# On the formation of surface active by-products during the electrochemical fluorination of tertiary amines

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**Abstract**

The electrochemical fluorination (ECF) of 2-phenyl-3,4-dimethylmorpholine led to the solubilization of the perfluoro products and HF foaming, which may be traced back to the formation of partially fluorinated, HF-soluble compounds which exhibit surface activity in HF. Some of the perfluoro products contain an asymmetric carbon atom attached directly to a cyclohexyl ring. This asymmetric centre leads to the non-equivalence of the fluorines bound to carbon atoms 2 and 6, respectively, of the cyclohexyl ring allowing them to be distinguished in the $^{19}F$ NMR spectra.

## Introduction

Electrochemical perfluorination in HF (ECF) is linked with the formation of partially fluorinated, HF-soluble intermediates and by-products. Their formation is one reason for the occurrence of the well-known induction period at the beginning of an ECF experiment [1]. However, if these partially fluorinated compounds possess surface activity in HF this would provide an additional explanation for the delayed occurrence of the perfluoro product. The formation of such surface-active compounds is described in this paper.

## Results and discussion

During the course of many ECF experiments, aimed at the synthesis of perfluorinated compounds for blood substitutes, we have repeatedly observed phenomena which indicate the generation of surface-active compounds in HF. A typical example occurred during the ECF of 2-phenyl-3,4-dimethylmorpholine (PDMM) (kindly supplied by ISIS-Chemie, Zwickau, Germany). This compound was of interest because of the expected [2] emulsion stability of its corresponding perfluoro product.

ECF of this material started smoothly; however, after *c.* 60% of the theoretically required amount of current had been applied, the electrolysis was progressively disrupted by increased foaming of the HF solution. The sole reason for this could only be the formation of surface-active compounds during the ECF process. ECF was performed semicontinuously in a 450 ml cell with a starting amount of PDMM of 40 g and after *c.* 200 A h the first of 12 portions (20 g each) of additional PDMM was added, the last after 1450 A h. All the electrolyte finally became foam-like (after the passage of *c.* 1600 A h) and the process had to be discontinued. After a further 30 min, the settled electrolyte could be drained from the cell.

As far as the product spectrum was concerned it seems that the ECF proceeded normally [3], i.e. it produced (i) the corresponding perfluoro(2-cyclohexyl-3,4-dimethylmorpholine) (PDMM), (ii) other liquid perfluorinated compounds, derived from expected cleavage reactions (see Table 1), (iii) fluorinated gaseous products and (iv) large amounts of partially fluorinated HF-soluble compounds ('HF phase' [1]) with an average F content of *c.* 50%.

Unexpectedly, in addition to partially fluorinated compounds, the electrolyte drained from the cell also contained crude perfluorinated product which could be separated by distillation or by centrifugation (3000 rpm, 30–60 min) but not by storage at 4 °C over more than 2 weeks. Obviously, the 'HF phase' is capable of stabilizing a perfluorocarbon-in-HF emulsion, i.e. the perfluoro product is solubilized in HF.

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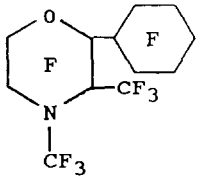
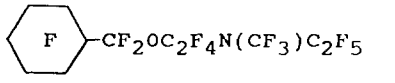
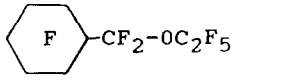
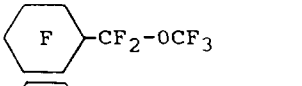
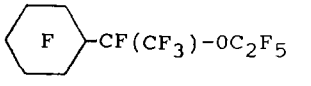
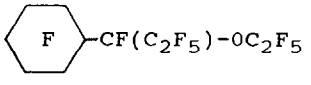
TABLE 1. Composition of the crude product arising from the ECF of PDMM

| Compounds | | Relative content (%)[a] |
|---|---|---|
|  | (1) | 20 |
|  | (2) | 23 |
|  | (3) | 15 |
|  | (4) | 13.5 |
|  | (5) | 9 |
|  | (6) | 7.5 |
| Others | | 12 |

[a]From GC analyses.

