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ELECTROCHEMICAL FLUORINATION OF N-CHLOROALKYL-SUBSTITUTED CYCLIC AMINES

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SUMMARY

The electrochemical fluorination of such N-chloroalkyl substituted cyclic amines as N-chloromethylpyrrolidine (1), N-(3-chloropropyl)pyrrolidine (2), N-chloromethylpiperidine (3), N-(2-chloroethyl)piperidine (4), N-(3-chloropropyl)piperidine (5), N-chloromethylmorpholine (6), N-(3-chloropropyl)morpholine (7), N-(2-chloroallyl)morpholine (8) has been conducted. Except in the cases of the N-chloromethyl-substituted ones (1,3 and 6), the corresponding chlorine-retaining-perfluoroamines were obtained in a yield of 5 ~ 20% together with perfluorinated ones (Yield = 20 ~ 60%). Neither chlorine-retaining amines nor perfluorinated amines, both of which having the original skeleton, was produced from fluorinations of 1,3 and 6 in an appreciable yield. The spectroscopic data and physical properties of newly synthesized perfluoro-N-chloroalkyl-substituted cyclic amines are presented.

INTRODUCTION

Electrochemical fluorination has been known as a good preparative route for perfluoroamines [1,2]. However, few works have yet been conducted on the electrochemical fluorination of N-chloroalkyl-substituted amines [1]. In a previous paper, we have shown that the electrochemical fluorination of several N-chloro-alkyl-substituted tertiary amines provides an easy route to corresponding perfluoro-N-chloroalkyl-substituted amines which are other wise difficult to obtain [3].

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For example, from the fluorination of N-(2-chloroethyl)-N,N-diemthylamine, $(CH_3)_2NCH_2CH_2Cl$, fluorinated amines like $(CF_3)_2NCF_2CF_2Cl$ and $(CF_3)_2CF_2CF_3$ were obtained in yields of 4.8% and 7.7% respectively. And from N-(2-chloroethyl)pyrrolidine, $\overline{CH_2(CH_2)_3NCH_2CH_2Cl}$, corresponding perfluoro[N-(2-chloroethyl)-pyrrolidine], $\overline{CF_2(CF_2)_3NCF_2CF_2Cl}$, was obtained in a yield of 19.2% together with perfluoro(N-ethylpyrrolidine), $\overline{CF_2(CF_2)_3NCF_2CF_3}$ (Y=41.6%).

In continuing our study on the preparation of chlorine-containing perfluoroamines, we have conducted the electrochemical fluorination of several kinds of N-chloroalkyl-substituted cyclic amines having the following formulas


N-R ; R = CH_2Cl (1), $CH_2CH_2CH_2Cl$ (2)


N-R ; R = CH_2Cl (3), CH_2CH_2Cl (4), $CH_2CH_2CH_2Cl$ (5)


N-R ; R = CH_2Cl (6), $CH_2CH_2CH_2Cl$ (7), $CH_2CCl=CH_2$ (8)

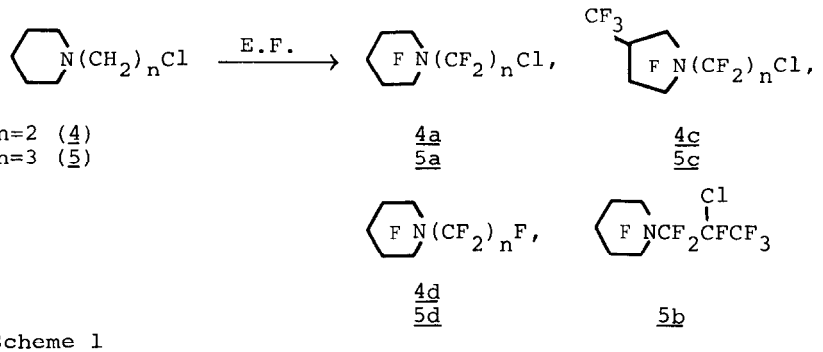
In this paper, we wish to report the results of the fluorination of these N-chloroalkyl-substituted cyclic amines.

