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FLUORINATIONS WITH COMPLEX METAL FLUORIDES. PART 7. FLUORINATIONS OF THE METHYL PYRIDINES WITH CAESIUM TETRAFLUOROCOBALTATE

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SUMMARY

4-Methylpyridine passed over caesium tetrafluorocobaltate at 330 - 340° gave tridecafluoro(1,3-dimethylpyrrolidine) (1) and its 3-difluoromethyl analogue (2), together with a range of polyfluoro-4-picolines (4 - 10) with $-CF_3$, $-CHF_2$ or $-CH_2F$ groups in the 4-position. 3-Methylpyridine similarly gave 1 and its 1,2-isomer (11) together with several polyfluoro-3-picolines (14 - 18). 2-Methylpyridine at 270° gave tridecafluoro(1-ethylpyrrolidine) (13), a trace of 11 and 2-trifluoromethyl- (22), 2-difluoromethyl- (23) and 2-fluoromethyl-tetrafluoropyridine (24); there were also products arising by loss of methyl. Other unidentified fluoroalkylpyridines besides those isolated were present in each case.

INTRODUCTION

In most early work on exhaustive fluorinations by high valency transition metal fluorides (HVMFs), functional groups were lost and saturated fluorocarbons made. Latterly, however production of fluorinated material retaining some functionality has been achieved, and this work extends a similar study [1] of the fluorination of pyridine by caesium tetrafluorocobaltate [2;3]. This reagent has so far given the highest proportion of arene-type fluorinated products from aromatic precursors such as benzene [3], naphthalene and tetralin [4].

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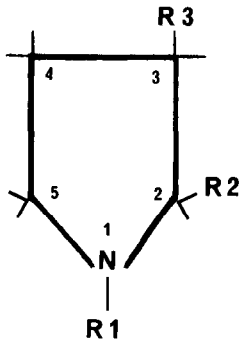
ISOLATION OF PRODUCTS

4-Methylpyridine was fluorinated at 330 - 340° to give a reasonable recovery of crude product (ca 1.5 x wt of input). An involved series of preparative glc separations gave the major products (Scheme 1 and Table 1), three categories being found. Firstly, were those with rearranged skeletons, saturated 5-membered rings; tridecafluoro(1,3-dimethylpyrrolidine) (1) the major product, and its 3-difluoromethyl-analogue (2). Secondly, there was an open chain fragment, bistrifluoromethylamine (3). Thirdly, fluoromethylpyridines were found; all with the original structure retained:- 4-trifluoromethyltetrafluoro- (4): 4-trifluoromethyl-2,3,6-trifluoro- (5); 4-difluoromethyltetrafluoro- (6); a mixture of 4-difluoromethyl-2,3,5- (7), and -2,3,6-trifluoro- (8); a mixture of 4-fluoromethyl-2,3-difluoro- (9); and 4-difluoromethyl-2-fluoro- (10) pyridines.

3-Methylpyridine gave a similar range of products (ca $1^{1}/_{3}$ x input), but with more short-retained degradation fragments. Pyrrolidine (1) was obtained again, but this time in an inseparable 2.2:1 mixture with its 1,2-isomer (11). A few percent of a fluoro-2-azahexene derivative (12) and of tridecafluoro(1-ethylpyrrolidine) (13) were present also. Bistrifluoromethylamine (3) was again found. The pyridine products all had methyl substituents on C_3 and were as follows:- 3-difluoromethyltetrafluoro- (14); 3-methyltetrafluoro- (15); 3-difluoromethyl-2,5,6- (16), and -4,5,6-trifluoro- (17); 3-fluoromethyltetrafluoro- (18) pyridines.

Fluorination of 2-methylpyridine went best at a rather lower temperature (270°) to give poorer recoveries (ca 1.2 x input) but with the highest proportion of aromatic fractions of the 3 isomers. Obtained were tridecafluoro(1-ethylpyrrolidine) (13) containing a little of the 1,2-bistrifluoromethyl isomer (11): undecafluoro(1-methylpyrrolidine) (20) undecafluoro-2-azahex-2-ene (19) and bistrifluoromethylamine (3) were also found. Pyridines present were the pentafluoro- (21) and the 2-trifluoromethyl- (22), 2-difluoromethyl- (23) and 2-fluoromethyl- (24) - tetrafluoropyridines.

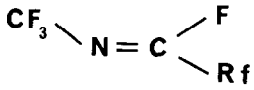
There were significant total amounts of unidentified material in all cases.



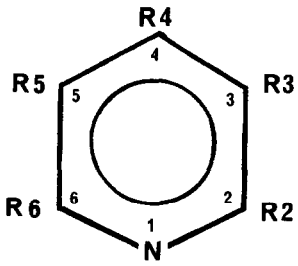
1 R1 = R3 = CF_3
2 R1 = CF_3 ; R3 = CHF_2
11 R1 = R2 = CF_3
13 R1 = C_2F_5
20 R1 = CF_3

CF_3NHCF_3

3



12 Rf unknown
19 Rf = C_3F_7



4 R4 = CF_3 : 5 R4 = CF_3 ; R5 = H : 6 R4 = CHF_2 :
7 R4 = CHF_2 ; R6 = H : 8 R4 = CHF_2 ; R5 = H :
9 R4 = CH_2F ; R5 = R6 = H : 10 R4 = CHF_2 ; R3 = R5 = R6 = H :
14 R3 = CHF_2 : 15 R3 = CH_3 : 16 R3 = CHF_2 ; R4 = H :
17 R3 = CHF_2 ; R2 = H : 18 R3 = CH_2F : 21 all R = F :
22 R2 = CF_3 : 23 R2 = CHF_2 : 24 R2 = CH_2F :

