The electrochemical fluorination of derivatives of morpholine, piperidine and carbazole

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Abstract

Electrochemical fluorination (ECF) of various heterocyclic compounds has been investigated. In the case of 1-morpholinocyclohexene, a survey of the products of ECF is given. ECF of α,ω-dimorpholino- and dipiperdino-alkanes of different chain length ($n = 1–6$) gave the perfluoro derivatives in yields up to 45%. The crystal and molecular structure of *F*-dimorpholinobutane is presented. 1,3-Bis(3-methylpiperidino)propane and 1,3-bis(4-methylpiperidino)propane were fluorinated. Perhydro-*N*-carbazoles were fluorinated by ECF as representatives of a new class of compounds. Electrochemical fluorination of 18-crown-6 was tried without success. The mechanism of ECF for these compounds is discussed on the basis of a steric model.

Introduction

Electrochemical fluorination (ECF) is one of the most commonly used methods for the fluorination of nitrogen-containing materials. Japanese groups have fluorinated a large variety of tertiary amines for use as blood substitutes [1–3]. Moore [4] has fluorinated aminoethers for use in many technical applications.

The mechanism of ECF is widely discussed in the literature [5–11]. In this work tertiary amines of potential use in the formulation of blood substitutes were fluorinated. Conclusions on the mechanism of ECF, based on a steric model, are discussed.

Results and discussion

The compounds found on ECF of 1-morpholinocyclohexene (**1**) are shown in Scheme 1. The starting material, 1-morpholinocyclohexene, was fluorinated without previous saturation of the double bond. The total yield of perfluorinated products was 45%. These contained 58% of *F*-cyclohexylmorpholine (**2**). As side-reactions, ring-contraction of the cyclohexyl ring took place leading to compounds **3**, **4** and **5**. Ring-opening reactions led to compounds **6** and **7**. As minor side-reactions, opening of the morpholine

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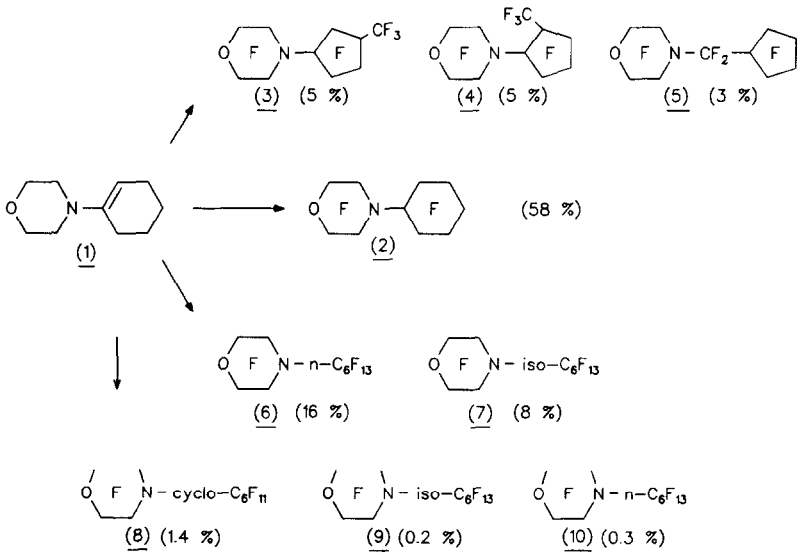


Scheme 1. Products of the electrochemical fluorination of 1-morpholinocyclohexene.

ring gave compounds **8, 9** and **10**. The distribution of the compounds observed was in accord with the results of Ono *et al.* [3] for ECF of piperidinocyclohexane.

If morpholinocyclohexane was used as the starting material, neither the yield of perfluorinated products nor the distribution was changed significantly.

Dimorpholinoalkanes, where $n = 1$–6, have also been fluorinated. The results obtained are shown in Table 1. With the exception of the alkane with $n = 1$, perfluorinated dimorpholinoalkanes were obtained as white solids in good yield. Where $n = 2$ and 3, the observed melting points were significantly higher than those published by Hayashi *et al.* [12]. In the case of $n = 1$, only very small amounts of perfluorinated products **11, 12** and **13** were found, and only traces of the desired *F*-dimorpholinomethane (**14**).

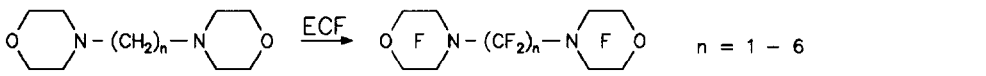
For *F*-1,4-dimorpholinobutane (**17**), it was possible to obtain the crystal structure. The substance crystallizes in the monoclinic space group $P2_1/n$. The lattice constants are $a = 1074.5$ pm, $b = 1101.1$ pm, $c = 822.2$ pm, $\alpha = 90°$, $\beta = 95.1°$ and $\gamma = 90°$. Unit cell volume and X-ray density were $V = 969.05 \times 10^6$ pm^3 and $\rho = 2.262$ g cm^{-3}. The number of molecules per unit cell was two. The confidence coefficient for the structure was $R = 0.047$.

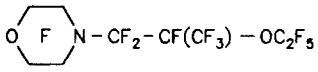
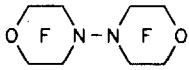
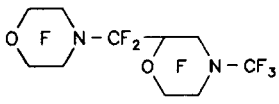
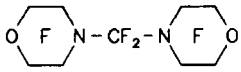
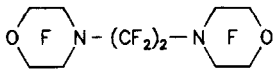
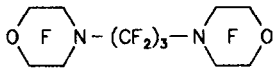
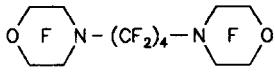
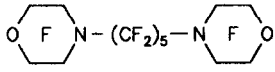
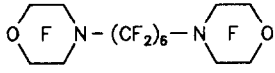
Figure 1 shows the molecular structure of *F*-1,4-dimorpholinobutane. Some geometrical parameters are listed in Table 2. The average C–F bond length of 1.33 Å is in accord with literature values [14]. The average C–C bond length is a little longer than that in alkanes. The angles between the heteroatoms and carbon are larger than in perfluorocyclohexane and deviate from tetrahedral geometry [15].

