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FLUORINATION OF TRIMETHYLAMINE OVER COBALT(III) FLUORIDE

NOVEL CYCLISATION OF TRIMETHYLAMINE TO POLYFLUORO-1,3-DIMETHYLIMIDAZOLIDINES (CHARACTERISED BY MASS SPECTROMETRY AND NMR SPECTROSCOPY); CATION-RADICAL MECHANISM OF FLUORINATION

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Abstract—Trimethylamine has been fluorinated with cobalt(III) fluoride to give eleven novel highly fluorinated products including seven polyfluoro-1,3-dimethylimidazolidines. Mass spectrometry and NMR spectroscopy were used to assign product structures. On fluorination under comparable conditions 1,2-bisdimethylamino-ethane and bisdimethylaminomethane gave mixtures containing all the products characterised from the title fluorination. A cation-radical mechanism of fluorination is proposed.

The fluorination of trimethylamine was studied in order to extend our search for new inhalational anaesthetics by the synthesis of novel molecules containing one or more highly fluorinated tertiary amine functions.[1]

Fluorinations of trimethylamine by CoF_3,[2,3] electrochemical fluorination[4] and a direct fluorination method[5] have been described. The only positively identified products were $(CF_3)_3N$,[3-5] $(CF_3)_2NF$,[2,3,5] $CF_3CF_2NF_2$,[5] CF_3NF_2,[3,5] NF_3,[4] C_2F_6,[5] CF_4,[4,5] and CHF_3.[4]

Additional products, believed to be volatile dimers [e.g. $(CF_3)_2NN(CF_3)_2$][3,5] and cyclic compounds,[2,3] were also present.

Apart from $(CF_3)_3N$,[2-12] the only known (poly) fluorinated derivatives of trimethylamine are $(CF_3)_2NCH_2F$,[1] $CF_3N(CH_3)_2$,[13,14] $CHF_2N(CH_3)_2$,[15,16] and $CH_2FN(CH_3)_2$.[17]

In this paper we describe a fluorination of trimethylamine with CoF_3 at 100° in a conventionally designed reactor.[1] A complex mixture of novel products (Table 1) was obtained. With the exception of 4 [$(CHF_2)_2NCHO$†] these were shown to be polyfluorinated derivatives of trimethylamine (1–3) and 1,3-dimethylimidazolidine (5–11). Compounds of the latter type were previously unknown.

Speculation on possible mechanisms which could account for the formation of 5–11 very soon led us to surmise that $Me_2NCH_2NMe_2$, $Me_2NCH_2CH_2NMe_2$ or (poly)fluorinated derivatives of these compounds could be important intermediates (Discussion and Table 1). Accordingly, fluorinations of these diamines were carried out with CoF_3 at 100°.

The mixture obtained from the fluorination of $Me_2NCH_2NMe_2$ was very similar to that obtained from our fluorination of trimethylamine; all the identified products (1–11) were the same in both cases. 1–11 were also characterised in the mixture from the fluorination of $Me_2NCH_2CH_2NMe_2$ but, in addition, three further new acyclic amines (12–14) were obtained.

†Glc evidence suggests that 4 arose from an acid hydrolysis of 3 [$(CHF_2)_3N$] which took place during distillation of the crude product mixtures.

From these results it was deduced that $Me_2NCH_2NMe_2$ and certain partially fluorinated derivatives could be important precursors to 5–11 in the fluorination of trimethylamine. It was also concluded that $Me_2NCH_2CH_2NMe_2$ and its fluorinated derivatives were unlikely to be important intermediates in the fluorination of the title compound.

Although the structures of 1–14 were established by NMR spectroscopy, mass spectrometry provided some useful confirmatory information.

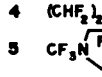
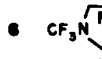
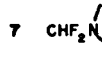
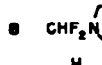
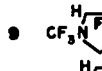
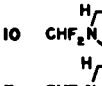
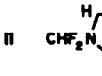
Mass spectrometry. Accurate mass measurements corresponding to M^+ or (M^+-F) ions were obtained in most cases but the strongest ions were usually smaller N-containing fragments. Thus a detailed analysis of the spectra of the polyfluoro-1,3-dimethylimidazolidines (Table 2) revealed strong peaks assigned to $C_3HF_6N^+$, $C_3H_2F_5N^+$, $C_2F_4N^+$ and $C_2HF_3N^+$ ions. In contrast to the precedent established for certain 6-membered heterocycles (polyfluoro-1,4-dioxans,[18] -oxathians[18] and -4-methylmorpholines[1]), ions due to polyfluoroethylene fragments ($C_2F_4^+$ and $C_2HF_3^+$) were always weak. A possible breakdown mechanism for 10 is outlined in Fig. 1.

