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ON THE ELECTROCHEMICAL FLUORINATION OF DERIVATIVES OF MORPHOLINE AND PIPERIDINE

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SUMMARY

Electrochemical fluorination (ECF) of α,ω-dimorpholino- and dipiperidino-alkanes of different chain length (n = 1-6) and of morpholinocyclohexene gave the perfluoro derivatives in yields up to 45%. By ring contractions, fragmentations and rearrangements several side products were obtained. Conclusions on the mechanism of ECF, based on a sterical model, were drawn.

INTRODUCTION

Since the pioneering work of J.H. Simons, ECF has been the subject of many investigations. This method allows the complete fluorination of a large number of organic compounds with the retention of functional groups. However, in many cases the reported yields are poor, due to the cleavage of the molecule during electrolysis, which leads to a variety of lower boiling by-products, as well as to polymeric tarry materials. Studies of numerous parameters involved in the process have been reported, but most of the published reports are concerned with elucidation of the reaction mechanism which is considered to be very complex. Several mechanisms have been suggested in order to explain this reaction.

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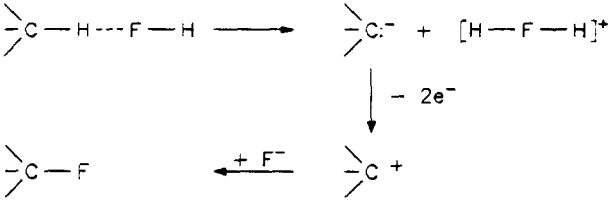
According to the one proposed by Simons [1], this process starts with the anodic oxidation of fluoride ions to F· radicals, which substitute the hydrogen atoms in the organic molecule after homolysis of the C-H bond.

Other theories suppose that the substitution of hydrogen atoms by fluorine atoms occurs by means of higher nickel fluorides as fluorinating agents [2] or through the adsorption on the anode of complexes of the organic compound with nickel fluorides [3].

RESULTS AND DISCUSSION

Our concept for electrofluorination of organic compounds is based on our assumption that the first step is the anodic oxidation of the part of a molecule with the lowest oxidation potential [4]. The electrochemical process is promoted by weakening of the C-H bonds due to hydrogen-fluorine bridges. After anodic withdrawal, the C-F bond is formed by insertion of a fluoride ion, present in the Helmholtz-double-layer at the electrode surface.

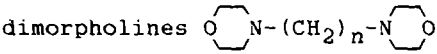


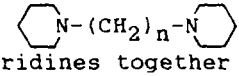
Electrofugal leaving of further hydrogen atoms linked at this carbon atom is promoted by insertion of the strongly electronegative fluoride ion and the formation of the C-F bond. Repetition of this mechanism leads to perfluorination. In these molecules the reaction proceeds until there is complete substitution of hydrogen atoms. After this the perfluorinated molecule leaves the adsorption layer at the anode and moves into the bath.

In general, this interpretation is in accord with the EC_bEC_N mechanism subsequently given by Burdon and co-workers [5], by Rozhkov [6] and by Gambaretto and coworkers [7]. According to this mechanism oxidation of the fluoride anions to radicals and a non-ionic origin for the C-F bond are excluded.

According to our concept [8], the initial anodic oxidation of the compound to be fluorinated is a normal part of electrofluorination. This means that the substitution of hydrogen atoms by fluorine atoms does not occur randomly (as it should do if a radical mechanism is operating), but proceeds with selection, starting at the carbon atom most easily oxidized.

In the course of our research on the synthesis of fluorinated compounds potentially suitable for biomedical application, we have prepared several derivatives of morpholine, piperidine and pyrrolidine via ECF. All runs were performed with the usual Simons equipment. Purification procedures are given in experimental.

ECF of dimorpholines  , n= 2 to 6, gave the corresponding perfluorocarbons. Crude products of these fluorinations were sublimable white solids, consisting of mixtures of perfluorinated products and compounds with residual hydrogen atoms. Hydrogen containing by-products were removed by autoclaving with KOH/ HNR_2 under autogenous pressure and at temperatures near the estimated boiling points. Hydrogen containing by-products cause depression of the melting point and boiling point elevation; see Table I.

ECF of dipiperidines  , n = 2 to 6, gave the corresponding F-dipiperidines together with ring-contracted isomers.

Throughout this article the 'F' symbol (also in the center of a ring) signifies all bonds are to fluorine and the 'F' system for naming perfluorinated organic compounds is based on the authorized ACS [9] nomenclature.

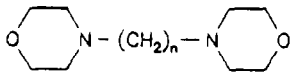
On ECF of morpholinocyclohexene, F-cyclohexylmorpholine and ring opened F-n-hexylmorpholine were obtained.

