Chemical properties of *N*-polyfluoroethylimidazole and -pyrrole derivatives

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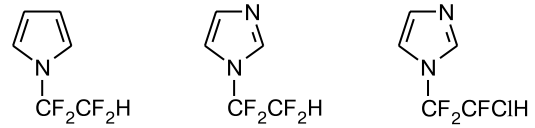
Bromination, acylation, nitration, and metallation of imidazole and pyrrole derivatives containing the difluoromethylene fragment at the N atom were studied. 1-(1,1,2,2-Tetrafluoroethyl)pyrrole, 1-(1,1,2,2-tetrafluoroethyl)imidazole, and 1-(2-chloro-1,1,2-trifluoroethyl)imidazole were used as substrates. 1-Alkyl-3-(1,1,2,2-tetrafluoroethyl)- and 1-alkyl-3-(2-chloro-1,1,2-trifluoroethyl)imidazolium iodides were obtained. These can be used as intermediates for preparation of new ionic liquids of the imidazole series and 1-alkyl-3-polyfluoroethylimidazole-2-thiones.

Key words: *N*-polyfluoroethylimidazoles, *N*-tetrafluoroethylpyrrole, imidazolium salts, carbenes, 1-alkyl-3-polyfluoroethylimidazole-2-thiones.

Many natural compounds belong to imidazole and pyrrole derivatives and often exhibit a high biological activity. Some of them with the carbon or nitrogen atoms bearing fluorine-containing groups have found use as drugs,[1] pesticides,[2] and ionic liquids.[3]

Ring-affecting reactions of nitrogen heterocycles with fluorine-containing groups at the N atom remain uninvestigated. Only reactions affecting fluorine-containing groups (CF=CFCl,[4] CF_2Br,[5] and CF_2SiMe_3[6]) directly bound to the heteroatom have been studied. It is known that fluorine atoms in the α-position with respect to the N atom of alkylamines are sufficiently reactive and hydrolyzed even by atmospheric moisture.[7] This ability allows one to transform alcohols into alkyl fluorides using Yarovenko reaction.[7a] In contrast to alkylamines, *N*-polyfluoroalkyl derivatives of nitrogen heterocycles are more resistant to nucleophilic displacement of the F atoms in the α-position with respect to the heteroatom since the lone electron pair of the N atom is involved in the formation of the 6π-electron aromatic system.

In the present work, we used accessible *N*-(1,1,2,2-tetrafluoroethyl)pyrrole (**1**),[8] *N*-(1,1,2,2-tetrafluoroethyl)imidazole (**2**),[9] and *N*-(2-chloro-1,1,2-trifluoroethyl)imidazole (**3**)[10] as model compounds and studied the possibility of obtaining various functional *N*-polyfluoroalkylimidazole and -pyrrole derivatives **1**—**3**.



1 **2** **3**

Results and Discussion

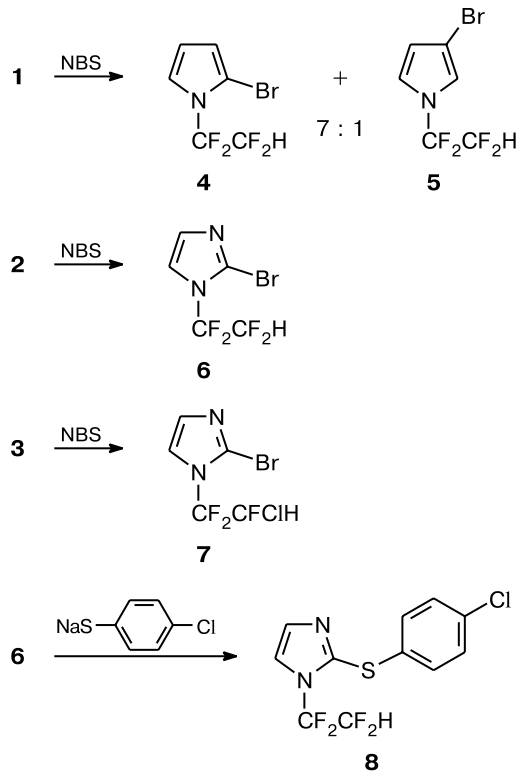
Halogenation of imidazole and pyrrole derivatives with free halogens usually gives mixtures of polyhalogenated products.[11] Use of *N*-bromosuccinimide (NBS) under mild conditions allowed selective bromination of *N*-alkylpyrroles in position 2.[12] However, this reaction with fluorine-containing pyrrole **1** yielded a difficult-to-separate mixture of 2- and 3-bromo derivatives **4** and **5** in the ratio 7 : 1 (Scheme 1). Apparently, the presence of the electron-withdrawing substituent at the N atom makes position 2 of the pyrrole ring less reactive toward electrophilic attacks, and thus bromination occurs at position 3. Bromination of imidazoles **2** and **3** under these conditions proceeds selectively to give 2-bromo-*N*-polyfluoroethylimidazoles **6** and **7** in high yields (see Scheme 1). The presence of two N atoms in the ring and of the electron-withdrawing polyfluoroalkyl group at the N atom activates the proton between the N atoms. Earlier, selective bromination of *N*-methylimidazole was carried out only *via* a lithium derivative.[13]

The bromine atom in *N*-alkyl-2-bromoimidazoles is highly inert. For instance, 2-bromo-*N*-methylimidazole does not react with piperidine even at 200 °C.[14] The presence of the electron-withdrawing fluorinated group at the N atom should make the Br atom more reactive. The reaction of compound **6** with sodium 4-chlorobenzenethiolate in Pr^iOH afforded 4-chlorophenyl *N*-(1,1,2,2-tetrafluoroethyl)imidazol-2-yl sulfide (**8**) (see Scheme 1). The tetrafluoroethyl group remains intact in this reaction.