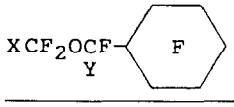
A similar observation was also made with triethylamine (TEA). In a typical experiment, ECF of TEA employing a 20% (w/w) solution ceased after the passage of *c.* 70% of the theoretically required amount of current. The clear, homogeneous HF solution was taken from the cell and the HF distilled off, when the receiver flask (at −78 °C) contained, beside HF, some drops of a second liquid which was immiscible with HF and which proved to be crude perfluorotriethylamine. This had obviously been solubilized in the electrolyte from the cell. Since we have made similar observations frequently, the phenomenon of solubilization is probably a normal rather than an exceptional occurrence in the ECF of tertiary amines, being dependent not only on the properties of the surface-active compounds in the HF phase but also to a substantial extent on the nature of the perfluoro compounds involved, as is known for perfluorocarbon-in-water emulsions [2].

Good physical preconditions exist for emulsification during ECF; firstly, the perfluoro products are formed anodically on a molecular basis, i.e. in a highly dispersed state, and secondly there is vigorous agitation of the HF solution caused by thermal convection and by $H_2$ liberation. If surface-active agents are present, the emulsion can be stabilized. In the systems under study, only the compounds present in the HF phase are potential interfacially active agents.

It was shown earlier [1] from the ECF of tertiary amines that products found in the HF phase have no fluorine atoms bound to the $\alpha$-C atoms. As a result, the basicity of the N atom is retained but at a reduced level, while the head groups of the alkyl chains become fluorophilic. Such compounds should be located predominantly at the perfluoride/HF interface. This effect should increase with the number of F atoms introduced at the $\beta$-C atoms but may pass through a maximum, because the basicities of highly fluorinated amines are too low (as reported for $(CF_3CH_2)_3N$ [4]) and a possible flattening of the amine molecule (as reported for perfluoroamines [5]). Hopefully, more information will be obtained from structural analyses of isolated partially fluorinated triethylamines (we are about to investigate this in collaboration with H. Oberhammer).

The consequences of these findings, which correspond well with observations during the ECF of other N-containing compounds, are as follows. Firstly, an additional explanation is provided for the occurrence of the well-known induction period at the beginning of an ECF experiment, viz. that due to emulsification the first PFC produced does not settle. Secondly, the partially fluorinated compounds produced prior to the perfluorinated products may possibly act as important

TABLE 2. $^{19}F$ chemical shift data for the fluorine atoms bound to positions 2 or 6 of monosubstituted *F*-cyclohexanes

|  | | Compound | Asymmetric C atom | Chemical shifts (ppm) | | |
|---|---|---|---|---|---|---|
| X | Y | | | $\delta_{F2a/6a}$ | $\delta_{F2e/6e}$ | $\Delta_{2a2e/6a6e}$[a] |
| F | F | **4** | no | 120.0 | 132.1 | 12.1 |
| $CF_3$ | F | **3** | no | 120.0 | 132.0 | 12.0 |
| $C_2F_5(CF_3)NCF_2$ | F | **2** | no | 120.0 | 131.9 | 11.9 |
| $CF_3$ | $CF_3$ | **5** | yes | 118.2; 118.5 | 131.5; 131.2 | 13.3; 12.7 |
| $CF_3$ | $C_2F_5$ | **6** | yes | 117.8; 119.0 | 131.3; 130.8 | 13.5; 11.8 |
| – | – | **1** | yes | 117.8; 118.8 | 128.2; 127.4 | 10.4; 8.6 |

[a]Differences between the chemical shifts of the respective axial and equatorial F atoms.

