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THE ELECTROCHEMICAL FLUORINATION OF NITROGEN-CONTAINING CARBOXYLIC ACIDS *. FLUORINATION OF METHYL ESTERS OF CYCLIC AMINO-GROUP SUBSTITUTED CARBOXYLIC ACIDS

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SUMMARY

Nine methyl esters of cyclic amino-group substituted carboxylic acids related to glycine, alanine or β-alanine were subjected to electrochemical fluorination. This afforded the corresponding perfluoroacid fluorides together with cleavage products in fair yields. As cyclic amino-substituents, pyrrolidino-, morpholino-, piperidino-, hexamethyleneimino- and N'-methylpiperazinyl-groups were investigated. The formation of cyclized by-products was not observed, which contrasts with the fluorination of aliphatic dialkylamino-substituted carboxylic acids. From such methyl 2-cyclic amino-propionates [cyclic amino-group: a pyrrolidino, a morpholino or a piperidino-group], the perfluorinated methyl esters were obtained together with the corresponding perfluoroacid fluorides in yields of 1～2 % and 14～29 % respectively. The formation of the former compounds is ascribed to the blocking effect of the bulky cyclic amino-groups. The physical properties of the new compounds obtained are reported together with their spectral (^{19}F NMR, Mass and IR) data.

INTRODUCTION

The preparation of perfluorocarboxylic acids is one of the most extensively studied subjects in organofluorine chemistry,

* Preceding paper of this series, see Ref.[2].

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because these compounds are important raw materials with well-established uses [1]. However, not many studies have been undertaken for the preparation of acids containing a nitrogen atom in their skeleton [2].

In the earlier paper, we have shown that several aliphatic perfluoro(dialkylamino-group substituted carboxylic acid fluorides) having a glycine, an alanine and/or a β-alanine type structure were formed in fair yields by the fluorination of corresponding methyl esters of N,N-dialkylamino-substituted carboxylic acids [2].

In this paper, we wish to report the preparation of perfluoroacid fluorides bearing a perfluorocyclic amino-group by the fluorination of methyl esters of the corresponding cyclic amino-substituted carboxylic acids. Although fluorinations of several kinds of 3-(cyclic amino-group)-substituted propionyl chloride·HCl salts have been reported in the patent literature [3], to our knowledge, those of cyclic amino-substituted carboxylic acids having a glycine or an alanine structure have not been examined previously.

The following nine methyl esters of cyclic amino-group substituted carboxylic acids were used:

$R\text{-}CH_2C(O)OMe$ (1) :R=pyrrolidino- (a), morpholino- (b), piperidino- (c)

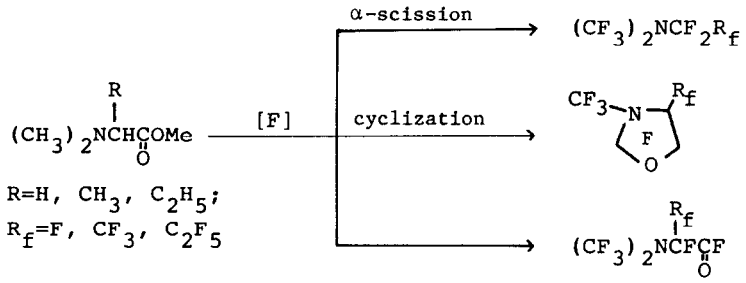
$R\text{-}CH(CH_3)C(O)OMe$ (2) :R=pyrrolidino- (a), morpholino- (b), piperidino- (c), hexamethyleneimino- (d), N'-methylpiperazinyl- (e)

$R\text{-}CH_2CH_2C(O)OMe$ (3) :R=hexamethyleneimino-

RESULTS AND DISCUSSION

It has been shown in the earlier paper that the major fluorination products obtained from each of the dimethylamino- or diethylamino-group substituted carboxylic acids having a glycine, an alanine and a β-alanine structure were a mixture composed of

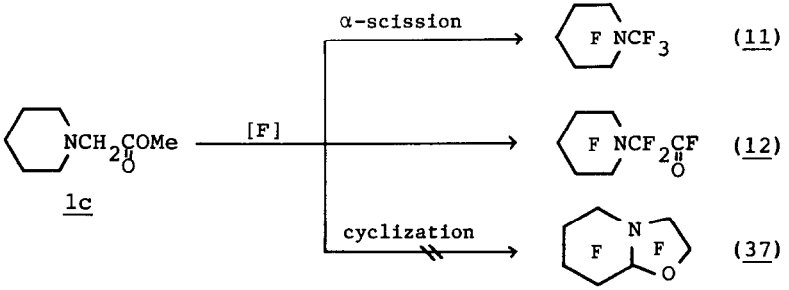
cleavage products due to α-scission at the carboxyl group, cyclization products and the desired perfluoroacid fluorides [2]. Thus, perfluorooxazolidines were invariably formed as by-products in small yields (Y = 2～8 %) from the fluorination of methyl esters of 2-(dimethylamino)-carboxylic acids.



Scheme 1.

However, all methyl esters of cyclic amino-group substituted carboxylic acids dealt with in this paper, when subjected to electrochemical fluorination, afforded characteristically only products consisting of cleaved ones arising from C-C and C-N bond scission and the desired perfluoroacid fluorides (Table 1).

