# Reactions involving Fluoride Ion. Part 20.[1] Competition between Isomerization and Nucleophilic Attack on a Perfluoroalkene

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Reaction of perfluoro-3,4-dimethylhex-3-ene (1) with amine gives products which arise from nucleophilic attack directly on (1) but also products derived from attack on isomers of (1), *i.e.* perfluoro-3,4-dimethylhex-2-ene (2) and perfluoro-3-methylene-4-methylhexane (3), promoted by fluoride ion which is generated during reaction. The products obtained depend critically on the steric requirements of the attacking amine, *e.g.* Et_2NH gives products arising exclusively from attack on isomer (3).

In an earlier part [2] we described some of the reactions of O-nucleophiles with the novel fluorinated alkene (1).[3,4] This system is particularly interesting because, in principle, equilibration between (1) and its isomers (2)
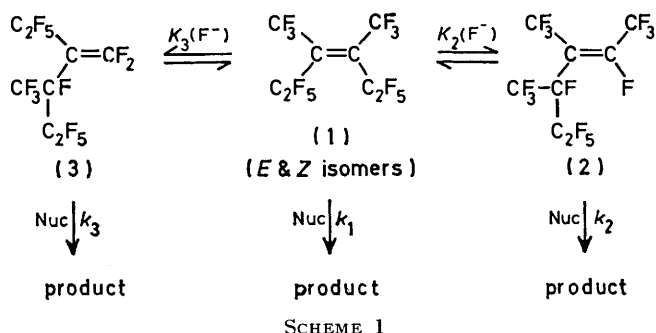
SCHEME 1

and (3) may be achieved by fluoride ion, generated by reaction of (1) with a nucleophile. Consequently, reactions of (1) with nucleophiles could give products arising from one or more of these isomers, see Scheme 1. In our earlier study [2] of reactions of (1) with O-nucleophiles, products were observed that were formed by reactions involving isomers (1) and (2) but there was no evidence for the involvement of (3). Nevertheless, a mixture containing each isomer was obtained recently,[5] by passing (1), in a stream of nitrogen, over hot iron or platinum under conditions where defluorination and fragmentation [6] were suppressed. It has now been clearly demonstrated [5] in reactions of compounds (1)—(3) with neutral methanol, that the reactivity order is $k_3 \gg k_2 \gg k_1$. Therefore, it is understandable that, even if the concentrations of (2) or (3) in the reaction mixture are small, it is still possible for significant reaction to occur *via* these isomers. In this paper we describe results of reactions of (1) with a variety of N-nucleophiles which give products arising from all of the isomers (1)—(3).

A process which accounts for the products obtained by reaction of ammonia with (1) is shown in Scheme 2. In a system containing water, only the nitrile (6) is obtained which, clearly, must be produced by direct reaction of isomer (1) with ammonia, as indicated. A more complex situation obtains, however, in a reaction with an-

hydrous ammonia because the composition of the product depends on the amount of ammonia used. Spectral evidence is available for the presence of compounds (4) and (5) in the product mixture obtained from reaction with anhydrous ammonia in the presence of caesium fluoride. Under these conditions, some attack on isomer (2) is clearly involved. However, in the absence of caesium fluoride only a compound corresponding to (5) is detected but not (4) and, with excess ammonia, (6) also the sole product under anhydrous conditions. It seems clear, therefore, that ammonium fluoride generated in the reaction does not promote the isomerisation of (1) to (2). Methylamine also reacts with isomer (1), exclusively, even under anhydrous conditions. The
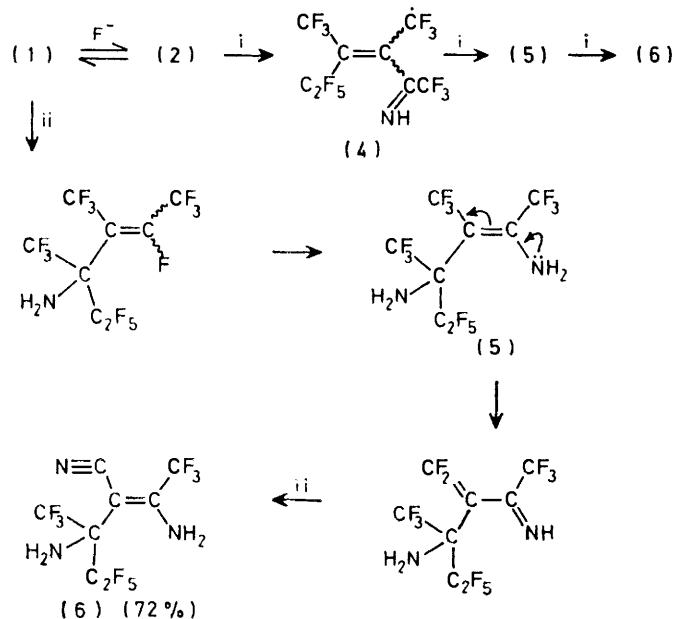
SCHEME 2   i, NH_3, Et_2O; ii, NH_3, H_2O, Et_2O

