.84, S 22.16; found C 45.68, H 3.11, N 4.81, S 21.78.

1-(Benzylsulfonyl)-1,1,2,2,3,3-hexafluoro-2-isothiocyanatopent-1-ene (4b): By the procedure described above for **4a**, compound **4b** was obtained as a red, viscous oil, which contained about 10% of impurities according to the NMR spectra. No special attempts were made to purify this product. IR (film): $\tilde{\nu}$ = 2100 cm^{-1} (NCS). ^{1}H NMR ($CDCl_3$): δ = 7.41 (m, 5 H, ArH), 6.45 (s, 1 H, CH=), 5.99 (tt, $^2J_{H,F}$ = 51.9, $^3J_{H,F}$ = 5.0 Hz, 1 H, CHF_2), 4.41 (s, 2 H, CH_2). ^{19}F NMR ($CDCl_3$): δ = −116.34 (m, 2 F, CF_2), −129.86 (m, 2 F, CF_2), −137.69 (dm, $^2J_{H,F}$ = 51.9 Hz, 2 F, CF_2H).

5-(Benzylsulfonyl)-6-(difluoromethyl)-3-methylpyrimidine-2,4(1*H*,3*H*)-dione (6a): A solution of **3a** (0.76 g, 2.4 mmol) in 5 mL of CH_3CN was added to a solution of KOH (0.25 g, 4.46 mmol) in 3 mL of methanol, followed by CH_3I (0.14 mL, 2.25 mmol). The solution was allowed to stand at room temperature for 24 h. A quantity of K salt **5a** precipitated as colorless crystals, which were collected and used for X-ray and NMR analyses. ^{1}H NMR ([D$_6$]DMSO): δ = 7.29 (m, 3 H, ArH), 7.19 (m, 2 H, ArH), 6.69 (t, $^2J_{H,F}$ = 55.3 Hz, 1 H, CHF_2), 4.58 (s, 2 H, CH_2), 3.13 (s, 3 H, NCH_3). ^{19}F NMR (CH_3CN): δ = −120.27 (d, $^2J_{H,F}$ = 55.3 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 162.36 (s, C4), 158.91 (t, $^2J_{C,F}$ = 21.3 Hz, C6), 157.92 (s, C2), 130.35 (s, ArC-*ortho*), 129.52 (s, ArC-*para*), 127.97 (s, ArC-*meta*), 127.92 (s, ArC-*ipso*), 108.21 (t, $^1J_{C,F}$ = 241.0 Hz, CF_2H), 102.23 (t, $^3J_{C,F}$ = 2.7 Hz, C5), 59.37 (s, CH_2), 26.76 (s, NCH_3). The solution was concentrated, the solid residue was dissolved in 15 mL of warm water, and 5 mL of conc. HCl was added to precipitate **6a**. Yield 86%, m.p. 211−213 °C (CH_3CN/H_2O, 2:1). ^{1}H NMR ([D$_6$]DMSO): δ = 7.37 (m, 3 H, ArH), 7.32 (m, 2 H, ArH), 7.13 (t, $^2J_{H,F}$ = 52.3 Hz, 1 H, CHF_2), 4.77 (s, 2 H, CH_2), 3.36 (broad, NH + H_2O), 3.21 (s, 3 H, NCH_3). ^{19}F NMR (CH_3CN): δ = −120.07 (d, $^2J_{H,F}$ = 52.3 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 159.17 (s, C4), 149.52 (s, C2), 148.66 (t, $^2J_{C,F}$ = 24.7 Hz, C6), 130.98 (s, ArC-*ortho*), 128.67 (s, ArC-*para*), 128.47 (s, ArC-*meta*), 127.75 (s, ArC-*ipso*), 110.23 (t, $^3J_{C,F}$ = 4.6 Hz, C5), 106.55 (t, $^1J_{C,F}$ = 244.7 Hz, CF_2H), 60.08 (s, CH_2), 27.31 (s, NCH_3). $C_{13}H_{12}F_2N_2O_4S$ (330.314): calcd. C 47.27, H 3.66, N 8.48, S 9.71; found C 47.18, H 3.58, N 8.47, S 9.54.

