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ELECTROCHEMICAL FLUORINATION OF SOME CYCLIC TERTIARY AMINES (°)

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SUMMARY

Electrochemical fluorination of N,N-diethylcyclohexylamine and N-ethyldicyclohexylamine gave the corresponding F-amines together with several other compounds arising from incomplete fluorination and fragmentation reactions. In the case of N,N-diethylcyclohexylamine yields of 51–52% were obtained and most of the reaction products were isolated and identified. With N-ethyldicyclohexylamine a lower yield (16%) was observed; the resultant reaction mixture was too complex to allow the identification of its components. Comments are made about the reaction mechanism, and NMR and IR data are reported for identified compounds.

INTRODUCTION

In the course of our research on the synthesis of fluorinated compounds potentially suitable for biomedical applications we have prepared several perfluorinated tertiary amines via electrochemical fluorination [1,2]. We report here the results obtained in the case of N,N-diethylcyclohexylamine and N-ethyldicyclohexylamine. Some information is also drawn about the reaction mechanism of the process.

RESULTS AND DISCUSSION

N,N-diethylcyclohexylamine

Electrochemical fluorination of this compound yielded a mixture of the corresponding perfluorinated amine with several other compounds. Most of these were isolated and identified; in

(°) This work was presented at the International Symposium in Paris (Moissan Centenary), August 1986.

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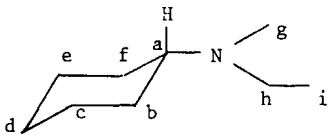
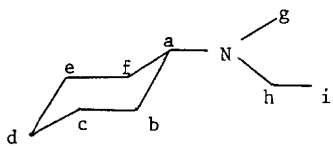
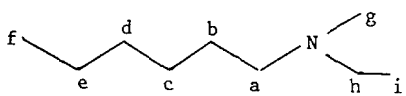
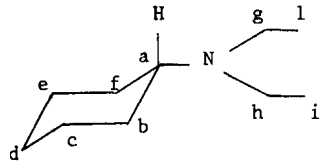
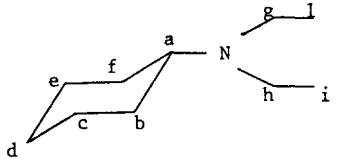
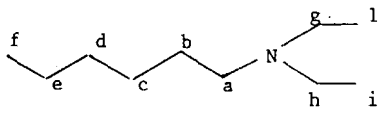
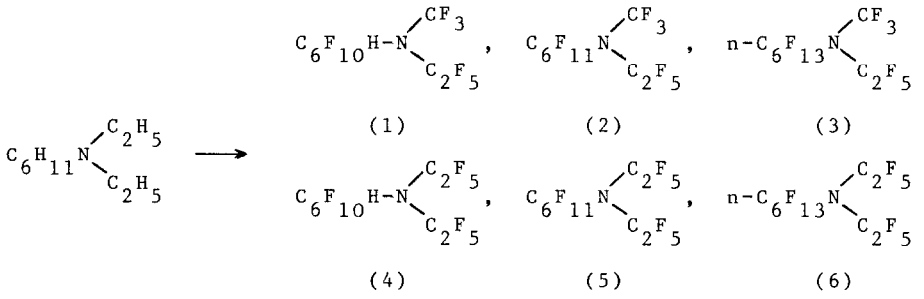
TABLE 1
^{19}F data of identified compounds isolated from the reaction mixture of electrochemical fluorination of N,N-diethylcyclohexylamine (°).

Compound	Structure	Chemical shift (ppm from int.$CFCl_3$)	Relative intensity	Assignment
1		145.7	2	c,e (eq)
		142.0	1	d (eq)
		125	7	b,f
		123		e,c,d (ax)
		99	2	h
		86.5	3	i
		52	3	g
2		155.5	1	a
		142.8	1	d (eq)
		139.1	2	c,e (eq)
		132.4	2	b,f (eq)
		123.6	1	d (ax)
		122.3	2	c,e (ax)
		118.3	2	b,f (ax)
		89.0	2	h
		84.4	3	i
		49.0	3	g
3		126.9	2	e
		123.0	4	c,d
		120.6	2	b
		93.3	2	h
		87.9	2	a
		84.6	3	f
		82.2	3	i
		51.3	3	g

4		146	2	c,e (eq)
		142.4	1	d (eq)
		125	7	b,f
		123		e,c,d (ax)
		97	2	g
		88.5	2	h
		84.5	3	l
		82.5	3	i
5		154.8	1	a
		142.5	1	d (eq)
		138.3	2	c,e (eq)
		133	2	b,f (eq)
		123.5	1	d (ax)
		122	2	c,e (ax)
		117.3	2	b,f (ax)
		85.5	4	g,h
		81.5	6	i,l
6		126.6	2	e
		123.0	4	c,d
		118.0	2	b
		88.9	4	g,h
		84.6	3	f
		81.9	2	a
		81.7	6	i,l

(°) Compounds 1 and 4 presented also a ^{1}H NMR signal at 4.5 and 4.6 ppm (from int. TMS) respectively.

accordance with their molecular structure, the reaction scheme can be represented as follows:



The compounds are numbered in order of increasing GLC retention time. Some of them (compounds 1 and 4) are not completely fluorinated, whereas the others by-products derive from the usual side reactions of fragmentation and isomerization.

