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N-HALOGENO-COMPOUNDS. PART 8. PERFLUORO-N-CHLOROPIPERIDINE

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SUMMARY

Perfluoro-1-azacyclohex-1-ylcaesium, produced by treatment of perfluoro-1-azacyclohexene with caesium fluoride, reacts with chlorine to yield perfluoro-N-chloropiperidine. UV-photolysis of this N-chloro-compound alone in silica gives perfluoro-NN'-bipiperidyl, perfluoro-2-aza-6-chlorohex-1-ene, and perfluoro-4-chlorobutyl isocyanate; similar photolysis in the presence of perfluorocyclobutene provides perfluoro-[N-(2-chlorocyclobutyl)piperidine].

INTRODUCTION

The chemistry of saturated six-membered cyclic N-fluoroamines of the fluorocarbon class like perfluoro-N-fluoropiperidine) (I), perfluoro-(N-fluoro-2,6-dimethylpiperidine) (II), and perfluoro-N-fluoromorpholine (III) has received a fair amount of attention [2] owing to the ease with which such substances can be prepared by electrochemical fluorination {Simons Process: e.g. pyridine ⟶ (I) [2a,3]; 2,6-lutidine ⟶ (II) [2b,4]; morpholine ⟶ (III) [2c,5]}. By contrast, information on analogous N-heterocycles carrying heavier halogens at ring nitrogen seems confined to a claim concerning the synthesis of perfluoro-N-bromopiperidine (IV)

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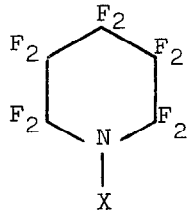
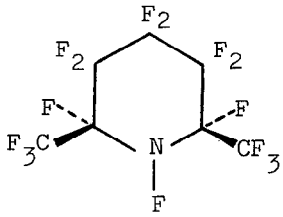


(I) X = F
(IV) X = Br
(IX) X = Cl



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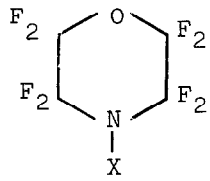
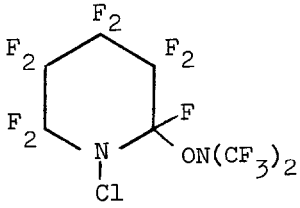


(III) X = F
(V) X = Cl
(VI) X = H



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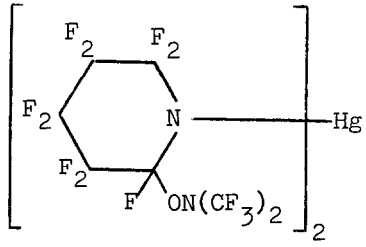

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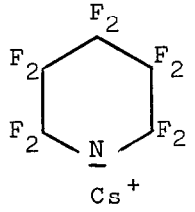
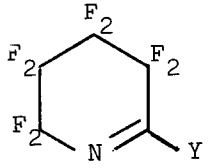
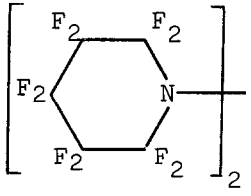


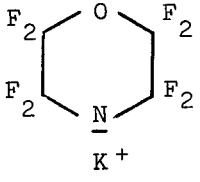
(X)



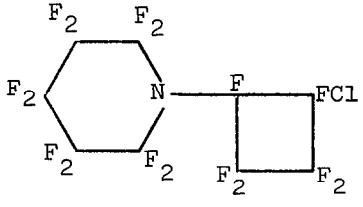
(XI) Y = F
(XII) Y = $ON(CF_3)_2$



(XIII)



(XVI)