N-Alkylpyrroles are easily formylated in the Vilsmeier reaction ($POCl_3$, DMF, 15 min, 70 °C).[15] The Vilsmeier

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 781—787, March, 2005.

Scheme 1



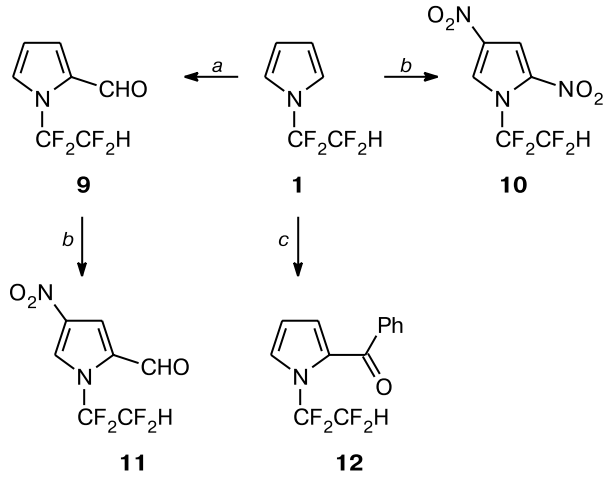
reaction with pyrrole **1** gave 2-formyl-*N*-(1,1,2,2-tetrafluoroethyl)pyrrole (**9**) in high yield; however, compared to *N*-alkylpyrroles, longer heating (3 h) was required (Scheme 2). This is due to the deactivating effect of the electron-withdrawing fluorinated group at the N atom. The ^{1}H NMR spectrum contains signals for three protons of the pyrrole ring with $J > 3$ Hz, which indicates substitution in position 2. The Vilsmeier reaction with imidazoles **2** and **3** did not occur.

Pyrrole derivatives are known to be unstable to strong acids, although nitration of pyrrole derivatives containing electron-withdrawing groups at the N atom has been reported.[16] The presence of a fluorinated group should make the pyrrole ring more resistant to acids. It turned out that the reaction of compound **1** with a mixture of nitric ($d = 1.52$) and sulfuric acids ($d = 1.84$) at -15 to -5 °C, though producing much resinification, gives dinitro product **10** with the retained tetrafluoroethyl group (see Scheme 2). The yield of compound **10** was 22%. Attempted syntheses of a mononitro derivative by the reaction with more diluted HNO_3 and H_2SO_4 were unsuccessful. Pyrrole derivatives containing, apart from the fluorinated group at the N atom, an electron-withdrawing substituent in the ring are more resistant to acids. Indeed, nitration of formylpyrrole **9** with a mixture of conc. HNO_3 and conc. H_2SO_4 afforded 2-formyl-4-nitro-*N*-(1,1,2,2-tetrafluoroethyl)pyrrole (**11**) in 45% yield. In this case, no resinification occurred (see Scheme 2).

The reaction of imidazole derivative **2** with a nitrating mixture yielded the corresponding imidazolium salt and no nitration products below 50 °C; treatment of the reaction mixture allowed the starting reagent to be recovered. Nitration at 100 °C resulted in destruction of the tetrafluoroethyl group to give 4-nitroimidazole.

We investigated acylation of compounds **1**—**3**. *N*-Phenylsulfonylpyrrole is known to enter into the Friedel—Crafts reaction with benzoyl chloride in the presence of Lewis acids.[17] It turned out that compound **1** reacts with benzoyl chloride in the presence of a weak Lewis acid ($ZnCl_2$ in CCl_4) to give 2-benzoyl-*N*-(1,1,2,2-tetrafluoroethyl)pyrrole (**12**) in 37% yield (see Scheme 2). Attempts to acylate compounds **2** and **3** under these conditions failed.

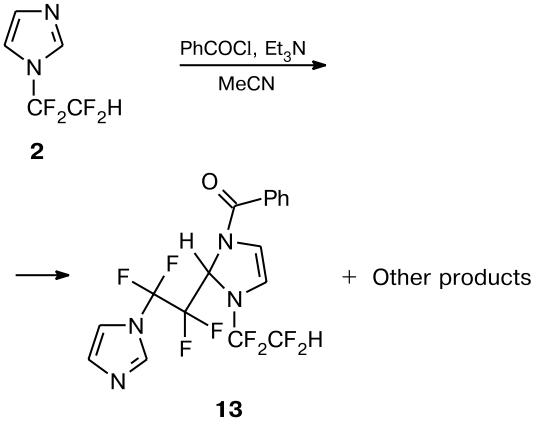
Scheme 2



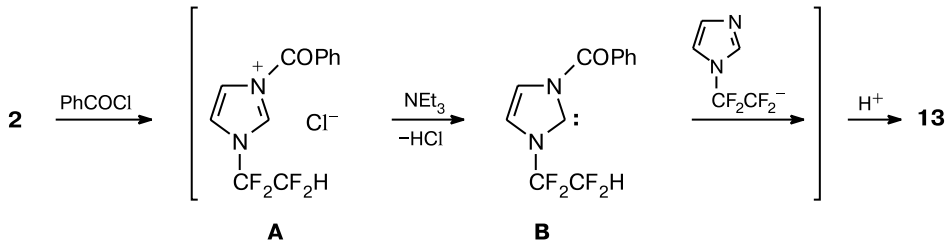
Reagents and conditions: *a*. $POCl_3$, DMF. *b*. HNO_3, H_2SO_4, -15 °C. *c*. $ZnCl_2$, PhCOCl.

