REACTION OF 1-(FLUOROALKYL)ALKANOLS WITH N-(1,1,2-TRIFLUORO-2-CHLOROETHYL)DIETHYLAMINE*

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The reaction of 2,2,3,3-tetrafluoropropanol (*II*), 2,2,3-trifluoro-3-chloropropanol (*III*) and 3,3,4-trifluoro-4-chloro-2-butanol (*IV*) with N-(1,1,2-trifluoro-2-chloroethyl)diethylamine (*I*) at temperatures higher than 150°C afforded products of substitution of hydroxyl with fluorine and chlorine, in the ratio about 25 : 75. N,N-Diethyldifluoroacetamide (*XVI*) was also isolated and difluoroacetates and N,N-diethylcarbamates of the alcohols *II*—*IV* were identified among the products. At room temperature, no substitution of hydroxyl with chlorine or fluorine takes place and the reaction mixture affords, upon hydrolysis, only chlorofluoroacetates of the alcohols *II*—*IV*. As shown by the mass and NMR spectra, the primary reaction product of the alcohol *II* is 2-diethylamino-1-chloro-1,2,5,5,6,6-hexafluoro-3-oxahexane (*VI*). The reaction of 2-methyl-3,3,4-trifluoro-4-chloro-2-butanol (*V*) with amine *I* leads only to dehydration product.

Substitution of hydroxyl group in fluoroalkanols proceeds with difficulty[1] and usually the direct reaction is circumvented by using reaction of the corresponding tosylates with alkali metal halides[2,3]. It was hitherto not known how fluoroalkanols react with N-(1,1,2-trifluoro-2-chloroethyl)diethylamine (*I*) which was suggested by Jarovenko and Rakša[4] as a reagent for the conversion of alcohols and acids into the corresponding alkyl and acyl fluorides. Since that time, the amine *I* was used in reactions with various types of hydroxy compounds[5] and it was particularly exploited in syntheses of fluoro derivatives of steroids[6–8].

In order to study the reaction of the amine *I* with fluoroalkanols, we chose 2,2,3,3-tetrafluoropropanol (*II*), 2,2,3-trifluoro-3-chloropropanol[9] (*III*), 3,3,4-trifluoro-4-chloro-2-butanol[10] (*IV*) and 2-methyl-3,3,4-trifluoro-4-chloro-2-butanol[11] (*V*) as representatives of primary, secondary and tertiary alcohols, containing an electronegative fluoroalkyl group in the α-position relative to hydroxyl. We have found that, unlike most non-fluorinated alcohols, the fluoroalkanols *II*—*IV* react with amine *I* at room temperature without substitution of the hydroxyl group with fluorine. Hydrolysis of the reaction mixture afforded mainly the corresponding fluorochloroacetates, in addition to the starting alcohols *II*—*IV* and N,N-diethylfluorochloroacetamide (*XVII*), arising by hydrolysis of the unreacted amine *I* (ref.[12]). Thus, alcohol

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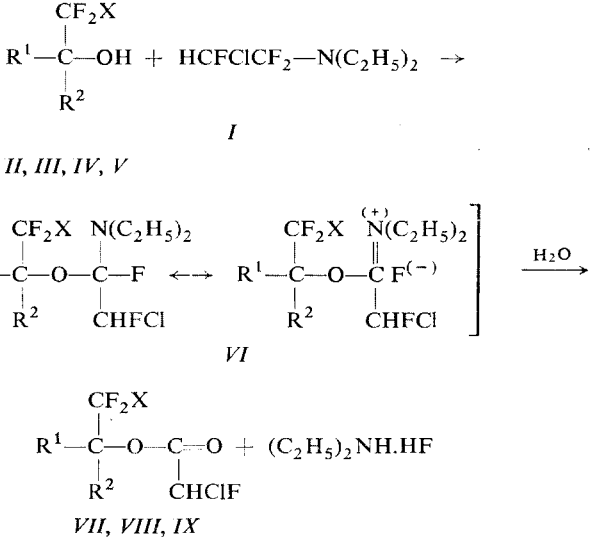
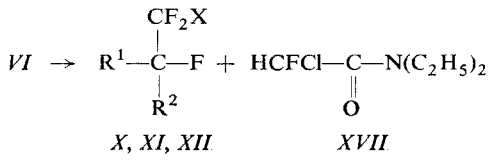
II gave 2,2,3,3-tetrafluoropropyl fluorochloroacetate (*VII*), (ν(C=O) 1790 and 1780 cm^{-1}), alcohol *III* afforded 2,2,3-trifluoro-3-chloropropyl fluorochloroacetate (*VIII*), ν(C=O) 1790 cm^{-1}, and alcohol *IV* gave rise to 1-methyl-2,3,3-trifluoro-3-chloropropyl fluorochloroacetate (*IX*), ν(C=O) 1778 and 1792 cm^{-1}. Addition of sodium hydroxide to the aqueous layer liberated diethylamine from its hydrofluoride.



In formulae *II*, *VI*, *VII*, $R^1 = R^2 = H$, $X = CF_2H$; *III*, *VI*, *VIII*, $R^1 = R^2 = H$, $X = CFClH$; *IV*, *VI*, *IX*, $R^1 = H$, $R^2 = CH_3$, $X = CFClH$; *V*, $R^1 = R^2 = CH_3$, $X = CFClH$.

