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HIGHLY FLUORINATED HETEROCYCLES. PART XVII. CHLORINATIONS OF 1-METHYLPOLYFLUOROPYRROLIDINES AND REACTIONS OF DERIVED PRODUCTS

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SUMMARY

Free-radical chlorination of 1-methyloctafluoropyrrolidine and -3H-heptafluoropyrrolidine gave progressive substitution of hydrogen by chlorine, but when oxygen was present the chloromethyl products were accompanied by the N-carbonyl chlorides. These were made also from the trichloromethyl compounds by sulphuric acid hydrolysis, and 1-dichloromethyl-3H-heptafluoropyrrolidine similarly gave the N-carbaldehyde. The 3H-1-trichloromethyl compound was dehydrofluorinated to the 3-ine. The 3H-N-carbonyl chloride gave an anilide and a methyl ester. 1-Fluoromethyloctafluoropyrrolidine was chlorinated to chlorofluoro- and dichlorofluoromethyl derivatives. 1-Methylhexafluoropyrrol-3-ine and chlorine gave dichloro adducts of the N-trichloride and N-carbonyl chloride, whilst with sodium methoxide the 3-methoxy-3-ine resulted, by addition-elimination. One chlorination of 1-methyl-3H-heptafluoropyrrolidine gave, in addition to the products outlined above, a 2,2,3-trichloro-N-carbonyl chloride involving an unusual replacement of fluorine. Methanolysis of this carbonyl chloride gave dimethyl chlorotrifluorosuccinate.

INTRODUCTION

As summarised in the previous part of this series [1] a range of polyfluoro-N-methylpyrrolidines has been made available by fluorination of 1-methylpyrrole or 1-methylpyrrolidine with cobalt(III) fluoride [1] or

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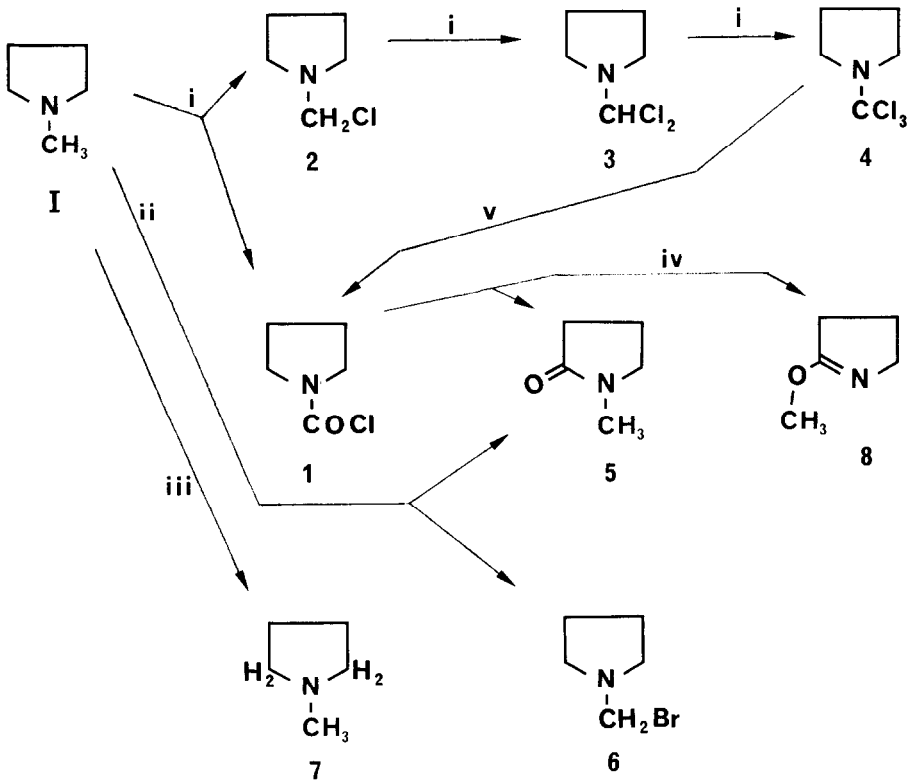
potassium tetrafluorocobaltate(III) [2]. Compounds with N-methyl side chains were made best by using $KCoF_4$, whilst CoF_3 afforded products with N-fluoromethyl and N-difluoromethyl groups. This paper describes some further compounds, derived, largely by chlorination sequences, from some of these earlier products. In the main Reaction Schemes , the starting materials in the left-hand column have their formulae allocated the same Roman numerals as those they were given in the original paper [2]. Formulae of new products made in the present study have Arabic numbers.



i Cl_2/uv ; ii Br_2/uv ; iii $AlCl_3$ then $LiAlH_4$; iv H_2O then CH_2N_2 ; v H_2SO_4 .

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SCHEME 1

RESULTS AND DISCUSSION

Reactions based on 1-methyloctafluoropyrrolidine(I) SCHEME 1

The two major products [2] of the 1-methylpyrrole/$KCoF_4$ reaction,were compounds I and III. These had, respectively, octafluoro- and 3H-hepta-fluoro-pyrrolidine rings carrying N-methyl groups : each has now been chlorinated under free radical conditions. Compound I and elemental chlorine were sealed together in a hard-glass Carius tube which was irradiated with ultraviolet light for two days. Since one of the products was a carbonyl chloride (1), the reaction was repeated with specially dried reagents, but the same range of products was obtained, compounds 1-4. The most volatile of these had a strong carbonyl absorption in the infrared, and elemental analysis and nmr and mass spectral characteristics showed it to be octafluoropyrrolidine-1-carbonyl chloride (1), i.e. the methyl group had been converted to -COCl. The other three products were shown by analysis and spectral data to be the expected 1-chloromethyl- (2), 1-dichloro-methyl- (3) and 1-trichloromethyl- (4) -octafluoropyrrolidine. A subsequent chlorination, without special drying, was done for seven days. Only one product was obtained, in excellent yield, the trichloromethyl compound (4). Further information on the chlorination process arose from reactions with compound III, and discussion will be deferred until these have been described.