For example, from the fluorination of methyl piperidinoacetate (1c), perfluoro-n-pentane (10), perfluoro(N-methyl piperidine) (11) and perfluoro(piperidino-acetyl fluoride) (12) were obtained as the major fluorination products. No cyclization

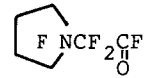
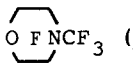
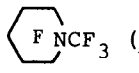
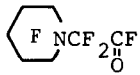


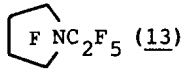
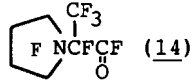
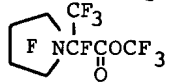
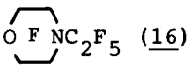
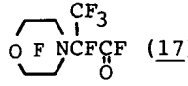
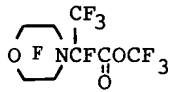
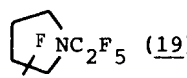
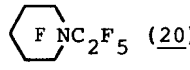
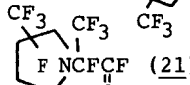
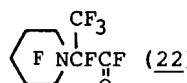
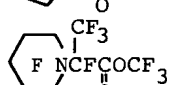
Scheme 2

product was formed from 1c, though the formation of the compound having the oxazolidine ring, perfluoro(1-aza-7-oxa-bicyclo-[4.3.0]nonane) (37), was expected. Analogous perfluorobicyclic

TABLE 1

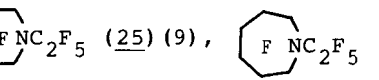
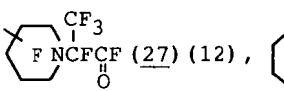
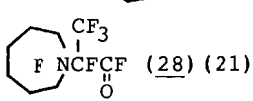
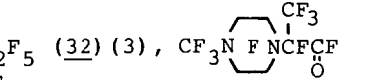
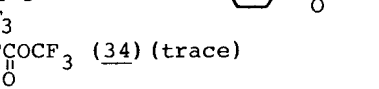
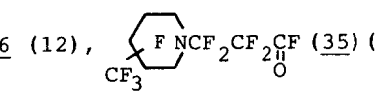
Results of the fluorination of methyl esters of cyclic amino-substituted carboxylic acids

Run	Sample g (mol)	Electricity passed (Ahr)	Fluorinated compds obtained (g) [a]	Products obtained (Yield %) [b]
1	1a, 25.1 (0.172)	154	21.1 (3.3)	$n\text{-}C_4F_{10}$ (4) (19),  (5) (21),  (6) (11)
2	1a, 41.3 (0.289)	232	28.9 (8.5)	4 (11), 5 (16), 6 (18)
3	1b, 24.8 (0.156)	135	9.6 (8.6)	$(C_2F_5)_2O$ (7) (8),  (8) (14),  (9) (16)
4	1b, 40.8 (0.257)	203	19.0 (24.2)	7 (9), 8 (17), 9 (29)
5	1c, 25.0 (0.159)	181	15.4 (3.2)	$n\text{-}C_5F_{12}$ (10) (12),  (11) (10),  (12) (6)
6	1c, 40.6 (0.259)	236	21.4 (22.6)	10 (17), 11 (17), 12 (12)

7	2a, 27.0 (0.172)	198	14.8 (15.9)	4 (7),  (13) (17),  (14) (20),  (15) (2)
8	2a, 40.3 (0.257)	227	17.6 (26.2)	4 (5), 13 (19), 14 (21), 15 (2)
9	2b, 26.1 (0.151)	173	13.9 (11.4)	7 (8),  (16) (24),  (17) (14),  (18) (1)
10	2b, 40.2 (0.232)	251	13.6 (19.7)	7 (7), 16 (13), 17 (17), 18 (2)
11	2c, 27.3 (0.160)	170	8.2 (20.3)	10[c] (6),  (19) (3),  (20) (16),  (21) (2),  (22) (14),  (23) (1)

(continued)

TABLE 1 (cont.)

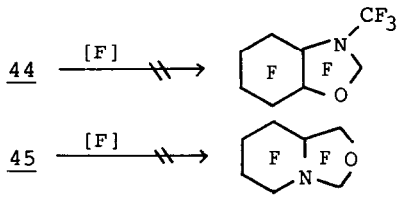
12	2c, 40.5 (0.237)	250	4.8 (56.7)	10[c] (2), 19 (4), 20 (20), 21 (5), 22 (29), 23 (2)
13	2d, 40.0 (0.216)	279	9.4 (52.0)	C_6F_{14}[c] (24) (6),  (25) (9), 26 (12),  (27) (12),  (28) (21)
14	2e, 40.1 (0.216)	193	9.3 (6.0)	$C_2F_5\overset{O}{\overset{\|}{C}}F$ (29) (1), $(C_2F_5)_2NCF_3$ (30) (2), $(C_2F_5)_3N$ (31) (5),  (32) (3), (33) (3),  (34) (trace)
15	3, 40.0 (0.216)	239	13.0 (47.4)	24[c] (8), 25 (13), 26 (12),  (35) (13)  (36) (8)

[a] Product collected in the -78 °C trap, and cell drainings, in (), are shown respectively.

[b] Products are arranged in order of elution time by GLC (Col.A).

[c] A mixture of n- and iso-isomer.

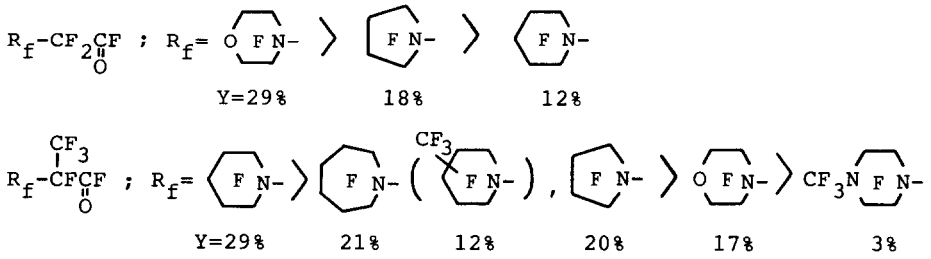
ethers were produced in fair yields by the fluorination of cyclohexyl or cyclohexenyl-substituted acetic acid derivatives [4]. However, for the development of new perfluorochemicals for use in artificial blood substitutes, we attempted to make new perfluorobicyclic compounds having both a nitrogen and an oxygen atom in their skeleton by fluorinating such compounds as methyl N-methyl-N-cyclohexylcarbamate (44), N-methoxycarbonyl-2-methylpiperidine (45) as well as 2c. However, we were not successful [5].



The reason why the formation of oxazolidine fused ring compounds from the fluorination of 1a~1c and 2a~2e is difficult is not clear. However, the incorporation of the nitrogen atom at the position of ring fusion of the expected bicyclic product may play an important role in preventing the ring closure, due to the enhanced strain as the degree of the fluorination progress. In this point, it is well known that perfluoro-tertiary amines have a larger bond angle than that of the usual ones [6].