NMR spectroscopy. ^1H NMR spectra (Table 3) were comparatively simple. $NCHF_2$ groups ($J_{CHF_2} \sim 55$–61 Hz) generally appeared as triplets (at 6.4–6.7δ), although in molecules containing ring H atoms these became distinct doublets of doublets. Protons in the $NCHF_2$ groups of 4 behaved anomalously compared with those of other products. Slow rotation about the amide C–N bond was observed, similar to that shown by DMF. Thus, two separate broadened triplets were observed for each CHF_2 group at 0°. These coalesced to one broad triplet at 35° and eventually to a sharp triplet (J = 58.0 Hz), centred at 7.09δ, at 60°.

NCH_2F groups ($J_{CH_2F} \sim 51$–55 Hz) were seen as doublets at 5.3–5.4δ. Ring H atoms in 9–11 appeared at 5.7–5.9δ and were split by both geminal ($J \sim 64$–66 Hz) and vicinal ($J \sim 5.5$–7.0 Hz) F atoms.

The ^{19}F NMR spectra (Table 3) provided the bulk of the information on which the structural assignments were based. The discussion ignores certain non-first

Table 1. Major products[a] from fluorinations of $(CH_3)_3N$, $(CH_3)_2NCH_2N(CH_3)_2$[D] and $(CH_3)_2NCH_2CH_2N(CH_3)_2$[E] with CoF_3.

	Product structure[b]	$(CH_3)_3N$	[D]	[E]
1	$CF_3N(CHF_2)_2$	11	2	7
2	$CF_3N(CH_2F)CHF_2$	3	4	6
3	$(CHF_2)_3N$	18	19	17
4	$(CHF_2)_2NCHO$	11[c]	1[c]	d
5		2	3	3
6		6	4	6
7		13	11	15
8		4	6	3
9		2[c]	3[c]	d
10		9	14	8
11		1	5	2
12	$(CHF_2)_2NCF_2CHF_2$	—	—	3
13	$CF_3N(CHF_2)CF_2(CHF_2)_2NCF_2$	—	—	6
14	$[(CHF_2)_2NCF_2]_2$	—	—	8

[a]The quoted figures are percentages by weight.
[b]'F' inside ring denotes that all unmarked bonds are to fluorine.
[c]Assumption made that the relative proportions of 4 and 9 in each distillation fraction remained unchanged.
[d]Combined percentage of 4 and 9 = 3.

order effects apparent in the spectra of some of the acyclic amines without affecting the validity of the structural assignments. For example, the spectrum of 3 is a distorted doublet of multiplets. The chemical shift and coupling constant of the doublet, taken in conjunction with those of the triplet visible in the ^1H NMR spectrum, indicated that the structure was probably $(CHF_2)_3N$. Information confirming this assignment was obtained from the mass spectrum of the compound.

As previously found with the polyfluoro-4-methylmorpholines,[1] F-substituted N–Me groups appeared in characteristic portions of the spectra: CH_2F fluorine at 170.5–174.0ϕ, CHF_2 fluorines at 94–102ϕ and CF_3 fluorines at 52–60ϕ.

F atoms in NCF_3, $NCHF_2$ and NCH_2F groups in the imidazolidines 5–8 showed all the possible four-bond F–C–N–C–F couplings ($J \sim 5.5$–8.5 Hz). Some couplings of this type were also shown by the acyclic amines (1–3 and 12–14) and the remaining imidazolidines (9–11). These were too complex for simple analysis with the exception of the couplings due to the fluorines of certain $NCHF_2$ groups in 9–11.

All four $NCHF_2$ groups in 9–11 appeared as AB patterns ($J \sim 221$–228 Hz), further split by geminal H atoms and some F atoms four bonds away. However, one pair (X) of AB patterns (in 9 and 10) was obviously less widely separated than the other pair (Y, in 10 and 11). It was assumed that the more distant the $NCHF_2$ group was from the asymmetric ring C atom, the narrower would be the separation. Further evidence for this conclusion was provided by reference to the consistent chemical shift (99.9ϕ) of $NCHF_2$ groups in imidazolidines (6–8) containing no ring H atoms. Thus the chemical shifts of the mid points of AB pair X were both within 0.1 ppm of this standard whilst those (98.0 and 98.1ϕ) of AB pair Y were relatively low, as a consequence of the close proximity of the ring H atom in each case. The fine splittings of AB pair Y provided further confirmation of these structural assignments. Thus the downfield arms of both AB signals were split as doublets ($J \sim 10$–11 Hz) whilst the upfield arms were split as doublets ($J \sim 5$–8 Hz) of doublets ($J \sim 5$–8 Hz). Since four-bond H–F couplings of this size are most unlikely, it seems reasonable to conclude that these are four-bond F–F couplings. The downfield F atoms must be coupled to single F atoms four bonds away whilst the upfield fluorines must be coupled to two dissimilar F atoms the same distance away. The fine splittings of AB pair X were obviously more complex, indicating the absence of H atoms four bonds away from the F atoms of the AB pair.