product (7) may be isolated but, with excess of methylamine, the azetine (9) is obtained, presumably *via* the intermediate ketenimine (8). Ketenimines have actually been isolated from comparable reactions of crowded primary amines and perfluoro-2-methylpent-2-ene.[7] Ethylamine, under anhydrous conditions, gave a more

complex product with (1) than the corresponding re-action with methylamine; the monosubstituted pro-ducts were characterised as (10)—(12). Obviously, these products arise from attack of the amine on all of
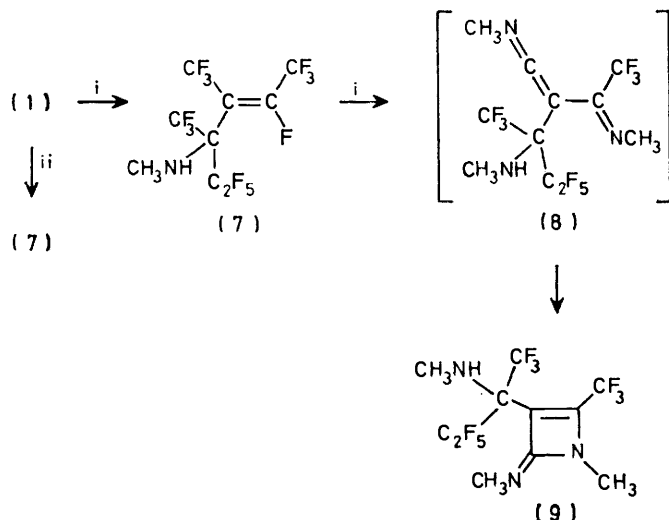
i, MeNH₂, Et₂O, H₂O; ii, MeNH₂, Et₂O

the isomers (1)—(3) and this indicates that the process k_1, Scheme 1, is slower for ethylamine than for methyl-amine.

A striking difference is observed with diethylamine, where the sole product now arises from reaction with (3), *i.e.* a process which was not observed at all in reactions with O-nucleophiles.²

The same selectivity was also observed in reaction with bulky t-butylamine, leading to products (15) and (16). On heating, compound (16) lost t-butyl fluoride giving the nitrile (17).

As outlined in Scheme 1, one of the factors determining product distribution will be the competition, for reaction

isomer (1) is most easily accounted for by the fact that ammonium fluoride does not promote equilibration of compounds (1)—(3).

For diethylamine there is no product detectable arising from direct attack on (1) and, the most obvious ex-planation for the formation of product (13), *i.e.* derived from isomer (3), is that direct attack by diethylamine on isomers (1) and even (2), is severely inhibited by steric effects. Evidence that steric effects are important in product formation also comes from the reaction with t-butylamine which gives products derived solely from isomer (3). Ethylamine is an interesting intermediate case, where steric effects must also be involved, to account for the additional product types obtained for ethylamine in comparison with methylamine. There must be a fine balance of effects operating in the case of ethylamine because this is the only example obtained, so far, of products arising from reaction with all three isomers (1)—(3).