RESULTS AND DISCUSSION

The starting N-chloroalkyl-substituted cyclic amines were added to the electrolytic cell, which contained 500 mℓ of electrically purified anhydrous hydrogen fluoride (AHF), in the form of hydrogen chloride salt (4 and 5) or free base (1,2,3,6,7 and 8). The evolution of gas (HCl) was observed when the former was added. The electrochemical fluorination was performed in the usual manner and the reaction proceeded smoothly in all cases.

Being different from the fluorination of N-2-chloroethyl- and N-3-chloropropyl-substituted cyclic amines, however, in the fluorination of N-chloromethyl-substituted ones (1,3 and 6), the formation of N-chlorodifluoromethyl-substituted perfluorocyclic amines was not observed. For example, in the fluorination of 3, only degradaded fluorocarbons consisting primarily of n-C_5F_{12}, and small amounts of n-C_4F_{10}, CF_4, CHF_3 and NF_3 were produced.

From N-2-chloroethyl- and N-3-chloropropyl-substituted cyclic amines, corresponding chlorine-retaining perfluoroamines and perfluoroamines were produced in good yields. Compounds arising from a ring-isomerization and a chlorine migration were also among the products.



Scheme 1

Thus, the fluorination of 4 afforded the perfluoro[N-(2-chloroethyl)piperidine](4a) in a yield of 5.0% and its isomer, perfluoro[N-(2-chloroethyl)-3-methylpyrrolidine](4c)(Y=0.7%) together with the corresponding perfluoro(N-ethylpiperidine)(4d) (Y=31.3%). The structure of 4c was determined on the basis of ^{19}F nmr spectra. It contained absorptions assigned to CF_3 and CF peaks at -71.9 ppm and -184.0 ppm, respectively. The absorption due to -CF group was considered to be the one attached to the 3-position of the pyrrolidine ring because the signals of the -CF group of 2-trifluoromethyl-substituted perfluoropyrrolidines appeared in the range of -160 ~ -166 ppm [4,5].

Similarly, the fluorination of N-(3-chloropropyl)piperidine (5) afforded the corresponding perfluoro[N-(3-chloropropyl)piperidine](5a)(Y=5.0%), perfluoro[N-(2-chloropropyl)piperidine](5b) (Y=2.0%), perfluoro[N-(3-chloropropyl)-3-methylpyrrolidine](5c) (Y=1.5%) and perfluoro(N-propylpiperidine)(5d)(Y=24.0%).

The migration of chlorine during electrolysis occurred considerably in the fluorination of N-(3-chloropropyl)pyrrolidine (2) and N-(3-chloropropyl)morpholine (7). From these starting materials, perfluoro(N-2-chloropropylpyrrolidine)(2b) from 2 and perfluoro(N-2-chloropropylmorpholine)(7b) from 7 were obtained in higher yields than those of the corresponding perfluoro(N-3-

chloropropylpyrrolidine)(2a) and perfluoro(N-3-chloropropylmorpholine)(7a) respectively. Thus, from 2, 2a and 2b were obtained in yields of 3.7% and 19.5%, respectively, and from 7, 7a and 7b were obtained in yields of 6.9% and 15.7%, respectively.

In the fluorination of N-(2-chloroallyl)morpholine (8), considerable amounts of tarry materials formed, which resulted in lowering the yield of the expected perfluoro(N-2-chloropropylmorpholine) produced (Y=10.7%). Other products like perfluoro(N-3-chloropropylmorpholine) were not obtained.

In the fluorination of N-chloromethyl-substituted amines (1,3 and 6), the formation of chlorofluoromethanes like CF_3Cl, which might be formed as a result of a fission of the nitrogen-carbon bond, was not detected. Furthermore, there was an obvious tendency in the fluorination of N-chloroalkyl-substituted amines that the yield of perfluoro-N-chloroalkyl cyclic amines formed increased as the number of bonds separating the nitrogen and chlorine increased in the starting N-chloroalkyl cyclic amines. Based on these results, it is considered that the chlorine atom of the N-chloromethyl-substituted ones (1,3 and 6) is very susceptible to substitution by fluoride ion due to interaction by the lone electron pair of nitrogen to afford N-fluoromethyl-substituted ones, like the case of the chloromethyl ethers [6].