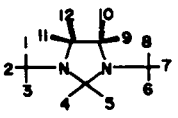
CF_2N groups in the acyclic amines 12–14 appeared as complex multiplets at 98–100ϕ. $NCF_2(C)$ groups in the imidazolidines 5–8 appeared at 91–95ϕ as multiplets (due to four-bond couplings) which could be analysed in sufficient detail for the relative positions of the CF_2 groups in 6 and 8 to be established. $NCF_2(C)$ groups in the imidazolidines 9–11 appeared as complex AB patterns ($J \sim 179$–181 Hz) at 79–104ϕ. $NCF_2(N)$ groups in 5–8 appeared as multiplets at 61.5–65.5ϕ whilst those in 9–11 appeared as complex AB patterns ($J \sim 126$–134 Hz) at 56–67ϕ.

Table 2. Fragments from the mass spectra of some polyfluoro-1,3-dimethylimidazolidines[a].

Compound No.	5	6	7	8	9	10	11
Fragment							
M	<1	1	14	2	4	1	24
183 (C_3F_7N)	90	33	<1	<1	1	<1	<1
165 (C_3HF_6N)	4	7	100	24	94	36	<1
147 ($C_3H_2F_5N$)	<1	<1	4	23	1	24	100
114 (C_2F_4N)	100	100	95	100	89	100	95
96 (C_2HF_3N)	2	17	25	26	100	76	93
78 ($C_2H_2F_2N$)	<1	<1	3	24	10	31	45

[a]Intensities are quoted as percentages of the base peak. No allowance has been made for the presence of ^{13}C in certain fragments (e.g. 165, C_3HF_6N and/or $^{12}C_2{}^{13}CF_6N$).

Table 3. Chemical shifts in polyfluoro-1,3-dimethylimidazolidines[a]. All compounds numbered as in



Compound No.	Position No. 1	2	3	4	5	6	7	8	9	10	11	12
5	58.55	b	b	65.35	b	58.55	b	b	94.6	b	b	b
6	56.55	b	b	62.65	b	99.9 ($J_{68} = J_{78} = 57.5$)	b	6.64[c]	91.65	b	93.35	b
7	99.9 ($J_{13} = J_{23} = J_{68} = J_{78} = 58.0$)	b	6.70[c]	61.95	b	99.9	b	6.70[c]	92.35	b	b	b
8	99.9 ($J_{13} = J_{23} = 57.5$)	b	6.58[c]	64.4	b	173.6 ($J_{67} = J_{68} = 53.5$)	5.40[c]	b	93.4	b	92.6	b
9	57.7	b	b	65.7 ($J_{45} = 126$)	58.5	102.0[d] ($J_{67} = 228$; $J_{68} = 55$; $J_{78} = 59$)	97.65[d]	6.52[c]	101.05 ($J_{9-10} = 181$)	79.7	145.2 ($J_{11-12} = 64$)	5.75[c]
10	100.7[e] ($J_{12} = 221$; $J_{13} \sim J_{23} \sim 58.5$)	95.3[e]	6.65[c]	65.8 ($J_{45} = 134$)	56.6	101.8[d] ($J_{67} = 225$; $J_{68} \sim J_{78} \sim 57$)	98.0[d]	6.55[c]	101.1 ($J_{9-10} = 180$)	79.9	143.7 ($J_{11-12} = 65$)	5.86[c]
11	100.75[e] ($J_{12} = 221$; $J_{13} \sim J_{23} \sim 58.5$)	95.45[e]	6.58[c]	66.9 ($J_{45} = 132$)	60.7	172.6 ($J_{67} = J_{68} = 54.5$)	5.35[c]	b	103.6 ($J_{9-10} = 179.4$)	80.2	144.0 ($J_{11-12} = 65.5$)	5.83[c]

[a] ^{19}F shifts in ϕ units; coupling constants in Hz.
[b] Identical to the preceding figure.
[c] ^{1}H shifts in δ units.
[d] AB pair X.
[e] AB pair Y.

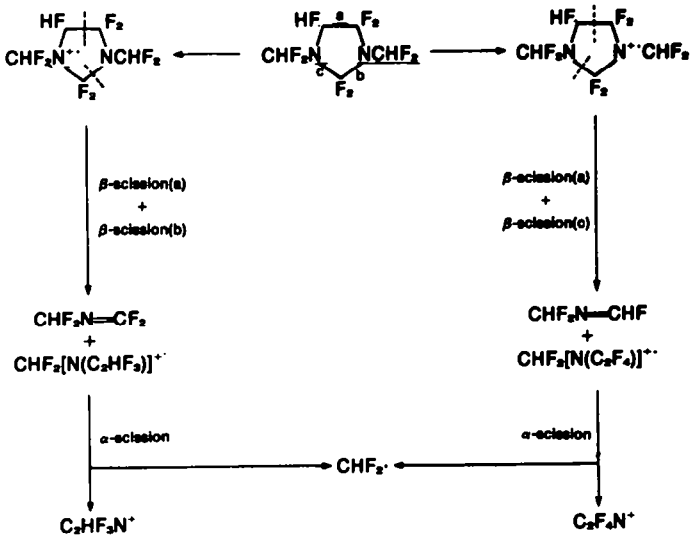


Fig. 1. A possible breakdown mechanism for 10.