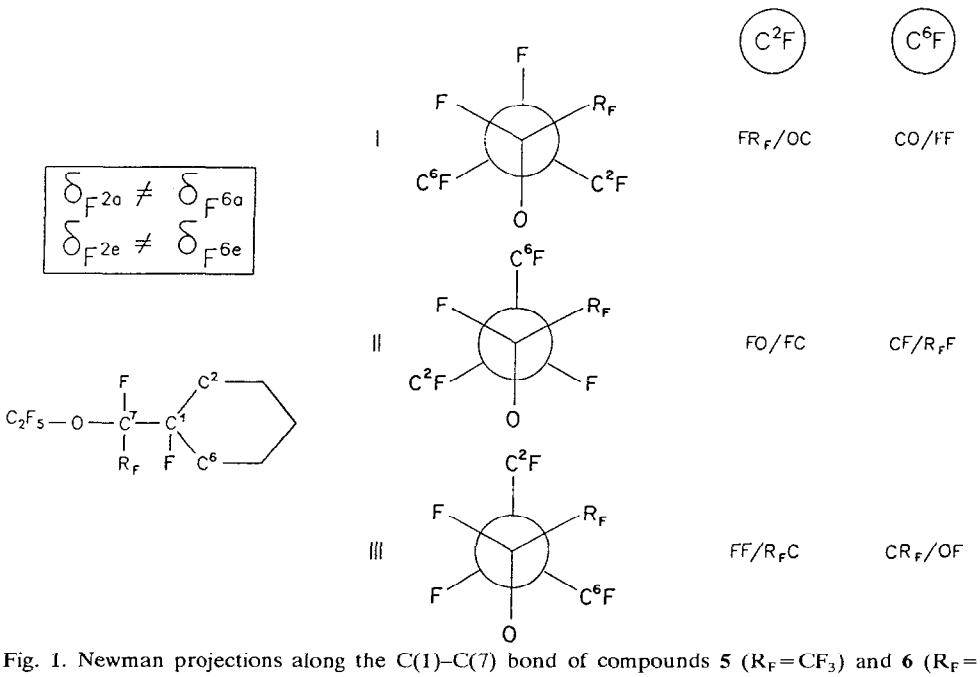



Fig. 1. Newman projections along the C(1)–C(7) bond of compounds **5** ($R_F = CF_3$) and **6** ($R_F = C_2F_5$).

auxiliary agents for the transportation of perfluorides or other anodic products from the anode. In this way, they could help to prevent the active area of the anode surface from becoming blocked.

$^{19}F$ NMR spectroscopic analysis of the identified perfluoro products (Table 1) shows the expected equivalence of the corresponding axial or equatorial fluorine atoms of the cyclohexyl ring system in positions 2 and 6, as well as in positions 3 and 5 in case of compounds **2**, **3** and **4**. However, in compounds **1**, **5** and **6**, which contain an asymmetric centre attached to the cyclohexyl ring, these respective F atoms are no longer equivalent (see Table 2). Such non-equivalence of the respective fluorine nuclei in the cyclohexyl ring system can be explained with the help of Newman projections. Newman projections show that the C(2) and the C(6) atoms are all in non-equivalent positions (Fig. 1); consequently, the F atoms bound to these C atoms also become non-equivalent. Similar effects are already known from the $^1H$ NMR spectra of hydrogen-containing compounds [6] and have also been reported recently for fluorinated compounds [7]. However, the results reported here are the first examples for cyclohexyl ring systems.

The signal assignments obtained by two-dimensional NMR analysis show (Fig. 2) that the differences in the chemical shift between the respective axial and equatorial fluorines are not equal for the C(2) and the C(6) positions (Table 2). In addition, the total two-dimensional spectrum shows that the fluorines at position C(2) and the corresponding ones at C(6) couple with different F nuclei.

A comparison of the $^{19}F$ NMR spectra for compounds **5** and **6** reveals another effect arising from the asymmetric centre. The $CF_2$ fluorines of the $CF_3CF_2-O$ side of the molecule should also give rise to an AB-type spectrum for both compounds **5** and **6**, as expected from the Newman projections. However, only compound **6** yielded the supposed AB-type spectrum, which may be explained as resulting from the additional influence of the $CF_2$ group linked to the asymmetric carbon atom. The fluorines of this $CF_2$ group – by becoming non-equivalent themselves (AB-type spectrum) – act on their environment in a diastereotopic manner.

## Experimental

*Electrochemical fluorinations*

ECF experiments were carried out in a 450 ml cell as described elsewhere [8].