(XVII)

via treatment of 'α,α,α -trichlorohexafluoropiperidine'* with bromine trifluoride [6]. Having failed in the past (i) to obtain [8] (but not, we believe [9], to generate) perfluoro-N-chloromorpholine (V) via thermal chlorination of perfluoromorpholine (VI) in the presence of anhydrous potassium fluoride (see comments later), and (ii) to isolate [10] perfluoro-[N-chloro-2-(dimethylamino-oxy)piperidine] (VII) following chlorination at 18 °C in Isceon 113 ($CF_2ClCFCl_2$) of material thought to contain the corresponding mercurial (VIII) {from perfluoro-1-azacyclohexene + $[(CF_3)_2NO]_2Hg$ [11]},** it was natural for us to seize the opportunity to synthesize perfluoro-N-chloropiperidine (IX) provided by the discovery [12] that perfluoro-1-azacyclohex-1-ylcaesium (X) can be generated from caesium fluoride and perfluoro-1-azacyclohexene (XI) (from perfluoro-N-fluoropiperidine + Ph_3P [14])in acetonitrile at ambient temperature under anhydrous conditions.

DISCUSSION

Since our initial report [12] on perfluoro-1-azacyclohexylcaesium (X), we have generated this nitranion source many times and established that when sufficient solvent [CH_3CN; ca. 1 cm^3 per mmol of perfluoro-1-azacyclohexene (XI)] is used the reaction mixture becomes homogeneous and conversion of the imine (XI) to the salt (X) is quantitative, according to ^{19}F NMR analysis. Also, the spectrum obtained comprises much sharper signals [at 13.0 (br. s; α-fluorines), - 51.4 (t;β) and - 55.3 (mult.;γ) p.p.m. (TFA)] than the original one [12], in keeping with the experience of investigators [13] who recommend sulpholar as a solvent.

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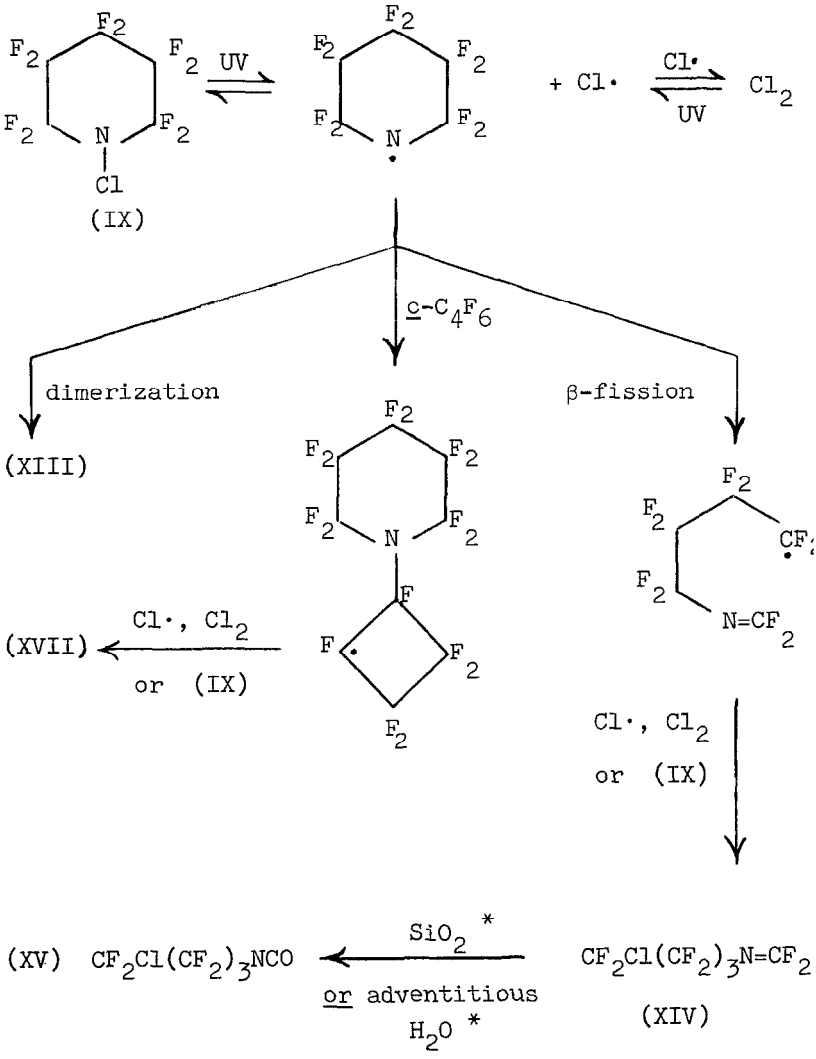
* Should this be the well-known [7] compound α,α,α -trichlorohexafluoro-Δ^1-piperideine?