All substituents are F, unless otherwise stated

SCHEME 1

TABLE 1

Approximate Percentages (estimated by glc) of products from Fluorinations of Methylpyridines

Component	From 2-Methyl-	From 3-Methyl	From 4-Methyl
Pyrrolidines			
$CF_3N[CF_2]_4$	7 (20)	-	-
$CF_3N[(CF_2)_3CFCF_3]1,3$	-	23 (1)	58 (1)
ditto 1,2	∿ 2 (11)	11 (11)	-
$C_2F_5N[CF_2]_4$	39 (13)	∿ 1 (13)	-
$CF_3N[(CF_2)_3CFCHF_2]1,3$	-	-	7 (2)
Open Chain			
CF_3NHCF_3	3 (3)	5 (3)	2 (3)
$CF_3N{=}CFRf$	∿ 1 (19)	∿ 1 (12)	∿ 1
Pyridines			
C_5F_5N	4 (21)	-	-
$CF_3 \cdot C_5F_4N$	6 (22)	-	8 (4)
$CF_3 \cdot C_5HF_3N$	-	-	2 (5)
$CHF_2 \cdot C_5F_4N$	21 (23)	4 (14)	5 (6)
$CHF_2 \cdot C_5HF_3N$	-	2(16):∿1(17)	3(8):2(7)
$CH_2F \cdot C_5F_4N$	6 (24)	2 (18)	-
$CH_3 \cdot C_5F_4N$	-	1 (15)	-
$CHF_2 \cdot C_5H_3FN$	-	-	∿ 1 (10)
$CH_2F \cdot C_5H_2F_2N$	-	-	∿ 1 (9)
Unidentified	13	50	12

(Numbers in brackets relate to Scheme 1)

CHARACTERISATION OF PRODUCTS

Preliminary classification was by elemental analysis, and ir spectroscopy, supplemented by mass spectrometry in some cases. Nmr spectrometry was then used for detailed assignment of structures.

(a) Pyrrolidines. Small amounts of these were found in the mixture from the pyridine/$KCoF_4$ reaction [5;6], but they were the major products here. Nmr parameters are recorded in Table 2. Considering the values cited for the previously-known 1-trifluoromethylpyrrolidine (20) [7], the presence of CF_3-N groups is shown in compounds 1, 2 and 11. Tertiary fluorine resonances are at 184.0 (1) 197.9 (2) and 138.2 (11). Those for 1 and 2 are close to the usual tertiary F position (e.g. ca 187 in the perfluorodecalins [8]) and indicate that the second polyfluoroalkyl group is in position 3 in both. However, the tertiary F value for 11 is close to 137.2, that for a tertiary F on a carbon next to nitrogen in perfluoro(N-cyclobutylpiperidine) [9], and 136.7, that in perfluoro-3-methyleneamino-1-isopropylcyclobutene [10]. Hence 11 is the 1,2-isomer of 1. Compound 13 has $>CF_2$ groups in the 2,5 and 3,4 positions absorbing very close to those in 20, and is clearly its N-C_2F_5 homologue.

(b) Pyridines. The full nmr parameters for the new pyridines isolated are recorded in Table 3. Table 4 lists the expected changes in the ^{19}F chemical shifts at each ring position based on values for the 3 isomeric tetrafluoropyridines with in each case the substituents H [cf. 6], CF_3 [11], CHF_2 (compounds 6,14 and 23), and CH_2F (compounds 9,18,and 24), and also 4-CH_3 [12] and 3-CH_3 (compound 15). The changes in the ^{19}F chemical shifts fall into an ordered pattern in Table 4. In Table 3, the ^{19}F chemical shift values calculated from the data in Table 4 are given in brackets for the other new compounds, and give unequivocal orientations in each case. The ^{1}H nmr chemical shifts also fall into an ordered pattern which agrees with the above, but here, the differences are smaller and the orientations are less precise.

DISCUSSION

The products were generally similar to those from the fluorination of pyridine itself [1]. Though all three methylpyridines gave fluoropicoline products (2>4>3), with no skeletal rearrangements, the small

TABLE 2

^{19}F Nmr Spectra of Fluoroalkylpyrrolidines

Compound	Chemical Shifts	Relative Intensity	Position	Couplings
1	R1=R3=CF_3 (done neat in a sealed tube)			
	55.5	3	1 (CF_3)	c
	73.2	3	3 (CF_3)	c
	82.5 and 92.3	2	2 (CF_2)	AB; J=187
	85.5 and 99.1	2	5 (CF_2)	AB; J=172
	125.0 and 130.2	2	4 (CF_2)	AB; J=257
	184.0	1	3 (F)	c
2	R1=CF_3, R3=CHF_2			
F	55.7	3	1 (CF_3)	tt; J_{15}=10.3, J_{12}=5.5
	82.0 and 95.6	2	2 (CF_2)	AB; J=187
	85.1 and 101.1	2	5 (CF_2)	AB; J=174
	125.7 and 131.9	2	4 (CF_2)	AB; J=265
	137.1	2	3 (CF_2H)	d; J_{HF}=51.9
	197.9	1	3 (F)	c
H	3.72	-	$\underline{C}\underline{H}F_2$	td; J_t=51.6, J_d=12.0