In order to check the effect of the initial solute-concentration, investigations were made on the fluorination of 1a, 1b, 1c, 2a, 2b and 2c employing a lower (ca.5.3 wt%) and a higher (ca. 8.2 wt%) concentration in a similar manner to experiments with methyl 2-(dimethylamino)-propionate [2]. Improvements in the yields of the perfluoroacid fluorides by raising the solute-concentration, were observed for 1a, 1b and 1c (Runs 2, 4 and 6 in Table 1). On the other hand, among 2a, 2b and 2c (Runs 8, 10 and 12), only 2c exhibited this effect clearly. These findings suggest that this effect is highly dependent not only on the carboxylic acid skeleton but also on the nature of the cyclic amino group present. For other samples like 2d, 2e and 3, fluorinations were conducted under comparable conditions employing only a higher solute-concentration (Runs 13, 14 and 15).

Thus, new difluoroacetyl fluorides and tetrafluoropropionyl fluorides carrying a perfluoro(cyclic amino)-group were obtained from 1 and 2 in the following decreasing order of yield:



Scheme 3.

Thus, in every case except the fluorination of methyl 2-(N'-methylpiperazinyl)-propionate (2e), the expected perfluoroacid fluorides were formed in yields of 12～29%. The low yield of 33 from 2e was considered to be due to the formation of significant amount of the quarternary ammonium salt during fluorination (see the Experimental Section).

Though the yields are very small, the structurally significant compounds, perfluoro(methyl 2-cyclic amino-propionates) (15, 18 and 23), which retained the same fundamental structures as the starting materials, were found to be formed together with the corresponding perfluoroacid fluorides (14, 17 and 22) from the fluorination of 2a, 2b and 2c, respectively.

As the ester linkage is easily destroyed by solvolysis in anhydrous hydrogen fluoride (AHF), it usually survives only by conversion into a hemi-acetal linkage during fluorination [7]. So, these cases seem to be the first, as far as we know, where the formation of perfluorinated esters was actually confirmed in electrochemical fluorination. Previously, perfluoroesters of carboxylic acids have been obtained as by-products from the reaction of silver perfluorocarboxylates with iodine [8], by the reaction of perfluoroacid fluorides with perfluoro-iso-propoxide [9], and/or by the direct fluorination of ethyl acetate with elementary fluorine using a cryogenic reactor [10].

TABLE 2

Comparison of physical properties and IR data between perfluoroacid fluorides (14, 17 and 22) and perfluoroesters (15, 18 and 23)

Compd	Bp (°C)	n_d^{20}	d_4^{20}	ν (C=O) (cm^{-1})
14	89.0 ~ 90.0	1.2927	1.7565	1897, 1880
15	99.0 ~ 99.5	1.2953	1.7703	1854, 1838
17	97.0 ~ 97.5	1.2988	1.7888	1898, 1883
18	108.5 ~ 109.5	1.2980	1.7870	1855, 1839
22	107.5 ~ 108.5	1.3005	1.8147	1898, 1883
23	118.0 ~ 119.5	1.3114		1852, 1839

We explain this remarkable formation of perfluoroesters (15, 18 and 23) in terms of the blocking effect due to the presence both of a cyclic amino and a methyl group at the α-carbon of the substituted methyl propionate which protected the ester linkage against cleavage. An analogous blocking effect which reduced the C-N bond scission of pyridines due to the presence of a methyl group at the 2- and/or 6-position has been reported [11]. After the finding of the formation of perfluoroesters 15, 18 and 23 from 2a ~ 2c, IR spectral data of the products from the fluorination of methyl 2-dimethylamino-propionate were surveyed in detail [2]. However, the expected perfluoroester could not be detected. With respect to this point, it was considered that the bulkiness of the cyclic amino-group (a, b and c) compared with that of dimethylamino one preserved the ester linkages in the starting materials 2a ~ 2c.

The isolation of these perfluoroesters by means of GLC made possible to compare their physical properties and IR spectra

with those of corresponding perfluoroacid fluorides (Table 2). These perfluoroesters could be easily distinguished by ^{19}F NMR and IR spectra. In the ^{19}F NMR spectra of compounds 15, 18 and 23, the CF_3O- signal was observed as a singlet at ϕ-59.4 ppm (Table 3), and their IR spectra showed characteristic medium strong ν(C=O) bands at ca. 1873~1855 cm^{-1}. The values are slightly lower than those of the perfluoroacid fluorides (ca. 1879~1898 cm^{-1}), but are within the range of the reported ν(C=O) values for known perfluoroesters.

Comparison of the fluorination products from 2d and 3 exhibited an interesting result about isomerization and ring size. The fluorination of 2d, whose hexamethyleneimino-group was connected with a branched substituent [$-CH(CH_3)C(O)OMe$], afforded 28 as the expected perfluoroacid fluoride together with ring-isomerized product (27) in yields of 21% and 12%, respectively. On the other hand, 3, which is an isomer of 2d having a straight chain substituent [$-CH_2CH_2C(O)OMe$], afforded the expected perfluoroacid fluoride (36)(Y=8%) and its isomerized compounds (35)(Y=13%). In the case of 2d, the ratio 27/28 was 0.57, which was reversed compared with that obtained for 3 (35/36 ratio=1.63). Furthermore, their combined yield (Y=34%) was considerably higher than that from the latter (Y=21%). The difference of the isomer ratio of the product between 2d and 3 appeared to be closely related to steric protection by the bulky alkyl group, not only to suppress the isomerization of the cyclic amino-group but also to diminish the cleavage of the C-N bond.

Finally, the broad scope and the utility of the newly prepared perfluoroacid fluorides having an alanine structure (2a~2d) are apparent because of having the same general structure as that of the perfluoro(2-alkoxy-propionic acids) which are important precursors for perfluorovinyl ethers (monomers of PFA resin), and also having a chiral carbon in the molecule. Thus, the usefulness of 2 as direct precursors for perfluorovinylamines has been shown by us recently [12]. Applications using 14, 17 and 22 as optically active agents have also been described [13].