Bromination of compound I was much more sluggish than chlorination, and very little product was obtained. Even then, the expected 1-bromo-methyloctafluoropyrrolidine (6) was the minor constituent. The majority (2:1) was 1-methylhexafluoropyrrolid-2-one (5). The structure was shown by its mass spectral cracking pattern [cf. 2], appropriate nmr peaks for 3 CF_2 groups, and an infrared carbonyl peak at 1800 cm^{-1}. However, it is not believed that product 5 arose via bromination. The crude product was dried over phosphoric oxide prior to final processing. Compound (5) almost certainly arose at this stage, via reaction of unchanged starting material I with phosphoric oxide/phosphoric acid. Sulphuric acid and compound I were found earlier [2] to give the 2,5-dione. The same 2-one (5) was subsequently made again as an unexpected product (see later).

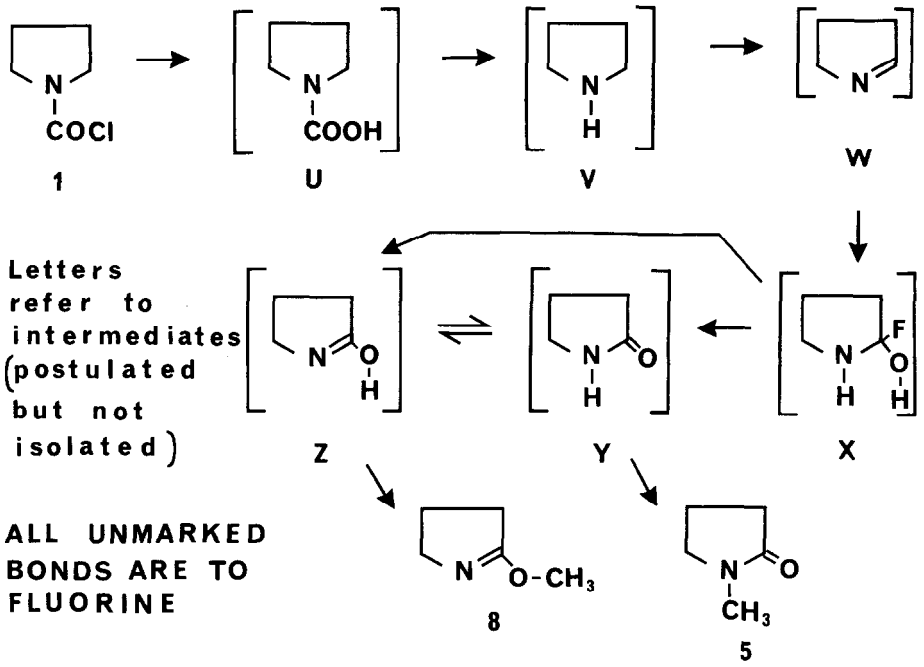
Aluminium chloride also is capable of replacing fluorine α to nitrogen, though in the two cases described previously, a $-CH_2F$ group was exchanged to $-CH_2Cl$ without affecting the $\geq CF_2$ groups in positions 2 and 5 [2], and attack on such $\geq CF_2$ groups was followed by dehydrochlorination (H was

present at positions 3 and 4) to give derivatives of 1-methylpyrrole [1]. Compound I reacted smoothly with aluminium chloride. The primary product was not isolated, but its nature was obvious, since reaction of the crude mixture with lithium aluminium hydride (well known [e.g. 3] to replace chlorine in chlorofluoro carbons specifically) afforded 1-methyl-3,3,4,4-tetrafluoropyrrolidine (7). Again, the structure was clearly shown by nmr and mass spectrometry.

Compound I displayed no acidic properties; with lithium methyl there was no evolution of methane, nor any evidence that an organometallic derivative had been formed (neither in fact was there with the 1-difluoromethyl analogue VIII [2]). Further, there were no obvious basic properties shown by compound I, with no evidence of salt formation by anhydrous hydrogen chloride. In contrast, the tetrafluoro-derivative (7) readily gave a hydrochloride salt (7a).

The N-trichloromethyl-derivative (4) was unaffected by strong aqueous potassium hydroxide at 110°, and was resistant to concentrated sulphuric acid at 15°. With oleum however there was good conversion to the carbonyl chloride (1).