The molecular structure of the compounds identified was based mainly on ^{19}F NMR data: the relative assignments are reported in Table 1. The quantitative data obtained from GLC analysis using the internal standard method are reported in Table 2, together with the molar yield of each compound based on the amount of amine fed.

A first interesting remark results from the molecular structure of incompletely fluorinated compounds. Residual hydrogen is always located in the cyclic part of the molecule and bound to the carbon atom next to nitrogen atom. This position, in accordance with the EC_bEC_N mechanism suggested for this process [3,4], is unlikely to undergo the anodic oxidation of the first step, due to the positive charge located on the nitrogen atom; therefore the corresponding hydrogen atom is substituted last. It may be inferred that the hydrogen substitution by fluorine starts from sites far away from nitrogen atom.

Other remarks follow from data of Table 2:

- identified compounds amounted to 65.3% of the reaction mixture;
- molar yield of perfluoro-N,N-diethylcyclohexylamine was somewhat low compared with those of other acyclic tertiary amines (13.8% as against 20-27%) [2];
- molar yields of compounds with residual hydrogen were much lower than those of perfluorinated compounds (5.3% as against 33.3%);
- as observed by other authors [5], fragmentation reactions producing ring opening were very important (i.e., compare the moles of compounds 5 and 6, or those of compounds 2 and 3); this side reaction was however less remarkable on linear chains (i.e., compare the moles of compounds 5 and 2), and almost negligible in the incompletely fluorinated compounds (i.e., compare the moles of compounds 4 and 1).

TABLE 2
Quantitative GLC analysis of reaction mixture obtained from electrochemical fluorination of N,N-diethylcyclohexylamine (DECHA).

Compound	% wt	g	Moles	Molar yield (%)
DECHA fed	-	857	5,5	-
1	1,5	23	0,05	0,9
2	9,2	140	0,29	5.3
3	9.0	136	0,26	4,7
4	8.1	123	0.24	4,4
5	26.9	407	0,76	13,8
6	10.6	160	0,52	9,5
others	34,7	525	-	-

N-ethyldicyclohexylamine

The reaction mixture obtained by electrochemical fluorination of this compound was so complex that the isolation and identification of its components were very difficult. Furthermore some difficulties were found during the experiment, due to the formation of great amounts of tar. GLC quantitative analysis of the reaction mixture gave a content of 26.7% by wt for perfluoro-N-ethyldicyclohexylamine, corresponding to a molar yield of 4,3% on the amine fed.

EXPERIMENTAL

Electrochemical fluorination

This process was carried out by the usual Simons equipment described elsewhere [1,2] . A cell of 1,2 liters was used, with a reflux condenser (-30 °C) and an anodic surface of 700 cm^2. In Table 3 are reported some experimental data.

TABLE 3
Experimental data of electrochemical fluorination of N,N-diethylcyclohexylamine (DECHA) and N-ethyldicyclohexylamine (EDCHA).

Experiment		Amine fed g	Amine fed moles	Ahr theor.	Ahr passed	Reaction mixture (g)	% Yield (°)
DECHA	1	200	1.3	1612	1644	358	51.7
	2	177	1,1	1430	1485	297	50.6
	3	480	3,1	3870	3912	859	52,0
EDCHA	1	649	3,0	4886	4924	343	16.5

(°) based on theoretical amount of the corresponding perfluoroamine.

The crude mixture drawn off the cell was washed with an aqueous solution of $NaHCO_3$ (5%) in order to remove the hydrogen fluoride. A small amount of the residual mixture was kept for GLC analysis; the remainder underwent a fractional distillation giving several fractions enriched with the different components of the mixture. In the case of DECHA the main components were then isolated in the pure state by preparative scale GLC; for EDCHA it was not possible to do that.

GLC analysis

Analytical GLC work was carried out on a 'Sigma 3' Perkin-Elmer gas chromatograph using a steel inox column (2 mm i.d., 2 m long) packed with Fomblin Y25 on Chromosorb P silanized 100-120 mesh (He carrier gas).

Preparative scale GLC was carried out on a 'Fractovap 2450' C. Erba gas chromatograph using a steel inox column (10 mm i.d., 5 m long) packed with Fomblin YR on Chromosorb P silanized 30-60 mesh or with 25% FS on Chromosorb P silanized 60-80 mesh (He carrier gas).