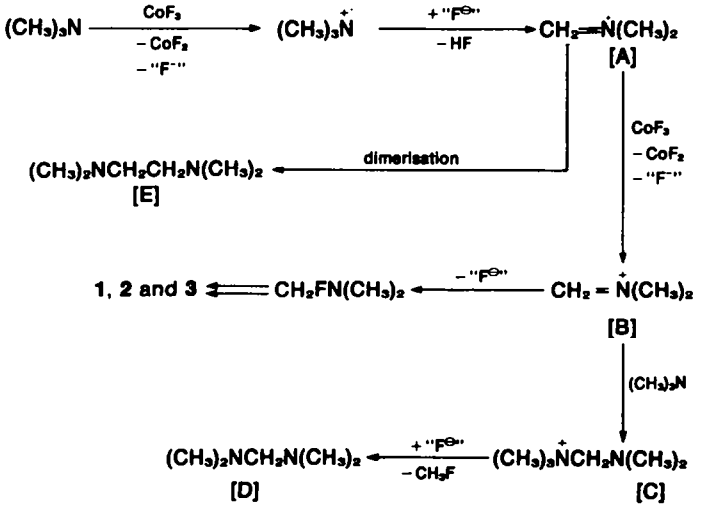


Fig. 2. Possible initial steps in the fluorination of $(CH_3)_3N$.

F atoms in CHFN groups in 9–11 appeared as doublets of multiplets at 143.5–145.5ϕ.

The structures of compounds not already considered individually always followed unambiguously from information derived from the ^{19}F NMR data.

DISCUSSION

The high degree of fluorination observed is consistent with a cation-radical mechanism[19,20] of fluorination since the ionisation potential (7.82 eV[21]) of trimethylamine is comparatively low. Mechanisms of this kind have previously been suggested to account for the products of fluorinations of certain cyclic amines (4-methylmorpholine,[1] pyridine,[22] 4-methylpyridine[22] and 1-methylpyrrole[23]) with high valency metal fluorides.

We outline some ideas on initial steps in the fluorination of trimethylamine in Fig. 2. The simple fluorinated monoamines (1–3) are believed to be formed from a series of oxidation-quenching steps via radicals and cations such as A and B, respectively. Intermediates of these types can also be invoked to explain the synthesis of the fluorinated imidazolidines (5–11).

A reaction which could account for the introduction of a second N atom is an attack of Me_3N† on a highly electrophilic imminium intermediate such as B‡. The resultant tetraalkyl ammonium species (C) could be quenched by "$F^{\ominus}$" to give $Me_2NCH_2NMe_2$[D].

Secondary amines could interact with B in a similar manner. Thus Me_2NH would give an adduct which could form (D) on deprotonation.

$$Me_2NH \xrightarrow{CH_2=\overset{+}{N}Me_2} Me_2\overset{+}{N}HCH_2NMe_2 \xrightarrow{-H^+} [D],$$

There is a possibility that Me_2NH could be produced transiently in the fluorination of Me_3N since its perfluoro derivative has been characterised from such a reaction[2,3] and it is known that Me_2NH may be obtained from Me_3N by oxidation.[24,25] In our system fluorinated analogues of Me_2NH could be obtained by an α-scission of a Me radical from intermediates of type A followed by HF addition to the imine thus formed.

$$CH_2=\dot{N}Me_2 \xrightarrow{-[Me^{\cdot}]} CH_2=NMe \xrightarrow{HF} CH_2FNHMe$$

Products arising from the incorporation of $(CF_3)_2N$ groups [via $(CF_3)_2NH$?] into the substrate have been isolated from complex mixtures obtained from fluorinations of pyridine with $KCoF_4$.[22]

A second method for the insertion of a N-containing species into the parent substrate was considered. This was a radical dimerisation of intermediate (A) to give $Me_2NCH_2CH_2NMe_2$[E]. Peroxide-catalysed dimerisations of some closely related radicals have been described,[26] e.g.,

$$C_6H_5NMe_2 \rightarrow C_6H_5NMeCH_2 \rightarrow [C_6H_5NMeCH_2]_2.$$

However, fluorinated derivatives of E were absent from the products identified from the fluorinations of trimethylamine and D, whilst two (13 and 14) were found amongst the products from the fluorinations of E. E is therefore unlikely to be a significant intermediate in the fluorination of trimethylamine whilst D could be an important intermediate.

The consequences of possible oxidative cleavage reactions of D (e.g. the formation of B by the β-scission shown in Fig. 3) followed by fluorination giving CH_2FNMe_2 could complicate the above conclusions. It is known that chlorinations of D carried out under mild reaction conditions give Me_2NCH_2Cl as the major product.[27] CH_2FNMe_2 may undergo all the modes of reaction so far outlined for Me_3N. However, the chemical properties of the fluoro derivatives of D (e.g. $Me_2NCHFNMe_2$) which form one significant group of products which could be generated from CH_2FNMe_2 may be modified in such a way that their most important reactions subsequently could be cyclisations to fluoro derivatives of 1,3-dimethylimidazolidine G (Fig. 3 for the analogous conversion of D to G via the diradical intermediate F‡).