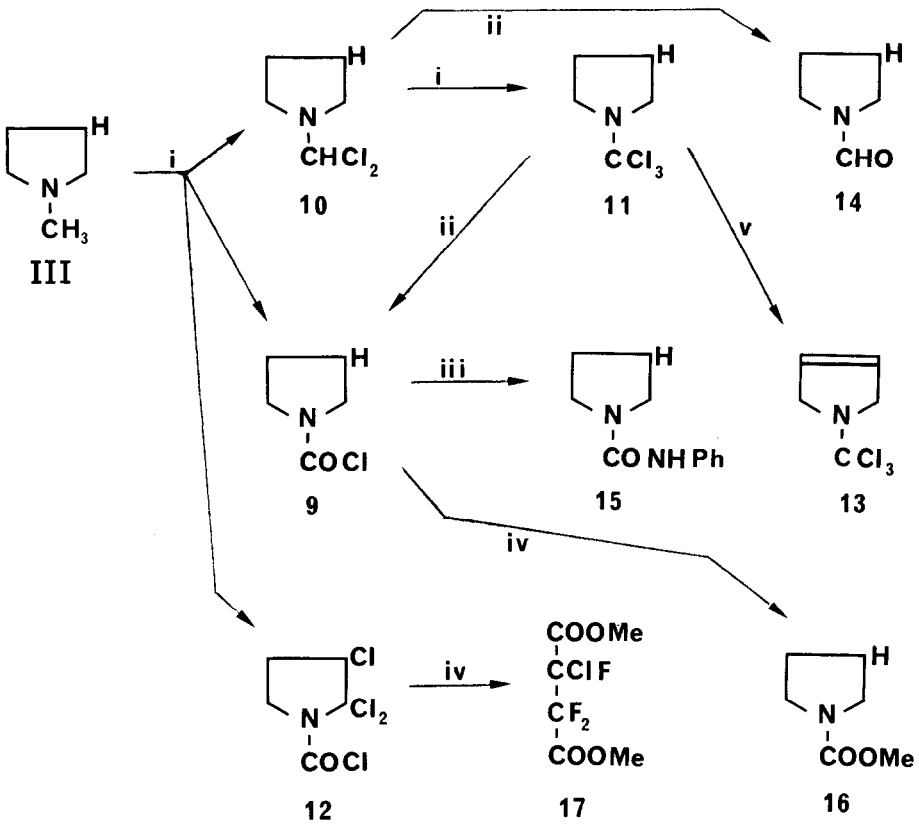
This compound (1) is a somewhat unusual derivative of a substituted carbamic acid. Perhaps not too surprisingly, classical reactions of acid chlorides were unsuccessful. Neither ammonia nor sodium azide afforded tractable products, and, whilst diazomethane afforded two, neither arose via the usual pathway. These two products were 2-methoxyhexafluoropyrrol-1-ine (8), and 1-methylhexafluoropyrrolid-2-one (5), the latter identical with the abnormal product from the bromination of compound I. Compound 8 had a ^{1}H nmr peak attributable to $-OCH_3$, an appropriate mass spectral cracking pattern, and an infrared band at 1670 cm^{-1} due to C=N. It seems most likely (Scheme 2) that the carbonyl chloride (1) reacted first with traces of water present in the ether solvent (a useful system sometimes for controlled hydrolysis, cf. [4]) to give the free carbamic acid (U), which then decarboxylated immediately to octafluoropyrrolidine (V). There would follow loss of HF from the resultant unstable $NH-CF_2$ system to give heptafluoropyrrolid-1-ine (W). Water addition to this would be extremely facile, to give X, and loss of HF would follow to give the pyrrolidone Y (H from oxygen) or the imide Z (H from nitrogen) which, in any case, are tautomers. Only at this stage apparently does the diazomethane get involved, methylating Y and Z to give the two actual products, 5 and 8 respectively.



SCHEME 2

Reactions based on 1-methyl-3H-heptafluoropyrrolidine(III) (SCHEME 3)

Chlorination with intensive drying, as for compound I, but over a longer time, gave three products, the 3H-heptafluoropyrrolidine derivatives with N-carbonyl chloride (9), N-dichloromethyl (10), and N-trichloromethyl (11) groups. A larger-scale reaction, without special drying, gave the same products. With compound III, there was no monochloro product, and no attack on the >CHF group. A reaction was then carried out with a little water added, but only two products were found, compounds 10 and 11, with the carbonyl chloride (9) absent. Clearly the carbonyl chlorides did not arise from the presence of water. It was realised only later that in the chlorinations of compounds I and III giving rise to carbonyl chlorides, the cooling of the Carius tubes prior to sealing was done by liquid nitrogen, whilst in the above reaction with added water, cooling was by solid carbon dioxide. Presumably, with liquid nitrogen cooling, some atmospheric oxygen was drawn inadvertently into the Carius tube and condensed during the filling. This oxygen could then react with intermediate radicals in the chlorination process, to give products 1 and 9.



i Cl_2/uv ; ii H_2SO_4 ; iii $PhNH_2$; iv MeOH ; v KOH .

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SCHEME 3

A further chlorination of III had been carried out previously under more forcing conditions, and presumably with oxygen involved similarly, though this was not established positively. Two products were found here, the trichloro-compound (11), and a new compound (12) which was a trichloro-pentafluoropyrrolidine-1-carbonyl chloride. ^{19}F nmr showed two $>CF_2$ groups, one adjacent and one removed from nitrogen, and a $\geq CClF$ group removed from nitrogen. The mass spectral cracking pattern showed the expected peaks, and a major one at 100 due to C_2F_4 (also a very small one at 148, due to C_2Cl_3F). Hence, compound 12 had the 2,2,3-trichloro structure. It seems likely that compound 12 arose from the carbonyl chloride 9, formed in the

presence of oxygen. Under the drastic conditions, chlorination of the hydrogen at position 3 presumably occurred, but was followed or accompanied by unexpected exchange of fluorine for chlorine at position 2. It appears that this is another manifestation of the relative reactivity of $\succ CF_2$ next to nitrogen in this series, in this case $\succ CF_2$ placed between $\succ NCOCl$ and the original $\succ CHF$ group. However, the exact pathway and reagents involved in this most unusual replacement of fluorine by chlorine are uncertain.

As with the perfluoro-trichloride (4), the 3H-analogue (11) reacted with sulphuric acid to give the corresponding carbonyl chloride (9). The CCl_3 group of compound 4 resisted alkaline hydrolysis, and this was also true of that in compound 11, but dehydrofluorination occurred at the 3,4 positions (as with N-methyl [1,2] and N-fluoromethyl [2] and N-difluoromethyl [2] analogues) to give 1-trichloromethylhexafluoropyrrolid-3-ine (13). The N-dichloromethyl-3H-compound (10) also reacted with sulphuric acid, giving 3H-heptafluoropyrrolidine-1-carbaldehyde (14). This did not appear to undergo normal aldehyde reactions at all readily; no 2,4-dinitrophenylhydrazone could be obtained.