Acylation of *N*-methoxymethylimidazoles with benzoyl chloride in the presence of triethylamine has been

Scheme 3



Scheme 4



documented.[18] However, using this method with *N*-tetrafluoroethylimidazole **2**, we obtained a complex mixture of products containing compounds with unsaturated fluorinated groups. Compound **13** was isolated from this mixture (Scheme 3).

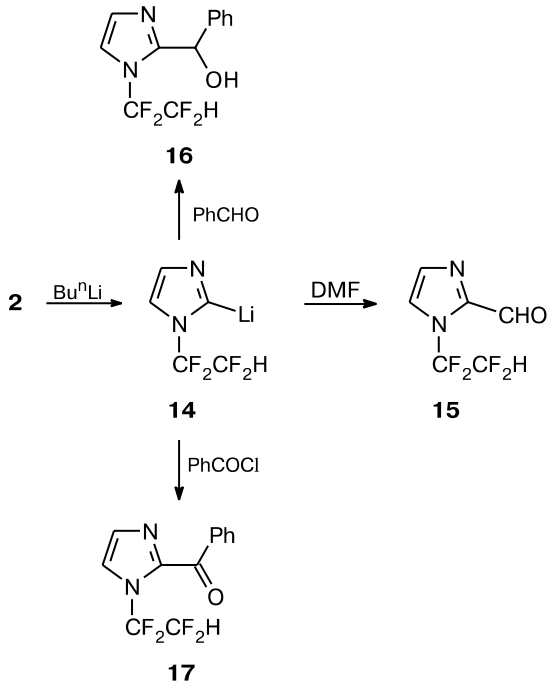
The composition and structure of compound **13** was confirmed by ^{1}H and ^{19}F NMR and mass spectra and elemental analysis data. The mass spectrum contains the molecular ion peak ($m/z = 440$); its fragmentation corresponds to structure **13**. The ^{19}F NMR spectrum shows, apart from a signal at δ_F –130 for the difluoromethyl group, three complex multiplets at δ_F –92, –95, and –135 for the difluoromethylene groups; their intensities correspond to six F atoms.

Apparently, benzoyl chloride initially adds to the N atom of imidazole. When treated with triethylamine, quaternary salt **A** with two electron-withdrawing groups at the N atoms easily forms carbene **B**, which then reacts with a carbanion generated by the tetrafluoroethyl group of compound **2** (Scheme 4).

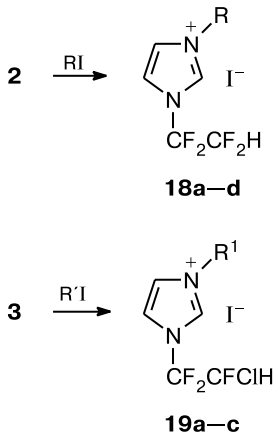
We found that the lithiation of compound **2** with butyllithium at –90 °C yields lithium derivative **14** with the retained tetrafluoroethyl group. The reactions of compound **14** with DMF, benzaldehyde, and benzoyl chloride gave 2-formyl-1-(1,1,2,2-tetrafluoroethyl)imidazole (**15**), phenyl[1-(1,1,2,2-tetrafluoroethyl)imidazol-2-yl]carbinol (**16**), and 2-benzoyl-1-(1,1,2,2-tetrafluoroethyl)imidazole (**17**), respectively (Scheme 5). The presence of the carbonyl function in compounds **15** and **17** was confirmed by the formation of the corresponding hydrazones **15a** and **17a** in the reaction with 2,4-dinitrophenylhydrazine.

When heated with alkyl iodides in acetonitrile, polyfluoroethylimidazoles **2** and **3** gave the corresponding quaternary imidazolium salts **18a—d** and **19a—c**. The reaction was completed over 8 to 40 h, depending on the alkyl (Scheme 6). Salts **18a—d** can be used to prepare new ionic liquids.[19]

Scheme 5



Scheme 6

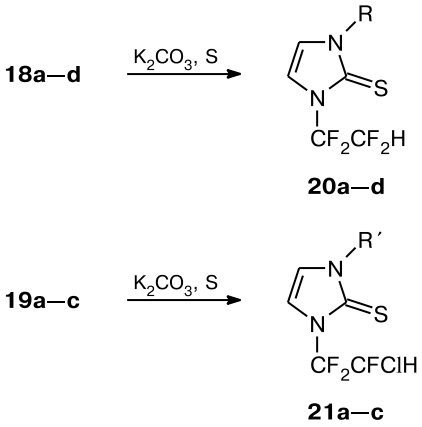


R = Me, Et, Pr^n, Bu^n
R´ = Me, Et, Pr^i

Quaternary imidazolium salts are known to form carbenes in the presence of bases.[20] One of the most characteristic reactions of such carbenes is addition of sulfur to give imidazole-2-thiones.[21]

Salts **18a—d** and **19a—c** can form carbenes. Their reactions with finely divided sulfur in methanol in the presence of K_2CO_3 afforded 1-alkyl-3-polyfluoroethylimidazole-2-thiones **20a—d** and **21a—c** (Scheme 7). These are low-melting solids, which can be distilled *in vacuo*.