11	R1=R2=CF_3 (done in a mixture with 1 in a sealed tube)			
	54.6	3	1 (CF_3)	c
	75.2	3	2 (CF_3)	c
	85.7 and 94.5	2	5 (CF_2)	AB; J=170
	127.2 and 136.6	2	3 and 4 (CF_2)	AB; J=253
	128.7 and 132.5	2		AB; J=262
	138.2	1	2 (F)	c
13	R1=C_2F_5			
	85.5	3	1 (CF_3CF_2)	p; J=7.5
	91.2	4	2,5 ($\overline{CF_2}$)	c
	97.5	2	1 (CF_3CF_2)	p; J=12.0
	133.3	4	3,4 ($\overline{CF_2}$)	s
20	R1=CF_3			
	55.5	3	1 (CF_3)	p; J=8.4
Ref [7]	93.8	4	2,5	q; J=8.5
adjusted to $CFCl_3$	133.8	4	3,4	bs

(s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, c = complex multiplet)

TABLE 3

Nmr Spectra of Fluoroalkyl pyridines

Compound		Chemical Shifts	Relative Intensity	Position	Couplings
5	F	63.4	3	4(CF_3)	d; J_{43}=12.4
		69.4(69.6)	1	6	dd; J_{63}=30.5,J_{62}=11.3
		83.1(85.0)	1	2	dd; J_{23}=22.6,J_{26}=11.3
		147.8(149.2)	1	3	c
	H	2.93	-	5(H)	c
6	F	88.1	1	2,6	part of AA'XX'
		116.9	1	4($C\underline{F_2}H$)	dt; J_{FH}=52.3,$J_{43,5}$=8.7
		144.4	1	3,5	c;part of AA'XX'
	H	3.06	-	4($C\underline{H}F_2$)	t; J_{H4F}=52.5
7 in admixture with 8	F	87.2(83.5)	1	2	dd; J_{26}=32.0,J_{23}=24.5
		116.8	2	4($C\underline{F_2}H$)	ddd; J_{FH}=51.9,J_{43}=J_{45}=9.0
		133.5(131.7)	1	5	dt; J_{52}=32.1,J_{54F}=9.0
		139.8(140.3)	1	3	dt; J_{32}=24.8,J_{34F}=9.0

(Contd.)7 in admixture with 8	H	3.14	1	4($\underline{CH}F_2$)	t; J_{H4F}=51.8
		2.09	1	6	c
8 in admixture with 7	F	70.1(69.3)	1	6	cdd; J_{63}=28.2, J_{62}=11.3
		85.2(84.7)	1	2	dd; J_{23}=22.6, J_{26}=12.4
		117.9	2	4($\underline{C}F_2H$)	cd; J_{FH}=54.1
		152.6(151.5)	1	3	dddt; J_{36}=28.2, J_{32}=22.6, J_{35}=3.1, J_{34F}=2.3
	H	3.17	1	4($\underline{CH}F_2$)	t; J_{H4F}=53.9
		3.04	1	5	dd; J_{53}=J_{56}=3.0
9 in admixture with 10	F	88.0	1	2	cd; J_{23}=25.9
		147.1	1	3	d; J_{32}=25.9
		232	1?	4($\underline{C}FH_2$)	t; J_{FH}=45-50
	H	4.48	2	4($\underline{CH}_2F$)	d; J_{H4F}=47.1
		ca. 2.72	1	5	?
		2.02	1	6	d; J_{65}=4.8

(continued overleaf)

TABLE 3 (Cont.)

Compound		Chemical Shifts	Relative Intensity	Position	Couplings
10 in admixture with 9	F	65.0(61.3)	1	2	s
		116.4	2	4($\underline{CF_2}$H)	d; J_{FH}=56.4
	H	3.38	1	4($\underline{CH}F_2$)	t; J_{H4F}=56.1
		2.98	1	3	bs
		2.72	1	5	d; J_{56}=5.0
		1.65	1	6	d; J_{65}=5.1
14	F	71.3	1	2	c
		78.7	1	6	c
		115.1	2	3($\underline{CF_2}$H)	c; part of AB_2; J_{HF}=53.0
		116.7	1	4	c; part of AB_2
		166.2	1	5	ddd; J_{52}=25.4, J_{56}=21.7, J_{54}=18.0
	H	3.16	-	3($\underline{CH}F_2$)	t; J_{H3F}=52.5
15	F	73.5	1	2	c
		88.8	1	6	c
		119.5	1	4	dddq; J_{45}=18.0, J_{46}=17.0, J_{42}=15.5, J_{43}=1.7

