Journal of Fluorine Chemistry, 23 (1983) 283–292
Received: December 17, 1982; accepted: January 25, 1983

FLUOROCARBON DERIVATIVES OF NITROGEN. PART IX [1]. SYNTHESIS OF SOME NEW 3,3,4,4,5,5-HEXAFLUORO-2,6-BIS(TRIFLUOROMETHYL)-1-AZACYCLOHEXENES $[\overline{CF_2(CF_2)_2C(CF_3)=NC}(CF_3)X$, X = H, Cl, SMe, $N_3]$

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SUMMARY

Treatment of perfluoro-(2,6-dimethyl-1-azacyclohexene) with triethylsilane, chlorotrimethylsilane, methyl trimethylsilyl sulphide, and azidotrimethylsilane yields, respectively, 6<u>H</u>-, 6-chloro-, 6-thiomethoxy-, and 6-azido-3,3,4,4,5,5-hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexene. Conversion of the thiomethoxy-compound into its 6<u>H</u>-analogue can be achieved using toluene-4-thiol, and treatment of perfluoro-(2,6-dimethyl-1-azacyclohexene) with aluminium chloride and sodium azide, respectively, provides alternative routes to the 6-chloro- and 6-azido-compounds.

INTRODUCTION

The work reported here stems from the isolation of perfluoro-2-chloro-1-azacyclohexene (I) and perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) (II) following attempts to trap anions (III) and (IV) with Me_3SiCl after mixing perfluoro-1-azacyclohexene (V) and perfluoro-(2,6-dimethyl-1-azacyclohexene) (VI), respectively, with caesium fluoride in acetonitrile [2].

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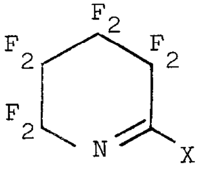
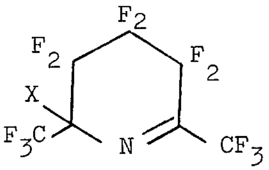


(I) X = Cl

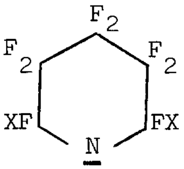
(V) X = F

(IX) X = Br



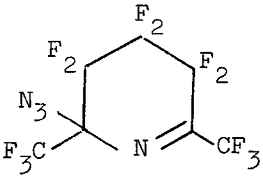
(II) X = Cl

(VI) X = F

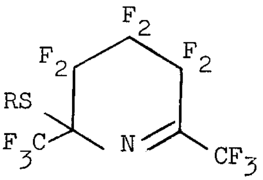


(III) X = F

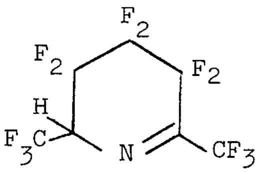
(IV) X = CF_3



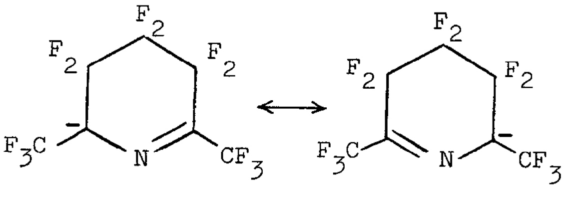
(VII)



(VIII)



(XI)



(X)

Detailed investigation of the perfluoro-1-azacyclohexene case revealed that chlorotrimethylsilane can effect smooth replacement of imidoyl fluorine by chlorine in this substrate with concomitant production of fluorotrimethylsilane [3]. In keeping with the addition-elimination mechanism proposed [3], Cl-for-F substitution [$\longrightarrow$ (II)] at C_6 has now been proved to occur when chlorotrimethylsilane attacks perfluoro-(2,6-dimethyl-1-azacyclohexene) (see Scheme 1). This observation, coupled with (a) the need to synthesise perfluoro-(6-azido-2,6-dimethyl-1-azacyclohexene) (VII) for research into ring-expansion reactions of cyclic fluorocarbon azides [4], and (b) problems encountered during attempts to prepare sulphur-containing derivatives (VIII) of perfluoro-(2,6-dimethyl-1-azacyclohexene) [5], led us to study the action of appropriate analogues (viz. Me_3SiN_3 and Me_3SiSMe) of chlorotrimethylsilane on the bistrifluoromethylated imine (VI).

