612. *Acyl Trifluoroacetates. Part I. The Reaction of Acetyl Trifluoroacetate with Phenols in Carbon Tetrachloride.*

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Acetyl trifluoroacetate reacts with phenols in carbon tetrachloride to give exclusively the phenyl acetates. The reaction does not appear to proceed through acetylium ions even when catalysed by trifluoroacetic acid. The rate constants for different phenols satisfy the Hammett equation with a ρ value of $-0{\cdot}82$. Very rapid and exclusive formation of the phenyl trifluoroacetates occurs when the solutions of acetyl trifluoroacetate (in large excess) and the phenol are mixed and immediately treated with saturated potassium hydrogen carbonate solution.

ACETYL TRIFLUOROACETATE can react with hydroxy-compounds to form the acetate and the trifluoroacetate esters. It has been established [1] that alcohols in carbon tetrachloride normally give a mixture of the esters but that phenol and certain trifluoro-alcohols form only the acetates. Interpretation of these results was based on the suggestion that the mixed anhydride acts as the trifluoroacetylating agent but that it can undergo heterolysis to acetylium ions $CH_3{\cdot}CO^+$ which are responsible for acetylation. Phenol and alcohols of similar acidity are less nucleophilic than simple alcohols and were consequently assumed to be reactive only to acetylium ions.

The present work reports kinetic studies on the reaction with various phenols in carbon tetrachloride, with the main study centred on *p*-chlorophenol.

Acetyl trifluoroacetate has been obtained in various ways,[2] but we have found that only reaction of the simple anhydrides in carbon tetrachloride gave a satisfactory product.

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[1] Bourne, Stacey, Tatlow, and Worrall, *J.*, 1958, 3268.
[2] Bourne, Stacey, Tatlow, and Worrall, *J.*, 1954, 2006.

EXPERIMENTAL

Materials.—" AnalaR " carbon tetrachloride was either redistilled from phosphoric oxide or dried over a molecular sieve. Trifluoroacetic acid, b. p. 72—74°, and " AnalaR " acetic anhydride, b. p. 139—140°, were both redistilled. " AnalaR " phenol was used directly. The following phenols were redistilled and collected at the b. p.s indicated: *p*-chlorophenol, 218°; *m*-chlorophenol, 214°; *p*-cresol, 201—202°; *m*-cresol, 200°; *m*-methoxyphenol, 240—244°. *p*-Methoxyphenol, m. p. 54—55°, was recrystallised from water.

Trifluoroacetic anhydride was prepared by distillation of a mixture of trifluoroacetic acid and phosphoric oxide,[3] followed by redistillation of the product from fresh phosphoric oxide; it had b. p. 38—39°.

Acetyl trifluoroacetate was always obtained by mixing equimolecular amounts of acetic and trifluoroacetic anhydride in carbon tetrachloride. The progress of the reaction was followed by infrared spectroscopic analysis in the regions 1700—1900 and 1000—1200 cm.$^{-1}$; in the former region, the acetic anhydride carbonyl absorption bands at 1760 and 1820 cm.$^{-1}$ and the analogous trifluoroacetic anhydride bands at 1800 and 1860 cm.$^{-1}$ were gradually replaced by bands at 1780 and 1850 cm.$^{-1}$ due to acetyl trifluoroacetate; in the latter region, the bands at 1120 cm.$^{-1}$ (acetic anhydride) and at 1040 cm.$^{-1}$ (trifluoroacetic anhydride) were gradually replaced by a band at 1080 cm.$^{-1}$ (acetyl trifluoroacetate).

Acetate esters of the phenols prepared by shaking acetic anhydride with an ice-cold solution of the phenol in aqueous sodium hydroxide are listed with their b. p.s: phenyl, 192—194°; *p*-chlorophenyl, 228—230°; *m*-chlorophenyl, 226—227°; *p*-tolyl, 212—214°; *m*-tolyl, 212—214°. Other esters made by refluxing the phenol with acetic anhydride and a little sulphuric acid were *m*- (b. p. 250—254°) and *p*-methoxyphenyl (crystallised from ether), m. p. 31°.

p-*Chlorophenyl trifluoroacetate* was obtained by refluxing the phenol with trifluoroacetic anhydride and sodium trifluoroacetate. Direct fractionation gave the trifluoroacetate, b. p. 181—182° (Found: C, 42·4; H, 1·9; F, 25·8; Cl, 16·1. $C_8H_4ClF_3O_2$ requires C, 42·8; H, 1·8; F, 25·4; Cl, 15·8%).

Infrared Spectroscopic Analysis.—All infrared spectra were measured with a Perkin-Elmer Infracord instrument. The esters formed during a reaction were identified by their spectra and determined by the optical density of their carbonyl absorption bands.[1] Optical densities for molar solutions of the acetate esters in a 1 mm. cell are: Phenyl, 50; *p*-chlorophenyl, 54; *m*-chlorophenyl, 55; *p*-tolyl, 52; *m*-tolyl, 49; *p*-methoxyphenyl, 51; *m*-methoxyphenyl, 47.