EXPERIMENTAL

Reagents

Except methyl 3-hexamethyleneimino-propionate, all N-containing carboxylic acids were prepared by reactions of appropriate methyl esters of chloro- or bromo-substituted carboxylic acids with cyclic amines [14]. Methyl 3-hexamethyleneimino-propionate was prepared by Michael addition using methyl acrylate and hexamethyleneimine in high yield.

These starting materials had following boiling points: methyl pyrrolidino-acetate, bp 58 °C/10 mmHg, methyl morpholino-acetate, bp 88.5～89.5 °C/7 mmHg, methyl piperidino-acetate, bp 137.5～138.5 °C/98 mmHg (reported: bp 205～207 °C)[15], methyl 2-pyrrolidino-propionate, bp 112.5～113.0 °C/57 mmHg, methyl 2-morpholino-propionate, bp 154.5～155.0 °C/98 mmHg, methyl 2-piperidino-propionate, bp 123.0～124.0 °C/53 mmHg, methyl 2-hexamethyleneimino-propionate, 138.5～139.5 °C/58 mmHg, methyl 2-(N'-methyl-N-piperazinyl)-propionate, bp 108.5～112.5 °C/6 mmHg, methyl 3-hexamethyleneimino-propionate, bp 162.0～163.5 °C/88 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 [2].

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

Infrared spectra were measured on a Hitachi EPI-G3 spectrometer, using a 6 cm gas cell with KBr windows.

^{19}F NMR spectra were measured at 56.46 MHz using CCl_3F as an internal standard. Mass spectra were measured on a Shimadzu GC/MS-7000 instrument at 70 eV.

Fluorination of methyl pyrrolidino-acetate (1a) (Run 2)

Sample 1a (41.3 g, 0.289 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 5.8～6.2 V, and a cell temperature of 7～8 °C over a period of 523 min (232 Ahr). At the final stage of the fluorination, the voltage reached 6.7 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 then bubbled through a fluoropolymer bottle containing water and a gas washing bottle containing aq. solution of a mixture of of K_2SO_3, KOH and KI, respectively. All products except new ones were identified by comparison of their infrared spectra and GLC retention times with those of authentic samples. New compounds were separated from other products by use of semi-preparative GLC, and their structures were determined on the basis of their infrared, ^{19}F NMR and mass spectra.

The products (compound number, g Yield) (28.9 g) condensed in the -78 °C trap consisted of perfluoro-n-butane (4) (7.6), perfluoro(N-methylpyrrolidine) (5) (12.1), and perfluoro(pyrrolidino-acetyl fluoride) (6) (9.2). Cell drainings (8.5 g) consisted of 5 (1.2) and 6 (7.3). The yield of 6 was 18% based on the sample fed. Attempts to isolate 6 were unsuccessful due to its facile change into free acid. So, further characterization of 6 was done on the methyl ester. Methyl perfluoro(pyrrolidino-acetate) (38) was prepared by mixing about 2 g of cell drainings with 1 mℓ of methanol. The reaction completed within a few minutes. Then, the lower layer of the reaction mixture was subjected to semi-preparative GLC (Col. D) to give pure 38.

Perfluoro(pyrrolidino-acetyl fluoride) (6) (nc): IR (gas): 1892 (s) ν(C=O), 1404 (w), 1339 (vs), 1313 (ms), 1231 (vs), 1185 (s), 1138 (ms), 1171 (ms), 1028 (w), 980 (s), 876 (w), 832 (m), 702 (w).

Methyl perfluoro(pyrrolidino-acetate) (38) (nc) had bp 119 121 °C, n_D^{20} 1.3167 and d_4^{20} 1.6401. IR (capillary film): 1792 (s) ν(C=O). Mass: 304 $[M-F]^+$(2.7), 276 $C_6F_{10}N^+$(4.3), 264 $C_5F_{10}N^+$ (27.6), 214 $C_4F_8N^+$(7.8), 176 $C_4F_6N^+$(4.3), 164 $C_3F_6N^+$(4.8), 145 $C_3F_5N^+$(10.7), 131 $C_3F_5^+$(6.7), 114 $C_2F_4N^+$(19.4), 109 $CF_2CO_2Me^+$ (11.6),100 $C_2F_4^+$(10.0), 81 $C_2F_3^+$(7.5), 79 $C_2F_2OH^+$(31.9), 69 CF_3^+(100). Found: C, 25.90%. Calculated for $C_7F_{10}NO_2H_3$: C, 26.00%. ^{19}F nmr spectra of 6 and 38 are shown in Table 3.

Fluorination of methyl morpholino-acetate (1b) (Run 4)

1b (40.8 g, 0.257 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 5.9~6.1 V, 7~8 °C, 470 min (203 Ahr). Work-up was as for the fluorination of 1a. Products collected in the -78 °C trap and cell drainings were subsequently analyzed by GLC (Col. A and B). Thus, the following compounds were obtained; products in the -78 °C trap (19.0 g) perfluorodiethyl ether) (7) (5.5), perfluoro(N-methylmorpholine) (8) (9.5), perfluoro(morpholino-acetyl fluoride) (9) (4.0). Cell drainings (24.2 g) 8 (3.9), 9 (20.3). The yield of 9 was 29% based on the sample fed.

Perfluoro(morpholino-acetyl fluoride) (9) (nc): IR (gas): 1894 (ms) ν(C=O), 1347 (m), 1310 (s), 1297 (ms,sh), 1232 (vs), 1179 (s), 1152 (ms), 1105 (w), 1088 (w), 1058 (w), 934 (m), 831 (w), 742 (w), 657 (w).

Methyl perfluoro(morpholino-acetate) (39) (nc) had bp 124~125 °C, n_D^{20} 1.3188 and d_4^{20} 1.6638. IR (capillary film): 1784 (s) ν(C=O). Mass: 320 $[M-F]^+$(3.7), 292 $C_6F_{10}NO^+$(3.7), 280 $[M-CO_2Me]^+$ (12.5), 119 $C_2F_5^+$ (28.4), 114 $C_2F_4N^+$(36.5), 109 $CF_2CO_2Me^+$(13.1),

100 $C_2F_4^+$(21.8), 81 $C_2F_3^+$(8.7), 79 $C_2F_2OH^+$(15.6), 69 CF_3^+ (100). Found: C, 24.70%. Calculated for $C_7F_{10}NO_3H_3$: C, 24.79%.