We infer from these facts that, in the case of the fluoroalkanols *II*–*IV*, the generally assumed intermediate, amino ether *VI* (ref.[4,6]), is relatively stable at room temperature and does not decompose to give the corresponding fluoro derivatives *X*–*XII*; only when hydrolysed, it affords the fluorochloroacetates *VII*-*IX* and diethylamine hydrofluoride. In the reaction of the alcohol *II* with the amine *I* we were able to isolate the primary intermediate, 2-diethylamino-1-chloro-1,2,5,5,6,6-hexafluoro-3-oxahexane (*VI*, $R^1 = R^2 = H$, $X = CHF_2$), and confirm its structure by ^{1}H-NMR, ^{19}F-NMR spectroscopy and mass spectrometry. In the reaction of alcohols *III* and *IV*, we did not try to isolate the corresponding derivatives of the amino ether *VI*. The increased stability of the amino ether *VI* can be explained by the inductive effect of the electronegative fluoroalkyl group which hinders the C—O fission in the amino ether *VI*.

Rapid decomposition of the amino ether *VI* takes place only above 150°C. In the volatile portion of the reaction mixture we identified products which arose by substitution of the hydroxyl group in the alcohols *II*–*IV* with fluorine and chlorine (in the



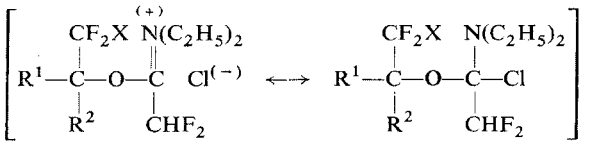
X, XI, XII *XVII*

In formulae *X*, $R^1 = R^2 = H$, $X = CF_2H$; *XI*, $R^1 = R^2 = H$, $X = CFClH$; *XII*, $R^1 = H$, $R^2 = CH_3$, $X = CFClH$.

ratio about 25 : 75). The alcohol *II* afforded a mixture of 1,1,2,2,3-pentafluoropropane[2] (*X*) and 1,1,2,2-tetrafluoro-3-chloropropane[2] (*XIII*), the alcohol *III* gave 1,2,2,3-tetrafluoro-1-chloropropane (*XI*) and 1,2,2-trifluoro-1,3-dichloropropane (*XIV*), and the alcohol *IV* afforded a mixture of 1,2,2,3-tetrafluoro-1-chlorobutane (*XII*) and 1,2,2-trifluoro-1,3-dichlorobutane (*XV*). The chloro derivatives *XIII*–*XV* were accompanied with N,N-diethyldifluoroacetamide (*XVI*), (ν(C=O) 1680 and 1700 cm^{-1}) which was always isolated together with the amide *XVII*. Among other minor products of the reaction we have found difluoroacetates and N,N-diethylcarbamates of the alcohols *II*–*IV* (Table I), *i.e.* from *II*: 2,2,3,3-tetrafluoropropyl difluoroacetate (*XIX*) and N,N-diethylcarbamate (*XXII*), from *III*: 2,2,3-trifluoro-3-chloropropyl difluoroacetate (*XX*) and N,N-diethylcarbamate (*XXIII*), and from *IV*: 2-methyl-3,3,4-trifluoro-3-chloropropyl difluoroacetate (*XXI*) and N,N-diethylcarbamate (*XXIV*).

The formation of the fluoro derivatives *X*–*XII* can be explained by the previously proposed mechanism[4,6], according to which the amino ether intermediate *VI* undergoes at the oxygen-bearing carbon a nucleophilic substitution with fluoride atom from the α-position of the amine part of *VI*; its reactivity is enhanced as a result of p-σ interaction, similarly[4] as in the starting amine *I*.

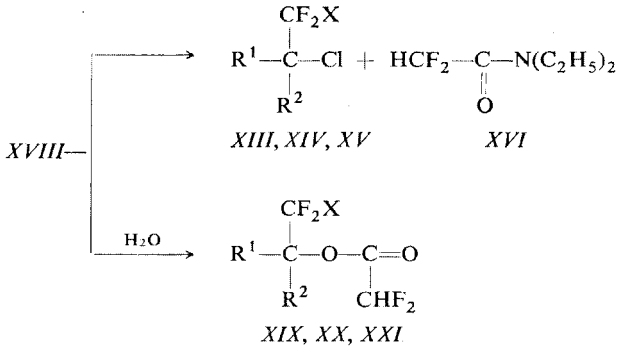
Substitution of the hydroxyl group with chlorine and formation of N,N-diethyl difluoroacetamide (*XVI*) is apparently connected with a further possible transformation of the amino ether *VI*. We assume that chlorine in the CHClF group is



XVIII

substituted with fluoride ion under formation of the amino ether *XVIII* which, analogously to the amino ether *VI*, decomposes to the chloro derivatives *XIII*–*XV* and N,N-diethyl difluoroacetamide (*XVI*). This explanation will obviously better describe the actual course of the reaction than the previously assumed cyclic mechanism[5].

