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Electrochemical fluorination of 1-ethylpiperazine and 4-methyl- and/or 4-ethylpiperazinyl substituted carboxylic acid methyl esters☆

Takashi Abe[a,*], Hajime Baba[b], Irina Soloshonok[a]

[a]*Department of Chemistry, National Industrial Research Institute of Nagoya, Hirate-cho 1-1, Kita-ku, Nagoya 462-8510, Japan*
[b]*Department for New Refrigerants Research, Research Institute of Innovative Technology for the Earth (RITE), c/o NIRIN, Hirate-cho 1-1, Kita-ku, Nagoya 462-8510, Japan*

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Abstract

Electrochemical fluorination (ECF) of 1-ethylpiperazine and eight methyl esters of 4-methyl- and/or 4-ethylpiperazinyl substituted carboxylic acids were studied. Corresponding perfluoro(4-fluoro-1-ethylpiperazine) was obtained from 1-ethylpiperazine in a small yield along with perfluoro(1-methyl-3-ethylimidazolidine), perfluoro[2-(*N*′,*N*′-difluoroaminoethyl)-*N*,*N*-diethylamine)] and perfluorotriethylamine. The corresponding mono-basic perfluoroacid fluorides with a perfluoro(4-alkylpiperazinyl) group were obtained in fair to good yields from the fluorination of methyl esters of 4-alkylpiperazinyl-substituted carboxylic acids. Yields of the targeted perfluoro(4-alkylpiperazinyl) group containing perfluorocarboxylic acid fluorides varied depending on both the type of *N*-alkyl (alkyl = CH_3^- or $C_2H_5^-$) group at the 4-position and the (ω-methoxycarbonylalkyl) group at the 1-position of the piperazine ring of the substrate. Higher yields of perfluoroacid fluorides were obtained by the ECF of 4-ethyl substituted piperazine derivatives than of the 4-methyl substituted piperazine derivatives when 4-alkylpiperazines with the same carboxylic acid ester group were fluorinated electrochemically. Spectroscopic data as well as physical properties are described for new perfluoro(1,4-dialkylpiperazines) and *N*-containing perfluorocarboxylic acids with a perfluoropiperazinyl group.

Keywords: Electrochemical fluorination; Perfluoroacid fluorides; Perfluoropiperazines; Perfluoromono-basic acids

1. Introduction

Electrochemical fluorination (ECF) is a very important method for the production of perfluoro-compounds[1] with a hetero-atom [1–3]. Although the ECF of several perfluoro(1,4-dialkylpiperazines) including various perfluoroheterocyclic compounds were reported by Russian chemists in 1965 [4], it was not until 1975 that the synthesis of perfluoro(1,4-difluoropiperazine), a perfluoroderivative of piperazine, was done by the ECF of piperazine by Banks et al. [5].

However, a need still exists for developing new perfluorocarboxylic acids especially those with a hetero-atom such as S, N, and O, because perfluorocarboxylic acids are important starting materials for products such as agrochemicals and pharmaceuticals [6,7].

We have previously shown that the ECF of two methyl esters of 4-methylpiperazinyl substituted carboxylic acids (methyl 2-(4-methylpiperazinyl)propionate, methyl 3-(4-methylpiperazinyl)-2-methylpropionate) resulted in fair to good yields of the corresponding perfluoroacid fluorides with a perfluoropiperazine ring [8,9]. Furthermore, we have shown in a previous paper that perfluoro[1,4-bis(ω-fluorocarbonylmethyl)piperazine] could be obtained by the ECF of 1,4-bis(2-hydroxyethyl)piperazine [10].

We have now embarked on the preparation of various perfluorocarboxylic acids with a perfluoropiperazine ring by ECF because little data are available on the ECF of piperazine derivatives with a functional group [11–14].[2] Though results of the ECF of methyl 2-(4-methylpiperazinyl)propionate (**4**) [8] and 3-(4-methylpiperazinyl)-2-methylpro-

☆ Electrochemical fluorination of *N*-containing carboxylic acids. Part 7.

* Corresponding author. Tel.: +81-52-911-2998; fax: +81-52-916-2802.
E-mail address: abe@nirin.go.jp (T. Abe).

[1] The prefix of "F-" in this paper designates "perfluoro-" (all C–H bonds are replaced by C–F bonds).

[2] It has been shown in brief by one of authors (TA) that *F*-[1,4-bis(1-fluorocarbonylethyl)piperazine] was obtained by the ECF of 1,4-bis(1-methoxycarbonylethyl)piperazine [13]. It was stated in brief that *F*-[1,4-bis(2-fluorosulfonylethyl)piperazine] was prepared by the ECF of 1,4-bis(2-fluorosulfonylethyl)piperazine [14].

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pionate (**6**) [9] have already been reported, these two samples were also examined in order to identify the by-products in detail under the same conditions as those applied for other samples for the purposes of comparison.

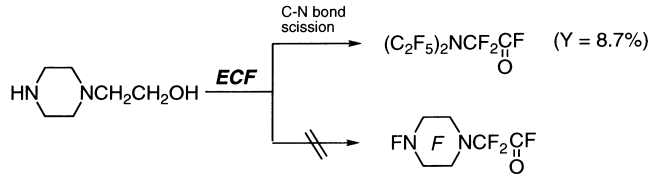
We herein report the results of the ECF of 1-ethylpiperazine (**1**) and the following eight derivatives of 4-methyl- and/or 4-ethylpiperazines with a ω-(methoxycarbonylalkyl) group at the 1-position of the piperazine ring (**2–9**): *c*-$C_2H_5N(C_2H_4)_2NH$ (**1**), *c*-$CH_3N(C_2H_4)_2NCH_2CH_2C(O)OMe$ (**2**), *c*-$C_2H_5N(C_2H_4)_2NCH_2CH_2C(O)OMe$ (**3**), *c*-$CH_3N(C_2H_4)_2NCH(CH_3)C(O)OMe$ (**4**), *c*-$C_2H_5N(C_2H_4)_2NCH(CH_3)C(O)OMe$ (**5**), *c*-$CH_3N(C_2H_4)_2NCH_2CH(CH_3)C(O)OMe$ (**6**), *c*-$C_2H_5N(C_2H_4)_2NCH_2CH(CH_3)C(O)OMe$ (**7**), *c*-$CH_3N(C_2H_4)_2NCH(CH_3)CH_2C(O)OMe$ (**8**), *c*-$C_2H_5N(C_2H_4)_2NCH(CH_3)CH_2C(O)OMe$ (**9**).

2. Results and discussion

We have shown that the ECF of *N*-(2-hydroxylethyl)piperazine does not produce perfluoro(4-fluoropiperazinyl-acetyl fluoride) as the expected product due to the extensive cleavage of the C–N bond of the *secondary* amine. Instead, perfluoro(*N,N*-diethylamino-acetyl fluoride) was formed as the cleaved product (Scheme 1) [10].

However, it has been shown that the ECF of 1-methylpiperazine yielded the corresponding perfluoro(4-fluoro-1-methylpiperazine) (GC yield = 6.8%), which retained its original structure, together with perfluoro(*N,N*-diethylmethylamine) (14.8%), perfluoro(1,3-dimethylimidazolidine) (2.6%) and perfluoro[2-(*N′,N′*-difluoroaminoethyl)-*N*-methyl,*N*-ethylamine)] [molecular formula: $C_2F_5(CF_3)NCF_2CF_2NF_2$] (2.0%) [15]. Among these products, perfluoro(1,3-dimethylimidazolidine) was formed as a result of the ring isomerization of the piperazine ring during fluorination.

In order to investigate the process of the ECF of 1-alkylpiperazine in more detail, we have examined the ECF of 1-ethylpiperazine (**1**) under almost comparable conditions to those applied in the ECF of 1-methylpiperazine. It was found that almost the same types of products as those obtained from 1-methylpiperazine were formed through the ECF of **1**, though their distribution patterns

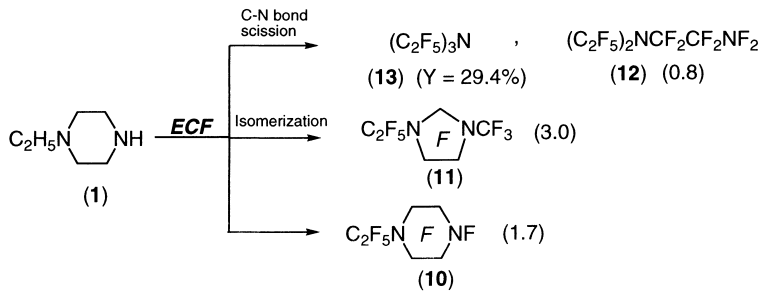


Scheme 1.

were different. The expected perfluoro(4-fluoro-1-ethylpiperazine) (**10**) was obtained at a small yield (GC yield = 1.7%) together with perfluoro(1-methyl-3-ethylimidazolidine) (**11**) [16], perfluoro[2-(*N′,N′*-difluoroaminoethyl)-*N,N*-diethylamine)] [molecular formula: $(C_2F_5)_2NCF_2CF_2NF_2$] (**12**) and perfluorotriethylamine (**13**) (major product) through the ECF of **1**, as shown in Scheme 2.

The second major product other than cleaved products was the ring-contracted compound **11** instead of **10** which was desired in this case. Though, an attempt to improve the yield of the corresponding perfluoro(4-fluoro-1-methylpiperazine) by the ECF of 1-methylpiperazine was made successfully by raising the initial substrate concentration (from 5.1 to 8.2%) in anhydrous hydrogen fluoride (AHF) [15] with the yield increasing from 0.8 to 6.8%, changing of the solute concentration did not produce the same effect in the case of **1** (see Section 3). Therefore, it was expected that some correlation would be observed from the results of the comparative ECF study where methyl esters of 4-alkylpiperazinyl substituted carboxylic acids were fluorinated by changing the *N*-alkyl group (alkyl = CH_3– or C_2H_5–) at the 4-position of the piperazine ring, because it is known that the ECF yield of the *tertiary* amines of the type of $CH_3NR_1(R_2)$ ($R_1 = C_nH_{2n+1}$, $R_2 = C_mH_{2m+1}$; $n, m > 2$) can be raised considerably by replacing the *N*-CH_3 group with other higher *N*-alkyl groups of the starting material [17].

We have investigated the ECF of 1,4-dialkylpiperazine derivatives which have a methyl and/or an ethyl group at the 4-position of the piperazine ring and a carboxylic acid methyl ester group at the 1-position. The results of the fluorination of (4-alkylpiperazinyl) substituted *n*- and/or *iso*-propionic acid methyl esters [alkyl = CH_3 (**2**, **4**), C_2H_5 (**3**, **5**)], and those of methyl 3-(4-alkylpiperazinyl)-2-methylpropionate [alkyl = CH_3 (**6**), C_2H_5 (**7**)] and methyl



Scheme 2.

Table 1
Results of the fluorination of **2**, **3**, **4** and **5**

Run	Sample g (mol)	Current passed (A h)	Fluorinated product (g)	Fluorinated products[c] (yield %)
1	(**2**) 39.5 (0.212)	233	9.5[a] (19.9)[b]	$(C_2F_5)_2NCF_3$ (**32**) (5.0), $(C_2F_5)_3N$ (**13**) (3.5), $CF_3N\langle F\rangle NCF_3$ (**33**) (3.8), $(C_2F_5)_2NCF_2CF_2C(O)F$ (**16**) (4.0), $CF_3N\langle F\rangle NC_2F_5$ (**17**) (5.8), $CF_3N\langle F\rangle NCF_2CF_2C(O)F$ (**14**) (8.0)
2	(**3**) 39.7 (0.198)	233	6.5[a] (30.2)[b]	$(CF_3)_2NC_2F_5$ (**31**) (2.3), **32** (1.1), $(CF_3)_2NCF_2CF_2C(O)F$ (**36**) (0.7), **13** (4.9), **16** (6.1), **17** (4.2), $C_2F_5N\langle F\rangle NC_2F_5$ (**18**) (12.8), $C_2F_5N\langle F\rangle NCF_2CF_2C(O)F$ (**15**) (14.3)
3	(**4**) 39.7 (0.213)	211	6.7[a] (16.0)[b]	**31** (1.6), **32** (1.7), $(CF_3)_2NCF(CF_3)C(O)F$ (**38**) (1.6), **13** (3.2), **33** (0.4), **17** (6.4), $CF_3N\langle F\rangle NCF(CF_3)C(O)F$ (**19**) (7.5), $CF_3N\langle F\rangle NCF(CF_3)C(O)OCF_3$ (**20**) (0.5)
4	(**5**) 39.2 (0.196)	209	5.1[a] (30.1)[b]	**31** (2.9), **32** (0.7), **39** (1.2), **13** (2.7), **17** (1.0), **18** (12.4), $C_2F_5N\langle F\rangle NCF(CF_3)C(O)F$ (**21**) (15.7), $C_2F_5N\langle F\rangle NCF(CF_3)C(O)OCF_3$ (**22**) (0.9)

[a] Products obtained in a cold trap.
[b] Products obtained as cell drainings.
[c] Arranged in order of the elution time on GC.