DISCUSSION

Perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) (II) and its 6-azido and 6-thiomethoxy analogues, (VII) and (VIII; R Me), were isolated in 83, 92, and 62% yield, respectively, after treatment of perfluoro-(2,6-dimethyl-1-azacyclohexene) with appropriate trimethylsilanes in the absence of solvent at room temperature (in the case of Me_3SiN_3*) or 100 - 110 °C (Me_3SiCl, Me_3SiSMe) for 15 days** (see Scheme 1). The azide (VII) and the thio-ether (VIII, R = Me) were new compounds; the chloro-compound (II), however, had been encountered previously during preliminary studies on reactions between cyclic perfluoro-imines and aluminium halides [6] and, more recently, as a product from attempted trapping of perfluoro-(2,6-dimethyl-1-azacyclohex-1-yl) anion (IV) with chlorotrimethylsilane (see the Introduction). The aluminium chloride route provides perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) in 79% yield based on 67% consumption of perfluoro-(2,6-dimethyl-1-azacyclohexene) during 4 days at ambient temperature. Similar reactions between perfluoro-1-azacyclohexene (V) and aluminium halides (chloride [3] and bromide [6]) lead to products [(I) and (IX), respectively] arising from replacement of imidoyl fluorine by a heavier halogen; so, as in the case of fluorine replacement via the agency of trimethylsilanes in the two types of perfluoro-imine under consideration [i.e. one containing a $CF{=}N$ group and the other a $C(CF_3){=}N$ moiety], a common mechanism can be proposed (see Scheme 2).

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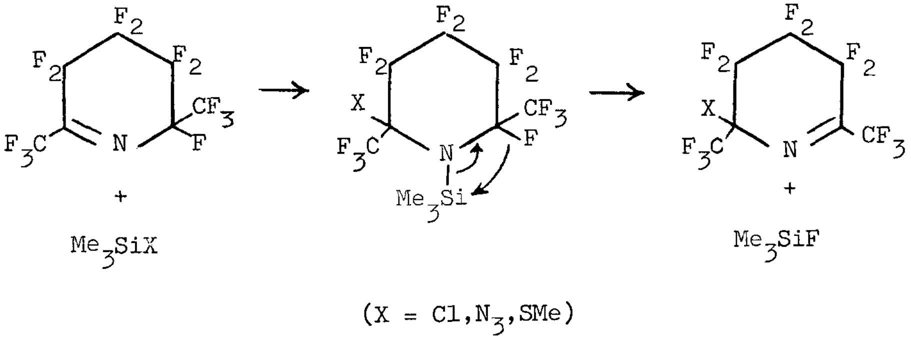
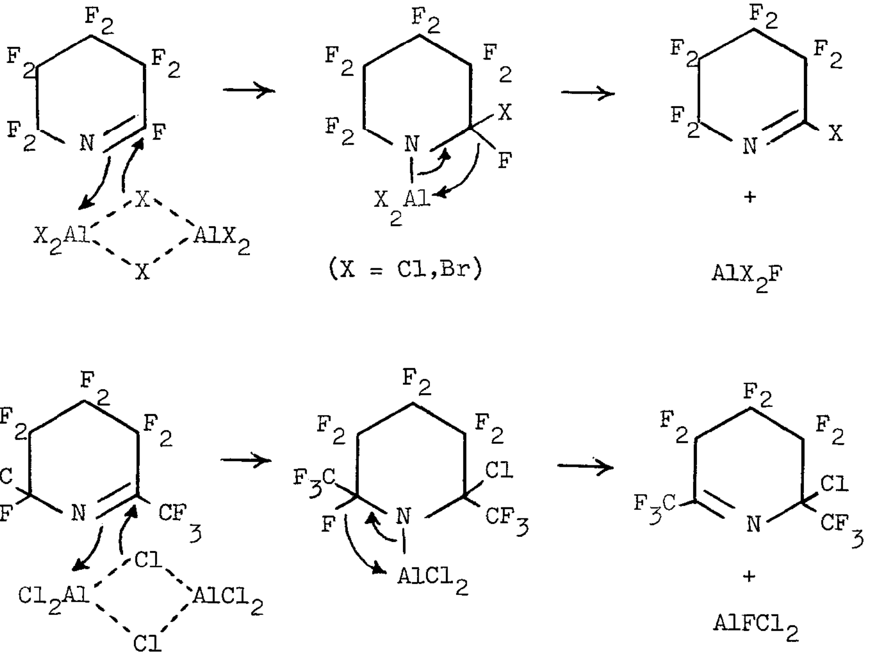
*Mild conditions were used here owing to the potential explosion hazard.