^{19}F nmr data of 9 and 39 are shown in Table 3.

Fluorination of methyl piperidino-acetate (1c) (Run 6)

1c (40.6 g, 0.259 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 6.0～6.1 V, 7～8 °C, 546 min (236 Ahr). Work-up gave; product in -78 °C trap (21.4 g), perfluoro-n-pentane (10) (12.3), perfluoro(N-methylpiperidine) (11) (6.7), unidentified (2.4). Cell drainings (22.6 g) 10 (0.6), 11 (8.3), perfluoro(piperidino-acetyl fluoride) (12) (11.5), unidentified (2.2). The yield of 12 was 12% based on the sample fed.

Perfluoro(piperidino-acetyl fluoride) (12) (nc): IR (gas): 1895 (ms) ν(C=O), 1376 (m), 1332 (s), 1276 (s), 1238 (s), 1198 1215 (vs), 1167 (m), 1130 (m), 1070 (ms), 1018 (m), 973 (s), 860 (w), 824 (w).

Methyl perfluoro(piperidino-acetate) (40) (nc) had bp 145～146 °C and n_D^{20}1.3218. IR (capillary film): 1793 (s) ν(C=O). Mass: 314 $[M-CO_2Me]^+$(7.8), 264 $C_5F_{10}N^+$(2.9), 176 $C_4F_6N^+$(2.6), 169 $C_3F_7^+$(2.6), 164 $C_3F_6N^+$(2.6), 145 $C_3F_5N^+$(4.3), 131 $C_3F_5^+$(9.2), 119 $C_2F_5^+$(6.5), 114 $C_2F_4N^+$(10.8), 109 $CF_2CO_2Me^+$(12.0), 100 $C_2F_4^+$ (6.5), 81 $C_2F_3^+$(6.5), 79 $C_2F_2OH^+$(26.4), 69 CF_3^+(100). Found: C, 25.71%. Calculated for $C_8F_{12}NO_2H_3$, 25.74%.

^{19}F nmr data of 12 and 40 are shown in Table 3.

Fluorination of methyl 2-pyrrolidino-propionate (2a) (Run 8)

2a (40.3 g, 0.257 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 5.7～5.9 V, 7～8 °C, 540 min (227 Ahr). After the usual work-up, the following compounds were obtained; product in the -78 °C trap (17.6 g) 4 (2.9), perfluoro(N-ethylpyrrolidine) (13) (11.6), perfluoro(2-pyrrolidino-

propionyl fluoride)(14)(2.3), unidentified (0.8). Cell drainings (26.2) 13 (4.3), 14 (16.8), perfluoro(methyl 2-pyrrolidino-propionate)(15)(2.3), unidentified (2.8). The yield of 14 and 15 were 21% and 2%, respectively. Among these products, 14 and 15 were isolated by GLC (Col.C) and their structure was determined by studying the IR and ^{19}F NMR. The physical properties of 14 and 15 are shown in Table 2.

Perfluoro(2-pyrrolidino-propionyl fluoride)(14)(nc): IR (gas): 1897 (ms) and 1880 (ms) ν(C=O), 1344 (s), 1297 (m), 1221~1262 (vs), 1178 (ms), 1125 (s), 1096 (ms), 1029 (m), 1013 (m), 966 (ms), 815 (w), 762 (w), 702 (w), 544 (w). Mass: 342 $[M-F]^+$ (5.4), 314 $[M-COF]^+$(33.6), 292 $C_6F_{10}NO^+$(8.2), 264 $C_5F_{10}N^+$(10.8), 219 $C_4F_9^+$(9.3), 214 $C_4F_8N^+$(5.0), 176 $C_4F_6N^+$(8.5), 164 $C_3F_6N^+$ (8.5), 150 $C_3F_6^+$(6.5), 145 $C_3F_5N^+$(7.6), 131 $C_3F_5^+$(15.6), 119 $C_2F_5^+$(33.0), 114 $C_2F_4N^+$(14.5), 100 $C_2F_4^+$(29.7), 69 CF_3^+(100),

Perfluoro(methyl 2-pyrrolidino-propionate)(15)(nc): IR (gas): 1854 (m) and 1838 (m) ν(C=O), 1344 (s), 1292 (s), 1259 (vs), 1222 (s), 1080 (ms), 1152 (vs), 1125 (s), 1104 (ms), 1032 (m), 1020 (m), 972 (ms), 882 (w), 839 (w), 794 (m), 754 (w). Mass: 408 $[M-F]^+$(1.0), 380 $C_7F_{14}NO^+$(1.5), 358 $[M-CF_3]^+$ (1.0), 314 $[M-COCF_3]^+$(12.3), 295 $C_6F_{11}N^+$(2.2), 264 $C_5F_{10}N^+$(4.4), 195 $C_4F_7N^+$(3.4), 176 $C_4F_6N^+$(3.7), 164 $C_3F_6^+$(3.6), 145 $C_3F_5N^+$ (2.9), 131 $C_3F_5^+$(5.0), 119 $C_2F_5^+$(9.1), 114 $C_2F_4N^+$(5.9), 100 $C_2F_4^+$(11.9), 69 CF_3^+(100).

^{19}F nmr data of 14 and 15 are shown in Table 3.

Fluorination of methyl 2-morpholino-propionate (2b)(Run 10)

2b (40.2 g, 0.232 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 6.1~6.3 V, 7~8 °C, 566 min (251 Ahr). Work-up gave; product in the -78 °C trap (13.6 g) perfluoro(diethyl ether)(7)(4.1), perfluoro(N-ethylmorpholine)(16)(6.8), perfluoro(2-morpholino-propionyl fluoride)(17)(1.0), unidentified (1.7). Cell drainings (19.7 g) 16 (3.9), 17 (13.6)

perfluoro(methyl 2-morpholino-propionate) (18) (2.2). The yield of 17 and 18 were 17% and 2%, respectively. The physical properties of 17 and 18 are shown in Table 2.