3-(4-alkylpiperazinyl)butyrate [alkyl = CH_3 (**8**), C_2H_5 (**9**)] are summarized in Tables 1 and 2, respectively.

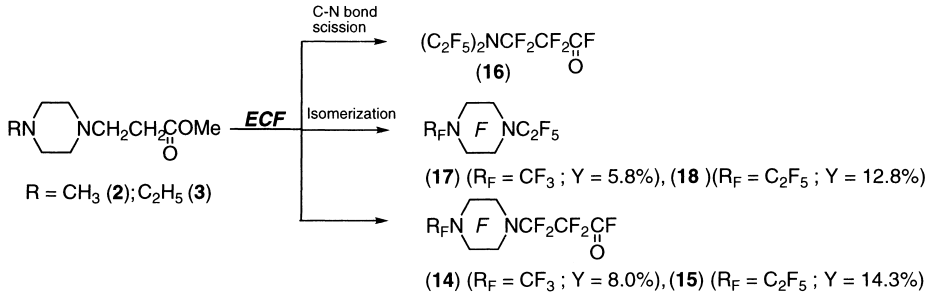
It was found that the desired perfluoro(4-alkylpiperazinyl) substituted perfluoro(carboxylic acid fluorides) could be obtained in fair yields by the ECF of corresponding carboxylic acid methyl esters with a 4-alkylpiperazinyl group [alkyl = CH_3^- (**2**, **4**, **6**, **8**), $C_2H_5^-$ (**3**, **5**, **7**, **9**)]. Although almost the same kind of the products and distribution pattern of the cleaved by-products were obtained through ECF of 4-alkylpiperazine derivatives in the case where an identical carboxylic acid group was attached at the 1-position, an obvious difference was observed in the yields of the targeted perfluoroacid fluorides between those with a perfluoro(4-methylpiperazinyl) group and those with a perfluoro(4-ethylpiperazinyl) group. Characteristically, the yields of the perfluoroacid fluorides were almost double that when were obtained from the ECF of 4-ethylpiperazinyl substituted substrate as compared with those from 4-methylpiperazinyl substituted substrate.

For example, the corresponding perfluoro[3-(4-methylpiperazinyl)propionyl fluoride] (**14**) and perfluoro[3-(4-ethylpiperazinyl)propionyl fluoride] (**15**) were obtained together

Table 2
Results of the fluorination of **6**, **7**, **8** and **9**

Run	Sample g (mol)	Current passed (A h)	Fluorinated product (g)	Fluorinated products[c] (yield %)
1	(**6**) 39.7 (0.199)	239	10.0[a] (40.2)[b]	*iso*-$C_3F_7C(O)F$ (**42**) (7.2), $(CF_3)_2NCF_2CF(CF_3)C(O)F$ (**43**) (4.3), **33** (0.8), **17** (1.3), $(C_2F_5)_2NCF_2CF(CF_3)C(O)F$ (**27**) (14.5), $CF_3N\langle F\rangle NC_3F_7(n)$ (**44**) (3.4), $CF_3N\langle F\rangle NCF_2CF(CF_3)C(O)F$ (**23**) (22.1)
2	(**7**) 40.0 (0.187)	232	6.6[a] (53.1)[b]	**42** (2.8), **31** (2.1), **38** (3.2), **27** (2.3), $C_2F_5N\langle F\rangle NC_3F_7(n)$ (**46**) (5.2), $C_2F_5N\langle F\rangle NCF_2CF(CF_3)C(O)F$ (**25**) (37.5)
3	(**8**) 40.5 (0.203)	229	12.0[a] (26.9)[b]	*n*-$C_3F_7C(O)F$ (**48**) (4.7), **32** (4.4), **13** (3.7), **17** (3.5), $CF_3N\langle F\rangle NC_3F_7(i)$ (**49**) (3.8), $CF_3N\langle F\rangle NCF(CF_3)CF_2C(O)F$ (**24**) (10.9), $CF_3N\langle F\rangle N\langle F\rangle O$ (**30**) (4.5)
4	(**9**) 40.3 (0.188)	237	7.1[a] (56.1)[b]	**48** (trace), **32** (1.8), **13** (3.4), **18** (11.0), $C_2F_5N\langle F\rangle NC_3F_7(i)$ (**28**) (9.5), $C_2F_5N\langle F\rangle NCF(CF_3)CF_2C(O)F$ (**26**) (20.2), $C_2F_5N\langle F\rangle N\langle F\rangle O$ (**29**) (9.7)

[a] Products obtained in a cold trap.
[b] Products obtained as cell drainings.
[c] Arranged in order of the elution time on GC.

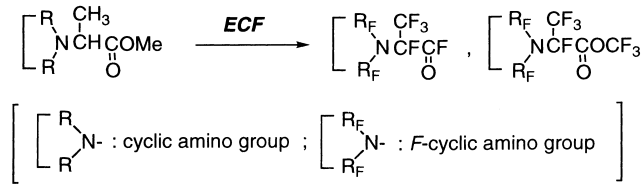


Scheme 3.

with cleaved products in yields as shown in Scheme 3 by the fluorination of **2** and **3**.

Other major by-products obtained were perfluoro[3-(*N,N*-diethylamino)propionyl fluoride] (**16**) and perfluoro(4-methyl-1-ethylpiperazine) (**17**) from **2**, and **16** and perfluoro(1,4-diethylpiperazine) (**18**) from **3**, respectively. In the case of the fluorination of **3**, it was found that not only the yield of the targeted **15** but also that of **18**, which resulted from the α-bond scission of the carboxylic acid, also increased as compared with that of the corresponding **17** from **2**. Among the targeted compounds (**14** and **15**), compound **15** is a known compound which has been filed in the patent literature [12]. Previously, compound **15** has been isolated as a cleaved by-product from the fluorination of 1,4-bis(β-propionyl chloride)piperazine dihydrochloride.

We have reported that various kinds of perfluoro[2-(*cyclic* amino)propionyl fluoride] could be obtained together with a small amount of perfluoro[methyl 2-(*cyclic* amino)propionate] by the ECF of methyl esters of 2-(*cyclic* amino)propionic acid [8] (Scheme 4).

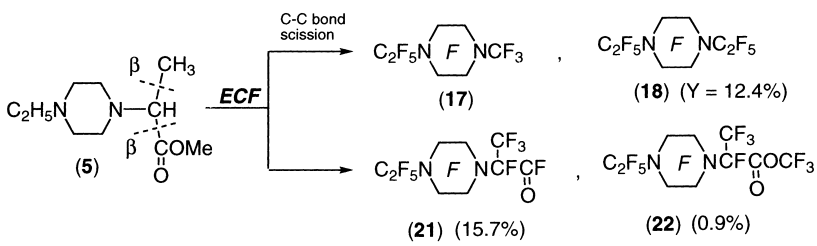


Scheme 4.

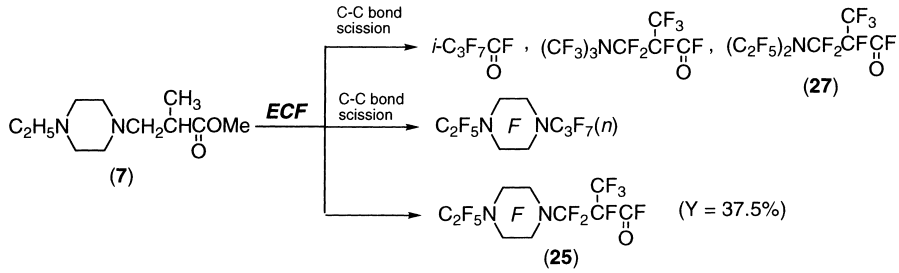
In accordance with these observations, a pair of the targeted perfluorocarboxylic acid derivatives, specifically, perfluoro[2-(4-methylpiperazinyl)propionyl fluoride] (**19**) and perfluoro[methyl 2-(4-methylpiperazinyl)propionate] (**20**), and perfluoro[2-(4-ethylpiperazinyl)propionyl fluoride] (**21**) and perfluoro[methyl 2-(4-ethylpiperazinyl)propionate] (**22**) were obtained by the fluorination of **4** and **5**, respectively. For example, several products including **21** and **22** were obtained in the fluorination of **5** as shown in Scheme 5.

Among the products, considerable quantities of perfluoro(1,4-diethylpiperazine) (**18**) was formed as a cleaved product resulting from the C–C bond scission. In the ECF of carboxylic acids (acid halides, methyl esters and amides), the cleavage of the α-bond to the carbonyl group is generally observed. While, in the ECF of *acyclic tertiary* amines with a branched alkyl group [alkyl = *N*-CHR$_1$(R$_2$); R$_1$ = C$_n$H$_{2n+1}$, R$_2$ = C$_m$H$_{2m+1}$; n, $m > 2$], the very easy cleavage of the C–C bond at the site of either a C–R$_1$ bond or a C–R$_2$ bond (β-bond from the amine) is widely acknowledged [17]. Therefore, compound **18** from the ECF of **5**, which is a *tertiary* amine with a branched propionic acid methyl ester, is thought to be formed due to a complex effect consisting of the α-bond scission at the carboxylic acid site and the β-bond scission at the amine site.

The formation of perfluoro(methyl esters) such as perfluoro[methyl 2-(4-ethylpiperazinyl)propionate] (**22**) can be easily identified by studying spectroscopic data (^{19}F NMR and IR). The CF_3O signal of the ester group was observed in the ^{19}F NMR spectra of **22** as a singlet at −59.4 ppm, and the IR spectra exhibited characteristic ν(C=O) bands which split into two peaks at 1854 and 1840 cm^{-1}. The values for ν(C=O) bands of the corresponding perfluoroacid fluoride (**21**), which similarly split into two peaks at 1898 and 1881 cm^{-1}, are slightly higher than those of the perfluoro(methyl ester) (**22**). The mass spectra of **22** were considerably different from those of **21**. The base peak was the CF_3^+ ion at *m/e* 69 for **19**, while that of **20** was the $C_2F_5^+$ ion at *m/e* 119.



Scheme 5.



Scheme 6.

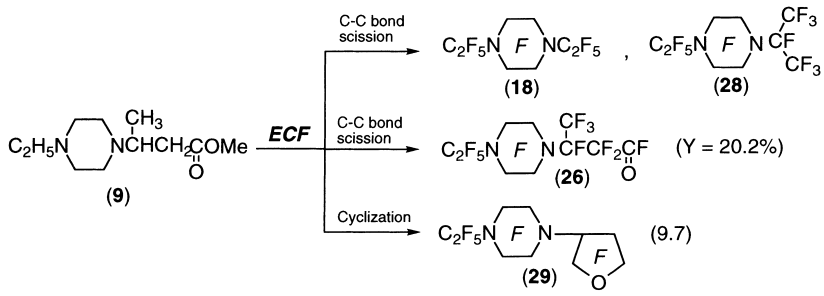
Relatively good yields of perfluoroacid fluorides were obtained from the ECF of 4-alkylpiperazines with a *n*- and/or an *iso*-butyric acid group at the 1-position of the piperazine ring as compared with those obtained from 4-alkylpiperazines with a *n*- and/or an *iso*-propionic acid group. Furthermore, the kinds of products obtained from the ECF of 4-alkylpiperazines with an *iso*-butyric acid group and/or a *n*-butyric acid one differed from each other. Relatively simple kinds of fluorinated products were formed from the ECF of the former substrates. In contrast, a complex mixture of cleaved products and a cyclization product as well as the targeted perfluoroacid fluoride were obtained from the ECF of the latter substrates. For example, the perfluoro[(4-ethylpiperazinyl)-2-methylpropionyl fluoride] (**25**) was formed at a yield as high as 37.5% together with cleaved products by the ECF of methyl 3-(4-ethylpiperazinyl)-2-methypropionate (**7**) as is shown in Scheme 6. The yield of **25** was almost doubled that of perfluoro[(4-methylpiperazinyl)-2-methylpropionyl fluoride] (**23**) obtained from the ECF of 4-methylpiperazinyl substituted substrate (**6**).