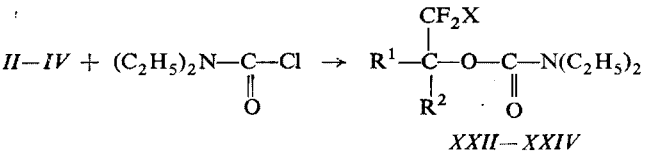
The formation of chloro derivatives *XIII*–*XV*, competitive with the formation of fluoro derivatives *X*–*XII*, was observed to take place to a small extent also in the reaction of alcohols containing no electronegative fluoroalkyl substituents[13,14]. The reason of predominant formation of fluoro derivatives from these alcohols and the amine *I* is obviously that the lesser stability of the aminoether intermediate without any electronegative groups in the vicinity of the reaction center facilitates its decomposition into the fluoro derivative according to the known mechanism[4-6]. Therefore the above-mentioned rearrangement, and thus the substitution of hydroxyl with



In formulae *XIII*, *XIX*, $R^1 = R^2 = H$, $X = CF_2H$; *XIV*, *XX*, $R^1 = R^2 = H$, $X = CFClH$; *XV*, *XXI*, $R^1 = H$, $R^2 = CH_3$, $X = CFClH$.

chlorine, will not take place to such extent as in the case of the fluoro alcohols. Substitution of hydroxyl group exclusively with more strongly nucleophilic chloride or bromide ions takes place in the reaction of steroid alcohols with the amine *I* in an excess of lithium chloride or bromide[15]. Reaction of the amine *I* with 1,2 : 3,4-di-O--isopropylidene-α-D-galactopyranose afforded only the corresponding 6-chloro-6--deoxy derivative together with 6-O-chlorofluoroacetate, although the reaction was carried out in an excess of potassium fluoride in dimethylformamide[16] which can even more facilitate the substitution of the chloro atom in the CHClF group[17]. The amide *XVI* which should arise in this reaction, was not detected[16], probably because of its hydrolysis with the aqueous–ethanolic sodium hydroxide solution during further work-up procedure. The formation of difluoroacetates *XIX*–*XXI* can be then explained by hydrolysis of aminoethers of the type *XVIII*.

The proposed reaction course does not explain satisfactorily the formation of N,N-diethylcarbamates *XXII*–*XXIV*, small amount of which was present among the reaction products, and which were identified by comparison of their mass spectra with that of the authentic carbamates *XXII*–*XXIV* prepared by the reaction of alcohols *II*–*IV* with N,N-diethylcarbamoyl chloride. Only in the case of the reaction



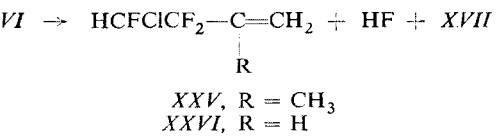
II–IV + $(C_2H_5)_2N{-}C(=O){-}Cl$ → $R^1{-}C(CF_2X)(R^2){-}O{-}C(=O){-}N(C_2H_5)_2$

XXII–XXIV

In formulae *XXII*, $R^1 = R^2 = H$, $X = CF_2H$; *XXIII*, $R^1 = R^2 = H$, $X = CFClH$; *XXIV* $R^1 = H$, $R^2 = CH_3$, $X = CFClH$.

of amine *I* with alcohol *II*, we isolated the carbamate *XXII* from a fraction in which it was accompanied with the amide *XVI* and *XVII*. The amides *XVI* and *XVII* were removed by hydrolysis with an aqueous sodium hydroxide solution and the pure carbamate *XXII* was identified by comparison (IR and NMR spectra) with the authentic standard. As indicated by our other results[18], the formation of *XXII–XXIV* can be ascribed to a thermal decomposition of the amine *I*.

The substitution reaction does not take place in the reaction of the tertiary alcohol *V* with the amine *I*: in this case the corresponding aminoether *VI* is decomposed only to 2-methyl-3,3,4-trifluoro-4-chloro-1-butene[19] (*XXV*), the amide *XVII* and hydrogen fluoride. Also the reaction of amine *I* with the secondary alcohol *IV* results in partial dehydration of *IV* to 3,3,4-trifluoro-4-chloro-1-butene (*XXVI*) (ref.[20]); we found 21% of *XXVI* in the volatile reaction products, together with 58% of the chloride *XV* (ref.[20]) and 21% of the fluoride *XII* (Table I).



VI → $HCFClCF_2{-}C(R){=}CH_2$ + HF + *XVII*

XXV, $R = CH_3$
XXVI, $R = H$

The structure of the products was determined by IR, NMR (Table II) and mass spectra (Table III). Some compounds were identified by comparison of their mass spectra, taken during chromatographic analysis, with that of the standards, prepared by another procedures (olefins *XXV* (ref.[20]), and *XXVI* (ref.[19]); dichlorotrifluorobutane[20] *XV*). Amide *XVI* was prepared by an independent synthesis from methyl difluoroacetate[21] and diethylamine.

EXPERIMENTAL

Temperature data are not corrected. IR spectra were measured in tetrachloromethane on UR-10, Zeiss, Jena, and Perkin Elmer 325 instruments. NMR spectra were taken in deuteriochloroform on Tesla BS 477 (60 MHz) and Varian XL 100 instruments, using tetramethylsilane as internal standard. The mass spectra were measured on a Gas Chromatograph-Mass Spectrometer LKB 9000. Analytical, as well as preparative, gas–liquid chromatography was performed on a Chrom III instrument with flame-ionisation detector, using polypropylene sebacate on Cellite as stationary phase, and nitrogen as carrier gas.