15 (Contd.)	F	168.8	1	5	ddd; J_{52}=24.3,J_{56}=21.4,J_{54}=18.6
	H	7.75	–	3(CH_3)	ddd; J_{32}=J_{34}=J_{36}=1.7
16	F	77.1(76.2)	1	2	cd; J_{25}=29.0
		82.3(83.6)	1	6	c
		114.8	2	3($\underline{CF_2}$H)	ddddd; J_{FH}=53.6,J_{32}=3.3,J_{34}=J_{35}=J_{36}=1.0
		144.2(145.1)	1	5	ddddt; J_{52}=29.3,J_{56}=22.3,J_{54}=7.9,J_{53F}= J_{53H}=1.0
	H	3.17	1	3($\underline{CHF_2}$)	ct; J_{H3F}=54.4
		2.04	1	4	cddd; J_{45}=7.9,J_{42}=J_{46}=7.4
17	F	78.4(74.1)	1	6	dd; J_{65}=25.0,J_{64}=24.0
		115.2	2	3($\underline{CF_2}$H)	cd; J_{FH}=54.8
		127.4(123.7)	1	4	dddt; J_{46}=24.3,J_{45}=19.0,J_{42}=7.8,J_{43F}=3.8
		163.9(162.1)	1	5	dd; J_{56}=24.8,J_{54}=19.0

(continued overleaf)

TABLE 3 (Cont.)

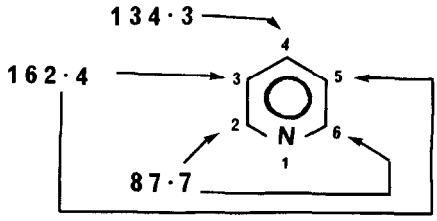
Compound		Chemical Shifts	Relative Intensity	Position	Couplings
17 (Contd.)	H	3.15	1	3($C\underline{H}F_2$)	t; J_{H3F}=54.0
		1.81	1	2	bd; J_{24}=7.5
23	F	82.4	1	6	ddd; J_{63}=27.0,J_{65}=23.0,J_{64}=18.6
		117.4	2	2($\underline{C}F_2H$)	ddd; J_{FH}=52.2,J_{23}=11.1,J_{25}=2.4
		137.1	1	4	ddd; J_{43}=J_{46}=18.0,J_{45}=17.5
		147.1	1	3	ddtd; J_{36}=27.0,J_{34}=18.6,J_{32F}=11.1,J_{35}=7.2
		153.4	1	5	dddt; J_{56}=23.4,J_{54}=17.3,J_{53}=7.2,J_{52F}=2.4
	H	3.5	-	2($C\underline{H}F_2$)	t; J_{H2F}=52.8
24	F	83.1	1	6	cddd; J_{63}=27.0,J_{65}=24.5,J_{64}=16.9
		139.3	1	4	ddd; J_{43}=18.0,J_{45}=17.5,J_{46}=17.0
		146.7	1	3	ddddt; J_{36}=26.8,J_{34}=18.3,J_{35}=J_{32F}=5.6, J_{32H}=2.9
		156.2	1	5	dddd; J_{56}=24.1,J_{54}=17.9,J_{53}=J_{52F}=6.1
		216.6	1	2($\underline{C}FH_2$)	tddd; J_{FH}=47.1,J_{23}=J_{25}=6.2,J_{26}=2.3
	H	4.69	-	2($C\underline{H}_2F$)	dd; J_{H2F}=47.1,J_{H3F}=2.9

(Chemical Shift figures in brackets are calculated values based on Table 4)

TABLE 4

Calculations of ^{19}F nmr Chemical Shifts for Fluoroalkylpyridines

Base Values for Pentafluoro -pyridine [6]



Substituent and Position [Compound No ( )]	Effect on ^{19}F Chemical Shift in Position					Literature Reference
	2	3	4	5	6	
2 H	-	-12.7	+7.0	-4.1	-4.6	[6]
2 CH_3	-	?	?	?	?	
2 CH_2F (24)	-	-15.7	+5.0	-6.2	-4.6	nc
2 CHF_2 (23)	-	-15.3	+2.8	-9.0	-5.3	nc
2 CF_3	-	-19.1	+2.5	-11.0	-5.5	[11]
3 H	-18.8	-	-18.5	+7.1	-3.4	[6]
3 CH_3 (15)	-14.2	-	-14.8	+6.4	+1.1	nc
3 CH_2F (18)	-15.2	-	-16.3	+4.7	-6.4	[1]
3 CHF_2 (14)	-16.4	-	-17.6	+3.8	-9.0	nc
3 CF_3	-22.1	-	-21.2	+3.3	-9.8	[11]
4 H	+4.9	-21.1	-	-21.1	+4.9	[6]
4 CH_3	+4.8	-18.4	-	-18.4	+4.8	[12]
4 CH_2F (9)	+8.3	-18.3	-	-18.3	+8.3	nc
4 CHF_2 (6)	+0.4	-18.0	-	-18.0	+0.4	nc
4 CF_3	+0.7	-20.3	-	-20.3	+0.7	[11]

