669. *Studies of Trifluoroacetic Acid. Part XV.* Further Investigations on the Reactions of Acyl Trifluoroacetates with Hydroxy-compounds.*

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Acyl trifluoroacetates with hydroxy-compounds give the trifluoroacetyl and other acyl esters, in proportions depending on the nature of the anhydride and hydroxy-compound; in most cases the " other acyl " ester predominates. The yields of acyl esters relative to trifluoroacetyl esters are usually increased by the presence of trifluoroacetic acid, and decreased by that of sodium trifluoroacetate and by solvents of low ionising ability. The manner in which the structure of a hydroxy-compound influences the course of its reactions with acyl trifluoroacetates is discussed. Alcohols capable of giving a stabilised carbonium ion react with acyl trifluoroacetate–trifluoroacetic acid mixtures by alkyl–oxygen fission.

It is well established that trifluoroacetic anhydride promotes acylations (as used in this paper the term excludes trifluoroacetylation) of hydroxy-compounds[1] and of compounds possessing reactive aromatic nuclei[2] by many carboxylic acids. These reactions proceed[3] *via* unsymmetrical anhydrides (acyl trifluoroacetates) formed from the acid and the trifluoroacetic anhydride. It has been suggested further,[4, 5] and supporting evidence based on conductivities has been adduced,[6] that these unsymmetrical anhydrides ionise to a limited extent into acylium ($R{\cdot}CO^+$) and trifluoroacetate ($CF_3{\cdot}CO_2^-$) ions, the former ions or solvated forms being the principal acylating species. The acylating, as opposed to trifluoroacetylating, power of acyl trifluoroacetates was considerably enhanced[3] by the trifluoroacetic acid liberated as they were formed in the above mixtures [equilibrium (1)]. With the unsymmetrical anhydrides in the absence of added acid, trifluoroacetylation became a more important process,[3] particularly in reactions with lower aliphatic alcohols and aromatic amines. This paper extends the investigations[3] of the reactions of acyl trifluoroacetates to cover different types of hydroxy-compounds and of acyl trifluoroacetates, and shows the broad effects on the process of the structures of the reactants.

$$R{\cdot}CO_2H + (CF_3{\cdot}CO)_2O \rightleftharpoons R{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 + CF_3{\cdot}CO_2H \quad . \; . \; . \; . \; . \; . \quad (1)$$

Results

Methods Used.—For the comprehensive studies envisaged, a new and simple method for the analysis of acyl and trifluoroacetyl ester products was required. Acyl trifluoroacetates derived from acetic, benzoic, and phenylacetic acid were available,[3] and it was shown that, in their infrared spectra, the carbonyl stretching frequencies for the esters of these acids in the range 1700—1800 cm.$^{-1}$ differed from those of the analogous trifluoroacetates by 25—65 cm.$^{-1}$, and this allowed an easy interpretation of their combined absorption spectra (see Table 6). The method required the preparation of each ester as a reference compound but was otherwise far superior to the anilide separation used before.[3]

Acetyl Trifluoroacetate Systems.—The reactions of acetyl trifluoroacetate, alone and in the presence of certain addenda, with a representative series of hydroxy-compounds were investigated, using the infrared method to provide a quantitative analysis of the products

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* Part XIV, *J.*, 1958, 1274.

[1] Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976.

[2] *Idem, J.*, 1951, 718.

[3] Bourne, Stacey, Tatlow, and Worrall, *J.*, 1954, 2006.

[4] Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942.

[5] Bourne, Randles, Stacey, Tatlow, and Tedder, *J. Amer. Chem. Soc.*, 1954, **76**, 3206.

[6] Randles, Tatlow, and Tedder, *J.*, 1954, 436.

obtained. The results of these reactions are given in Table 1. The conditions used before [3] for the reactions of *n*-, *sec.*-, and *tert.*-butyl alcohol with acetyl trifluoroacetate in ether are roughly comparable with those of columns III and IV of Table 1. The hydroxy-compounds now investigated may be divided into two broad groups, both of which can be further subdivided making four sub-groups, 1a, 1b, 2a, 2b, each with a distinctive mode of reaction.

TABLE 1. *Esters formed in reactions of acetyl trifluoroacetate* (1·3 *mol.*) *with hydroxy-compounds* (ca. 0·0025 *mole*).

(For 2 hr. at 20° unless otherwise stated.)

	I		II		III		IV	
Addenda:	—		$CF_3·CO_2H$ (1·3 mol.)		CCl_4 (0·5 c.c.)		$CF_3·CO_2H$ (1·3 mol.) CCl_4 (0·5 c.c.)	
R in ROH	ROAc (%)	RO·CO·CF_3 (%)	ROAc (%)	RO·CO·CF_3 (%)	ROAc (%)	RO·CO·CF_3 (%)	ROAc (%)	RO·CO·CF_3 (%)
Group 1a								
Bu^n	58	37	79	18	21	78	67	33
Et	73	25	87	12	29	66	76	22
$Ph·CH_2$	72	28	81	18	46	52	81	15
Bu^s	78	20	89	8	56	40	87	11
$[CH_2]_5{>}CH$	86	14	91	8	68	32	92	7
p-$NO_2·C_6H_4·CH_2$	93	4	96	4	86	14	86	14
Group 1b								
$CF_3·CMe_2$	96	—	99	—	95	—	99	—
$CF_3·CHMe$	96	—	96	—	96	—	96	—
$CF_3·CH_2$	100	—	100	—	98	—	96	—
Ph	98	—	96	—	98	—	95	—
Group 2a								
Bu^t	55	41	4	90	96	3	36	64
Ph·CHMe	61	39	4	94	74	24	4	94
Group 2b								
Ph_2CH	Polymers		Polymers		29	68	11	89
p-$MeO·C_6H_4·CHPh$	Polymers		Polymers		12	87	Polymers	

	V		VI		VII	
Addenda:	CCl_4 (25 c.c.)		$CF_3·CO_2H$ (1·3 mol.) CCl_4 (25 c.c.)		$CF_3·CO_2Na$ (1·5 mol.)	
R in ROH	ROAc (%)	RO·CO·CF_3 (%)	ROAc (%)	RO·CO·CF_3 (%)	ROAc (%)	RO·CO·CF_3 (%)
Group 1a						
Bu^n	6 *	90 *	9 *	90 *	15	79
$Ph·CH_2$	18 *	81 *	28 *	71 *		
Bu^s	30 *	67 *	30 *	68 *	20	74
$[CH_2]_5{>}CH$	35 *	64 *	33 *	67 *	—	—
p-$NO_2·C_6H_4·CH_2$					33	66
Group 1b						
$CF_3·CMe_2$	21 *	—	67 *	—		
$CF_3·CHMe$	50 *	—	79 *	—		
$CF_3·CH_2$	91 *	—	98 *	—	36	61
Ph	90 *	—	96 *	—	44	50
Group 2a						
Bu^t	50 *	4 *	70 *	4 *	84	15
Ph·CHMe	42	54	67	30	35	64
Group 2b						
Ph_2CH	74	26	39	57		
p-$MeO·C_6H_4·CHPh$	16	84	6	87		

* Reaction for 1 hr.

Trifluoroacetic acid clearly plays an important rôle in esterifications with acetyl trifluoroacetate. It should be noted that it is liberated when the anhydride reacts with a hydroxy-compound to give an acetate [equation (2)], whilst if a trifluoroacetate is produced acetic acid is formed [equation (3)]. Acetic acid can itself react with acetyl trifluoroacetate with the formation[7] of acetic anhydride and trifluoroacetic acid [equilibrium (4)].