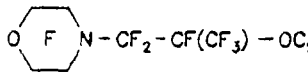
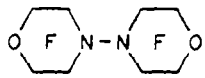
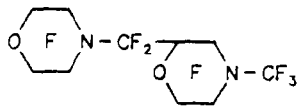
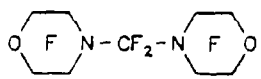
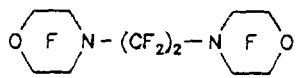
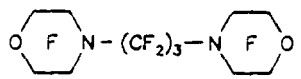
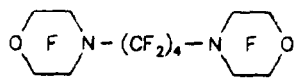
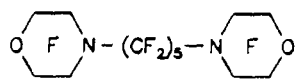
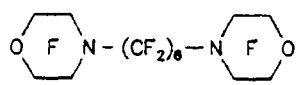
On ECF of dimorpholinomethane or dipiperidinomethane only very small amounts of the corresponding perfluoro methanes were formed, due to a previous reaction of HF with the starting methanes.

ECF results are listed in Table I.

TABLE I

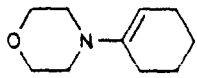
ECF of morpholino- and piperidino-derivatives

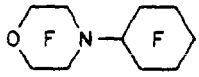
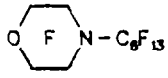
starting material:  ; n = 1 – 6

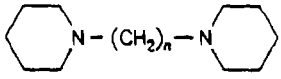
sample	perfluorocarbon obtained		yield	bp [°C] / mp [°C]
n=1		(1a)	0.5%	140–144
		(1b)	0.4%	130–135 137 [10]
		(1c)	0.4%	164–167
		(1d)	0.1%	
n=2		(2a)	28%	163–165 / 75.0–75.5 171.5–172.5/50.5–51.5 [11]
n=3		(3a)	25%	181–183 / 55.5–56.5 184.0–184.5/26.5–27.5 [11]
n=4		(4a)	30%	197–199 / 65.0–66.0
n=5		(5a)	26%	214–216 / 59.5–60.5
n=6		(6a)	20%	224–226 / 79.0–80.0

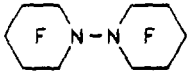
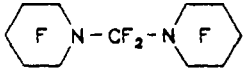
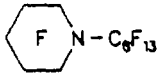
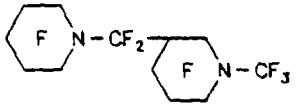
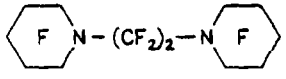
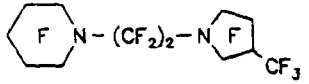
(continued)

TABLE I (cont.)

starting material:  (7)

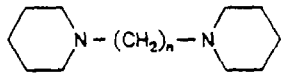
perfluorcarbon obtained	yield	bp [°C]
	31%	148.5–149.5
	12%	149.0–150.5
$(CF_3-O-C_2F_4)-CF_2N-C_6F_{13}$	<0.5%	

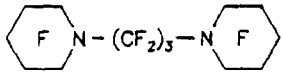
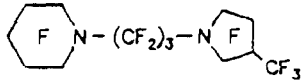
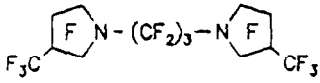
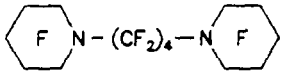
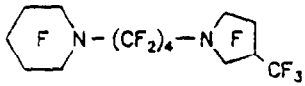
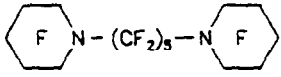
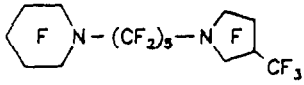
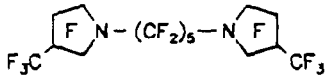
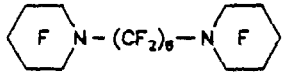
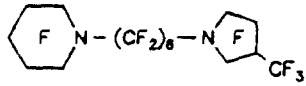
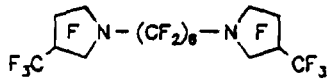
starting material:  ; n = 1 – 6

sample	perfluorcarbon obtained		yield	bp [°C] / mp [°C]
n=1		(8a)	0.1%	
		(8b)	0.1%	
		(8c,d)	1.3%	
		(8e)	0.1%	
n=2		(9a)	25%	185–187 / 87.5–88.5 192.5–193.5/76.0–76.5 [11]
		(9b)	1%	183–185 192–193 [11]

(continued)

TABLE I (cont.)