We have information here on the structure of this type of perfluoro compound for the first time. Data obtained from this structure were helpful

TABLE 1

Electrochemical fluorination of α,ω-dimorpholinoalkanes



	Perfluorocarbon		Yield (%)	B.p. (°C)/m.p. (°C)
$n=1$		(11)	0.5	140–144
		(12)	0.4	130–135 137 [13]
		(13)	0.4	164–167
		(14)	<0.1	152–155
$n=2$		(15)	28	164/75.5 171.5–172.5/50.5–51.5 [12]
$n=3$		(16)	44	182/56.0 184.0–184.5/26.5–27.5 [12]
$n=4$		(17)	39	198/65.6
$n=5$		(18)	43	215/60.0
$n=6$		(19)	20	225/79.5

in developing the concept of the insertion of morpholines into the anode Helmholtz layer. EFC of α,ω-dipiperidines with $n=1$–6 gave the products shown in Table 3. For $n=1$, only very small amounts of perfluorinated products were found and the desired *F*-dipiperidinomethane (**20**) was obtained in 0.3% yield. In the other cases, yields up to 25% for the straight perfluorinated product and varying amounts of ring-contraction products were found, with either single or two-fold ring contraction occurring in the latter case. For $n=3$ and 5, large amounts of ring-contraction products were formed, with yields of 17% and 18%, respectively. On the other hand, for $n=2$ and 4

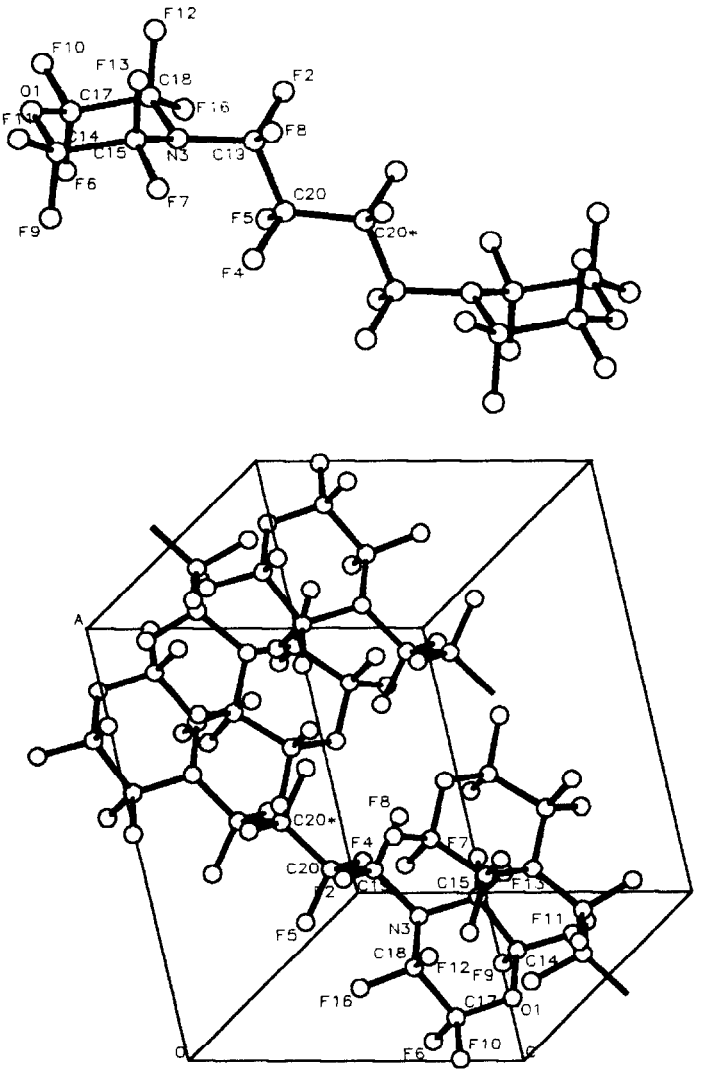


Fig. 1. Molecular and crystal structure of perfluoro-1,4-dimorpholinobutane.

only small yields of 1% and 2%, respectively, were observed. In the case of $n=2$ and 3, the same products as described by Hayashi *et al.* [12] were found.

As far as the mechanism of ECF is concerned, we believe that it proceeds via an EC_bEC_N process [11]. If dimorpholinopropane is considered as in the Helmholtz layer of the anode, as shown in Fig. 2, the axial hydrogens next to oxygen are nearest to the anode and will be fluorinated first. ECF will thus begin α to oxygen and proceed until the whole molecule is fluorinated. This is in accord with the results of Gambaretto *et al.* [5, 6] for the ECF