Perfluoro(2-morpholino-propionyl fluoride) (17) (nc): IR (gas): 1898 (ms) and 1883 (ms) ν(C=O), 1346 (m), 1310 (s), 1291 (s), 1221~1261 (vs), 1153 (s), 1111 (m,sh), 1088 (w), 1065 (w), 987 (m), 936 (w), 919 (w), 817 (w), 703 (w), 613~626 (w). Mass: 358 $[M-F]^+$(2.8), 330 $[M-COF]^+$(11.1), 214 $C_4F_8N^+$(5.5), 192 $C_3F_8N^+$(5.3), 164 $C_3F_6N^+$(28.8), 145 $C_3F_5N^+$(6.5), 119 $C_2F_5^+$(100), 114 $C_2F_4N^+$(22.0), 100 $C_2F_4^+$(49.7), 69 CF_3^+(38.4).

Perfluoro(methyl 2-morpholino-propionate) (18) (nc): IR (gas): 1855 (m) and 1839 (ms) ν(C=O), 1342 (m,sh), 1310 (ms,sh), 1291 (s), 1257 (vs), 1232 (vs), 1182 (s), 1152 (vs), 1107 (m,sh), 1089 (w), 1065 (w), 1021 (m), 972 (w), 922~937 (w), 853 (w), 810 (w), 790 (w), 752 (w). Mass: 396 $C_7F_{14}NO_2^+$(1.0), 374 $[M-CF_3]$ (1.3), 330 $[M-CO_2CF_3]^+$(8.3), 311 $C_6F_{11}NO^+$(2.4), 214 $C_4F_8N^+$(4.0), 195 $C_4F_7N^+$(2.5), 192 $C_3F_8N^+$(2.3), 164 $C_3F_6N^+$(13.8), 145 $C_3F_5N^+$ (4.6), 119 $C_2F_5^+$(42.2), 114 $C_2F_4N^+$(10.2), 100 $C_2F_4^+$(38.4), 69 CF_3^+(100).

^{19}F nmr data of 17 and 18 are shown in Table 3.

Fluorination of methyl 2-piperidino-propionate (2c) (Run 12)

2c (40.5 g, 0.237 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 5.9~6.0 V, 7~8 °C, 592 min (250 Ahr). Work-up gave; product in the -78 °C trap (4.8 g), 10 (1.5), perfluoro(N-ethyl methylpyrrolidine) (19) (0.3), perfluoro(N-ethylpiperidine) (20) (1.5), unidentified (1.5). Cell drainings (56.7) 19 (3.3), 20 (16.6), perfluoro[2-(methylpyrrolidino)-propionyl fluoride] (21) (4.9), perfluoro(2-piperidino-propionyl fluoride) (22) (27.9), perfluoro(methyl 2-piperidino-propionate) (23) (2.2), unidentified (1.8). The yield of 22 and 23 were 29% and 2%, respectively. The physical properties of 22 and 23 are shown in Table 2.

Perfluoro(2-piperidino-propionyl fluoride) (22) (nc): IR (gas): 1898 (m,sh) and 1883 (s) ν(C=O), 1370 (m), 1316~1325 (ms), 1266~1278 (vs), 1239 (vs), 1204 (vs), 1179 (s), 1164 (ms), 1134 (m), 1104~1116 (m), 1096 (ms), 1071 (ms), 1016 (s), 993 (m), 962 (ms), 947 (m,sh), 844 (w), 809 (w), 763 (w), 716 (w), 701 (w), 657 (w), 634 (w). Mass: 392 $[M-F]^+$(5.9), 364 $[M-COF]^+$ (34.7), 342 $C_7F_{12}NO^+$(11.6), 314 $C_6F_{12}N^+$(9.9), 269 $C_5F_{11}^+$(7.5), 264 $C_5F_{10}N^+$(4.7), 226 $C_5F_8N^+$(7.9), 181 $C_4F_7^+$(7.7), 176 $C_4F_6N^+$ (7.7), 169 $C_3F_7^+$(8.1), 164 $C_3F_6N^+$(14.2), 145 $C_3F_5N^+$(7.7), 131 $C_3F_5^+$(38.7), 119 $C_2F_5^+$(48.3), 114 $C_2F_4N^+$(18.3), 100 $C_2F_4^+$(53.3), 69 CF_3^+(100).

Perfluoro(methyl 2-piperidino-propionate) (23) (nc): IR (gas): 1852 (w,sh) and 1839 (m) ν(C=O), 1369 (w), 1292 (s), 1270 (vs), 1240 (ms), 1205 (s), 1182 (m,sh), 1153 (vs), 1137 (ms,sh), 1087 (m), 1069 (w), 1018 (ms), 968 (m), 802 (w), 789 (w), 752 (w), 662 (w), 636 (w). Mass: 408 $[M-CF_3]^+$(1.2), 364 $C_7F_{14}N^+$(8.9), 345 $C_7F_{13}N^+$(2.4), 342 $C_7F_{12}NO^+$(1.4), 314 $C_6F_{12}N^+$(3.3), 226 $C_5F_8N^+$(2.6), 219 $C_4F_9^+$(1.8), 195 $C_4F_7N^+$(1.8), 181 $C_4F_7^+$(1.9), 176 $C_4F_6N^+$(3.4), 169 $C_3F_7^+$(2.0), 164 $C_3F_6N^+$(4.1), 145 $C_3F_5N^+$(3.9), 131 $C_3F_5^+$(13.4), 119 $C_2F_5^+$(12.4), 114 $C_2F_4N^+$ (5.9), 100 $C_2F_4^+$(14.5), 69 CF_3^+(100).

^{19}F nmr data of 22 and 23 are shown in Table 3.