The results described in this paper do, indeed, illustrate
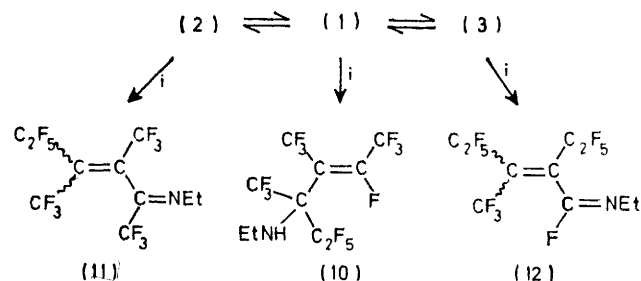
i, EtNH₂, tetraglyme

the unusual situation outlined in Scheme 1. Observed rate constants for product formation *via* isomers (2) and (3) are products of equilibrium- and rate-constants, *i.e.* K_2k_2 and K_3k_3. With all nucleophiles, the order of reactivity will be $k_3 > k_2 > k_1$ but the considerable range
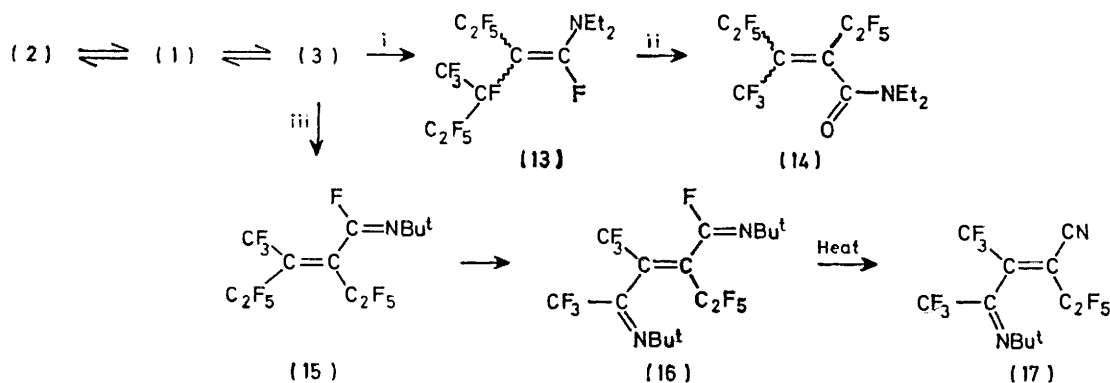
i, Et₂NH, Et₂O or tetraglyme; ii, dil. NaOH; iii, ButNH₂, Et₂O

of isomer (1), between amine and fluoride ion. There-fore, for the stronger bases, products arising from direct attack on (1) would be expected to be dominant. This is clearly not the case and so, other factors must be involved. That reaction of ammonia occurs exclusively with

in product distribution observed, arises from factors which (a) affect k_1, *i.e.* reaction with the most abundant isomer and (b) affect the setting up of equilibria K_2 and K_3 by fluoride ion produced in the reaction. Fluorides generated from ButNH₂ are obviously very effective in

promoting the equilibrium (1)–(3), whereas those produced from reaction with ammonia or methylamine are ineffective.

EXPERIMENTAL

^{19}F and ^{1}H n.m.r. spectra were measured at 40 °C, using a Varian A56/60D spectrometer, with trichlorofluoromethane or tetramethylsilane as external reference. Upfield ^{19}F shifts are quoted as positive. Unless otherwise stated, percentage yields and conversions were determined by g.l.c. analysis (using a gas-density balance detector) of the crude product mixture. G.l.c. columns were packed with 30% silicone gum rubber SE-30 (Col. O), or 20% di-isodecyl-phthalate (Col. A) on Chromosorb P.

Reactions of Perfluoro-3,4-dimethylhex-3-ene (1).—(a) *With aqueous ammonia.* A mixture containing (1) (7.7 g, 19.3 mmol), aqueous ammonia (10 ml, 0.88 s.g.), and ether (8 ml) was stirred at room temperature for 71 h. (*N.B.* in a separate experiment it was noted that, in the absence of ether, no reaction was apparent after 30 min but rapid development of colour occurred on the addition of ether.) Water (50 ml) and ether (50 ml) were added and the ether layer was separated, washed, and dried (MgSO$_4$). Analysis by g.l.c. (Col. ' O ', 200 °C) showed one major component. Ether was removed under reduced pressure leaving a pale yellow solid (4.9 g, 72% crude yield) which was fractionally sublimed at 100 °C (0.005 mmHg) giving trans-2,4-*diamino-3-cyano-4-trifluoromethyloctafluorohex-2-ene* (6), m.p. 73—74 °C

(6)
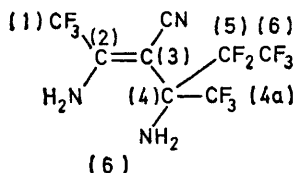
(Found: C, 27.5; F, 59.3; N, 12.2%; M^+, 351. $C_8H_4F_{11}N_3$ requires C, 27.4; F, 59.5; N, 12.0%; M, 351), $\lambda_{max.}$ (chloroform) 260 nm (ε 15 400).