TABLE 2

Geometrical parameters of *F*-1,4-dimorpholinobutane

Bond lengths (Å) (±0.005)					
$C_{14}-F_9$	1.339	$C_{14}-F_{11}$	1.321	$C_{15}-F_7$	1.361
$C_{15}-F_{13}$	1.350	$C_{17}-F_6$	1.341	$C_{17}-F_{10}$	1.360
$C_{18}-F_{12}$	1.353	$C_{18}-F_{16}$	1.327	$C_{19}-F_2$	1.335
$C_{19}-F_8$	1.359	$C_{20}-F_4$	1.343	$C_{20}-F_5$	1.361
$C_{18}-C_{17}$	1.575	$C_{14}-C_{15}$	1.576	$C_{19}-C_{20}$	1.572
$C_{14}-O_1$	1.412	$C_{17}-O_1$	1.377	$C_{15}-N_3$	1.440
$C_{18}-N_3$	1.475	$C_{19}-N_3$	1.483		
Bond angles (°)					
$F_9-C_{14}-O_1$	110.6(±0.4)	$F_{11}-C_{14}-F_9$	109.4(±0.3)	$F_{11}-C_{14}-O_1$	106.1(±0.3)
$C_{15}-C_{14}-O_1$	114.0(±0.3)	$C_{15}-C_{14}-F_9$	107.9(±0.3)	$C_{15}-C_{14}-F_{11}$	108.0(±0.3)
$F_7-C_{15}-N_3$	110.2(±0.3)	$F_{13}-C_{15}-N_3$	112.3(±0.3)	$F_{13}-C_{15}-F_7$	107.1(±0.3)
$C_{14}-C_{15}-N_3$	110.7(±0.3)	$C_{14}-C_{15}-F_7$	109.9(±0.3)	$C_{14}-C_{15}-F_{13}$	107.4(±0.3)
$F_6-C_{17}-O_1$	111.2(±0.4)	$F_{10}-C_{17}-O_1$	106.0(±0.3)	$F_{10}-C_{17}-F_6$	107.6(±0.3)
$C_{18}-C_{17}-O_1$	112.9(±0.3)	$C_{18}-C_{17}-F_6$	110.3(±0.3)	$C_{18}-C_{17}-F_{10}$	110.3(±0.3)
$F_{12}-C_{18}-N_3$	112.1(±0.3)	$F_{16}-C_{18}-N_3$	110.6(±0.3)	$F_{16}-C_{18}-F_{12}$	108.2(±0.3)
$C_{17}-C_{18}-N_3$	111.7(±0.3)	$C_{17}-C_{18}-F_{12}$	106.7(±0.3)	$C_{17}-C_{18}-F_{16}$	107.4(±0.3)
$N_3-C_{19}-F_2$	109.0(±0.3)	$F_8-C_{19}-F_2$	108.6(±0.3)	$F_8-C_{19}-N_3$	111.1(±0.3)
$C_{20}-C_{19}-F_2$	109.7(±0.3)	$C_{20}-C_{19}-N_3$	110.8(±0.3)	$C_{20}-C_{19}-F_8$	107.6(±0.3)
$F_5-C_{20}-F_4$	109.2(±0.3)	$C_{19}-C_{20}-F_4$	108.0(±0.3)	$C_{19}-C_{20}-F_5$	106.3(±0.3)
$C_{18}-N_3-C_{15}$	115.0(±0.3)	$C_{19}-N_3-C_{15}$	116.6(±0.3)	$C_{19}-N_3-C_{18}$	118.3(±0.3)
$C_{17}-O_1-C_{14}$	115.0(±0.3)				

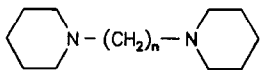
of morpholines. If one now places the analogous piperidino derivative at the anode, the same hydrogens are nearest to the anode and will be fluorinated first (see Fig. 2).

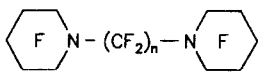
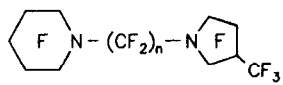
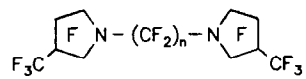
Scheme 2 shows what happens during substitution of the first hydrogen by fluorine in piperidino derivatives. The hydrogen in the 3-position is abstracted. The resulting carbonium ion (**I**) can now add a fluoride ion and will be fluorinated to the corresponding perfluoropiperidino derivative (**II**). The other possibility is a ring contraction to a five-membered ring, leading to a perfluorinated pyrrolidino derivative substituted in the 3-position by a methyl group (**III**). This product also arises if fluorination starts at the 4-position of the piperidine ring. If fluorination starts α to nitrogen, a pyrrolidino derivative substituted in the 2-position is to be expected.

To enable further investigation of this ring-contraction reaction, two methyl-substituted derivatives of dipiperidinopropane were synthesized. The results of ECF are shown in Table 4. On ECF of 1,3-di(3-methylpiperidino)propane (**34**), the perfluoro compound **36** was formed in 29% yield but no five-membered ring systems were found. The only by-products were a ring-expansion product **37** and hydrogen-containing material **38**. ECF of 1,3-di(4-methylpiperidino)propane (**35**) gave the corresponding perfluoro compound **40** in 10% yield. Several ring-contraction products with an ethyl group in the five-membered ring (**39** and **41**) and ring-expansion products

TABLE 3

Electrochemical fluorination of α,ω-dipiperidinoalkanes

Starting material:  ; n = 1 – 6

									
		Yield (%)	B.p. (°C)/m.p. (°C)		Yield (%)	B.p. (°C)/m.p. (°C)		Yield (%)	B.p. (°C)/m.p. (°C)
$n=1$	**(20)**	0.3							
$n=2$	**(21)**	25	186/88.0 192.5–193.5/76.0–76.5 [12]	**(26)**	1	184 192–193 [12]			
$n=3$	**(22)**	24	191/30.0 199–200/47.0–47.5 [12]	**(27)**	15	189 198–199 [12]	**(31)**	2	186
$n=4$	**(23)**	20	213/65.0	**(28)**	2	210			
$n=5$	**(24)**	24	229	**(29)**	14	227	**(32)**	4	223
$n=6$	**(25)**	8	240/65.5	**(30)**	6	236	**(33)**	2	232