Perfluoro[3-(*N,N*-diethylamino)-2-methylpropionyl fluoride] (**27**) was formed due to the C–N bond scission between the 3- and 4-position of the piperazine ring in a small yield (2.3%) as a cleaved product from **7**. This compound was also obtained from **6** as a common cleaved product at a higher yield (yield = 14.5%) than that obtained from **7**. Therefore, in the case of the ECF of **7** having a 4-ethylpiperazinyl group, the degree of the C–N bond scission at the 4-position of the piperazine ring was considerably lower than the case of **6** with a 4-methylpiperazinyl group, which resulted in an increased amount of the formation of the corresponding perfluoroacid fluoride.

The targeted perfluoro[3-(4-methylpiperazinyl)butyryl fluoride] (**24**) and perfluoro[3-(4-ethylpiperazinyl)butyryl fluoride] (**26**) were obtained in fair yields together with cleaved and cyclization products by the fluorination of methyl 3-(4-methylpiperazinyl)butyrate (**8**) and methyl 3-(*N*-ethylpiperazinyl)butyrate (**9**).

As a typical example, the reaction pathway for each of the fluorination products from the ECF of **9** can be explained as shown in Scheme 7.

Among them, perfluoro(1,4-diethylpiperazine) (**18**) and perfluoro[4-ethyl-1-(*iso*-propyl)piperazine] (**28**) were formed as major cleaved products. Compound **28** was formed as a result of the α-bond scission of the carboxylic acid skeleton. Compound **18** is thought to be formed due to the β-bond scission (from the side of the amine) of the butyric acid skeleton as is shown in Scheme 5 by looking at the cleavage pattern of the products from ECF of **5** which resulted in perfluoro(1,4-diethylpiperazine) (**18**) as the main cleaved product. Another major product obtained was the perfluoro[3-(4-ethylpiperazinyl)oxolane] (**29**) which is a specific product from the ECF of the substrate with a $-CH(CH_3)CH_2C(O)OMe$ group. We have shown that perfluoroalkylamines bearing a perfluorooxolane group are formed in the fluorination of a series of methyl 3-(dialkylamino)butyrates as a result of the intramolecular cyclization [9]. Corresponding perfluoro[3-(4-methylpiperazinyl)oxolane] (**30**) was similarly formed as the expected cyclization product ($Y = 4.5\%$) by the fluorination of **8**. The yields of these cyclization products (**29** and **30**) amounted to almost half of those of the corresponding perfluoroacid fluorides (**26** and **24**), respectively. Accordingly, it can be concluded that this cyclization is one of the major reasons for lowered yield



Scheme 7.

Scheme 8.

of the targeted perfluoroacid fluorides in the case of the fluorination of those substrates with a 4-alkylpiperazinyl group.

It has been reported by Moore and co-workers at 3M Co. that there is a relationship between the structure and the ECF yield for substrates which have a dialkylamino-substituted ether structure [18]. They found that good product yields were obtained when an *iso*-propyl group was incorporated into the ether linkage (**I** and **II**) compared with the case where the N and O atoms are separated by three methylene groups (**III**) (Scheme 8).

Similarly we have found that there is a correlation between the yields of the desired perfluoroacid fluoride and the structure of the substrate consisting of (*N,N*-dialkylamino) substituted carboxylic acids with respect to both the dialkylamino-group and the carboxylic acid skeleton [8,9]. The *cyclic* amino group substituted carboxylic acids result in higher yields of perfluoroacid fluoride than those from *acyclic* amino group substituted carboxylic acids. Furthermore, good yields of the corresponding perfluoro(*N,N*-dialkylamino) substituted perfluoroacid fluorides are obtained in the case of *iso*-butyric acid (the precursor for **D** form in Scheme 9) compared with those of *n*-/*iso*-propionic acid (the precursor for **A** and **B** forms) and *n*-butyric acid (the precursor for **C** form) as the substrate in regard to the structure of the carboxylic acid bearing a *N,N*-dialkylamino-group. Generally, the following order of increasing yields was observed as shown in Scheme 9.

So, it has become possible to determine the relationship between the yields of corresponding perfluoroacid fluorides and the structure of the substrate by studying the data, in which 4-methyl and/or ethylpiperazinyl groups bearing one of four kinds of (methoxycarbonylalkyl) groups are fluorinated. It was found that, in accordance with the general rule shown in Scheme 9, the following order of the increasing yield was obtained for the series of perfluoro[4-methylpiperazinyl] substituted perfluoroacid fluorides; **19** (**B** form), **14** (**A** form) < **24** (**C** form) < **23** (**D** form). The comparison of the ECF yields in a series of perfluoro[4-ethylpiperazinyl] group substituted perfluoroacid fluorides showed the same increasing order of the yield as was observed in that for perfluoro[4-methylpiperazyniyl] group substituted perfluoroacid fluorides; **15** (**A** form) < **21** (**B** form) < **26** (**C** form) < **25** (**D** form).

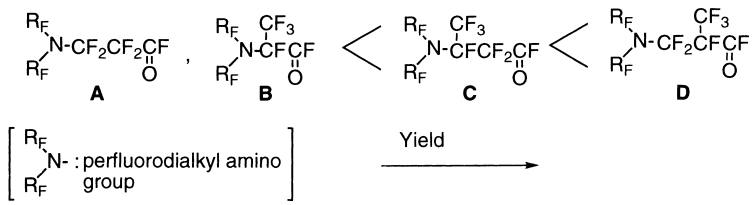
Our study on the preparation of *N*-containing perfluoroacid fluorides is in progress and the results of the ECF of piperazines with bis(ω-methoxycarbonylalkyl) groups at the 1- and 4-positions of the piperazine ring will be reported in a subsequent paper.

3. Experimental details

Boiling points were uncorrected. The 1-ethylpiperazine (**1**) was used as commercial grade. Methyl esters of 2-(4-alkylpiperazinyl)propionic acids were prepared by the reaction of corresponding 4-alkylpiperazine with methyl 2-bromopropionate in the presence of Na_2CO_3 and small quantities of H_2O according to the method described in the literature [19]. Methyl esters of 3-(4-alkylpiperazinyl)-propionic acids, methyl esters of 3-(4-alkylpiperazinyl)-2-methylpropionic acids, and methyl esters of 3-(*N*-alkylpiperazinyl)butyric acids were prepared by the Michael reaction of corresponding 1-alkylpiperazine with methyl acrylate, methyl methacrylate and methyl crotonate, respectively.

The substrates synthesized for fluorination had the following boiling points: methyl 3-(4-methylpiperazinyl)propionate (**2**), bp 103–104°C/5 mmHg; methyl 3-(4-ethylpiperazinyl)propionate (**3**), bp 107°C/3 mmHg; methyl 2-(4-methylpiperazinyl)propionate (**4**), bp 79°C/5 mmHg; methyl 2-(4-ethylpiperazinyl)propionate (**5**), 86°C/3 mmHg; methyl 3-(4-methylpiperazinyl)-2-methylpropionate (**6**), 267–170°C/15 mmHg; methyl 3-(4-ethylpiperazinyl)-2-methylpropionate (**7**), 142°C/17 mmHg; methyl 3-(4-methylpiperazinyl)butyrate (**8**), 132°C/19 mmHg; methyl 3-(4-ethylpiperazinyl)butyrate (**9**), 134°C/17 mmHg.

Purity of anhydrous hydrogen fluoride (AHF) (Daikin Industries Co.) was more than 99.8%. The electrolytic fluorination apparatus and operating procedures were similar to those described previously [20]. Analytical GLC work was carried out with a Shimadzu GC-14B gas chromatograph using stainless steel columns (3 mm diameter) packed



Scheme 9.

with 25% Fomblin YR on Chromosorb PAW (6.4 m). For a semi-preparative work, a GASUKURO LL-75 modified gas chromatograph using stainless steel columns (10 mm diameter) packed with 30% KelF wax on Chromosorb PAW (4.9 m), and a Varian model 920 GC using an aluminum column (3/8 in. diameter) packed with 20% Fomblin YR on Chromosorb PAW (20 ft) were used. The carrier gas was helium in all cases. Infrared spectra were measured on a Shimadzu FTIR-8000PC spectrometer using a 6 cm gas cell with KBr windows. ^{19}F NMR spectra were measured on a Varian Unity Inova 300 spectrometer (282.238 MHz for ^{19}F and 299.95 MHz for ^{1}H, respectively). Chemical shifts for ^{19}F and ^{1}H NMR spectra were reported relative to $CFCl_3$ and TMS, respectively. Positive shifts are downfield from the reference ($CFCl_3$ and TMS). MS spectra were measured on a Shimadzu GC/MS-QP5000 and a Shimadzu GC/MS-QP1100EX instruments fitted with a capillary column (Neutra Bond-1, 30 m long, 0.25 mm i.d., 1.5 μm thick) at 70 eV. Elemental analyses were performed by Mikroanalytisches Laboratorium Beller in Göttingen, Germany.

*3.1. Fluorination of 1-ethylpiperazine at a lower solute concentration (**1**)*

Sample **1** (28.6 g, 0.250 mol) was charged into a cell containing 420 ml electrolytically purified AHF, and the solution was subjected to fluorination with an anodic current density of 3.2 A/dm^2, a cell voltage of 5.7–5.8 V, and a cell temperature of 7–8°C over a period of 690 min (261 A h). At the final stage of the fluorination, the voltage reached 6.2 V.

The effluent gases from the cell were passed over NaF pellets and then condensed in a trap cooled to −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 an aqueous solution of a mixture of K_2CO_3, KOH and KI. All products except new ones were identified by comparison of their infrared spectra and GLC retention times with those of authenticated samples. New compounds were separated from the other products by use of semi-preparative GLC, and their structures were determined on the basis of their spectral data (IR, ^{19}F NMR and MS) and elemental analysis (carbon and fluorine).

The products (21.1 g) condensed in the −78°C trap consisted of perfluoro(*N,N*-dimethylethylamine) (**31**) (3.3 g), perfluoro(*N,N*-diethylmethylamine) (**32**) (5.6 g), perfluorotriethylamine (**13**) (9.1 g), perfluoro(3-methyl-1-ethylimidazolidine) (**11**) [16] (0.7 g), perfluoro(4-fluoro-1-ethylpiperazine) (**10**) (0.1 g) and unidentified products (2.3 g) (products are arranged in order of elution on GC). Cell drainings (24.2 g) consisted of **32** (1.3 g), **13** (18.1 g), **11** (2.1 g), **10** (1.4 g), perfluoro[2-(*N*′,*N*′-difluoroaminoethyl)-*N,N*-diethylamine)] (**12**) (0.9 g) and unidentified products (0.4 g). The GC yield of **10** was 1.7%. ^{19}F NMR data of **11** were the same as those of the reported one [16]. The physicochemical properties and spectral data (IR and MS) of **11**, **10** and **12** are shown below. ^{19}F NMR data of **10** are shown in Table 3 together with those of other new compounds isolated in this study.

Perfluoro(3-methyl-1-ethylimidazolidine) (**11**): bp 76.0–77.0°C (reported bp 70–75°C) [16], d_4^{20} 1.7653, $n_D^{20} < 1.28$. IR (gas): 1366 (vs), 1340 (s), 1304 (ms), 1248 (vs), 1219 (s), 1188 (ms), 1077 (m), 1008 (w), 1922 (m), 824 (w), 748 (w), 709 (w), 665 (w). MS: 347 $[M-F]^+$ (15.8), 297 $C_5F_{11}N_2^+$ (22.2), 259 $C_5F_9N_2^+$ (6.6), 214 $C_4F_8N^+$ (3.4), 209 $C_4F_7N_2^+$ (13.5), 164 $C_3F_6N^+$ (59.3), 119 $C_2F_5^+$ (33.6), 114 $C_2F_4N^+$ (100), 100 $C_2F_4^+$ (13.4), 69 CF_3^+ (96.9), 50 CF_2^+ (11.1).