TABLE I

Reaction of the Amine *I* with Fluoroalkanols *II*—*V*

	Fluoroalkanol g (mol) (ether, ml)	Amine *I* g (mol) (ether, ml)	Procedure	Volatile components				Distillation residue after hydrolysis						
				g	rel. %			g						rel. %
II,	13·6 (0·103)	20·7 (0·109)	*A*	8·6	*X*	*XIII*	—	19·7	*XVII*	*XVI*	*VII*	*XIX*	*XXII*	*II*
					20	80			49	26	7	6	5	7
II,	20·3 (0·154)	36·1 (0·190)	*A*	15·6	*X*	*XIII*	—	28·9	*XVII*	*XVI*	*VII*	*XIX*	*XXII*	*II*
					22	78			54	27	7	2	8	2
II,	13·2 (0·100)	21·6 (0·114)	*A*	6·1	*X*	*XIII*	—		*XVII*	*XVI*	*VII*	*XIX*	*XXII*	*II*
					25	75			46	26	7	7	9	4
II,	13·0 (0·099) (10)	23·3 (0·123) (25)	*B*	—	—	—	—	39·0	*XVII*	—	*VII*	—	—	*II*
									37		56			7
III,	5·6 (0·038)	10·4 (0·055)	*A*	2·8	*XI*	*XIV*	—	8·1	*XVII*	*XVI*	*VIII*	*XX*	*XXIII*	*III*
					20	80			43	21	16	4	5	11
III,	5·0 (0·034) (10)	7·3 (0·039) (10)	*B*	—	—	—	—	9·5	*XVII*	—	*VIII*	—	—	*III*
									26		49			25
IV,	12·2 (0·076)	18·0 (0·100)	*A*	9·6	*XII*	*XV*	*XXVI*	14·4	*XVII*	*XVI*	*IX*	*XXI*	*XXIV*	*IV*
					21	58	21		56	19	8	3	6	8
IV,	5·0 (0·031) (10)	6·8 (0·036) (10)	*B*	—	—	—	—	8·4	*XVII*	—	*IX*	—	—	*IV*
									26		58			16
V,	10·0 (0·057)	10·8 (0·057)	*A*	1·2	—	—	*XXV*	8·3	*XVII*	—	—	—	—	*V*
							100		78					20
V,	5·0 (0·028)	6·2 (0·033)	*B*	3·4	—	—	*XXV*	5·2	*XVII*	—	—	—	—	*V*
							100		84					16

TABLE II

^{1}H-NMR Spectra of Compounds *II*, *VII*–*XVII*, *XIX*, and *XXII*–*XXIV*

Proton[a,b]	*II*[c]	*VII*	*VIII*	*IX*	*X*	*XI*	*XII*	*XIII*	*XIV*	*XV*	*XVI*	*XVII* (ref. [23])	*XIX*	*XXII*	*XXIII*	*XXIV*
		5·87 (tt)	6·22 (ddd)	6·20 (dt)									5·90 (tt)	5·88 (tt)		6·24 (dt)
H—CFX	5·93 (tt)	6·35[d] (d)	6·33[d] (d)	6·27[d] (d)	5·85 (ttd)	6·36 (dt)	—	5·94 (tt)	6·39 (dt)	6·59 (ddd)	6·25[d] (t)	6·48[d] (d)	6·00[d] (t)		6·26 (ddd)	6·22 (ddd)
		52	48	47									53			48
$^2J_{HF}$	53	50[d]	50[d]	50[d]	53	48	—	53	49	49	54[d]	51[d]	53[d]	53	48	48
$^3J_{HF}$	4	3	6 and 7·5	7·5	4·5 2[e]	7	—	3·8	6·5	9 6	—	—	3·5	4	6 8	7·5 6 and 8
CF_2—CH—	3·98 (t)	4·64 (tt)	4·68 (td)	5·40 (m)	4·69 (dtt)	4·69 (d)	4·99[f] (dm)	3·82 (t)	3·92 (td)	4·48 (m)			4·66 (tt)	4·50 (tt)	4·55 (td)	5·35 (m)
$^3J_{HF}$	13	12·5	12	—	12[g]	[g]	—	13·5	12·5	—	—	—	13	13	12	—
$^4J_{HF}$	—	1·6	1·5	—	1·8	—	—	1·5	1·5	—	—	—	1·4	1·8	1·2	—
CH_3	—	—	—	1·45 (d)	—	—	1·51 (dd)	—	—	1·75 (d)	1·27 1·34 (t)	1·22 1·14 (t)	—	1·16 (t)	1·16 (t)	1·13 (t) 1·42[h] (d)
CH_2	—	—	—	—	—	—	—	—	—	—	3·54 3·57 (q)	3·39 3·45 (q)	—	3·31 (q)	3·32 (q)	3·29 (q)
$^3J_{HH}$	—	—	—	6·5	—	—	7	—	—	6·5	7	7	—	7·2	7·2	7·6 6[h]

[a] Chemical shifts in δ; [b] values of the coupling constants in Hz; [c] OH = 2·12δ(s); [d] data for HCFX—CO— (X = Cl, F); [e] $^4J_{HF}$; [f] $^3J_{HF}$ = 24Hz; [g] $^2J_{HF}$ = 46 Hz; [h] for $\underline{CH_3}$—CH.