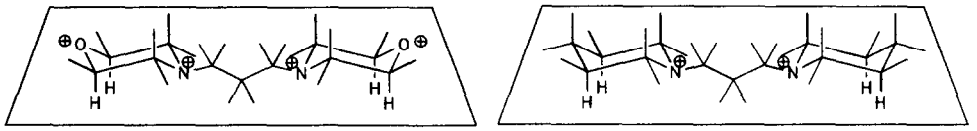
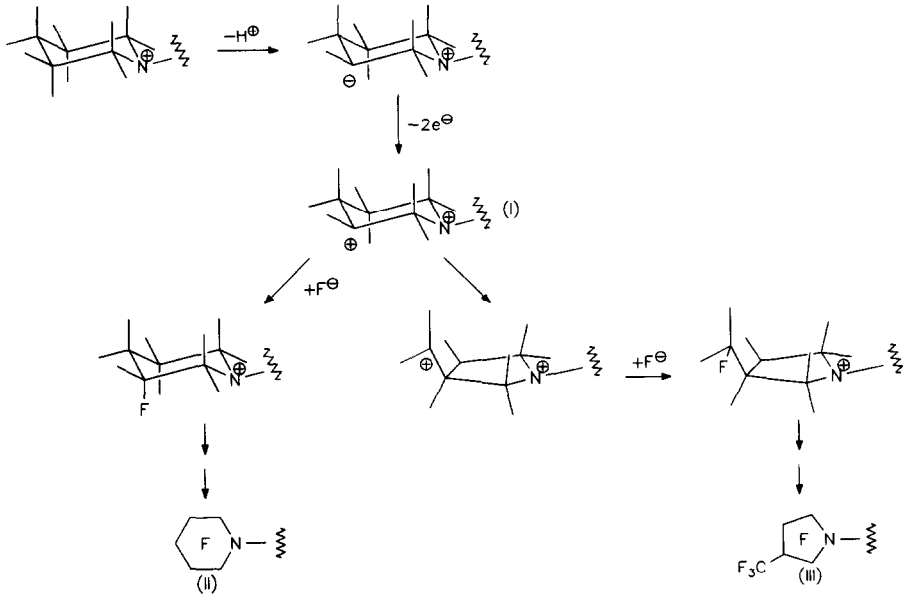


Fig. 2. Insertion of 1,3-dimorpholinopropane and 1,3-dipiperidinopropane in the anode.



Scheme 2. Isomerization of piperidino derivatives during ECF.

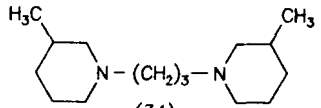
(**41**, **42** and **43**) were formed in minor yield. No five-membered ring with two attached methyl groups occurred.

These results make the ring-contraction process shown in Scheme 3 likely. The axial hydrogen in position 3 is abstracted and the resulting carbonium ion (**IV**) now has the possibility of isomerization to an ethyl-pyrrolidino derivative (**V**). By addition of a fluoride ion to the carbonium ion, the corresponding perfluoro derivative (**VI**) is formed. The products found can only be explained by assuming that ECF starts in the 3-position of the piperidino ring. In the lower part of the Scheme, the mechanism for the formation of the seven-membered ring is given. Here hydrogen abstraction takes place in the methyl group and either the corresponding perfluoro derivative (**VI**) or the seven-membered ring (**VIII**) is formed.

Since they were previously uninvestigated, heterocyclic perhydro-*N*-carbazoles (**50a, b**) were also fluorinated. The total yield of perfluorinated material was 10% for R = methyl and 17% for R = ethyl, boiling over the ranges 193–197 °C and 210–214 °C, respectively. Table 5 lists the perfluorinated products obtained. The yields are expressed as percentages of the perfluorinated products. In both cases, a very similar distribution of products is found with about 70% of the perfluorinated starting material (**44a** and

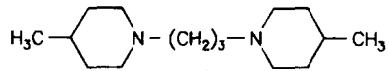
TABLE 4

Electrochemical fluorination of 1,3-di(methylpiperidino)propanes

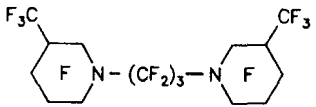
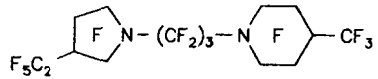
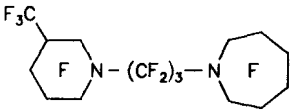
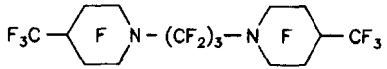
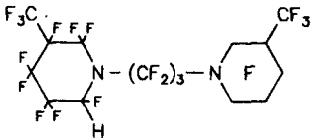
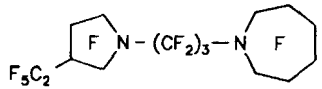
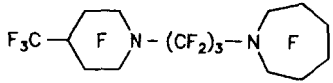
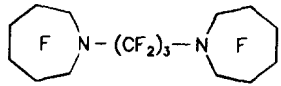