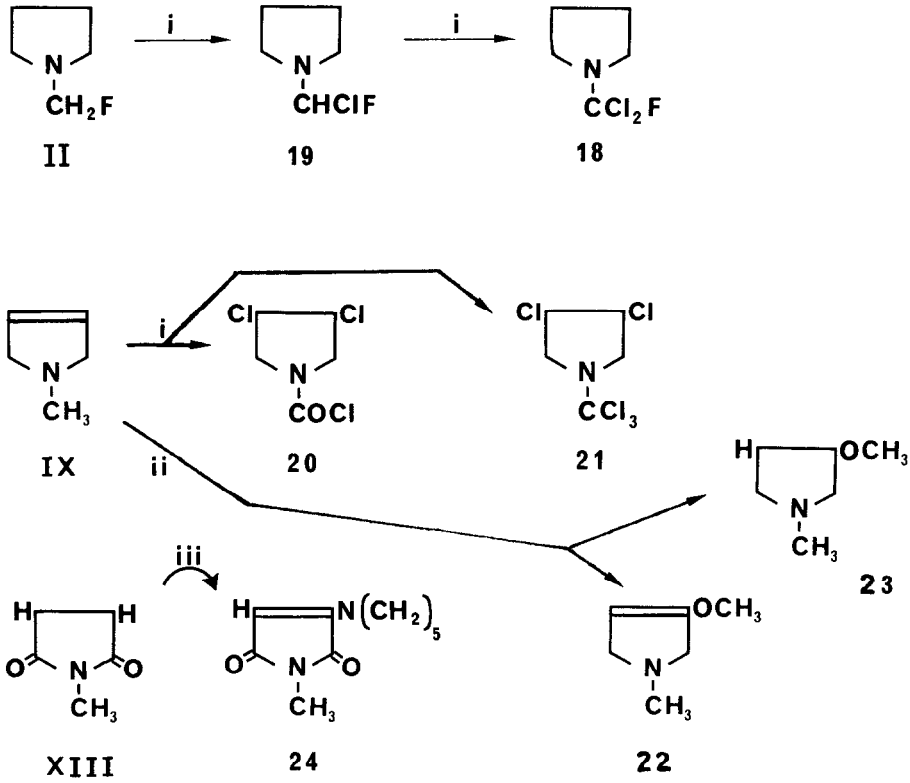
The 3H-carbonyl chloride (9) reacted with aniline and with methanol to give the corresponding carbanilide (15) and methyl ester (16), respectively. In the latter case, the presence of some fluorosilicate indicated partial deep-seated decomposition with loss of fluorine. Reaction of chloride 9 with ammonia did not give a tractable product. Presumably, with a stronger base than aniline, more deep-seated reaction occurred. The behaviour of the carbonyl chloride (9) with water was rather surprising; after being shaken for 1 week at room temperature, no hydrolysis had occurred. With sodium bicarbonate solution however, there was rapid reaction with effervescence, but no useful product could be isolated. It was found [5] that bistrifluoromethylcarbamic acid could not be isolated from the acid fluoride obtained by electrochemical fluorination; complete degradation of the trifluoromethyl groups occurred.

The trichloro-carbonyl chloride (12) was treated with methanol and reacted vigorously. Fluoride ion was lost and the organic product turned out to be dimethyl chlorotrifluorosuccinate (17) (appropriate analysis, and nmr, ir, and mass spectrometric peaks). Obviously, the 2,5 positions lose halogen readily. This could be by a sequence analogous to that of Scheme 2, with the intermediate corresponding to species Y

dehydrofluorinating again to give ultimately a 2,5-dione. This must then have undergone methanolysis, catalysed by the hydrogen halides previously liberated, so that the eventual product was the diester (17).

Miscellaneous reactions (SCHEME 4)

1-Fluoromethyloctafluoropyrrolidine(II) was chlorinated as usual, and, whatever the conditions, the products were the chlorofluoromethyl (19) and dichlorofluoromethyl (18) analogues, with no carbonyl chloride formed.



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SCHEME 4

1-Methylhexafluoropyrrolid-3-ine(IX) was chlorinated, with oxygen presumably present, and two products, each an inseparable mixture of stereoisomers, were isolated. 1-Trichloromethyl-3,4-dichlorohexafluoropyrrolidine (21) was accompanied by the corresponding carbonyl chloride (20). Olefin IX was reacted with methoxide, to study the expected addition-elimination sequence. Reaction with sodium methoxide in dimethylformamide was spontaneous; the product was rather unstable, and, though satisfactory elemental analysis could not be obtained, the nmr, ir, and mass spectrometric data were clear. The compound was the expected 3-methoxy-3-ine (22). The reaction with methoxide in methanol was more interesting, in that the ine (22) was accompanied by an equal amount of 1-methyl-3-methoxy-4H-hexafluoropyrrolidine (23), the methanol adduct of starting material IX. This is formed by protonation of the intermediate carbanion (as opposed to loss of fluoride ion to give compound 22). Such protonation is quite uncommon among cyclic structures. Unfortunately, not only were both products (22 and 23) relatively unstable, but they were difficult to separate from each other. Consequently, though compound 23 was clearly the major constituent of one fraction, as shown by nmr spectroscopy, adequate characterisation was not possible.

It was hoped to make derivatives of fluoromaleic acid from the 2,5-dione XIII, but controlled dehydrofluorination could not be achieved. Reaction with piperidine went smoothly, but dehydrofluorination was followed by addition-elimination, to give the fluorine-free piperidinoenamine (24).

EXPERIMENTAL

General Gas chromatography was as before [1] with other columns also used : tube h, silicone gum/Universal B (1:40) : tube i, Kel F oil on Chromasorb P (1:10).
Spectroscopic measurements were done as before [1].

Reactions of 1-Methyloctafluoropyrrolidine(I)

(i) With chlorine (experiment A) Compound I (2.3 g; dried over P_2O_5) and chlorine (5.0 g; dried by bubbling through concentrated sulphuric acid) were sealed (liquid N_2 cooled) in a Carius tube, and exposed to ultraviolet light (Hanovia 500A lamp at 30 cm distance) for 48 hours. The tube was cooled in liquid nitrogen, opened, and warmed carefully to 15°. The liquid contents were washed with aqueous sodium metabisulphite, water, and dried ($MgSO_4$). The product (2.5 g) gave by glc (a, 100°, 4) :

(i) octafluoropyrrolidine-1-carbonyl chloride (1) nc (0.8 g) b.p. 93-94° (Found: C, 21.9; Cl, 12.8; F, 54.3; N, 5.1. C_5ClF_8NO requires C, 21.6; Cl, 12.8; F, 54.8; N, 5.0%); m/e 242 (M-Cl); ir 1810 cm^{-1} (s; C=O) :