NMR, IR and MS-GLC analysis

NMR spectra were recorded on a Varian XL 200 spectrometer at 200 MHz for ^{1}H and 188 MHz for ^{19}F, using TMS and $CFCl_3$ as an internal standard for ^{1}H and ^{19}F respectively.

Mass spectra were recorded on a Varian MAT CH7A spectrometer; infrared spectra were recorded on a Perkin-Elmer 782 spectrophotometer.

Identified compounds

IR data and the boiling points observed are reported for the identified compounds. MS data are reported for compounds 4 and 5 only.

a) N(trifluoromethyl),N(pentafluoroethyl)-2,2,3,3,4,4,5,5,6,6-decafluorocyclohexylamine

B.p. 117 °C; IR (film, cm^{-1}) 1340-1180 (s, broad), 1145 (s), 1100 (m), 1070 (w), 1020 (s), 990 (s), 975 (s), 930 (s), 820 (w), 810 (w), 740 (s), 710 (w), 695 (w), 670 (w), 640 (m), 625 (m).

b) (Perfluoro)N(methyl),N(ethyl)cyclohexylamine

B.p. 127,5 °C; IR (film, cm^{-1}) 1340-1190 (s, broad), 1150 (w), 1125 (w), 1090 (s), 1060 (m), 1050 (m), 1000 (s), 965 (s), 925 (s), 915 (w), 840 (w), 810 (s), 790 (s), 745 (s), 730 (s), 665 (w), 640 (s), 625 (w).

c) (Perfluoro)N(methyl),N(ethyl)-*n*-hexylamine

B.p.: 129 °C; IR (film, cm^{-1}) 1340-1190 (s, broad), 1150 (w), 1100 (s), 1000 (m), 985 (m), 930 (s), 880 (m), 860 (w), 800 (m), 790 (w), 755 (w), 735 (s) 720 (w), 710 (m), 665 (m).

d) N,N(perfluorodiethyl)-2,2,3,3,4,4,5,5,6,6-decafluorocyclohexylamine

B.p.: 129.5 °C; IR (film, cm^{-1}) 1300-1205 (s, broad), 1180 (w), 1165 (w), 1135 (m), 1090 (s), 1030 (s), 1015 (s), 985 (s), 935 (s), 895 (s), 810 (m), 740 (s), 710 (m), 705 (m), 675 (w), 625 (s); MS (given in the following order: mass number, formula, % intensity of base peak): 514 (M-H, 0.05), 496 (M-F, 0.08), 446 ($M-CF_3$, 3.5), 396 ($C_8F_{15}HN$, 0.3), 358 ($C_8F_{13}HN$, 2.8), 308 ($C_7F_{11}HN$, 1.8), 243 (C_5F_7, 1.1), 208 (C_5F_7HN, 0.9), 181 (C_4F_7, 1.1), 164 (C_3F_6N, 1.0), 146 (C_3F_5HN, 1.5), 131 (C_3F_5, 4.5), 119 (C_2F_5, 100), 100 (C_2F_4, 4), 69 (CF_3, 40), 51 (CF_2H, 2), 50 (CF_2, 2), 31 (CF, 5).

e) (Perfluoro)N,N-diethylcyclohexylamine

B.p. 136.5 °C; IR (film, cm^{-1}) 1280-1250 (m, broad), 1225 (s, broad), 1180 (w), 1130 (m), 1090 (s), 1050 (w), 1030 (s), 980 (m), 965 (s), 875 (s), 785 (s), 745 (s), 735 (s), 635 (w); MS 533 (M^+, 0.1), 464 ($M-CF_3$, 0.3), 376 ($C_8F_{14}N$, 2), 326 ($C_7F_{12}N$, 1), 288 ($C_7F_{10}N$, 0.2), 281 (C_6F_{11}, 0.7), 276 ($C_6F_{10}N$, 0.25), 238(C_6F_8N, 0.5), 231 (C_5F_9, 0.8), 226 (C_5F_9N, 1.5), 181 (C_4F_7, 2.3), 164 (C_3F_6N, 2.5), 131 (C_3F_5, 13), 119 (C_2F_5, 100), 100 (C_2F_4, 5), 69 (CF_3, 52), 50 (CF_2, 7), 31 (CF, 14).

f) (Perfluoro)N,N-diethyl-*n*-hexylamine

B.p. 141.5 °C; IR (film, cm^{-1}) 1280-1230 (s, broad), 1150 (m, broad), 1100 (m), 1010 (w), 1000 (w), 985 (s), 970 (w), 925 (w), 875 (s), 800 (m), 775 (m), 755 (w), 740 (s), 715 (w), 705 (w), 690 (m), 665 (w, broad), 645 (w, broad).

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