Figure 3 also shows various routes to the products characterised from the fluorination of E.

In summary, E and its (poly) fluorinated derivatives are unlikely to be significant intermediates in the fluorination of trimethylamine whilst D, or, more likely, certain (poly) fluorinated derivatives could be important precursors to the polyfluorinated 1,3-dimethylimidazolidines characterised from the title fluorination.

We were disappointed to find that the major products isolated from the fluorinations were valueless as anaesthetics.

EXPERIMENTAL§

IR spectra, recorded on all pure samples, were measured on a Perkin Elmer Model 157 Spectrophotometer. ^{1}H NMR spectra (samples in $CDCl_3$ soln with internal TMS as standard) were measured on Varian HA 100D (100 MHz), Varian A60 (60 MHz) or Perkin–Elmer R12 (60 MHz) instruments. ^{19}F NMR spectra (samples in $CDCl_3$ soln with internal CCl_3F as standard) were measured at 35° on a Bruker HX 90E (84.69 MHz) instrument linked to a Nicolet 1080E computer. Relative sizes of ^{1}H and ^{19}F NMR integrals were always in agreement with the proposed structures. Mass spectra (MS) were recorded on an AEI MS9 instrument, *m/e* values being obtained in amu. Entries such as NMR or MS after a compound indicate that details of these measurements appear elsewhere.

Analytical and preparative glc separations were carried out with Pye 104 and 105 glc machines operated under standard conditions. Both machines were equipped with glass columns containing either Di(2-ethylhexyl) Sebacate (15%) on Universal Support (Column A, Pye 105) or Carbowax 20M (20%) on Chromosorb W (Column B, Pye 105). Details of some intermediate fractions have been omitted from descriptions of the preparative glc separations.

Fluorination of trimethylamine with CoF_3. Trimethylamine (48.4 g) was vaporized over 5 hr into a stirred bed of CoF_3 (3 kg) at 100° in a stream of dry N_2 (400 ml min^{-1}). Crude product, collected in a trap at −78°, was removed after the system had been purged with N_2 for a further 4 hr at 100–200°. After ice-water washing (2 × 50 ml aliquots) the mixture (47.6 g) was further washed with excess sat $NaHCO_3$aq and dried ($MgSO_4$). An aliquot (38.9 g) of this material was distilled (Vigreux column; 30 cm × 6 mm) to give six fractions.

†Analogous reactions may be undergone by partially fluorinated derivatives. Although this statement is valid for many later stages in the mechanism, for the sake of clarity no mention of these additional possibilities has been made in the ensuing discussion, except in cases of special relevance.

‡D could be converted to G by a cyclisation of the substituted imminium intermediate $CH_2=\overset{+}{N}MeCH_2NMe_2$ to a charged 1,3-diazetidine species, followed by rearrangement and deprotonation.

§Further details of glc separations, NMR and mass spectra are available on request from the authors.

