359. *The Mechanism of Sulphoacetic Acid Formation in the System* H_2SO_4–Ac_2O–AcOH.

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It is shown that the rate of formation of sulphoacetic acid from sulphuric acid and acetic anhydride, in an excess of acetic acid as solvent, is of the first-order in the free sulphate concentration, and displays the same, somewhat complex kinetic dependence on anhydride concentration as does acetylation of hydroxylic compounds in the same system. The two reactions, therefore, probably involve common intermediates. This conclusion is made the basis of a discussion of the mechanism of sulphoacetic acid formation.

The formation of sulphoacetic acid, from mixtures of sulphuric acid and acetic anhydride, has long been known.[1] It has usually been reported when the reagents have been heated together in equivalent quantities. When an excess of anhydride is used a somewhat less

$$Ac_2O + H_2SO_4 \longrightarrow HO_3S{\cdot}CH_2{\cdot}CO_2H + AcOH$$

well-defined species, considered to be the acetyl derivative of sulphoacetic acid, possibly of structure $AcO{\cdot}SO_2{\cdot}CH_2{\cdot}CO_2H$, is formed to some extent.[1-3] However, there is little doubt about the formation or structure of sulphoacetic acid itself. Indeed the free acid and its derivatives have been prepared [4] by reaction of monochloroacetic acid and sodium sulphite. This route clearly supports the formulation above. The dissociation constant of the free acid, and the solubility of its salts, have also been studied.[5]

$$Na_2SO_3 + CH_2Cl{\cdot}CO_2H \longrightarrow NaO{\cdot}SO_2{\cdot}CH_2{\cdot}CO_2H + NaCl$$

A solution of sulphoacetic acid in acetic acid may be prepared by allowing equivalent quantities of acetic anhydride and sulphuric acid to react in this solvent until a negligible amount of free sulphate remains.[3] The kinetics of this reaction have been studied once previously, by Murray and Kenyon.[6] Their sulphuric acid, and particularly their anhydride, concentrations were large, and their variations of the latter must have changed the nature of the reaction medium considerably. This fact makes conclusions drawn from their observed reaction order for anhydride equivocal. They found the loss of free sulphate to be a first-order process.

Murray and Kenyon also studied the corresponding propionic and butyric systems. Their general conclusions were effectively that the acyl hydrogen sulphate is formed in a rapid pre-equilibrium and then undergoes slow, unimolecular rearrangement to give the product; *e.g.*, for acetic anhydride:

$$Ac_2O + H_2SO_4 \rightleftharpoons AcHSO_4 + AcOH \qquad \text{Fast}$$

$$AcHSO_4 \longrightarrow HO_3S{\cdot}CH_2{\cdot}CO_2H \qquad \text{Slow}$$

However, as noted, these conclusions are to be treated with reserve. This is especially so because, as shown in a preceding paper,[3b] the kinetics of the acylation of phenols by anhydrides in carboxylic acid solvents seem best interpreted by using the assumption that two active intermediates ($AcHSO_4$ and Ac_2SO_4) are formed from the anhydride and sulphuric acid. Thus at the outset of this study there were three possibilities for the mechanism of sulphoacetic acid formation. (*a*) It could proceed *via* $AcHSO_4$ only, as suggested by Murray and Kenyon (*i.e.*, not *via* Ac_2SO_4). If so, the kinetic form would be

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[1] See, *e.g.*, Franchimont, *Rec. Trav. chim.*, 1888, **7**, 27.

[2] Dommoni, U.S.P. 2,411,823.

[3] Jeffery and Satchell, *J.*, 1962, (*a*) 1876, (*b*) 1887.

[4] Stillich, *Ber.*, 1905, **83**, 1241; Collmann, *Annalen*, 1867, **148**, 109.

[5] Smith and Elliott, *J. Amer. Chem. Soc.*, 1953, **75**, 3566; Banks and Zimmerman, *J. Org. Chem.*, 1956, **21**, 1439; Backer, *Z. phys. Chem.*, 1927, **130**, 177.

[6] Murray and Kenyon, *J. Amer. Chem. Soc.*, 1940, **62**, 1230.

different from that found for acylation. (*b*) It could proceed *via* both $AcHSO_4$ and Ac_2SO_4. In this case the kinetics could possibly be of similar pattern to those of acylation. (*c*) It could proceed by quite other intermediates, the kinetics then probably differing in detail from those for acylation.

We have studied the reaction under kinetically more satisfactory conditions than did Murray and Kenyon.[6] Rather small concentrations of sulphuric acid and acetic anhydride were used to minimise medium effects. In view of the form of the results, we have also compared the rate of formation of sulphoacetic acid with the rate of acetylation of *m*-nitrophenol at the same temperature and under similar conditions.

