The electrochemical fluorination of N-containing carboxylic acids (Part 4*). Fluorination of methyl 3-dialkylamino-isobutyrates and methyl 3-dialkylamino-n-butyrates

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Abstract

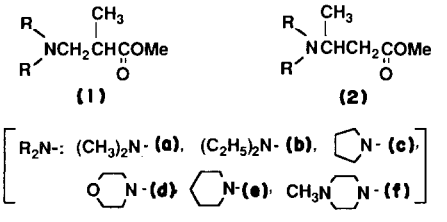
Several methyl esters of 3-dialkylamino-substituted n- and isobutyric acids have been subjected to electrochemical fluorination to give the corresponding perfluoroacid fluorides. Dimethyl, diethyl, pyrrolidino, morpholino, piperidino and *N*-methylpiperazino groups were investigated as dialkylamino substituents. The structure/yield relationship was evaluated both in terms of the structure of the acid and the kind of amino group, respectively. Better yields of perfluoroacid fluorides were obtained from methyl esters having isobutyric acid skeletons than those having n-butyric acid groups, and from the acids containing cyclic amino groups than those containing acyclic ones.

Introduction

Although many approaches to the preparation of perfluorocarboxylic acids have been reported, there is still need to develop a convenient method for making these compounds. In view of our interest in the preparation of new nitrogen-containing perfluorocarboxylic acids by the fluorination of methyl esters of the corresponding carboxylic acids [1], we have extended our study to a series of n- and isobutyric acids having cyclic and acyclic substituents.

For the preparation of nitrogen-containing perfluoroacid fluorides, electrochemical fluorination is the most feasible technique [2]. For this to become economically feasible, however, good product yields both at the fluorination stage and in the preparation of the starting material using cheap raw materials are essential. We have found that methyl 3-dialkylamino-isobutyrates and methyl 3-dialkylamino-n-butyrates are very good starting materials for the preparation of the corresponding nitrogen-containing perfluoroacid fluorides.

The following two series of methyl esters of dialkylamino-substituted butyric acid were fluorinated:



Results and discussion

Methyl 3-dialkylamino-isobutyrates (**1**) and methyl 3-dialkylamino-n-butyrates (**2**) were good starting materials for the preparation of a series of perfluoro(dialkylamino-substituted butyryl fluorides). Compounds **1** and **2** can be easily prepared in high yield by a one-flask preparation (Michael reaction) from the appropriate secondary amines and methyl methacrylate [3] and/or methyl crotonate [4], respectively.

The results of the fluorination of **1** and **2** are listed in Tables 1 and 2, respectively. As compounds **1** and **2** are isomers, it was possible to compare the results in terms of yield and the kind of products arising from the difference in the skeleton of the carboxylic acid.

Fluorination of methyl-3-dialkylamino-isobutyrates (1)

It was found that good product yields were obtained from the fluorination of **1**. The yields of the corre-

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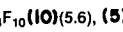
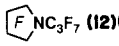
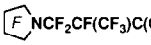
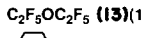
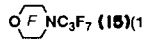
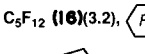
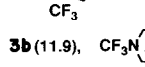
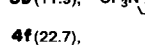
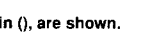
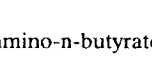
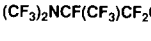
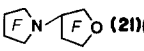
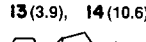
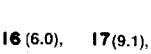
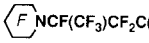
TABLE 1. Fluorination of methyl 3-dialkylamino-iso-butyrates (**1**)

Run	Sample g (mol)	Current passed [Ahr]	Fluorinated products (g)	Products obtained[b] (Yield %)
1	**1a**, 41.1 (0.284)	259	29.5[a] (28.6)	$C_2F_5C(O)F$ (4.2), i-$C_3F_7C(O)F$ **(5)**(11.0), $C_3F_7N(CF_3)_2$ **(6)**(5.1) $(CF_3)_2NCF_2CF(CF_3)C(O)F$ **(3a)**(36.4), $(CF_3)_2NCF(CF_3)CF_2C(O)CF_3$ (*Z*)(2.1)
2	**1b**, 41.1 (0.238)	266	9.9 (43.0)	**5** (6.6), $(C_2F_5)_3N$ **(8)**(2.7), $(C_2F_5)_2NC_3F_7$ **(9)**(5.4), $(C_2F_5)_2NCF_2CF(CF_3)C(O)F$ **(3b)**(31.2)
3	**1c**, 40.4 (0.236)	235	11.8 (50.8)	C_4F_{10} **(10)**(5.6), **(5)**(1.6),  **(11)**(0.7),  **(12)**(9.2),  **(3c)**(43.3)
4	**1d**, 41.3 (0.221)	217	7.4 (70.1)	$C_2F_5OC_2F_5$ **(13)**(1.7),  (1.6),  **(14)**(1.1), **(15)**(12.6),  **(3d)**(63.7)
5	**1e**, 40.9 (0.221)	226	3.9 (55.1)	C_5F_{12} **(16)**(3.2),  (0.6),  **(17)**(0.2), **(18)** (5.6),  (8.9),  **(4d)**(39.7)
6	**1f**, 40.3 (0.202)	241	13.3 (44.5)	**3b** (11.9), CF_3N  (4.4), CF_3N **4f** (22.7),

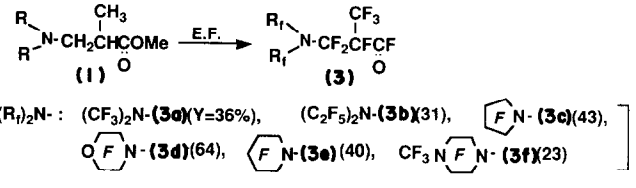
[a] Products collected in the -78 °C trap, and cell drainings, in (), are shown.
[b] Products are arranged in order of elution time by GLC (Col.A).