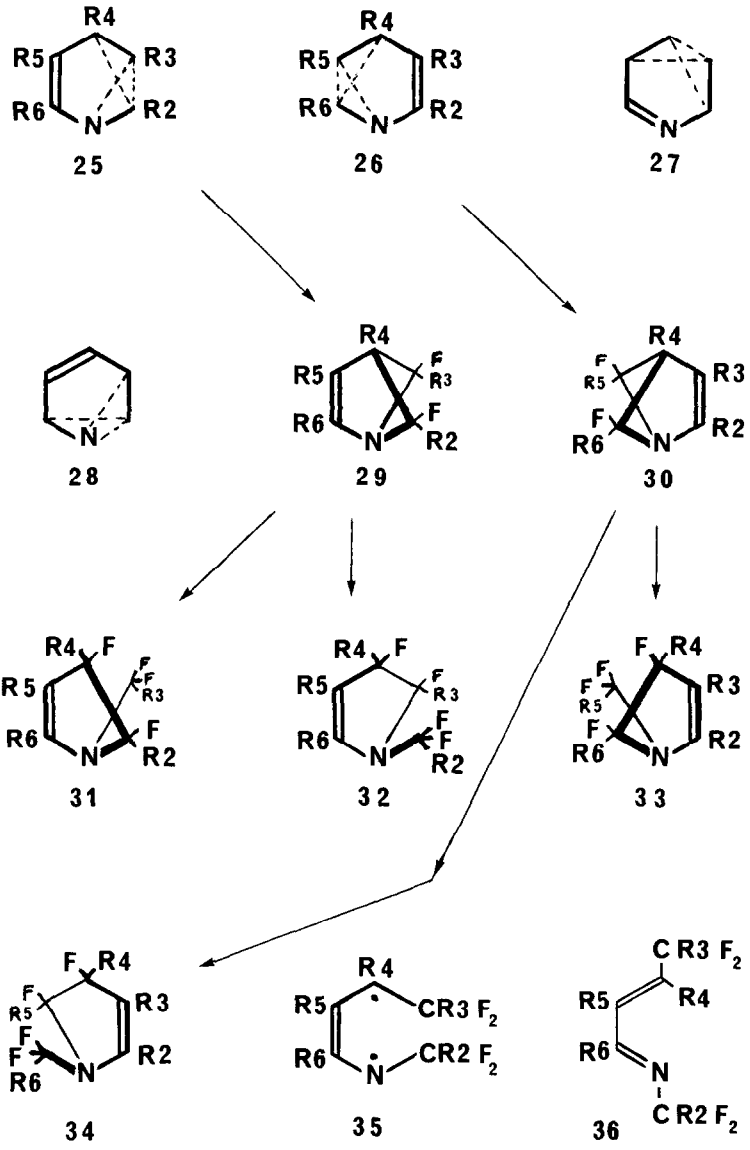
amounts formed and the complexity of the mixtures were rather disappointing. One product only, 2-difluoromethyltetrafluoropyridine (23) was found in significant proportion.

The pyrrolidines were found in greater amounts, though even here isolation of pure products was not easy. These products all arose by ring contraction following the rupture of the 2-3 (5-6) bond in the original pyridine ring. This rupture could occur in highly fluorinated pyridines or their difluoro-adducts, the corresponding azacyclohexadienes [13]. Such a pathway has been proposed recently [10] to explain the photochemical conversions of fluoro-azacyclohexadienes to cyclobutenes, the first step being the formation of an open-chain aza-triene. In our cases this would then either cyclise to give pyrrolidines, or fluorinate further to give 2-azahexadienes and azahexenes (12 and 19). Compounds of both the latter types are present in much greater amounts from the fluorinations of pyridine and 4-methylpyridine by $KCoF_4$ at 200 - 230° [5;6].

An amplification of this pathway which explains the pyrrolidine products obtained in a much more specific way, invokes transition states of type 25 or 26 (Scheme 2). Valence bond isomers of this type (benzvalenes) have been isolated from hexakistrifluoromethylbenzene [14;15] and studied in detail [16]. We suggest that the driving force for the formation of benzvalene intermediates in our fluorination reactions, is the inability of the reagents readily to form N-F bonds. Those of type 27 would therefore be unimportant. Benzvalene 25 (and 26) would quickly react further, and the original C_2-C_3 (C_5-C_6) bond would be most likely to break. Intermediate 25 (and 26) need not have independent existence, the C_2-C_3 (C_5-C_6) bond breaking, with take-up of fluorine, as the N-C_3 and C_2-C_4 (or N-C_5 and C_4-C_6) bonds form. In any event, bicyclic species of types 29 and 30 are the next key stage. If all this is so, benzvalenes of type 28 would lead to compounds with N-F bonds and so can be ignored. Further C-C bond breaking, in species 29 (or 30), of either the "new" C_2-C_4 bond or the 'old' C_3-C_4 bond give rise to the pyrrolidines isolated (31-34)

A similar pathway could operate from 1-azacyclohexa-1,3-dienes, which can arise from partial saturation of the pyridine ring [13]. The 4H-hexafluoride of this type was isolated from pyridine and 4H-tetrafluoropyridine/$KCoF_4$ [6].

2-Azahexadienes could also be formed from open chain intermediates of the type postulated by Chambers [10], which derive from 25 and 26 if it is


R4
R5
R3
R6
N
R2
25
26
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28
29
30
F
R5
R3
R6
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31
32
33
34
35
36
CR3 F2
CR2 F2

SCHEME 2

accepted that the 'new' bonds fail to form at all in the transition state as the C_2-C_3 bond breaks: perhaps more fluorine adds to the C_2 and C_3 positions preferentially, to give something like the diradical 35 which can then stabilize to give 2-azahexadienes of type 36. For these products it seems that the route from pyridines is more likely than that from azacyclohexa-1,3-dienes: it is even possible that pyridines give azahexadienes and azacyclohexadienes give N-alkylpyrrolidines.

Consideration in more detail of various fluorinations leads to the following observations (intermediates 25-34 could all be saturated, if they derive from the corresponding 1,3-diene).