**Conditions were not optimized. This period may be excessively long.



Scheme 1



Scheme 2

An alternative (and preferred) route to perfluoro-(6-azido-2,6-dimethyl-1-azacyclohexene) (VII) comprises treatment of perfluoro-(2,6-dimethyl-1-azacyclohexene) with sodium azide in acetonitrile at room temperature. The straightforward Ad_N-E reaction [cf. 7] involved proceeds in high yield (ca. 80%), gives a purer product than when azidotrimethylsilane is used, is ca. ten times less expensive to undertake than the silane method, and has been employed on a 60 mmole scale [i.e. to give ca. 18 g of azide (VII) per run] without mishap.

By contrast, it seems probable that the corresponding alternative (i.e. use of MeSNa) in the case of conversion of perfluoro-(2,6-dimethyl-1-azacyclohexene) into its 6-thiomethoxy derivative (VIII, R = Me) via the agency of the trialkylsilane Me_3SiSMe will prove unsuccessful, because attempts to prepare analogous derivatives from the parent imine and the salts NaSH, p-MeC_6H_4SNa, and EtOC(S)SK in acetonitrile have so far yielded only unidentified F- and N-containing red gums and the known disulphides $(p\text{-}MeC_6H_4S)_2$ and $[EtOC(S)S]_2$ [5]. We conjecture that these disulphides could have arisen via nucleophilic attack by the anions p-$MeC_6H_4S^-$ and $EtOC(S)S^-$, respectively, on sulphur in the corresponding 6-substituted hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexenes [(VIII), R = p-MeC_6H_4, EtOC(S)] generated initially, with the mesomeric carbanion (X) produced concomitantly becoming involved in gum formation. Partial* support for this proposal comes from the discovery that hexafluoro-6-thiomethoxy-2,6-(bistrifluoromethyl)-1-azacyclohexene (VIII, R = Me) loses its thiomethoxy group when treated with the thiocresol p-MeC_6H_4SH in acetonitrile at room temperature, the fluorocarbon product being 6H-hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexene (XI) (73% yield after g.l.c. separation); in this respect, the perfluoro-(2,6-dimethyl-1-azacyclohex-1-en-6-yl) group in the thiomethoxy derivative (VIII, R = Me) displays pseudohalogen character.

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*Regrettably, thorough investigation of the complex hydrocarbon product was not undertaken.

Direct conversion of perfluoro-(2,6-dimethyl-1-azacyclohexene) into 6_H_-hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexene can be effected with triethylsilane, but under the conditions of the single experiment performed here (125 °C, 15 days) a complex product was obtained from which the 6_H_-compound could be isolated in only _ca_. 15% yield.