** The compound believed to be the N-chloroamine (VII)decomposed [⟶ (XII)] during an attempt to separate it by GLC from perfluoro-[2-(dimethylamino-oxy)-1-azacyclohexene] (XII) also produced during the chlorination.



Scheme

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* This type of conversion is well known in fluorocarbon chemistry [16].

Perfluoro-N-chloropiperidine (IX), b.p. 80 °C, can be isolated in at least 58% yield following treatment of pre-formed perfluoro-1-azacyclohexylcaesium with chlorine at temperatures up to 18 °C; separation of this product from solvent acetonitrile is easily achieved using perfluoropentane as an extractant. As expected, the N-chloro-compound is a photochemical source of perfluoro-N-piperidyl radical; thus, UV-irradiation in silica provides the radical's dimer, perfluoro-NN'-bipiperidyl (XIII) plus the acyclic imine $CF_2Cl(CF_2)_3N{=}CF_2$ (XIV) and the corresponding isocyanate, $CF_2Cl(CF_2)_3NCO$ (XV) (see the Scheme). Formation of the chlorine-containing imine (XIV) provides support for the proposal [9] that perfluoro-N-chloromorpholine (V) can be generated *via* thermal treatment of perfluoromorpholine (VI) with potassium fluoride [⟶ the corresponding nitranion (XVI)] in the presence of chlorine: this reaction provides the imine $CF_2ClOCF_2CF{=}NCF_3$, *i.e.* the expected product of fluoride-initiated isomerization of the 5-oxa-analogue $CF_2ClOCF_2CF_2N{=}CF_2$ of (XIV).

Trapping of perfluoro-N-piperidyl radical from UV-photolysis of perfluoro-N-chloropiperidine using perfluorocyclobutene provides perfluoro-[N-(2-chlorocyclobutyl)piperidine] (XVII) (in *ca.* 33% yield when the ratio of N-chloro-compound to olefin is *ca.* 1:1), which corresponds to the formation of perfluoro-(N-cyclobutylpiperidine) from perfluorocylobutene and perfluoro-N-fluoropiperidine in the presence of UV light [15].

EXPERIMENTAL

Spectroscopic analysis

^{19}F NMR and mass spectra were obtained with a Perkin-Elmer R32 instrument (84.6 MHz; ext. CF_3CO_2H ref., shifts to high field designated negative) and an A.E.I. MS/2H spectrometer (electron beam energy 70 eV), respectively.

Starting materials

Perfluoro-1-azacyclohexene was obtained by defluorination (with Ph_3P [14]) of perfluoro-N-fluoropiperidine produced by electrochemical fluorination (Simons Process) of pyridine [2a];

it was contaminated with traces of perfluoro-(N-methylpyrrolidine) and perfluoro-n-pentane, inert compounds formed in the fluorination stage. Perfluorocyclobutene was prepared by dechlorination (with Zn [17]) of 1,2-dichlorohexafluorocyclobutane procured by thermal dimerization of commercial chlorotrifluoroethylene. Immediately prior to use, commercial powdered caesium fluoride was dried at 150-200 °C under dynamic vacuum for ca. 5 h in the Pyrex tubes (fitted with Rotaflo stopcocks) subsequently used as reaction vessels. AnalaR acetonitrile was dried over molecular sieves (3Å) [18] prior to use.