starting material:  ; n = 1 – 6

sample	perfluorcarbon obtained		yield	bp [°C] / mp [°C]
n=3		(10a)	24%	190–192 / 29–31 199–200/47.0–47.5 [11]
		(10b)	15%	188–190 198–199 [11]
		(10c)	2%	185–187
n=4		(11a)	20%	212–214
		(11b)	2%	209–212
n=5		(12a)	24%	228–231
		(12b)	14%	225–228
		(12c)	4%	220–224
n=6		(13a)	8%	238–242
		(13b)	6%	233–237
		(13c)	2%	229–232

As part of our studies on PFC-oxygen-transport emulsions we found these perfluorinated morpholino-, piperidino- and pyrrolidino-derivatives exhibit favorable properties as oxygen-carrying agents in terms of emulsifiability, particle size stability and pharmacodynamical properties. The polar centers in these heterocyclic compounds improve emulsifiability and the excretion rate by the decrease of the fluorine/carbon ratio. Within the same series of perfluoro-dimorpholines, -dipiperidines and -pyrrolidines a continuous change in the molecular weights and physical properties arises because of the different length of the bridging CF_2-chains.

Our ECF results on morpholino- and piperidinoderivatives give more insights and allow an extension of our explanation of the ECF mechanism.

At a detailed level it must be considered in which direction the molecule moves into the Helmholtz-double-layer and in which sterical position this molecule is adsorbed at the anode which is covered with F^-, HF_2^-, $H_2F_3^-$, etc. ions.

Morpholines and piperidines are heterocycles with electronegative oxygen and nitrogen atoms, which will be protonated in liquid HF and with carbon atoms of different chemical environment. Furthermore bridging with CH_2-groups increases the distance between the heterocycles and leads to different stereo isomers. From the electrofluorinated products conclusions can be drawn on the steric arrangement of the starting material in the anode layer.

ECF of morpholinocyclohexene-(1)

On ECF of morpholinocyclohexene-(1) the main products F-cyclohexylmorpholine and F-n-hexylmorpholine are formed. In a side reaction additional splitting of the morpholine ring takes place.

From our own experiments and according to Gambaretto [7] it can be derived that ECF starts at the morpholine cycle. After its perfluorination the cyclohexene is fluorinated.

ECF of dimorpholines

All heterocyclic molecules considered here are dissolved in liquid hydrogenfluoride by protonation oxygen and nitrogen atoms and by hydrogen-fluorine bridging of the C-H bonds.

Molecules such like dimorpholinopropane could be adsorbed at the anode in such a way that heteroatoms bearing positive charges are furthest from the surface of the anode. These heterocycles have chair conformations. Therefore the steric arrangement is suggested to be as in Fig. 1.

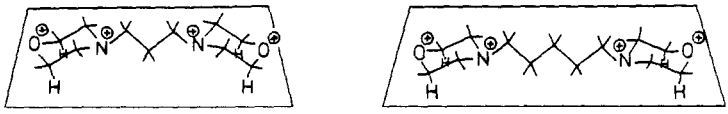


Fig.1.

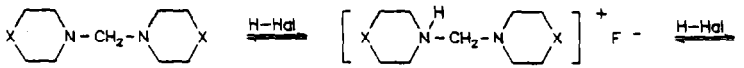
It can be seen that the two axial hydrogen atoms of C-H bonds alpha to oxygen in each ring are nearest to the anode, adsorbed in the Helmholtz layer. These hydrogen atoms bound to the carbon atoms next to the electron-withdrawing oxygen are preferred for electrofugal leaving [4,8]. Cleaving these C-H bonds by loss of a proton and formation of a carbanion gives high electron density at the residual carbon atoms. After oxidation of these carbanions C-F bonds are formed by addition of fluoriode ions.

According to our own experiments and in agreement with Gambaretto [7] in the heterocycles fluorination begins alpha to oxygen and proceeds until there is a complete substitution of hydrogen atoms. After the ring fluorination the same procedure is continued on the bridging CH_2-chain.

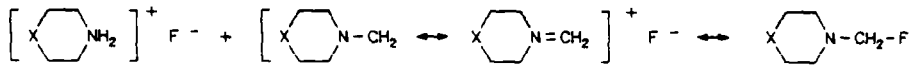
As can be seen in Fig.1, in the case of the propane chain, there are two hydrogen atoms adjacent to the anode and therefore sterically preferred for substitution. It must also be considered, that alpha to nitrogen there are also strongly favoured electrofugal leaving positions, however these may be sterically hindered. Up to now, we cannot define at which position the fluorination of the chain starts. At the end all the hydrogen atoms are substituted.

Accordingly the yield of perfluorinated dimorpholinopropane is very high (34%) and there are no side products.

Our results on ECF in dimorpholinomethane differ from the other alkane derivatives considered here. In hydrogen halide solvents diaminomethanes are cleaved by protons between the methylene group and the ammonium nitrogen [13]. According to an equilibrium reaction large amounts of ammonium salts (IV) and halogenated amines (III) are present in liquid HF.