For most of the kinetic work on *p*-chlorophenol the Infracord spectrophotometer was calibrated by using mixed solutions of known concentrations of the acetate and trifluoroacetate esters to a total molarity of 0·01. A calibration curve for each ester was constructed from the results of analysis of the mixed solutions.

Kinetic Measurements.—Reactions were carried out at 25° ± 0·05°. The phenol solution (0·01M) in carbon tetrachloride (2 ml.) was run into the solution of acetyl trifluoroacetate in the same solvent (20 ml.) to start reaction. Samples (*ca.* 2 ml.) were removed at fixed time intervals and immediately shaken with saturated aqueous potassium hydrogen carbonate solution (*ca.* 5 ml.). The organic layer was separated and dried ($MgSO_4$) and its spectrum recorded in the carbonyl absorption region. In all kinetic runs reported here the rate of formation of acetate ester was of the first order in the phenol. Results of a typical run are given in the Table, at the initial concentrations indicated. The significance of the trifluoroacetate and total ester molarities is discussed below.

Reaction of acetyl trifluoroacetate (0·228M) and *p*-chlorophenol (0·0097M) at 25°.

Time (sec.)	415	535	665	840	1080	1320	1560	1800	24 hr.
Acetate (10^4M)	25	34	40	47	58	65	72	75	91
Trifluoroacetate (10^4M)	67	61	52	44	35	31	25	19	3
Total esters (10^4M)	92	95	92	91	93	96	97	94	94
10^4k (sec.$^{-1}$)	7·1	8·1	8·1	7·8	8·5	8·3	8·7	8·3	—

Mean value of k = 8·1 × 10^{-4} sec.$^{-1}$.

RESULTS

The aliquot portion of the reaction solution removed immediately after mixing the solutions of *p*-chlorophenol and acetyl trifluoroacetate indicated, on analysis, that the only ester present

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

was the trifluoroacetate in almost quantitative yield. Subsequent portions were found, on analysis, to contain increasing amounts of the acetate ester with correspondingly diminished amounts of trifluoroacetate. The final result was an almost quantitative yield of acetate with the virtual absence of trifluoroacetate.

Earlier studies have established that phenyl trifluoroacetate is not converted into phenyl acetate by acetyl trifluoroacetate under the conditions of these kinetic measurements. The action of potassium hydrogen carbonate was therefore suspected and it was discovered that, on omission of the carbonate and shaking with water only, no trifluoroacetate ester could be detected in the products at any stage of the reaction. Since it was not possible to remove completely the acids and anhydride from samples by using water alone, the carbonate treatment was necessary, but in calculating rate constants the trifluoroacetate formation was ignored.

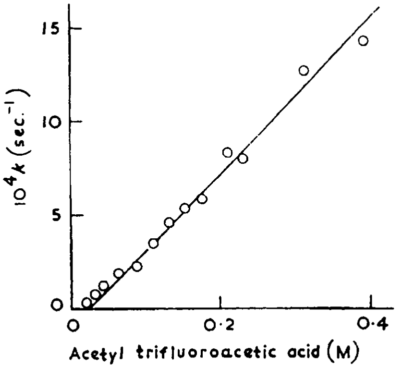

FIG. 1. Variation of rate constant (k) with initial acetyl trifluoroacetate concentration.

Three series of runs were carried out, all in carbon tetrachloride. In the first, *p*-chlorophenol (0·01M) was treated with an excess of acetyl trifluoroacetate (0·02—0·40M). The results of these runs were calculated by using the calibration curve for the acetate and trifluroacetate obtained from the mixed solutions. In all cases the reactions were of the first order in *p*-chlorophenol. The variations of the rate constant with the initial molarity is given in Fig. 1.

In the second series, *p*-chlorophenol (0·01M), acetyl trifluoroacetate (0·086M), and concentrations of trifluoroacetic acid up to 0·09M were used. The results were calculated as for the first series and the reactions were again of the first order in *p*-chlorophenol. Variation of the rate constant with initial trifluoroacetic acid molarity is shown in Fig. 2.

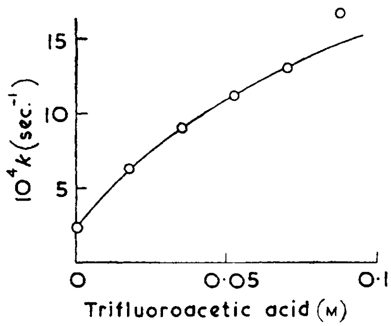

FIG. 2. Variation of rate constant (k) with trifluoroacetic acid molarity.

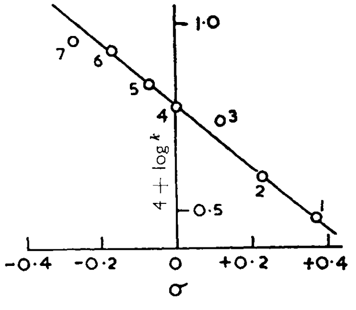

FIG. 3. Variation of rate constant (k) with Hammett σ value. 1, *m*-Cl. 2, *p*-Cl. 3, *m*-MeO. 4, H. 5, *m*-Me. 6, *p*-Me. 7, *p*-MeO.