(a) 4-Methylpyridine. Several fluoropyridines were isolated with no skeletal rearrangements detected. The pyrrolidine products (1) and (2) would be obtained from the two pyridines isolated in largest amounts (4 and 6 respectively) by the sequence given above and at some stage saturation of double bonds, all pathways giving the same products.

(b) 3-Methylpyridine. Here, despite a large proportion of unidentified material (most of it short-retained degradation products) and an absence of the expected tetrafluorotrifluoromethylpyridine, the pyrrolidines isolated were of particular significance. If R3=CF_3 and all other R=F (Scheme 2), 31 would give rise to compound 13; 32 to 11; 33 and 34 to 1. In fact, all these pyrrolidines were found: 1 (2 parts); 11 (1 part); and a little of 13. It is known, in general fluorocarbon chemistry, that C-C bonds involving quaternary and tertiary carbons are broken more readily than those with exclusively secondary or primary carbons [17]. Bonds involving quaternary C and tertiary nitrogen are probably also relatively unstable. Thus, in this case, bond forming to give intermediate 30 should be easier, but C_2-C_3 bond breaking to give 29 should be easier than C_5-C_6 to give 30. Experimentally, the route through 30 is preferred, but $^1/_3$ or so of the reaction proceeds via 29. However, 29 gives almost entirely 11 (from 32) by rupture of the C_4-C_2 (tertiary-secondary) bond, rather than 13 (from 31) by C_4-C_3 (tertiary-tertiary) rupture. Possibly the 'new' C_4-C_2 (energy-rich?) bond always breaks more readily than the original C_4-C_3 bond, despite other factors.

(c) 2-Methylpyridine. Here, unless more pyridine impurity (>10%) was present in the starting material than was realised, significant loss of the methyl at C_2 occurred, to give rise to pentafluoropyridine (21)

and its related products (19 and 20; cf. [1]). Since product 13 is the major one, the route to pyrrolidines via 30 is not favoured, and that through 29 is followed by predominant C_4-C_2 rupture. This is both a 'new' bond and a tertiary-tertiary one.

(d) Pyridine/$KCoF_4$ [6]. Pyrrolidine products were the 1-difluoromethyl-3H, (which could arise from the 2,3,5- ; 2,3,6- ; 2,4,6- and 2,4,5-trifluoropyridines: the first three were also isolated as products) and the 1-difluoromethyl-3H,4H (which could arise from the 2,5- and 2,6-difluoropyridines: both were also isolated as products, but the 2,6-isomer was degraded on further fluorination).

1-Azahexadienes found could have arisen from 2,3,5,6-tetrafluoro- and 2,3,6-trifluoro-pyridine,both found as products. An interesting issue here is the trans-nature of the groups around the double bonds in all these products; i.e. all have CF_3-N=C$\begin{matrix}R\\Rf\end{matrix}$ and CH=CH and CH=CF in the trans-orientations, even the degradation products related to trifluorocrotonic acid. This could be because there is saturation of the original C_2 and C_3 positions by fluorine as the C_2-C_3 bond breaks, and the new groups formed on these carbons move away from each other to take up the most favourable positions sterically. Radical 35 therefore will form conjugated double bonds to stabilize itself exclusively in the conformation corresponding to the all-trans diene 36.

(e) Pyridine/$CsCoF_4$ [1]. The products are explained by this pathway, but with no special diagnostic features.

(f) Quinoline/$CsCoF_4$ and quinoline/CoF_3 [18]. The major product is formed by rearrangement explicable as above.

Summarising, it seems that the key stage in the rearrangement to pyrrolidines is the formation of the N-C_3 (or N-C_5) bond. Intermediates 25, 26, 29 and 30 may or may not have real if transitory existence, but the new bond to nitrogen can be clearly identified in all cases. The relationship to the open chain products also seems too close for random ring opening to be responsible.

EXPERIMENTAL

General

Fluorination Reactors. Fluorinations were carried out in a standard unit [1] 1080 mm x 150 mm int. diam. containing ca 6.5 Kg of $CsCoF_4$.

Gas-liquid chromatography. Columns used for preparative work all had 30-60 mesh Chromosorb P as solid supports: column a, dinonyl phthalate (1:5), in a copper tube 4.88 m x 75 mm int. diam. with a Katharometer detector: other columns, used in Pye series 104 or 105 instruments, were in glass tubes 9.14 m x 8 mm int. diam; column d, Ucon oil (LB 550-x) (1:4); column e, Ucon oil (50-HB-2000) (1:4); column g, di-isodecyl phthalate (1:3); column h, carbowax 6000 (1:4). Recorded for each separation are the column used, temperature (°C) and nitrogen flow rate ($\ell\ h^{-1}$) or overpressure (p.s.i).

Spectroscopy. As in Part 6 [1].

Fluorination of 4-Methylpyridine. At a reactor temperature of 330 - 340°, portions of 50 g each in a stream of nitrogen (10 $\ell\ h^{-1}$) were passed during 150 min. The reactor was swept with nitrogen (25 $\ell\ h^{-1}$) for 3 h further. The products, collected in a trap cooled in solid CO_2, were allowed to warm to ca 15°, washed with ice-water, separated, and dried ($MgSO_4$).