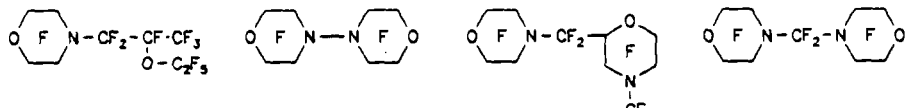


X = O, CH_2



IV III

Therefore on electrolysis of dimorpholinomethane the main products are F-N-methylmorpholine and F-morpholine together with F-1-morpholino-2-ethoxy-propane (1a), F-bimorpholyl (1b) and F-2-(morpholinomethyl)-4-methyl-morpholine (1c) and unidentified products. By GC/MS F-dimorpholinomethane (1d) is only formed in yields <1%.



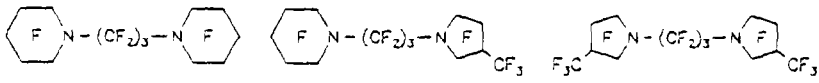
(1a) (1b) (1c) (1d)

ECF of dipiperidines

Because of geometrical similarity dipiperidines should be adsorbed at the anode like the analogous dimorpholines.

Fig.2.

Contrary to dimorpholines, on ECF of dipiperidines besides the expected F-dipiperidines, significant amounts of ring contracted F-3-methylpyrrolidines are formed.
e.g.: in the ratio ca. 12 : 7 : 1



The anodic oxidation process must be explained as follows: Taking dipiperidinopropane, this molecule is adsorbed in the Helmholtz-layer in such an arrangement, that the four axial hydrogen atoms of the C-H bonds beta to nitrogen are nearest to the anode and favoured for electrofugal leaving and with the protonated nitrogen furthest from the electrode. The resulting free electron pair is oxidized. The carbonium-cation formed now has two possibilities for further reactions.

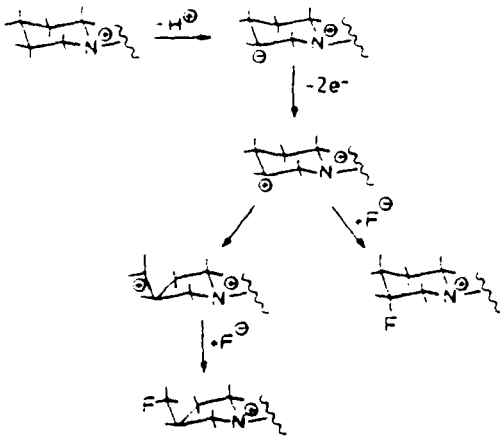
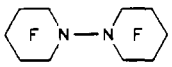


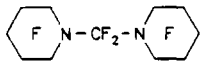
Fig.3.

By addition of a fluoride ion a C-F bond is formed and the fluorination proceeds until the piperidine ring is perfluorinated.The second path is a rearrangement to a five-membered ring, bearing a CH_2^+-group in position 3. The driving force for this contraction is lowering of ring strain. The next step is the addition of a fluoride ion to the CH_2^+-group and so on till perfluorination. The relatively high yields of isomerization products indicate, that an initial oxidation in the alpha position relative to nitrogen is not preferred.

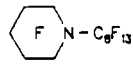
Dipiperidinomethane behaves in liquid HF like dimorpholinomethane. Therefore ECF produces mainly F-N-methylpiperidine and F-piperidine, but F-bipiperidyl (8a), F-dipiperidinomethane (8b), F-n-hexylpiperidine (8c), F-i-hexylpiperidine (8d), F-3-(piperidinomethyl)-1-methylpiperidine (8e) and ring-contracted isomers are formed.



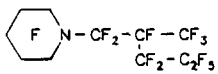
(8a)



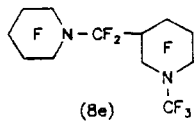
(8b)



(8c)



(8d)



(8e)

These results are in good agreement with our steric model of ECF.

EXPERIMENTAL

Reagents

Starting materials for ECF were synthesized by known methods. Dimorpholinomethane and dipiperidinomethane were synthesized from morpholine or piperidine and formalin. Morpholinocyclohexene-(1) was obtained from morpholine and cyclohexanone. Dimorpholino- (n=2-6) and dipiperidino-derivatives (n=2-6) were prepared from morpholine or piperidine and dibromo- or dichloroalkanes.

Hydrogen fluoride (>99,5% pure, KaliChemie) used for ECF was dried by electrolysis.

Apparatus

Fluorination

ECF was carried out in the usual Simons equipment [1]. Conductivity additives were not used in the experiments. Experimental conditions are given in Table II.