Obviously, therefore, the reactions of acetyl trifluoroacetate with hydroxy-compounds will always be complicated by these effects, and those in which no reactive addenda were included (Table 1, columns I, III, and V) are really composite reactions in which, in the later stages, the effects of the liberated acids may be quite pronounced.

$$X{\cdot}OH + CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \longrightarrow X{\cdot}O{\cdot}CO{\cdot}CH_3 + CF_3{\cdot}CO_2H \quad . \; . \; . \; . \; . \quad (2)$$

$$X{\cdot}OH + CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \longrightarrow X{\cdot}O{\cdot}CO{\cdot}CF_3 + CH_3{\cdot}CO_2H \quad . \; . \; . \; . \; . \quad (3)$$

$$CH_3{\cdot}CO_2H + CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \rightleftharpoons (CH_3{\cdot}CO)_2O + CF_3{\cdot}CO_2H \quad . \; . \; . \; . \quad (4)$$

Sub-group 1*a*. With acetyl trifluoroacetate alone, the compounds of group 1a, the simple primary and secondary alcohols, gave mainly acetate esters, but these were accompanied by appreciable amounts of trifluoroacetates (Table I, column 1). The effect of the addition of trifluoroacetic acid is noteworthy (column II); it increased the acetate formed at the expense of the trifluoroacetate. Reaction of the hydroxy-compounds of sub-group 1a with acetyl trifluoroacetate and with acetyl trifluoroacetate–trifluoroacetic acid, under normal conditions with no diluent, is very rapid, and rates could only be determined after considerable dilution of the reactants with carbon tetrachloride. Samples of reaction mixtures (0·1M with respect to hydroxy-compound) were withdrawn at intervals and analysed for ester content. This dilution with carbon tetrachloride had a marked effect on the products [columns (V) and (VI) of Table 1] obtained with the alcohols of group 1a, and trifluoroacetylation became the main reaction. Trifluoroacetic acid had no appreciable effect on either the rates or the products of these reactions at high dilution. The primary alcohols reacted more rapidly and gave less acetate ester than the secondary alcohols. Since trifluoroacetylation was predominant, the rates of reaction of *n*- and *sec.*-butyl alcohol with trifluoroacetic acid, which could have been responsible for this type of acylation, were studied under the same conditions. Trifluoroacetylation did in fact occur but very much more slowly; again the primary reacted more rapidly than the secondary alcohol. The considerable influence exercised on the reactions of acetyl trifluoroacetate by a non-ionising solvent such as carbon tetrachloride, even in fairly small amounts, is shown in columns III and IV of Table 1. The proportions of trifluoroacetate formed were increased. The addition of sodium trifluoroacetate to acetyl trifluoroacetate also enhanced the formation of trifluoroacetate esters (column VII).

Sub-group 1*b*. The hydroxy-compounds of group 1b, phenol and fluoro-alcohols, reacted much more slowly with acetyl trifluoroacetate and gave exclusively acetate esters; however, with this group the rates of acetylation were increased greatly on addition of trifluoroacetic acid, even in high dilution with carbon tetrachloride. Differences in rates of reaction were also observed between the members of this sub-group. 2 : 2 : 2-Trifluoroethanol reacted more rapidly than 1-trifluoromethylethanol, and this more rapidly than 2 : 2 : 2-trifluoro-1 : 1-dimethylethanol. Dilution with carbon tetrachloride did not give rise to any trifluoroacetate, but addition of sodium trifluoroacetate did give over 50% of trifluoroacetate from phenol and from trifluoroethanol.

Group 2. Alcohols of group 2 gave quite different results. Diphenylmethanol and its 4-methoxy-derivative (group 2b) gave polymeric products when no inert diluent was used; in the presence of carbon tetrachloride, the addition of trifluoroacetic acid increased the yields of trifluoroacetate esters. With *tert.*-butyl alcohol and 1-phenylethanol (group 2a), the same effect applied in reactions involving trifluoroacetic acid with no diluent (columns I and II) or with little diluent (columns III and IV), and, contrary to the cases in group 1a, the addition of carbon tetrachloride increased the yields of acetate esters relative to those

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[7] Bourne, Tatlow, and Worrall, *J.*, 1957, 315.

obtained from the neat mixtures. At much lower concentrations in carbon tetrachloride, however (columns V and VI), the effect of trifluoroacetic acid was to increase the proportion of acetate esters (general behaviour similar to that shown by members of group 1). Also, in the case of *tert.*-butyl alcohol, the rate of reaction under these conditions was increased by trifluoroacetic acid, as for group 1b. With *tert.*-butyl alcohol, the addition of sodium trifluoroacetate to acetyl trifluoroacetate considerably enhanced the production of acetate ester relative to reactions with no addenda or with added trifluoroacetic acid.

L-1-Phenylethanol and Acetyl Trifluoroacetate Systems.—Except for the reactions with group 2a at high dilution, the behaviour of the members of group 2 was clearly anomalous, and processes involving alkyl–oxygen fission at some stage were obviously indicated. The behaviour of L-1-phenylethanol and its esters with various reaction mixtures was therefore studied. A chromatographic separation of the acetate and trifluoroacetate of this alcohol was developed, which enabled this to be done. The results are given in Table 2.

With acetyl trifluoroacetate–trifluoroacetic acid under mild conditions, the L-alcohol gave extensively racemised trifluoroacetate (76%) together with inactive acetate (24%) showing that alkyl–oxygen fission had indeed occurred at some stage. The system was complex, however, since, while acetic acid or acetic anhydride did not appear to have any effect on the esters, trifluoroacetic acid alone readily racemised both the L-acetate and L-trifluoroacetate and converted much of the former into the trifluoroacetate. The presence of carbon tetrachloride inhibited both the interconversion and the racemisation. Trifluoroacetic acid and the L-alcohol gave the racemic trifluoroacetate. Acetyl trifluoroacetate alone had no effect on the L-acetate or the L-trifluoroacetate, but with the L-alcohol it gave partly racemised esters. The addition of progressively greater amounts of carbon tetrachloride to the last system first decreased and then increased the proportion of trifluoroacetate ester obtained; no racemisation occurred under these conditions. In the absence of diluent however, acetyl trifluoroacetate–trifluoroacetic acid gave much more extensive racemisation than when no acid was added. Acetyl trifluoroacetate–sodium trifluoroacetate and the L-alcohol afforded acetate ester (35%) and trifluoroacetate (64%), both however with complete retention of optical activity. These results show clearly that trifluoroacetic acid causes racemisation, presumably by protonation, but suggest that acetyl trifluoroacetate alone does not.

Acetyl Trifluoroacetate–Heptafluorobutyric Acid.—A brief study was made next of the system acetyl trifluoroacetate–heptafluorobutyric acid to confirm the probability that there was ready interchange between the acid and the anhydride in mixtures of this type. First, the system acetic anhydride–heptafluorobutyric anhydride was examined by infrared spectroscopy and it was established that the equilibrium favoured the unsymmetrical anhydride [equation (5)] as in the analogous case with trifluoroacetic

$$\mathrm{Ac_2O + (C_3F_7{\cdot}CO)_2O \rightleftharpoons 2Ac{\cdot}O{\cdot}CO{\cdot}C_3F_7} \quad . \; . \; . \; . \; . \; . \; . \; . \tag{5}$$

$$\mathrm{Ac{\cdot}O{\cdot}CO{\cdot}CF_3 + C_3F_7{\cdot}CO_2H \rightleftharpoons Ac{\cdot}O{\cdot}CO{\cdot}C_3F_7 + CF_3{\cdot}CO_2H} \quad . \; . \; . \; . \; . \; . \tag{6}$$

anhydride.[3] Infrared spectroscopic analysis of mixtures showed that equilibrium (6) was indeed established and that the equilibrium constant was very approximately 1. In its reaction with phenetole, acetyl trifluoroacetate–heptafluorobutyric acid gave a good yield (78%) of ketone in only 3 hr.; this acid thus had an effect comparable with that of trifluoroacetic acid[3] on the acylating power of the anhydride.