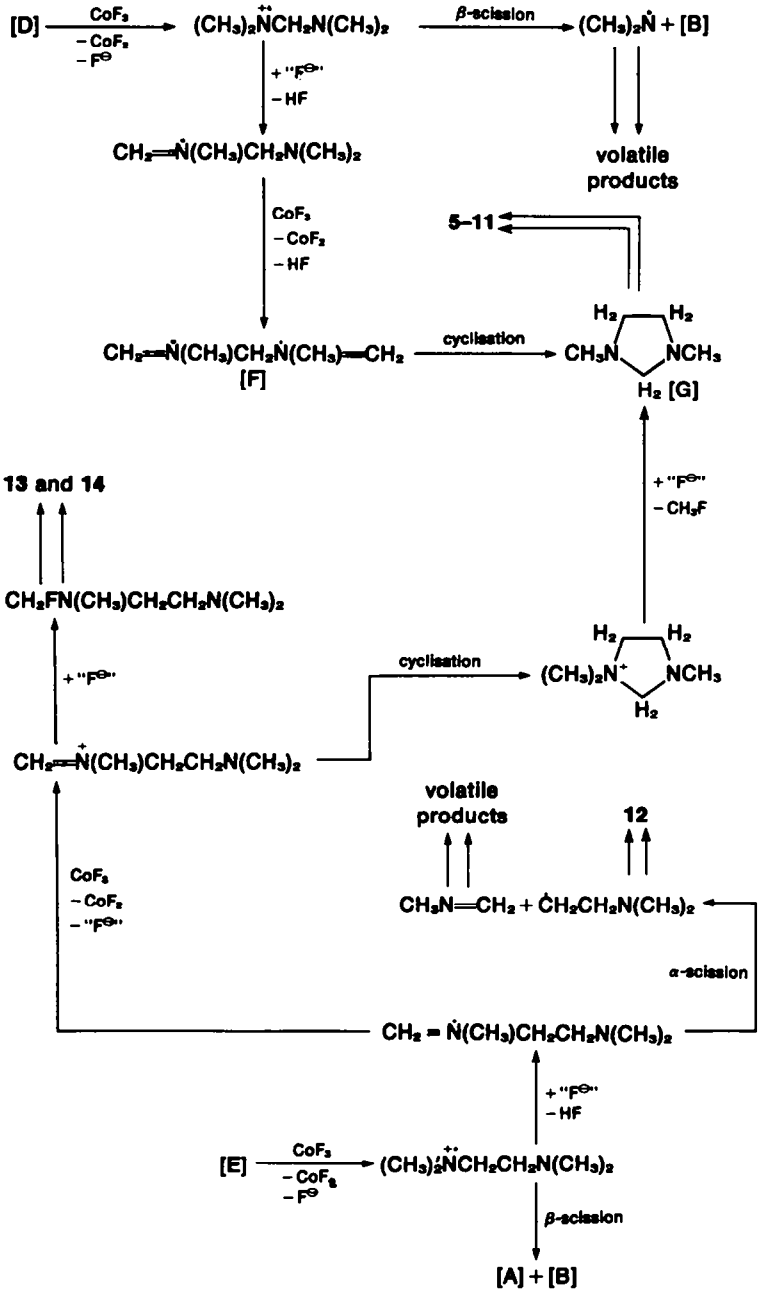


Fig. 3. Possible mechanisms for the fluorinations of [D] and [E].

Volatiles (0.9 g; b.p. ≤ 26°): mainly **1** (0.3 g), **3** (0.4 g) and **5** (0.1 g) (analytical glc).

Fraction 1 (6.9 g; b.p. 26–39°). Separation (A, 52°) of an aliquot (6.25 g) gave: (i) a 1:1 mixture (0.40 g) of **5** and an unidentified component, contaminated by some **1**; (ii) **1**, ***bisdifluoromethyl-trifluoromethylamine*** (1.76 g), b.p. 25.5–27.5°, ^{1}H[$(CHF_2)_2N$, triplet, J = 58.2 Hz, at 6.60δ] and ^{19}F[CF_3, pentet, J = 6.0 Hz, at 57.0ϕ; $(CHF_2)_2N$, doublet, J = 58.1 Hz, of quartets, J = 6.0 Hz, at 97.6ϕ]NMR, MS[*m/e* at 185.019 ($C_3H_2F_7N$ requires 185.019), 166, 134, 116, 115, 114, 96, 69, 32]; and (iii) **3**, ***trisdifluoromethylamine*** (1.13 g), b.p. 44.0–45.0°, ^{1}H(CHF_2, triplet, J = 59.4 Hz, at 6.67δ) and ^{19}F(CHF_2, doublet, J = 61.5 Hz, at 96.2ϕ)NMR, MS[*m/e* at 167.017 ($C_3H_3F_6N$ requires: 167.017), 166, 165, 148, 116, 98, 97, 96, 78, 51, 32].

Fraction 2 (6.5 g; b.p. 39–73°): mainly **1** (0.4 g), **2** (0.7 g), **3** (2.9 g), **4** (0.8 g), **5** (0.1 g), **6** (1.1 g), **7** (0.1 g) and **9** (0.1 g) (analytical glc).

Fraction 3 (10.6 g; b.p. 73–99°). Separation (A, 102°) of an aliquot (6.51 g) gave: (i) a complex mixture (1.44 g) containing **3**, **4**, **6**, **9** and one other unidentified major component; (ii) a mixture (1.43 g), a portion of which was further separated (B, 103°) to give (ii) (a) **9**[28] (0.04 g) and (ii) (b) **4**, N,N-***bisdifluoromethyl-formamide*** (0.40 g), b.p. 87.0–88.0°, IR[$\nu_{max(C=O)}$ 1750 cm^{-1}], ^{1}H[$(CHF_2)_2N$, broadened triplet, J = 58.0 Hz, at 7.09δ; CHO, singlet at 8.84δ] and ^{19}F[$(CHF_2)_A$, broadened doublet, J = 58 Hz, at 95.6ϕ; $(CHF_2)_B$, broadened doublet, J = 58 Hz, at 104.7ϕ]NMR, MS[*m/e* at 145.014 ($C_3H_3F_4NO$ requires: 145.015), 117, 116, 94.012 ($C_2H_2F_2NO$ requires: 94.013), 78, 66, 51, 48]; and (iii) **7**, 1,3-***bisdifluoromethyl-hexafluoroimidazolidine*** (1.90 g), b.p. 94.5–95.5°, NMR, MS (Found: *m/e* at 280.007. $C_5H_2F_{10}N_2$ requires: 280.006).

Fraction 4 (5.4 g; b.p. 99–120°). Separation (A, 110°) of this material gave: (i) a mixture (0.19 g) containing several major components including **4**, **7** and **9**; (ii) **7**[28] (0.17 g); (iii) **8**, 1-

difluoromethyl - 3 - monofluoromethyl - hexafluoroimidazolidine (0.76 g) b.p. 111.0–113.0°, NMR, MS (Found: *m/e* at 262.015. $C_5H_3F_9N_2$ requires: 262.015); (iv) **10**, 1,3-*bisdifluoromethyl*-2, 2, 4, 4, 5-*pentafluoroimidazolidine* (2.07 g), b.p. 114.5–116.5°, NMR, MS (Found: *m/e* at 262.015); and (v) a complex mixture (0.10 g) containing some **10** and **11**.