TABLE 2. Fluorination of methyl 3-dialkylamino-n-butyrates (**2**)

Run	Sample g (mol)	Current passed [Ahr]	Fluorinated products (g)	Products obtained[b] (Yield %)
1	**2a**,40.9 (0.282)	263	33.6[a] (18.7)	$CF_3OC_3F_7$ (2.4), $C_2F_5N(CF_3)_2$ (6.1), **6** (5.3), $(CF_3)_2NCF_2CF_2C(O)F$ (4.1), $(CF_3)_2NCF_2CF_2CF_2OCF_3$ (3.4), $(CF_3)_2N$  **(19)**(2.8), $(CF_3)_2NCF(CF_3)CF_2C(O)F$ **(4a)**(16.9)
2	**2c**, 40.3 (0.236)	221	13.0 (45.1)	**10** (7.9), **11** (8.2), **12** (9.1),  **(20)**(2.3), **(21)**(10.0),  **(4c)**(21.2)
3	**2d**, 40.7 (0.218)	228	10.4 (61.6)	**13** (3.9), **14** (10.6), **15** (12.3),  **(22)**(2.8), **(23)**(6.9),  **(4d)**(43.2)
4	**3c**, 40.3 (0.218)	243	8.6 (50.8)	**16** (6.0), **17** (9.1), **18** (7.4),  **(24)**(6.3), **(4c)**(21.0)

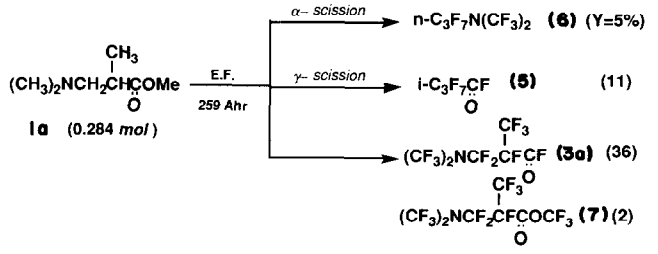
[a] Products collected in the -78 °C trap, and cell drainings, in (), are shown.
[b] Products are arranged in order of elution time by GLC (Col.A).

sponding perfluoroacid fluoride **3** ranged from 23 to 64%, viz.

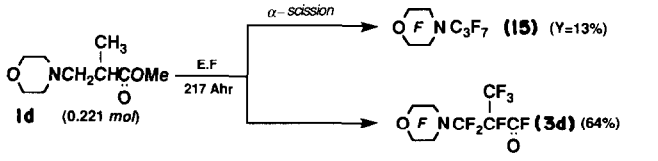


However, some differences were observed in the kind of fluorination product generated from **1** in terms of acyclic amino and cyclic amino-substituted reactants. In the case of the former [**1a** and **1b**], γ-scission as well as α-scission of the acid occurred affording perfluoro(isobutyryl fluoride) (**5**) as the main cleaved product [11% from **1a** and 7% from **1b**, respectively].

The formation of the main products from **1a**, for example, are explained as follows.



From **1a**, the perfluoromethyl ester **7** is formed in small yield (yield = 2%) together with the corresponding perfluoro(3-dimethylamino-isobutyryl fluoride) (**3a**) (yield = 36%). From **1** having cyclic amino-substituents, cleaved products arising from α-scission were the main by-products. A typical example occurs in the fluorination of **1d**.

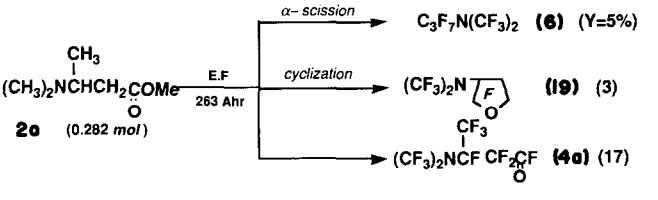


It should be noted that the highest yield of perfluoroacid fluoride **3d** (64%) was obtained for **1d** in this work.

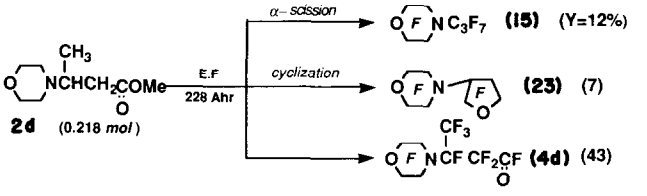
From **1f**, the expected perfluoro[3-(*N*-methylpiperazino)isobutyryl fluoride] (**3f**) was obtained in a yield of 23% together with the perfluoro(3-diethylamino-isobutyryl fluoride) (**3b**) (yield = 12%). Compound **3b** was formed as a result of C—N bond scission in the piperazino ring during fluorination.

Fluorination of methyl-3-dialkylamino-n-butyrates (2)

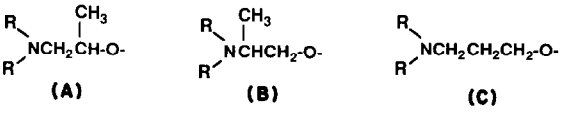
In the fluorination of **2**, it was observed that the yields of the corresponding perfluoroacid fluoride **4** were more affected by the kind of the alkyl amino group than in the case of **1**. Furthermore, cyclization products (**19** from **2a**, **21** from **2c**, **23** from **2d**, and **24** from **2e**, respectively) were invariably formed from **2**, this being the major cause of the decrease in the yield of **4**. A similar trend was observed in the yield of **4** from **2** when an acyclic amino-substituted **2** was employed relative to a cyclic amino-substituted **2**: higher yields of **4** were obtained in the latter case than in the former. Thus, the fluorination products from **2a** may be explained as follows, which indicates α-scission and a considerable incidence of cyclization giving perfluoro(3-dimethylamino-n-butyryl fluoride) (**4a**) in a low yield.



The fluorination of **2b** to give the corresponding perfluoroacid fluoride (**4b**) was not successful, since many complicated products were formed (the yield of **4b** was estimated to be *c.* 5%; see Experimental section). Yields of **4** were improved considerably when **2** having a cyclic amino substituent instead of an acyclic one was fluorinated. Thus, from **2d**, the following products were obtained.

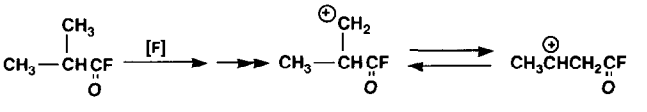


Moore *et al.* have widely investigated the fluorination of various dialkylamino-substituted ethers and have obtained interesting information about the structure/yield relationship for the substrates [5]. It was stated that cyclic amines generally gave better yields than acyclic ones, and that good product yields were obtained when an isopropyl group was incorporated in the ether linkage (**A** and **B**) compared with arrangement **C** where the N and O atoms are separated by three methylene groups.



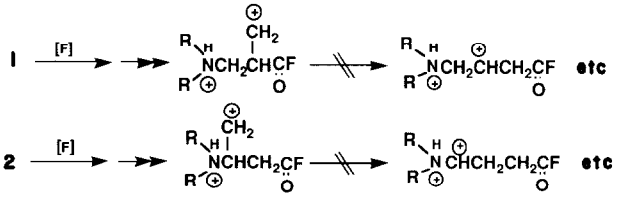
Although we have not attempted the fluorination of methyl 4-dialkylamino-n-butyrates which have a linear structure similar to **C**, our studies have shown that 3-dialkylamino-isobutyric acids (**A** type) give perfluoroacid fluorides in better yield than 3-dialkyl-amino-n-butyric acids (**B** type).