5-(Benzylsulfonyl)-6-(1,1,2,2,3,3-hexafluoropropyl)-3-methylpyrimidine-2,4(1*H*,3*H*)-dione (6b): Compound **6b** was obtained from **3b** (1.0 g, 2.4 mmol), in the same manner as **6a**. Yield 89%, m.p. 214−216 °C (CH_3CN/H_2O, 2:1). ^{1}H NMR ([D$_6$]DMSO): δ = 7.32 (m, 3 H, ArH), 7.25 (m, 2 H, ArH), 6.96 (tt, $^2J_{H,F}$ = 52.5, $^3J_{H,F}$ = 5.8 Hz, 1 H, CHF_2), 4.69 (s, 2 H, CH_2), 4.20 (broad, NH + H_2O), 3.18 (m, 3 H, NCH_3). ^{19}F NMR (CH_3CN): δ = −102.00 (m, 2 F, CF_2), −122.35 (m, 2 F, CF_2), −137.78 (dm, $^2J_{H,F}$ = 52.5 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 160.63 (s, C4), 151.90 (s, C2), 148.73 (t, $^2J_{C,F}$ = 28.5 Hz, C6), 131.03 (s, ArC-*ortho*), 128.39 (s, ArC-*ipso*), 128.28 (s, ArC-*para*), 128.19 (s, ArC-*meta*), 113.36 (tt, $^1J_{C,F}$ = 264.9, $^2J_{C,F}$ = 31.7 Hz, $CF_2CF_2CF_2H$), 110.86 (tm, $^1J_{C,F}$ = 264.9 Hz, $CF_2CF_2CF_2H$), 110.46 (s, C5), 108.79 (tt, $^1J_{C,F}$ = 251.8, $^2J_{C,F}$ = 29.8 Hz, CF_2H), 60.72 (s, CH_2), 27.32 (s, NCH_3). $C_{15}H_{12}F_6N_2O_4S$ (430.334): calcd. C 41.87, H 2.81, N 6.51, S 7.45; found C 41.83, H 2.80, N 6.58, S 7.57.

5-(Benzylsulfonyl)-2,4-dichloro-6-(polyfluoroalkyl)pyrimidines 7. General Procedure: PCl_5 (6 mmol) was added to a suspension of pyrimidinedione **3** (2 mmol) in 15 mL of benzene and the mixture was heated under reflux for 12 h. After cooling, the solution was decanted and the solvents were evaporated under vacuum. The residue was triturated with cool hexane, and solid was filtered off and crystallized from hexane.

Dichloride 7a: Yield 82%, m.p. 128−130 °C. ^{1}H NMR ($CDCl_3$): δ = 7.36 (m, 3 H, ArH), 7.23 (m, 2 H, ArH), 6.89 (t, $^2J_{H,F}$ = 53.1 Hz, 1 H, CHF_2), 4.72 (s, 2 H, CH_2). ^{19}F NMR (C_6H_6): δ = −118.36 (d, $^2J_{H,F}$ = 53.1 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 164.14 (t, $^2J_{C,F}$ = 24.1 Hz, C6), 163.82 (s, C4), 163.31 (s, C2), 130.96 (s, ArC-*ortho*), 130.39 (s, ArC-*para*), 129.63 (s, ArC-*meta*), 129.44 (t, $^3J_{C,F}$ = 3.2 Hz, C5), 125.46 (s, ArC-*ipso*), 107.26 (t, $^1J_{C,F}$ = 246.2 Hz, CF_2), 62.19 (s, CH_2). $C_{12}H_8Cl_2F_2N_2O_2S$ (353.178): calcd. Cl 20.08, N 7.93, S 9.08; found Cl 20.01, N 7.95, S 9.20.

Dichloride 7b: Yield 94%, m.p. 108−110 °C. ^{1}H NMR ($CDCl_3$): δ = 7.46−7.31 (m, 5 H, ArH), 6.47 (tt, $^2J_{H,F}$ = 52.6, $^3J_{H,F}$ = 5.5 Hz, 1 H, CHF_2), 4.75 (s, 2 H, CH_2). ^{19}F NMR (C_6H_6): δ = −102.20 (m, 2 F, CF_2), −125.89 (m, 2 F, CF_2), −136.32 (dm, $^2J_{H,F}$ = 52.6 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 165.49 (s, C4), 161.79 (s, C2), 160.67 (t, $^2J_{C,F}$ = 30.0 Hz, C6), 132.94 (s, C5), 131.55 (s, ArC-*ortho*), 130.09 (s, ArC-*para*), 129.35 (s, ArC-*meta*), 124.68 (s, ArC-*ipso*), 113.62 (tt, $J_{C,F}$ = 263.3, $^2J_{C,F}$ = 30.8 Hz,

C$F_2CF_2CF_2H$), 111.24 (tm, $^1J_{C,F}$ = 266.4 Hz, CF_2*C*F_2CF_2H), 108.75 (tt, $^1J_{C,F}$ = 254.1, $^2J_{C,F}$ = 30.8 Hz, CF_2H), 62.78 (s, CH_2). $C_{14}H_8Cl_2F_6N_2O_2S$ (453.198): calcd. Cl 15.65, N 6.18, S 7.08; found Cl 15.39, N 6.16, S 7.09.