Scheme 7



R = Me, Et, Pr^n, Bu^n
R′ = Me, Et, Pr^i

Thus, we demonstrated that imidazole and pyrrole derivatives with the tetrafluoroethyl or chlorotrifluoroethyl group at the N atoms can enter into electrophilic and nucleophilic substitution reactions and metallation, as well as form quaternary salts and carbenes with the retained fluorine-containing groups.

Experimental

^1H and ^{19}F NMR spectra were recorded at 20 °C on a Varian VXR-300 instrument (300 (^1H) and 282 MHz (^{19}F)) in $CDCl_3$ with Me_4Si and CCl_3F as the internal standards, respectively. IR spectra were recorded on a UR-20 instrument (Carl Zeiss Co.) (KBr pellets). Mass spectra were recorded on an Agilent Mat-112 instrument (direct inlet probe). Silica gel (MN-Kieselgel-60) was used. Tetrahydrofuran was dried by distillation over a Na/K alloy; CCl_4 and DMF were distilled over P_2O_5 and BaO, respectively.

Synthesis of 2-bromo-1-(1,1,2,2-tetrafluoroethyl)pyrrole (4), 3-bromo-1-(1,1,2,2-tetrafluoroethyl)pyrrole (5), 2-bromo-1-(1,1,2,2-tetrafluoroethyl)imidazole (6), and 2-bromo-1-(2-chloro-1,1,2-trifluoro)imidazole (7) (general procedure). *N*-Bromosuccinimide (1.78 g, 0.01 mol) was added to a solution of the corresponding heterocycle (**1**, **2**, or **3**) (0.01 mol) in anhydrous THF (15 mL). The reaction mixture was stirred at room temperature for 24 h and concentrated. The product was extracted with CCl_4. The extract was washed with aqueous $Na_2S_2O_3$ (5 g in 50 mL of water) and dried with $MgSO_4$. The solvent was removed and the product was distilled *in vacuo* to give a mixture of compounds **4** and **5** as a colorless oil. The yield of the mixture was 1 g (41%), b.p. 42—44 °C (15 Torr). The ratio of products **4** and **5** was 7 : 1. Found (%): C, 29.06; H, 1.85; Br, 32.25. $C_6H_4BrF_4N$. Calculated (%): C, 29.28; H, 1.63; Br, 32.48. ^1H NMR, δ: **4**: 7.16 (d, 1 H, J = 5 Hz); 7.17 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.27 (t, 1 H, J = 5 Hz); 7.90 (d, 1 H, J = 5 Hz). ^{19}F NMR, δ: **4**: −97.00 (s, 2 F, CF_2); −136.10 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz). ^{19}F NMR, δ: **5**: 6.87 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.22 (s, 1 H); 7.76 (d, 1 H, J = 3 Hz); 7.86 (d, 1 H, J = 3 Hz). ^{19}F NMR, δ: −97.63 (s, 2 F, CF_2); −135.60 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz).

Compound **6** (1.65 g, 67%), colorless liquid, b.p. 67—68 °C (15 Torr). Found (%): C, 24.44; H, 1.48; Br, 32.01. $C_5H_3BrF_4N_2$. Calculated (%): C, 24.30; H, 1.22; Br, 32.37. ^1H NMR, δ: 6.25 (t, 1 H, CF_2H, $J_{H,F}$ = 53 Hz); 7.07 (s, 1 H); 7.21 (s, 1 H). ^{19}F NMR, δ: −95.81 (s, 2 F, CF_2); −135.35 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz).

Compound **7** (1.81 g, 69%), colorless oil, b.p. 90—91 °C (15 Torr). Found (%): C, 22.85; H, 0.96; N, 10.18. $C_5H_3BrClF_3N_2$. Calculated (%): C, 22.78; H, 1.14; N, 10.63. ^1H NMR, δ: 6.64 (dq, 1 H, CFClH, $^2J_{H,F}$ = 48 Hz, $^3J_{H,F}$ = 5 Hz); 7.00—7.14 (m, 1 H); 7.19—7.24 (m, 1 H). ^{19}F NMR, δ: −93.46 (AB system, 2 F, CF_2, $J_{F,F}$ = 219 Hz); −153.65 (d, 1 F, CFClH, $J_{H,F}$ = 48 Hz).

4-Chlorophenyl 1-(1,1,2,2-tetrafluoroethyl)imidazol-2-yl sulfide (8). 4-Chlorobenzenethiol (0.72 g, 0.005 mol) was added to a solution of sodium isopropoxide prepared from metallic Na (0.115 g, 0.005 mol) and Pr^iOH (10 mL). After 10 min, imidazole **6** (1.23 g, 0.005 mol) was added to the resulting solution of sodium 4-chlorobenzenethiolate. The reaction mixture was refluxed for 3 h, concentrated, and diluted with water (30 mL). The oily product was extracted with ether (3×30 mL). The extract was dried with $MgSO_4$, the solvent was removed, and the product was purified by column chromatography with $CHCl_3$ as the eluent (R_f = 0.4) to give compound **8** (0.75 g, 48%) as colorless crystals, m.p. 42—43 °C (from hexane). Found (%): C, 42.25; H, 2.38; S, 10.06. $C_{11}H_7ClF_4N_2S$. Calculated (%): C, 42.52; H, 2.27; S, 10.32. ^1H NMR, δ: 6.37 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.20—7.50 (m, 6 H). ^{19}F NMR, δ: −96.39 (s, 2 F, CF_2); −135.97 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz).