It is generally difficult to obtain perfluoroacid fluorides having a branched perfluoroalkyl group in good yield by ECF methods because of isomerization (iso- → n-) of the alkyl group [6].



This isomerization is considered to be an unavoidable side-reaction due to anodic fluorination. In the cases we have studied (except for **2b**), however, the desired perfluoroacid fluorides were obtained in fair to good yield, since no isomerization of the branched group to a linear one occurred. It was considered that the formation of an ammonium salt on the alkyl group of both **1** and **2** in anhydrous hydrogen fluoride (AHF) suppressed the isomerization, which occurs via a car-

bocation-like intermediate [7] at the initial stage of the fluorination.



Perfluorocarboxylic acids have been utilized as versatile starting materials for the synthesis of organofluorine chemicals. Similarly, nitrogen-containing perfluorocarboxylic acids can be used as new raw materials not only for useful organofluorine chemicals such as surface-active agents [8], inert perfluorinated fluids*, perfluoro-olefins [9] etc., but also for chiral derivatizing agents and as starting materials for ferroelectric liquid crystals using the chiral centre adjacent to the carboxy group and taking advantage of the bulky perfluorodialkylamino group at the asymmetric carbon in the case of **3** [10]. Thus, fair to good yields of the nitrogen-containing perfluoroacid fluorides from **1** and **2** have strengthened the ECF process for the preparation of perfluorocarboxylic acids as compared to indirect methods [11], and have opened the door for new applications as the chiral building block using **3**.

Experimental

Reagents

All N-containing carboxylic acids were prepared by the reaction of appropriate secondary amines and methyl methacrylate or methyl crotonate as described in the literature.

These starting materials had the following boiling points: methyl 3-dimethyl-amino-isobutyrate, b.p. 87 ~ 88 °C/48 mmHg (lit. value [3]: b.p. 73 °C/40 mmHg), methyl 3-diethylamino-isobutyrate, b.p. 95 ~ 96 °C/18 mmHg (lit. value [12]: b.p. 88.5 °C/15 mmHg), methyl 3-pyrrolidino-isobutyrate, b.p. 92 ~ 93 °C/14 mmHg (lit. value [13]: b.p. 86°C/13 mmHg), methyl 3-morpholino-isobutyrate, b.p. 106 ~ 107 °C/9 mmHg (lit. value [12]: b.p. 112 °C/13 mmHg), methyl 3-piperidino-isobutyrate, b.p. 103 °C/15 mmHg (lit. value [12]: b.p. 99.5 ~ 100 °C/13 mmHg; lit. value [14]: b.p. 127 ~ 129 °C/30 mmHg), methyl 3-(*N*-methylpiperazino)isobutyrate, b.p. 125 ~ 126 °C/15 mmHg, methyl 3-dimethylamino-n-butyrate, b.p. 71 ~ 72 °C/12 mmHg (lit. value [3]: b.p. 82 ~ 84 °C/40 mmHg; lit. value [4]: b.p. 66 °C/17 mmHg), (lit. value [3]: b.p. 88.5 °C/15 mmHg), methyl 3-diethylamino-n-butyrate, b.p. 71 ~ 72 °C/12 mmHg, methyl 3-pyrrolidino-n-butyrate, b.p. 106 ~ 107 °C/19 mmHg (lit. value [4]: b.p. 100 ~ 102 °C/23 mmHg), methyl 3-morpholino-n-butyrate, b.p. 121 ~ 123 °C/16 mmHg, methyl 3-piperidino-n-butyrate, b.p. 113 ~ 114 °C/16 mmHg. Anhydrous hydrogen fluoride (AHF) (Daikin Industries Co.) was better than 99.8% pure.

Apparatus

The electrolytic fluorination apparatus and operating procedures were similar to those described previously [1c].

Analytical GLC work was carried out using a Shimadzu GC-2C gas chromatograph with stainless-steel columns (3 mm diameter) packed with 30% 1,6-bis(1,1,7-trihydroperfluoroheptyloxy)hexane on Chromosorb PAW (6.4 m) (column A) or 30% 1,6-bis(1,1,12-trihydroperfluorododecyloxy)hexane on Chromosorb PAW (6.4 m) (column B). For semi-preparative work, a GASUKURO LL-75 modified gas chromatograph was used employing stainless-steel columns (10 mm diameter) packed with 30% 1,6-bis(1,1,12-trihydroperfluorododecyloxy)hexane on Chromosorb PAW (4.9 m) (column C) or 30% Silicone QF-1 on Chromosorb PAW (4.9 m) (column D). The carrier gas was helium in all cases.

Infrared (IR) spectra were measured on a Hitachi EPI-G3 spectrometer, using a 6-cm gas cell with KBr windows. ^{19}F NMR spectra were measured using CCl_3F as an internal standard either on Hitachi R-20B (56.46 MHz) or Hitachi R-90F (84.68 MHz) spectrometers. Mass spectra were measured on a Shimadzu GC–MS 7000 instrument at 70 eV.

*Fluorination of methyl 3-dimethylamino-isobutyrate (**1a**)*

Sample **1a** (41.1 g, 0.284 mol) was charged into the cell which contained 450 ml electrically purified AHF, and the solution was subjected to fluorination with an anodic current density of 3.5 A dm^{-2}, a cell voltage of 6.1 ~ 6.2 V and a cell temperature of 7 ~ 8 °C over a period of 595 min (259 A h). At the final stage of the fluorination, the voltage reached 6.3 V.

The effluent gases from the cell were passed over NaF pellets and then condensed in a trap cooled at −78 °C. The gaseous products which did not condense in the −78 °C trap were first bubbled through a fluoropolymer bottle containing water and then through a gas washing bottle containing an aqueous solution of a mixture of K_2CO_3, KOH and KI. All products except new ones were identified by comparison of their IR spectra and GLC retention times with those of authentic samples. New compounds were separated from other products by the use of semi-preparative GLC, and their structures were determined on the basis of their IR ^{19}F NMR and mass spectra.