Perfluoro(4-fluoro-1-ethylpiperazine) (**10**) (nc): bp 85.0–85.5°C, d_4^{20} 1.8030, $n_D^{20} < 1.2835$. IR (gas): 1381 (m), 1334 (s), 1287 (ms), 1247 (vs), 1229 (vs), 1183 (s), 1140 (w), 1120 (w), 1071 (s), 970 (m), 951 (ms), 824 (m), 734 (m), 706 (w), 665 (w), 626 (w). MS: 347 $[M-F]^+$ (4.9), 297 $C_5F_{11}N_2^+$ (4.2), 259 $C_5F_9N_2^+$ (1.5), 209 $C_4F_7N_2^+$ (16.8), 164 $C_3F_6N^+$ (42.3), 159 $C_3F_7^+$ (4.1), 145 $CF_3N_2^+$ (11.0), 119 $C_2F_5^+$ (100), 114 $C_2F_4N^+$ (99.6), 100 $C_2F_4^+$ (40.7), 95 $C_2F_3N^+$ (7.1), 69 CF_3^+ (88.9), 50 CF_2^+ (19.0). Analysis: Calc. for $C_6F_{14}N_2$: C, 19.67%; F, 72.7%. Found: C, 19.72; F, 72.4%.

Perfluoro[2-(*N*′,*N*′-difluoroaminoethyl)-*N,N*-diethylamine) (**12**) (nc): bp 95.0–95.5°C, d_4^{20} 1.8075, $n_D^{20} < 1.2800$. IR (gas): 1348 (w), 1816 (m), 1286 (vs), 1241 (vs), 1171 (m), 1158 (m), 1109 (ms), 1050 (w), 939 (w), 879 (m), 841 (w), 788 (w), 755 (w), 742 (w). MS: 302 $[M-CF_2NF_2]^+$ (1.1), 247 $C_4F_9N_2^+$ (1.3), 214 $C_4F_8N^+$ (8.9), 195 $C_2F_5N_2^+$ (3.2), 164 $C_3F_6N^+$ (15.3), 119 $C_2F_5^+$ (100), 114 $C_2F_4N^+$ (10.7), 100 $C_2F_4^+$ (11.4), 76 $N_2F_2^+$ (1.3), 69 CF_3^+ (66.5), 50 CF_2^+ (6.8). ^{19}F NMR: δ 18.1 (m, 2F, NF_2), −81.8 (m, 6F, $(\mathbf{CF_3}CF_2)_2NCF_2^-$), −86.2 (m, 2F, $(CF_3CF_2)_2N\mathbf{CF_2}^-$), −89.9 (m, 4F, $(CF_3\mathbf{CF_2})_2NCF_2$), −112.0 (m, 2F, $-\mathbf{CF_2}NF_2$). Analysis: Calc. for $C_6F_{16}N_2$: C, 17.82%; F, 75.3%. Found: C, 17.92; F, 75.0%.

*3.2. Fluorination of 1-ethylpiperazine (**1**) at a higher solute concentration*

Sample **1** (40.2 g, 0.352 mol) was fluorinated similarly under the following conditions: 3.2 A/dm^2, 5.6–5.8 V, 7–8°C, 846 min (321 A h). The work-up gave the following products in the −78°C trap (18.1 g): **31** (3.3 g), **32** (5.8 g), **13** (6.7 g), **11** (0.4 g), and unidentified products (1.9 g). Cell drainings (29.2 g): **32** (1.3 g), **13** (21.4 g), **11** (3.3 g), **10** (1.6 g), **12** (1.2 g) and unidentified products (0.4 g). The GC yield of **11** was 1.3%.

*3.3. Fluorination of methyl 3-(4-methylpiperazinyl)propionate (**2**)*

Sample **2** (39.5 g, 0.212 mol) was fluorinated similarly under the following conditions: 3.2 A/dm^2, 5.8–6.4 V, 7–8°C, 638 min (233 A h). The work-up gave the following products in the −78°C trap (9.5 g): **32** (3.4 g), **13** (1.8 g),

Table 3
^{19}F NMR of compounds **10**, **14**, **15**, **21**, **22**, **24**, **25**, **26**, **28**, **29**, **30**, **34**, **37**, **40**, **44**, **45**, **46**, **47**, **49**, **50** and **51**

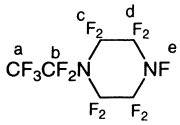
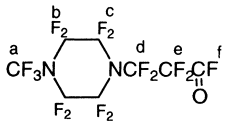
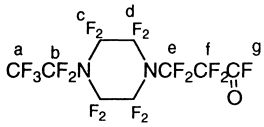
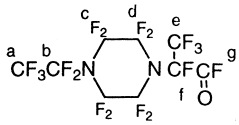
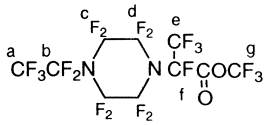
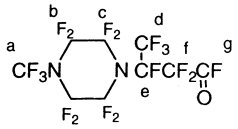
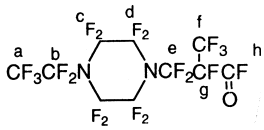
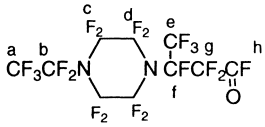
Compound	Formula	Chemical shift[a,b]		J (Hz)[b]
10		a	−87.1 (quintet)	a–c = 8.7
		b	−97.2 (quintet)	b–c = 17.2
		c	−89.6 (broad)	
		d	−109.6	
		e	−107.7 (s)	
14		a	−52.4 (quintet)	a–b = 13.8
		b	−93.5 (quartet)	b–a = 13.8
		c	−90.6 (m)	
		d	−91.0 to −91.4 (m)	
		e	−118.9 (double quintet)	e–f = e–c = 10.4
		f	26.0 (m)	
15		a	−86.8 (quintet)	a–b = 6.8
		b	−96.6 (quintet)	b–c = 18.9
		c	−92.4 (m)	
		d	−92.2 (m)	
		e		
		f	−119.8 (double quintet)	f–d = 8.8, f–g = 8.5
		g	26.3 (m)	
21		a	−86.1 (quintet)	a–c = 7.1
		b	−93.8, −97.7	J_{AB} = 238
		c	−87.2, −95.4	J_{AB} = 192
		d	−87.1, −93.5	J_{AB} = 191
		e	−75.8 (m)	
		f	−140.8 (m)	
		g	24.9 (m)	
22		a	−86.0 (m)	
		b	−93.3, −98.0	J_{AB} = 238
		c	−86.3, −96.2	J_{AB} = 189
		d	−86.3, −94.0	J_{AB} = 190
		e	−75.8 (m)	
		f	−142.3 (m)	
		g	−59.1 (s)	
24		a	−52.9 (quintet)	a–b = 11.9–13.8
		b	−89.8, −92.8	J_{AB} = 191
		c	−84.9, −87.6	J_{AB} = 189
		d	−76.1 (m)	
		e	−158.2 (quintet)	e–c = 20.6–24.0
		f	−112.0, −112.9	J_{AB} = 271
		g	25.8	
25		a	−87.0 (m)	
		b	−96.9 (quintet)	b–c = 18.9
		c	−92.9	
		d	−92.6	
		e	−82.7, −86.6	J_{AB} = 243
		f	−73.3 (m)	
		g	−177.2 (m)	
		h	33.8	
26		a	−85.2 (m)	
		b	−94.9 (quintet)	b–c = 18.9
		c	−88.0, −90.3	J_{AB} = 193
		d	−86.8, −88.9	J_{AB} = 179
		e	−75.9	
		f	−158.1 (m)	
		g	−112.3, −112.9	J_{AB} = 276
		h	25.9	

Table 3 (*Continued*)

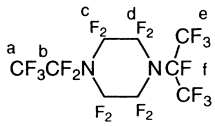
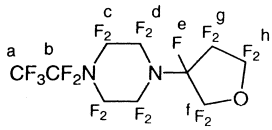
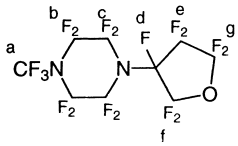
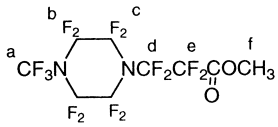
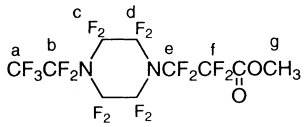
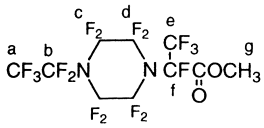
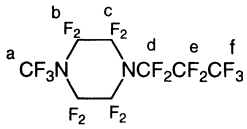
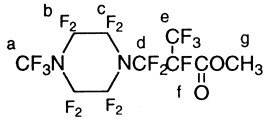
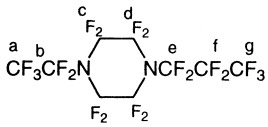
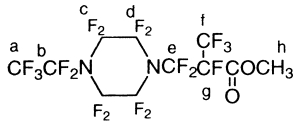
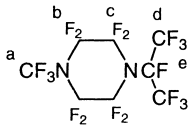
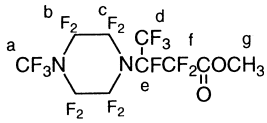
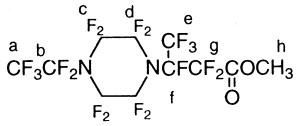
Compound	Formula	Chemical shift[a,b]		*J* (Hz)[b]
28		a	−85.2 (quintet)	a–c = 8.5–8.8
		b	−95.0 (quintet)	b–c = 18.9
		c	−89.4 (m)	
		d	−88.0 (m)	
		e	−77.3 (quintet)	e–d = 8.6
		f	−160.5 (quintet)	f–d = 24.1
29		a	−86.1 (quintet)	a–c = 6.8
		b	−95.6, −96.2	J_{AB} = 238 (F_1–c= 18.9–20.6; F_2–c= 17.2–20.9)
		c	−90.4, −91.6	J_{AB} = 200
		d	−90.4 (m)	
		e	−136.0 (m)	
		f	−70.4, −83.5	J_{AB} = 135
		g	−117.2, −127.4	J_{AB} = 250
		h	−79.8, −91.3	J_{AB} = 127
30		a	−52.8 (quintet)	a–b = 13.0
		b	−91.7, −92.9	J_{AB} = 189
		c	−89.4, −90.1	J_{AB} = 192
		d	−135.4 (m)	
		e	−117.2, −127.4	J_{AB} = 257
		f	−70.1, −83.3	J_{AB} = 133
		g	−80.0, −91.4	J_{AB} = 127
34		a	−52.5 (quintet)	a–b = 12.1
		b	−93.7 (quintet)	b–a = 13.8
		c	−90.7 (m)	
		d	−91.7 (quintet)	d–c = 18.9
		e	−119.7 (quintet)	e–c = 11.3
		f	δ 3.99 (s)	
37		a	−86.9 (quintet)	a–c = 8.5
		b	−96.7 (quintet)	b–c = 18.9
		c	−92.6	b–a = 13.8
		d	−92.3	
		e	−92.9 (quintet)	e–d = 17.2–18.9
		f	−120.6 (quintet)	f–d = 8.5
		g	δ 3.98 (s)	
40		a	−86.0 (m)	
		b	−93.3, −98.2	J_{AB} = 238
		c	−86.3, −96.3	J_{AB} = 206
		d	−86.0, −94.5	J_{AB} = 197
		e	−76.7 (m)	
		f	−142.4 (m)	
		g	δ 4.00 (s)	
44		a	−52.4 (quintet)	a–b = 13.8
		b	−93.7 (quintet)	b–a = 13.8
		c	−90.8 (m)	
		d	−91.1 (m, broad)	
		e	−127.5 (quintet)	e–c = 10.4–11.9
		f	−81.3 (triplet)	f–d = 8.8–10.2
45		a	−52.3 (quintet)	a–b = 13.8
		b	−93.9, −94.8	J_{AB} = 195
		c	−90.7, −92.1	J_{AB} = 190
		d	−83.8, −84.7	J_{AB} = 239
		e	−73.6 (m)	
		f	−178.7 (m)	
		g	δ 3.97 (s)	

Table 3 (*Continued*)