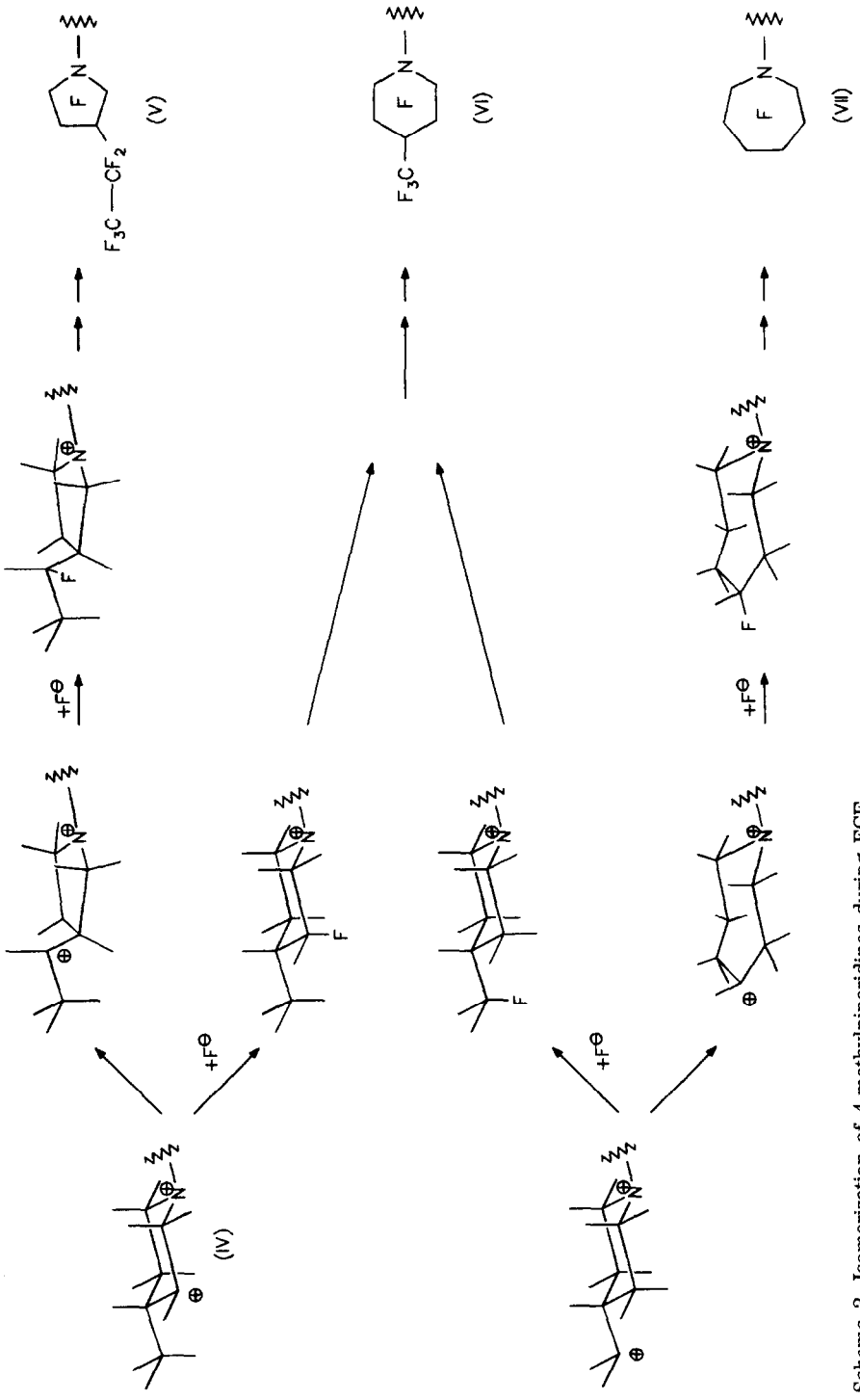
(34)

starting material



(35)

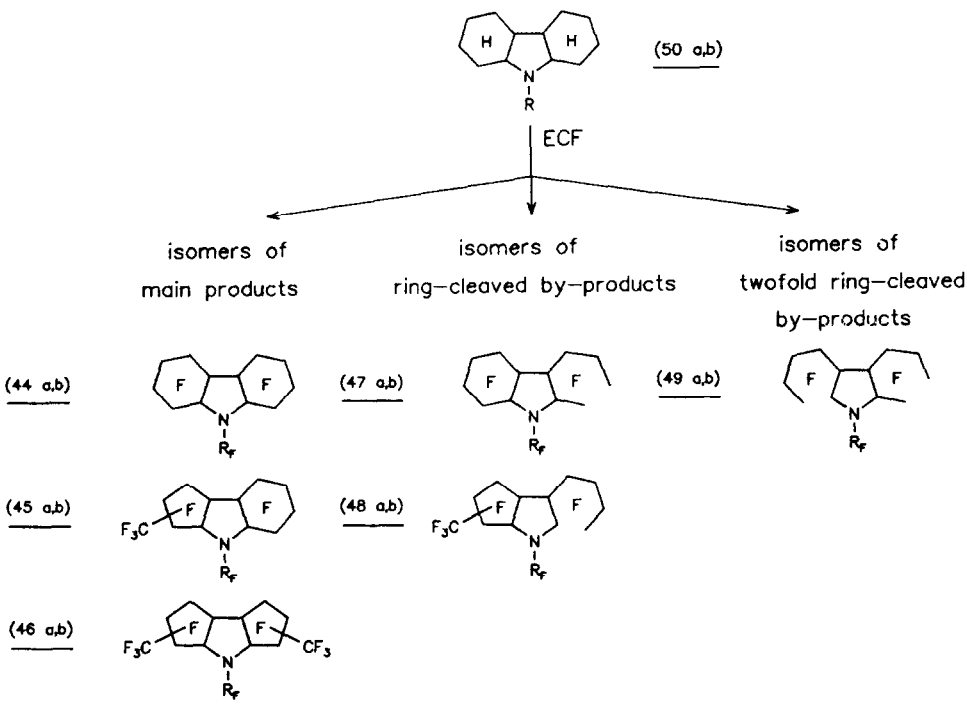
Perfluorocarbon		Yield (%)	Perfluorocarbon		Yield (%)
	(36)	29.2		(39)	2.9
	(37)	0.5		(40)	10.1
	(38)	5.9		(41)	1.3
				(42)	7.3
				(43)	0.2



Scheme 3. Isomerization of 4-methylpiperidines during ECF.

TABLE 5

Products of ECF of perhydro-*N*-alkylcarbazoles



R_F = CF_3 (a)	69 %	23 %	8 %
= C_2F_5 (b)	73 %	21 %	6 %

44b) and ring-contraction products (**45a, b** and **46a, b**), about 20% of products with one ring cleaved (**47a, b** and **48a, b**) and about 7% of two-fold ring-cleaved products (**49a, b**). No product was found in which the five-membered ring had been cleaved.

After these experiments were completed a patent, by Sargent [16] from ISC Chemicals Limited appeared in the literature. He fluorinated carbazoles via the cobalt trifluoride process and his results are consistent with ours.