The products (29.5 g) condensed in the −78 °C trap consisted of pentafluoropropionyl fluoride (2.0 g), per-

*Fluoroinert liquids, a 3M company.

fluoro(isobutyryl fluoride)(**5**)(6.8 g), perfluoro(*N*,*N*-dimethylpropylamine)(**6**)(4.0 g), perfluoro[3-(*N*,*N*-dimethylamino)isobutyryl fluoride](**3a**)(12.7 g) and unidentified materials (4.0 g). Cell drainings (28.6 g) consisted of **3a** (23.3 g) and perfluoro[methyl 3-(*N*,*N*-dimethylamino)isobutyrate] (**7**) (2.4 g) and unidentified materials (2.4 g). The yield of **3a** was 36.4% based on the sample feed.

Perfluoro(3-dimethylamino-isobutyryl fluoride) (**3a**) (nc): b.p. 60.5~61.5 °C, n_D^{20}<1.28, d_4^{20} 1.7120. IR (gas) (cm^{-1}): 1890; 1887 (ms) (C=O); 1360 (vs); 1345 (s); 1248 (vs); 1225 (s); 1150 (ms); 1012 (m); 989 (s); 932 (w); 865 (m); 775 (w); 762 (w); 737 (w). MS *m/z*: 330 $[M-F]^+$ (3.0); 264 $C_5F_{11}N^+$ (2.8); 202 $C_3F_9N^+$ (16.5); 197 $C_3F_8^+$ (13.0); 169 $C_3F_7^+$ (18.6); 131 $C_3F_5^+$ (7.6); 119 $C_2F_5^+$ (14.8); 114 $C_2F_4N^+$ (27.2); 100 $C_2F_4^+$ (9.2); 69 CF_3^+ (100).

Perfluoro(methyl 3-dimethylamino-isobutyrate) (**7**) (nc): IR (gas) (cm^{-1}): 1884; 1872 (ms) (C=O); 1337~1356 (vs); 1282 (s); 1220~1259 (s~vs); 1199 (s); 1147 (vs); 1099 (w); 1027 (w); 996 (s); 931 (w); 866 (m); 840 (w); 771 (m); 756 (w); 734 (m); 670 (w). MS *m/z*: 330 $[M-OCF_3]^+$ (6.7); 202 $C_3F_8N^+$ (26.0); 197 $C_4F_7O^+$ (10.5); 169 $C_3F_7^+$ (10.1); 150 $C_3F_6^+$ (27.2); 131 $C_3F_5^+$ (9.7); 114 $C_2F_4N^+$ (22.0); 100 $C_2F_4^+$ (9.6); 69 CF_3^+ (100). ^{19}F NMR data for **3a** are listed in Table 3.

Fluorination of methyl 3-diethylamino-isobutyrate (1b)

Sample **1b** (41.1 g, 0.238 mol) was fluorinated similarly under the following conditions: 3.5 A dm^{-2}, 6.0~6.1 V, 7~8 °C, 616 min (266 A h). Work-up was as for the fluorination of **1a**. Products collected in the −78 °C trap and cell drainings were subsequently analyzed by GLC methods (columns A and B). The following compounds were obtained. Products in the −78 °C trap (9.9 g), **5** (3.4 g), perfluoro(triethylamine)(**8**)(2.4 g), perfluoro(diethyl-n-propylamine)(**9**)(1.2 g), perfluoro(3-diethylamino-isobutyryl fluoride)(**3b**)(0.7 g) and unidentified materials (2.2 g). Cell drainings (43.0 g): **8** (4.2 g), **3b** (33.8 g) and unidentified materials (5.0 g). The yield of **3b** was 31.2%.

Perfluoro(3-diethylamino-isobutyryl fluoride)(**3b**)-(nc): B.p. 105~106 °C, n_D^{20} 1.2880, d_4^{20} 1.8002. IR (gas) (cm^{-1}): 1894; 1878 (C=O); 1290~1315 (vs~s); 1275 (s, sh); 1245 (vs); 1233 (s, sh); 1160 (m); 1105 (m); 1078 (m); 1090 (w); 985 (w); 878 (m); 838 (m); 758 (w); 743 (m); 712 (w). MS *m/z*: 414 $C_8F_{16}N^+$ (1.0); 380 $C_7F_{14}NO^+$ (3.8); 352 $C_6F_{14}N^+$ (1.7); 302 $C_5F_{12}N^+$ (8.0); 264 $C_5F_{10}N^+$ (2.4); 197 $C_3F_8^+$ (24.3); 169 $C_3F_7^+$ (44.3); 164 $C_3F_6N^+$ (25.4); 119 $C_2F_5^+$ (67.9); 114 $C_2F_4N^+$ (100); 100 $C_2F_4^+$ (93.0); 69 CF_3^+ (49.6). ^{19}F NMR data for **3b** are listed in Table 3.

Fluorination of methyl 3-pyrrolidino-isobutyrate (1c)

Sample **1c** (40.4 g, 0.236 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 6.5~6.7 V, 7~8 °C, 485 min (235 A h). Work-up gave: products in the −178 °C trap (11.8 g): n-C_4F_{10} (**10**) (2.5 g), **5** (0.8 g), perfluoro(*N*-ethylpyrrolidine)(**11**)(0.5 g), perfluoro(*N*-propylpyrrolidine)(**12**)(1.9), perfluoro(3-pyrrolidino-isobutyryl fluoride)(**3c**)(0.5 g) and unidentified materials (2.8 g). Cell drainings (50.8 g): **12** (6.5 g), **3c** (41.5 g) and unidentified materials (2.8 g). The yield of **3c** was 43.3%.

Perfluoro(3-pyrrolidino-isobutyryl fluoride)(**3c**)(nc): B.p. 105~106 °C, n_D^{20} 1.2943, d_4^{20} 1.7833. IR (gas) (cm^{-1}): 1890; 1874 (ms) (C=O); 1402 (w); 1346 (vs); 1313 (m); 1244 (vs); 1227 (s, sh); 1180 (ms); 1149 (ms); 1123 (w); 1037 (m); 1009 (w); 971 (s); 876 (w); 796 (m); 657 (w); 614 (w). MS *m/z*: 392 $[M-F]^+$ (3.7); 364 $C_7F_{14}N^+$ (2.5); 264 $C_5F_{10}N^+$ (100); 214 $C_4F_{10}N^+$ (19.2); 197 $C_3F_8^+$ (29.7); 176 $C_4F_6N^+$ (9.9); 169 $C_3F_7^+$ (47.2); 164 $C_3F_6N^+$ (9.9); 150 $C_3F_6^+$ (24.8); 131 $C_3F_5^+$ (14.1); 119 $C_2F_5^+$ (11.8); 114 $C_2F_4N^+$ (25.1); 100 $C_2F_4^+$ (44.6); 69 CF_3^+ (97.0). ^{19}F NMR data for **3c** are listed in Table 3.