Compound	Formula		Chemical shift[a,b]	J (Hz)[b]
46		a	−86.8 (quintet)	a–c = 7.1
		b	−96.7 (quintet)	b–c = 18.9
		c	−92.7 (m)	
		d	−92.3 (m)	
		e	−92.0 (m)	
		f	−128.3 (quintet)	f–d = 10.4
		g	−81.3 (triplet)	g–e = 8.8–10.4
47		a	−81.7 (quintet)	a–c = 7.1–8.5
		b	−97.0 (quintet)	b–c = 17.2–20.6
		c	−92.8 to −92.9 (m)	
		d	−92.8 to −92.9 (m)	
		e	−84.5, −85.7	J_{AB} = 237
		f	−73.6 (m)	
		g	−178.9 (m)	
		h	δ 3.96 (s)	
49		a	−52.4 (quintet)	a–b = 12.1–13.8
		b	−91.5	
		c	−87.7	
		d	−77.4 (double quintet)	d–c = 10.2, d–e = 3.4
		e	−160.9 (heptet)	e–d = 3.4
50		a	−52.9 (quintet)	a–b = 13.5
		b	−87.7, −95.3	J_{AB} = 195
		c	−85.0, −89.5	J_{AB} = 196
		d	−75.3 (m)	
		e	−158.3 (triple triplet)	e–c = 22.3–26.8
		f	−114.1 (m)	
		g	δ 3.98 (s)	
51		a	−85.1 (quintet)	a–c = 8.7
		b	−93.4 (F_1), −96.5(F_2)	J_{AB} = 239, F_2-c = 18.9
		c	−86.7, −91.6	J_{AB} = 190
		d	−85.1, −90.1	J_{AB} = 195
		e	−75.1 (m)	
		f	−158.3 (quintet)	f–d = 20.6–27.9
		g	−114.2 (double quartet)	g–e = g–f = 10.4
		h	δ 3.98 (s)	

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

perfluoro(1,4-dimethylpiperazine) (**33**) (1.2 g), perfluoro[3-(*N,N*-diethylamino)propionyl fluoride] (**16**) [21] (0.4 g), perfluoro(4-methyl-1-ethylpiperazine) (**17**) (0.6 g) and unidentified products (2.1 g). Cell drainings (19.9 g): **13** (1.0 g), **33** (1.8), **16** (2.9 g), **17** (4.9 g), perfluoro[3-(4-methylpiperazinyl)propionyl fluoride] (**14**) (7.5 g) and unidentified products (1.8 g). The GC yield of **14** was 8.0%. Spectral data (IR and MS) of **14** are shown below. ^{19}F NMR data of **14** are shown in Table 3.

Perfluoro[3-(4-methylpiperazinyl)propionyl fluoride] (**14**) (nc): IR (gas): 1886 ν(C=O) (ms), 1358 (vs), 1338 (m), 1311 (vs), 1268 (ms), 1230 (vs), 1180 (ms), 1121 (m), 1092 (w), 1077 (w), 986 (w), 959 (ms), 896 (w), 800 (w), 742 (w), 731 (w), 691 (w). MS: 425 $[M - F]^+$ (0.7), 347 $[M - CF_2C(O)F]^+$ (9.6), 259 $C_5F_9N_2^+$ (7.7), 214 $C_4F_8N^+$ (0.9), 209 $C_4F_9N_2^+$ (1.4), 171 $C_4F_5N_2^+$ (3.1), 164 $C_3F_6N^+$ (15.9), 147 $C_2F_5N_2^+$ (3.4), 145 $C_3F_5N^+$ (1.8), 119 $C_2F_5^+$ (64.8), 114 $C_2F_4N^+$ (39.3), 100 $C_2F_4^+$ (39.2), 95 $C_2F_3N^+$ (2.5), 81 $C_3F_3^+$ (1.2), 76 $C_2F_2N^+$ (2.3), 69 CF_3^+ (100), 50 CF_2^+ (6.8).

Further characterization of **14** was conducted in a form of the methyl ester. Methyl ester (**34**) of **14** were prepared by mixing about 5 g of cell drainings with 2 ml of methanol. The reaction was completed within a few minutes. The lower layer of the reaction mixture was separated by means of semi-preparative GC to give **34**.

Methyl perfluoro[3-(4-methylpiperazinyl)propionate] (**34**) (nc) had bp 171.0–171.7°C, d_4^{20} 1.7675 and n_D^{20} 1.3223. IR (capillary film): 2968 (w) ν(CH), 1789 ν(C=O) (s), 1444 (w), 1351 (s), 1302 (vs), 1269 (s), 1217 (s), 1166 (vs), 1087 (m), 1071 (m), 1015 (m), 954 (s), 894 (m), 853 (w), 826 (w), 792 (m), 729 (m), 744 (m), 679 (w). MS: 437 $[M - F]^+$ (0.6), 347 $[M - CF_2C(O)OCH_3]^+$ (7.8), 259 $C_5F_9N_2^+$ (4.5), 171 $C_4F_5N_2^+$ (1.8), 164 $C_3F_6N^+$ (7.3),

159 $C_2F_4C(O)CH_3^+$, $C_3F_5N_2^+$ (8.3), 145 $C_3F_5N^+$ (2.4), 131 $C_3F_5^+$ (14.0), 119 $C_2F_5^+$ (15.2), 114 $C_2F_4N^+$ (19.5), 100 $C_2F_4^+$ (27.8), 97 $C_2F_3O^+$ (3.2), 95 $C_2F_3N^+$ (1.3), 81 $C_2F_3^+$ (8.1), 76 $C_2F_2N^+$ (1.2), 69 CF_3^+ (43.7), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (2.6). Analysis: Calc. for $C_9F_{15}N_2O_2H_3$: C, 23.68%; F, 62.5%. Found: C, 23.80%; F, 62.3%. ^{19}F NMR data of **34** are shown in Table 3.

Compound **14** was derivatized into an amide of *p*-methoxyaniline for further characterization also: into a 100 ml polytetrafluoroethylene beaker, was placed 0.23 g (1.9 mmol) of *p*-methoxyaniline dissolved in 10 ml of dichloromethane and 0.23 g (2 mmol) of triethylamine, and compound **14** (1.01 g, 2 mmol) which was isolated by preparative GC was added dropwise while shaking. The mixture was left standing in the draft overnight. The residue was dissolved in a mixture of hexane and acetonitrile (1:1) and analyzed by TLC. The crude product was purified by column chromatography (hexane/acetonitrile as eluent) to give perfluoro[3-(4-methylpiperazinyl)propionyl]-*p*-methoxyanilide (**35**) as white crystals (0.52 g, 46% yield).

Perfluoro[3-(4-methylpiperazinyl)propionyl]-*p*-methoxyanilide (**35**) (nc) had mp 82.3–83.0°C. IR (KBr): 1701 *v*(C=O) (ms). MS: 547 $[M+1]^+$ (0.9), 149 $C(O)NHPhOCH_3^+$ (54.6), 134 $C(O)NHPhO^+$ (22.5), 122 $NHPhOCH_3$ (100), 119 $C_2F_5^+$ (17.2), 114 $C_2F_4N^+$ (19.1), 100 $C_2F_4^+$ (17.2), 95 $C_2F_3N^+$ (18.3), 69 CF_3^+ (54.1), 52 $CF_2H_2^+$ (23.3), 51 CF_2H^+ (11.9) 50 CF_2^+ (8.4). ^{19}F NMR ($CDCl_3$): δ −52.4 (quintet, 3F, J_{F-F} = 13.8 Hz, $\mathbf{CF_3}N$), δ −90.5 [m, 4F, *c*-$CF_3N(CF_2\mathbf{CF_2})_2N$], δ −91.2 [quintet, 2F, J_{F-F} = 18.9−20.9 Hz, $N\mathbf{CF_2}CF_2C(O)O)$], δ −93.6 [quartet, 4F, 11.9–13.8 Hz, *c*-$CF_3N(\mathbf{CF_2}CF_2)_2N$], δ −120.8 (quintet, 2F, J_{F-F} = 10.4 Hz, $NCF_2\mathbf{CF_2}C(O)O$), ^1H NMR ($CDCl_3$): δ 7.90 (s, 1H, NH), δ 7.45 (d, 2H), δ 6.91 (d, 2H), δ 3.81 (s, 3H, OCH_3). Analysis: Calc. for $C_{15}F_{15}N_3O_2H_8$: C, 32.91%; F, 52.10%. Found: C, 33.04%; F, 51.9%.

3.4. Fluorination of methyl 3-(4-ethylpiperazinyl)propionate (3)

Sample **3** (39.7 g, 0.198 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.8–6.1 V, 7–8°C, 638 min (233 A h). The work-up gave the following products in the −78°C trap (6.5 g): **31** (1.2 g), **32** (0.7 g), perfluoro[3-(*N,N*-dimethylamino)propionyl fluoride] (**36**) [22] (0.4 g), **13** (2.4 g), **17** (0.4 g), perfluoro(1,4-diethylpiperazine) (**18**) (0.5 g) and unidentified products (0.9 g). Cell drainings (31.8 g): **13** (1.2 g), **16** (0.5 g), **17** (3.1 g), **18** (11.3 g), perfluoro[3-(4-ethylpiperazinyl)propionyl fluoride] (**15**) (14.0 g) and unidentified products (1.7 g). The GC yield of **15** was 14.3%. Spectral data (IR and MS) of **15** will be shown below as no data except the bp (86–88°C/0.6 mmHg) and mp (56–59°C) of perfluoro[3-(4-ethylpiperazinyl)propionic acid] which was derived by a hydrolytic reaction of **15** are described in the patent literature [12]. ^{19}F NMR data of **15** are shown in Table 3.

Pefluoro[3-(4-ethylpiperazinyl)propionyl fluoride] (**15**) [12]: IR (gas): 1885 *v*(C=O) (m), 1340 (s), 1304 (s), 1270 (ms), 1252 (vs), 1214 (m, sh), 1185 (s), 1121 (w), 1102 (w), 1068 (m), 987 (w), 956 (m), 824 (w), 796 (w), 731 (w), 662 (w). MS: 475 $[M-F]^+$ (0.8), 425 $[M-CF_3]^+$ (1.2), 397 $[M-CF_2C(O)F]^+$ (10.8), 309 $C_6F_{11}N_2^+$ (3.8), 259 $C_5F_9N_2^+$ (4.9), 214 $C_4F_8N^+$ (1.4), 171 $C_4F_5N_2^+$ (3.8), 164 $C_3F_6N^+$ (15.4), 147 $C_3F_5O^+$ (2.8), 145 $C_3F_5N^+$ (1.6), 119 $C_2F_5^+$ (100), 114 $C_2F_4N^+$ (33.4), 100 $C_2F_4^+$ (32.6), 95 $C_2F_3N^+$ (1.8), 76 $C_2F_2N^+$ (1.9), 69 CF_3^+ (45.8), 50 CF_2^+ (4.4).

Methyl ester (**37**) of **15** were prepared in a similar manner as explained for **14**.

Methyl perfluoro[3-(4-ethylpiperazinyl)propionate] (**37**) (nc) had bp 181.2–181.7°C, d_4^{20} 1.7712 and n_D^{20} 1.3193. IR (capillary film): 2968 *v*(CH) (w), 1788 *v*(C=O) (s), 1444 (w), 1333 (s), 1297 (vs), 1260–1227 (s–vs), 1200–1166 (s–vs), 1101 (w), 1063(s), 1015 (s), 951 (s), 821 (s), 756 (s), 739 (s), 726 (m), 696 (m), 676 (m), 656 (ms), 623 (m), 613 (w). MS: 447 $[M-C(O)OCH_3]^+$ (0.5), 397 $[M-CF_2C(O)OCH_3]^+$ (8.6), 309 $C_6F_{11}N_2^+$ (2.1), 259 $C_5F_9N_2^+$ (4.3), 214 $C_4F_8N^+$ (1.3), 171 $C_4F_5N_2^+$ (2.9), 164 $C_3F_6N^+$ (10.2), 159 $C_3F_5N_2^+$ (11.9), 149 $C_3F_5O^+$ (1.0), 145 $C_3F_5N^+$ (2.7), 131 $C_3F_5^+$ (22.1), 119 $C_2F_5^+$ (52.8), 114 $C_2F_4N^+$ (24.7), 100 $C_2F_4^+$ (40.3), 97 $C_2F_3O^+$ (5.4), 95 $C_2F_3N^+$ (1.6), 81 $C_2F_3^+$ (12.0), 76 $C_2F_2N^+$ (1.4), 69 CF_3^+ (32.3), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (3.7). Analysis: Calc. for $C_{10}F_{17}N_2O_2H_3$: C, 23.72%; F, 63.8%. Found: C, 23.80%; F, 63.7%. ^{19}F NMR data of **37** are shown in Table 3.