TABLE III

Mass Spectra of Compounds *VII*—*XVII*, *XIX*—*XXIV*, and *XXVI*

Compound Formula (mol. wt.) b.p., °C	Principial ionic species, *m/e*/relative intensity, %
VII $C_5H_4ClF_5O_2$ (226·5) 99—100/15 Torr	226/0·42 and 228/0·14 $(M)^+$; 207/0·42 and 209/0·14 $(M - F)^+$; 191/0·42 $(M - Cl)^+$; 179/0·85 and 181/0·28 $(M - F—CO)^+$; 175/0·42 and 177/0·14 $(M - HCF_2)^+$; 163/2·1 $(M - Cl—CO)^+$; 159/18 $(M - HCFCl)^+$; 125/6·4 and 127/2·1 $(HCFClCO_2CH_2)^+$; 115/32 $(HCF_2CF_2CH_2)^+$; 95/11 $(C_3H_2F_3)^+$ or $(HCFClCO)^+$; 82/4·8 $(C_2HF_3)^+$; 67/70 $(HCFCl)^+$; 69/28 $(HCFCl)^+$ and $(CF_3)^+$; 64/11 $(C_2H_2F_2)^+$; 60/22 $(C_2HFO)^+$; 51/100 $(HCF_2)^+$; 32/20 $(CHF)^+$; 31/17; 29/17; 28/12; 27/14
VIII $C_5H_4Cl_2F_4O_2$ (243·0)	207/0·56 and 209/0·19 $(M - Cl)^+$; 175/3·7 and 177/1·1 $(M - HCFCl)^+$; 159/0·37 and 161/0·11 $(HCFClCF_2CH_2CO)^+$; 131/31 and 133/11 $(M - HCFClCO_2)^+$; 67/100 $(HCFCl)^+$; 69/35 $(HCFCl)^+$ and $(CF_3)^+$; 60/11 $(C_2HFO)^+$; 51/26 $(HCF_2)^+$
IX $C_6H_6Cl_2F_4O_2$ (257·0)	220/0·1 $(M - HCl)^+$; 212/0·29 $(M - CO_2)^+$; 189/0·61 and 191/0·26 $(M - HCFCl)^+$; 173/0·45 and 175/0·15 $(M - Cl—HF—CO)^+$; 145/13 and 147/4·4 $(M - HCFClCO_2)^+$; 139/29 and 141/10 $(M - HCFClCF_2)^+$; 125/17 and 127/5·8 $(M - HCFClCO_2—HF)^+$; 111/10 $(HCFClCO_2)^+$; 109/29 $(C_4H_4F_3)^+$; 89/18 $(C_4H_3F_2)^+$; 77/17 $(C_3H_3F_2)^+$; 67/100; 69/35; 65/24 $(C_2H_3F_2)^+$; 63/17 $(C_2HF_2)^+$; 60/14; 59/10 $(C_3H_5F)^+$; 51/12; 47/24 $(C_2H_4F)^+$; 43/14; metastable ions for $145^+ \rightarrow 125^+ + HF$; $109^+ \rightarrow 89^+ + 20$
X $C_3H_3F_5$ (134·1) 28	101/8 $(M - CH_2F)^+$; 83/80 $(M - CHF_2)^+$; 82/11 $(C_2HF_3)^+$; 64/19 $(C_2H_2F_2)^+$; 51/100; 33/31 $(CH_2F)^+$
XI $C_3H_3ClF_4$ (150·5)	150/1·3 and 152/0·4 $(M)^+$; 117/8·4 and 119/2·8 $(HCFClCF_2)^+$; 83/100 $(M - HCFCl)^+$; 82/14; 67/70; 69/31; 64/75; 51/56; 33/44
XII $C_4H_5ClF_4$ (164·5)	164/0·23 and 166/0·08 $(M)^+$; 144/0·23 and 146/0·08 $(M - HF)^+$; 117/1·5 and 119/0·5; 98/10 and 100/3 $(C_2HClF_2)^+$; 97/13 $(M - HCFCl)^+$; 82/49; 77/15; 67/17; 69/11; 65/11; 51/21; 47/100; 32/11; metastable ions for: $109^+ \rightarrow 89^+ + 20$; $97^+ \rightarrow 77^+ + 20$
XIII $C_3H_3ClF_4$ (150·5)	150/3·6 and 152/1·2 $(M)^+$; 130/5·5 and 132/1·8 $(M - HF)^+$; 114/5·5 $(M - HCl)^+$; 101/16 $(M - CH_2Cl)^+$; 99/39 $(M - HCF_2)^+$; 98/11; 67/11; 64/19; 51/100; 49/23 $(CH_2Cl)^+$

TABLE III
(*Continued*)