The N-chloroalkyl cyclic amines isolated in the present work have the boiling points about 20 °C higher than those of the corresponding perfluoro-N-alkyl cyclic amines. Refractive indexes and densities of these chloropolyfluoroamines were found to be slightly higher than those of the corresponding perfluoroamines. The properties of chloropolyfluoroamines are summarised in Table 1.

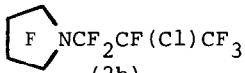
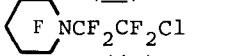
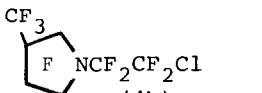
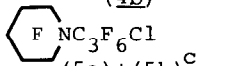
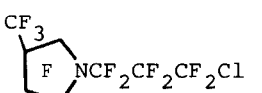
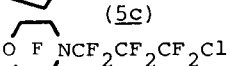
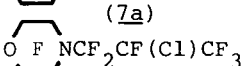
EXPERIMENTAL

Reagents

N-chloromethylpyrrolidine (1), N-chloromethylpiperidine (3) and N-chloromethylmorpholine (6) were prepared by the reaction of bromochloromethane (Tokyo Kasei Co.) with the corresponding amines (Wako Junyaku Co.) according to the method described in the literature [7]. N-(3-chloropropyl)pyrrolidine (2) and N-(3-chloropropyl)morpholine (7) were prepared by the

Table 1

Properties of chloropolyfluorocyclic amines

Compounds	Source	BP (°C)[a]	n_D^{20}	d_4^{20}	Elemental Analysis		
					C(%)	N(%)	F(%)
 (2b)	2	102.5~103.5	1.3035	1.7866	20.29 (21.04)[b]	3.67 (3.51)	66.4 (66.6)
 (4a)	4	103.5~104.5	1.3050	1.7969	20.98 (21.04)	3.70 (3.51)	66.2 (65.6)
 (4b)	4	102.5~103.5	1.3031		20.93 (21.04)	3.80 (3.51)	66.2 (66.1)
 (5a)+(5b)[c]	5	122.5~123.0	1.3086	1.8320	21.24 (21.37)	3.13 (3.12)	67.4 (67.6)
 (5c)	5	122.5~124.0	1.3087	1.8288	21.32 (21.37)	3.31 (3.12)	67.3 (67.6)
 (7a)	7	113.5~114.0	1.3066	1.8150	20.10 (20.23)	3.57 (3.37)	64.5 (64.3)
 (7b)	7,8	113.0~113.5	1.3067	1.8204	20.40 (20.23)	3.55 (3.37)	63.8 (64.0)

[a] Boiling points are not corrected. [b] Calculated values in parentheses.
[c] A mixture of perfluoro(N-3-chloropropylpiperidine) (5a) (76%) and perfluoro(N-2-chloropropylpiperidine) (5b) (24%).

reaction of 3-bromo-1-chloropropane (Aldrich Chemicals Co.) with corresponding amines [8]. Other chlorinated amines were purchased from Aldrich Chemicals Co. and were used as received. Anhydrous hydrogen fluoride (Daikin Industry Co.) was more than 99.9% pure.

Apparatus

Fluorination was carried out in a similar way to that reported previously [6] using a 500 mℓ electrolytic cell fitted with a reflux condenser (-20 °C) on the top of the cell. The electrodes (nickel plates) were consisted of 7 anodes and 8 cathodes arranged alternately. The effective anodic surface area was 7.5 dm^2.

A gas chromatographic analysis (composition was calculated on the basis of chromatographic peak area, assuming equal weight sensitivities for all components) was carried out with a Shimadzu GC-1C gas chromatograph using a stainless column (3 mm dia) packed with 30% 1,6-bis(1,1,7-trihydroperfluoroheptyloxy)hexane on Chromosorb PAW (60/80 mesh)(6.4 m) for products in cold traps and with 30% 1,6-bis(1,1,12-trihydroperfluorododecyloxy)hexane on Chromosorb PAW (60/80 mesh)(6.4 m) for cell drainings respectively

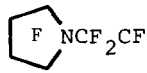
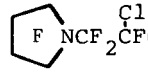
For semi-preparative work, the fluorination products were separated roughly into few aliquots with a Shimadzu GC-6C gas chromatograph using a copper column (10 mm dia) packed with 30% Silicone DC QF-1 on Chromosorb PAW (4.9 m), and then each of them was purified with a Shimadzu GC-1C gas chromatograph using a stainless column (10 mm dia) packed with 30% 1,6-bis(1,1,12-trihydroperfluorododecyloxy)hexane on Chromosorb PAW (60/80 mesh) (4.0 m).