Fortunately acetylation and the concurrent sulphoacetic acid formation may be made to proceed at markedly different rates. The acid formation proves to be of the first order in sulphuric acid (see below), and the reaction half-life is therefore independent of the initial sulphate concentration. The half-life for acetylation is, however, inversely proportional to the catalyst concentration.[3b] Thus for the latter reaction we chose a sulphuric acid concentration high enough to ensure that the loss of catalyst during the runs would be negligible. For sulphoacetic acid formation the restrictions on the sulphuric acid concentration were (*a*) that it should be small compared with the anhydride concentration, thus leaving the latter unaffected during a run, and so keeping the kinetic form as simple as possible, and (*b*) that it should, in principle, be as small as possible so that its change in concentration during a run would not constitute a large medium effect.

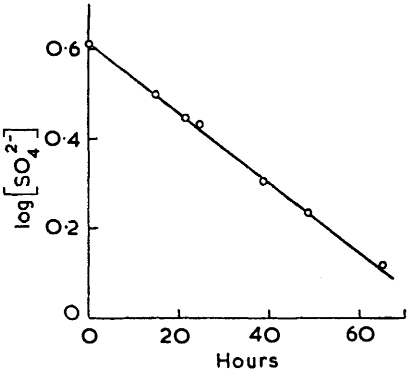

FIG. 1. First-order loss of free sulphate.

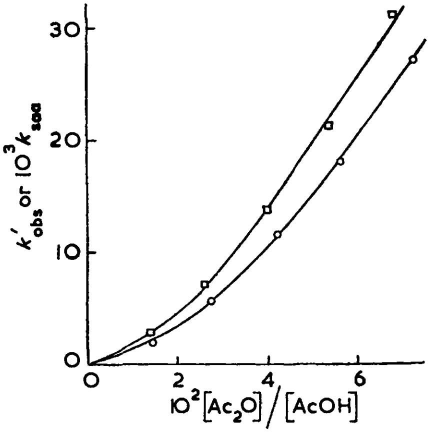

FIG. 2. Dependence on ^{f} $[Ac_2O]$ for acylation (○) and for formation of sulphoacetic acid (□).

Reaction Orders and Mechanism.—Experiments concerning reaction orders for sulphoacetic acid formation showed (Table 1, Figs. 1 and 2) it to be of the first order in the loss of sulphuric acid and dependent on the anhydride concentration to a power greater than unity. The observed order in sulphuric acid agrees with Murray and Kenyon's findings,[6]

TABLE 1.

The rate of formation of sulphoacetic acid at 50°.

k_{saa} = First-order rate constant, in min.$^{-1}$; square brackets represent concentrations (M) in both Tables.

$10^2[Ac_2O]/[AcOH]$ * ...	1·49	2·77	4·20	5·63	7·23	1·42
$10^2[H_2SO_4]$	5·0	5·0	5·0	5·0	5·0	2·5
10^3k_{saa}	1·80	5·75	11·5	17·95	27·6	1·96

* [AcOH] does not vary by more than *ca.* 5% throughout the experiments.

and implies that only one molecule of this compound is concerned in the slow step of the reaction. The non-integral order in acetic anhydride is reminiscent of that found in sulphuric acid-catalysed acetylation.[3b] We therefore re-measured some acetylation rates at the higher temperature of 50° (which is more convenient for the slower sulphoacetic acid formation) over the range of anhydride concentrations used for the sulphoacetic acid reaction, and at constant catalyst concentration. The results are in Table 2 and are plotted together with those for sulphoacetic acid formation in Fig. 2. To discover whether the curves were of mathematically similar form for the two reactions, the respective values of k_{saa} and k'_{obs},* corresponding to various given anhydride concentrations, were obtained from Fig. 2. They are plotted against each other in Fig. 3. The good straight line produced implies that the dependence on acetic anhydride is of essentially identical form for the sulphoacetic and acetylation reactions and presumably has the same explanation for both. Since for the latter we reject one based on medium effects,[3b] we must do so also for the former, and must suggest instead a common mechanism for both reactions in which the anhydride provides the same intermediates, playing similar *kinetic* roles. [Thus alternative (*b*) on p. 1914 probably operates.] Such a mechanism could be as follows:

TABLE 2.

Acetylation of *m*-nitrophenol by acetic anhydride catalysed by sulphuric acid at 50°.

$k_{obs}' = k_{obs}/[H_2SO_4]$, where $k_{obs} = -d[ArOH]/dt$.

$10^2[Ac_2O]/[AcOH]$ *	1·43	2·64	4·01	5·37	6·90
$10^2[H_2SO_4]$	0·210	0·206	0·202	0·198	0·193
k'_{obs}	2·86	6·99	13·8	21·1	31·1

* See Table 1.