Liquid perfluorinated products were drained off from the cell bottom and also condensed from the gas stream (*F*-triethylamine). Partially fluorinated compounds were separated from the HF solution by distilling off the excess HF, followed by an alkaline work-up procedure [8].

*Analytical investigations*

Gas chromatography was carried out on a Varian 3700 GC instrument with packed columns (10% FS16 on N-AW-DMCS, 3.7 m) or on a Varian 3400 capillary GC machine (60 m column coated with DB5 silicon phase).

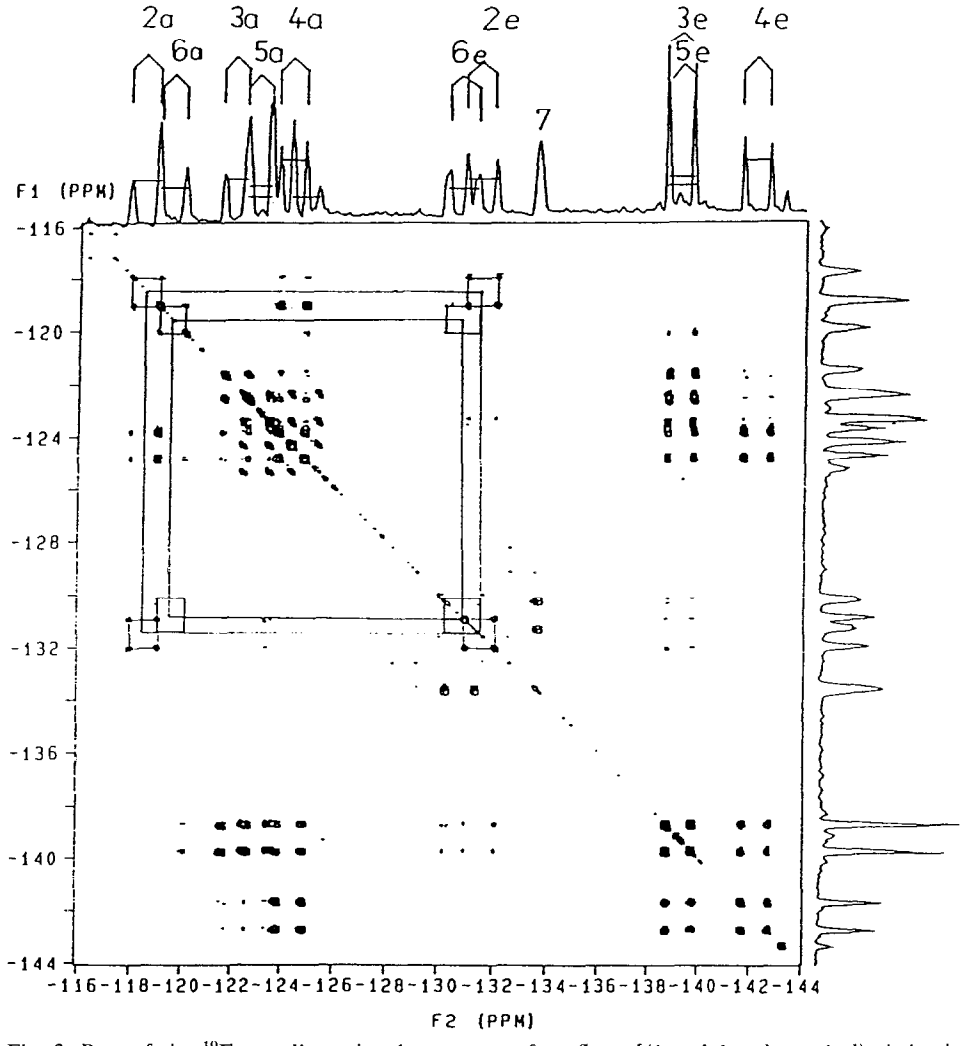



Fig. 2. Part of the $^{19}F$ two-dimensional spectrum of perfluoro[(1-cyclohexylprop-1-yl)ethyl ether] (**6**).

Mass spectra were recorded using a Finnigan MAT 212 (double focus) instrument at EI = 70 eV, or with a Finnigan MAT GC-MS 5100 (quadrupole) system, GC = 50 m SE30, EI = 70 eV.