Compound Formula (mol. wt.) b.p., °C	Principial ionic species, *m/e*/relative intensity, %
XIV $C_3H_3Cl_2F_3$ (167·0) 85	166/1·5 and 168/0·83 and 170/0·21 $(M)^+$; 146/12 and 148/7·7 and 150/1·5 $(M - HF)^+$; 130/8·7 and 132/2·9 $(M - HCl)^+$; 99/100 and 101/32 $(M\text{-}HCFCl)^+$; 98/23 and 100/10; 95/16; 67/58; 69/25; 64/37; 51/52; 49/32
XV $C_4H_5Cl_2F_3$ (181·0) 105	180/0·71 and 182/0·5 and 184/0·1 $(M)^+$; 160/2·6 and 162/1·7 and 164/0·3 $(M - HF)^+$; 113/30 and 115/10 $(M - HCFCl)^+$; 144/6·7 and 146/2·5 $(M - HCl)^+$; 109/14; 82/19; 77/28; 67/29; 69/12; 63/100 and 65/38 $(CH_3CHCl)^+$; 51/20; 28/15; metastable ion for: $109^+ \rightarrow 89^+ + 20$
XVI $C_6H_{11}F_2NO$ (151·2) 63°/9 Torr	151/53 $(M)^+$; 136/58 $(M - 15)^+$; 122/17 $(M - 29)^+$; 108/28 $(HCF_2 . CONH{=}CH_2)^+$; 100/46; 72/100; 58/89; 56/20; 51/37; 44/89; 42/29; 41/10; 30/46; 29/99; 28/44; 27/51; metastable ions for: $136^+ \rightarrow 108^+ + 28$; $100^+ \rightarrow 72^+ + 28$
XVII $C_6H_{11}ClFNO$ (167·6)	167/24 and 169/8·4 $(M)^+$; 152/31 and 154/11 $(M - 15)^+$; 132/30 $(M - Cl)^+$; 124/5·9 and 126/2·1 $(CFClHCONH{=}CH_2)^+$; 100/72 $(C_4H_{10}CNO)^+$; 72/100 $(C_4H_{10}N)^+$; 67/17 and 69/5·9; 58/68 $(C_2H_5{-}NH{=}CH_2)^+$; 56/17 $(CH_2{=}CHNH{=}CH_2)^+$; 44/45 $(CH_3NH{=}CH_2)^+$; 42/23 $(CH_2{=}{=}C{=}NH_2)^+$; 30/15; 29/68; 28/26; metastable ion for: $100^+ \rightarrow 72^+ + 28$
XIX $C_5H_4F_6O_2$ (210·1)	159/10 $(M - HCF_2)^+$; 114/13 $(C_3H_2F_4)^+$; 81/20 $(HCF_2O{=}CH_2)^+$; 51/100; 28/17 $(CO)^+$
XX $C_5H_4ClF_5O_2$ (226·5)	226/0·02 (M^+); 191/0·42 $(M - Cl)^+$; 175/0·52 and 177/0·21 $(M - HCF_2)^+$ 159/9·4 $(M - HCFCl)^+$; 131/25 and 133/8·4 $(HCFClCF_2CH_2)^+$; 109/9·4 $(HCF_2CO_2CH_2)^+$; 98/22 and 100/7·3; 81/31 and 83/10 $(HCFClCH_2)^+$; 82/37; 69/19; 67/50; 51/100; 33/14; 31/71; 29/23
XXI $C_6H_6ClF_5O_2$ (240·6)	173/0·6 $(M - HCFCl)^+$; 123/24 $(M - HCFClCF_2)^+$; 109/12 $(C_4H_4F_3)^+$; 95/21 $(HCF_2CO_2)^+$; 89/9·2; 77/11; 69/62; 67/17; 51/38; 47/15; 45/100 $(CH_3CH{=}OH)^+$; 43/18; 29/12; 27/11; metastable ion for: $109^+ \rightarrow 89^+ + 20$
XXII $C_8H_{13}F_4NO_2$ (231·2) 110–115/40 Torr	231/14 $(M)^+$; 216/100 $(M - 15)^+$; 212/1·7 $(M - F)^+$; 202/0·84 $(M - 29)^+$; 144/14 $(M - 15 - 28 - 44)^+ = (HCF_2CF_2CH_2{-}NH{=}CH_2)^+$; 115/13; 100/19; 72/17; 56/13; 51/46; 44/20; 42/14; metastable ions for: $216^+ \rightarrow$ $\rightarrow 188^+ + 28$; $188^+ \rightarrow 144^+ + 44$; $144^+ \rightarrow 124^+ + HF$; $100^+ \rightarrow 72^+ + 28$

TABLE

Mass Spectra of Compounds *VII—XVII, XIX—XXIV,* and *XXVI*

Compound Formula (mol. wt.) b.p., °C	Principial ionic species, *m/e*/relative intensity, %
XXIII $C_8H_{13}ClF_3NO_2$ (247·7) 110/36 Torr	247/11 and 249/3·5 $(M)^+$; 232/100 and 234/34 $(M - 15)^+$; 131/10 and 133/3·5; 116/13 $(OCON(C_2H_5)_2)^+$; 100/25; 72/24; 69/15; 67/40; 58/18; 56/17; 51/23; 44/28; 42/25; metastable ions for: $232^+ \rightarrow 204^+ + 28$; $204^+ \rightarrow 160^+ + 44$; $160^+ \rightarrow 140^+ + HF$; $100^+ \rightarrow 72^+ + 28$
XXIV $C_9H_{15}ClF_3NO_2$ (261·7) 100/20 Torr	261/10 and 263/3·3 $(M)^+$; 246/69 and 248/24 $(M - 15)^+$; 202/11 and 204/3·7 $(M - 15 - 44)^+$; 174/6·7 and 176/2·2$(M - 15 - 44 - 28)$; 145/2·7 $(HCFClCF_2CHCH_3)^+$; 125/8·9 and 127/3·0 $(C_4H_4ClF_2)^+$; 116/27; 109/18; 102/10; 100/45; 89/13; 72/38; 67/19; 65/15; 59/10; 58/100; 56/18; 47/20; 44/37; 42/27; 29/55; 28/21; metastable ions for: $246^+ \rightarrow 202^+ + 44$; $202^+ \rightarrow 174^+ + 28$; $174^+ \rightarrow 154^+ + 20$; $100^+ \rightarrow 72^+ + 28$
XXVI $C_4H_4ClF_3$ (144·5) 68	144/0·3 and 146/0·1 $(M)^+$; 125/0·45 and 127/0·15 $(M - F)^+$; 109/2·6 $(M - Cl)^+$; 89/8·7; 82/3·2; 77/100 $(M - HCFCl)^+$; 67/6·6; 69/3·3; 51/30; 32/10; metastable ion for: $109^+ \rightarrow 89^+ + 20$