5-(Benzylsulfonyl)-2-chloro-6-(difluoromethyl)pyrimidine-4-amine (8a): Ammonia gas was passed at 5−10 °C for 1 h through a solution of dichloride **7a** (0.71 g, 2 mmol) in 40 mL of diethyl ether, and the solvent was evaporated. The remained solid was washed with water and recrystallized. Yield 75%, m.p. 208−210 °C (CH_3CN). ^{1}H NMR ([D$_6$]DMSO): δ = 9.05 (broad, 1 H, NH), 7.69 (broad, 1 H, NH), 7.42−7.31 (m, 5 H, ArH), 6.82 (t, $^2J_{H,F}$ = 53.1 Hz, 1 H, CHF_2), 4.85 (s, 2 H, CH_2). ^{19}F NMR ([D$_6$]DMSO): δ = −118.82 (d, $^2J_{H,F}$ = 53.1 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 162.52 (s, C4), 161.97 (s, C2), 160.80 (t, $^2J_{C,F}$ = 22.9 Hz, C6), 131.37 (s, ArC-*ortho*), 129.12 (s, ArC-*para*), 128.71 (s, ArC-*meta*), 126.82 (s, ArC-*ipso*), 110.53 (t, $^3J_{C,F}$ = 4.0 Hz, C5), 107.41 (t, $^1J_{C,F}$ = 242.1 Hz, CF_2H), 60.78 (s, CH_2). $C_{12}H_{10}ClF_2N_3O_2S$ (333.737): calcd. Cl 10.62, N 12.59, S 9.61; found Cl 10.59, N 12.51, S 9.81.

5-(Benzylsulfonyl)-6-(1,1,2,2,3,3-hexafluoropropyl)pyrimidine-2,4-diamine (8b): Ammonia gas was passed at 5−10 °C for 0.5 h through a solution of dichloride **7b** (0.91 g, 2 mmol) in 40 mL of diethyl ether, and the solvent was evaporated. The remained solid was washed with water and recrystallized. Yield 94%, m.p. 198−200 °C (benzene). ^{1}H NMR ([D$_6$]DMSO): δ = 7.70−6.90 (overlapped, 10 H, 5 ArH + CHF_2 + 2 NH_2), 4.55 (s, 2 H, CH_2). ^{19}F NMR (Et_2O): δ = −104.41 (m, 2 F, CF_2), −129.07 (m, 2 F, CF_2), −136.65 (dm, $^2J_{H,F}$ = 51.4 Hz, 2 F, CF_2H). ^{13}C NMR ([D$_6$]DMSO): δ = 162.65 (s, C4), 161.14 (s, C2), 156.81 (t, $^2J_{C,F}$ = 29.5 Hz, C6), 131.16 (s, ArC-*ortho*), 128.57 (s, ArC-*para*), 128.36 (s, ArC-*meta*), 127.82 (s, ArC-*ipso*), 114.33 (tt, $^1J_{C,F}$ = 264.0, $^2J_{C,F}$ = 26.2 Hz, *C*$F_2CF_2CF_2H$), 111.97 (tm, $^1J_{C,F}$ = 260.3 Hz, CF_2*C*F_2CF_2H), 110.26 (tt, $^1J_{C,F}$ = 251.9, $^2J_{C,F}$ = 29.5 Hz, CF_2H), 101.37 (s, C5), 62.04 (s, CH_2). $C_{14}H_{12}F_6N_4O_2S$ (414.334): calcd. C 40.58, H 2.92, N 13.52, S 7.74; found C 40.75, H 3.02, N 13.53, S 7.69.