Most (332.5 g) of the products (354.3 g) from 5 such runs (input 242 g) were separated by glc (a, 95°, 75) in 4 aliquots to give 6 crude fractions (A-F). Fraction A (183.1 g) was an impure compound; further glc (d, 24°, 6.5) on 2.15 g, afforded tridecafluoro(1,3-dimethylpyrrolidine) (1) nc (0.96 g), b.p. 49.5 - 50.5° (Found: C, 21.6; F, 73.8; N, 3.9. $C_6F_{13}N$ requires C, 21.6; F, 74.2; N, 4.2%) (m/e 332.979. $C_6F_{13}N^+$ requires 332.982).

Fraction B (26.1 g) was another impure compound; an aliquot (2.30 g) being purified by glc (d, 57°, 6.5) to give heptafluoro-3-difluoromethyl-1-trifluoromethylpyrrolidine (2) nc (0.71 g), b.p. 75 - 76° (Found: C, 22.7; H, 0.4; F, 72.7. $C_6HF_{12}N$ requires C, 22.9; H, 0.3; F, 72.4%) (m/e 314.991. $C_6HF_{12}N^+$ requires 314.992).

Fraction C (5.1 g) was bistrifluoromethylamine (3) (m/e 153. Calc. for C_2HF_6N: 153) identified by ir [19].

Fraction D (12.5 g) was a mixture of 8 compounds, with 4 and 5 the major ones.

Fraction E (18.4 g) was a mixture, an aliquot (3.9 g) of which by glc (d, 118°, 7.5) gave:- E(i), tetrafluoro-4-trifluoromethylpyridine (4) (2.3 g), b.p. 99.5 - 101.5° (Found: C, 33.0; F, 60.4; N, 6.6. Calc. for C_6F_7N: C, 32.9; F, 60.7; N, 6.4%) [20], with correct nmr parameters [11]: E(ii), a 1:1 mixture (0.1 g) of 4 and 5: E(iii), 2,3,6-trifluoro-4-trifluoromethylpyridine (5) nc (0.7 g), b.p. 104 - 106° (Found: C, 35.6; H, 0.7; F, 56.7. C_6HF_6N requires C, 35.8; H, 0.5; F, 56.7; N, 7.0%); ir 1643 (m), 1603 (m), 1480 (s), and 1445 (s) cm^{-1}: E(iv), a mixture (0.2 g) of 3 compounds including 5.

Fraction F (39.8 g) was a complex mixture, an aliquot (3.8 g) of which by glc (d, 140°, 4.5) gave:- F(i), a mixture (0.5 g) of 9 compounds principally 6: F(ii), tetrafluoro-4-difluoromethylpyridine (6) nc (0.7 g), b.p. 121.5 - 123.5° (Found: C, 36.1; H, 0.8; F, 56.8; N, 6.8%), ir 1655 (m), 1610 (w), 1480 (vs) cm^{-1}: F(iii), a 1:1 mixture (0.1 g) of 6 and 7 + 8: F(iv), a 1:1.2 mixture (0.7 g) of 2,3,5- (7) and 2,3,6-trifluoro-4-difluoromethylpyridine (8) (Found: C, 39.3; H, 1.4; F, 51.9. $C_6H_2F_5N$ requires C, 39.4; H, 1.1; F, 51.9%), ir 1643 (m), 1601 (m), 1480 (s), 1460 (s), 1442 (s) cm^{-1}: F(v), a mixture (0.4 g) of 6 compounds including 9 and 10: F(vi), a 1:4 mixture (0.1 g) of 2,3-difluoro-4-fluoromethylpyridine (9), and 2-fluoro-4-difluoromethylpyridine (10), b.p. 158.5 - 160.5° (m/e 147. $C_6H_4F_3N^+$ requires 147), ir 1624 (m), 1582 (m), 1484 (m), and 1453 (s) cm^{-1}.

Fluorination of 3-Methylpyridine. As before, this (226.8 g) gave dried product (305.5 g), but there was a higher proportion of short-retained degradation products in this case. Preliminary glc separation (a, 92 - 97°, 75.0: 282.6 g in 3 portions) gave 6 crude fractions (G-L). Fraction G was a complex mixture (129.6 g), containing one major glc peak. An aliquot (5.6 g) was purified by two glc separations (d, 66°, 7.0: d, 24°, 4.5) to give an inseparable 1:2.2 mixture (1.5 g) of tridecafluoro(1,2-dimethylpyrrolidine) (11) and its 1,3-isomer (1), b.p. 52 - 54° (Found: C, 21.4%; m/e 332.983): ir and nmr spectra indicated the presence of a 2-aza-2-alkene (12) (ir 1778 cm^{-1}) and of tridecafluoro-(1-ethylpyrrolidine) (13) (<5% of each).

Fraction H was a mixture (23.7 g) with 10 glc peaks, containing some 11 + 1.

Fraction I was bistrifluoromethylamine (3) (12.3 g).

Fraction J was a mixture (12.7 g) of 11 glc peaks and was mainly aromatic, with CH_3, CH_2F, CHF_2, CF_3, and F groups shown in nmr spectra.

Fraction K (9.3 g) had 13 glc peaks and was essentially identical with fraction L.

Fraction L (26.0 g) was separated by glc (e, 153°, 4.5) in aliquots (6.5 g), each of which gave sub-fractions L(i) (2.3 g); L(ii) (1.8 g); L(iii) (1.1 g); L(iv) (0.4 g).