Benzoyl and Phenylacetyl Trifluoroacetate.—Benzoyl trifluoroacetate was found previously[3] to effect trifluoroacetylation much more readily than did acetyl trifluoroacetate. Infrared spectroscopy of esters has now been applied to the reactions of other hydroxy-compounds with benzoyl trifluoroacetate, alone and in the presence of certain addenda (Table 3). The series cannot be divided into clear-cut groups as before, but the hydroxy-compounds are arranged roughly in order of increasing yield of benzoate esters with benzoyl trifluoroacetate alone (column I). With the alcohols at the beginning of the series, trifluoroacetylation was the predominant reaction, but phenol at the end of the series gave a good yield (75%) of the benzoate (column I). Addition of trifluoroacetic acid did not appreciably affect yields of benzoate esters with the alcohols in the series up to *p*-nitrobenzyl alcohol, but with this and the remainder of the hydroxy-compounds it caused a substantial increase in benzoate production (column II). When treated with benzoyl trifluoroacetate in carbon tetrachloride (columns IV and V) all the alcohols in the series up to and including *p*-nitrobenzyl alcohol gave exclusively trifluoroacetate esters even when the reactions were carried out in the presence of trifluoroacetic acid. Of the remaining hydroxy-compounds, with the unsymmetric anhydride alone in carbon

TABLE 2. *Reactions of* L-1-*phenylethanol and its esters.*

	Reactants (g.)					
	L-PhMeCH·O·R					
Expt. No.	R = H	R = Ac	R = CO·CF_3	$CF_3·CO_2H$	$CF_3·CO_2Ac$	CCl_4
1	—	0·64	—	0·90	—	—
2	—	0·28	—	0·39	—	16
3	—	0·31	—	—	0·36	—
4	—	0·72	—	0·66	0·97	—
5	—	0·21	—	0·19	0·26	16
6	—	—	0·30	0·31	—	—
7	—	—	0·19	0·20	—	1·6
8	—	—	0·18	0·20	—	16
9	—	—	0·27	—	0·26	—
10	—	—	0·27	0·33	0·46	—
11	—	—	0·18	0·13	0·17	16
12	1·22	—	—	2·28	—	—
13	1·08	—	—	—	1·81	—
14	1·20	—	—	1·48	2·05	—
15	1·36	—	—	—	2·28	8
16	1·22	—	—	—	2·04	300
17	0·39	—	—	0·20 *	0·65	—

		Esters formed							
		L-PhMeCH·O·CO·R′		Properties of product isolated			Properties of alcohol obtained by hydrolysis		
Expt. No.	Reaction time (hr.) at 20°	R′	Yield (% by infrared)	Yield (%)	B. p./ 15 mm.	Optical activity (%age retained)	Yield (%)	B. p./ 15 mm.	Optical activity (%age retained)
1	2	Me	28	24	96°	6	81	93°	6
		CF_3	69	48	74	0	78	94	0
2	2	Me	—	78	95	100	—	—	—
3	2	Me	—	82	96	100	—	—	—
4	2	Me	24	24	95	0	—	—	—
		CF_3	76	37	74	0	77	94	0
5	2	Me	—	89	95	100	—	—	—
6	2	CF_3	—	84	72	0	—	—	—
7	2	CF_3	—	66	72	83	—	—	—
8	2	CF_3	—	69	70	100	—	—	—
9	2	CF_3	—	76	72	100	—	—	—
10	4·5	CF_3	100	72	70	5	—	—	—
11	2	CF_3	—	72	70	100	—	—	—
12	4	CF_3	—	70	72	0	81	94	0
13	2	Me	61	45	94	42	85	93	42
		CF_3	39	23	75	12	57	93	12
14	0·5	Me	24	14	95	0	—	—	—
		CF_3	76	50	76	10	75	93	11
15	1	Me	76	61	94	100	—	—	—
		CF_3	21	13	73	100	81	93	100
16	4	Me	46	43	94	100	75	94	100
		CF_3	52	24	74	100	74	93	100
17	2	Me	35	24	93	100	—	—	—
		CF_3	64	26	70	100	—	—	—

* $CF_3·CO_2Na$.

tetrachloride (column IV), only phenol gave a reasonable yield (76%) of benzoate ester, but the yields from the fluoro-alcohols were greatly increased on addition of trifluoroacetic acid (column V). When the reactions of *n*- and *sec.*-butyl and of *p*-nitrobenzyl alcohol with benzoyl trifluoroacetate were carried out in the presence of a large excess (10 mol.) of trifluoroacetic acid (column III) the proportions of benzoate esters were greatly increased and even the butyl alcohols gave reasonable yields (38 and 57% respectively).

TABLE 3. *Reactions of benzoyl trifluoroacetate* (1·3 *mol.*) *with hydroxy-compounds* (2 *hr. at* ca. 20°).

	I		II		III	
Addenda:	—		$CF_3{\cdot}CO_2H$ (1·3 mol.)		$CF_3{\cdot}CO_2H$ (10 mol.)	
R in ROH	ROBz (%)	$RO{\cdot}CO{\cdot}CF_3$ (%)	ROBz (%)	$RO{\cdot}CO{\cdot}CF_3$ (%)	ROBz (%)	$RO{\cdot}CO{\cdot}CF_3$ (%)
Bu^n	6	93	8	92	38	59
$Ph{\cdot}CH_2$	3	94	4	93		
Bu^s	5	92	8	92	57	40
$[CH_2]_5{>}CH$	5	94	9	90		
Et	12	84	13	81		
Bu^t	13	74	23	73	—	83
$p\text{-}NO_2{\cdot}C_6H_4{\cdot}CH_2$ *	16	83	64	35	92	8
$CF_3{\cdot}CMe_2$	29	15	82	16		
$CF_3{\cdot}CHMe$	18	57	94	6		
$CF_3{\cdot}CH_2$	44	53	82	17		
Ph *	75	25	88	11		

	IV		V	
Addenda:	CCl_4 (0·5 c.c.)		$CF_3{\cdot}CO_2H$ (1·3 mol.) CCl_4 (0·5 c.c.)	
R in ROH	ROBz (%)	$RO{\cdot}CO{\cdot}CF_3$ (%)	ROBz (%)	$RO{\cdot}CO{\cdot}CF_3$ (%)
Bu^n	—	97	—	99
$Ph{\cdot}CH_2$	—	99	—	99
Bu^s	—	95	—	99
$[CH_2]_5{>}CH$	—	96	—	99
Et	—	96	—	97
Bu^t	—	86 *	—	87 *
$p\text{-}NO_2{\cdot}C_6H_4{\cdot}CH_2$ *	—	99	—	99
$CF_3{\cdot}CMe_2$	21	13	50	25
$CF_3{\cdot}CHMe$	11	51	85	15
$CF_3{\cdot}CH_2$	20	67	80	19
Ph *	76	19	93	7

* Reaction for 2 hr. at *ca.* 50°.

The rates of reaction of butan-1-ol and of phenol with benzoyl trifluoroacetate, alone and in the presence of trifluoroacetic acid, in excess of carbon tetrachloride, showed that even phenol now gave mainly the trifluoroacetate. The reactions with butan-1-ol were as rapid as for acetyl trifluoroacetate. In the early stages of the reaction of benzoyl trifluoroacetate alone with phenol the same is true, but the main effect of trifluoroacetic acid here was to slow down considerably the formation of phenyl trifluoroacetate; the formation of phenyl benzoate was also enhanced somewhat.

Phenylacetyl trifluoroacetate seems to occupy an intermediate position as regards acylating power. The reactions of some hydroxy-compounds with phenylacetyl trifluoroacetate and phenylacetyl trifluoroacetate–trifluoroacetic acid were examined by infrared spectroscopy (Table 4), the hydroxy-compounds with the exception of *tert.*-butyl alcohol being listed in order of increasing yields of phenylacetate esters. The alcohols at the beginning of the list gave only low yields of phenylacetate with phenylacetyl trifluoroacetate, increased when the reactions were carried out in the presence of trifluoroacetic acid, while trifluoroethanol and phenol gave exclusively the phenylacetate esters. *tert.*-Butyl alcohol behaved as it did with acetyl trifluoroacetate, the yield of the phenylacetate

TABLE 4. *Reactions of phenylacetyl trifluoroacetate* (1·3 *mol.*) *with hydroxy-compounds* (2 *hr. at* ca. 20°).

R in ROH	RO·CO·CH$_2$Ph (%)	RO·CO·CF$_3$ (%)	+ CF$_3$·CO$_2$H (1·3 mol.) RO·CO·CH$_2$Ph (%)	+ CF$_3$·CO$_2$H (1·3 mol.) RO·CO·CF$_3$ (%)
Bu^n	16	84	28	71
[CH$_2$]$_5$>CH	28	71	56	44
Bu^s	35	63	58	42
p-NO$_2$·C$_6$H$_4$·CH$_2$	55	41	84	16
CF$_3$·CH$_2$	100	—	98	—
Ph	100	—	98	—
Bu^t	52	45	13	87

ester being decreased when the reaction was carried out in the presence of trifluoroacetic acid, suggesting that again the mechanism involved alkyl–oxygen fission of the tertiary alcohol.

DISCUSSION OF REACTION MECHANISMS.