5-(Benzylsulfonyl)-4-chloro-6-(1,1,2,2,3,3-hexafluoropropyl)-2-methoxypyrimidine (9b): Methanol (1 mL) was added to a solution of dichloropyrimidine **7b** (0.91 g, 2 mmol) in 40 mL of diethyl ether, and the solution was allowed to stand for 24 h. The solvent was evaporated, and the residue was recrystallized from ethanol/H_2O (4:1). Yield 79%, m.p. 121−123 °C. ^{1}H NMR ($CDCl_3$): δ = 7.37 (m, 5 H, ArH), 6.50 (tt, $^2J_{H,F}$ = 52.8, $^3J_{H,F}$ = 5.3 Hz, 1 H, CHF_2), 4.70 (s, 2 H, CH_2), 4.16 (s, 3 H, OCH_3). ^{19}F NMR (Et_2O): δ = −102.25 (m, 2 F, CF_2), −126.07 (m, 2 F, CF_2), −136.41 (dm, $^2J_{H,F}$ = 52.8 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 165.95 (s, C4), 163.96 (s, C2), 161.49 (t, $^2J_{C,F}$ = 29.6 Hz, C6), 131.55 (s, ArC-*ortho*), 129.75 (s, ArC-*para*), 129.18 (s, ArC-*meta*), 127.03 (s, C5), 125.62 (s, ArC-*ipso*), 113.75 (tt, $^1J_{C,F}$ = 263.1, $^2J_{C,F}$ = 29.0 Hz, *C*$F_2CF_2CF_2H$), 111.37 (tm, $^1J_{C,F}$ = 265.9 Hz, CF_2*C*F_2CF_2H), 108.85 (tt, $^1J_{C,F}$ = 253.5, $^2J_{C,F}$ = 29.7 Hz, CF_2H), 62.74 (s, CH_2), 57.32 (s, OCH_3). $C_{15}H_{11}ClF_6N_2O_3S$ (448.777): calcd. Cl 7.90, N 6.24; found Cl 7.72, N 6.26.

5-(Benzylsulfonyl)-6-(difluoromethyl)-2,4-dimethoxypyrimidine (10a): Methanol (1 mL) was added to a solution of dichloropyrimidine **7a** (0.71 g, 2 mmol) in 40 mL of diethyl ether. The solution was allowed to stand for 24 h and the solvent was evaporated. The residue, as indicated by NMR spectroscopic data (two sets of signals in a 1:1 ratio), was found to be a mixture of monomethoxy-substituted chloropyrimidines **V**. This mixture was dissolved in 30 mL of toluene, methanol (1 mL) and pyridine (0.5 mL) were added, and the mixture was heated under reflux for 4 h. The solvent was evaporated, and the residue was treated with CH_3OH/H_2O (10:1), filtered off, and recrystallized from methanol. Yield 72%, m.p. 134−136 °C. ^{1}H NMR ($CDCl_3$): δ = 7.35−7.28 (m, 3 H, ArH), 7.20−7.16 (m, 2 H, ArH), 7.04 (t, $^2J_{H,F}$ = 53.6 Hz, 1 H, CHF_2), 4.55 (s, 2 H, CH_2), 4.20 (s, 3 H, OCH_3), 4.09 (s, 3 H, OCH_3). ^{19}F NMR (toluene): δ = −119.63 (d, $^2J_{H,F}$ = 53.6 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 169.45 (s, C4), 166.67 (s, C2), 163.36 (t, $^2J_{C,F}$ = 23.5 Hz, C6), 130.71 (s, ArC-*ortho*), 129.48 (s, ArC-*para*), 129.06 (s, ArC-*meta*), 127.33 (s, ArC-*ipso*), 112.55 (s, $^3J_{C,F}$ = 3.8 Hz, C5), 107.41 (t, $^1J_{C,F}$ = 243.1 Hz, CF_2H), 62.19 (s, CH_2), 56.24 (s, OCH_3), 56.15 (s, OCH_3). $C_{14}H_{14}F_2N_2O_4S$ (344.334): calcd. C 48.83, H 4.10, N 8.14, S 9.31; found C 48.78, H 4.12, N 8.16, S 9.34.

5-(Benzylsulfonyl)-2,4-bis(dialkylamino)-6-(polyfluoroalkyl)-pyrimidines 11, 12. General Procedure: A solution of morpholine (0.39 mL, 4.5 mmol) in 5 mL of benzene was added dropwise to a solution of dichloropyrimidine **7** (1 mmol) (for dimethylamino derivatives: dimethylamine was passed through a solution of dichloride) in 15 mL of benzene and mixture was stirred for 0.5 h. The solvent was evaporated, and the residue was carefully washed with water, dried, and recrystallized.