Organically bound fluorine was determined by the Wickboldt method [9] using fluoride-sensitive electrodes.

$^{19}F$ NMR spectra were recorded at 282 MHz on a Varian spectrometer with TFA as external reference. Values are given relative to $CFCl_3$ ($\delta_{CFCl_3} = \delta_{TAA} + 78$), those upfield of $CFCl_3$ being designated positive. Two-dimensional NMR experiments were performed using a spectral window of 18 692 Hz with 4096 points in the $t_2$ direction and 512 increments in $t_1$ direction using $CDCl_3$ as solvent.

*ECF of PDMM*

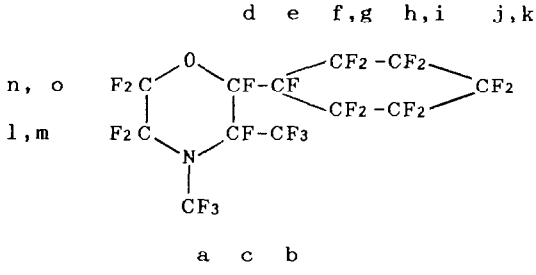
Using a 450 ml cell 40 g PDMM were electrofluorinated. After 200 A h had passed, 12 portions (each of 20 g PDMM) were added progressively up to a total of 280 g PDMM, HF being added as necessary. ECF was terminated at 1600 A h, the current density having diminished from 3 A dm initially to nearly zero due to extensive foaming of the HF solution, with the foam passing through the reflux condenser. Crude liquid perfluoro compounds (160 g) were obtained, mainly by distillation of the electrolyte (together with HF), in addition to *c.* 250 g of partially fluorinated HF-soluble compounds ('HF phase') of *c.* 50% F content, and gaseous products, mainly $CF_4$, $NF_3$, $(C_2F_5)_2O$, $C_2F_5OCF_3$ and $CF_3OCF_3$, as identified by GC methods according to ref. 8. The liquid perfluoro products (Table 1) were identified by MS and $^{19}F$ NMR spectral methods.

*Compounds*

Compounds **1** and **2** formed a mixture which could not be separated by distillation. NMR data were obtained from several mixtures (between *c.* 3:1 and 1:3) boiling in the range 182–187 °C. Of the two possible isomers of **1** ($F_d$–$F_c$: *trans* or *cis*), the *trans* compound

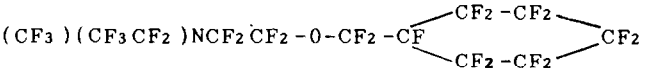
(**1**, *trans*) was present exclusively in the mixtures. For all compounds, the peak areas correspond to the appropriate numbers of fluorines.

Compound **1** (nc):



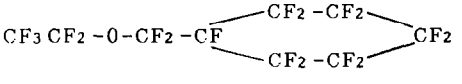

$^{19}$F NMR $\delta$: a, 51.0; b, 73.3; c, 150.1; d, 108; e, 182.8; f, 117.8; f', 118.8; g, 128.2; g', 127.4; h, 122.7; i, 140; j, 125.2; k, 143.2; l, 84.7; m, 88.5; n, 78.3; o, 81.4 ppm ($J_{n,o}$, 148.5; $J_{f,m}$, 193.5; $J_{j,k}$, 288.7; $J_{h,i}$, 290; $J_{f,g}$, 300 Hz). MS *m/z*: 592 [M − F] (0.2%); 542 [M − $CF_3$] (0.3%); 476 [M − $C_2F_5O$] (0.2%); 309 [$C_6F_{11}CO$] (1%); 281 [$C_6F_{11}$] (1%); 164 [$NC_3F_6$] (18%); 131 [$C_3F_5$] (15%); 119 [$C_2F_5$] (20%); 114 [$NC_2F_4$] (16%); 100 [$C_2F_4$] (90%); 69 [$CF_3$] (100%).