TABLE II

cell volume	960 ml	300 ml
anodic surface area	1500 cm^2	450 cm^2
cell temperature	-8°C - + 10°C	-5°C - + 10°C
current density	2 - 13 mA/cm^2	2 - 20 mA/cm^2
voltage	5.0 - 7.5 V	5.0 - 7.0 V

The gaseous products, collected in traps, were subjected to purification with alkali fluoride and washed with an aqueous solution of $NaHCO_3$.

The crude liquid or solid products drawn off the cell were washed with an aqueous solution of $NaHCO_3$ and treated with KOH and secondary amine. The residue was fractionally distilled. The main components were isolated by preparative scale gas chromatography and identified by ^{19}F-nmr, GC, MS, IR and total fluorine content.

Gas chromatography

GC was carried out on a Gira CAP 12 gas chromatograph, equipped with a thermal conductivity detector using columns I, II, III for analytical and preparative scale separations (Helium as carrier gas).

I: copper column (3 m x 6 mm id) packed with 30% SE 30 on Chromosorb P 60-80 mesh
II: copper column (5 m x 4 mm id) packed with 10% SE 30 on Chromosorb P 80-100 mesh
III: glass column (1.7 m x 3 mm id) packed with molecular sieve 5 A, 40-60 mesh

Spectroscopy

NMR spectra were recorded on a Varian EM 360 L spectrometer operating at 60 MHz for ^1H and 56.4 MHz for ^{19}F. The F-nmr chemical shifts are expressed in terms of (-) ppm upfield of internal $CFCl_3$. Mass spectra were recorded on a Varian Mat 711 at 70 eV.

TABLE III

^{19}F and MS data of products (1a-6a) obtained on ECF of morpholino-derivatives

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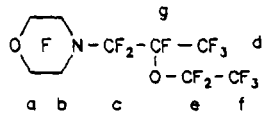
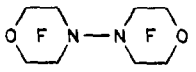
(1a) 

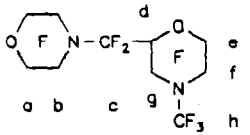
^{19}F: chemical shift (ppm*), assignment
-87.2 (a); -91.9 (b); -84.7 (c); -78.7 (d); -90.0 (e); -86.5 (f); -141.4 (g)

MS: mass number (formula; relative intensity for significant fragments) m/z 496 ($M-F^+$; 2.3), 380 ($C_7F_{14}NO^+$; 5.2), 285 ($C_5F_{11}O^+$; 10.1), 280 ($C_5F_{10}NO^+$; 50.7), 119 ($C_2F_5^+$; 100)

(1b) 

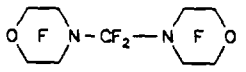
^{19}F: -86.6 (a); -96.6 (b)

MS: m/z 460 (M^+; 8.4), 441 ($M-F^+$; 15.8), 100 ($C_2F_4^+$; 100)

(1c) 

^{19}F: -86.6 (a); -90.8 (b); -83.1 (c); -122.1 (d); -84.7 (e); -87.4 (e); -90.8 (f); -88.1 (g); -51.3 (h)

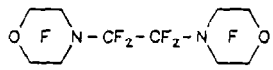
MS: m/z 541 ($M-F^+$; 9.9), 330 ($C_6F_{12}NO^+$; 11.1), 280 ($C_5F_{10}NO^+$; 100), 119 ($C_2F_5^+$; 70.8)

(1d) 

MS: m/z 491 ($M-F^+$; 3.9), 280 ($C_5F_{10}NO^+$; 100)

(continued)

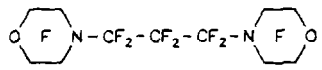
TABLE III (cont.)

(2a) 

a b c

^{19}F: -87.3 (a); -92.7 (b); -94.9 (c)

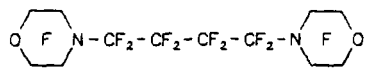
MS: m/z 541 ($M-F^+$; 3.3), 330 ($C_6F_{12}NO^+$; 9.3), 280 ($C_5F_{10}NO^+$; 88.0), 119 ($C_2F_5^+$; 100)

(3a) 

a b c d

^{19}F: -87.1 (a); -92.2 (b); -90.0 (c); -124.6 (d)

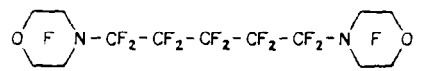
MS: m/z 591 ($M-F^+$; 2.8), 380 ($C_7F_{14}NO^+$; 6.9), 280 ($C_5F_{10}NO^+$; 100), 169 ($C_3F_7^+$; 35.4), 119 ($C_2F_5^+$; 77.2)