3.5. Fluorination of methyl 2-(4-methylpiperazinyl)-propionate (4)

Sample **4** (39.7 g, 0.213 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.6–6.7 V, 7–8°C, 575 min (211 A h). The work-up gave the following products in the −78°C trap (6.7 g): **31** (0.9 g), **32** (1.2 g), perfluoro[2-(*N,N*-dimethylamino)propionyl fluoride] (**38**) [22] (1.0 g), **13** (1.7 g), **33** (0.3 g), **17** (0.5 g) and unidentified products (1.1 g). Cell drainings (16.0 g): **13** (0.9 g), perfluoro(4-methyl-1-ethylpiperazine) (**17**) (5.2 g), perfluoro[2-(4-methylpiperazinyl)propionyl fluoride] (**19**) (7.1 g), perfluoro[methyl 2-(4-methylpiperazinyl)propionate] (**20**) (0.6 g) and unidentified products (2.2 g). The GC yields of **19** and **20** were 7.5 and 0.5%, respectively.

Spectral data (IR, Mass and ^{19}F NMR) of **19** and **20**, and the methyl ester of perfluoro[2-(4-methylpiperazinyl)propionic acid] have been reported in our previous paper [8]. Therefore, the physical property (mp) and spectral data (IR, MS and ^{19}F and ^1H NMR) of *p*-methoxyanilide (**39**) of perfluoro[2-(4-methylpiperazinyl)propionic acid], which was prepared in a similar manner as explained for **14**, will be reported.

Perfluoro[2-(4-methylpiperazinyl)propionyl]-*p*-methoxyanilide (**39**) (nc) had mp 124.0–124.5°C (55% yield). IR (KBr disk): 1705 *v*(C=O) (s). MS: 547 $[M+1]^+$ (0.7), 149

$C(O)NHPhOCH_3^+$ (30.7), 134 $C(O)NHPhO^+$ (9.7), 122 $NHPhOCH_3$ (100), 119 $C_2F_5^+$ (22.1), 114 $C_2F_4N^+$ (12.5), 100 $C_2F_4^+$ (12.8), 95 $C_2F_3N^+$ (15.7), 77 $C_2F_2NH^+$ (11.4), 69 CF_3^+ (42.9), 53 ? (11.1), 52 $CF_2H_2^+$ (19.1), 51 CF_2H^+ (10.3). ^{19}F NMR ($CDCl_3$): δ −52.8 (triple triplet, 3F, $J_{F-F} = 8.8$ and 10.2 Hz, $\mathbf{CF_3}N$), δ −85.6, −99.3 [4F, $J_{AB} = 192$ Hz, c-$C_2F_5N(\mathbf{CF_2}CF_2)_2N$], δ −83.4, −94.8 [4F, $J_{AB} = 189$ Hz, c-$C_2F_5N(CF_2\mathbf{CF_2})_2N$], δ −73.7 [m, 3F, $NCF(\mathbf{CF_3})$], δ −133.6 [m, 1F, $NC\mathbf{F}(CF_3)$]. ^1H NMR ($CDCl_3$): δ 7.88 (s, 1H, NH), δ 7.43 (d, 2H), δ 6.92 (d, 2H), δ 3.82 (s, 3H, OCH_3). Analysis: Calc. for $C_{15}F_{15}N_3O_2H_8$: C, 32.91%; F, 52.1%. Found: C, 33.03%; F, 52.2%.

*3.6. Fluorination of methyl 2-(4-ethylpiperazinyl)propionate (**5**)*

Sample **5** (39.2 g, 0.196 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.8–6.3 V, 7–8°C, 572 min (209 A h). The work-up gave the following products in the −78°C trap (5.1 g): **31** (1.5 g), **32** (0.4 g), **38** (0.7 g), **13** (1.6 g), **17** (0.3 g), **18** (0.2 g) and unidentified products (0.4 g). Cell drainings (30.1 g): **13** (0.4 g), **17** (0.5 g), **18** (11.2 g), perfluoro[2-(4-ethylpiperazinyl)propionyl fluoride] (**21**) (15.2 g), perfluoro[methyl 2-(4-ethylpiperazinyl)propionate] (**22**) (1.0 g) and unidentified products (1.8 g). The GC yields of **21** and **22** were 15.7 and 0.9%, respectively.

Spectral data (IR and Mass) of **21** and **22** including the physicochemical properties for the former one are shown below. ^{19}F NMR data of **21** and **22** are shown in Table 3.

Perfluoro[2-(4-ethylpiperazinyl)propionyl fluoride] (**21**) (nc) had bp 138.5–139.5°C, n_D^{20} 1.3007 and d_4^{20} 1.8386. IR (gas): 1898 (m) and 1881 (ms) ν(C=O), 1326 (s), 1302 (s), 1247 (vs, broad), 1185 (vs), 1135 (m), 1107 (w), 1186 (w), 1071 (w), 1053 (ms), 1044 (ms), 981 (m), 955 (m), 824 (w), 810 (w), 741 (ms), 697 (w). MS: 475 $[M-F]^+$ (0.7), 447 $[M-COF]^+$ (4.0), 425 $[M-CF_3]^+$, 309 $C_6F_{11}N_2^+$ (4.3), 259 $C_5F_9N_2^+$ (1.2), 214 $C_4F_8N^+$ (9.4), 171 $C_4F_5N_2^+$ (1.6), 164 $C_3F_6N^+$ (19.7), 145 $C_3F_5N^+$ (1.8), 126 $C_3F_4N^+$ (0.5), 119 $C_2F_5^+$ (100), 114 $C_2F_4N^+$ (26.5), 100 $C_2F_4^+$ (31.9), 95 $C_2F_3N^+$ (2.1), 76 $C_2F_2N^+$ (2.8), 69 CF_3^+ (50), 50 CF_2^+ (5.6).

Perfluoro[methyl 2-(4-ethylpiperazinyl)propionate] (**22**) (nc): IR (gas): 1854 (m) and 1840 (m) ν(C=O), 1324 (m), 1289 (ms), 1256 (vs), 1219 (m), 1185 (ms), 1153 (ms), 1107 (w), 1089 (w), 1054 (w), 1019 (w), 955 (w), 824 (w), 788 (w), 741 (w). MS: 491 $[M-F]^+$ (0.2), 447 $[M-C(O)OCF_3]^+$ (2.0), 397 $C_7F_{15}N_2^+$ (0.5), 309 $C_6F_{11}N_2^+$ (6.3), 259 $C_5F_9N_2^+$ (0.3), 214 $C_4F_8N^+$ (3.0), 195 $C_4F_7N^+$ (1.8), 164 $C_3F_6N^+$ (6.3), 145 $C_3F_5N^+$ (1.5), 119 $C_2F_5^+$ (30.2), 114 $C_2F_4N^+$ (7.7), 100 $C_2F_4^+$ (12.7), 76 $C_2F_2N^+$ (1.1), 69 CF_3^+ (100), 50 CF_2^+ (5.3).

Methyl ester (**40**) and *p*-methoxyanilide (**41**) of perfluoro[2-(4-methylpiperazinyl)propionic acid] were prepared in a similar manner as explained for **16**. ^{19}F NMR data of **40** are shown in Table 3.

Methyl perfluoro[2-(4-ethylpiperazinyl)propionate] (**40**) (nc) had bp 180.0–180.7°C, n_D^{20} 1.3212 and d_4^{20} 1.7808. IR (capillary film): 2968 ν(CH) (w), 1789 (s) ν(C=O), 1443 (m), 1408 (w), 1340–1225 (s–vs), 1175 (vs), 1125 (s), 1084 (ms), 1067 (ms), 1046 (s), 951 (s), 932 (w), 919 (w), 842 (w), 820 (ms), 841 (w), 820 (w), 792 (w), 776 (m, sh), 739 (s), 719 (w), 689 (w), 676 (w), 668 (w), 641 (w), 624 (w). MS: 487 $[M-F]^+$ (0.5), 447 $[M-C(O)OCH_3]^+$ (0.9), 309 $C_6F_{11}N_2^+$ (2.2), 214 $C_4F_8N^+$ (2.2), 195 $C_4F_7N^+$ (2.8), 164 $C_3F_6N^+$ (7.4), 159 $[C_2F_4C(O)OCH_3]^+$ (1.2), 145 $C_3F_5N^+$ (1.8), 131 $C_3F_5^+$ (12.9), 119 $C_2F_5^+$ (21.1), 114 $C_2F_4N^+$ (7.7), 100 $C_2F_4^+$ (13.9), 97 $C_2F_3O^+$ (1.8), 81 $C_2F_3^+$ (3.9), 69 CF_3^+ (14.5), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (1.6). Analysis: Calc. for $C_{10}F_{17}N_2O_2H_3$: C, 23.72%; F, 63.8%. Found: C, 23.85%; F, 63.6%.

Perfluoro[2-(4-ethylpiperazinyl)propionyl]-*p*-methoxyanilide (**41**) (nc) had mp 105.5–106.0°C (60% yield). IR (KBr disk): 1712 ν(C=O) (ms). MS: 597 $[M+1]^+$ (0.5), 221 ? (0.9), 164 $C_3F_6N^+$ (0.8), 150 $C_3F_6^+$ (1.0), 149 $C_8H_7NO_2^+$ (32.8), 134 $C_2F_5NH^+$ (8.9), 123 $C_7H_9NO_2^+$ (7.9), 122 $C_7H_8NO_2^+$ (100), 119 $C_2F_5^+$ (35.7), 114 $C_2F_4N^+$ (12.4), 100 $C_2F_4^+$ (15.2), 95 $C_2F_3N^+$ (16.0), 77 $C_2F_2NH^+$ (10.6), 69 CF_3^+ (25.2), 53 ? (11.0), 52 $CF_2H_2^+$ (20.5), 51 CF_2H^+ (10.5). ^{19}F NMR ($CDCl_3$): δ −73.8 (m, 3F, $NCF(\mathbf{CF_3})$, δ −84.2, −85.5 (2F, $J_{AB} = 184$ Hz, $CF_3\mathbf{CF_2}N$) δ −85.4, −97.5 [4F, $J_{AB} = 203$ Hz, c-$C_2F_5N(\mathbf{CF_2}CF_2)_2N$], δ −84.1, −94.4 [4F, $J_{AB} = 195$ Hz, c-$C_2F_5N(CF_2\mathbf{CF_2})_2N$], δ −85.7 [quintet, $J_{F-F} = 8.8$, $\mathbf{CF_3}CF_2N$], δ −134.3 [m, 1F, $NC\mathbf{F}(CF_3)$]. ^1H NMR ($CDCl_3$): δ 7.86 (s, 1H, NH), δ 7.43 (d, 2H), δ 6.92 (d, 2H), δ 3.82 (s, 3H, OCH_3). Analysis: Calc. for $C_{16}F_{17}N_3O_2H_8$: C, 32.16%; F, 54.1%. Found: C, 32.12%; F, 54.2%.

*3.7. Fluorination of methyl 3-(4-methylpiperazinyl)-2-methylpropionate (**6**)*

Sample **6** (39.7 g, 0.199 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.8–6.1 V, 7–8°C, 656 min (239 A h). The work-up gave the following products in the −78°C trap (10.0 g): perfluoro(*iso*-propionyl fluoride) (**42**) (3.1 g), perfluoro[3-(*N,N*-dimethylamino)-2-methylpropionyl fluoride] (**43**) [9] (2.2 g), **33** (0.5 g), **17** (1.0 g), perfluoro[3-(*N,N*-diethylamino)-2-methylpropionyl fluoride] (**27**) [9] (0.9 g) and unidentified products (2.3 g). Cell drainings (40.2 g): **43** (0.9 g), **27** (12.1 g), perfluoro[4-methyl-1-(propyl)piperazine] (**44**) (3.1 g), perfluoro[3-(4-methylpiperazinyl)-2-methylpropionyl fluoride] (**23**) (21.7 g) and unidentified products (2.4 g). The GC yield of **23** was 22.1%.