General Behaviour of Acyl Trifluoroacetates.—In previous papers[3-6] it has been postulated that the unsymmetrical anhydride formed in considerable quantity when a carboxylic acid (R·CO$_2$H) is dissolved in trifluoroacetic anhydride is, in its molecular form, mainly a trifluoroacetylating agent. Further, however, it has been considered to be capable of dissociating slightly to give acylium (R·CO$^+$) and trifluoroacetate (CF$_3$·CO$_2$$^-$) ions, the former species being largely responsible for acylation, reacting with many compounds much more readily than the molecular anhydride is able to do. We still believe this to be true in general. It seems unlikely that other entities which might be present and capable of such a reaction, namely, the free carboxylic acid (R·CO$_2$H) and its symmetric anhydride [(R·CO)$_2$O], play a significant part in acylation in these systems. Both are in extremely small concentrations in an equimolecular mixture of a carboxylic acid and trifluoroacetic anhydride and the introduction of more trifluoroacetic acid should suppress the concentration of the symmetric anhydride [(R·CO)$_2$O] even further[7] [equilibrium (4)] although it probably would increase that of the acid (R·CO$_2$H) somewhat. The conjugate acids R·CO$_2$H$_2$$^+$, (R·CO)$_2$·OH$^+$, and (R·CO·O·CO·CF$_3$:H)$^+$, or any solvated species would be expected to break down to, or to react essentially as, acylium ions, and no attempt is made here to distinguish them. It seems likely however that the unsymmetrical anhydride in its molecular form may be an acylating agent in some specialised cases (see later).

The entities potentially capable of effecting trifluoroacetylation in the above systems containing unsymmetrical anhydrides are presumably trifluoroacetic anhydride, trifluoroacetic acid, trifluoroacetate anion (CF$_3$·CO$_2$$^-$), trifluoroacetylium cation (CF$_3$·CO$^+$), and the unsymmetrical anhydrides in their molecular forms. The first of these does not seem to be present in any appreciable concentration,[3] except possibly when a large excess of trifluoroacetic acid is introduced. Measurements of rates of reaction showed that trifluoroacetate esters were formed from the butyl alcohols and acetyl trifluoroacetate very much more rapidly than with trifluoroacetic acid, so that this acid can play only a minor rôle in trifluoroacetylation by the direct reaction. Alkyl–oxygen fission of a hydroxy-compound is a pre-requisite for reaction with the free trifluoroacetate anion (CF$_3$·CO$_2$$^-$), which must be associated with a cation, presumably acylium ion (R·CO$^+$). This type of fission has been demonstrated only with the specialised alcohols of group 2; otherwise it may be regarded as being of little importance. It seems unlikely that trifluoroacetylium cation (CF$_3$·CO$^+$) could exist in significant concentrations in these systems. It was inferred therefore that almost all of the trifluoroacetate esters formed arose from reactions of hydroxy-compounds with the molecular forms of the unsymmetrical anhydrides. From orthodox electronic theory the latter should be principally trifluoroacetylating agents (cf. the work[8] on anhydrides from acetic and the chloroacetic acids), reacting always by acyl–oxygen fission.

Reactions of Acetyl Trifluoroacetate with Hydroxy-compounds of Sub-group 1*a*.—The mechanism suggested above is in general accord with the experimental results found with these systems. The rapidity of acylations of the types under discussion will presumably be determined largely by two factors, (*a*) the availability of electrons at the oxygen atom of the hydroxyl group, and (*b*) the accessibility of this group. Acetylations with the strongly electrophilic acetylium cation carrying a formal positive charge should not be influenced greatly by fine degrees of electron availability (*e.g.*, acetyl trifluoroacetate can acetylate[7] the hydroxyl group of acetic acid); and the steric factor, though obviously important, should be at a minimum with a fairly small attacking species such as this. In contrast, for trifluoroacetylations by molecular acetyl trifluoroacetate, since it is relatively less electrophilic and also larger, both factors (*a*) and (*b*) will be much more important. For the alcohols of sub-group 1a, however, neither factor should be sufficient to prevent the occurrence to an appreciable extent of this type of trifluoroacetylation. Though less reactive than the acetylium cation, molecular acetyl trifluoroacetate is present in vastly greater concentration. The order of increasing acetate : trifluoroacetate ratio in which the primary alcohols of sub-group 1a are arranged in Table 1 is that which would be predicted from simple electronic theory for increasing acidity, and hence presumably decreasing electron-availability on the oxygen atom of the un-ionised forms. *sec.*-Butyl alcohol and *cyclo*hexanol should be more basic than ethanol or butan-1-ol, but have much less accessible hydroxyl groups, so that the increased proportions of acetate obtained from the secondary alcohols can be explained by the greater difficulty of approach of molecular acetyl trifluoroacetate to the oxygen atom.

Addition of sodium trifluoroacetate to acetyl trifluoroacetate considerably decreased its acetylating power, presumably because of a decrease in the concentration of acetylium cations by a common-ion effect, which slowed the acetylation considerably. An inert non-polar solvent such as carbon tetrachloride (ε_{20} 2·23) should also decrease the overall ionisation and hence the proportion of acetate formed, again in accordance with the observed effects.

Trifluoroacetic acid promoted acetylation quite markedly with alcohols of this group. This obviously could not be a direct effect of normal dissociation of the acid on the ionisation of acetyl trifluoroacetate. The value for the dielectric constant[9] (ε_{20} 8·4) suggests that trifluoroacetic acid is not intrinsically a particularly highly ionising medium. Further, there is an indication of a maximum,[9b] well above the value for trifluoroacetic acid alone, in the dielectric constants of mixtures of acetic and trifluoroacetic anhydride. Thus it seems that the promotion of acetylation by the acid cannot be due merely to its properties as a polar solvent. Ready exchange of anions ($CF_3{\cdot}CO_2^-$) between the acid and acetyl trifluoroacetate occurs almost certainly, since it has been demonstrated for the system acetyl trifluoroacetate–heptafluorobutyric acid. This could presumably give a transient liberation of acetylium cations, but need not necessarily, and in any case should not increase their overall concentration.

Trifluoroacetic acid is known to promote the polymerisation[10,11] of certain olefins such as styrene and α-methylstyrene. One reason for its high activity here may well be the ease with which it can solvate its own negative ions,[11] after initiation of the polymerisation by protonation, so that chain termination is inhibited. A very similar effect could well apply in our esterifications. The powerful influence of trifluoroacetic acid would then be due largely to its ability to solvate the asymmetric anhydride (this could be by addition to the fluorocarbonyl group, a process known to proceed readily in other

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[8] Emery and Gold, *J.*, 1950, 1443, 1447, 1455.

[9] (*a*) Dannhauser and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 6105; (*b*) Tedder, *J.*, 1954, 2646.

[10] Bourne and Tatlow, unpublished observations.

[11] Throssell, Sood, Szwarc, and Stannett, *J. Amer. Chem. Soc.*, 1956, **78**, 1122.

connections, *e.g.*, hydration of fluoro-aldehydes and -ketones). Under ionising conditions, the actual liberation of a solvated anion would then be favoured with promotion of acylation by the acetylium cation released concomitantly.

Trifluoroacetic acid will presumably protonate the alcohol to some extent with consequent lower reactivity of the protonated species towards electrophilic reagents. It seems unlikely that this effect could assume major importance, however, since the acid will ionise only to a limited extent under these conditions.

Reactions of Acetyl Trifluoroacetate with Hydroxy-compounds of Sub-group 1b.—These hydroxy-compounds are all appreciably acidic (K_a values[12]: $CF_3{\cdot}CMe_2{\cdot}OH$, $2{\cdot}5 \times 10^{-12}$; $CF_3{\cdot}CHMe{\cdot}OH$, $6{\cdot}3 \times 10^{-12}$; $CF_3{\cdot}CH_2{\cdot}OH$, $4{\cdot}0 \times 10^{-12}$; $C_6H_5{\cdot}OH$, $1{\cdot}7 \times 10^{-10}$). Therefore, the electrons on the oxygen atoms of all these compounds should be relatively less readily available for interaction with weakly electrophilic reagents than is the case with the alcohols of sub-group 1a. Attack by molecular acetyl trifluoroacetate should thus be very slow. In fact, trifluoroacetyl esters are produced from members of sub-group 1b only in the presence of sodium trifluoroacetate. Also, the effect of added trifluoroacetic acid in speeding up reaction is most marked with these hydroxy-compounds.