Fluorination of methyl 3-morpholino-isobutyrate (1d)

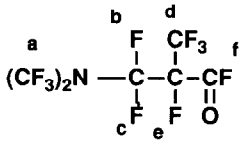
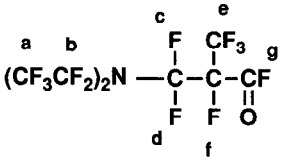
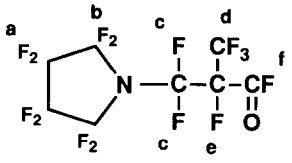
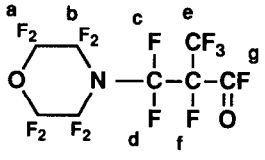
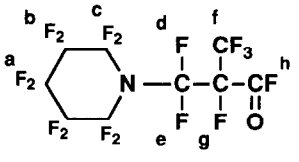
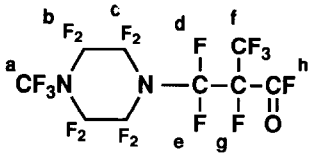
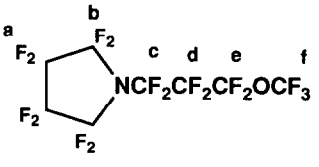
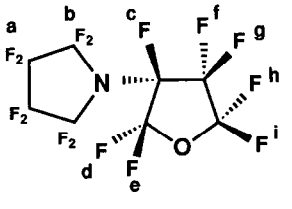
Sample **1d** (41.3 g, 0.221 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 7.1~7.6 V, 7~8 °C, 452 min (217 A h). Work-up gave: product in the −78 °C trap (7.4 g) perfluoro(diethylether)-(**13**)(1.0 g), perfluoro(*N*-methylmorpholine) (1.1 g), perfluoro(*N*-ethylmorpholine)(**14**)(0.8 g), perfluoro(*N*-propylmorpholine)(**15**)(2.3 g), perfluoro(3-morpholino-isobutyryl fluoride)(**3d**)(1.6 g) and unidentified materials (0.6 g). Cell drainings (70.1 g): **15** (8.8 g), **3d** (58.4 g) and unidentified materials (2.9 g). The yield of **3d** was 63.7%.

Perfluoro(3-morpholino-isobutyryl fluoride)(**3d**)(nc): B.p. 113~114 °C, n_D^{20} 1.2967, d_4^{20} 1.8021. IR (gas) (cm^{-1}): 1890; 1875 (ms) (C=O); 1349 (ms); 1309 (vs); 1251 (vs); 1226; 1196 (ms); 1166 (s); 1154 (s); 1103 (m); 1012 (w); 979 (w); 973 (w); 933 (m); 795 (m); 640 (w); 716 (w). MS *m/z*: 408 $[M-F]^+$ (1.5); 280 $C_5F_{10}NO^+$ (68.4); 197 $C_4F_7O^+$ (39.0); 169 $C_3F_7^+$ (63.4); 164 $C_3F_6N^+$ (26.0); 119 $C_2F_5^+$ (92.4); 114 $C_2F_4N^+$ (68.9); 100 $C_2F_4^+$ (100); 69 CF_3^+ (78.9). ^{19}F NMR data for **3d** are listed in Table 3.

Fluorination of methyl 3-piperidino-isobutyrate (1e)

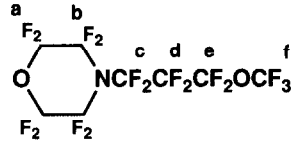
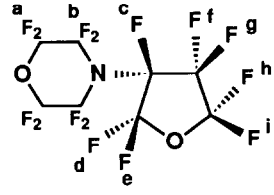
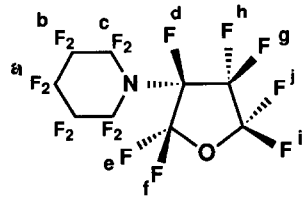
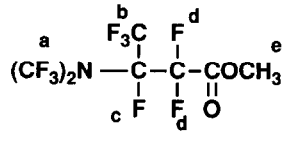
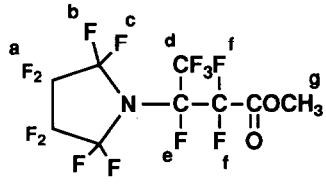
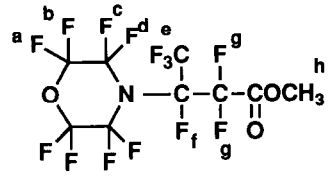
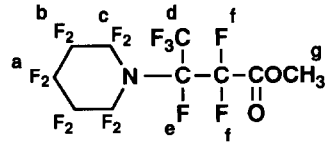
Sample **1e** (40.9 g, 0.221 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 6.1~6.3 V, 7~8 °C, 513 min (226 A h). Work-up gave: product in the −78 °C trap (3.9 g): perfluoropentane (**16**) (2.0 g), perfluoro(*N*-methylpiperidine)(0.4 g), perfluoro(*N*-ethylpiperidine)(**17**)(0.2 g), perfluoro(*N*-propylpiperidine) (**18**) (0.3 g) and unidentified material (0.1 g).

TABLE 3. ^{19}F NMR spectra of compounds **3a**, **3b**, **3c**, **3d**, **3e**, **3f**, **20**, **21**, **22**, **23**, **24**, **25**, **26**, **27** and **28**

Comp.	Formula		Chemical shift[a,b]	J (Hz)[b]
3a		a	−52.6	a–b = a–c = 16.1
		b	−81.3	a–e = 11.6
		c	−86.6	b–c = 256
		d	−73.6	
		e	−173.8	
		f	32.7	
3b		a	−73.4	d–e = 244
		b	−88.9	
		c	−73.2	
		d	−83.9	
		e	−73.4	
		f	−169.3	
		g	31.7	
3c		a	−133.6	
		b	−91.2	
		c	−86.2	
		d	−73.6	
		e	−177.9	
		f	32.8	
3d		a	−88.1	b–c = b–d = 16.8
		b	−93.1	b–f = 16.9
		c	−82.5	
		d	−86.0	
		e	−73.6	
		f	−176.8	
		g	32.9	
3e		a	−134.5	d–e = 244
		b	−132.3	
		c	−90.7	
		d	−84.9	
		e	−81.2	
		f	−73.3	
		g	−176.3	
		h	32.8	
3f		a	−52.5	
		b	−93.7	
		c	−90.5	
		d	−81.5	
		e	−85.9	
		f	−73.5	
		g	−176.3	
		h	32.9	
20		a	−133.4	e–f = 9.6
		b	−90.7	
		c	−93.0	
		d	−126.7	
		e	−85.3	
		f	−55.8	
21		a	−134.2	d–e = 136
		b	−91.3	f–g = 248
		c	−137.7	h–i = 132
		d	−63.6	
		e	−89.6	
		f	−131.0	
		g	−117.0	
		h	−80.4	
		i	−91.6	