Compound **2** (nc):



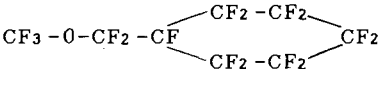

$^{19}$F NMR $\delta$: a, 51.5; b, 84.5; c, 93.1; d, 93.5; e, 84.9; f, 72.2; g, 187.8; h, 120; i, 131.9; j, 123.1; k, 141; l, 125.2; m, 143.2 ppm ($J_{l,m}$, 290; $J_{j,k}$, 288; $J_{h,i}$, 298 Hz). MS *m/z*: 630 [M − F] (0.1%); 331 [$C_6F_{11}CF_2$] (3%); 309 [$C_6F_{11}CO$] (1%); 252 [$CF_3N$ ($C_2F_5$)$CF_2$] (20%); 164 [$NC_3F_6$] (60%); 131 (18%); 119 (100%); 114 (30%); 100 (15%), 69 (95%).

Compound **3** (nc):B.p. 117.9–119 °C.



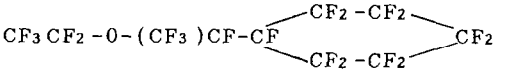

$^{19}$F NMR $\delta$: a, 88.3; b, 89.1; c, 72.2; d, 188; e, 120; f, 132; g, 123.2; h, 141; i, 125; j, 143.2 ppm ($J_{e,f}$, 298; $J_{g,h}$, 286; $J_{i,j}$, 288 Hz). MS *m/z*: 331 [$C_6F_{11}CF_2$] (1.5%); 309 (1%); 281 (1%); 243 (2.3%); 231 (2%); 185 (12%); 181 (10%); 162 (5%); 131 (20%); 119 (100%).

Compound **4**: B.p. 104 °C.



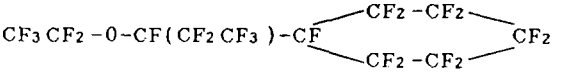

$^{19}$F NMR $\delta$: a, 56.3; b, 74.3; c, 188; d, 120; e, 132.1; f, 123.2; g, 141.2; h, 125; i, 143.3 ppm (reported in ref. 10: a, 58.7; b, 73.0; c, 189.7; d–i, 119.1–148.7 ppm) ($J_{d,e}$, 291.1; $J_{f,g}$, 289; $J_{h,i}$, 289.8 Hz). MS *m/z*: 347 [$C_6F_{11}CF_2O$] (0.1%); 331 (3%); 309 (1.2%); 281 (0.9%); 243 (1.5%); 231 (1.2%); 181 (4%); 162 (2%); 135 (16%); 131 (10%); 69 (100%).

Compound **5** (nc): B.p. 137.1–137.7 °C.




$^{19}$F NMR $\delta$: a, 87.9; b, 85.7; c, 80.5; d, 134.7; e, 183.7; f, 118.2; f', 118.5; g, 131.5; g', 131.2; h, 122.8; i, 140.4; j, 124.8; k, 143.1 ppm ($J_{j,k}$, 287.5; $J_{h,i}$, 296.5; $J_{f,g}$, 303 Hz). MS *m/z*: 447 [M − $CF_3$] (0.6%); 381 [$C_6F_{11}CF(CF_3)$] (5%); 309 (5%); 281 (2%); 243 (2%); 231 (4%); 181 (6%); 162 (2%); 131 (10%); 119 (100%).

Compound **6** (nc): B.p. 155.1–155.8 °C.




$^{19}$F NMR $\delta$: a, 87.4; b, 83.3; c, 84.9; d, 132.6; e, 122.6; f, 124.5; g, 80.3; h, 181.3; i, 117.8; i', 119.0; j, 131.3; j', 130.8; k, 121.5–123.7; l, 139.9; m, 124.4; n, 142.9 ppm ($J_{b,c}$, 145; $J_{e,f}$, 288; $J_{i,j}$, 300; $j_{k,e}$, 290; $J_{m,n}$, 288 Hz). MS *m/z*: 447 [M − $C_2F_5$] (0.5%); 431 [$C_6F_{11}CF(C_2F_5)$] (4%); 309 (4%); 281 (2.5%); 243 (1.5%); 231 (2.8%); 181 (4%); 162 (2%); 131 (8%), 119 (100%).

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