(ii) 1-chloromethyloctafluoropyrrolidine (2) nc (0.2 g) b.p. 97-98° (Found: C, 22.7; H, 0.8; Cl, 13.3; F, 57.3. $C_5H_2ClF_8N$ requires C, 22.8; H, 0.8; Cl, 13.5; F, 57.7%); m/e 265, 263 (M) :

(iii) 1-dichloromethyloctafluoropyrrolidine (3) nc (0.2 g) b.p. 110° (Found: C, 20.3; H, 0.4; Cl, 23.9; F, 50.7. $C_5HCl_2F_8N$ requires C, 20.2; H, 0.3; Cl, 23.8; F, 51.0%); m/e 264, 262 (M-Cl) :

(iv) 1-trichloromethyloctafluoropyrrolidine (4) nc (0.8 g) b.p. 134° (Found: C, 17.9; Cl, 32.1; F, 45.7; N, 4.3. $C_5Cl_3F_8N$ requires C, 18.1; Cl, 32.0; F, 45.7; N, 4.2%); m/e 300, 298, 296 (M-Cl).

(ii) With chlorine (experiment B) Without special drying, compound I (6.7 g) and chlorine (10.1 g) were sealed (solid CO_2 cooled) in a Carius tube and irradiated (lamp at a distance of 5 cm) for 7 days. The only product isolated (yield ca. 95%) was the trichloromethyl compound (4).

(iii) With bromine Compound I (2.3 g) and bromine (6.4 g) were sealed in a Carius tube and irradiated as in experiment A above for 3 days. The organic layer was pipetted from excess bromine, washed with aqueous sodium metabisulphite, and distilled in vacuo from phosphorus pentoxide to give a colourless liquid (2.1 g). This was separated by glc (a, 100°, 4) to give:- (i), compound I (glc and ir) : (ii), 1-methylhexafluoropyrrolid-2-one (5) nc (0.2 g) b.p. 98-99° (Found: C, 29.2; H, 1.6; N, 7.0. $C_5H_3F_6NO$ requires C, 29.0; H, 1.5; N, 6.8%); m/e 207.0147 (required M=207.0119); 188 (M-F), 178 (M-CHO), 150 (C_3F_6), 100 (C_2F_4), 57 (C_2H_3NO); ir 1800 cm^{-1} (s: C=O) : (iii), 1-bromomethyloctafluoropyrrolidine (6) nc (0.1 g); m/e 289, 287 (M-HF).

(iv) With aluminium chloride followed by lithium aluminium hydride
To a stirred suspension of aluminium chloride (5.33 g) in diethyl ether (10 cm^3) prepared and maintained at 0° in an atmosphere of nitrogen, was ad dropwise a solution of compound I (6.9 g) in ether (3 cm^3). The mixture was allowed to warm to 15°, and stirring was continued for 15 hours. The solid was filtered off and washed with ether (10 cm^3). The combined filtrate and washings were added dropwise to a stirred slurry of lithium aluminium hydride (1.71 g) in ether (10 cm^3), maintained in an atmosphere of nitrogen. The mixture was stirred for 15 hours, and then water added cautiously, dropwise. The organic layer was separated off, and the

aqueous layer ether-extracted. The ether layers were dried ($MgSO_4$), and ether distilled off through a short fractionating column. The residue, by glc (b, 100°, 9) gave:- (i), ether : (ii), 1-methyl-3,3,4,4-tetrafluoropyrrolidine (7) nc (1.22 g) b.p. 114-115° (Found: C, 38.0; H, 4.6; F, 48.6; N, 9.1. $C_5H_7F_4N$ requires C, 38.2; H, 4.5; F, 48.4; N, 8.9%); m/e 157 (M), 57 (C_3H_7N), 42 (C_2H_4N).

Dry hydrogen chloride gas was bubbled through a solution of compound 7 (0.08 g) in dry diethyl ether (3 cm^3) for two minutes. The white precipitate was filtered off, washed with ether and dried to give the hydrochloride (7a) nc (0.09 g), m.p. 120-121° (Found: C, 30.9; H, 4.0; Cl, 18.3; F, 38.8; N, 7.2. $C_5H_8ClF_4N$ requires C, 31.0; H, 4.2; Cl, 18.3; F, 39.3; N, 7.2%).

Hydrolysis of 1-trichloromethyloctafluoropyrrolidine (4)

Compound 4 (1.0 g) and a solution of oleum in concentrated sulphuric acid (25%; 3 g) were stirred together at 15° for 12 hours. The reactants were added carefully dropwise onto ice (20 g), more water (10 cm^3) added, and the system extracted with ether (2 x 10 cm^3). The extracts were dried ($MgSO_4$), and most of the ether distilled off through a short column. Isolation by glc (h, 80°, 10 p.s.i.) gave : (i), ether : (ii), octafluoropyrrolidine-1-carbonyl chloride (1) (0.7 g) (glc and ir).

After compound 4 and excess aqueous potassium hydroxide (18 M) had been stirred together at 110° for 3 hours, only unreacted 4 was present.

2-Methoxyhexafluoropyrrol-1-ine (8) and 1-methylhexafluoropyrrolid-2-one (5) from Octafluoropyrrolidine-1-carbonyl chloride (1)

To a solution of diazomethane in diethyl ether, prepared in the usual way from N-nitroso-N-methyl-p-toluene sulphonamide (20 g), was added dropwise and with stirring at 0°, the acid chloride (1) (0.7 g) in ether (20 cm^3). When effervescence ceased, the bulk of ether was distilled off through a short column. The residue was distilled in vacuo and the distillate by glc (i, 30°, 10 p.s.i.) gave:- (i), ether : (ii), 2-methoxyhexafluoropyrrol-1-ine (8) nc (0.1 g), b.p. 80-81°; m/e 207.0141 (required M=207.0119), 188 (M-F), 177 ($M-CH_2O$), 157 ($M-CF_2$), 100 (C_2F_4), 92 (C_2F_2NO), 31 (CH_3O); ir 1670 cm^{-1} (s; C=N) : (iii), 1-methylhexafluoropyrrolid-2-one (5) (0.15 g) (ir).