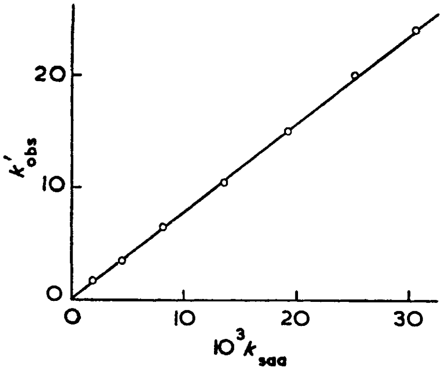

FIG. 3. Rates of formation of sulphoacetic acid (k_{saa}) and acylation (k'_{obs}) at chosen concentrations of acetic anhydride.

$$Ac_2O + H_2SO_4 \rightleftharpoons Ac_2OH^+HSO_4^- \qquad \text{Fast}$$

$$2Ac_2O + H_2SO_4 \rightleftharpoons (Ac_2OH^+)_2SO_4^{2-} \qquad \text{Fast}$$

$$Ac_2OH^+HSO_4^- \left\{ \begin{array}{l} \xrightarrow{ArOH} ArO{\cdot}COMe + AcOH + H_2SO_4 \\ \longrightarrow HO_3S{\cdot}CH_2{\cdot}CO_2H + AcOH \end{array} \right. \qquad \text{Slow}$$

$$(Ac_2OH^+)_2SO_4^{2-} \left\{ \begin{array}{l} \xrightarrow{ArOH} ArO{\cdot}COMe + AcOH + Ac_2O + H_2SO_4 \\ \longrightarrow HO_3S{\cdot}CH_2{\cdot}CO_2H + Ac_2O + AcOH \end{array} \right. \qquad \text{Slow}$$

Left like this, the slow steps beg several questions. The necessary rearrangement of the protonated species, if indeed they exist to any extent,[3b] seems likely to proceed through

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* For definitions see Tables.

subsequent and simpler intermediates. This was one of our reasons for rejecting a scheme such as that above for the acetylation.[3b]

Our preferred scheme for acetylation (see p. 1913) involves the acyl sulphates, and sulphoacetic acid formation is therefore now assumed to involve them also, as in the following scheme:

$$\begin{array}{rclll} \mathrm{Ac_2O + H_2SO_4} & \rightleftharpoons & \mathrm{AcHSO_4 + AcOH} & K_1 & \text{Fast (1)} \\ \mathrm{2Ac_2O + H_2SO_4} & \rightleftharpoons & \mathrm{Ac_2SO_4 + 2AcOH} & K_2 & \text{Fast (2)} \\ \mathrm{AcHSO_4} & \longrightarrow & \mathrm{HO_3S{\cdot}CH_2{\cdot}CO_2H} & k_3 & \text{Slow (3)} \\ \mathrm{Ac_2SO_4} & \longrightarrow & \mathrm{AcO{\cdot}SO_2{\cdot}CH_2{\cdot}CO_2H} & k_4 & \text{Slow (4)} \\ \mathrm{AcO{\cdot}SO_2{\cdot}CH_2{\cdot}CO_2H + AcOH} & \rightleftharpoons & \mathrm{Ac_2O + HO_3S{\cdot}CH_2{\cdot}CO_2H} & & \text{Fast (5)} \end{array}$$

The product, in view of the excess of anhydride used, will partly exist as acetylsulphoacetic acid though, as previously shown,[3b] equilibrium (5) probably lies well to the right. From equations (1)—(4), in which k represents a rate constant and K an equilibrium constant, the rate of loss of total free sulphate (C) may be seen to be (square brackets representing concentration):

$$-\mathrm{d[C]/d}t = k_3[\mathrm{AcHSO_4}] + k_4[\mathrm{Ac_2SO_4}],$$

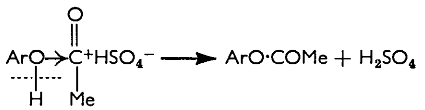
or

$$-\mathrm{d[C]/d}t = (k_3K_1 + k_4K_2A)A[\mathrm{C}]/(1 + K_1A),$$

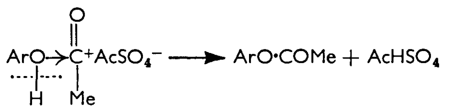
where $A = [\mathrm{Ac_2O}]/[\mathrm{AcOH}]$, and equilibrium (2) has been assumed (as for acetylation) to lie well to the left. Hence

$$-\mathrm{d}\ \ln\,[\mathrm{C}]/\mathrm{d}t = (k_3K_1 + k_4K_2A)A/(1 + K_1A). \quad . \quad . \quad . \quad . \quad (6)$$