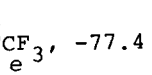
Infrared spectra were measured on a Hitachi EPI-G3 spectrometer, using a 6 cm gas cell with KBr windows. ^{19}F nmr spectra were measured on a Hitachi R-20B high resolution spectrometer operating at 56.46 MHz using CCl_3F as an internal standard. Mass spectra were measured on a Hitachi RMU-7 instrument at 70 eV.

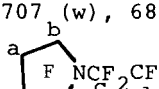
Fluorination of N-(3-chloropropyl)pyrrolidine (2)

Sample (2)(20.0 g) was dissolved into electrically purified anhydrous hydrogen fluoride (500 mℓ), and the resulting solution was electrolyzed over a period of 325 min (152 Ahr) with an anodic current density of 3.7 A/dm^2, a cell voltage of 6.1～7.9 V and a cell temperature of 7～12 °C. Helium (50 mℓ/min) was introduced through the bubbler at the bottom of the cell.

The gaseous products evolving from the cell were passed through a sodium fluoride tube, gas-washing bottles filled with a 20% aqueous solution of potassium sulfite containing a small amount of potassium iodide, and then led to a series of cold traps immersed in ice, dry ice - acetone mixture and liquid N_2, respectively. The products sunk at the bottom of the cell were also collected after the completion of electrolysis. These products were subjected to gas chromatographic analysis. Thus, the following products were found: n-C_4F_{10} (3.7 g),

 (2d)(lit. [4])(26.2 g),  (2b) (10.9 g),  (2a)(2.1 g) and unidentified (1.3 g).

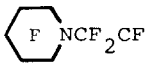
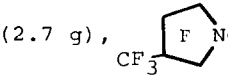
(2b)(nc): IR (gas): 1381 (m), 1344 (vs), 1313 (s,sh), 1292 (s), 1255 (s,sh), 1239 (vs), 1207 (s,sh), 1189 (s), 1173 (s), 1129 (s), 1042 (m), 1011 (m), 980 (s), 946 (m), 931 (w,sh), 897 (m), 863 (w), 841 (w), 790 (m), 734 (m), 722 (m), 616 (w), 570 (w). Mass: 380 $[M-F]^+$(6.1), 364 $[M-Cl]^+$(1.7), 264 $[C_5F_{10}N]^+$ (49.6), 69 $[CF_3]^+$(100). ^{19}F nmr:  , -77.4 (CF_3^e), -81.3 (CF_2^b), -84.6 (CF_2^c), -133.1 (CF_2^a), -135.3 (CF^d).

(2a)(nc): IR (gas): 1400 (w), 1347 (vs), 1310 (m,sh), 1296 (m), 1255 (m), 1132 (m), 1073 (w), 1052 (m), 1032 (m), 1018 (m), 979 (w), 887 (m), 873 (m), 790 (w), 780 (m), 753 (m), 736 (w,sh) 707 (w), 680 (w), 618 (w), 556 (w). ^{19}F nmr:  , -68.3 (CF_2^e), -81.4 (CF_2^b), -90.6 (CF_2^c), -120.9 (CF_2^d), -133.3 (CF_2^a).

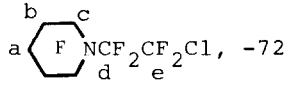
The properties of 2b and the results of the elemental analysis are shown in Table 1.

Fluorination of N-(2-chloroethyl)piperidine (4)

The sample (4)·HCl (25.0 g) was fluorinated similarly under the following conditions; 4.0 A/dm^2, 5.6~6.7 V, 8~12 °C 167 Ahr (335 min), and the following compounds were obtained:

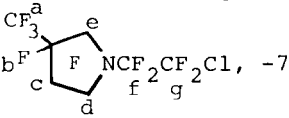
$n\text{-}C_4F_{10}$ (4.1 g), $n\text{-}C_5F_{10}$ (6.7 g),  (4d)(lit. [4]) (16.3 g),  (4a)(2.7 g),  (4c)(0.4 g) and unidentified (2.2 g).