Fluorination of methyl 2-hexamethyleneimino-propionate (2d) (Run 13)

2d (40.0 g, 0.216 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 6.0~6.4 V, 7~8 °C, 606 min (258 Ahr). Work-up gave; product in the -78 °C trap (9.4 g) 4 (1.0), 10 (2.3), perfluorohexane (24) (4.6), perfluoro(N-ethyl methylpiperidine) (25) (0.8), perfluoro(N-ethylhexamethyleneimine) (26) (0.7). Cell drainings (52.0 g) 25 (7.8), 26 (10.8), perfluoro[2-(methylpiperidino)-propionyl fluoride] (27) (12.0), perfluoro(2-hexamethyleneimino-propionyl fluoride) (28) (21.4). The yields of 27 and 28 were 12% and 21%, respectively. 27 was determined on the basis of the GLC analysis, and its correct

assignment was verified from the results of the pyrolytic reaction of a mixture of 27 and 28 over K_2CO_3, which gave a mixture of perfluoro(N-vinyl methylpiperidine) and perfluoro(N-vinyl hexamethyleneimine) respectively [12].

Perfluoro(2-hexamethyleneimino-propionyl fluoride) (28) (nc) had bp 137.0~137.5 °C, n_D^{20}1.3082 and d_4^{20}1.8746. IR (gas): 1894 (m,sh) and 1880 (ms) ν(C=O), 1284 (s), 1219~1259 (vs~s), 1186 (s), 1157 (s), 1134 (s), 1119 (s), 1062 (m), 1042 (m), 1009 (ms), 988 (s), 954 (m), 944 (m), 932 (s), 767 (m), 737 (w), 727 (m), 699 (m), 632 (w). Mass: 442 $[M-F]^+$(10.5), 414 $[M-COF]^+$(43.4), 392 $C_8F_{14}NO^+$(12.9), 364 $C_7F_{14}N^+$(8.2), 295 $C_6F_{11}N^+$(4.8), 269 $C_5F_{11}^+$(4.5), 226 $C_5F_8N^+$(11.9), 195 $C_4F_7N^+$(6.2), 181 $C_4F_7^+$(6.6), 164 $C_3F_6N^+$(13.9), 145 $C_3F_5N^+$(6.3), 131 $C_3F_5^+$(90.9), 119 $C_2F_5^+$ (17.3), 100 $C_2F_4^+$(11.4), 69 CF_3^+(100).

^{19}F nmr data of 28 are shown in Table 3.

Fluorination of methyl 2-(N'-methylpiperazinyl)-propionate (2e) (Run 14)

2e (40.1 g, 0.216 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 6.1~6.4 V, 7~8 °C, 456 min (193 Ahr). The residual AHF was dark chocolate-coloured with good fluidity and dissolved easily in water, which suggested the formation of the quarternary ammonium salt. Work-up gave; product in the -78 °C trap (9.3 g) perfluoropropionyl fluoride (29) (0.4), perfluoro(N,N-diethylmethylamine) (30) (1.3), perfluoro(triethylamine) (31) (3.4), perfluoro(N'-methyl-N-ethylpiperazine) (32) (1.9), unidentified (2.3). Cell drainings (6.0 g) 31 (0.2), 32 (2.2), perfluoro[2-(N'-methylpiperazinyl)-propionyl fluoride] (33) (3.2), perfluoro[methyl 2-(N'-methylpiperazinyl)-propionate] (34) (trace), unidentified (0.4). 34 was determined by IR and GLC analysis. The yield of 33 was 3% based on the sample fed.

Perfluoro[2-(N'-methylpiperazinyl)-propionyl fluoride] (33) had bp 119~121 °C, n_D^{20}1.3067 and d_4^{20}1.8360. IR (gas): 1898 (m) and 1881 (m) ν(C=O), 1360 (vs), 1307 (s), 1288 (ms), 1260 (s),

1225～1243 (vs～s), 1176 (ms), 1133 (w), 1105 (w), 1065 (m), 1011 (w), 981 (w), 959 (m), 938 (m), 896 (w), 808 (w), 732 (m), 698 (w). Mass: 425 $[M-F]^+$(5.8), 397 $[M-COF]^+$(10.7), 385 $C_6F_{15}N_2^+$ (5.8), 309 $C_6F_{11}N_2^+$(4.1), 259 $C_5F_9N_2^+$(6.2), 214 $C_4F_8N^+$(11.5), 164 $C_3F_5N^+$(31.1), 119 $C_2F_5^+$(60.0), 114 $C_2F_4N^+$(38.6), 100 $C_2F_4^+$ (48.2), 69 CF_3^+(100).

Perfluoro[methyl 2-(N'-methylpiperazinyl)-propionate](34) (nc): IR (gas) 1854 (m) and 1837 (m) ν(C=O), 1360 (s), 1309 (ms), 1290 (s), 1258 (vs), 1225 (s), 1200 (ms), 1174 (ms), 1151 (s), 1074 (m), 1017 (m), 960 (m), 897 (m), 850 (w), 788 (w), 731 (m).

^{19}F nmr data of perfluoro[2-(N'-methylpiperazinyl)-propionic acid](41) in place of 33 are shown in Table 3 due to the decomposition in NMR tube during long shelf storing.

Fluorination of methyl 3-hexamethyleneimino-propionate (3) (Run 15)

3 (40.0 g, 0.216 mol) was fluorinated similarly under the following conditions; 3.5 A/dm^2, 6.1～6.2 V, 7～8 °C, 527 min (239 Ahr). Work-up gave, product in the -78 °C trap (13.0 g) 4 (1.9), 10 (2.8), 24 (5.7), 25 (0.7), 26 (0.3), unidentified (1.6). Cell drainings (47.7 g) 25 (11.1), 26 (10.6), perfluoro-[3-(methylpiperidino)-propionyl fluoride](35) (13.0), perfluoro-(3-hexamethyleneimino-propionyl fluoride)(36)(7.5). The yield of 35 and 36 were 13% and 8%, respectively. Attempts to isolate 35 and 36 by preparative GLC failed due to the facile hydrolytic reaction. So, they were characterized in the form of methyl esters.

Methyl [3-(methylpiperidino)-propionate](42)(nc) had bp 169～172 °C, n_D^{20}1.3243 and d_4^{20}1.7810. IR (capillary film): 1787 (s) ν(C=O). Mass: 414 $[M-CO_2Me]^+$(1.5), 364 $[M-CF_2CO_2Me]^+$ (12.7), 314 $C_6F_{12}N^+$(2.2), 276 $C_6F_{10}N^+$(3.6), 159 $CF_2F_2CO_2Me^+$ (7.2), 131 $C_3F_5^+$(18.6), 119 $C_2F_5^+$(21.3), 114 $C_2F_4N^+$(9.6), 100 $C_2F_4^+$(27.0), 81 $C_2F_3^+$(10.1), 79 $C_2F_2OH^+$(33.8), 69 CF_3^+(100).