Chlorination of 1-methyl-3H-heptafluoropyrrolidine(III)

Experiment A With conditions as for experiment A compound I, chlorine (5.0 g) and compound III (2.1 g) were sealed in a Carius tube (liquid N_2) and irradiated with ultraviolet light for 88 hours. Glc (a, 100°, 5) afforded:- (i), 3H-heptafluoropyrrolidine-1-carbonyl chloride (9) nc (0.5 g) b.p. 127° (Found: C, 22.9; H, 0.6; Cl, 13.7; F, 51.5; N, 5.8. C_5HClF_7NO requires C, 23.1; H, 0.4; Cl, 13.7; F, 51.3; N, 5.4%); ir 1795 cm^{-1} (s; C=O) : (ii), 1-dichloromethyl-3H-heptafluoropyrrolidine (10) nc (0.2 g), b.p. 135° (Found: C, 21.1; H, 0.8; Cl, 25.1; F, 47.6, N, 4.7. $C_5H_2Cl_2F_7N$ requires C, 21.4; H, 0.7; Cl, 25.3; F, 47.5; N, 5.0%) : (iii), 1-trichloromethyl-3H-heptafluoropyrrolidine (11) nc (1.2 g), b.p. 154° (Found: C, 18.8; H, 0.3; F, 42.6. $C_5HCl_3F_7N$ requires C, 19.1; H, 0.3; F, 42.3%); m/e 282, 280, 278 (M-Cl).

Experiment B Compound III (12.6 g) and chlorine (17.0 g) (no special drying) were treated as for experiment A (lamp distance 20 cm; reaction time 94 hours). Glc (c, 95°, 7) gave:- (i), compound 9 (4.2 g) : (ii), compound 10 (1.2 g) : (iii), compound 11 (7.8 g) : all were identified by glc and ir.

Experiment C Compound III (7.0 g) chlorine (8.0 g) and water (0.4 g) were sealed (solid CO_2 cooled) in a Carius tube and irradiated as before (lamp distance 15 cm; reaction time 7 days). Separation by glc (h, 150°, 20 p.s.i.) gave : (i), compound 10 : (ii), compound 11 : recovery was comparable to the total yields above, with the relative proportions of 10 and 11 similar : identification was by glc and ir.

Experiment D Compound III (15 g) and chlorine (19 g) (cooling uncertain) were irradiated (lamp distance 10 cm, reaction time 9 days). Isolated product (20 g) was separated by glc (h, 160°, 12 p.s.i.) to give:- (i), compound 11, (60%) (glc and ir) : (ii), 2,2,3-trichloropentafluoropyrrolidine-1-carbonyl chloride (12) nc (40%) b.p. 178° (Found: C, 18.6; Cl, 43.4; F, 29.6; N, 4.3. $C_5Cl_4F_5NO$ requires C, 18.4; Cl, 43.4; F, 29.1; N, 4.3%); m/e 294, 292, 290 (M-Cl), other significant peaks at 257 and 255 ($M-Cl_2$), 146 ($C_2Cl_2F_2N$), 116 (C_2ClF_3), 100 (C_2F_4); ir 1810 cm^{-1} (s; C=O).

Reactions of 1-trichloromethyl-3H-heptafluoropyrrolidine (11)

(i) With sulphuric acid Compound 11 (1.0 g) and concentrated sulphuric acid (6 g) were stirred together at 15° for 15 hours. The reactants were

partitioned cautiously between iced brine (20 cm^3) and diethyl ether (20 cm^3). The ether layer was dried ($MgSO_4$), most of the ether distilled off up a short column, and the residue separated by glc (h, 90°, 20 p.s.i.) to give:- (i), ether : (ii), 3H-heptafluoropyrrolidine-1-carbonyl chloride (9) (0.6 g) (glc and ir).

(ii) With potassium hydroxide Compound 11 (6.3 g) was dissolved in dry benzene (7 cm^3) and powdered potassium hydroxide (5.6 g) added. After 2 hours at 80°, the volatile constituents were distilled off in vacuo, and separated by glc (c, 100°, 9) to give:- (i), benzene : (ii), 1-trichloromethylhexafluoropyrrol-3-ine (13) nc (3.97 g), b.p. 146-148° (Found: C, 20.5; Cl, 36.1; F, 38.4; N, 5.0. $C_5Cl_3F_6N$ requires C, 20.4; Cl, 36.1; F, 38.7; N, 4.8%); m/e 262, 260, 258 ($M-Cl$), other major peaks at 117 (CCl_3), 93 (C_3F_3), 62 (C_2F_2); ir 1815 (s; C=C).

Reaction of 1-dichloromethyl-3H-heptafluoropyrrolidine (10) with sulphuric acid

Compound 10 (0.7 g) and concentrated sulphuric acid (6 g) were reacted together as for compound 11. Glc (b, 120°, 20 p.s.i.) gave:- (i), ether : (ii), 3H-heptafluoropyrrolidine-1-carbaldehyde (14) nc (0.4 g) b.p. 125-126° (Found: C, 26.5; H, 1.0; F, 59.1; N, 6.3. $C_5H_2F_7NO$ requires C, 26.7; H, 0.9; F, 59.1; N, 6.2%); m/e 225 (M), 178 ($M-CFO$), 177 ($M-CHFO$), 29 (CHO); ir 1750 cm^{-1} (s; C=O).

Reactions of 3H-heptafluoropyrrolidine-1-carbonyl chloride (9)

(i) With aniline Acid chloride (9) (0.9 g) in dry diethyl ether (30 cm^3) was added slowly with stirring to aniline (0.6 g; freshly distilled) in ether (15 cm^3). After 10 min further, the solution was filtered, washed with sulphuric acid (2 x 15 cm^3 : 2 M), then water, and dried ($MgSO_4$). Evaporation of ether left a viscous liquid, which was dried (P_2O_5) and distilled in vacuo to give 3H-heptafluoropyrrolidine-1-carbanilide (15) nc (0.8 g) b.p. 240° decomp. (Found: C, 41.2; H, 2.2; F, 42.3; N, 8.6. $C_{11}H_7F_7N_2O$ requires C, 41.8; H, 2.2; F, 42.1; N, 8.9%); m/e 316 (M), strong peaks at 177 (C_4HF_6N), 119 (C_7H_5NO), 92 (C_2F_2NO), 77 (C_6H_5); ir 1730 (bs; C=O).