2-Formyl-1-(1,1,2,2-tetrafluoroethyl)pyrrole (9). A mixture of pyrrole **1** (5 g, 0.03 mol), anhydrous DMF (8 mL), and $POCl_3$ (5 mL) was stirred at 75 °C for 3 h. On cooling, the solution was added to 5% $NaHCO_3$ (100 mL). The resulting oil was extracted with ether (3×30 mL). The extract was washed with water (3×100 mL) and dried with $MgSO_4$. The solvent was removed and the product was distilled *in vacuo* to give compound **9** (4.1 g, 70%) as a colorless liquid, b.p. 54—55 °C (15 Torr). Found (%): C, 43.17; H, 2.70; F, 38.77. $C_7H_5F_4NO$. Calculated (%): C, 43.09; H, 2.58; F, 38.94. ^1H NMR, δ: 6.44 (t, 1 H, J = 5 Hz); 6.71 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.20 (d, 1 H, J = 5 Hz); 7.39 (d, 1 H, J = 5 Hz); 9.79 (s, 1 H, CHO). ^{19}F NMR, δ: −96.00 (s, 2 F, CF_2); −136.17 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz). IR, ν/cm^{-1}: 1700 (C=O).

2,4-Dinitro-1-(1,1,2,2-tetrafluoroethyl)pyrrole (10). Pyrrole **1** (1.67 g, 0.01 mol) was added dropwise at −15 °C for 1 h to a mixture of HNO_3 (d = 1.52) (2 mL) and H_2SO_4 (d = 1.84) (3 mL). The reaction mixture was stirred at −15 to 5 °C for 30 min. The resulting solution was poured into ice (100 g). The dark oil that formed was extracted with ether (3×30 mL). The extract was washed with 5% $NaHCO_3$ (100 mL) and dried with $MgSO_4$. The solvent was removed *in vacuo* (15 Torr) and the product was purified by column chromatography with $CHCl_3$ as the eluent (R_f = 0.7) to give compound **10** (0.56 g, 22%) as light

yellow crystals, m.p. 46—47 °C (from hexane). Found (%): C, 28.53; H, 0.99; N, 16.42. $C_6H_3F_4N_3O_4$. Calculated (%): C, 28.03; H, 1.17; N, 16.34. ^{1}H NMR, δ: 6.75 (t, 1 H, CF_2H, $J_{H,F}$ = 53 Hz); 7.81 (s, 1 H); 8.02 (s, 1 H). ^{19}F NMR, δ: –97.88 (s, 2 F, CF_2); –138.27 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz).

2-Formyl-4-nitro-1-(1,1,2,2-tetrafluoroethyl)pyrrole (11). Pyrrole **9** (1.95 g, 0.01 mol) was added dropwise at –15 °C for 1 h to a mixture of HNO_3 (d = 1.52) (2 mL) and H_2SO_4 (d = 1.84) (3 mL). The reaction mixture was stirred at 0 °C for 30 min. The resulting solution was poured into ice (100 g). The yellow oil that formed was extracted with ether (3×30 mL). The extract was washed with 5% $NaHCO_3$ (100 mL) and dried with $MgSO_4$. The solvent was removed and the product was recrystallized from hexane to give compound **11** (1.08 g, 45%) as yellow crystals, m.p. 51—52 °C (from hexane). Found (%): C, 34.69; H, 1.79; N, 11.73. $C_7H_4F_4N_2O_3$. Calculated (%): C, 35.01; H, 1.68; N, 11.67. ^{1}H NMR, δ: 6.69 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.67, 8.14 (both s, 1 H each), 9.61 (s, 1 H, CHO). ^{19}F NMR, δ: –97.08 (s, 2 F, CF_2); –136.37 (d, 2 F, CF_2H, $J_{H,F}$ = 53 Hz). IR, ν/cm^{-1}: 1705 (C=O).

2-Benzoyl-1-(1,1,2,2-tetrafluoroethyl)pyrrole (12). Anhydrous $ZnCl_2$ (0.5 g) was gradually added to a vigorously stirred solution of pyrrole **1** (1.67 g, 0.01 mol) and benzoyl chloride (1.48 g, 0.0105 mol) in anhydrous CCl_4 (20 mL). The reaction mixture was refluxed for 5 h, with hourly addition of new portions of $ZnCl_2$ (0.5 g). On cooling, the precipitate was filtered off and washed with CCl_4. The filtrate was washed with 5% $NaHCO_3$ and water and dried with $MgSO_4$. The solvent was removed *in vacuo* (15 Torr). The product was purified by column chromatography with $CHCl_3$—CCl_4 (1 : 2) as the eluent (R_f = 0.4) and distilled *in vacuo* to give compound **12** (1 g, 37%) as a colorless oil, b.p. 86—87 °C (0.3 Torr). Found (%): C, 58.07; H, 3.52; N, 5.29. $C_{13}H_9F_4NO$. Calculated (%): C, 57.57; H, 3.34; N, 5.17. ^{1}H NMR, δ: 6.34 (t, 1 H, J = 5 Hz); 6.79—6.88 (m, 1 H); 7.14 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.25—7.37 (m, 1 H); 7.45—7.52 (m, 2 H); 7.55—7.65 (m, 1 H); 7.80—7.95 (m, 2 H). ^{19}F NMR, δ: –96.60 (s, 2 F, CF_2); –137.25 (d, CF_2H, 2 F, $J_{H,F}$ = 53 Hz). IR, ν/cm^{-1}: 1720 (C=O).