The i.r. spectrum of (6) showed NH$_2$ stretching vibrations and bands at 1 625 (C=C str) and 2 220 cm^{-1} (C≡N str); the ^{1}H n.m.r. spectrum showed two signals corresponding to NH$_2$, δ_H 7.9br (undergoing slow exchange) and 3.3 (fast exchange); δ_F, 68.7 (1-CF$_3$), 73.6 (4a-CF$_3$; J_{4a-5}, 12.5 Hz), 80.2 (6-CF$_3$; J_{4a-6}, 4 Hz) 118.9, 119.1 p.p.m. (5-CF$_2$).

(b) *With anhydrous ammonia.* (i) *In the presence of caesium fluoride.* Compound (1) (7.89 g, 19.7 mmol) containing a small quantity of caesium fluoride was stirred during the passage of anhydrous ammonia gas; a solid yellow mass developed. The system was made mobile by addition of Et$_2$O and a further quantity of ammonia was passed. Solid was removed by filtration and analysis of the solution by mass spec.–g.l.c. showed components which corresponded to (4) (P^+ 358. $C_8HF_{14}N$ requires M – 19, 358), (5) (two isomers) (P^+, 357. $C_8H_4F_{14}N_2$ requires M – 19, 375), and compound (6) (see above).

(ii) *Without caesium fluoride.* In a reaction similar to that described above, the product contained components corresponding to (5) and (6) but not (4).

(iii) *Using an excess of ammonia.* In a reaction similar to that described in (b) (i) but using a sealed system with ammonia contained in a flexible rubber bladder, stirring was continued over several days. Filtration and removal of ether under reduced pressure left only compound (6), identified by comparison of spectra, see (a).

(c) *With aqueous methylamine.* A mixture containing (1) (8.5 g, 21.3 mmol), 25/30% (w/v) aqueous methylamine (20 ml), and ether (10 ml) was stirred for 74 h. The liquid product (7.5 g) was isolated as in (a) above and g.l.c. showed that it contained two major and several minor components (Col. ' O ', 200 °C). The two main components were separated by reduced-pressure fractional distillation and preparative-scale g.l.c. The ^{19}F n.m.r. spectrum of the


(9)
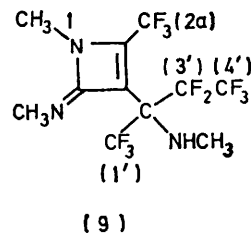
more volatile component showed that it contained several isomers or compounds and was not investigated further. The spectral and analytical data of the less volatile component are consistent with 3-(1-*methylamino-1-trifluoromethylper-fluoropropyl*)-4-*methylimino*-N-*methyl-2-trifluoromethyl-2-azetine* (9) (Found: C, 33.6; F, 53.5%; N, 10.7%; M^+, 393; $C_{11}H_{10}F_{11}N_3$ requires C, 33.60; F, 53.15; N, 10.69%; M, 393); $\lambda_{max.}$ (cyclohexane) 290 nm (ε 13 600); $\nu_{max.}$ 1 710 (C=C str) and 1 685 cm^{-1}; (C=N str); δ_F 67.0br (2a-CF$_3$,), 70.4 (1'-CF$_3$, $J_{1',2a}$ 10 Hz), 82.3 (4'-CF$_3$), and 118.3 p.p.m. (3'-CF$_2$, multiplet); δ_H 2.9 (CH$_3$), 3.2 (2 × CH$_3$), and 7.7 (NH).