(ii) With methanol Methanol (1.0 g) was added to the acid chloride (9) (0.9 g) in ether (2 cm^3). After being refluxed for 1 hour, ether (20 cm^3) was added to the cooled solution, and the white inorganic precipitate was filtered off. The filtrate was washed, dried and concentrated, the residue giving by glc (b, 120°, 12 p.s.i.):- (i), ether : (ii), 3H-heptafluoropyrrolidine-1-carboxylic acid methyl ester (16) nc (0.4 g), b.p. 156-157° (Found: C, 28.2; H, 1.6; F, 52.3; N, 5.4. $C_6H_4F_7NO_2$ requires

C, 28.2; H, 1.6; F, 52.1; N, 5.5%); m/e 255 (M), other major peaks at 224 (M-CH_3O), 192 (C_4F_6NO), 113 (C_3HF_4), 92 (C_2F_2NO), 59 ($C_2H_3O_2$); ir 1775 cm^{-1} (bs; C=O).

Reaction of 2,2,3-trichloropentafluoropyrrolidine-1-carbonyl chloride (12) with Methanol.

Acid chloride 12 (1.3 g) and methanol (1.0 g) were mixed (heat developed) and stirred for 1 hour. There was a precipitate of fluorosilicate, and the liquid product was distilled off in vacuo and separated by glc (h, 150°, 5) to give : (i), methanol : (ii), dimethyl-2-chloro-2,3,3-trifluorosuccinate (17) nc, b.p. 202-203° (Found: C, 30.8; H, 2.8; Cl, 14.6; F, 24.6. $C_6H_6ClF_3O_4$ requires C, 30.7; H, 2.6; Cl, 15.1; F, 24.3%); m/e 192, 190 (M-CO_2), other major peaks at 155 (M-CO_2Cl), 116 (C_2ClF_3), 59 ($C_2H_3O_2$); ir 1760 cm^{-1} (bs; C=O).

Chlorination of 1-fluoromethyloctafluoropyrrolidine(II).

Compound II(4.94 g) and chlorine (7.1 g) were irradiated as before (lamp distance 25 cm; reaction time 5 days). Glc (a, 60°, 9) afforded:- (i), unreacted II (0.15 g) (glc and ir) : (ii), 1-dichlorofluoromethyloctafluoropyrrolidine (18) nc (1.1 g) b.p. 100-101° (Found: C, 18.9; Cl, 22.5; N, 4.4. $C_5Cl_2F_9N$ requires C, 19.0; Cl, 22.4; N, 4.4%); m/e 282, 280 (M-Cl) : (iii), 1-chlorofluoromethyloctafluoropyrrolidine (19) nc (1.75 g) b.p. 84-86° (Found: C, 21.2; H, 0.2; Cl, 12.6; F, 60.4; N, 4.7. C_5HClF_9N requires C, 21.3; H, 0.4; Cl, 12.6; F, 60.7; N, 5.0%); m/e 264, 262 (M-F), 246 (M-Cl).

Reactions of 1-methylhexafluoropyrrolid-3-ine(IX)

(i) With chlorine Compound IX (2.86 g) and chlorine (5.3 g) were sealed in a Carius tube (liquid N_2) and irradiated (distance from lamp 25 cm; reaction time 3 days). Glc (d, 130°, 8) afforded : (i), 3,4-dichlorohexafluoropyrrolidine-1-carbonyl chloride (20) nc (0.58 g) (Found: C, 19.2; Cl, 34.6; F, 36.6; N, 4.4. $C_5Cl_3F_6NO$ requires C, 19.3; Cl, 34.3; F, 36.7; N, 4.5%); m/e 278, 276, 274 (M-Cl), base peak 63 (COCl); ir 1780, 1810 cm^{-1} (s, C=O) : (ii), 1-trichloromethyl-3,4-dichlorohexafluoropyrrolidine (21) nc (3.15 g) (Found: C, 16.1; Cl, 48.3; F, 30.9; N, 3.8. $C_5Cl_5F_6N$ requires C, 16.4; Cl, 48.5, F, 31.2; N, 3.8%); m/e 334, 332, 330, 328 (M-Cl).

(ii) With sodium methoxide in dimethylformamide Compound IX (2.0 g), sodium methoxide (0.8 g) and dimethylformamide (10 cm^3) were stirred together at 15° for 2 hours. Water (50 cm^3) was added and the mixture extracted with ether (3 x 50 cm^3). Isolation as usual followed by glc

TABLE 1

^{1}H and ^{19}F nmr Data for all New Compounds

(measurements were in solution in carbon tetrachloride unless otherwise stated)

Compound Number		Chemical Shifts	Relative Intensity	Position in Formula	Couplings
1	F	93.7	1	2,5	c
(in CD_3COCD_3)		133.6	1	3,4	c
2	H	4.89	-	1	s
	F	95.3	1	2,5	cs
		132.8	1	3,4	c
3	H	2.89	-	1	s
	F	94.0	1	2,5	c
		133.7	1	3,4	c
4	F	90.7	1	2,5	c
		134.7	1	3,4	c
5	H	6.91	-	1 (NCH_3)	cs
	F	100.8	1	5	bs
		127.1	1	3	t, J_{34}=6.0
		134.3	1	4	tt, J_{43}=6.2, J_{45}=4.4
6	H	4.90	-	1	s
	F	96.3	1	2,5	cs
		132.8	1	3,4	cs
7	H	6.98	4	2,5	t, J_{23}=J_{54}=13
(in $CDCl_3$)		7.64	3	1	s
	F	117.9	-	3,4	ct, J_{32}=J_{45}=13

(continued overleaf)

TABLE 1 (Continued)