3-Benzoyl-2-[tetrafluoro-2-(imidazol-1-yl)ethyl]-1-(1,1,2,2-tetrafluoroethyl)-2*H*-imidazole (13). Benzoyl chloride (1.4 g, 0.01 mol) was added at 0 °C to a solution of imidazole **2** (1.68 g, 0.01 mol) in acetonitrile. After 5 min, triethylamine (1.2 g, 0.012 mol) was added at the same temperature. The reaction mixture was stirred at room temperature for 6 h and then at 30 to 40 °C for 4 h. The resulting oil was extracted with ether (3×30 mL). The extract was washed with water and dried with $MgSO_4$. The solvent was removed *in vacuo* (15 Torr). The product was purified by column chromatography with $CHCl_3$ as the eluent (R_f = 0.5) and twice recrystallized from $CHCl_3$—hexane (1 : 1) to give compound **13** (0.33 g, 15%) as colorless crystals, m.p. 81—83 °C (from $CHCl_3$—hexane). Found (%): C, 46.51; H, 2.81; N, 12.89. $C_{17}H_{12}F_8N_4O$. Calcu-

Table 1. Characteristics of 1-alkyl-3-polyfluoroethylimidazolium iodides **18a—d** and **19a—c**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) I	Molecular formula	NMR (acetone-d_6), δ (J/Hz) ^{1}H	NMR (acetone-d_6), δ (J/Hz) ^{19}F
18a	95.0	140—142	40.55 / 40.93	$C_6H_7F_4IN_2$	4.20 (s, 3 H, Me, $J_{H,H}$ = 7); 7.46 (t, 1 H, CF_2H, $J_{H,F}$ = 52); 8.21, 8.28, 10.30 (all s, 1 H each)	–99.5 (s, 2 F, CF_2); –137.0 (d, 2 F, CF_2H, $J_{H,F}$ = 52)
18b	82.3	90—91	38.89 / 39.16	$C_7H_9F_4IN_2$	1.67 (s, 3 H, Me, $J_{H,H}$ = 7); 4.60—4.67 (m, 2 H, CH_2); 7.55 (t, 1 H, CF_2H, $J_{H,F}$ = 52); 8.31, 8.34, 10.40 (all s, 1 H each)	–99.1 (s, 2 F, CF_2); –137.0 (d, 2 F, CF_2H, $J_{H,F}$ = 52)
18c	62.1	77—79	37.13 / 37.53	$C_8H_{11}F_4IN_2$	1.13 (s, 3 H, Me, $J_{H,H}$ = 7); 2.03—2.09 (m, 2 H, CH_2); 4.52—4.65 (m, 2 H, CH_2); 7.70 (t, 1 H, CF_2H, $J_{H,F}$ = 52); 7.70, 7.96, 10.56 (all s, 1 H each)	–99.7 (s, 2 F, CF_2); –137.0 (d, 2 F, CF_2H, $J_{H,F}$ = 52)
18d	65.0	73—75	36.51 / 36.04	$C_9H_{13}F_4IN_2$	1.00 (s, 3 H, Me, $J_{H,H}$ = 7); 1.40—1.48 (m, 2 H, CH_2); 2.03—2.09 (m, 2 H, CH_2); 4.61—4.71 (m, 2 H, CH_2); 7.57 (t, 1 H, CF_2H, $J_{H,F}$ = 52); 8.34, 8.39, 10.52 (all s, 1 H each)	–99.2 (s, 2 F, CF_2); –137.2 (d, 2 F, CF_2H, $J_{H,F}$ = 52)
19a	80.0	104—105	39.00 / 38.87	$C_6H_7ClF_3IN_2$	4.50 (s, 3 H, Me); 8.10 (dq, 1 H, CHClF, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5); 8.15, 8.30, 10.30 (all s, 1 H each)	–94.1 (AB system, 2 F, CF_2, $J_{F,F}$ = 660); –154.8 (d, 1 F, CHClF, $J_{H,F}$ = 48)
19b	79.5	94—95	37.48 / 37.27	$C_7H_9ClF_3IN_2$	1.67 (s, 3 H, Me, $J_{H,H}$ = 7); 4.67 (m, 2 H, CH_2); 8.20 (dq, 1 H, CHClF, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5); 8.37, 8.38, 10.42 (all s, 1 H each)	–94.1 (AB system, 2 F, CF_2, $J_{F,F}$ = 660); –154.8 (d, 1 F, CHClF, $J_{H,F}$ = 48)
19c	62.1	92—93	35.90 / 35.79	$C_8H_{11}ClF_3IN_2$	1.78 (d, 6 H, Me, $J_{H,H}$ = 7); 5.03—5.28 (m, 1 H, CH); 7.54 (dq, 1 H, CHClF, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5); 7.82, 8.11, 10.40 (all s, 1 H each)	–94.1 (AB system, 2 F, CF_2, $J_{F,F}$ = 660); –154.8 (d, 1 F, CHClF, $J_{H,F}$ = 48)