Preparation of perfluoro-N-chloropiperidine

A mixture of perfluoro-1-azacyclohexene (15.2 g, 62.0 mmol), anhydrous caesium fluoride (9.41 g, 62.0 mmol), and dry acetonitrile (20 cm^3) was stirred magnetically overnight at ambient temperature under anaerobic conditions in a Pyrex tube (300 cm^3). The tube was cooled to -196 °C, charged with chlorine (4.26 g, 60.0 mmol) in vacuo, re-sealed and left at room temperature for 20 h with the stirrer in motion. Volatile product was transferred, in vacuo, to a cold (-196 °C) trap, warmed to room temperature, then extracted continuously for several hours with perfluoropentane* (b.p. 29 °C; ca. 200 cm^3) in a conventional liquid-liquid extractor [for a dense extractant (cf. C_5F_{12}, d_4^{20} 1.620 g cm^{-3}; CH_3CN, d_4^{20} 0.786 g cm^{-3})] fitted with a cold finger condenser (methylated spirit-Drikold) and guard tube ($CaCl_2$). Distillation of the extract, first using a column (10 x 1 cm) packed with Heli-pak Hastelloy B wire coils (0.05 x 0.10 x 0.10 in.) (to remove most of the C_5F_{12}) and finally with a Vigreux column (10 x 1 cm) gave ca. 98% pure (by GLC) perfluoro-N-chloropiperidine (10.7 g, 35.7 mmol, 58%) (nc), b.p. 77-80 °C, which was identified by comparison (GLC and IR) with a sample [(Found: C, 20.1; Cl, 11.5; F, 63.4 .

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* Mainly the n-isomer, obtained here as by-product from ECF of pyridine [→ (I)] (available commercially as Flutec® PP50 [19]).

$C_5ClF_{10}N$ requires C, 20.0; Cl, 11.85; F, 63.4%), b.p. 80-81 °C (Siwoloboff), δ_F (neat liq.) -22.0 (br. m; 2-,2-,6-6-F), -54.0 (m; 3-,3-,5-,5-F), and -57.2 (m; 4-,4-F) p.p.m., m/z 301 ($C_5{}^{37}ClF_{10}N^+$, 11.4%), 299 ($C_5{}^{35}ClF_{10}N^+$, 36.5%)] isolated by GLC (SE 30, 80 °C) following a similar experiment on a 10 mmol scale in which the extraction step was omitted.

Reactions of perfluoro-N-chloropiperidine

(a) Photolysis alone

The N-chloro-compound (3.25 g, 10.85 mmol) was condensed, in vacuo, into a cold (-196 °C) silica tube (300 cm^3) which previously had been flamed-out in vacuo; the tube was sealed, in vacuo, warmed to 18 °C and then irradiated for 18 hours with light from a 500-W medium-pressure Hanovia UV lamp placed 20 cm distant. The product was freed from chlorine (0.21 g, 2.9 mmol) by shaking it with mercury (5 g), leaving a 6-component (by GLC) mixture; this was worked-up by preparative GLC (4 m, 50:50 OV/17: SE30, 69 °C) to provide perfluoro-NN'-bipiperidyl (estimated yield 30%) [Found: C, 22.6; N, 5.6%; M (mass spec.), 528 . Calc. for $C_{10}F_{20}N_2$: C, 22.7; N, 5.3%; M, 528], which was identified spectroscopically (IR, NMR [15]), and binary mixtures of perfluoro-N-chloropiperidine (total estimated recovery 16%) with (i) perfluoro-2-aza-6-chlorohex-1-ene (nc) [yield, based on analytical GLC (uncalibrated) peak areas, 22%] { $\nu_{max.}$ (vap.) 1800 cm^{-1} (C=N str.; cf. $n\text{-}C_3F_7N{=}CF_2$, 1814 cm [20]); m/z (GC-MS) 282 [M^+ (^{37}Cl) - F·, 0.2%], 280 [M^+(^{35}Cl) -F· , 0.8%], 264 (M^+ - Cl·, 2.1%), 245 (M^+ - Cl· - F·, 10.7%), 145 ($C_3F_5N^+$, 84.3%), 114 ($C_2F_5N^+$, 55.0%), 100 ($C_2F_4{}^+$, 56.4%), 87 ($C^{37}ClF_2{}^+$, 26.5%), 85 ($^{35}ClF_2$, 85.7%), 69 ($CF_3{}^+$, 100%); δ_F (neat liq. mixture) 47.7 and 31.7 (each v.br. s; $N{=}CF_2$), 13.9 [t (13 Hz); CF_2Cl], - 15.2 [t (12 Hz; $CF_2{=}NCF_2$), -43.0 and -47.1 (each br. complex; $NCF_2CF_2CF_2$) p.p.m. } and (ii) perfluoro-4-chlorobutyl isocyanate (nc) [yield, based on analytical GLC (uncalibrated) peak areas, 27%] { $\nu_{max.}$ (vap.) 2295 cm^{-1} (asym. N=C=O str.); cf. [16] $n\text{-}C_3F_7NCO$, 2288 cm^{-1}; m/z (GC-MS) 260 [M^+(^{37}Cl) - F·, 0.6%], 258 [M^+(^{35}Cl) - F·, 1.9%], 145 ($C_3F_5N^+$, 100%), 114 ($C_2F_4N^+$,