Fraction 5 (3.9 g; b.p. > 120°): a complex mixture (2 layers) containing some **10** (0.1 g) and **11** (0.1 g) and several significant unidentified, high boiling components (analytical glc).

Fluorinations of 1,2 - *bisdimethylamino ether* [$Me_2NCH_2CH_2NMe_2$] *and bisdimethylaminomethane* [$Me_2NCH_2NMe_2$] *with* CoF_3.

The title amines were fluorinated under experimental conditions similar to those previously described for trimethylamine. The injection sizes of starting material were slightly different in each case, i.e. 36.5 g [$Me_2NCH_2CH_2NMe_2$] and 38.3 g [$Me_2NCH_2NMe_2$]. The ice-water washed products (46.5 g and 48.0 g respectively) were further washed with excess sat $NaHCO_3$aq and dried ($MgSO_4$).

Aliquots (37.6 g and 35.4 g respectively) of these products were distilled as before.

Compositions of distillation fractions from the fluorination of $Me_2NCH_2CH_2NMe_2$.

Volatiles (0.3 g; b.p. ≤ 28°): mainly **1** (0.10 g), **2** (0.03 g), **3** (0.06 g) and **5** (0.09 g) (analytical glc).

Fraction 1 (5.7 g; b.p. 28–45°). Separation (A, 53°) of an aliquot (2.14 g) gave: (i) **5**, 1,3-*bistrifluoromethyl-hexafluoroimidazolidine* (0.14 g), b.p. 46.5–48.5°, NMR, MS (Found: *m/e* at 296.989. $C_5F_{11}N_2$ requires 296.989); (ii) 1^{28} (0.40 g); (iii) a mixture (0.05 g) of **1**, **2** and **6**; (iv) **2**, *difluoromethyl-monofluoromethyl-trifluoromethylamine* (0.13 g), b.p. 48.0–50.0°, $^1H(CHF_2$, triplet, J = 58.5 Hz, of multiplets at 6.49δ; CH_2F, doublet, J = 53.0 Hz, of multiplets at 5.33δ) and $^{19}F(CF_3$, multiplet at 59.1ϕ; CHF_2, doublet, J = 59 Hz, of multiplets at 96.75ϕ; CH_2F, triplet, J = 51 Hz, of multiplets at 170.9ϕ) NMR, MS (*m/e* at 167.016, 166, 148, 116, 98, 97, 96, 78, 69, 51); and (v) 3^{28} (0.42 g).

Fraction 2 (6.0 g; b.p. 45–57°): mainly **1** (0.49 g), **2** (1.13 g), **3** (2.82 g), a mixture (0.05 g) of **4** and **9** (not further resolved), **5** (0.10 g), **6** (0.47 g), **7** (0.21 g) and **12** (0.19 g) (analytical glc).

Fraction 3 (3.5 g; b.p. 57–85°). Separation (A, 80°) of an aliquot (2.69 g) gave: (i) a complex mixture (0.13 g) containing some **1** and **6**; (ii) **6**, 3 - *difluoromethyl* - 1 - *trifluoromethyl* - *hexafluoroimidazolidine* (0.51 g), b.p. 68.0–70.0°, NMR, MS (Found: *m/e* at 297.996. $C_5HF_{11}N_2$ requires: 297.997); (iii) a mixture (0.21 g) of **2**, **3** and **6**; (iv) mainly 3^{28} (0.26 g); (v) **12**, 1 - *bisdifluoromethylamino* - 1,1,2,2-*tetrafluoroethane* (0.09 g), b.p. 68.0–70.0°, $^1H[(CHF_2)_2N$, triplet, J = 58.0 Hz, of multiplets at 6.61δ; CHF_2CF_2, triplet, J = 53.5 Hz, of multiplets at 6.00δ] and $^{19}F[(CHF_2)_2N$, doublet, J = 58 Hz, of multiplets at 94.3ϕ; CHF_2CF_2, multiplet at 99.2ϕ; CHF_2CF_2, doublet, J = 54 Hz, of multiplets at 136.6ϕ]NMR, MS[*m/e* at 198 ($C_4H_3F_7N$)]; (vi) a mixture (0.09 g) of **4**, **7**, **9** and **12**; (vii) 7^{28} (0.27 g); (viii) a mixture (0.07 g) containing **7**, **8** and **10**.

Fraction 4 (7.8 g; b.p. 85–108°): mainly **2** (0.06 g), **3** (0.40 g), a mixture (0.70 g) of **4** and **9**, **6** (0.58 g), **7** (2.45 g), **8** (0.19 g), **10** (0.99 g), **11** (0.10 g), **12** (0.51 g), **13** (0.42 g) and **14** (0.13 g) (analytical glc).