(d) *With anhydrous methylamine.* Anhydrous methylamine (2.6 g, 84 mmol) was bubbled into compound (1) (6.47 g, 16 mmol); a white solid was formed in an exothermic reaction. During the reaction, ether (10 ml) was added, to inhibit blocking by the solid. Water was added and a white solid (0.6 g) which was insoluble in ether or water separated but was not identified. The ether layer was dried (MgSO$_4$) and the ether removed by distillation, leaving a mixture (3.0 g) which was shown by g.l.c. (Col. ' A ', 108 °C) to contain (1) (39%), major product (7) (46%), and minor components. A sample of the major product was isolated by preparative scale g.l.c. giving trans-4-*methylamino-3,4-bistrifluoromethylnonafluorohex-2-ene* (7) (Found: C, 26.5; F, 68.9; N, 3.7%; M^+, 411. $C_9H_4F_{15}N$ requires C, 26.29; F, 69.30; N, 3.41%; M^+, 411); δ_F 54.79, 65.07, 69.70, 81.31 (CF$_3$), 95.39 (=CF), and 118.44 p.p.m. (CF$_2$); assignments can be made by comparison with compound (10), see (e).


(10)
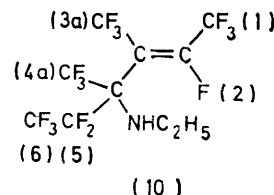
(e) *With anhydrous ethylamine.* Ethylamine (2.4 g, 53.3 mmol) was added to compound (1) (10 g, 25 mmol) and tetraglyme (20 ml) at 0 °C. The mixture was stirred at room temperature for 18 h after which time water (100 ml) was added and the product (6.9 g) recovered as in (a). Transference under vacuum gave a less-volatile fraction (3.4 g) and a volatile fraction (3.5 g). The volatile fraction contained two main components which were separated by

preparative-scale g.l.c. (Col. ' A ', 145 °C) giving trans-4-*ethylamino*-3,4-*bistrifluoromethylnonafluorohex-2-ene* (10), b.p. 127 °C (Found: F, 66.5%; M^+, 425. $C_{10}H_6F_{15}N$ requires F, 67.0%; M, 425); δ_F 53.7 (3a-CF$_3$), 63.8 (4a-CF$_3$), 68.8 (1-CF$_3$, $J_{1,3a}$ = 15 Hz, $J_{1,2}$ = 2 Hz), 80.3 (6-CF$_3$), 96.4 (2-F), and 117.6 p.p.m. (5-CF$_2$); δ_H 1.2 (CH$_3$), 1.9 (NH) [*N.B.* this is a remarkably low value, *cf.* compounds (6) and (9)], and -2.7 (CH$_2$); and a mixture of *cis*-,*trans*-2-ethyl-imino-3,4-bistrifluoromethyloctafluorohex-3-ene (11) and *cis*-, *trans*-3-(*N*-ethyliminofluoromethyl)-4-trifluoromethyl-decafluorohex-3-ene (12) [unresolved by g.l.c., ratio (11) : (12)

(11)   (12)
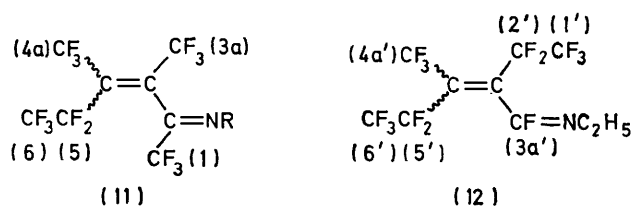
is 2 : 1 by ^{19}F n.m.r. spectroscopy] (Found: C, 29.3; F, 65.1; N, 3.5%; M^+, 405. Calc. for $C_{10}H_5F_{14}N$: C, 29.6; F, 65.7; N, 3.5%; M, 405); $\nu_{max.}$ 1 640 (C=C str), 1 670 [CF$_3$C=N str, (11)], 1 750 cm^{-1} [CF=N str, (12)]; the δ_F data are consistent with a mixture of (11) and (12), 17.6, 20.2 (br, 3a'-F), 57—61 (overlapping multiplets, 3a, 4a, 4a'-CF$_3$), 70.5 (1-CF$_3$), 80—81.7 (overlapping multiplets, 1', 6', 6-CF$_3$); 105.7—109.2 p.p.m. (overlapping multiplets, 2', 5', 5-CF$_2$).