Sub-fraction L(i), (1.98 g) on further glc separation (d, 128°, 4.5) gave L(i) a, impure 14 (0.10 g): L(i) b, tetrafluoro-3-difluoromethylpyridine (14) nc (0.88 g), b.p. 126 - 128° (Found: C, 35.6; H, 0.7; F, 56.4%), ir 1646 (s), 1630 (s), 1501 (vs), 1470 (s) cm^{-1}: L(i) c, impure 15 (0.18 g) containing 14: L(i) d, tetrafluoro-3-methylpyridine (15) nc (0.18 g), b.p. 127 - 128.5° (Found: C, 43.4; H, 1.8; F, 46.1; N, 8.5. $C_6H_3F_4N$ requires C, 43.6; H, 1.8; F, 46.0; N, 8.5%), ir 2942 (w), 1641 (s), 1603 (m), 1498 (s), 1469 (s) cm^{-1}.

Sub-fraction L(ii) (1.38 g) was separated by glc (d, 132°, 8.0) to give L(ii) a, impure 16 (0.02 g): L(ii) b, mainly one compound (0.27 g) was purified (d, 133°, 4.5; 0.24 g passed) giving 2,5,6-trifluoro-3-difluoromethylpyridine (16) nc (0.16 g), b.p. 131 - 133° (Found: C, 39.7; H, 1.2; F, 51.9%) (m/e 183.010, $C_6H_2F_5N^+$ requires 183.011), ir 3083 (w), 1631 (s), 1480 (s), 1443 (s) cm^{-1}: L(ii) c, (0.17 g) a mixture of 16, 17 and 18: L(ii) d, a mixture (0.35 g), an aliquot (0.20 g) of which gave by glc (g, 133°, 7.0) L(ii) dI, (0.01 g) impure, unidentified; L(ii) d II, 4,5,6-trifluoro-3-difluoromethylpyridine (17) nc (0.04 g), b.p. 133 - 135° (m/e 183.007), ir 1641 (m), 1613 (s), 1589 (m), 1501 (s), 1479 (s) cm^{-1}; L(ii) dIII, tetrafluoro-3-fluoromethylpyridine (18) (0.10 g) [1]: L(ii) e, a mixture (0.07 g) of 17, 18 and 2 other compounds.

Sub-fraction L(iii) was a mixture (1.1 g) of 6 unidentified peaks.

Sub-fraction L(iv) was a complex mixture (0.4 g), solid at 15°, containing aromatic-type fluoro-compounds.

Fluorination of 2-Methylpyridine. This was done in 4 runs each on 80 g, at 270°, and lasting 180 - 200 min, a total of 388.6 g crude dried material being obtained. Preliminary glc (338.7 g in 3 portions; a, 92 - 96°, 75) gave 8 fractions (M-T).

Fraction M (157.0 g) was further separated (3.8 g; d, 25°, 4.5) to give M(i), (0.3 g) a 1:9 mixture of undecafluoro-2-azahex-2-ene (19) [7] and undecafluoro(1-methylpyrrolidine) (20) [7]: M(ii), (0.3 g) mainly 13, contaminated by 19 and 20: M(iii), tridecafluoro(1-ethylpyrrolidine) (13) nc (1.7 g), b.p. 47 - 49° (Found: C, 21.8; F, 74.8%: m/e 314 [M-F]; 264 [M-CF_3]; 214 [M-C_2F_5]); some tridecafluoro-1,2-dimethylpyrrolidine (11) (<10%) was present by nmr: M(iv), a complex mixture (0.1 g) containing 13.

Fraction N was a mixture (12.7 g) of 4 major and several minor unidentified compounds.

Fraction O (8.8 g) was bistrifluoromethylamine (3).

Fraction P (13.9 g) was impure pentafluoropyridine (21). An aliquot (3.1 g) gave by glc (d, 137°, 6.0) a pure sample (1.9 g) [1].

Fraction Q (19.8 g) was impure tetrafluoro-2-trifluoromethylpyridine (22); an aliquot (2.2 g) gave by glc (d, 138°, 5.5) a pure sample (1.4 g) b.p. 103.5 - 105° (Found: C, 32.6; F, 60.4%) with correct nmr parameters [11].

Fraction R (9.5 g) contained 12 peaks, and included 22 and 23.

Fraction S (68.0 g) was impure tetrafluoro-2-difluoromethylpyridine (23). Glc (d, 135°, 5.5) on a portion (2.7 g) gave a pure sample of 23 nc (2.0 g), b.p. 124.5 - 126° (Found: C, 35.7; H, 0.4; F, 56.9%); ir 3005 (w), 1631 (m), 1620 (m), 1525 (s), 1479 (vs), 1456 (m) cm^{-1}.

Fraction T (29.4 g) was a mixture, an aliquot (3.8 g) of which by glc (e, 146°, 5.5) gave:- T(i), a mixture (0.2 g) containing 24: T(ii), an impure compound (1.5 g), a portion (1.35 g) of which gave by glc (h, 125°, 6.0) tetrafluoro-2-fluoromethylpyridine (24) nc (0.72 g), b.p. 136 - 138° (Found: C, 39.7; H, 1.1; F, 52.1%); ir 2977 (w), 1630 (s), 1619 (m), 1515 (s), 1475 (vs) cm^{-1}: T(iii), a mixture (0.2 g) of 4 compounds including 24: T(iv) (0.3 g) and T(v) (0.2 g) mixtures.

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