(*continued*)

TABLE 3 (*continued*)

Comp.	Formula		Chemical shift[a,b]	J (Hz)[b]
22		a	−88.0	b–d = 11.9
		b	−92.6	c–e = 9.8
		c	−91.1	e–f = 9.6
		d	−127.4	
		e	−85.7	
		f	−56.1	
23		a	−86.0	d–e = 132
		b	−90.8	f–g = 249
		c	−135.6	h–i = 130
		d	−84.1	
		e	−70.2	
		f	−127.7	
		g	−116.9	
		h	−80.2	
		i	−91.7	
24		a	−134.3	c–f = 132
		b	−133.5	g–h = 250
		c	−92.0	i–j = 130
		d	−133.5	
		e	−83.1	
		f	−70.2	
		g	−117.0	
		h	−126.7	
		i	−91.7	
		j	−80.2	
25		a	−51.5	a–b = 7.6
		b	−75.7	a–e = 17.5
		c	−156.8	
		d	−112.8	
		e	3.94	
26		a	−133.8	b–c = 176
		b	−87.9	
		c	−90.7	
		d	−76.1	
		e	−162.0	
		f	−114.7	
		g	3.93	
27		a	−82.8	a–b = 147
		b	−85.0	c–d = 200
		c	−85.3	c–f = d–f = 32.2
		d	−88.7	
		e	−75.1	
		f	−157.6	
		g	−114.1	
		h	3.94	
28		a	−133.2	c–e = 32.2
		b	−130.4	
		c	−87.7	
		d	−74.1	
		e	−153.4	
		f	−112.2	
		g	3.91	

[a] ^{19}F chemical shifts in ppm relative to internal CCl_3F (negative shifts are upfield) and ^1H chemical shifts in ppm relative to TMS.
[b] Only obvious chemical shifts and coupling constants are given.

Cell drainings (55.1 g): perfluoro[*N*-propyl-(methylpyrrolidine)](0.5 g), **18** (5.1 g), perfluoro[3-(methylpyrrolidino)isobutyryl fluoride](9.1 g) and perfluoro(3-piperidino-isobutyryl fluoride)(**3e**)(40.5 g). The yield of **3e** was 39.7%.

Perfluoro(3-piperidino-isobutyryl fluoride)(**3e**)(nc): B.p. 121~123 °C, n_D^{20} 1.2997, d_4^{20} 1.8270. IR (gas) (cm^{-1}): 1890; 1875 (m) (C=O); 1368 (m); 1333 (vs); 1308 (w); 1275 (s); 1246 (vs); 1208 (s); 1190 (s); 1163 (ms); 1128 (ms); 1068 (w); 1028 (s); 1012 (w); 990 (w); 974 (s); 851 (w); 788 (m); 760 (w); 635 (m). MS *m/z*: 442 $[M-F]^+$ (4.5); 414 $C_8F_{16}N^+$ (4.9); 314 $C_6F_{12}N^+$ (100); 264 $C_5F_{10}N^+$ (15.3); 219 $C_4F_9^+$ (16.2); 197 $C_3F_8^+$ (26.7); 169 $C_3F_7^+$ (41.5); 164 $C_3F_6N^+$ (9.4); 150 $C_3F_6^+$ (9.9); 131 $C_3F_5^+$ (31.2); 119 $C_2F_5^+$ (20.8); 114 $C_2F_4N^+$ (15.0); 100 $C_2F_4^+$ (36.1); 69 CF_3^+ (78.2). ^{19}F NMR data for **3e** are listed in Table 3.

Fluorination of methyl 3-(N-methylpiperazino)-isobutyrate (1f)

Sample **1f** (40.3 g, 0.202 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 6.5~6.7 V, 7~8 °C, 546 min (241 A h). Work-up gave: product in the −78 °C trap (13.3 g) consisted mainly of aliphatic tertiary amines having low boiling points. Cell drainings (44.5 g): **3b** (11.2 g), perfluoro(*N'*-methyl-*N*-propylpiperazine)(4.1 g), perfluoro[3-(*N*-methylpiperazino)-isobutyryl fluoride] (**3f**)(22.7 g) and unidentified materials (6.5 g). The yield of **3f** was 22.7%.

Perfluoro[3-(*N*-methylpiperazino)isobutyryl fluoride]-(**3f**): B.p. 167~170 °C, n_D^{20} 1.3180, d_4^{20} 1.8838. IR (gas) (cm^{-1}): 1887; 1873 (m) (C=O); 1364 (vs); 1332(s); 1305 (vs); 1264 (s); 1217; 1227 (vs); 1167(s); 1094 (m); 1071 (w); 1009 (w); 987 (w); 973 (m); 956 (s); 894 (w); 976 (w). MS *m/z*: 475 $[M-F]^+$ (3.1); 347 $[M-C_2F_5]^+$ (14.2); 259 $C_5F_9N_2^+$ (16.2); 197 $C_3F_7N_2^+$ (16.2); 169 $C_3F_7^+$ (24.2); 164 $C_3F_6N^+$ (17.2); 119 $C_2F_5^+$ (15.1); 114 $C_2F_4N^+$ (36.1); 100 $C_2F_4^+$ (62.5); 69 CF_3^+ (100). ^{19}F NMR data for **3f** are listed in Table 3.

Fluorination of methyl 3-dimethylamino-n-butyrate (2a)

Sample **2a** (40.9 g, 0.282 mol was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 6.1~6.2 V, 7~8 °C, 509 min (263 A h). Product in the −78 °C trap (33.6 g) and cell drainings (18.7 g) were combined. Work-up gave: perfluoro(methyl propyl ether) (1.7 g), perfluoro(*N,N*-dimethylethylamine)(4.6 g), **6** (4.8 g), perfluoro(3-dimethylaminopropionyl fluoride)-[1a](3.5 g), perfluoro(3-dimethylaminopropylmethyl ether)[1a](3.7 g), perfluoro(3-dimethylamino-n-butyryl fluoride)(**4a**)(16.6 g), perfluoro(3-dimethylaminooxolane)(**19**)[1a](2.7 g) and unidentified materials (14.6 g). The yield of **4a** was 16.9%. Analysis of perfluoro(3-dimethylamino-n-butyryl fluoride)(**4a**) was undertaken as the methyl ester.