Reaction of Alcohols *II—IV* with Amine *I*

A) *At temperatures above* 150°C: The alcohol *II* (20·3 g, 0·15 mol) was mixed with the amine *I* (36·1 g, 0·19 mol), the homogeneous mixture warmed up spontaneously and after about 20 minutes two layers separated. The mixture was heated and at 150—170°C a vigorous reaction set in. The fraction, distilling at 50—80°C (column head), was collected (15·6 g), washed with ice-cold water, sodium hydrogen carbonate solution, dried over magnesium sulphate and analysed by gas liquid chromatography. The main components were shown to be pentafluoropropane *X* and tetrafluorochloropropane *XIII* (20 : 80). Rectification afforded the pure components: *X*, b.p. 28°C (ref.[2] 26°C), and *XIII*, b.p. 54°C (ref.[2] 54°C). Their NMR spectra are given in Table II, mass spectra in Table III. The residue, remaining after the distillation of *X* and *XIII*, was diluted with ether, the solution washed with water and sodium hydrogen carbonate solution, dried over magnesium sulphate, and taken down (28·9 g). Gas–liquid chromatographic analysis has shown following components (compound, relative amount, retention time in cm): difluoroacetate *XIX*, 6%, 4·0 cm; alcohol *II*, 7%, 4·8 cm; fluorochloroacetate *VII*, 7%, 7·2 cm; N,N-diethyldifluoroacetamide *XVI*, 26%, 8·8 cm; 2,2,3,3-tetrafluoropropyl N,N-diethylcarbamate *XXII*, 5%, 11·6 cm; N,N-diethylfluorochloroacetamide *XVII*, 49%, 20·5 cm. These compounds were identified by comparison of retention times (gas–liquid chromatography) with that of the authentic samples, and also by comparison of mass spectra, taken during the gas–liquid chromatography, with standards.

B) *At room temperature*: A solution of the alcohol *II* (13·0 g, 0·099 mol) in ether (10 ml) was mixed under cooling with a solution of the amine *I* (23·3 g, 0·123 mol) in ether (25 ml). In about 15 minutes an emulsion was formed, and gradually an oily layer separated at the bottom of the

flask. The mixture was allowed to stand for 5 days at room temperature, with intermittent stirring. Then it was decomposed with water (25 ml) under cooling, the ethereal layer was separated, washed with a sodium hydrogen carbonate solution, dried over magnesium sulphate, taken down and analysed by gas–liquid chromatography. Following three compounds were found (compound, relative amount, retention time in cm): alcohol *II*, 7%, 3·5 cm; amide *XVII*, 37%, 15 cm; fluorochloroacetate *VII*, 56%, 5·2 cm. The acetate *VII*, b.p. 99–100°/115 Torr, was obtained in the pure state by rectification and identified by IR, NMR (Table II) and mass (Table III) spectra.

The reactions of alcohols *III*–*V* with the amine *I* were carried out following the procedures *A* and *B*; the reaction conditions and results are listed in Table I. The reaction products were isolated by rectification or preparative gas–liquid chromatography, and identified by IR, NMR (Table II) and mass (Table III) spectra.

Preparation of N,N-Diethylcarbamates *XXII*–*XXIV*

Esters *XXII*–*XXIV* were prepared by heating N,N-diethylcarbamoyl chloride with the corresponding alcohols *II*–*IV* at 120–150°C till the evolution of hydrogen chloride ceased, and the products were isolated by distillation *in vacuo*. Reaction of the alcohol *II* (3·95 g, 0·03 mol) with N,N-diethylcarbamoyl chloride (4·47 g, 0·03 mol) afforded 4·8 g (69%) of the ester *XXII*, b.p. 110–115°C/40 Torr, ν(C=O) 1 720 cm^{-1} (vs); treatment of alcohol *III* (1·48 g, 0·01 mol) with N,N-diethylcarbamoyl chloride (1·35 g, 0·01 mol) gave 1·8 g (73%) of the ester *XXIII*, b.p. 110°C/36 Torr, ν(C=O) 1 720 cm^{-1} (vs); alcohol *IV* (1·62 g, 0·01 mol) reacted with N,N-diethylcarbamoyl chloride (1·35 g, 0·01 mol) under formation of ester *XXIV* (2·0 g; 76%), b.p. 100°C/20Torr, ν(C=O) 1 716 cm^{-1} (vs). The pertinent NMR and mass spectra are listed in Table II and III.

The esters *XXII*–*XXIV*, which were present in the reaction mixtures after the reaction of the alcohols *II*–*IV* with the amine *I*, were identified by comparison of their mass spectra with that of the authentic *XXII*–*XXIV* prepared by the preceding method. Only the ester *XXII* was isolated from the reaction mixture of alcohol *II* with amine *I* using following procedure. The fraction, (5,7 g) b.p. 95–105°C/22 Torr, containing according to gas–liquid chromatography 6% of *XVI*, 19% of *XXII* and 75% of *XVII*, was heated under stirring with a solution of sodium hydroxide (4 g) in water (10 ml) to 70–90°C for 15 hours. The decrease of the amides *XVI* and *XVII* during the reaction was followed by gas–liquid chromatography. After hydrolysis of the amides had been complete, the mixture was extracted with ether, the ethereal layer dried over magnesium sulphate, and taken down, leaving 0·8 g of the ester, b.p. 87–93°C/20 Torr, identical (IR, NMR and mass spectra) with an authentic sample of *XXII*.