(4a) 

a b c d

^{19}F: -87.2 (a); -92.0 (b); -90.0 (c); -123.5 (d)

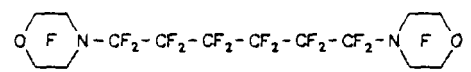
MS: m/z 641 ($M-F^+$; 4.6), 430 ($C_8F_{16}NO^+$; 8.4), 280 ($C_5F_{10}NO^+$; 100), 219 ($C_4F_9^+$; 3.3)

(5a) 

a b c d

^{19}F: -87.3 (a); -92.2 (b); -90.1 (c); -123.4 (d)

MS: m/z 691 $M-F^+$; 7.8), 480 ($C_9F_{18}NO^+$; 5.4), 280 ($C_5F_{10}NO^+$; 100), 269 ($C_5F_{11}^+$; 5.5)

(6a) 

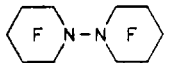
a b c d e

^{19}F: -87.3 (a); -92.0 (b); -90.0 (c); -121.7 (d); -122.6 (e)

MS: m/z 741 ($M-F^+$; 7.5), 530 ($C_{10}F_{20}NO^+$; 3.0), 319 ($C_6F_{13}^+$; 1.5), 280 ($C_5F_{10}NO^+$; 100)

TABLE IV

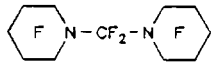
^{19}F and MS data of products (8a-13c) obtained on ECF of dipiperidino-derivatives (n=1-6)

(8a) 

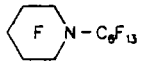
a b c

^{19}F: -132.9 (a); -131.7 (b); -96.0 (c)

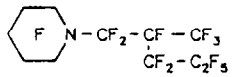
MS: m/z 528 (M^+; 6.68), 509 ($M-F^+$; 16.6)

(8b) 

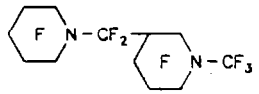
MS: m/z 559 ($M-F^+$; 4.2), 314 ($C_6F_{12}N^+$; 100), 264 ($C_5F_{10}N^+$; 5.1)

(8c) 

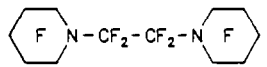
MS: m/z 564 ($M-F^+$; 15.6), 319 ($C_6F_{13}^+$; 19.9), 314 ($C_6F_{12}N^+$; 36.6)

(8d) 

MS: m/z 564 ($M-F^+$; 15.3), 319 ($C_6F_{13}^+$; 19.1), 314 ($C_6F_{12}N^+$; 58.6)

(8e) 

MS: m/z 609 ($M-F^+$; 8.5), 314 ($C_6F_{12}N^+$; 84.5)

(9a) 

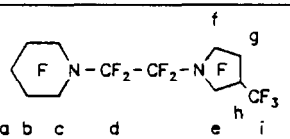
a b c d

^{19}F: -134.4 (a); -131.9 (b); -91.0 (c); -93.4 (d)

MS: m/z 609 ($M-F^+$; 3.4), 364 ($C_7F_{14}N^+$; 9.7), 314 ($C_6F_{12}N^+$; 89.2), 119 ($C_2F_5^+$; 100)

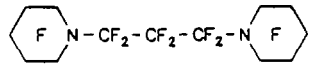
(continued)

TABLE IV (cont.)

(9b) 

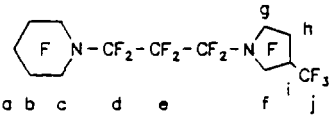
^{19}F: -134.4 (a); -131.9(b); -91.2 (c); -93.5 (d); -79.9 and -83.0 (e) J=170Hz; -97.3 and -97.9 (f) J=215Hz; -125.6 and -130.5 (g) J=240Hz; -184.0 (h); -73.5 (i)

MS: m/z 609 ($M-F^+$; 7.6), 364 ($C_7F_{14}N^+$; 12.3), 314 ($C_6F_{12}N^+$; 84.7), 119 ($C_2F_5^+$; 100)

(10a) 

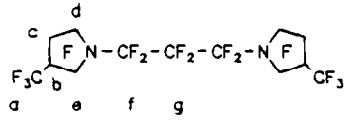
^{19}F: -135.1 (a); -132.8 (b); -91.7 (c); -90.2 (d); -125.3 (e)

MS: m/z 659 ($M-F^+$; 2.0), 414 ($C_8F_{16}N^+$; 12.8), 314 ($C_6F_{12}N^+$; 100), 169 ($C_3F_7^+$; 35.2)

(10b) 