The influence of accessibility of the hydroxyl group was shown very clearly in the measurements of the rates of reaction of acetyl trifluoroacetate with the fluoro-alcohols (of which the acidities do not differ greatly) to give acetate esters. The rates decreased markedly with increasing substitution of the carbon atom carrying the hydroxyl group. Further, the very profound effects exerted by a trifluoromethyl group on the properties of alcohols are well illustrated by a comparison of the behaviour of 2 : 2 : 2-trifluoro-1 : 1-dimethylethanol and of *tert.*-butyl alcohol (see below) towards acetyl trifluoroacetate–trifluoroacetic acid. In complete contrast to the latter, the tertiary fluoro-alcohol underwent no reactions involving alkyl–oxygen fission and behaved normally, but was rather unreactive, presumably because of both the steric effect and the electron-withdrawal by the fluorine atoms. This type of compound might well be employed usefully for studying steric factors of this type in general reactions of alcohols.

Reactions of Acetyl Trifluoroacetate with Hydroxy-compounds of Group 2.—Of the butyl alcohols, *tert.*-butyl alcohol should be the most basic but have the least accessible hydroxyl group. Reaction with acetyl trifluoroacetate in carbon tetrachloride was slower than for the isomers but gave a high proportion of acetate. This ester was also obtained in good yield in the reaction with acetyl trifluoroacetate–sodium trifluoroacetate. Some of the acetate produced will arise from attack by acetylium ion, of which however only a very low concentration should be present under these conditions of suppressed ionisation, so that an additional route to the acetate seems likely. It may well be that with an alcohol such as *tert.*-butyl alcohol, possessing an inaccessible hydroxyl group, in a reaction with molecular acetyl trifluoroacetate the relatively large trifluoromethyl group will hinder approach of the alcohol to the adjacent carbonyl group. The slower, but less hindered, attack on the acetyl group should then become of importance because of the reactivity of (electron-availability on) the hydroxyl group. Somewhat similar postulates have been made[8] to explain certain reactions of anhydrides of chloroacetic acids. This effect will probably be significant only with secondary and tertiary alcohols with both hindered and reactive hydroxyl groups (*i.e.*, not with members of group 1b) under essentially non-ionic conditions and should make only a very limited contribution to normal esterifications with trifluoroacetic acid present and inert solvents absent.

Under the reaction conditions so far discussed in this section esterification of *tert.*-butyl alcohol proceeded by normal acyl–oxygen fission. The behaviour of the alcohol with acetyl trifluoroacetate in the absence of a solvent or in the presence of trifluoroacetic acid was very different however. *tert.*-Butyl trifluoroacetate was a major product, particularly when the free acid was added, and a mechanism involving alkyl–oxygen fission at some stage was clearly indicated. However, both the acetate and the alcohol were attacked

[12] Henne and Pelley, *J. Amer. Chem. Soc.*, 1952, **74**, 1426.

by trifluoroacetic acid itself in the absence of solvents to give the trifluoroacetate ester. It is likely that these, particularly the first, are major routes to the last product in the esterifications with acetyl trifluoroacetate–trifluoroacetic acid. Presumably, in this type of reaction, the acid protonates the alcohol or acetate, and a neutral molecule (H_2O or HOAc) is then eliminated, the resultant carbonium cation finally reacting with a trifluoroacetate anion.

It is well known [13] that the phenyl group confers a greater degree of stability on carbonium ions than does a methyl group, and, as expected, L-1-phenylethanol and *tert.*-butyl alcohol behaved similarly. Under conditions of low acidity and suppressed ionisation *e.g.*, with carbon tetrachloride or sodium trifluoroacetate present, the L-alcohol gave appreciable amounts of acetate (behaviour similar to that of an alcohol at the end of sub-group 1a), but no racemisation occurred. Racemisation was demonstrated only when trifluoroacetic acid was present; if it was liberated in the reaction, *i.e.*, no great amount was present, some optical activity was retained in the ester products. It seems very likely that in these systems only attack by a free perfluoro-carboxylic acid causes alkyl–oxygen fission and that acylium ions themselves do not. If they do, it is under conditions of high acidity when the acid itself will also give the same effect.

Diphenylmethanol, and its 4-methoxy-derivative which can give even more stabilised carbonium cations, afforded polymeric products very easily. Both gave considerable amounts of their trifluoroacetates even in the presence of much carbon tetrachloride, but the addition of trifluoroacetic acid considerably increased the yield of its esters.

These results are in general accord with data on the formation and hydrolysis of esters by processes involving alkyl–oxygen fission, of which full accounts of the mechanisms established have been given.[13] Direct evidence for the ionisation of tertiary alcohols, in an acidic medium, to give carbonium ions has been obtained [14] from cryoscopic measurements in concentrated sulphuric acid.

Esterifications with Benzoyl Trifluoroacetate.—Benzoyl trifluoroacetate showed much more tendency to give trifluoroacetates and thus presumably to react in its molecular form than did acetyl trifluoroacetate. A possible explanation of this is resonance stabilisation of the benzoylium cation ($C_6H_5{\cdot}CO^+$) with consequent lowering of the density of the positive charge on the carbonyl group. This should slow down the reactions of the cation with hydroxy-functions and allow attack by the molecular anhydride to assume greater relative importance.

The acetylium cation cannot be stabilised in this way. Also, owing to the very slightly increased electronegativity, benzoyl trifluoroacetate may be a more reactive trifluoroacetylating agent than is acetyl trifluoroacetate. The greater size of the phenyl group than of methyl should also mean that steric factors would not favour benzoylation in this case.

It appeared that only in the presence of excess trifluoroacetic acid was benzoylation important with members of sub-group 1a, and that, even with those of sub-group 1b, trifluoroacetylation occurred to an appreciable extent. The rate of reaction of benzoyl trifluoroacetate with phenol in an excess of carbon tetrachloride to give the trifluoroacetate was decreased when trifluoroacetic acid was added. This could be due to solvation by the acid of the molecular anhydride.

Very many hydroxy-compounds are not normally acylated by processes involving alkyl–oxygen fission. For these, the following appear favourable conditions for use in reactions with carboxylic acid–trifluoroacetic anhydride: (*a*) the use of a stoicheiometric proportion of carboxylic acid to hydroxy-compound, with a slight excess of trifluoroacetic anhydride; (*b*) use of an excess of trifluoroacetic acid; (*c*) exclusion of any components

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[13] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 751; Davies and Kenyon, *Quart. Rev.*, 1955, **9**, 203.

[14] Newman, Craig, and Garrett, *J. Amer. Chem. Soc.*, 1949, **71**, 869; Newman and Deno, *ibid.*, 1951, **73**, 3644.

which would give rise to any appreciable concentration of trifluoroacetate anions; (*d*) absence of non-polar solvents.

EXPERIMENTAL

Unless otherwise stated, dry reagents and anhydrous conditions were employed.

Preparation of Esters as Reference Compounds.—(a) *Trifluoroacetates.* With the exception of ethyl trifluoroacetate,[15] trifluoroacetate esters were prepared by treatment [16] of the corresponding hydroxy-compounds with trifluoroacetic anhydride–sodium trifluoroacetate. Four standard methods of isolation were evolved.

(i) The hydroxy-compound (1·0—3·3 g.) was treated with trifluoroacetic anhydride (1·3 mol.) and sodium trifluoroacetate (*ca.* 0·1 g.) and after the initial vigorous reaction had subsided, the mixture was heated under reflux for 15 min. Water (1 c.c.) was then added and the aqueous phase was neutralised rapidly with 2N-sodium hydroxide until it had pH 7—8 (Universal indicator). The organic phase was separated, dried ($MgSO_4$), filtered, and distilled.

TABLE 5. *Trifluoroacetate esters* ($R{\cdot}O{\cdot}CO{\cdot}CF_3$).