lated (%): C, 46.36; H, 2.75; N, 12.72. ^{1}H NMR, δ: 5.87 (t, 1 H, CF_2H, $J_{H,F}$ = 53 Hz); 6.01, 6.44 (both d, 1 H each, J = 4 Hz); 6.68—6.90 (m, 1 H); 7.05, 7.11, 7.18 (all s, 1 H each); 7.45—7.59 (m, 5 H). ^{19}F NMR, δ: –95.60, –97.90 (both m, 2 F each); –133.75 (d, 2 F, $J_{H,F}$ = 54 Hz); –137.5——137.7 (m, 2 F). IR, ν/cm^{-1}: 1715 (C=O). MS (EI, 70 eV), m/z (I_{rel} (%)): 440 $[M]^+$ (11.98), 335 $[M - COPh]^+$ (1.59), 220 $[M - COPh - NCF_2CF_2H]^+$ (2.68), 181 $[Im - CF_2CF_2 - CH + H]^+$ (1.47), 168 $[Im - CF_2CF_2 + H]^+$ (0.97), 105 $[COPh]^+$ (100), 77 $[C_6H_5]^+$ (23.74), 51 $[CF_2H]^+$ (4.09).

Synthesis of 2-formyl-1-(1,1,2,2-tetrafluoroethyl)imidazole (15), phenyl[1-(1,1,2,2-tetrafluoroethyl)imidazol-2-yl]carbinol (16), and 2-benzoyl-1-(1,1,2,2-tetrafluoroethyl)imidazole (17) (general procedure). A 2.5 *N* solution of BuLi (4.4 mL, 0.011 mol) in hexane was added at –90 °C to a solution of imidazole **1** (1.68 g, 0.01 mol) in anhydrous THF (20 mL). The reaction mixture was stirred at this temperature for 30 min and then the corresponding reagent (DMF, benzaldehyde, or benzoyl chloride) (0.012 mol) was added dropwise. The reaction mixture was warmed to room temperature and poured into water (100 mL). The resulting solution was neutralized with 15% HCl to pH 5. The oily product was extracted with ether (3×30 mL). The extract was washed with water (3×30 mL) and dried with $MgSO_4$. The solvent was removed *in vacuo*

Table 2. Characteristics of 1-alkyl-3-polyfluoroethylimidazole-2-thiones **20a—d** and **21a—c**

Compound	Yield (%)	M.p. /°C	B.p. /°C (Torr)	Found / Calculated (%)			Molecular formula
				C	H	S	
20a	54	32—33	74—75 (1)	33.56 / 33.64	2.70 / 2.82	15.04 / 14.97	$C_6H_6F_4N_2S$
20b	47	18—19	79—80 (0.7)	36.91 / 36.84	3.50 / 3.53	13.98 / 14.05	$C_7H_8F_4N_2S$
20c	41	—	83—85 (0.5)	39.61 / 39.66	4.10 / 4.16	13.30 / 13.23	$C_8H_{10}F_4N_2S$
20d	56	—	91—92 (0.5)	41.95 / 42.18	4.50 / 4.74	12.52 / 12.51	$C_9H_{12}F_4N_2S$
21a	48	41—42	77—78 (1)	31.22 / 31.24	2.60 / 2.62	13.77 / 13.90	$C_6H_6ClF_3N_2S$
21b	46	22—23	83—85 (0.5)	34.27 / 34.36	3.22 / 3.29	12.97 / 13.10	$C_7H_8ClF_3N_2S$
21c	66	50—51	86—89 (0.5)	37.15 / 37.14	3.70 / 3.89	12.22 / 12.39	$C_8H_{10}ClF_3N_2S$

Table 3. ^{1}H and ^{19}F NMR spectra ($CDCl_3$) of 1-alkyl-3-polyfluoroethylimidazole-2-thiones **20a—d** and **21a—c**