Spectral data (IR, MS and ^{19}F NMR) of **23** have been reported in our previous paper [9]. Therefore, physicochemical properties and spectral data of **44** and methyl perfluoro[3-(4-methylpiperazinyl)-2-methylpropionate] (**45**), which had not been characterized yet, will be described. ^{19}F NMR data of **44** and **45** are shown in Table 3.

Perfluoro[4-methyl-1-(propyl)piperazine] (**44**) (nc) had bp 121.2–121.8°C, n_D^{20} 1.2874 and d_4^{20} 1.8386. IR (gas): 1359 (s), 1311 (s), 1273 (ms), 1233 (vs), 1179 (ms), 1151 (w), 1136 (w), 1102 (w), 1076 (w), 979 (m), 959 (ms), 895 (w), 796 (w), 739 (ms), 666 (w), 626 (w). MS: 447 $[M-F]^+$ (2.1), 347 $[M-C_2F_5]^+$ (13.1), 259 $C_5F_9N_2^+$ (11.1), 214 $C_4F_8N^+$ (2.4), 209 $C_4F_7N_2^+$ (1.3), 171 $C_4F_5N_2^+$ (2.8), 169 $C_3F_7^+$ (34.7), 164 $C_3F_6N^+$ (13.3), 145 $C_3F_5N^+$ (2.0), 121 $C_3F_3N_2^+$ (2.0), 119 $C_2F_5^+$ (16.3), 114 $C_2F_4N^+$ (30.7), 100 $C_2F_4^+$ (46.7), 95 $C_2F_3N^+$ (2.2), 76 $C_2F_2N^+$ (1.7), 69 CF_3^+ (100), 50 CF_2^+ (4.0). Analysis: Calc. for $C_8F_{18}N_2$: C, 20.60%; F, 73.1%. Found: C, 20.58%; F, 73.0%.

Methyl perfluoro[3-(4-methylpiperazinyl)-2-methylpropionate] (**45**) had bp 179.5–180.0°C, n_D^{20} 1.2874 and d_4^{20} 1.8386. IR (capillary film): 2969 *v*(CH) (w), 1793 (ms) and 1780 (m) *v*(C=O), 1443 (w), 1351 (s), 1301 (vs), 1262 (s), 1226 (vs), 1164 (s), 1090 (m), 1070 (w), 1045 (m), 1034 (m), 1019 (w), 968 (m), 953 (s), 892 (m), 852 (m), 808 (w), 780 (m), 743 (w), 729 (w), 701 (w), 620 (w). MS: 347 $[M-CF(CF_3)C(O)OCH_3]^+$ (2.3), 259 $C_5F_9N_2^+$ (2.2), 209 $C_3F_6C(O)OCH_3^+$, $C_4F_7N_2^+$ (5.5), 197 $C_4F_7N_2^+$ (2.0), 169 $C_3F_7^+$ (2.8), 164 $C_3F_6N^+$ (4.1), 150 $C_3F_6^+$ (9.1), 145 $C_3F_5N^+$ (1.1), 131 $C_3F_5^+$ (3.6), 119 $C_2F_5^+$ (4.8), 114 $C_2F_4N^+$ (12.9), 100 $C_2F_4^+$ (10.8), 81 $C_2F_3^+$ (10.4), 69 CF_3^+ (31.5), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (1.4). Analysis: Calc. for $C_{10}F_{17}N_2O_2H_3$: C, 23.72%; F, 63.8%. Found: C, 23.70%; F, 63.8%.

3.8. Fluorination of methyl 3-(4-ethylpiperazinyl)-2-methylpropionate (7)

Sample **7** (40.0 g, 0.187 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.6–6.0 V, 7–8°C, 632 min (232 A h). The work-up gave the following products in the −78°C trap (6.6 g): **42** (1.2 g), **31** (1.1 g), **43** (2.1 g) and unidentified products (2.2 g). Cell drainings (53.1 g): **27** (1.9 g), perfluoro[4-ethyl-1-(propyl)piperazine] (**46**) (5.0 g), perfluoro[3-(4-ethylpiperazinyl)-2-methylpropionyl fluoride] (**25**) (38.2 g) and unidentified products (8.0 g). The GC yield of **25** was 37.5%.

Physicochemical properties and spectral data (IR and MS) of **25** and **46** are shown below. ^{19}F NMR data of **25** and **46** are shown in Table 3.

Perfluoro[3-(4-ethylpiperazinyl)-2-methylpropionyl fluoride] (**25**) had bp 138.5–139.5°C, n_D^{20} 1.3005 and d_4^{20} 1.8512. IR (gas): 1890 (m) and 1875 (m) *v*(CO), 1340 (s), 1230 (s), 1271 (s), 1252 (vs), 1184 (ms), 1155 (w), 1069 (ms), 1011 (w), 988 (w), 970 (w), 955 (m), 824 (w), 789 (w), 756 (w), 741 (m), 692 (w), 630 (w). MS: 525 $[M-F]^+$ (0.3), 475 $[M-CF_3]^+$ (2.3), 397 $[M-C_2F_4C(O)F]^+$ (4.3), 309 $C_6F_{11}N_2^+$ (1.5), 259 $C_5F_9N_2^+$ (3.9), 214 $C_4F_8N^+$ (1.5), 197 $C_4F_7N_2^+$ (22.3), 171 $C_4F_5N_2^+$ (1.8), 169 $C_3F_7^+$ (32.9), 164 $C_3F_6N^+$ (14.2), 150 $C_3F_6^+$ (3.2), 145 $C_3F_5N^+$ (1.9), 131 $C_3F_5^+$ (2.3), 128 $C_4F_4N_2^+$ (2.4), 119 $C_2F_5^+$ (51.8), 114 $C_2F_4N^+$ (33.8), 100 $C_2F_4^+$ (69.0), 95 $C_2F_3N^+$ (2.1), 76 $C_2F_2N^+$ (1.8), 69 CF_3^+ (100), 50 CF_2^+ (5.7).

Perfluoro[4-ethyl-1-(propyl)piperazine] (**46**) (nc) had bp 137.0–137.6°C, n_D^{20} 1.2883 and d_4^{20} 1.8384. IR (gas): 1340 (s), 1307 (s), 1271 (s), 1252 (vs), 1235 (s), 1184 (s), 1137 (w), 1108 (w), 1070 (ms), 978 (ms), 956 (ms), 824 (w), 793 (w), 741 (ms), 665 (w), 647 (w). MS: 497 $[M-F]^+$ (1.8), 447 $[M-CF_3]^+$ (2.8), 397 $C_7F_{13}N_2^+$ (11.7), 359 $C_7F_{13}N_2^+$ (2.0), 309 $C_6F_{11}N_2^+$ (9.5), 264 $C_5F_{10}N^+$ (2.0), 259 $C_5F_9N_2^+$ (7.7), 214 $C_4F_8N^+$ (5.1), 171 $C_4F_5N_2^+$ (6.1), 169 $C_3F_7^+$ (65.9), 164 $C_3F_6N^+$ (26.7), 145 $C_3F_5N^+$ (3.2), 119 $C_2F_5^+$ (97.3), 114 $C_2F_4N^+$ (55.4), 100 $C_2F_4^+$ (83.7), 95 $C_2F_3N^+$ (3.1), 81 $C_2F_3^+$ (1.3), 76 $C_2F_2N^+$ (2.8), 69 CF_3^+ (100), 50 CF_2^+ (7.7). Analysis: Calc. for $C_9F_{20}N_2$: C, 20.93%; F, 73.6%. Found: C, 20.83%; F, 73.3%.

For the further characterization of **25**, it was derivatized into the corresponding methyl ester (**47**) similarly. It was a compound like sherbet at room temperature.

Methyl perfluoro[3-(4-ethylpiperazinyl)-2-methylpropionate] (**47**) (nc) had bp 192.0–192.5°C. IR (capillary film): 2969 *v*(CH) (w), 1792 and 1980 *v*(CO) (ms), 1443 (w), 1335 (s), 1295 (s), 1250–1245 (s–vs), 1226 (s), 1201 (m), 1165 (s), 1099 (w), 1065 (s), 1046 (m), 1034 (m), 967 (w), 951 (s), 823 (m), 807 (w), 780 (m), 755 (w), 739 (ms), 697 (w), 674 (w), 642 (m). MS: 397 $[M-CF(CF_3)C(O)OCH_3]^+$ (1.9), 309 $C_6F_{11}N_2^+$ (0.8), 259 $C_5F_9N_2^+$ (1.6), 209 $C_3F_7C(O)OCH_3^+$, $C_4F_7N_2^+$ (7.7), 197 $C_3F_7N_2^+$ (2.4), 169 $C_3F_7^+$ (3.3), 164 $C_3F_6N^+$ (4.9), 159 $C_3F_5N_2^+$ (1.1), 150 $C_3F_6^+$ (10.5), 145 $C_3F_5N^+$ (1.0), 131 $C_3F_5^+$ (4.1), 119 $C_2F_5^+$ (18.6), 114 $C_2F_4N^+$ (14.7), 100 $C_2F_4^+$ (11.6), 81 $C_2F_3^+$ (11.9), 69 CF_3^+ (21.3), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (1.4). Analysis: Calc. for $C_{11}F_{19}N_2O_2H_3$: C, 23.74%; F, 64.9%. Found: C, 23.90%; F, 65.2%.

^{19}F NMR data of **46** and **47** are shown in Table 3.

3.9. Fluorination of methyl 3-(4-methylpiperazinyl)butyrate (8)

Sample **8** (40.5 g, 0.203 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.9–6.1 V, 7–8°C, 619 min (229 A h). The work-up gave the following products in the −78°C trap (12.0 g): perfluoro(propionyl fluoride) (**48**) (2.1 g), **32** (2.9 g), **13** (2.7 g), **17** (0.9 g) and unidentified products (3.4 g). Cell drainings (26.9 g): **17** (2.0 g), perfluoro[4-methyl-1-(*iso*-propyl)piperazine] (**49**) (3.2 g), perfluoro[3-(4-methylpiperazinyl)butyryl fluoride] (**24**) (10.9 g), perfluoro[3-(4-methylpiperazinyl)oxolane] (**30**) (4.6 g) and unidentified products (6.2 g). The GC yield of **24** was 10.9%.

Spectral data (IR and MS) of **24** and physicochemical properties and spectral data (IR and Mass) of **30** and **49** are shown below. ^{19}F NMR data of **49** isolated by preparative GC revealed that it contained small quantities of perfluoro[4-methyl-1-(propyl)piperazine] (**43**). ^{19}F NMR data of **24**, **49** and **30** are shown in Table 3.

Perfluoro[3-(4-methylpiperazinyl)butyryl fluoride] (**24**) (nc): IR (gas): 1886 *v*(CO) (ms), 1413 (w), 1360 (vs), 1296 (s), 1270 (s), 1227 (vs), 1199 (m), 1177 (ms), 1124 (w), 1092 (w), 1075 (w), 1031 (w), 960 (ms), 928 (w), 897 (m), 855 (w), 788 (w), 732 (m). MS: 425 $[M-F]^+$ (0.8), 397 $[M-C(O)F]^+$ (4.9), 359 $C_7F_{13}N_2^+$ (0.4), 309 $C_6F_{11}N_2^+$ (1.5), 264 $C_5F_{10}N^+$ (3.2), 259 $C_5F_9N_2^+$ (1.9), 214 $C_4F_8N^+$ (5.7), 197 $C_3F_7N_2^+$ (1.3), 171 $C_4F_5N_2^+$ (1.3), 169 $C_3F_7^+$ (6.6), 164 $C_3F_6N^+$ (18.6), 145 $C_3F_5N^+$ (2.2), 131 $C_3F_5^+$ (1.5), 119 $C_2F_5^+$ (52.3), 114 $C_2F_4N^+$ (18.1), 100 $C_2F_4^+$ (21.7), 95 $C_2F_3N^+$ (2.1), 76 $C_2F_2N^+$ (2.3), 69 CF_3^+ (100), 50 CF_2^+ (4.7).