Compound 11a: Yield 82%, m.p. 121−122 °C (hexane/benzene, 4:1). ^{1}H NMR ($CDCl_3$): δ = 7.33−7.14 (m, 5 H, ArH), 6.97 (t, $^2J_{H,F}$ = 54.3 Hz, 1 H, CHF_2), 4.42 (s, 2 H, CH_2), 3.24 (m, 3 H, NCH_3), 3.09 (m, 9 H, 3 NCH_3). ^{19}F NMR ($CDCl_3$): δ = −120.22 (d, $^2J_{H,F}$ = 54.3 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.59 (s, C4), 163.10 (t, $^2J_{C,F}$ = 21.8 Hz, C6), 159.97 (s, C2), 130.87 (s, ArC-*ortho*), 128.78 (s, ArC-*para*), 128.62 (s, ArC-*meta*), 128.43 (s, ArC-*ipso*), 109.72 (t, $^1J_{C,F}$ = 241.5 Hz, CF_2H), 102.59 (s, C5), 64.62 (s, CH_2), 42.34 (s, NCH_3), 37.01 (s, NCH_3). $C_{16}H_{20}F_2N_4O_2S$ (370.414): calcd. C 51.88, H 5.44, N 15.13, S 8.66; found C 51.30, H 5.68, N 15.12, S 8.26.

Compound 11b: Yield 95%, m.p. 144−146 °C (hexane/benzene, 9:1). ^{1}H NMR ($CDCl_3$): δ = 7.34 (m, 5 H, ArH), 6.56 (tt, $^2J_{H,F}$ = 53.4, $^3J_{H,F}$ = 6.2 Hz, 1 H, CHF_2), 4.61 (s, 2 H, CH_2), 3.19 (s, 6 H, CH_3), 3.14 (broad d, 6 H, CH_3). ^{19}F NMR (C_6H_6): δ = −106.73 (m, 2 F, CF_2), −129.02 (m, 2 F, CF_2), −136.30 (dm, $^2J_{H,F}$ = 53.4 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.09 (s, C4), 159.19 (t, $^2J_{C,F}$ = 27.8 Hz, C6), 158.59 (s, C2), 131.36 (s, ArC-*ortho*), 128.73 (s, ArC-*para*), 128.63 (s, ArC-*meta*), 128.41 (s, ArC-*ipso*), 113.74 (tt, $^1J_{C,F}$ = 261.0, $^2J_{C,F}$ = 29.2 Hz, *C*$F_2CF_2CF_2H$), 111.43 (tm, $^1J_{C,F}$ = 265.1 Hz, $CF_2CF_2CF_2H$,), 108.94 (tt, $^1J_{C,F}$ = 252.6, $^2J_{C,F}$ = 29.2 Hz, CF_2H), 104.46 (s, C5), 63.84 (t, *J* = 5.1 Hz CH_2), 41.65 (s, NCH_3), 37.10 (s, NCH_3). $C_{18}H_{20}F_6N_4O_2S$ (470.434): calcd. C 45.96, H 4.29, N 11.91, S 6.82; found C 45.97, H 4.24, N 11.89, S 7.09.

Compound 12a: Yield 78%, m.p. 155−156 °C (hexane/benzene, 3:2). ^{1}H NMR ($CDCl_3$): δ = 7.32−7.18 (m, 3 H, ArH), 7.23 (t, $^2J_{H,F}$ = 54.4 Hz, 1 H, CHF_2), 7.10 (m, 2 H, ArH), 4.38 (s, 2 H, CH_2SO_2), 3.90 (m, 2 H, NCH_2CH_2O), 3.75 (m, 10 H, NCH_2CH_2O), 3.41 (m, 4 H, NCH_2CH_2O). ^{19}F NMR (C_6H_6): δ = −119.13 (d, $^2J_{H,F}$ = 54.5 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 165.35 (s, C4), 163.26 (t, $^2J_{C,F}$ = 22.0 Hz, C6), 159.58 (s, C2), 130.53 (s, ArC-*ortho*), 128.76 (s, ArC-*para*), 128.49 (s, ArC-*meta*), 128.29 (s, ArC-*ipso*), 109.00 (t, $^1J_{C,F}$ = 242.7 Hz, CF_2H), 104.91 (s, C5), 66.66 (s, CH_2SO_2), 66.65 (s broad, OCH_2), 64.29 (s, OCH_2), 51.82 (s, NCH_2), 44.33 (broad s, NCH_2). $C_{20}H_{24}F_2N_4O_4S$ (454.484): calcd. N 12.33, S 7.05; found N 12.26, S 7.28.