EXPERIMENTAL

^{19}F N.m.r. spectra were recorded at 84.6 MHz (ext. CF_3CO_2H; chemical shifts to high field designated negative) and ^{1}H spectra at 90 MHz (ext. Me_4Si) using a Perkin-Elmer R32 instrument. Mass spectra were obtained with an A.E.I. MS/2H or MS/902 spectrometer (electron beam energy 70 eV).

Perfluoro-(2,6-dimethyl-1-azacyclohexene) was prepared as described previously [7].

Preparation of perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene)

(a) _Using chlorotrimethylsilane_

Perfluoro-(2,6-dimethyl-1-azacyclohexene) (4.08 g, 11.8 mmol) was condensed, _in vacuo_, into a cold (-196 °C) Pyrex ampoule (300 cm^3) containing anhydrous caesium fluoride (1.82 g, 12.0 mmol); the tube was sealed, shaken at 20 °C for 2 days, then cooled (-196 °C) and opened to a vacuum system to allow chlorotrimethylsilane (1.30 g, 12.0 mmol) to be introduced. The tube was resealed and shaken at 20 °C for 4 days. Work-up of the volatile product by a combination of trap-to-trap fractional condensation, _in vacuo_, and g.l.c. (2 m Kel-F No. 10 oil/Celite, 75 °C) gave perfluoro-(2,6-dimethyl-1-azacyclohexene) (0.84 g, 2.43 mmol, 21% recovery) and perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) (nc) (1.44 g, 4.0 mmol, 42.5% based on $C_7F_{13}N$ consumed) [Found: C, 23.0; Cl, 10.1; F, 63.3; N, 3.6%; _M_ (mass spec.), 361.5 . $C_7ClF_{12}N$ requires C, 23.2; Cl, 9.8; F, 63.1; N, 3.9%; _M_, 361.5], $\lambda_{max.}$ (liq. film) 5.88 µm (C=N str.), δ_F (neat liq.) 7.3 (2-CF_3), 1.8 (6-CF_3), -31.3 and -51.9 (3-CF_2; J_{AB} 322 Hz), -45.7 (5-CF_2), and -45.8 and -67.8 (4-CF_2; J_{AB} 280 Hz) p.p.m.*

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*See ref. 7 for a discussion of ^{19}F n.m.r. assignments for 6-substituted perfluoro-(2,6-dimethyl-1-azacyclohexenes).

Similar work-up of the product formed by stirring magnetically a mixture of perfluoro-(2,6-dimethyl-1-azacyclohexene) (3.45 g, 10.0 mmol) and chlorotrimethylsilane (1.08 g, 10.0 mmol) at 100 °C for 15 days under anaerobic conditions in a Pyrex tube (300 cm^3) provided perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) (3.0 g, 8.3 mmol, 83%) and fluorotrimethylsilane (0.83 g, 9.0 mmol). The identity of the former product was checked by elemental analysis and spectroscopic methods (i.r., n.m.r., and mass), and that of the latter by i.r. spectroscopy.

(b) Using aluminium chloride

Perfluoro-(2,6-dimethyl-1-azacyclohexene) (2.24 g, 6.49 mmol) was condensed, in vacuo, onto aluminium trichloride (12 g, 90 mmol) contained in a cold (-196 °C) Pyrex tube (60 cm^3). The tube was sealed and shaken mechanically for 4 days at room temperature. Distillation of the volatile product in a semi-micro Vigreux still yielded a mixture (1.50 g) of perfluoro-(2,6-dimethyl-1-azacyclohexene) (0.75 g, 2.17 mmol, 33% recovery) and perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) (0.75 g, 2.07 mmol) [analysed by g.l.c. (2 m SE30 at 25 °C)] and perfluoro-(6-chloro-2,6-dimethyl-1-azacyclohexene) (0.49 g, 1.36 mmol, total yield based on $C_7F_{13}N$ converted = 79%) [Found: M (Regnault), 363. $C_7ClF_{12}N$ requires M, 361.5], b.p. (Siwoloboff) 94 °C, with correct spectroscopic (i.r. and ^{19}F n.m.r.) properties.