(4a)(nc): IR (gas): 1362 (s), 1353 (s,sh), 1338 (vs), 1279 (s), 1263 (s), 1225 (s), 1199 (s), 1190 (s), 1166 (s), 1131 (s), 1101 (m), 1069 (m), 1023 (s), 963 (s), 949 (m), 890 (m), 864 (w), 851 (w), 819 (w), 791 (m), 769 (m), 734 (w), 715 (w), 709 (w), 652 (w), 641 (m), 631 (m). Mass: 380 $[M\text{-}F]^+$(15.3), 364 $[M\text{-}Cl]^+$ (6.3), 314 $[C_6F_{12}N]^+$(64.0), 69 $[CF_3]^+$(100). ^{19}F nmr:



CF_2^c), -91.6 (CF_2^d), -95.9 (CF_2^c), -132.4 (CF_2^b), -135.1 (CF_2^a).

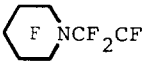
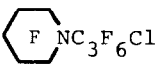
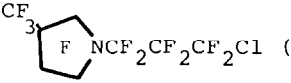
(4c)(nc): IR (gas): 1382 (m), 1342(s,sh), 1338 (vs), 1312 (s,sh), 1262 (s), 1248 (vs), 1169 (s), 1131 (m), 1108 (m), 1088 (m), 1031 (w), 1016 (m), 1000 (m), 968 (m), 910 (m,sh), 893 (m), 790 (w), 772 (m), 722 (w). Mass: 380 $[M\text{-}F]^+$(15.3), 364 $[M\text{-}Cl]^+$ (6.3), 314 $[C_6F_{12}N]^+$(64.0), 69 $[CF_3]^+$(100). ^{19}F nmr:



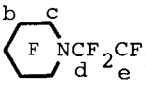
and -92.8 (CF_2^e), -95.8 (CF_2^d), -127.0 and -129.0 (CF_2^c), -184.0 (CF^b).

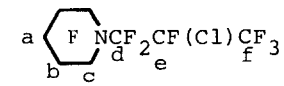
The properties of 4a and 4c and the results of the elemental analysis are shown in Table 1.

Fluorination of N-(3-chloropropyl)piperidine (5)

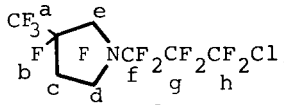
The sample (5)·HCl (25.0 g) was fluorinated; 4.0 A/dm^2, 5.2～8.2 V, 8～14 °C, 171 Ahr (314 min). The following compounds were obtained: $n\text{-}C_4F_{10}$ (4.7 g), $n\text{-}C_5F_{12}$ (6.2 g),  (5d) (lit. [9]) (13.1 g),  (5a) + (5b) (3.3 g),  (5c) (0.9 g) and unidentified (2.2 g).

Compounds 5a and 5b could not be resolved by GLC and these were assigned by means of ^{19}F nmr. The mixing ratio was 5a/5b = 1 : 0.32. The mass spectrum of the mixture had the peak of 430 $[M-F]^+$(5.3) and such fragment ions as 414 $[M-Cl]^+$(1.7), 314 $[C_6F_{12}N]^+$(39.5), 185 $[C_3F_6Cl]^+$(25.4), 69 $[CF_3]^+$(100).

^{19}F nmr:  (5a), -134.5 (CF_2^a), -132.2 (CF_2^b), -90.9 (CF_2^c and CF_2^d), -127.6 (CF_2^e), -77.9 (CF_2^f).

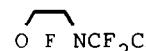
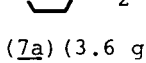
 (5b), -134.5 (CF_2^a), -132.2 (CF_2^b), -90.9 (CF_2^c), -84.5 (CF_2^d), -68.9 (CF^e), -81.5 (CF_3^f).