Compound 12b: Yield 80%, m.p. 187−189 °C (hexane/benzene, 5:1). ^{1}H NMR ($CDCl_3$): δ = 7.33−7.21 (m, 5 H, ArH), 6.37 (tt, $^2J_{H,F}$ =

52.8, $^3J_{H,F}$ = 5.8 Hz, 1 H, CHF_2), 4.56 (s, 2 H, CH_2SO_2), 3.73 (m, 10 H, NCH_2CH_2O), 3.63 (m, 6 H, NCH_2CH_2O). ^{19}F NMR (C_6H_6): δ = −105.70 (m, 2 F, CF_2), −127.68 (m, 2 F, CF_2), −136.64 (dm, $^2J_{H,F}$ = 52.8 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.61 (s, 2C4), 159.49 (t, $^2J_{C,F}$ = 27.7 Hz, C6), 158.01 (s, C2), 131.09 (s, ArC-*ortho*), 128.93 (s, ArC-*para*), 128.73 (s, ArC-*meta*), 128.32 (s, ArC-*ipso*), 114.20 (tt, $^1J_{C,F}$ = 258.9, $^2J_{C,F}$ = 29.4 Hz $CF_2CF_2CF_2H$), 110.08 (tm, $^1J_{C,F}$ = 261.2 Hz, $CF_2CF_2CF_2H$), 109.22 (tt, $^1J_{C,F}$ = 253.8, $^2J_{C,F}$ = 29.1 Hz, CF_2H), 105.47 (s, C5), 66.70 (s, OCH_2), 66.56 (s broad, OCH_2), 64.25 (t,[25] J = 4.1 Hz, CH_2SO_2), 50.71 (s, NCH_2), 44.46 (broad s, NCH_2). $C_{22}H_{24}F_6N_4O_4S$ (554.504): calcd. N 10.10, S 5.78; found N 10.02, S 5.85.

2,4-Bis(dialkylamino)-6-(polyfluoroalkyl)pyrimidines 13, 14. General Procedure: A mixture of compound **3/11/12** (2 mmol) and HMPTA (3 mL) was heated at 215−220 °C for 1−4 h, the reaction being monitored by ^{19}F NMR spectroscopy. When the reaction was complete, water (50 mL) was added and the mixture was extracted with $CHCl_3$ (3×20 mL). After drying with Na_2SO_4 and evaporation of solvent, diethyl ether (10−15 mL) was added to the obtained residue, and a large quantity of undissolved *N*-(dimethylamino)benzylsulfonamide was filtered off [m.p. 98−100 °C, ref.[25] m.p. 101 °C. ^1H NMR ($CDCl_3$): δ = 7.39 (m, 5 H, ArH), 4.24 (s, 2 H, CH_2), 2.72 (s, 6 H, NCH_3)]. The mother liquor was concentrated and the crude product was purified by crystallization as detailed below.

Compound 13a: This compound was prepared by the general procedure described above, starting either from compound **3a** (time of reaction 1 h) or from compound **11a** (time of reaction 3.5 h), and purified by distillation followed by low-temperature crystallization from pentane. Yield 71% (starting from **3a**), 52% (starting from **11a**), b.p. 60−66 °C (0.05 Torr), m.p. 36−38 °C− ^1H NMR ($CDCl_3$): δ = 6.26 (t, $^2J_{H,F}$ = 55.8 Hz, 1 H, CHF_2), 6.03 (s, 1 H, C5-H), 3.14 (s, 6 H, CH_3), 3.08 (s, 6 H, CH_3). ^{19}F NMR ($CDCl_3$): δ = −120.05 (d, $^2J_{H,F}$ = 55.8 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.56 (s, C4), 162.21 (s, C2), 159.72 (t, $^2J_{C,F}$ = 24.7 Hz, C6), 113.95 (t, $^1J_{C,F}$ = 241.0 Hz, HCF_2), 87.03 (t, $^3J_{C,F}$ = 4.1 Hz, C5), 37.03 (s, CH_3), 36.85 (s, CH_3). $C_9H_{14}F_2N_4$ (216.230): calcd. C 49.99, H 6.53, N 25.91; found C 49.92, H 6.67, N 25.87.