Compound	NMR, δ (J/Hz)	
	^{1}H	^{19}F
20a	3.74 (s, 3 H); 6.76 (d, 1 H, J = 4); 7.02 (m, 1 H); 7.56 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53, $^3J_{H,F}$ = 4)	–100.56 (s, 2 F); –135.76 (d, 2 F, CF_2H, $J_{H,F}$ = 53)
20b	1.37 (t, 3 H, J = 7); 4.00—4.11 (m, 2 H); 6.76 (d, 1 H, J = 4); 7.04 (m, 1 H); 7.8 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53, $^3J_{H,F}$ = 4)	–100.56 (s, 2 F); –135.76 (d, 2F, CF_2H, $J_{H,F}$ = 53)
20c	1.37 (t, 3 H, J = 7); 1.82—1.93 (m, 2 H); 3.90—3.99 (m, 2 H); 6.76 (d, 1 H, J = 4); 7.03 (m, 1 H); 7.57 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53, $^3J_{H,F}$ = 4)	–100.56 (s, 2 F); –135.76 (d, 2F, CF_2H, $J_{H,F}$ = 53)
20d	1.37 (t, 3 H, J = 7); 1.70—1.83 (m, 2 H); 2.61—2.69 (m, 2 H); 4.02—4.11 (m, 2 H); 6.76 (d, 1 H, J = 4); 7.02 (m, 1 H); 7.55 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53, $^3J_{H,F}$ = 4)	–100.56 (s, 2 F); –135.76 (d, 2 F, CF_2H, $J_{H,F}$ = 53)
21a	3.74 (s, 3 H); 6.76 (d, 1 H, J = 4); 7.02 (m, 1 H); 8.06 (tt, 1 H, CFClH, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5)	–96.56 (AB system, 2 F, J = 219); –135.76 (dt, 1 F, CFClH, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5)
21b	1.37 (t, 3 H, J = 7); 4.00—4.15 (m, 2 H); 6.76 (d, 1 H, J = 4); 7.03 (m, 1 H); 7.99 (tt, 1 H, CFClH, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5)	–96.56 (AB system, 2 F, J = 219); –135.76 (dt, 1 F, CFClH, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5)
21c	1.37 (t, 6 H, J = 7); 4.99 (sept, 1 H, J = 7); 6.76 (d, 1 H, J = 4); 7.02—7.09 (m, 1 H); 8.01 (tt, 1 H, CFClH, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5)	–96.56 (AB system, 2 F, J = 219); –135.76 (dt, 1 F, CFClH, $^2J_{H,F}$ = 48, $^3J_{H,F}$ = 5)

(15 Torr). The products were distilled *in vacuo* (**15**) or crystallized (**16**, **17**).

Compound **15**, colorless crystals, yield 0.65 g (33%), b.p. 74—75 °C (15 Torr), m.p. 44—46 °C (from pentane). ^{1}H NMR, δ: 6.14 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 7.35, 7.49 (both s, 1 H each); 9.91 (s, 1 H, CHO). ^{19}F NMR, δ: −96.60 (s, 2 F, CF_2); −137.25 (d, CF_2H, 2 F, $J_{H,F}$ = 53 Hz). IR, ν/cm^{-1}: 1715 (C=O). **Hydrazone 15a**, m.p. 175—176 °C. Found (%): C, 38.45; H, 2.30; N, 22.01. $C_{12}H_8F_4N_6O_4$. Calculated (%): C, 38.30; H, 2.15; N, 22.34.

Compound **16**, colorless crystals, yield 1.53 g (56%), m.p. 77—79 °C (from hexane). Found (%): C, 52.33; H, 3.85; N, 10.62. $C_{12}H_{10}F_4N_2O$. Calculated (%): C, 52.55; H, 3.68; N, 10.22. ^{1}H NMR, δ: 3.40 (br.s, 1 H, OH); 5.60 (tt, 1 H, CF_2H, $^2J_{H,F}$ = 53 Hz, $^3J_{H,F}$ = 4 Hz); 5.85, 7.04 (both s, 1 H each); 7.11 (s, 1 H); 7.35—7.55 (m, 5 H). ^{19}F NMR, δ: −97.10 (AB system, 2 F, CF_2, $J_{F,F}$ = 222 Hz); −136.05 (d, CF_2H, 2 F, $J_{H,F}$ = 53 Hz).

Compound **17**, colorless crystals, yield 0.83 g (30%), m.p. 158—160 °C (from benzene—hexane (1 : 1)). Found (%): C, 51.31; H, 3.35; N, 10.26. $C_{12}H_8F_4N_2O \cdot 0.5H_2O$. Calculated (%): C, 51.25; H, 3.23; N, 9.96. ^{1}H NMR, δ: 5.64 (tt, 1 H, CF_2H, $J_{H,F}$ = 53 Hz); 7.52—7.78 (m, 6 H); 8.17 (d, 1 H, J = 3 Hz). ^{19}F NMR, δ: −97.10 (AB system, 2 F, CF_2, $J_{F,F}$ = 222 Hz); −136.05 (d, CF_2H, 2 F, $J_{H,F}$ = 53 Hz). **Hydrazone 17a**, m.p. 165—166 °C. Found (%): C, 47.95; H, 2.40; N, 19.00. $C_{12}H_8F_4N_6O_4$. Calculated (%): C, 47.79; H, 2.68; N, 18.58.

1-Alkyl-3-polyfluoroethylimidazolium iodides 18a—d and 19a—c. A solution of imidazole **2** or **3** (0.01 mol) and the corresponding alkyl iodide (0.011 mol) were heated in MeCN (20 mL) at 80 °C for 8 (MeI), 16 (EtI), 24 (Pr^nI), 36 (Pr^iI), and 40 h (BuI). The solvent was removed *in vacuo* (15 Torr) and the residue was crystallized from ethyl acetate (Table 1).

1-Alkyl-3-polyfluoroethylimidazole-2-thiones 20a—d and 21a—c. Potassium carbonate (2.8 g, 0.02 mol) and finely divided sulfur (0.64 g, 0.02 mol) were added to a solution of salt **18a—d** or **19a—c** (0.01 mol) in anhydrous methanol (30 mL). The suspension was stirred at room temperature for 8 h. The precipitate was filtered off and washed with methanol. The methanolic solutions were combined and concentrated *in vacuo* (15 Torr). The product was purified by column chromatography with $CHCl_3$—CCl_4 (1 : 1) as the eluent (R_f = 0.5—0.8) (Tables 2, 3).

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Received September 3, 2004;
in revised form February 2, 2005