Fraction 5 (8.7 g; b.p. 108–127°). Separation (A, 112°) of an aliquot (8.25 g) gave: (i) mainly 7^{28} (1.2 g); (ii) a mixture (1.3 g), an aliquot (1.18 g) of which was further separated (B, 132°) to give (ii) (a) **13**, 2 - *bisdifluoromethylamino* - 1 - (*difluoromethyl* - *trifluoromethylamino*) - *tetrafluoroethane* (0.68 g), b.p. 123.0–124.0°, $^1H[CHF_2NCF_3$, triplet, J = 55.0 Hz, of multiplets at 6.40δ; $(CHF_2)_2N$, triplet, J = 57.0 Hz, at 6.45δ] and $^{19}F[CF_3$, multiplet at 52.9ϕ; CHF_2NCF_3, doublet, J = 55.0 Hz, of multiplets at 96.45ϕ; CF_2CF_2, multiplet at 98.4ϕ; $(CHF_2)_2N$, doublet, J = 58.0 Hz, of multiplets at 94.9ϕ]NMR, MS[*m/e* at 331, 311.003 ($C_6H_2F_{11}N_2$ requires: 311.004), 261, 211, 191, 184, 166, 146, 116, 114, 96, 69, 51] and (ii) (b) 8^{28} (0.28 g); (iii) mainly 10^{28} (0.95 g); (iv) 11^{28} (0.20 g); and (v) an impure compound (0.55 g) which was further purified (B, 132°) to give **14**, 1,2 - *bis*(*bisdifluoromethylamino*) - *tetrafluoroethane*, b.p. 139.5–141.5°, $^1H(CHF_2$, triplet, J = 57.0 Hz, of multiplets at 6.46δ) and $^{19}F(CHF_2$, doublet, J = 57.0 Hz, of pentets, J = 6.9 Hz, at 94.85ϕ; CF_2, multiplet at 98.45ϕ)NMR, MS[*m/e* at 313.019 ($C_6H_4F_{11}N_2$ requires: 313.020), 293, 243, 193, 173, 166, 146, 116, 100, 97, 96, 78, 69, 66, 51, 50].

Fraction 6 (3.5 g; b.p. > 127°): a complex mixture containing **8** (0.05 g), **10** (0.17 g), **11** (0.13 g), **13** (0.14 g), **14** (1.75 g) and several unidentified components.

Compositions of distillation fractions from the fluorination of $Me_2NCH_2NMe_2$.

Volatiles (0.2 g; b.p. ≤ 28°): mainly **1** (0.02 g), **2** (0.02 g), **3** (0.09 g) and **5** (0.05 g) (analytical glc).

Fraction 1 (5.7 g; b.p. 28–45°): mainly **1** (0.56 g), **2** (0.74 g), **3** (3.06 g), **5** (0.92 g) and **6** (0.09 g) (analytical glc).

Fraction 2 (5.0 g; b.p. 45–85°). Separation (A, 54°) of an aliquot (2.44 g) gave: (i) a complex mixture (0.50 g) containing **2**, **3** and **6**; (ii) 3^{28} (0.85 g); and (iii) a complex mixture (0.25 g) containing **3**, **4**, **7** and **9**.

Fraction 3 (6.3 g; b.p. 85–111°). Separation (A, 102°) of an aliquot (3.82 g) gave: (i) a complex mixture (0.89 g) containing **2**, **3**, **4**, **6** and **9**; (ii) a 4:1 mixture (0.23 g) of **9**(3 - *difluoromethyl* - 1 - *trifluoromethyl* - 2,2,4,4,5 - *pentafluoroimidazolidine*) and **4** respectively, b.p. 86–88°, NMR, MS† (Found: *m/e* at 280.005); (iii) 7^{28} (0.97 g); (iv) 8^{28} (0.16 g); and (v) 10^{28} (0.60 g).

Fraction 4 (6.8 g; b.p. 111–119°): mainly **4** (0.04 g), **6** (0.02 g), **7** (0.82 g), **8** (1.27 g), **9** (0.14 g), **10** (2.60 g) and **11** (0.96 g) (analytical glc).

Fraction 5 (2.5 g; b.p. 119–123°). Separation (A, 111°) of an aliquot (1.05 g) gave: (i) a complex mixture (0.28 g) containing **7** and **8**; (ii) impure 10^{28} (0.31 g); and (iii) **11**, 1 - *difluoromethyl* - 3 - *monofluoromethyl* - 2,2,4,4,5 - *pentafluoroimidazolidine* (0.19 g), b.p. 132.0–133.0°, NMR, MS (Found: *m/e* at 244.024. $C_5H_4F_8N_2$ requires: 244.025).

Fraction 6 (7.1 g; b.p. > 123°): a complex mixture (2 layers) containing some **8** (0.03 g), **10** (0.05 g) and **11** (0.08 g), as well as several significant unidentified compounds (analytical glc).

Several additional fluorinations of trimethylamine and the two diamines were carried out at 100°. Details of these experiments have been omitted since (under optimum experimental conditions) product yields and distributions were always comparable with those found for the corresponding examples described in the Experimental.

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†The sample was run on a Carbowax 20M glc column so that a spectrum of pure **9** could be obtained.

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