(5c) (nc): IR (gas): 1381 (m,sh), 1333 (vs), 1319 (s,sh), 1299 (s), 1277 (s,sh), 1254 (vs), 1248 (s,sh), 1201 (s), 1191 (s), 1161 (m,sh), 1132 (m), 1084 (w), 1021 (m), 1005 (m,sh), 972 (s), 956 (m,sh), 891 (m), 859 (w), 784 (m), 740 (m), 716 (w). Mass: 430 $[M-F]^+$(4.4), 414 $[M-Cl]^+$(1.9), 380 $[M-CF_3]^+$(8.5), 314 $[C_6F_{12}N]^+$(41.2), 185 $[C_3F_6Cl]^+$(23.5), 69 $[CF_3]^+$(100). ^{19}F nmr:

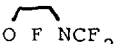
 , -67.8 (CF_2^h), -72.8 (CF_3^a), -77.1 (CF_2^g), -81.1 (CF_2^f), -90.3 (CF_2^e), -96.9 (CF_2^d), -126.4 and -131.8 (CF_2^c), -183.4 (CF^b).

The properties of 5c and the results of the elemental analysis are shown in Table 1.

Fluorination of N-(3-chloropropyl)morpholine (7)

Sample (7) (20.5 g) was fluorinated; 3.6 A/dm^2, 6.1~8.1 V, 5~12 °C, 127 Ahr (275 min). The following compounds were obtained: $(C_2F_5)_2O$ (3.1 g),  (7d)(lit. [10]) (29.9 g),  (7a)(3.6 g), (7b) (7.8 g).

(7a) (nc): IR (gas): 1402 (w), 1348 (m), 1308 (s), 1239 (vs), 1227 (vs), 1185 (s), 1170 (m,sh), 1156 (s), 1135 (m), 1106 (m), 1047 (w), 1032 (m), 935 (m), 887 (m), 871 (w), 790 (w), 778 (m), 756 (m), 716 (w), 685 (w), 659 (w), 625 (w), 570 (w), 491 (w). Mass: 396 $[M-F]^+$(3.5), 380 $[M-Cl]^+$(1.3), 280 $[C_4F_8NOCF_2]^+$(67.2), 185 $[C_3F_6Cl]^+$(40.5), 119 $[C_2F_5]^+$(100).

^{19}F nmr:  , -68.1 (CF_2^e), J_{de}=10.3, -87.1 (CF_2^a), -89.1 (CF_2^b), -98.1 (CF_2^b), -121.1 (CF_2^d), J_{ed}=9.7, J_{cd}=9.7.

(7b) (nc): IR (gas): 1402 (w), 1345 (s), 1304 (s), 1290 (vs), 1252 (vs), 1229 (vs), 1221 (s,sh), 1191 (s), 1166 (s), 1155 (s,sh), 1131 (s), 1102 (s), 974 (s), 951 (m), 833 (s), 786 (m), 779 (m), 741 (w), 734 (w), 696 (w), 662 (s), 625 (m), 573 (w), 554 (w), 492 (w). Mass: 396 $[M-F]^+$(4.7), 380 $[M-Cl]^+$(1.2), 280 $[C_4F_8NOCF_2]^+$(66.7), 186 $[C_3F_6Cl]^+$(38.7), 119 $[C_2F_5]^+$(100).

^{19}F nmr:  , -77.4 (CF_3^e), J_{de}=5.7, -85.1 (CF_2^a), -87.1 (CF_2^b), -92.3 (CF_2^c), -137.3 (CF^d).

The properties of 7a and 7b and the results of the elemental analysis are shown in Table 1.

Fluorination of N-(2-chloroallyl)morpholine (8)

Sample (8) (20.5 g) was fluorinated; 3.6 A/dm^2, 6.1～6.8 V, 3～8 °C, 139 Ahr (305 min). The following compounds were obtained: $(C_2F_5)_2O$ (2.8 g), (7d) (11.7 g), (7b) (5.7 g).

As a typical fluorination of N-chloromethyl cyclic amines, the fluorination of N-chloromethylpyrrolidine will be described.

Fluorination of N-chloromethylpyrrolidine (1)

Sample (1) (20.0 g) was fluorinated; 3.7 A/dm^2, 5.9～6.9 V, 6～12 °C, 139 Ahr (334 min). The compounds (25.3 g) collected at -196 °C trap were CF_4 and C_2F_6. The compounds (16.4 g) collected at -78 °C trap consisted primarily of n-C_4F_{10}(14.2 g) and a trace of  other than unidentified (2.0 g).

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