(f) *With anhydrous diethylamine (with P. D. Philpot)*. A mixture containing compound (1) (10 g, 25 mmol), sulpholan (20 ml), and diethylamine (3.6 g, 49.3 mmol) was stirred vigorously for 16 h at room temperature. The reaction mixture was then poured into water (50 ml) and the products (10 g) separated as a lower organic layer. Compound (1) remaining in the product was removed under reduced pressure leaving a higher-boiling residue (8.3 g) which was shown by analytical scale g.l.c. (125 °C, Col. ' O ') to contain a single component, identified as 3-*trifluoromethyl*-4-*diethylaminofluoromethyleneundecafluorohexane* (13), (73%), b.p. 93 °C (18 mmHg) (Found: C, 32.0; H, 2.4; F, 62.5;


(13)
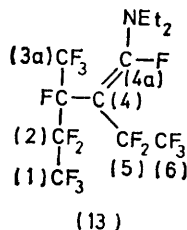
N, 3.5%; M^+, 453. $C_{12}H_{10}NF_{15}$ requires C, 31.8; H, 2.2; F, 62.9; N, 3.1%; M^+, 453); δ_F, 42.0 (4a-F), 77.2 (3a-CF$_3$), 82.5 (J = 18 Hz), 84.1 (J = 28 Hz) (1- and 6-CF$_3$),

103.5br (5-CF$_2$), 117.0, 122.4 (multiplets, 2-CF$_2$), and 181.5-br, p.p.m. (3-F).

Compound (13) (6 g, 12.2 mmol) was stirred vigorously with sodium hydroxide solution (20 ml; 2M), for 2 days, after which the lower layer (4 g) was withdrawn and dried (MgSO$_4$). G.l.c. (Col. ' O ', 125°) indicated one component, identified as *cis*- and *trans*-3-trifluoromethyl-4-(*N*,*N*-diethyl-amido)decafluorohex-3-ene (14) (70%) (Found: C, 33.2; F, 57.3; N, 3.6%; M^+, 431. $C_{12}H_{10}F_{13}NO$ requires C, 33.4; F, 57.3; N, 3.3%; M^+, 431); δ_F, isomer A: 58.0 (3a-CF$_3$), 81.1, 82.2 (1- and 6-CF$_3$), and 106.3 and 110.5 p.p.m. (complex, 2- and 5-CF$_2$); isomer B: 60.2 (3a-CF$_3$), 81.1, 82.2 (1- and 6-CF$_3$), and 106.3 and 110.5 p.p.m. (2- and 5-CF$_2$).

(g) *With anhydrous t-butylamine*. Addition of an excess of t-butylamine (1.75 g, 24 mmol) to a sample of (1) (1.1 g. 2.8 mmol) formed a white solid mass in an exothermic reaction. Pyridine (10 ml) was added and the mixture was stirred for several days, after which water was added and a lower layer (0.8 g) separated. Analysis by g.l.c. (Col. ' A ' 140°) showed the presence of one main component (*ca.* 80%), compound (16) (Found: $M^+ - F$, 447. $C_{16}H_{18}F_{12}N_2$ requires M, 466); δ_F, 11.8 ($J_{3a,4a}$ = 15 Hz, 4a-F), 59.5 ($J_{3a,1}$ = 8.5 Hz,

(14)
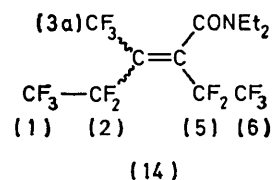
3a-CF$_3$), 69.3 (1-CF$_3$), 81.9 (6-CF$_3$), and 107.7 p.p.m. (5-CF$_2$); δ_H 1.4 and 1.45 (singlets). Attempted separation of compound (16) by preparative-scale g.l.c. (Col. ' A ', 150 °C), gave a mixture containing (16) (15 mol % by n.m.r.) and a compound identified as the nitrile (17) (Found: $M^+ - CH_3$. 375. $C_{12}H_9F_{11}N_2$ requires M, 390); $\nu_{max.}$ 1 625 (C=C str.), 1 685 (C=N str) and 2 225 cm^{-1} (C≡N str); δ_F, 61.1 ($J_{3a,1}$ = 8.5 Hz, 3a-CF$_3$), 70.0 (1-CF$_3$), 80.9 (multiplet, 6-CF$_3$), and 108.4br p.p.m. (5-CF$_2$); δ_H 1.4 (s).

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