^{19}F: -135.1 (a); -132.7 (b); -91.5 (c); -89.8 (d) -124.2 (e); -79.7 and -82.8 (f) J=175Hz; -97.1 and -97.7 (g) J=220Hz; -125.5 and -130.5 (h) J=250Hz; -184.1 (i); -73.6 (j)

MS: m/z 659 ($M-F^+$; 6.3), 414 ($C_8F_{16}N^+$; 17.9), 314 ($C_6F_{12}N^+$; 100), 169 ($C_3F_7^+$; 31.6)

(10c) 

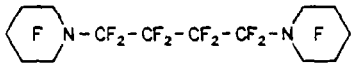
^{19}F: -73.0 (a); -183.4 (b); -124.9 and -129.9 (c) J=250Hz; -96.9 and -97.5 (d) J=220Hz; -79.4 and -82.3 (e) J=175Hz; -89.7 (f); -123.1 (g)

MS: m/z 659 ($M-F^+$; 3.0), 414 ($C_8F_{16}N^+$; 21.3). 314 ($C_6F_{12}N^+$; 100), 169 ($C_3F_7^+$; 40.4)

(continued)

TABLE IV (cont.)

(11a)

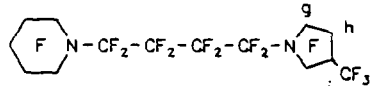


a b c d e

^{19}F: -134.5 (a); -132.1 (b); -90.5 (c); -89.0 (d); -123.3 (e)

MS: m/z 709 ($M-F^+$; 3.2), 464 ($C_9F_{18}N^+$; 9.7),
314 ($C_8F_{16}N^+$; 100), 219 ($C_4F_9^+$; 40.3)

(11b)

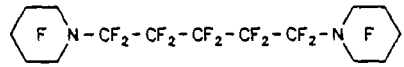


a b c d e f i j

^{19}F: -134.4 (a); -132.1 (b); -90.5 (c); -89.1 (d); -123.6 (e);
-79.5 and -82.6 (f) J=180Hz; -97.0 and -97.6 (g) J=210Hz;
-125.4 and -130.3 (h) J=255Hz; -183.9 (i); -73.4 (j)

MS: m/z 709 ($M-F^+$; 8.1), 464 ($C_9F_{18}N^+$; 13.9),
314 ($C_8F_{16}N^+$; 100), 219 ($C_4F_9^+$; 33.5)

(12a)

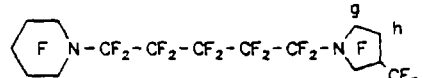


a b c d e

^{19}F: -134.3 (a); -131.8 (b); -90.6 (c); -88.9 (d); -122.5 (e)

MS: m/z 759 ($M-F^+$; 5.8), 514 ($C_{10}F_{20}N^+$; 11.0),
314 ($C_6F_{12}N^+$; 100), 269 ($C_5F_{11}^+$; 13.9)

(12b)



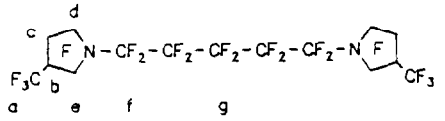
a b c d e f i j

^{19}F: -134.5 (a); -132.0 (b); -90.7 (c); -89.1 (d); -122.8 (e);
-79.5 and -82.4 (f) J=170Hz; -97.0 and -97.6 (g) J=220Hz;
-125.4 and -130.1 (h) J=250Hz; -184.3 (i); -73.4 (j)

MS: m/z 759 ($M-F^+$; 4.6), 514 ($C_{10}F_{20}N^+$; 16.2),
314 ($C_6F_{12}N^+$; 100), 269 ($C_5F_{11}^+$; 15.2)

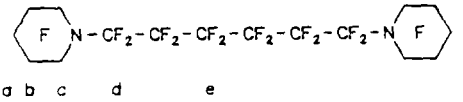
(continued)

TABLE IV (cont.)

(12c) 

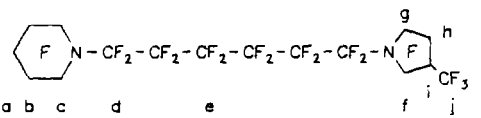
^{19}F: -73.3 (a); -183.9 (b); -125.3 and -130.4 (c) J=250Hz; -96.9 and -97.5 (d) J=220Hz; -79.5 and -82.6 (e) J=170Hz; -89.2 (f); -122.6 (g)

MS: m/z 759 ($M-F^+$; 6.5), 514 ($C_{10}F_{20}N^+$; 20.7), 314 ($C_6F_{12}N^+$; 100), 269 ($C_5F_{11}^+$; 19.0)

(13a) 