Preparation of hexafluoro-6-thiomethoxy-2,6-bis(trifluoromethyl)-1-azacyclohexene

Perfluoro-(2,6-dimethyl-1-azacyclohexene) (3.45 g, 10.0 mmol) and methyl trimethylsilyl sulphide (1.20 g, 10.0 mmol) were condensed separately, in vacuo, into a cold (-196 °C) Pyrex tube (300 cm^3) fitted with a PTFE needle valve (Rotaflo) and containing a PTFE-coated magnetic stirrer follower. The tube was sealed, allowed to warm to room temperature then, with the stirrer in motion, kept at 110 °C for 15 days. Volatile product was transferred, in vacuo, to a conventional Pyrex vacuum system and subjected to trap-to-trap fractional condensation; the material which condensed at -78 °C was subjected to preparative g.l.c. (5 m Kel-F oil No. 10/Celite at 80 °C) to provide 3,3,4,4,5,5-hexafluoro-6-thiomethoxy-2,6-bis(trifluoromethyl)-1-azacyclohexene (nc) (2.3 g, 6.2 mmol, 62%) (Found: C, 25.9; H, 0.8; N, 3.4; S, 8.6. $C_8H_3F_{12}NS$ requires C, 25.7; H, 0.8; N, 3.75; S, 8.6%), $\lambda_{max.}$ (liq. film) 5.88 μm (C=N str.), δ_F (neat liq.) 8.0 (2-CF_3), -30.6 and -52.9 (3-CF_2; J_{AB} 320 Hz), -40.0 and -66.2 (4-CF_2; J_{AB} 270 Hz), -44.3 and -48.2 (5-CF_2; J_{AB} 285 Hz), and 4.8 (6-CF_3) p.p.m., and δ_H 2.13 (s) p.p.m.

Preparation of 6*H*-hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexene

(a) From hexafluoro-6-thiomethoxy-2,6-bis(trifluoromethyl)-1-azacyclohexene

A mixture of the thiomethoxy-compound (1.12 g, 3.00 mmol), toluene-4-thiol (0.37 g, 2.98 mmol) and dry (distilled off P_2O_5) acetonitrile (5 cm^3) was shaken mechanically for 2 weeks under anaerobic conditions in a Pyrex ampoule (100 cm^3) at room temperature. Volatile product was allowed to distil from the ampoule, *in vacuo*, and was collected in a trap cooled to -196 °C; the material thus isolated was shown by g.l.c. analysis to be a mixture of acetonitrile and 6*H*-3,3,4,4,5,5-hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexene (nc), and a sample of the latter (0.72 g, 2.20 mmol, 73%) {[Found: C, 25.7; H, none detected; F, 70.1; N, 4.5%; *M* (mass spec.), 327. $C_7HF_{12}N$ requires C, 25.7; H, 0.3; F, 69.7; N, 4.3%; *M*, 327), $\lambda_{max.}$ (liq. film) 3.37 (C-H str.) and 5.85 (C=N str.) μm, δ_F (neat liq.) 7.1 (2-CF_3), -32.9 and -55.5 (3-CF_2; J_{AB} 321 Hz), -53.3 and -73.3 (4-CF_2; J_{AB} 275 Hz), -50.7 and -53.6 (5-CF_2; J_{AB} 279 Hz), and 6.4 (6-CF_3) p.p.m., δ_H (neat liq.) 4.4 (v. br. s) p.p.m. (spin-decoupling involving the fluorines of the 6-CF_3 group sharpened up this absorption considerably), and *m*/*z* 327 ($M^{+\cdot}$, 37.5%), 308 ($M^{+\cdot}$ - F·, 54%), 307 ($M^{+\cdot}$ - HF, 70%), 227 [$M^{+\cdot}$ - C_2F_4 (retro Diels-Alder cleavage), 42%], and 69 (CF_3^+, 100%)} was isolated by preparative g.l.c. (5 m OV17, 60 °C). ^{19}F N.m.r. analysis of the yellowish oily residue left in the reaction vessel failed to reveal the presence of any fluorine-containing material, and g.l.c. analysis showed it to contain at least 5 components.