Methyl perfluoro(3-dimethylamino-n-butyrate)(**25**) was prepared by mixing about 2 g of cell drainings with 1 ml of methanol. The reaction was complete within a few minutes. The lower layer of the reaction mixture was then subjected to semi-preparative GLC (column D) to give pure **25**.

Methyl perfluoro(3-dimethylamino-n-butyrate)(**25**)-(nc): B.p. 125~126 °C, n_D^{20} 1.3067, d_4^{20} 1.6843. IR (capillary film) (cm^{-1}): 1788 (C=O). MS *m/z*: 342 $[M-F]^+$ (2.3); 252 $C_4F_{10}N^+$ (28.8); 214 $C_4F_8N^+$ (13.7); 209 $C_5F_7O^+$ (9.3); 164 $C_3F_6N^+$ (30.4); 150 $C_3F_6^+$ (16.0); 145 $C_3F_5N^+$ (5.6); 131 $C_3F_5^+$ (5.7); 114 $C_2F_4N^+$ (9.7); 100 $C_2F_4^+$ (10.2); 81 $C_2F_3^+$ (9.4); 69 CF_3^+ (100); 59 CO_2Me^+ (64.2). ^{19}F NMR data for **24** are listed in Table 3.

Fluorination of methyl 3-pyrrolidino-n-butyrate (2c)

Sample **2c** (40.3 g, 0.236 mol) was fluorinated similarly under the following conditions: 3.5 A dm^{-2}, 6.4~6.5 V, 7~8 °C, 509 min (221 A h). Work-up gave: products in the −78 °C trap (13.0 g): **10** (3.5 g), **11** (4.4 g), **12** (2.0 g) and unidentified materials (3.0 g). Cell drainings (45.1 g): **11** (2.0 g), **12** (6.2 g), perfluoro(3-pyrrolidinopropylmethyl ether)(**20**)(2.4 g), perfluoro(3-pyrrolidino-n-butyryl fluoride)(**4c**)(20.5 g), perfluoro(3-pyrrolidinooxolane)(**21**)(9.7 g) and unidentified materials (6.7 g). The yield of **4c** was 21.2%. Characterization of **4c** was as for **4a**.

Perfluoro(3-pyrrolidinopropylmethyl ether)(**20**): B.p. 105~106 °C, n_D^{20} 1.2819, d_4^{20} 1.7916. IR (gas) (cm^{-1}): 1347 (s); 1279 (s); 1227~1247 (vs); 1182 (s); 1157 (s); 1135 (ms); 1042 (m); 980 (s); 895 (w); 873 (w); 795 (w); 776 (ms); 737 (w). MS *m/z*: 430 $[M-F]^+$ (5.5); 364 $C_7F_{14}N^+$ (15.9); 342 $C_7F_{12}NO^+$ (5.9); 314 $C_6F_{12}N^+$ (9.8); 264 $C_5F_{10}N^+$ (9.1); 214 $C_4F_8N^+$ (17.5); 169 $C_3F_7^+$ (27.7); 131 $C_3F_5^+$ (12.4); 119 $C_2F_5^+$ (22.1); 114 $C_2F_4N^+$ (15.7); 100 $C_2F_4^+$ (24.9); 69 CF_3^+ (100).

Perfluoro(3-pyrrolidinooxolane)(**21**)(nc): B.p. 107~108 °C, n_D^{20} 1.2997, d_4^{20} 1.8273. IR (gas) (cm^{-1}): 1337~1357 (m~ms); 1307 (ms); 1257; 1272 (vs); 1223 (vs); 1202 (s, sh); 11.86 (s); 1172 (s); 1135 (m); 1112 (s); 1084 (s); 1042 (ms); 985 (ms); 945 (m); 910 (w); 852 (w); 795 (w); 768 (ms); 730 (w). MS *m/z*: 392 $[M-F]^+$ (16.2); 364 $C_7F_{14}N^+$ (15.2); 345 $C_7F_{13}N^+$ (14.6); 95 $C_6F_{11}N^+$ (61.7); 245 $C_5F_9N^+$ (17.0); 176 $C_4F_6N^+$ (27.2); 169 $C_3F_7^+$ (22.5); 150 $C_3F_6^+$ (38.0); 131 $C_3F_5^+$ (29.2); 119 $C_2F_5^+$ (14.2); 100 $C_2F_4^+$ (100); 69 CF_3^+ (61.5).

Methyl perfluoro(3-pyrrolidino-n-butyrate)(**26**)(nc): B.p. 151~153 °C, n_D^{20} 1.3220, d_4^{20} 1.7444. IR (capillary film) (cm^{-1}): 1788 (C=O). MS *m/z*: 404 $[M-F]^+$ (2.4); 364 $C_7F_{14}N^+$ (4.9); 314 $C_6F_{12}N^+$ (19.8); 264 $C_5F_{10}N^+$ (5.4); 209 $C_5F_7O^+$ (7.6); 176 $C_4F_6N^+$ (5.5); 169 $C_3F_7^+$ (8.4); 150 $C_3F_6^+$ (11.4); 131 $C_3F_5^+$ (9.7); 119 $C_2F_5^+$ (9.6); 100 $C_2F_4^+$ (14.4); 81 $C_3F_3^+$ (5.8); 69 CF_3^+ (37.7);

59 CO_2Me^+ (100). ^{19}F NMR data for **20**, **21** and **26** are listed in Table 3.

Fluorination of methyl 3-morpholino-n-butyrate (2d)

Sample **2d** (40.7 g, 0.218 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 7.2~7.6 V, 7~8 °C, 530 min (228 A h). Work-up gave: product in the −78 °C trap (10.4 g): **13** (2.2 g), **14** (4.1 g), **15** (2.5 g) and unidentified materials (1.7 g). Cell drainings (61.6 g): **14** (4.0 g), **15** (n/iso ratio = 1:10) (8.2 g), perfluoro(3-morpholinopropylmethyl ether)(**22**)(2.8 g), perfluoro(3-morpholinooxolane)(**23**)(6.4 g), perfluoro-(3-morpholino-n-butyryl fluoride)(**4d**)(40.2 g) and unidentified materials (2.8 g). The yield of **4d** was 43.2%. Characterization of **4d** was as for **4a**.