As far as the mechanism of ECF of perhydrocarbazoles is concerned, many conformers are possible in this case. We believe that the three isomers *cis–anti–cis* (**VIII**), *trans–syn–trans* (**IX**) and *trans–syn–cis* (**X**) are formed preferentially as shown in Fig. 3, which shows how these isomers are inserted on the anode. In every case, the positively charged nitrogen is furthest from the anode. The marked axial hydrogen atoms of the six-membered ring are nearest to the anode and will be abstracted first. The resulting carbonium ion now has the possibility of fluorination or isomerization.

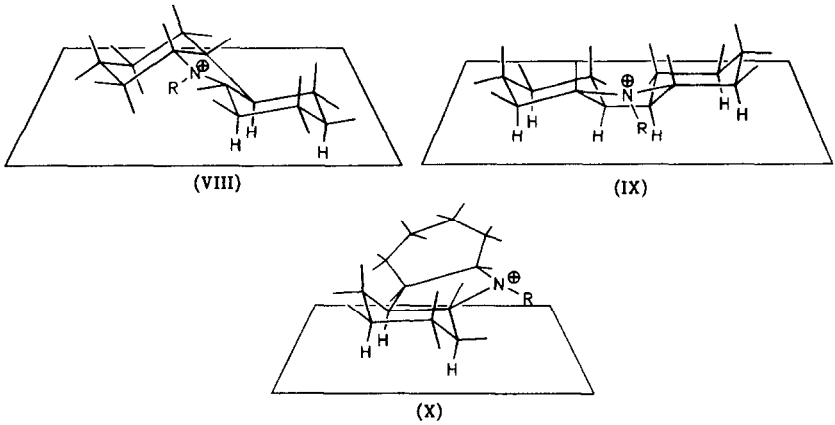


Fig. 3. Insertion of perhydro-*N*-alkylcarbazoles in the anode.

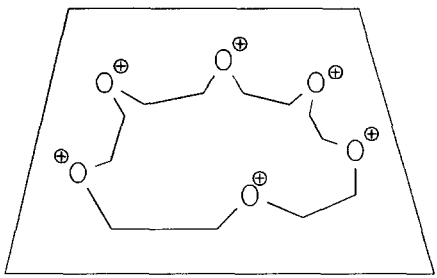


Fig. 4. Insertion of 18-crown-6 in the anode. The positively charged oxygens are furthest from the anode.

Subsequently, studies on the ECF of crown ethers were undertaken. ECF of 18-crown-6 gave only about 1% of fragmentation products such as $CF_3-O-(CF_2)_2-COF$ (**51**), $CF_3-O-C_2F_5$ (**52**) and *F*-dioxan (**53**). In addition, large amounts of gaseous products, such as CF_4 and OF_2, and tarry residues were isolated.

We believe that 18-crown-6 is inserted on the surface of the anode as shown in Fig. 4. The positively charged oxygens are furthest from the anode. A large number of hydrogen atoms (not shown) are near the anode and undergo fluorine exchange at once with so much energy release that the molecule breaks into fragments.

Experimental

Reagents

Starting materials were synthesized by known methods. 1,3-Bis(3-methylpiperidino)propane (**34**) and 1,3-bis(4-methylpiperidino)propane (**35**) had previously been described only as dihydrochlorides [17]. The pure products

were synthesized as follows. The methyl-substituted piperidine (2.1 mol) was dissolved in 300 ml benzene. After heating to 60 °C, 0.5 mol 1,3-dibromopropane was then added. The mixture was refluxed for 2 h and sucked through a Büchner funnel. After removal of the solvent, the liquid oil was distilled in vacuum. The yield was 66% for 1,3-bis(4-methylpiperidino)propane (**35**), boiling at 115 °C/0.5 mbar and 72% for 1,3-bis(3-methyl-piperidino)propane (**34**) boiling at 126 °C/0.5 mbar.

Hydrogen fluoride (>99.5% pure, Solvay Fluor und Derivate GmbH) used for ECF was dried by electrolysis.

Apparatus

Electrochemical fluorination was carried out as described elsewhere [11]. NMR spectra were recorded on a Varian EM 360 L spectrometer operating at 60 MHz for ^1H nuclei and 56.4 MHz for ^{19}F nuclei. ^1H NMR chemical shifts are expressed in ppm for TMS in $CDCl_3$. The ^{19}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. Data for compounds not listed here are described elsewhere [11].

Analyses for 1,3-bis(3-methylpiperidino)propane (**34**) and 1,3-bis(4-methylpiperidino)propane (**35**) were as follows:

Compound **34**: ^1H NMR δ: 2.8 (t, 4H, CH_2-N); 2.3 (t, 4H, CH_2-N); 1.5–1.8 m (m, other 12H); 0.9 (d, 6H, CH_3) ppm.

Compound **35**: ^1H NMR δ: 2.8 (d, 4H, CH_2-N); 2.3 (t, 4H, CH_2-N); 1.9 (d, 4H, CH_2-N); 1.7 (d, 2H, CH); 1.3 (m, 6H, CH_2); 0.9 (d, 6H, CH_3) ppm.

Products of the fluorination of 1-morpholinocyclohexene (**1**) gave the following analyses:

Compound **7**: ^{19}F NMR δ: −87.7 (4F, CF_2-O); −92.4 (4F, CF_2-N); −90.3 (2F, CF_2-N); −120.3 (2F, CF_2); −115.5 (2F CF_2-CF); −185.4 (1F, CF); −72.3 (6F, CF_3) ppm.

Compound **10**: MS *m/z*: 568 ($M-F^+$, 0.5); 319 ($C_6F_{13}^+$, 13.7); 318 ($C_5F_{12}NO^+$, 10.1); 69 (CF_3^+, 100).

Minor products **3**, **4**, **5**, **8** and **9** were not isolated and identified completely, but spectroscopic data indicated their structures.