(b) From perfluoro-(2,6-dimethyl-1-azacyclohexene) and triethylsilane

Treatment of perfluoro-(2,6-dimethyl-1-azacyclohexene) (3.45 g, 10.0 mmol) with triethylsilane (1.16 g, 10.0 mmol) at 125 °C for 15 days under anaerobic conditions (as described above for reaction of the azacyclohexene with Me_3SiSMe) gave a complex reaction product from which 6*H*-3,3,4,4,5,5-hexafluoro-2,6-bis(trifluoromethyl)-1-azacyclohexene (nc) with correct spectroscopic properties (i.r. and n.m.r.; see above) was isolated by g.l.c. (5 m Kel-F No. 10 oil/Celite, 70 °C) in *ca*. 15% yield.

Preparation of perfluoro-(6-azido-2,6-dimethyl-1-azacyclohexene)

(a) Using azidotrimethylsilane

The azidosilane (1.15 g, 10 mmol) and perfluoro-(2,6-dimethyl-1-azacyclohexene) (3.45 g, 10.0 mmol) were condensed separately, *in vacuo*, into a Pyrex Rotaflo tube (300 cm^3) equipped for magnetic stirring. After the tube had warmed to room temperature (18 °C), the reaction mixture was stirred for 15 days then the volatile product was fractionated, *in vacuo*, to provide fluorotrimethylsilane (9.3 mmol; -196 °C trap, identified by i.r. spectroscopy) and perfluoro-(6-azido-2,6-dimethyl-1-azacyclohexene) (nc) (3.38 g, 9.18 mmol, 92%) with a correct elemental composition (Found: C, 22.5; F, 61.9; N, 15.5 . $C_7F_{12}N_4$ requires C, 22.8; F, 62.0; N, 15.2%) but, compared with the product from sodium azide and perfluoro-(2,6-dimethyl-1-azacyclohexene) (see below), its i.r. spectrum showed bands (at 5.75 and 11.6 μm) indicative of an impurity not detected by ^{19}F n.m.r. spectroscopy.

(b) Using sodium azide

A mixture of perfluoro-(2,6-dimethyl-1-azacyclohexene) (3.45 g, 10.0 mmol), sodium azide (0.65 g, 10.0 mmol), and dry acetonitrile (10 cm^3) was stirred magnetically under anaerobic conditions at room temperature for 5 days. Distillation of the liquid product provided a fraction (b.p. 42 °C at 10 mmHg) which separated into two layers, the upper being acetonitrile and the lower perfluoro-(6-azido-2,6-dimethyl-1-azacyclohexene) (nc) (3.0 g, 8.15 mmol, 81.5%) (Found: C, 23.0; F, 62.1; N, 15.4.

$C_7F_{12}N_4$ requires C, 22.8; F, 62.0; N, 15.2%), $\lambda_{max.}$ 4.67 (N_3 asym. str.) and 5.85 (C=N str.) μm, δ_F (neat liq.) 7.4 (2-CF_3), -32.2 and -52.0 (3-CF_2; $\underline{J}_{AB}$ 321 Hz), -49.6 and -69.0 (4-CF_2; $\underline{J}_{AB}$ 270 Hz), -47.7 and -52.6 (5-CF_2; $\underline{J}_{AB}$ 285 Hz), and 1.0 (6-CF_3) p.p.m. On a 60 mmol scale, the yield of perfluoro-(6-azido-2,6-dimethyl-1-azacyclohexene) was still very good (80%).

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