Methyl 3-hexamethyleneimino-propionate (43)(nc) had bp 181~182 °C, n_D^{20} 1.3305 and d_4^{20} 1.8067. IR (capillary film): 1788 (s) ν(C=O). Mass: 414 $[M-CO_2Me]^+$(0.5), 364 $[M-CF_2CO_2Me]^+$(6.6), 314 $C_6F_{12}N^+$(1.1), 276 $C_6F_{10}N^+$(2.3), 226 $C_5F_8N^+$(2.0), 169 $C_3F_7^+$(4.2), 159 $CF_2CF_2CO_2Me^+$(6.2), 131 $C_3F_5^+$(23.2), 119 $C_2F_5^+$(19.4), 114 $C_2F_4N^+$(27.1), 100 $C_2F_4^+$(27.1), 81 $C_2F_3^+$(13.6), 79 $C_2F_2OH^+$(35.6), 69 CF_3^+(100). Found: C, 25.35%. Calculated for $C_{10}F_{16}NO_2H_3$: C, 25.37%.

^{19}F nmr data of 43 are shown in Table 3.

TABLE 3

^{19}F nmr data of 6, 9, 12, 14, 15, 17, 18, 22, 23, 27, 38, 39, 40, 41 and 43

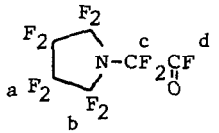
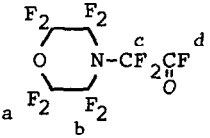
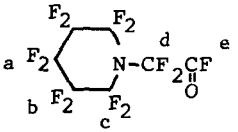
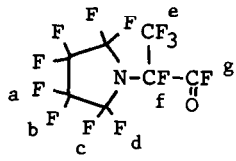
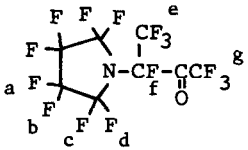
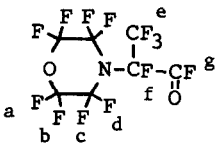
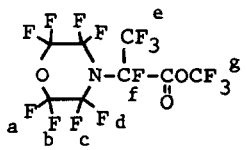
Compd	Formula		Chemical shift[a,b]	J (Hz)[b]
6		a	-132.8	b-c=9.1
		b	-91.3	
		c	-88.7	
		d	15.7	
9		a	-85.7	
		b	-91.6	
		c	-86.5	
		d	14.2	
12		a	-134.2	
		b	-132.1	
		c	-91.8	
		d	-84.4	
		e	14.0	

TABLE 3 (cont.)

14		a	-89.2	a-b=172
		b	-92.4	
		c	-132.8	c-d=250
		d	-135.6	
		e	-75.6	
		f	-136.5	
		g	28.2	
15		a	-88.1	a-b=174
		b	-92.7	
		c	-132.1	c-d=250
		d	-136.1	
		e	-75.1	
		f	-137.6	
		g	-59.4	
17		a	-84.4	a-b=146
		b	-88.1	
		c	-88.4	c-d=196
		d	-92.5	
		e	-76.0	
		f	-140.6	
		g	24.4	
18		a	-84.2	a-b=148
		b	-88.3	
		c	-87.7	c-d=198
		d	-92.7	
		e	-75.7	
		f	-141.0	
		g	-59.4	

(continued)

TABLE 3 (cont.)

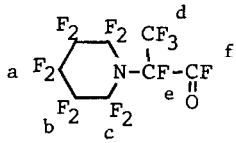
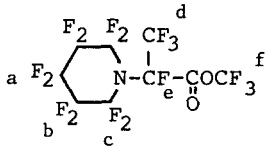
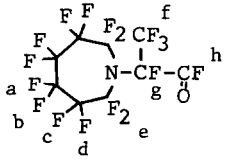
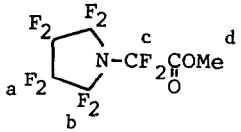
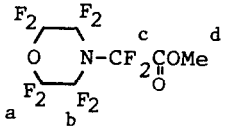
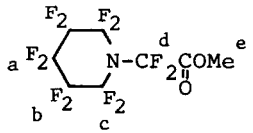
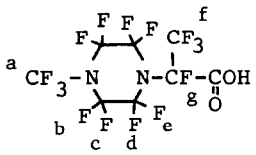
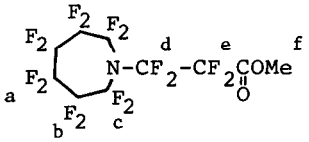
22		a	-133.6	
		b	-132.3	
		c	-91.0	
		d	-77.4	
		e	-141.2	
		f	24.4	
23		a	-133.4	
		b	-132.6	
		c	-90.8	
		d	-76.4	
		e	-141.0	
		f	-59.4	
27		a	-124.1	J_{AB} a-b=296
		b	-132.4	
		c	-119.1	J_{AB} c-d=277
		d	-121.6	
		e	-84.0	
		f	-77.5	
		g	-146.8	
		h	20.1	
38		a	-133.1	
		b	-91.6	
		c	-87.7	
		d	δ3.99	
39		a	-85.8	
		b	-91.8	
		c	-85.5	
		d	δ3.99	

TABLE 3 (cont.)

40		a	-134.1	
		b	-132.2	
		c	-91.6	
		d	-83.7	
		e	δ3.79	
41		a	-53.0	
		b	-87.2	b-c=192
		c	-98.3	J_{AB}
		d	-83.6	d-e=197
		e	-94.3	J_{AB}
		f	-76.3	
		g	-142.5	
43		a	-130.0	
		b	-125.0	
		c, d	-88.2	
		e	-118.4	
		f	δ3.97	

a ^{19}F chemical shift in ppm relative to internal CCl_3F in CCl_4.
b Only evident chemical shifts and coupling constants are given.

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