Compound Number		Chemical Shifts	Relative Intensity	Position in Formula	Couplings
8	H	5.84	-	2 (OCH_3)	s
	F	91.6	1	5	bs
		123.9	1	3	t, J_{34}=6.3
		131.8	1	4	tt, J_{43}=6.2, J_{45}=4.4
9	H	4.77	-	3	cd, J_{3H3F}=48
(in CD_3COCD_3)	F	87.8	2	2	AB, J=193, Δυ=549
		93.4	2	5	AB, J=186, Δυ=142
		128.2	2	4	AB, J=270, Δυ=433
		215.8	1	3	cd, J_{3F3H}=49
10	H	2.90	1	1 ($C\underline{H}Cl_2$)	s
		4.95	1	3	cd, J_{3H3F}=50
	F	87.9	2	2	AB, J=194, Δυ=517
		93.4	2	5	cs
		128.1	2	4	AB, J=269, Δυ=433
		213.9	1	3	cd, J_{3F3H}=51
11	H	4.91	-	3	cd, J_{3H3F}=49.5
	F	83.6	2	2	AB, J=195, Δυ=520
		89.9	2	5	AB, J=186, Δυ=235
		128.7	2	4	AB, J=270, Δυ=482
		213.5	1	3	cd, J_{3F3H}=49
12	F	91.5	2	5	AB, J=180, Δυ=378
		128.2	2	4	ddd, J_{43}=10.5
		141.4	1	3	dt, J_{34}=10.5, Jd=6
13	F	86.3	2	2,5	cd, $J_{23}=J_{54}$=8
(in $CDCl_3$)		156.7	1	3,4	ct, $J_{32}=J_{45}$=8

TABLE 1 (Continued)

Compound Number		Chemical Shifts	Relative Intensity	Position in Formula	Couplings
14	H	1.46	1	1 (CHO)	s
		4.96	1	3	cd, J_{3H3F}=48
	F	86.8	2	2	AB, J=204, Δυ=641
		93.6	2	5	AB, J=190, Δυ=198
		127.8	2	4	AB, J=270, Δυ=474
		214.0	1	3	dp, J_{3F3H}=49, $J_{32}=J_{34}$=9.5
15	H	2.55-2.95	5	C_6H_5	cm
		3.05	1	NH	b
		4.90	1	3	cd, J_{3H3F}=49
	F	85.2	2	2	AB, J=192, Δυ=585
		92.5	2	5	collapsed AB
		127.9	2	4	AB, J=264, Δυ=414
		214.2	1	3	dp, J_{3F3H}=50, $J_{32}=J_{34}$=10
16	H	5.06	1	3	cd, J_{3H3F}=49
		6.04	3	1 (OCH_3)	s
	F	88.5	2	2	AB, J=198, Δυ=678
		95.0	2	5	AB, J=186, Δυ=120
		128.2	2	4	AB, J=270, Δυ=481
		214.0	1	3	dp, J_{3F3H}=50, $J_{32}=J_{34}$=10
17	H	6.08	-	1 and 4 (OCH_3)	s
	F	114.1	2	3	dAB, J_{AB}=288, Δυ=426, J_{32}=8 and 13
		129.3	1	2	dd, J_{23}=8 and 13

(continued overleaf)

TABLE 1 (Continued)

Compound Number		Chemical Shifts	Relative Intensity	Position in Formula	Couplings
18	F	34.2	1	1($\underline{C}FCl_2$)	p, $J_{12}=J_{15}=13$
		92.1	4	2,5	d, $J_{21}=J_{51}=13$
		133.9	4	3,4	s
19	H	2.92	-	1($\underline{C}HClF$)	cd, $J_{1H1F}=50.4$
(neat)	F	92.4	4	2,5	AB, J=180, Δυ=194
		96.7	1	1($CHCl\underline{F}$)	cd, $J_{1F1H}=50$
		133.4	4	3,4	AB, J=250, Δυ=205
20	F	87.8	2	2,5	AB, J=171, Δυ=1214
(in $CDCl_3$)	major isomer	123.0	1	3,4	cd
	minor	87.0	2	2,5	AB, J=171, Δυ=488
	isomer	134.4	1	3,4	cd
21	F	84.0	2	2,5	AB, J=175, Δυ=1200
(neat)	major isomer	122.8	1	3,4	cd
	minor	83.2	2	2,5	AB, J=175, Δυ=245
	isomer	133.9	1	3,4	cd
22	H	5.95	1	3(OCH_3)	d, $J_{3H4F}=3$
		7.35	1	1($N\underline{CH_3}$)	s
	F	92.5	4	2,5	c
		172.3	1	4	c
23	H	5.02	1	4	s
		6.32	4	3($N[CH_2]_2$)	c
		7.17	3	1(NCH_3)	s
		8.37	6	3($[CH_2]_3$)	c

(e, 100°, 4) gave 1-methyl-3-methoxypentafluoropyrrol-3-ine (22) nc (0.5 g), b.p. 79° (decomp.), m/e 203 (M) other major peaks at 188 ($M-CH_3$), 184 (M-F), 160 ($M-C_2H_3O$); ir 1760 cm^{-1} (s; C=C).

Reaction of 1-methyl-3,4-difluoropyrrolid-2,5-dione(XIII) with piperidine

Piperidine (3.0 g) was added dropwise to a stirred solution of the title compound (1.0 g) in dry benzene (20 cm^3) at 60°. After 12 hours at 60°, the volatile material was removed by distillation in vacuo to leave an orange solid (1.3 g). Sublimation and recrystallisation from n-hexane gave yellow crystals of 1-methyl-3-(N'-piperidino)pyrrolid-3-ine-2,5-dione (24) nc,m.p. 88° (Found: C, 61.6; H, 7.0; N, 14.7. $C_{10}H_{14}N_2O_2$ requires C, 61.8; H, 7.3; N, 14.4%); m/e 194 (M); ir 1610 (s) 1700 (s) cm^{-1}; uv maxima at 389 nm (ε 4590), 251 (ε4950), 205 (ε4950).

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