Products of the fluorination of **34** gave the following analyses:

Compound **36**: ^{19}F NMR δ: −69.7 (6F, CF_3); −71.0 and −92.6 (4F, CF_2-N, $J=228$ Hz); −78.4 and −103 (4F, CF_2-N, $J=215$ Hz); −88.5 (4F, CF_2-N); −120.8 and −132.4 (4F, CF_2-CF, $J=300$ Hz); −120.8 and −139.2 (4F, CF_2, $J=266$ Hz); −123.5 (2F, CF_2); −181 (2F, CF) ppm. MS *m/z*: 759 ($M-F^+$, 4.1); 464 ($M-C_6F_{12}N^+$, 17.4); 364 ($C_7F_{14}N^+$, 100); 169 ($C_3F_7^+$, 38.0).

Compound **37**: ^{19}F NMR δ: −69.9 (3F, CF_3); −71.4 and −92.8 (2F, CF_2-N, $J=236$ Hz); −78.2 and −103.6 (2F, CF_2-N, $J=226$ Hz); −86.1 (6F, CF_2-N); −88.8 (2F, CF_2-N); −121.6 (2F, CF_2); −121.9 and −140.3 (2F, CF_2, $J=268$ Hz); −121.9 and −132.6 (2F, CF_2-CF, $J=284$ Hz); −122.9 (4F, CF_2); −128.1 (4F, CF_2); −181.7 (1F, CF) ppm. MS *m/z*: 778

(M^+, 0.6); 759 ($M-F^+$, 2.7); 464 ($M-C_6F_{12}N^+$, 22.1); 364 ($C_7F_{14}N^+$, 100); 169 ($C_3F_7^+$, 54.6).

Compound **38**: ^{19}F NMR δ: −69.7 (3F, CF_3); −71.2 and −93.5 (2F, CF_2−N, J=230 Hz); −73.5 (3F, CF_3); −78.6 and −102.8 (2F, CF_2−N, J=200 Hz); −83.7 (2F, CF_2−N, J=245 Hz); −86.4 (2F, CF_2−N); −89 (2F, CF_2−N); −121.8 and −133.1 (2F, CF_2−N, J=300 Hz); −121.8 and −140.3 (2F, CF_2−CF, J=255 Hz); −124.7 (2F, CF_2); −125.6 (4F, CF_2, J=294 Hz); −146.3 (1F, CFH−N, J=48 Hz); −181.8 (1F, CF) ppm. MS m/z: 760 (M^+, 0.9); 741 ($M-F^+$, 9.2); 464 ($M-C_6F_{11}HN^+$, 21.5); 446 ($M-C_6F_{12}N^+$, 11.1); 364 ($C_7F_{14}N^+$, 100); 346 ($C_7F_{13}HN^+$, 52.2); 169 ($C_3F_7^+$, 52.0).

Products of the fluorination of **35** gave the following analyses:

Compound **39**: ^{19}F NMR δ: −69.9 (3F, CF_3−CF); −74.6 and −95.2 (2F, CF_2−N, J=195 Hz); −76.2 and −102.9 (4F, CF_2−N, J=212 Hz); −81.5 (3F, CF_3−CF_2); −82.4 and −97.9 (2F, CF_2−N, J=270 Hz); −89.2 (4F, CF_2−N); −118.6 and −130.6 (4F, CF_2−CF, J=274 Hz); −120.4 (2F, CF_2−CF_3); −122.8 (2F, CF_2); −126.3 (2F, CF_2−CF, J=164 Hz); −180.9 (1F, CF); −189.2 (1F, CF) ppm. MS m/z: 759 ($M-F^+$, 8.0); 464 ($M-C_6F_{12}N^+$, 19.6); 426 ($C_9F_{14}N^+$, 6.3); 364 ($C_7F_{14}N^+$, 100); 275 ($C_6F_{10}N^+$, 8.8); 160 ($C_3F_7^+$, 32.8).

Compound **40**: ^{19}F NMR δ: −69.8 (6F, CF_3); −75.8 and −102.1 (8F, CF_2−N, J=204 Hz); −88.6 (4F, CF_2−N); −117.8 and −129.9 (8F, CF_2−CF, J=281 Hz); −123 (2F, CF_2); −188.2 (2F, CF) ppm. MS m/z: 759 ($M-F^+$, 3.7); 464 ($M-C_6F_{12}N^+$, 13.7); 364 ($C_7F_{14}N^+$, 100); 276 ($C_6F_{10}N^+$, 13.1); 169 ($C_3F_7^+$, 34.0).

Compound **41**: ^{19}H NMR δ: −75.2 and −95.8 (2F, CF_2−N, J=192 Hz); −82 (3F, CF_3); −82.9 and 98.1 (2F, CF_2−N, J=259 Hz); −86.4 (6F, CF_2−N); −89.7 (2F, CF_2−N); −120.7 (2F, CF_2−CF_3); −121 (2F, CF_2); −123.1 (4F, CF_2); −126.5 (2F, CF_2−CF, J=264 Hz); −128.3 (4F, CF_2; −181.8 (1F, CF) ppm. MS m/z: 778 (M^+, 0.9); 759 ($M-F^+$, 8.2); 464 ($M-C_6F_{12}N^+$, 28.9); 426 ($C_9F_{14}N^+$, 13.5); 364 ($C_7F_{14}N^+$, 100); 276 ($C_6F_{10}N^+$, 12.0); 169 ($C_3F_7^+$, 42.5).

Compound **42**: ^{19}F NMR δ: −69.7 (3F, CF_3); −75.9 and −102.7 (4F, CF_2−N, J=216 Hz); −85.6 (6F, CF_2−N); −89.1 (2F, CF_2−N); −118.5 and −130.3 (4F, CF_2−CF, J=288 Hz); −121 (2F, CF_2); −122.4 (4F, CF_2); −127.7 (4F, CF_2); −189.1 (1F, CF) ppm. MS m/z: 778 (M^+, 0.9); 759 ($M-F^+$, 3.0); 464 ($M-C_6F_{12}N^+$, 21.2); 364 ($C_7F_{14}N^+$, 100); 276 ($C_6F_{10}N^+$, 18.5); 169 ($C_3F_7^+$, 49.0).