No.	R	Method	Yield (%)	B. p./mm.	n_D ($t°$)	Previous values B. p.	Previous values n_D ($t°$)	Ref.
I	Bu^n	ii	73	104°/745	1·3394 (18°)	102·7—102·8°	1·3391 (20°)	*a*
II	Bu^s	ii	57	93—94/740	1·3343 (18)	—	—	
III	Bu^t	i	62	85—86/750	1·3295 (19)	—	—	
IV	$[CH_2]_5{>}CH$	ii	76	150/759	1·3827 (19)	—	—	
V	Ph	iii	86	147/750	1·4197 (20)	146·5—147·0	1·4183 (25)	*b*
VI	$Ph{\cdot}CH_2$	iii	82	177—178/755	1·4363 (18)	173—174/760	—	*c*
VII	Ph·CHMe	iv	80	73/15	1·4329 (22)	—	—	
VIII	$Ph_2{\cdot}CH$	iv	79	131/13	1·5030 (19)	—	—	
IX	p-$MeO{\cdot}C_6H_4{\cdot}CHPh$	iv	79	167/13	1·5107 (19)	—	—	
X	$CF_3{\cdot}CH_2$		21	55·5/752	1·280 (20)	55	1·2812 (20)	*d*
XI	$CF_3{\cdot}CHMe$	i	52	63—64/746	1·291 (16)	—	—	
XII	$CF_3{\cdot}CMe_2$	i	19	73/743	1·3080 (20)	—	—	

No.	Formula	Required (%) C	H	F	equiv.	Found (%) C	H	F	equiv.
I	$C_6H_9O_2F_3$	42·4	5·3	—	170	42·7	5·3	—	170
II	,,	,,	,,	—	,,	42·5	5·5	—	172
III	,,	,,	,,	33·5	,,	42·1	5·2	32·9	171
IV	$C_8H_{11}O_2F_3$	49·0	5·65	29·1	196	49·5	5·7	28·9	200
VII	$C_{10}H_9O_2F_3$	55·05	4·2	26·1	218	55·5	4·0	25·8	217
VIII	$C_{15}H_{11}O_2F_3$	64·3	4·0	—	280	64·2	3·9	—	282
X	$C_4H_2O_2F_6$	24·5	1·0	—	196	24·8	1·35	—	195
XI	$C_5H_4O_2F_6$	28·6	1·9	—	210	28·8	2·0	—	209
XII	$C_6H_6O_2F_6$	32·2	2·7	—	224	32·5	2·9	—	220

IX Stable only for 15 min. after isolation.
XII Purified by preparative-scale gas chromatography.[e]
p-Nitrobenzyl trifluoroacetate [16] had m. p. 47°.

(*a*) Campbell, Knobloch, and Campbell, *J. Amer. Chem. Soc.*, 1950, **72**, 4380. (*b*) Clark and Simons, *ibid.*, 1953, **75**, 6305. (*c*) Weygand and Leising, *Chem. Ber.*, 1954, **87**, 248. (*d*) Swarts, *Bull. Soc. chim. Belg.*, 1934, **43**, 471. (*e*) Evans and Tatlow, *J.*, 1955, 1184.

(ii) The neutral aqueous phase was extracted with ether, and the extract was dried ($MgSO_4$), filtered, and distilled through a short Vigreux column to give ether and then the trifluoroacetate.

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[15] Gilman and Jones, *ibid.*, 1943, **65**, 1458.

[16] Bourne, Tatlow, and Tatlow, *J.*, 1950, 1367.

(iii) Direct distillation through a short Vigreux column afforded a mixture of trifluoroacetic acid and the excess of anhydride, and then the trifluoroacetate.

(iv) Trifluoroacetic anhydride (1·3 mol.) was added slowly to a cooled solution of the hydroxy-compound in ether (5 c.c.) and, after 10 min. at 20°, ether (25 c.c.) was added. The solution was washed with sodium hydrogen carbonate solution, then with water, dried ($MgSO_4$), filtered, and distilled under reduced pressure, to give the trifluoroacetate.

The experimental details are given in Table 5. The *esters* to which no references are given are new. The equivalents were determined by hydrolysis with excess of alkali and back-titration.

(b) *Acetates, benzoates, and phenylacetates.* Many of these were available commercially or were prepared by standard methods. The benzoates of the fluorine-containing hydroxy-compounds, and 2 : 2 : 2-trifluoroethyl phenylacetate, were prepared by treatment of the hydroxy-compound with the appropriate acid chloride in pyridine. 2 : 2 : 2-*Trifluoroethyl benzoate* (84%) had b. p. 83°/19 mm., n^{16} 1·4508 (Found: C, 52·9; H, 3·5%; equiv., 202. $C_9H_7O_2F_3$ requires C, 52·95; H, 3·5%; equiv., 204); 2 : 2 : 2-*trifluoro*-1-*methylethyl benzoate* (87%) had b. p. 88°/20 mm., n^{17} 1·4476 (Found: C, 55·0; H, 4·2%; equiv., 217. $C_{10}H_9O_2F_3$ requires C, 55·05; H, 4·2%; equiv., 218); 2 : 2 : 2-*trifluoro*-1 : 1-*dimethylethyl benzoate* (50%) had b. p. 93°/18 mm., n^{15} 1·4523 (Found: C, 56·9; H, 4·8%; equiv., 230. $C_{11}H_{11}O_2F_3$ requires C, 56·9; H, 4·8%; equiv., 232); 2 : 2 : 2-*trifluoroethyl phenylacetate* (57%) had b. p. 99·5°/15 mm., n^{19} 1·4467 (Found: C, 55·4; H, 4·4%; equiv., 214).

Absorption Bands Used in the Infrared Spectroscopic Analysis.—The infrared spectra of the esters in carbon tetrachloride (*ca.* 0·08M) were determined over the range 1700—1900 cm.$^{-1}$, by use of a Grubb-Parsons spectrometer with a rock-salt prism. The frequencies (cm.$^{-1}$) of the carbonyl absorption bands and the optical densities (O.D. of M-solutions in a cell of thickness *ca.* 0·1 mm.) of the esters are given in Table 6.

TABLE 6. *Infrared analysis of esters.*

	$RO·CO·CF_3$		ROAc		ROBz		$RO·CO·CH_2Ph$	
R	cm.$^{-1}$	O.D.	cm.$^{-1}$	O.D.	cm.$^{-1}$	O.D.	cm.$^{-1}$	O.D.
Et	1786	6·8	1743	7·0	1723	7·6	—	—
Bu^n	1787	7·3	1735	6·6	1723	6·6	1736	6·4
Bu^s	1779	7·2	1733	7·1	1719	7·9	1735	6·6
Bu^t	1777	7·8	1736	5·8	1715	7·1	1735	6·3
$[CH_2]_5{>}CH$	1777	7·2	1734	6·3	1720	8·1	1739	6·4
Ph	1795	7·2	1764	5·7	1740	7·6	1755	4·2
$Ph·CH_2$	1776	6·9	1749	5·7	1726	7·2	—	—
Ph·CHMe	1783	6·7	1738	4·6	—	—	—	—
Ph_2CH	1786	7·2	1741	6·2	—	—	—	—
p-$MeO·C_6H_4·CHPh$	1786	6·3	1741	5·0	—	—	—	—
p-$NO_2·C_6H_4·CH_2$	1789	7·1	1755	5·7	1729	7·3	1749	5·6
$CF_3·CH_2$	1802	3·6	1764	4·4	1740	7·1	1761	4·3
$CF_3·CHMe$	1790	4·7	1754	5·3	1729	7·1	—	—
$CF_3·CMe_2$	1792	6·1	1752	5·9	1727	6·8	—	—

Reactions of Acetyl Trifluoroacetate with Hydroxy-compounds.—The hydroxy-compound (*ca.* 0·0025 mole) was treated with acetyl trifluoroacetate (1·3 mol.) for 2 hr. at 20° and then carbon tetrachloride (10 c.c.) was added. The solution was washed with sodium hydrogen carbonate solution, and the organic layer, together with extracts of the aqueous phase, was dried ($MgSO_4$), filtered, and diluted to 25 c.c. with carbon tetrachloride. The infrared spectrum of the solution (ester concentration *ca.* 0·1M) was then determined over the frequency range 1700—1900 cm.$^{-1}$. A comparison of the calculated optical densities (M-hydroxy-compound in a cell of thickness *ca.* 0·1 mm.), at the appropriate frequencies, with those of solutions of the pure acetate and trifluoroacetate enabled the proportion of each ester produced in the reaction to be determined. To check the accuracy of the method a mixture of ethyl acetate and ethyl trifluoroacetate in carbon tetrachloride (each 0·08M) was submitted to the same procedure. Recoveries of 97% and 96% respectively were observed. It was also shown that acetic and trifluoroacetic acid, the by-products of the reaction, were completely removed by the extraction process. The accuracy of the analysis is estimated at ±5%. The results of the reactions of a number of hydroxy-compounds with acetyl trifluoroacetate alone and in the presence of trifluoroacetic acid, carbon tetrachloride, carbon tetrachloride–trifluoroacetic acid, and sodium trifluoroacetate are given in Table 1.