27.7%), 100 ($C_2F_4^+$, 76.2%), 92 (CF_2NCO^+, 96.9%), 87 ($C^{37}ClF_2$, 23.9%), 85 ($C^{35}ClF_2$, 68.8%), 69 (CF_3^+, 97.5%); δ_F (neat liq. mixture) 18.9 (t, CF_2Cl), - 3.1 (t, CF_2NCO), - 42.8 and - 45.6 (each br. complex; $C\underline{F}_2C\underline{F}_2CF_2NCO$) p.p.m. }.

(b) Photolysis in the presence of perfluorocyclobutene

Perfluoro-N-chloropiperidine (2.07 g, 6.91 mmol) and perfluorocyclobutene (1.17 g, 7.22 mmol) were condensed separately into a cold (-196 °C) evacuated silica tube (300 cm^3) which was then sealed, allowed to warm to room temperature, and irradiated for 18 hours with light from a 500-W medium-pressure Hanovia UV lamp placed 20 cm distant. Gaseous product (containing unchanged starting material in amounts not determined) was transferred, in vacuo, to a cold trap (-196 °C), leaving a colourless liquid which was separated by preparative GLC (4 m, 50:50 OV17/SE 30, 100 °C) into perfluoro-NN'-bipiperidyl [estimated yield (by analytical GLC) 10%], perfluoro-[N-(2-chlorocyclobutyl)piperidine] (nc) (33%) (Found: C, 23.5; Cl, 8.4; F, 65.3; N, 3.2. $C_9ClF_{16}N$ requires C, 23.4; Cl, 7.7; F, 65.9; N, 3.0%), m/z 444 [M^+ (^{37}Cl) - F·, 5.5%], 442 [M^+(^{35}Cl) - F·, 16.8%] (top mass peaks), 363 ($C_5F_{10}NCFCF^{37}Cl^+$, 18.8%), 361 ($C_5F_{10}NCFCF^{35}Cl^+$, 57.3%), 345 ($C_5F_{10}NCFCF_2^+$, 100%), 118 ($CF_2CF^{37}Cl^+$, 25.1%), 116 ($CF_2CF^{35}Cl^+$, 73.8%), 100 ($CF_2CF_2^+$, 58.8%), δ_F (neat liq.) - 16.2 (br. s; 2-,2-,6-,6-F), - 44.5 and - 52.8 [AB system (J ca. 210 Hz); 3'-,3'-F or 4'-,4'-F], - 47.2 (two overlapping absorptions; 2'-F and 4'-,4'-F or 3'-,3'-F), - 56.0 (two overlapping absorptions; 3-,3-,4-,4-, 5-,5-F), and - 57.4 (br. s; 1'-F) p.p.m. (rel. int. 4:2:3:6:1), and material which may be/contain perfluoro-2,2'-dichlorobicyclobutyl* (13% by analytical GLC) but was not isolated in sufficient amount for positive identification.

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*Cf. the formation of perfluorobicyclobutyl via photolysis of perfluoro-N-fluoropiperidine in the presence of perfluorocyclobutene [15].

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