Compound 13b: This compound was prepared by the general procedure described above, starting either from compound **3b** (time of reaction 1 h) or from compound **11b** (time of reaction 4 h), and purified by crystallization from hexane/diethyl ether (4:1). Yield 78% (starting from **3b**), 57% (starting from **11b**), m.p. 70−72 °C. ^1H NMR ($CDCl_3$): δ = 6.65 (tt, $^2J_{H,F}$ = 53.2, $^3J_{H,F}$ = 6.2 Hz, 1 H, CHF_2), 6.14 (s, 1 H, C5-H), 3.12 (s, 6 H, CH_3), 3.10 (broad s, 6 H, CH_3). ^{19}F NMR ($CDCl_3$): δ = −118.91 (m, 2 F, CF_2), −134.37 (m, 2 F, CF_2), −138.81 (dm, $^2J_{H,F}$ = 53.2 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.39 (s, C4), 161.83 (s, C2), 155.82 (t, $^2J_{C,F}$ = 26.0 Hz, C6), 113.16 (tt, $^1J_{C,F}$ = 255.2, $^2J_{C,F}$ = 28.5 Hz, $CF_2CF_2CF_2H$), 111.02 (tm, $^1J_{C,F}$ = 261.6 Hz, $CF_2CF_2CF_2H$),

Table 2. Crystal data and structure refinement parameters for compounds **2b**, **5a**, **8a**, and **9b**

	2b	**5a**	**8a**	**9b**
Empirical formula	$C_{20}H_{25}F_6N_3O_4S$	$C_{13}H_{11}F_2KN_2O_4S$	$C_{12}H_{10}ClF_2N_3O_2S$	$C_{15}H_{11}ClF_6N_2O_3S$
Cell parameters				
a [Å]	10.956(2)	9.206(2)	7.986(2)	18.757(3)
b [Å]	22.053(3)	15.509(2)	5.508(1)	10.054(2)
c [Å]	11.049(2)	10.594(3)	30.956(7)	19.649(7)
β [°]	117.84(1)	93.00(2)	93.99(3)	90
V [Å^3]	2360.4(7)	1510.5(8)	1358.2(5)	3705.3(1.6)
Z	4	4	4	8 (two independent molecules)
$D_{calcd.}$ [g·cm^{-3}]	1.46	1.62	1.63	1.61
Crystal system	monoclinic	monoclinic	monoclinic	orthorhombic
Space group	$P2_1/a$	$P2_1/n$	$P2_1/c$	$Pca2_1$
μ [cm^{-1}]	19.18	48.13	42.60	36.39
M	517.49	368.40	333.74	448.77
F(000)	1077	757	685	1812
Crystal size [mm]	0.56 × 0.56 × 0.56	0.31 × 0.59 × 0.65	0.12 × 0.19 × 0.37	0.12 × 0.50 × 0.63
Index ranges	$0 < h < 12$	$0 < h < 11$	$0 < h < 9$	$-1 < h < 22$
	$0 < k < 25$	$0 < k < 18$	$0 < k < 6$	$-1 < k < 11$
	$-12 < l < 12$	$-12 < l < 12$	$-36 < l < 36$	$-1 < l < 22$
θ_{max} [°]	70	70	65	65
No. of reflections:				
collected	4363	3072	2709	4039
independent	4009	2773	2251	3165
in refinement	3530 [$I > 3\sigma(I)$]	2410 [$I > 3\sigma(I)$]	1875 [$I > 3\sigma(I)$]	1984 [$I > 2\sigma(I)$]
R(int)	0.011	0.021	0.034	0
No. of refined parameters	315	208	199	395
Obsd./var.	11.2	11.6	9.4	5.0
Final R indices				
R	0.043	0.055	0.036	0.063
R_w	0.045	0.065	0.040	0.063
GOF	1.097	1.115	1.127	1.193
Weighting coefficients	2.10, −0.60, 0.93, −0.67	4.13, 2.61, 2.88	1.13, 0.05, 0.68, −0.16, 0.11	1.42, 0.78, 0.79, 0.16, 0.41
Largest peak/hole [e·cm^{-3}]	0.32/−0.32	0.46/−0.73	0.22/−0.34	0.27/−0.24

108.71 (tt, $^1J_{C,F}$ = 253.7, $^2J_{C,F}$ = 29.0 Hz, HCF_2), 88.98 (t, $^3J_{C,F}$ = 5.7 Hz, C5), 37.04 (s, CH_3), 36.80 (s, CH_3). $C_{11}H_{14}F_6N_4$ (316.250): calcd. C 41.78, H 4.46, N 17.72; found C 41.70, H 4.60, N 17.78.