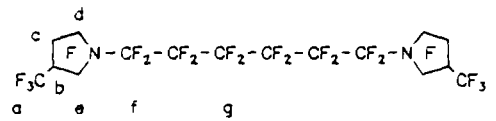
^{19}F: -134.1 (a); -131.9 (b); -90.8 (c); -89.1 (d); -122.1 (e)

MS: m/z 809 ($M-F^+$; 6.9), 564 ($C_{11}F_{22}N^+$; 8.4), 319 ($C_6F_{13}^+$; 2.2), 314 ($C_6F_{12}N^+$; 100)

(13b) 

^{19}F: -134.7 (a); -132.4 (b); -91.3 (c); -89.5 (d); -122.8 (e); -79.3 and -82.4 (f) J=175Hz; -96.8 and -97.4 (g) J=220Hz; -125.2 and -129.9 (h) J=250Hz; -183.9 (i); -73.3 (j)

MS: m/z 809 ($M-F^+$; 10.3), 564 ($C_{11}F_{22}N^+$; 9.8), 319 ($C_6F_{13}^+$; 1.5), 314 ($C_6F_{12}N^+$; 100)

(13c) 

^{19}F: -73.1 (a); -183.7 (b); -125.0 and -129.9 (c) J=250Hz; -96.7 and -97.3 (d) J=220Hz; -79.2 and -82.3 (e) J=175Hz; -89.7 (f); -123.0 (g)

MS: m/z 809 ($M-F^+$; 11.2), 564 ($C_{11}F_{22}N^+$; 12.9), 319 ($C_6F_{13}^+$; 2.0), 314 ($C_6F_{12}N^+$; 100)

ECF of dimorpholino- and dipiperidino-alkanes

In a typical experiment a total of 57g 1.4-dimorpholino-butane was dissolved in 150 ml HF. During the run, the solution was added periodically to the cell maintaining the concentration of organic material between 5-10%. The electrolysis was carried out with a cell voltage of 5.0-6.5 V, an anodic current density of 2-15 mA/cm^2 and a cell temperature between -5 and +8°C. HF was added as needed to replace that consumed in the reaction and also lost through the condensing system. The resulting solid crude product was collected (80 g), washed with water and 2M $NaHCO_3$ solution and then treated with a mixture of 8M aq. KOH and dibutylamine (1:1 by volume) in an autoclave at 200°C for 72 hours. The lower layer was separated, washed with water, 2M HCl, water and acetone and then fractionated to yield 50 g F-dimorpholinobutane (product-yield 30%, bp. 197 - 198°C). Structure and purity were confirmed by GC, ^{19}F-nmr, MS, IR and elemental analysis.

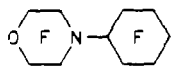
ECF of morpholinocyclohexene-(1)

A total of 125 g morpholinocyclohexene dissolved in HF was electrolysed at 5.0-6.7 V, 20-2 mA/cm^2, -3 - +10 °C to give 240 g fluorinated product which was periodically drained off the cell. The crude product was purified as described above to yield a bulk fraction (164 g ≈ 43%) boiling at 149°C-154°C. The fraction contained mainly two components: 71% of F-cyclohexylmorpholine (bp. 148-149°C) and 28% of F-n-hexylmorpholine (bp. 149-150 °C). These components were isolated by preparative scale gas chromatography using column II and identified by ^{19}F-nmr and MS. According to MS the minor product (<1%) was F-N-(2 methoxy)ethyl-N,N-methylhexylamine.

Another separation of the reaction products was found by means of molecular sieves with pore diameters of 5Å [14]. Only the acyclic perfluoro-chains could be retained in such pores whereas the fluorinated cycles are too large to move inside. In this way F-n-hexylmorpholine was separated from F-cyclohexylmorpholine.

TABLE V

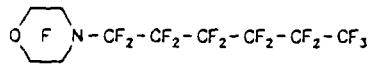
^{19}F and MS data of products obtained on ECF of morpholino-cyclohexene-(1)



a b c d e f

^{19}F: -85.0 (a); -86.5 (b) J=28Hz; -156.2 (c); -118.5 and -133.0 (d) J=293Hz; -121.5 and -138.5 (e) J=295Hz; -123.0 and -142.0 (f) J=298Hz

MS: m/z 511 (M^+; 4.3), 492 ($M-F^+$; 9.7), 326 ($C_7F_{12}N^+$; 6.2), 281 ($C_6F_{11}^+$; 3.1), 280 ($C_5F_{10}NO^+$; 6.0)



a b c d e f g

^{19}F: -87.7 (a); -92.4 (b); -90.3 (c); -122.6 (d); -123.0 (e); -126.4 (f); -81.5 (g)

MS: m/z 530 ($M-F^+$; 3.8), 319 ($C_6F_{13}^+$; 7.8), 280 ($C_5F_{10}NO^+$; 50.8)

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