Compound **43**: ^{19}F NMR δ: −86.4 (12F, CF_2−N); −119.5 (2F, CF_2); −123.2 (8F, CF_2); −128.6 (8F, CF_2) ppm. MS m/z: 778 (M^+, 0.8); 759 ($M-F^+$, 1.5); 464 ($M-C_6F_{12}N^+$, 21.1); 364 ($C_7F_{14}N^+$, 100); 276 ($C_6F_{10}N^+$, 20.6); 169 ($C_3F_7^+$, 53.8).

Products of the fluorination of perhydro-*N*-methylcarbazole gave the following analyses:

Compound **44a**: ^{19}F NMR δ: −52 (3F, CF_3−N); −105 to −145 (other 18F); −169 to −185 (2F, CF) ppm. MS m/z: 607 (M^+); 588 ($M-F^+$).

Compound **45a**: ^{19}F NMR δ: −52 (3F, CF_3−N); −72 (3F, CF_3−CF); −105 to −145 (other 14F); −169 to −185 (3F, CF) ppm. MS *m/z*: 607 (M^+); 588 ($M-F^+$).

Compound **46a**: ^{19}F NMR δ: −52 (3F, CF_3−N); −72 (6F, CF_3−CF); −105 to −145 (other 10F); −169 to −185 (4F, CF) ppm. MS *m/z*: 607 (M^+); 588 ($M-F^+$).

Compound **47a**: ^{19}F NMR δ: −52 (3F, CF_3−N); −70 (3F, CF_3−CF); −80 (3F, CF_3-CF_2); −105 to −145 (other 14F); −169 to −185 (2F, CF) ppm. MS *m/z*: 645 (M^+); 626 ($M-F^+$).

Compound **48a**: ^{19}F NMR δ: −52 (3F, CF_3−N); −72 (3F, CF_3−CF); −80 (3F, CF_3-CF_2); −85 (2F, CF_2−N); −105 to −145 (other 11F); −169 to −185 (3F, CF) ppm. MS *m/z*: 645 (M^+); 626 ($M-F^+$).

Compound **49a**: ^{19}F NMR δ: −52 (3F, CF_3−N); −70 (3F, CF_3−CF); −80 (6F, CF_3-CF_2); −85 (2F, CF_2−N); −105 to −145 (other 11F); −169 to −185 (2F, CF) ppm. MS *m/z*: 683 (M^+); 664 ($M-F^+$).

Products of the fluorination of perhydro-*N*-ethylcarbazole gave the following analyses.

Compound **44b**: −80 (3F, CF_3-CF_2); −87 (2F, CF_2−N); −105 to −145 (other 18F); −169 to −185 (2F, CF) ppm. MS *m/z*: 657 (M^+); 638 ($M-F^+$); 588 ($M-CF_3^+$).

Compound **45b**: ^{19}F NMR δ: −72 (3F, CF_3−CF); −80 (3F, CF_3-CF_2); −87 (2F, CF_2−N); −105 to −145 (other 14F); −169 to −185 (3F, CF) ppm. MS *m/z*: 657 (M^+); 638 ($M-F^+$); 588 ($M-CF_3^+$).

Compound **46b**: ^{19}F NMR δ: −72 (6F, CF_3−CF); −80 (3F, CF_3-CF_2); −87 (2F, CF_2−N); −105 to −145 (other 10F); −169 to −185 (4F, CF) ppm. MS *m/z*: 657 (M^+); 638 ($M-F^+$); 588 ($M-CF_3^+$).

Compound **47b**: ^{19}F NMR δ: −70 (3F, CF_3−CF); −80 (6F, CF_3-CF_2); −87 (2F, CF_2−N); −105 to −145 (other 14F); −169 to −185 (2F, CF) ppm. MS *m/z*: 695 (M^+); 676 ($M-F^+$); 626 ($M-CF_3^+$).

Compound **48b**: ^{19}F NMR δ: −72 (3F, CF_3−CF); −80 (6F, CF_3-CF_2); −85 to −93 (4F, CF_2−N); −105 to −145 (other 11F); −169 to −185 (3F, CF) ppm. MS *m/z*: 695 (M^+); 676 ($M-F^+$); 626 ($M-CF_3^+$).

Compound **49b**: ^{19}F NMR δ: −72 (3F, CF_3−CF); −80 (9F, CF_3-CF_2); −85 to −93 (4F, CF_2−N); −105 to −145 (other 11F); −169 to −185 (2F, CF) ppm. MS *m/z*: 714 ($M-F^+$); 664 ($M-CF_3^+$).

Products of the fluorination of 18-crown-6 gave the following analyses:

Compound **51**: ^{19}F NMR δ: −56 (3F, CF_3−O); −87 (2F, CF_2−O) ppm. MS *m/z*: 213 ($M-F^+$).

Compound **52**: ^{19}F NMR δ: −56 (3F, CF_3−O); −90 (2F, CF_2−O); −86 (3F, CF_3) ppm. MS *m/z*: 185 ($M-F^+$).

Compound **53**: ^{19}F NMR δ: −88 (8F, CF_2−O) ppm. MS *m/z*: 213 ($M-F^+$).

The X-ray experiments were undertaken on a Philips PW-1100 diffractometer, using Mo Kα radiation. The crystal size was 0.6×0.3×0.2 mm. The method of solution was the direct method used in the program SHELX [18]. Perfluoro-1,4-dimorpholinobutane crystallizes in the monoclinic space

group $P2_1/n$. The lattice constants were $a=1074.5$ pm, $b=1101.1$ pm, $c=822.2$ pm, $\alpha=90°$, $\beta=95.1°$ and $\gamma=90°$. The unit cell volume and X-ray density were $V=969.05\times10^6$ pm^3 and $\rho=2.262$ g cm^{-3} respectively. The number of molecules per unit cell was two. The confidence coefficient for the final refinement cycle was $R=0.047$.

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