Compound 14a: This compound was prepared by the general procedure described above, starting from compound **12a** (time of reaction 4 h), and purified by crystallization from hexane/diethyl ether (4:1). Yield 47%, m.p. 117−119 °C. ^{1}H NMR ($CDCl_3$): δ = 6.26 (t, $^2J_{H,F}$ = 56.0 Hz, 1 H, CHF_2), 6.14 (s, 1 H, C5-H), 3.75 (m, 12 H, NCH_2CH_2O), 3.61 (m, 4 H, NCH_2CH_2O). ^{19}F NMR ($CDCl_3$): δ = −119.99 (d, $^2J_{H,F}$ = 56.0 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.46 (s, C4), 161.55 (s, C2), 160.42 (t, $^2J_{C,F}$ = 24.6 Hz, C6), 113.50 (t, $^1J_{C,F}$ = 242.1 Hz, HCF_2), 88.29 (t, $^3J_{C,F}$ = 3.7 Hz, C5), 66.92 (s, CH_2O), 65.58 (s, CH_2O), 44.30 (s, 2 CH_2N). $C_{13}H_{18}F_2N_4O_2$ (300.300): calcd. C 51.99, H 6.04, N 18.66; found C 51.83, H 6.09, N 18.57.

Compound 14b: This compound was prepared by the general procedure described above, starting from compound **12b** (time of reaction 4 h), and was crystallized from hexane/diethyl ether (7:1) after standing at −20 °C overnight. Yield 64%, m.p. 131−133 °C. ^{1}H NMR ($CDCl_3$): δ = 6.39 (tt, $^2J_{H,F}$ = 52.8, $^3J_{H,F}$ = 6.1 Hz, 1 H, CHF_2), 6.23 (s, 1 H, C5-H), 3.73 (m, 12 H, NCH_2CH_2O), 3.62 (m, 4 H, NCH_2CH_2O). ^{19}F NMR ($CDCl_3$): δ = −119.10 (m, 2 F, CF_2), −133.73 (m, 2 F, CF_2), −138.58 (dm, $^2J_{H,F}$ = 52.8 Hz, 2 F, CF_2H). ^{13}C NMR ($CDCl_3$): δ = 163.38 (s, C4), 161.44 (s, C2), 156.63 (t, $^2J_{C,F}$ = 25.7 Hz, C6), 112.94 (tt, $^1J_{C,F}$ = 256.0, $^2J_{C,F}$ = 29.4 Hz, $CF_2CF_2CF_2H$), 110.75 (tm, $^1J_{C,F}$ = 262.3 Hz, $CF_2CF_2CF_2H$), 108.37 (tt, $^1J_{C,F}$ = 253.7, $^2J_{C,F}$ = 29.2 Hz, HCF_2), 90.42 (t, $^3J_{C,F}$ = 5.3 Hz, C5), 66.88 (s, CH_2O), 66.59 (s, CH_2O), 44.49 (s, CH_2N), 44.39 (s, CH_2N). $C_{15}H_{18}F_6N_4O_2$ (400.320): calcd. C 45.01, H 4.53, N 14.00; found C 45.11, H 4.54, N 14.05.

X-ray Crystallographic Study: Crystal data, data collection and processing parameters are given in Table 2. All crystallographic measurements were performed at 20 °C with a CAD-4 Enraf−Nonius diffractometer (Cu-K_α radiation) using ω-2θ scan mode (the ratio of the scanning rates ω/2θ = 1.2). All data were corrected for Lorentz and polarization effects and an empirical absorption correction based on azimuthal scan data[26] was applied. The structures were solved by direct methods. Non-hydrogen atoms were refined by full-matrix, least-squares techniques in the anisotropic (isotropic/anisotropic for **9b**) approximation. The Chebushev weighting scheme[27] was used. All hydrogen atoms in **2b**, **5a**, and **8a** were located in the difference Fourier maps, in **9b** they were placed in calculated positions. All H atoms were included in the final refinement with the fixed positional and thermal parameters. Only the atoms H(3) and H(4) in **2b** and H(41) and H(42) in **9b** were refined isotropically. The Flack test[28] was applied for the absolute configuration determinations of **9b** [the enantiopole parameter was refined to 0.11(8) using 2044 reflections with the nonaveraged Friedel equivalents]. All structural calculations were carried out with the CRYSTALS program package.[29] CCDC-166789 (**2b**), -166790 (**5a**), -166787 (**8a**), and -166788 (**9b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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