In the third series of runs, acetyl trifluoroacetate (0·093M) was treated separately with seven different *meta*- or *para*-substituted phenols (0·01M). In this series the concentration of acetate in the samples was calculated from the optical density of the acetate alone in carbon tetrachloride solution. This method is less accurate than that used in the other series. Since the same method was used for all the phenols and only a comparison between them was required it was thought permissible to use it. All the reactions were of the first order in phenol. The rate constant is plotted against the Hammett σ constant for each phenol in Fig. 3. The substituent constants used are those given by Hine [4] and are derived from the ionisation of benzoic acids.

DISCUSSION

The reaction of acetyl trifluoroacetate with each of the phenols used produces only the acetate ester, as previously reported for phenol itself.[1] All the reactions are of the first order in phenol and therefore, at least for an initial phenol concentration of 0·01M, the rate step must involve the phenol. This suggests that the reaction is a direct attack of the phenol on the anhydride:

$$ArOH + CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \longrightarrow ArO{\cdot}CO{\cdot}CH_3 + CF_3{\cdot}CO_2H$$

The trifluoroacetic acid produced in the reaction must have a catalytic effect (see Fig. 2 and later discussion), but its magnitude is difficult to assess and, in fact, no significant increase was observed in the rate constants during any of the kinetic runs reported here.

The dependence of the rate constant of the *p*-chlorophenol reaction on the initial acetyl trifluoroacetate molarity shown in Fig. 1 is linear over nearly the whole range studied. This is in agreement with the suggested mechanism. The fact that the line does not pass through the origin is partly due to the use of initial as opposed to average anhydride molarities. Most of this displacement, however, cannot yet be explained.

Fig. 3 shows that the reaction obeys the Hammett equation. Thus the same mechanism is followed by all the phenols. The value of the reaction constant, ρ, is $-0{\cdot}82$, the sign of which is in accord with a nucleophilic attack of the phenol on the anhydride.

If the reaction with the phenol was preceded by ionisation of the anhydride, as shown in (1) and (2), reaction (2) almost certainly would be very rapid and reaction (1) would be the rate-determining step. In this case the rate of reaction would not depend on the phenol concentration. Ionisation (1) is hardly likely to be important in carbon tetrachloride and the main evidence for such an ionisation [5] relates to the very different system acetic anhydride–trifluoroacetic anhydride–water.

$$CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3 \longrightarrow CH_3{\cdot}CO^+ + CF_3{\cdot}CO_2^- \qquad (1)$$

$$CH_3{\cdot}CO^+ + ArOH \longrightarrow ArO{\cdot}CO{\cdot}CH_3 + H^+ \qquad (2)$$

If reaction does occur through the undissociated anhydride we have to account for the formation of the phenyl acetates. Two opposing effects must be considered in the reaction of the anhydride with a nucleophile.[6] The electronic effect of the fluorine atoms will make the carbonyl-carbon atom adjacent to the trifluoromethyl group more reactive than that of the other carbonyl group. The greater size of the trifluoromethyl group, however, will restrict reaction at this point. The extent to which the anhydride is acetylating or trifluoroacetylating depends on the balance between these effects. From our results it appears that in the reaction with phenols the steric effect predominates, and consequently acetylation alone occurs. A similar conclusion has been reached regarding the reaction of acetyl trichloroacetate and aniline.[6]

Since alcohols are more powerful nucleophiles than phenols they will react more easily with the anhydride, and this increase in reactivity may overcome the steric effect of the trifluoromethyl group. However, a general increase in reactivity would not necessarily change the product composition. The results suggest rather that there is less steric hindrance offered by the alcohols and that a partial shift of the point of attack from the acetyl to the trifluoroacetyl carbonyl group occurs, *i.e.*, for alcohols the electronic effect increases in importance relative to the steric effect. This shift to trifluoroacetylation

[4] Hine, " Physical Organic Chemistry," McGraw-Hill, New York, 1956, p. 72.

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

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

decreases in the order, butan-1-ol, butan-2-ol, t-butyl alcohol, in accordance with decreased accessibility of the hydroxyl group.[1]

The formation of the phenyl trifluoroacetates on treating the reactant solutions with aqueous alkali hydrogen carbonate may be relevant to this interpretation. The order of increasing nucleophilicity will be: phenol, alcohol, phenoxide anions. Phenoxides would be expected to react very rapidly with the anhydride and, since they are more nucleophilic than alcohols, to give even more trifluoroacetate. As the reaction occurring on shaking with aqueous carbonate is rapid and yields only trifluoroacetate it may proceed entirely through the phenoxide anion.

We have as yet no satisfactory explanation of the catalysis by trifluoroacetic acid shown in Fig. 2. Since we have detected no ionisation of the anhydride the suggestion that trifluoroacetic acid aids this ionisation and hence speeds up the reaction cannot apply here. It is significant that this acid has little or no catalytic effect with simple alcohols and does not affect the ratio of ester products obtained.[1] Catalysis appears to require a more acidic hydroxyl group which through a hydrogen-bonded complex with the acid might achieve an enhanced reactivity towards the acylating agent.

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