In the reactions in carbon tetrachloride (columns III and IV), with ethanol, butan-1-ol, and *tert.*-butyl alcohol, some reactions were done with amounts of trifluoroacetic acid below 1·3 mol. The products obtained had the expected compositions, intermediate between those in columns III and IV.

Rates of Reaction of Hydroxy-compounds with Acetyl Trifluoroacetate and with Acetyl Trifluoroacetate–Trifluoroacetic Acid.—A 0·1M-carbon tetrachloride solution (25 c.c.) of the hydroxy-compound was kept in a thermostat at 25° ± 0·1° for 1 hr. before acetyl trifluoroacetate (1·3 mol.) was added with thorough mixing. Samples (*ca.* 2 c.c. each) were withdrawn at noted time intervals during 1 hr., and plunged into sodium hydrogen carbonate solution with vigorous shaking. After separation and drying ($MgSO_4$) the samples were analysed for ester content as before. A similar experiment was carried out in which acetyl trifluoroacetate (1·3 mol.) and trifluoroacetic acid (1·3 mol.) were added. The results, in the form: time of reaction (min.), acetate ester produced (%), trifluoroacetate ester produced (%), respectively in each case, are given below for the reaction of hydroxy-compounds with (A) acetyl trifluoroacetate and (B) acetyl trifluoroacetate–trifluoroacetic acid:

Bu^nOH. (A) 0·5, 4, 64; 1, 5, 74; 3, 6, 86; 6, 6, 89; 17, 6, 89; 60, 6, 90.
(B) 0·5, 3, 58; 1, 6, 68; 2, 8, 75; 4, 9, 78; 8, 9, 85; 15, 9, 90; 60, 9, 90.
Bu^sOH. (A) 0·5, 8, 14; 1, 10, 18; 2, 11, 25; 4, 22, 36; 8, 25, 47; 15, 27, 62; 30, 28, 67; 60, 30, 67.
(B) 0·5, 7, 14; 1, 8, 19; 2, 10, 28; 4, 17, 39; 8, 22, 47; 15, 24, 60; 30, 27, 65; 60, 30, 68.
Bu^tOH. (A) 2, 0, 0; 4, 5, 0; 8, 9, 0; 16, 18, 1; 32, 27, 3; 60, 50, 4.
(B) 2, 7, 0; 4, 13, 0; 8, 18, 0; 16, 30, 1; 32, 54, 2; 60, 70, 4.
$C_6H_5\cdot CH_2\cdot OH$. (A) 1, 12, 32; 2, 14, 48; 4, 18, 62; 6, 18, 70; 8, 18, 71; 15, 18, 78; 29, 18, 80.
(B) 1, 12, 49; 2, 18, 58; 4, 21, 61; 6, 23, 64; 8, 23, 67; 15, 28, 70; 29, 28, 71.
$[CH_2]_5{>}CH\cdot OH$. (A) 1, 15, 20; 2, 19, 23; 4, 23, 33; 9, 30, 49; 15, 32, 51; 30, 33, 56; 45, 34, 61; 58, 35, 64.
(B) 1, 14, 22; 2, 16, 25; 4, 17, 33; 9, 24, 51; 15, 28, 54; 30, 32, 61; 45, 33, 65; 58, 33, 67.
PhOH. (A) 2, 16, 0; 4, 21, 0; 8, 33, 0; 18, 61, 0; 28, 81, 0; 38, 86, 0; 48, 88, 0; 58, 90, 0.
(B) 2, 47, 0; 4, 68, 0; 8, 79, 0; 18, 88, 0; 28, 91, 0; 38, 93, 0; 48, 95, 0; 58, 96, 0.
$CF_3\cdot CH_2\cdot OH$. (A) 1, 14, 0; 2, 18, 0; 4, 30, 0; 8, 45, 0; 15, 57, 0; 30, 75, 0; 45, 84, 0; 60, 91, 0.
(B) 1, 23, 0; 2, 34, 0; 4, 52, 0; 8, 73, 0; 15, 84, 0; 30, 89, 0; 45, 93, 0; 60, 98, 0.
$CF_3\cdot CHMe\cdot OH$. (A) 2, 2, 0; 4, 4, 0; 8, 8, 0; 17, 15, 0; 28, 23, 0; 38, 31, 0; 48, 40, 0; 58, 50, 0.
(B) 2, 12, 0; 4, 21, 0; 8, 29, 0; 17, 50, 0; 28, 60, 0; 38, 67, 0; 48, 73, 0; 58, 79, 0.
$CF_3\cdot CMe_2\cdot OH$. (A) 2, 0, 0; 4, 0, 0; 8, 0, 0; 15, 2, 0; 25, 3, 0; 35, 10, 0; 45, 15, 0; 55, 21, 0.
(B) 2, 3, 0; 4, 6, 0; 8, 14, 0; 15, 26, 0; 25, 39, 0; 35, 51, 0; 45, 63, 0; 55, 67, 0.

The yields in each series after 60 min. are given in Table 1, columns V and VI.

Rates of Reaction of Trifluoroacetic Acid with the Butyl Alcohols.—The butyl alcohols in carbon tetrachloride (0·1M; 25 c.c.) were treated with trifluoroacetic acid (1·3 mol.), and the ester produced determined in the manner described before for the reactions with acetyl trifluoroacetate. With *n*-butyl alcohol, the yields of trifluoroacetate ester after 2·3, 4·0, 6·3, and 8·0 hr., were 25%, 41%, 58%, and 69% respectively. With *sec.*-butyl alcohol they were 6%, 15%, 25%, and 33%, whilst with *tert.*-butyl alcohol no trifluoroacetate was detected even after 4 days.

Reaction of L-1-*Phenylethanol with Acetyl Trifluoroacetate, Acetyl Trifluoroacetate–Trifluoroacetic Acid, and Trifluoroacetic Acid.*—The hydrogen phthalate of DL-1-phenylethanol was resolved with L-brucine according to Houssa and Kenyon's method,[17] and on hydrolysis with 2N-sodium hydroxide afforded L-1-phenylethanol (23%), b. p. 98°/20 mm., n_D^{18} 1·5264, α_D^{19} $-20·45°$ (l 0·5), $[\alpha]_D^{20}$ $-42·8°$ (c 2·48 in EtOH), $[\alpha]_D^{20}$ $-53·5°$ (c 2·58 in $CHCl_3$). Houssa and Kenyon [17] gave b. p. 93°/14 mm., α_{5893}^{20} $-10·94°$ (l 0·25).

Prepared in the same way as the DL-ester, L-1-phenylethyl trifluoroacetate (87%) had b. p. 74°/15 mm., n_D^{19} 1·4328, $\alpha_D^{21·5}$ $-66·15°$ (l 0·5), $[\alpha]_D^{19}$ $-110·0°$ (c 2·20 in $CHCl_3$), $[\alpha]_D^{19}$ $-114·3°$ (c 1·49 in CCl_4) (Found: C, 55·5; H, 4·0; F, 25·8%; equiv., 217. Calc. for $C_{10}H_9O_2F_3$: C, 55·0; H, 4·1; F, 26·1%; equiv. 218). Hydrolysis of the L-trifluoroacetate afforded L-1-phenylethanol (82%), b. p. 95—96°/15 mm., $n_D^{18·5}$ 1·5233, α_D^{16} $-20·35°$ (l 0·5), $[\alpha]_D^{19}$ $-42·4°$ (c 2·31 in EtOH), $[\alpha]_D^{19}$ $-53·1°$ (c 2·41 in $CHCl_3$).