This expression predicts the first-order loss of free sulphate and a formal dependence on A similar to that found for acetylation.[3b] This is a required result. However, the linearity of Fig. 3 implies something more, namely, that the values of the two terms in the numerator of equation (6) have effectively the same ratio for both acetylation and sulphoacetic acid formation, or, since K_1 and K_2 apply to equilibria common to the two reactions, that the relative reactivities of the two intermediates are the same in both reactions. This simple conclusion is remarkable in that the substrate phenol is involved in the slow step for acetylation, yet no similar species, and therefore no exactly similar process, can be involved for the slow step in sulphoacetic acid formation. In view of this conclusion it seems sensible to choose slow processes for the two reactions as similar as possible. On the basis of the intermediates that we favour, this seems easiest if it is assumed that the ionised forms ($\mathrm{Ac^+HSO_4^-}$ and $\mathrm{Ac^+AcSO_4^-}$) of the acyl derivatives are involved (these will be in equilibrium with the un-ionised forms). Then for acetylation we may have attack by oxygen on the positive centre:

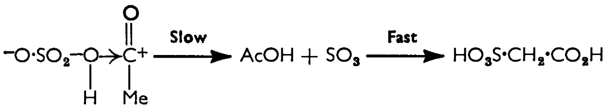


$$\underset{\mathrm{H}}{\mathrm{ArO}}{\rightarrow}\underset{\mathrm{Me}}{\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}}{}^{+}\mathrm{HSO_4^-} \longrightarrow \mathrm{ArO{\cdot}COMe + H_2SO_4} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

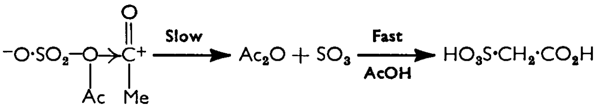


$$\underset{\mathrm{H}}{\mathrm{ArO}}{\rightarrow}\underset{\mathrm{Me}}{\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}}{}^{+}\mathrm{AcSO_4^-} \longrightarrow \mathrm{ArO{\cdot}COMe + AcHSO_4} \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and for the rearrangement a somewhat similar process involving the gegen-ion and producing sulphur trioxide, followed by the fast attack of sulphur trioxide on acetic acid, a process which we have previously[3b] suggested, on other grounds, produces sulphoacetic acid rapidly even at low temperatures:



$$^{-}O\cdot SO_2{-}\underset{\mid\atop H}{O}{\rightarrow}\overset{O\atop \|}{\underset{\mid\atop Me}{C^+}} \xrightarrow{\text{Slow}} AcOH + SO_3 \xrightarrow{\text{Fast}} HO_3S\cdot CH_2\cdot CO_2H \quad . \; . \; . \; . \; . \; (9)$$



$$^{-}O\cdot SO_2{-}\underset{\mid\atop Ac}{O}{\rightarrow}\overset{O\atop \|}{\underset{\mid\atop Me}{C^+}} \xrightarrow{\text{Slow}} Ac_2O + SO_3 \xrightarrow[\text{AcOH}]{\text{Fast}} HO_3S\cdot CH_2\cdot CO_2H \quad . \; . \; . \; . \; . \; (10)$$

It seems possible that the relative rates of the pairs of processes (7)–(8) and (9)–(10) could be dominated by the relative availabilities of Ac^+, which would be the same for each pair. Further speculation about the rearrangement seems unjustified.

It should be noted that the above conclusions about the relative reactivities of the intermediates is simply the form taken, in our explanation, to explain the result that the same complex order in anhydride is found for two reactions which have different rate-determining steps. This will have to be dealt with in any alternative explanation.

EXPERIMENTAL

Materials.—The purification of materials has been previously described.[3] The water content of the solvent was $<0\cdot02$M.

Kinetic Methods.—All experiments were at 50°.

(a) *Sulphoacetic acid formation.* Reaction mixtures were made up, in 25-ml. volumetric flasks, from acetic acid (solvent), a stock solution of sulphuric acid in acetic acid, and acetic anhydride. A small correction was applied to allow for the volume change on going from room temperature to 50°. At appropriate intervals samples were withdrawn and run into water (to quench the reaction). The free sulphate remaining was estimated by Miller's volumetric method.[7] The use of a volumetric, rather than a gravimetric,[6] method allowed low sulphuric acid concentrations to be used and also, of course, reduced the labour.

(b) *Acylation experiments.* The method was as previously described.[3]

For both reactions the acetic anhydride concentrations were corrected for the water content of the medium, which would be rapidly destroyed.

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[7] Miller, *J.*, 1940, 401.