Perfluoro[4-methyl-1-(*iso*-propyl)piperazine] (**49**) (nc) had bp 121.0–121.6°C, n_D^{20} 1.2895 and d_4^{20} 1.8564. IR (gas):1413 (w), 1360 (vs), 1320–1272 (vs), 1245–1229 (vs), 1176 (m), 1149 (w), 1075 (w), 1060 (w), 978 (m), 959 (s), 897 (w), 857 (w), 796 (w), 740 (m), 730 (w), 629 (w), 546 (w). MS: 447 $[M-F]^+$ (3.2), 397 $[M-CF_3]^+$ (19.9), 359 $C_7F_{15}N_2^+$ (3.6), 309 $C_6F_{11}N_2^+$ (3.9), 264 $C_5F_{10}N^+$ (12.7), 259 $C_5F_9N_2^+$ (3.3), 214 $C_4F_8N^+$ (10.6), 171 $C_4F_5N_2^+$ (1.8), 169 $C_3F_7^+$ (4.4), 164 $C_3F_6N^+$ (29.7), 145 $C_3F_5N^+$ (3.1), 119 $C_2F_5^+$ (66.2), 114 $C_2F_4N^+$ (29.2), 100 $C_2F_4^+$ (47.7), 95 $C_2F_3N^+$ (2.6), 81 $C_2F_3^+$ (1.2), 76 $C_2F_2N^+$ (3.5), 69 CF_3^+ (100), 50 CF_2^+ (5.8). Analysis: Calc. for $C_8F_{18}N_2$: C, 20.60%; F, 73.4%. Found: C, 20.50%; F, 73.1%.

Perfluoro[3-(4-methylpiperazinyl)oxolane] (**30**) (nc) had bp 145.0–145.5°C, n_D^{20} 1.3055 and d_4^{20} 1.8756. IR (gas): 1360 (s), 1316 (s), 1254 (s), 1227 (vs), 1186 (ms), 1124 (w), 1084 (m), 1073 (w), 1011 (w), 972 (m), 927 (w), 8976 (w), 764 (w), 732 (w). MS: 428 $[M-CF_3]^+$ (3.7), 378 $C_7F_{14}N_2^+$ (11.4), 321 $C_7F_{11}N_2^+$ (1.1), 295 $C_6F_{11}N^+$ (4.7), 264 $C_5F_{10}N^+$ (4.0), 245 $C_5F_9N^+$ (7.3), 221 $C_5F_7N_2^+$ (1.3), 214 $C_4F_8N^+$ (4.6), 176 $C_4F_6N^+$ (7.7), 169 $C_3F_7^+$ (2.4), 164 $C_3F_6N^+$ (9.9), 152 ? (1.8), 150 $C_3F_6^+$ (7.3), 145 $C_3F_5N^+$ (21.9), 131 $C_3F_5^+$ (10.1), 119 $C_2F_5^+$ (35.6), 114 $C_2F_4N^+$ (21.0), 100 $C_2F_4^+$ (74.4), 95 $C_2F_3N^+$ (3.2), 81 $C_2F_3^+$ (2.3), 76 $C_2F_2N^+$ (4.2), 69 CF_3^+ (100), 50 CF_2^+ (6.1). Analysis: Calc. for $C_9F_{18}N_2O$: C, 21.86%; F, 69.2%. Found: C, 21.76%; F, 69.1%.

For the further characterization of **24**, it was derivatized into the methyl ester (**50**) similarly.

Methyl perfluoro[3-(4-methylpiperazinyl)butyrate] (**50**) (nc) had bp 185.5–185.8°C, n_D^{20} 1.3262 and d_4^{20} 1.7971. IR (capillary film): 2969 *v*(CH) (w), 1792 *v*(C=O) (s), 1444 (w), 1411 (w), 1352 (s), 1340–1171 (vs), 1070 (ms), 1050 (m), 1034 (m), 955 (s), 895 (ms), 881 (w), 853 (w), 817 (m), 776 (m), 729 (ms), 691 (w), 673 (w), 627 (m), 576 (w). MS: 447 $[M-C(O)OCH_3]^+$ (0.3), 397 $[M-CF_2C(O)OCH_3]^+$ (6.1), 309 $C_6F_{11}N_2^+$ (1.1), 264 $C_5F_{10}N^+$ (1.5), 259 $C_5F_9N_2^+$ (1.1), 214 $C_4F_8N^+$ (2.7), 209 $C_3F_6C(O)OCH_3^+$, $C_4F_7N_2^+$ (8.0), 181 $C_4F_7^+$ (1.2), 164 $C_3F_6N^+$ (6.7), 150 $C_3F_6^+$ (7.8), 145 $C_3F_5N^+$ (2.1), 131 $C_3F_5^+$ (2.9), 119 $C_2F_5^+$ (15.8), 114 $C_2F_4N^+$ (13.1), 100 $C_2F_4^+$ (10.9), 95 $C_2F_3N^+$ (1.1), 81 $C_2F_3^+$ (2.1), 76 $C_2F_2N^+$ (1.1), 69 CF_3^+ (36.3), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (1.6). Analysis: Calc. for $C_{10}F_{17}N_2O_2H_3$: C, 23.72%; F, 63.8%. Found: C, 23.81%; F, 63.5%. ^{19}F NMR data of **50** are shown in Table 3.

*3.10. Fluorination of methyl 3-(4-ethylpiperazinyl)butyrate (**9**)*

Sample **9** (40.3 g, 0.188 mol) was fluorinated similarly under the following conditions; 3.2 A/dm^2, 5.9–6.0 V, 7–8°C, 656 min (237 A h). The work-up gave the following products in the −78°C trap (7.1 g): **48** (trace), **32** (1.1 g), **13** (2.4 g), **18** (0.3 g) and unidentified products (3.3 g). Cell drainings (56.1 g): **18** (9.3 g), perfluoro[4-ethyl-1-(*iso*-propyl)piperazine] (**28**) (9.3 g), perfluoro[3-(4-ethylpiperazinyl)butyryl fluoride] (**26**) (20.7 g), perfluoro[3-(4-ethylpiperazinyl)oxolane] (**29**) (10.0 g) and unidentified products (6.8 g). The GC yield of **26** was 20.2%.

Spectral data (IR and MS) of **26** and physicochemical properties and spectral data (IR and Mass) of **28** and **29** are shown below. ^{19}F NMR of **26**, **28** and **29** are shown in Table 3.

Perfluoro[3-(4-ethylpiperazinyl)butyryl fluoride] (**26**) (nc): IR (gas): 1886 *v*(C=O) (m), 1323 (ms), 1292 (s), 1254 (vs), 1182 (ms), 1072 (w), 1030 (m), 955 (m), 928 (w), 826 (w), 741 (m). MS: 525 $[M-F]^+$ (0.4), 475 $[M-CF_3]^+$ (0.7), 447 $[M-CF_2C(O)F]^+$ (4.2), 425 $C_8F_{16}N_2O^+$ (0.2), 359 $C_7F_{13}N_2^+$ (0.4), 309 $C_6F_{11}N_2^+$ (2.8), 264 $C_5F_{10}N^+$ (3.3), 214 $C_4F_8N^+$ (6.4), 197 $C_3F_7N_2^+$ (1.2), 171 $C_4F_5N_2^+$ (1.5), 169 $C_3F_7^+$ (5.5), 164 $C_3F_6N^+$ (14.9), 150 $C_3F_6^+$ (1.3), 145 $C_3F_5N^+$ (1.5), 131 $C_3F_5^+$ (1.5), 119 $C_2F_5^+$ (100), 114 $C_2F_4N^+$ (20.3), 100 $C_2F_4^+$ (23.2), 95 $C_2F_3N^+$ (1.6), 76 $C_2F_2N^+$ (2.1), 69 CF_3^+ (57.8), 50 CF_2^+ (4.4).

Perfluoro[4-ethyl-1-(*iso*-propyl)piperazine] (**28**) (nc) had bp 137.3–137.9°C, n_D^{20} 1.2929 and d_4^{20} 1.8734. IR (gas): 1324 (s), 1290 (vs), 1268 (vs), 1247 (vs), 1204 (ms), 1180 (s), 1147 (w), 1123 (w), 1086 (w), 1072 (w), 1041 (m), 978 (m), 956 (m), 826 (w), 796 (w), 741 (ms), 729 (m), 676 (w), 621 (w). MS: 497 $[M-F]^+$ (0.7), 447 $[M-CF_3]^+$ (5.9), 387 $C_7F_{15}N_2^+$ (2.7), 309 $C_6F_{11}N_2^+$ (4.4), 259 $C_5F_9N_2^+$ (3.5), 214 $C_4F_8N^+$ (5.0), 171 $C_4F_5N_2^+$ (2.7), 169 $C_3F_7^+$ (23.0), 164 $C_3F_6N^+$ (18.8), 145 $C_3F_5N^+$ (1.9), 119 $C_2F_5^+$ (76.2), 114 $C_2F_4N^+$ (33.1), 100 $C_2F_4^+$ (43.4), 95 $C_2F_3N^+$ (2.2), 76 $C_2F_2N^+$ (2.3), 69 CF_3^+ (100), 50 CF_2^+ (4.8). Analysis: Calc. for $C_9F_{20}N_2$: C, 20.93%; F, 73.6%. Found: C, 20.91%; F, 73.3%.

Perfluoro[3-(*N*-ethylpiperazinyl)oxolane] (**29**) (nc) had bp 159.5–160.0°C, n_D^{20} 1.3065 and d_4^{20} 1.8986. IR (gas): 1312 (m, broad), 1254 (vs), 1236 (s, sh), 1188 (ms), 1128 (w), 1190 (w), 1067 (w), 1011 (w), 968 (w), 923 (w), 826 (w), 762 (w), 741 (w). Mass: 525 $[M-F]^+$ (1.2), 478 $C_9F_{18}N_2^+$ (2.0), 428 $C_8F_{16}N_2^+$ (6.7), 295 $C_6F_{11}N^+$ (2.1), 264 $C_5F_{10}N^+$ (5.1), 245 $C_5F_9N^+$ (4.7), 214 $C_4F_8N^+$ (4.3), 195 $C_4F_7N^+$ (16.0), 176 $C_4F_6N^+$ (5.4), 169 $C_3F_7^+$ (2,5), 164 $C_3F_6N^+$ (14.6), 150 $C_3F_6^+$ (8.3), 145 $C_3F_5N^+$ (13.8), 131 $C_3F_3^+$ (10.3), 119 $C_2F_5^+$ (100), 114 $C_2F_4N^+$ (34.5), 100 $C_2F_4^+$ (86.7), 81 $C_3F_3^+$ (2.7), 76 $C_2F_2N^+$ (5.0), 69 CF_3^+

(85), 50 CF_2^+ (7.7). Analysis: Calc. for $C_{10}F_{20}N_2O$: C, 22.06%; F, 69.9%. Found: C, 22.03%; F, 69.8%.

For the further characterization of **26**, it was derivatized into the methyl ester (**51**) similarly.

Methyl perfluoro[3-(4-ethylpiperazinyl)butyrate] (**51**) (nc) had bp 199.0–199.5°C, n_D^{20} 1.3253 and d_4^{20} 1.8216. IR (capillary film): 2968 *v*(CH) (w), 1792 *v*(C=O) (s), 1444 (w), 1350–1230 (s–vs), 1173 (vs), 1111 (m, sh), 1068 (ms), 1034 (ms), 951 (s), 917 (w), 855 (w), 825 (ms), 817 (ms), 776 (m), 740 (ms), 675 (w), 691 (w), 675 (w), 620 (w), 567 (w), 541 (w). MS: 447 $[M - CF_2C(O)OCH_3]^+$ (3.3), 309 $C_6F_{12}N_2^+$ (1.8), 264 $C_5F_{10}N^+$ (1.5), 214 $C_4F_8N^+$ (2.2), 209 $C_3F_6C(O)OCH_3^+$ (6.9), 164 $C_3F_6N^+$ (7.9), 150 $C_3F_6^+$ (7.2), 145 $C_3F_5N^+$ (2.4), 131 $C_3F_5^+$ (2.5), 119 $C_2F_5^+$ (31.2), 114 $C_2F_4N^+$ (16.0), 100 $C_2F_4^+$ (12.7), 81 $C_2F_3^+$ (1.7), 76 $C_2F_2N^+$ (1.0), 69 CF_3^+ (20.8), 59 $[C(O)OCH_3]^+$ (100), 50 CF_2^+ (3.4). Analysis: Calc. for $C_{11}F_{19}N_2O_2H_3$: C, 23.74%; F, 64.9%. Found: C, 23.85%; F, 64.5%. ^{19}F NMR data of **51** are shown in Table 3.

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