Acetylation of the L-alcohol with acetic anhydride and pyridine afforded L-1-phenylethyl acetate (70%), b. p. 99°/18 mm., n_D^{20} 1·4923, α_D^{20} $-58·23°$ (l 0·5), $[\alpha]_D^{21}$ $-105·2°$ (c 3·84 in EtOH), $[\alpha]_D^{21}$ $-104·7°$ (c 4·26 in $CHCl_3$) (Found: C, 73·1; H, 7·3%; equiv., 166. Calc. for $C_{10}H_{12}O_2$: C, 73·1; H, 7·4%; equiv., 164). Hydrolysis gave L-1-phenylethanol (86%), b. p. 96°/18 mm., $n_D^{18·5}$ 1·5239, α_D^{22} $-20·14°$ (l 0·5), $[\alpha]_D^{22}$ $-42·2°$ (c 2·18 in EtOH), $[\alpha]_D^{22}$ $-53·1°$ (c 3·84 in $CHCl_3$). Cited values [18] for the DL-acetate were b. p. 88°/10 mm., n_D^{18} 1·5003.

The acetate and trifluoroacetate were separable chromatographically on carefully neutralised aluminium oxide. Neutralisation of the aluminium oxide was effected by heating it under reflux for 30 min., first with a 20% solution of ethyl formate in light petroleum (b. p. 60—80°) and then with a 2% solution of ethyl trifluoroacetate in the same solvent. The oxide was filtered and dried before use. In a trial separation a mixture of the esters (0·5 g. each) in light petroleum (5 c.c.) was put on to a column of neutralised aluminium oxide (100 g.; 33 × 2·5 cm.) which was then eluted with light petroleum (b. p. 60—80°). The trifluoroacetate ester in the eluate was identified by its absorption band at 1786 $cm.^{-1}$ and when this had been removed completely from the column, the acetate was eluted with ether. The esters were isolated by distillation and recoveries of 70% and 87% respectively were obtained.

The experimental details of the reactions of L-1-phenylethanol with acetyl trifluoroacetate, acetyl trifluoroacetate–trifluoroacetic acid, and trifluoroacetic acid are given in Table 2, as are control experiments in which the L-acetate and the L-trifluoroacetate esters were treated with the same reactants. The changes in optical rotations of the reaction mixtures with time were observed. If, after the requisite period, the reaction mixture could have contained only one ester (as when the L-alcohol and the L-trifluoroacetate were treated with trifluoroacetic acid) it was dissolved in ether and the solution was washed with dilute sodium hydrogen carbonate solution. After drying ($MgSO_4$), the organic phase was filtered and distilled under reduced pressure, to give the required ester which was examined polarimetrically. If the reaction mixture could have contained both acetate and trifluoroacetate esters, a small portion, sufficient to give a total ester concentration of 0·1M, was withdrawn, diluted to 2 c.c. with carbon tetrachloride, and analysed by infrared spectroscopy for ester content as previously described. The remainder of the reaction mixture was dissolved in ether and washed with dilute sodium hydrogen carbonate solution, dried ($MgSO_4$), filtered, and evaporated to give a mixture of esters which was separated on a column of neutralised aluminium oxide (100 g.; 33 × 2·5 cm.) as described above. The optical activities were then determined. In some cases, the esters were hydrolysed and the properties of the alcohols also measured.

When the L-acetate and L-trifluoroacetate were treated with acetic acid or acetic anhydride there was no change either in the composition or in the optical activity.

Reactions of Benzoyl and of Phenylacetyl Trifluoroacetate with Hydroxy-compounds.—The results are recorded in Tables 3 and 4 for the reactions of a number of hydroxy-compounds with benzoyl and with phenylacetyl trifluoroacetate, which were carried out in the same way as with acetyl trifluoroacetate.

Rates of Reaction of Hydroxy-compounds with Benzoyl Trifluoroacetate and with Benzoyl Trifluoroacetate–Trifluoroacetic Acid.—These were carried out as for acetyl trifluoroacetate. Results are given for time of reaction (min.), benzoate ester produced (%), trifluoroacetate

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[17] Houssa and Kenyon, *J.*, 1930, 2260.

[18] Olsson, *Z. phys. Chem.*, 1928, **133**, 293.

ester produced (%), respectively, for the reaction of each hydroxy-compound with (A) benzoyl trifluoroacetate and (B) benzoyl trifluoroacetate–trifluoroacetic acid.

Bu^{n}OH. (A) 1, 0, 93, 2, 0, 99; 15, 0, 99.
(B) 1, 0, 93; 2, 0, 100; 15, 0, 100.
PhOH. (A) 2, 0, 39; 4, 0, 42; 8, 0, 44; 15, 1, 53; 30, 3, 57; 45, 3, 61; 60, 3, 67.
(B) 2, 0, 14; 4, 1, 15; 8, 3, 18; 15, 4, 18; 30, 7, 26; 45, 7, 31; 60, 8, 36.

Anhydride Systems involving Acetyl Heptafluorobutyrate.—(a) *Acetyl heptafluorobutyrate from acetic anhydride–heptafluorobutyric anhydride.* An infrared spectroscopic analysis of this system was impossible over the frequency range 1000—1250 cm.$^{-1}$ because of the close proximity of absorption bands of acetic anhydride (1121 cm.$^{-1}$), heptafluorobutyric anhydride (1134 cm.$^{-1}$), and acetyl heptafluorobutyrate (1126 cm.$^{-1}$). The analysis was possible however in carbon tetrachloride (*ca.* 0·1M in a cell of thickness *ca.* 0·1 mm.) over the frequency range 1700—1900 cm.$^{-1}$. The absorption bands of heptafluorobutyric anhydride (1799 and 1864 cm.$^{-1}$) and of acetic anhydride (1761 and 1829 cm.$^{-1}$) were entirely absent from the spectrum of an equimolecular mixture of acetic and heptafluorobutyric anhydrides which had been warmed at 40° for 15 min., and were replaced by bands (1780 and 1853 cm.$^{-1}$) which were characteristic of acetyl heptafluorobutyrate.

(b) *Equilibria in the systems acetyl trifluoroacetate–heptafluorobutyric acid and acetyl heptafluorobutyrate–trifluoroacetic acid.* The infrared analysis of these systems was carried out in carbon tetrachloride (*ca.* 0·05M) over the frequency range 1000—1250 cm.$^{-1}$ by using the bands at 1072 cm.$^{-1}$ and 1126 cm.$^{-1}$ for the analysis of acetyl trifluoroacetate and acetyl heptafluorobutyrate respectively. The calculated optical densities (M in a cell of thickness *ca.* 0·1 mm.) of the appropriate solutions were then used to estimate by comparison the proportion of each of these unsymmetrical anhydrides in mixtures of acetyl trifluoroacetate–heptafluorobutyric acid, and acetyl heptafluorobutyrate–trifluoroacetic acid. Heptafluorobutyric acid showed a weak absorption band (1125 cm.$^{-1}$) which interfered with the estimation of acetyl heptafluorobutyrate (1126 cm.$^{-1}$), and the latter absorbed weakly over the range 1063—1085 cm.$^{-1}$ which interfered with the estimation of acetyl trifluoroacetate. Allowance was made for these absorptions when estimating the proportions of the unsymmetrical anhydride compounds. The results are recorded in Table 7; the accuracy of the method is estimated as ±10%.

TABLE 7. *Infrared spectroscopic analysis of the system*

$$\text{AcO·CO·CF}_3 + \text{C}_3\text{F}_7\text{·CO}_2\text{H} \rightleftharpoons \text{AcO·CO·C}_3\text{F}_7 + \text{CF}_3\text{·CO}_2\text{H}$$

Original components (mol.)				Components measured	
AcO·CO·CF$_3$	C$_3$F$_7$·CO$_2$H	AcO·CO·C$_3$F$_7$	CF$_3$·CO$_2$H	AcO·CO·CF$_3$ (1072 cm.$^{-1}$)	AcO·CO·C$_3$F$_7$ (1126 cm.$^{-1}$)
1·0	0·5	—	—	0·7	0·3
1·0	1·0	—	—	0·55	0·45
1·0	2·0	—	—	0·3	0·7
—	—	1·0	0·5	0·3	0·7
—	—	1·0	1·0	0·5	0·5
—	—	1·0	2·0	0·65	0·35

(c) *Reaction of acetyl trifluoroacetate–heptafluorobutyric acid with phenetole.* A mixture of phenetole (0·483 g.), acetyl trifluoroacetate (0·925 g.), and heptafluorobutyric acid (1·24 g.) was kept at 20° for 3 hr. After dilution of the solution with water (1 c.c.), and neutralisation with sodium hydroxide, *p*-ethoxyacetophenone was isolated as its semicarbazone (78%); m. p. and mixed m. p. 182°.

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