N,N-Diethyldifluoroacetamide (*XVI*)

A solution of methyl difluoroacetate (7·0 g, 0·064 mol) in ether (20 ml) was mixed with diethylamine (6 g, 0·083 mol) and the mixture was set aside for 6 hours. The ether was evaporated *in vacuo* and the residue was distilled, affording 1·2 g (43%) of an amide, b.p. 63°C/9 Torr (ref.[22] b.p. 79°C/25 Torr), identical in all respects with the amide *XVI*, isolated by preparative gas–liquid chromatography from the reactions of the alcohols *II*–*IV* with the amine *I* according to the procedure *A*.

1-Chloro-2-diethylamino-1,2,5,5,6,6-hexafluoro-3-oxahexane (*VI*)

Alcohol *II* (6·6 g, 0·05 mol) was added dropwise under stirring and cooling with ice to the amine *I* (9·5 g, 0·05 mol). The reaction mixture separated into two layers. The under layer was predominantly a mixture of the starting compounds, the upper one consisted of the aminoether *VI*

($R^1 = R^2 = H, X = CF_2H$). For $C_9H_{14}ClF_6NO$ (301·7) calculated: 35·84% C, 4·67% H, 37·80% F, 11·75% Cl, 4·65% N; found: 34·80% C, 4·74% H, 39·21% F, 12·24% Cl, 5·08% N. ^{1}H-NMR spectrum, δ (p.p.m.): 6·16 (d, 1 H, $^2J_{HF} = 48·5$ Hz, CHFCl); 5·94 (tt, 1 H, $^2J_{HF} = 53$ Hz, $^3J_{HF} = 5·0$ Hz, CHF_2); 4·12 (tt, 2 H, $^3J_{HF} = 12·0$ Hz and $^4J_{HF} = 1·5$ Hz, CH_2CF_2); 2·93 (q, 2 H, $^3J_{HH} = 7·0$ Hz, CH_2N); 1·14 (t, 3 H, $^3J_{HH} = 7·0$ Hz, CH_3). ^{19}F-NMR spectrum, δ (p.p.m. relative to $CFCl_3$): 148 (d, 1 F, $^2J_{HF} = 48·5$ Hz, CFClH); 141 (d, 2 F, $^2J_{HF} = 53$ Hz, CF_2H); 126 (s, CF_2); 113·5 to 116 (m, N—CF—O). Mass spectrum, (principal ionic species, *m/e*/relative intensity %): 281/13 and 283/4 $(M - HF)^+$, 266/3 and 268/1 $(M - HF—CH_3)^+$, 246/40 $(M - HF—Cl)^+$, 186/16 $(M-115)^+$, 166/74 and 168/25 $(M - HF-115)^+$, 158/16, 152/12, 150/16, 138/20, 122/20, 122/24 and 124/8, 115/20 $(C_3H_3F_4)^+$, 100/19 $(CONEt_2)^+$, 95/24 $(C_3H_2F_3)^+$, 94/27 and 96/9 $(CFCl{=}CO)^+$, 72/93, 70/23, 67/32 and 69/10 $(CHClF)^+$, 60/15, 56/75, 51/100 $(CHF_2)^+$, 44/86, 42/47.

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REFERENCES

1. Duncan W. G., Silverstein R. M.: J. Chem. Eng. Data *11*, 129 (1966).
2. Cohen W. V.: J. Org. Chem. *26*, 4021 (1961).
3. Tiers G. V. D., Brown H. A., Reid T. S.: J. Am. Chem. Soc. *75*, 5978 (1953).
4. Jarovenko N. N., Rakša M. A.: Ž. Obšč. Chim. *29*, 2159 (1959).
5. Liška F.: Chem. listy *66*, 189 (1972).
6. Ayer D. E.: Tetrahedron Lett. *1962*, 1065.
7. Knox L. H., Velarde E., Berger S., Cuadriello D., Cross A. D.: Tetrahedron Lett. *1962*, 1249.
8. Knox L. H., Velarde E., Berger S., Delfín I., Grezemkovsky R., Cross A. D.: J. Org. Chem. *30*, 4160 (1965).
9. Liška F., Šimek S. This Journal *35*, 1752 (1970).
10. Liška F., Dědek V., Chutný B.: This Journal *33*, 1299 (1967).
11. Liška F., Němec M., Dědek V.: This Journal *37*, 2091 (1972).
12. Pruett R. L., Barr J. T., Rapp K. E., Bahner C. T., Gibson J. D., Lafferty R. H. jr: J. Am. Chem. Soc. *72*, 3646 (1950).
13. Paleček J., Mitera J.: This Journal *39*, 2037 (1974).
14. Závada J.: Personal communication.
15. Bailey E. J., Fazakerley H., Hill M. E., Newall C. E., Phillips G. H., Stephenson L., Tulley A.: J. Chem. Soc. D, *1970*, 106.
16. Wood K. R., Fischer D., Kent P. W.: J. Chem. Soc. C, *1966*, 1994.
17. Sheppard W. A., Sharts C. M.: *Organic Fluorine Chemistry*, p. 86. Benjamin, New York 1969.
18. Dědek V., Liška F., Cvak L.: This Journal, in press.
19. Dědek V., Liška F.: This Journal *32*, 4297 (1967).
20. Dědek V., Liška F., Fikar J., Chvátal Z., Pohořelský L.: This Journal *40*, 1008 (1975).
21. Paleta O., Liška F., Pošta A.: This Journal *35*, 1303 (1970).
22. England D. C., Melby L. R., Dietrich M. A., Lindsey R. V., jr: J. Am. Chem. Soc. *82*, 5116 (1960).
23. Schaumburg K. J. Magnetic Resonance *7*, 177 (1972).

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