Perfluoro(3-morpholinopropylmethyl ether)(**22**)(nc): B.p. 115~117 °C, n_D^{20} 1.2827, d_4^{20} 1.8038. IR (gas) (cm^{-1}): 1349 (ms); 1286~1209 (ms~s); 1227~1247 (vs); 1193 (s); 1167 (s); 1152 (vs); 1125 (m); 1105 (m); 985 (w); 934 (ms); 895 (w); 775 (ms); 667 (w); 623 (w). MS *m/z*: 446 $[M-F]^+$ (0.9); 280 $C_5F_{10}NO^+$ (14.1); 169 $C_3F_7^+$ (14.2); 64 $C_3F_6N^+$ (8.7); 119 $C_2F_5^+$ (44.6); 114 $C_2F_4N^+$ (25.2); 100 $C_2F_4^+$ (37.5); 69 CF_3^+ (100).

Perfluoro(3-morpholinooxolane)(**23**)(nc): B.p. 118~109 °C, n_D^{20} 1.3033, d_4^{20} 1.8596. IR (gas) (cm^{-1}): 1315 (m); 1300 (m); 1257 (s); 1230 (vs); 1186 (s); 1146 (m); 1132 (m); 1090 (w); 1008 (w); 967 (w); 890~898 (w); 768 (w). MS *m/z*: 408 $[M-F]^+$ (2.8); 361 $C_7F_{13}NO^+$ (2.8); 311 $C_6F_{11}NO^+$ (11.1); 295 $C_6F_{11}N^+$ (5.8); 245 $C_5F_9N^+$ (5.4); 214 $C_4F_8N^+$ (5.8); 195 $C_4F_7N^+$ (7.2); 176 $C_4F_6N^+$ (9.5); 145 $C_3F_5N^+$ (17.2); 131 $C_3F_5^+$ (12.1); 119 $C_2F_5^+$ (88.5); 100 $C_2F_4^+$ (100); 69 CF_3^+ (57.8).

Methyl perfluoro(3-morpholino-n-butyrate)(**27**)(nc): B.p. 160~163 °C, n_D^{20} 1.3248, d_4^{20} 1.7671. IR (capillary film) (cm^{-1}): 1793 (C=O). MS *m/z*: 420 $[M-F]^+$ (2.3); 381 $C_8F_{15}^+$ (4.6); 331 $C_7F_{13}^+$ (20.9); 214 $C_4F_8N^+$ (9.2); 209 $C_3F_6CO_2Me^+$ (16.6); 164 $C_3F_6N^+$ (22.7); 150 $C_3F_6^+$ (22.9); 119 $C_2F_5^+$ (72.1); 114 $C_2F_4N^+$ (14.2); 100 $C_2F_4^+$ (40.0); 69 CF_3^+ (24.9); 59 $CO_2CH_3^+$ (100). ^{19}F NMR data for **22**, **23** and **27** are listed in Table 3.

Fluorination of methyl 3-piperidino-n-butyrate (2e)

Sample **2e** (40.3 g, 0.218 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 6.1~6.3 V, 7~8 °C, 549 min (243 A h). Work-up gave: product in the −78 °C trap (8.6 g); **16** (3.8 g), **17** (2.1 g) and unidentified materials (2.7 g). Cell drainings (50.8 g): **17** (5.5 g), **18** (n/iso ratio = 1:2) (7.0 g), perfluoro-[3-(methylpyrrolidino)-n-butyryl fluoride] (6.5 g), perfluoro(3-piperidinooxolane)(**27**)(6.3 g), perfluoro(3-piperidino-n-butyryl fluoride)(**4e**)(21.1 g) and unidentified materials (4.8 g). The yield of **4e** was 21.0%. Characterization of **4e** was as for **4a**.

Perfluoro(3-piperidinooxolane)(**24**)(nc): B.p. 129~132 °C, n_D^{20} 1.3062, d_4^{20} 1.8748. MS *m/z*: 442 $[M-F]^+$ (6.5); 414 $C_8F_{16}N^+$ (4.0); 395 $C_6F_{12}N^+$ (4.1); 376 $C_8F_{10}N^+$ (3.5); 345 $C_5F_{10}N^+$ (17.5); 276 $C_6F_8N^+$ (13.0); 226 $C_5F_8N^+$ (8.0); 176 $C_4F_6N^+$ (21.0); 169 $C_3F_7^+$ (10.5); 131 $C_3F_5^+$ (78.1); 119 $C_2F_5^+$ (17.7); 100 $C_2F_4^+$ (96.0); 69 CF_3^+ (100).

Methyl perfluoro(3-piperidino-n-butyrate)(**28**)(nc): B.p. 167~168 °C, n_D^{20} 1.3271, d_4^{20} 1.7958. IR (capillary film) (cm^{-1}): 1788 (C=O). MS *m/z*: 454 $[M-F]^+$ (1.1); 414 $C_8F_{16}N^+$ (10.6); 364 $C_7F_{14}N^+$ (42.9); 314 $C_6F_{12}N^+$ (5.3); 226 $C_5F_{10}N^+$ (5.0); 209 $C_3F_6CO_2Me^+$ (16.4); 169 $C_3F_7^+$ (9.5); 164 $C_3F_6N^+$ (6.3); 150 $C_3F_6^+$ (22.0); 131 $C_3F_5^+$ (23.0); 119 $C_2F_5^+$ (17.8); 114 $C_2F_4N^+$ (17.8); 100 $C_2F_4^+$ (100); 69 CF_3^+ (37.0); 59 CO_2Me^+ (100). ^{19}F NMR data for **24** and **28** are listed in Table 3.

Fluorination of methyl 3-diethylamino-n-butyrate (2b)

Sample **2b** (40.6 g, 0.234 mol) was fluorinated similarly under the following conditions; 3.5 A dm^{-2}, 6.6~6.7 V, 7~8 °C, 577 min (249 A h). Work-up was as for the fluorination of **1a**. Products collected in the −78 °C trap (24.8 g) consisted mainly of **5** (14.3 g), perfluoro(*N*,*N*-diethylmethylamine)(4.6 g) and **9** (3.7 g). Perfluoro(*N*,*N*-diethylpropylamine)(1.8 g) and perfluoro(3-diethylaminopropionyl fluoride) [1c] (2.6 g) were found in the cell drainings (23.6 g), and most of the products remained unidentified. Among them, two perfluoroacid fluorides were found as a mixture, 5.4 g and 5.2 g, respectively. Determination of the structure in the form of their methyl esters was unsuccessful due to the complex ^{19}F NMR data obtained. However, we have assigned them as perfluoro[3-(*N*-methyl-*N*-ethylamino)-n-propionyl fluoride] for the former and perfluoro[3-(*N*,*N*-diethylamino)-n-propionyl fluoride] (**4b**) for the latter from their GC data. The yields of the former and the latter (**4b**) corresponded to 5.5% and 4.7%, respectively.

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