326. *Kinetic Measurements of the Acetylation of Anisole by Acetic Acid in the Presence of Boron Trifluoride.*

By V. GOLD and T. RILEY.

In the presence of large concentrations of boron trifluoride in acetic acid, anisole is converted into 4-methoxyacetophenone. The reaction velocity is very dependent on catalyst concentration, and it is tentatively suggested that acetylation is due to the acetyl cations formed in the equilibrium, $[AcOH_2]^+[BF_3{\cdot}OAc]^- \rightleftharpoons Ac^+ + BF_3{\cdot}OH^- + AcOH$.

THE aralkylation of anisole catalysed by sulphuric acid,[1,2] zinc chloride,[3] or boron trifluoride [4] in acetic acid solution can be conveniently observed without interference by disturbing side-reactions. During kinetic studies of these reactions it was found that, in the absence of an aralkylating agent, the interaction of acetic acid and anisole is slow and comparatively unimportant at catalyst concentrations in the range used in the aralkylation experiments. However, when much higher concentrations of boron trifluoride were used, anisole was acetylated at a conveniently measurable velocity, and these kinetic results are now reported. The reaction results in the introduction of one acetyl group, in qualitative agreement with earlier preparative work [5] under more drastic conditions.

EXPERIMENTAL

The preparation and analysis of catalyst solutions [4] and the purification of anisole [2] (samples of which were stored in the dark over sodium [6]) have been described previously.

4-Methoxyacetophenone was prepared (i) by Noller and Adams's procedure [7] (acetylation with acetic anhydride and aluminium trichloride in carbon disulphide; yield 68%; m. p. 38·5°), (ii) by a method involving conditions similar to those of the kinetic runs, and (iii) by the use of zinc chloride, hydrogen chloride, and acetic anhydride in acetic acid. In procedure (ii) anisole (3·2 g.) was added to a solution of boron trifluoride–acetic acid complex (40 ml.

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[1] Bethell and Gold, *J.*, 1958, 1905.

[2] Bethell, Gold, and Riley, *J.*, 1959, 3134.

[3] Bethell and Gold, *J.*, 1958, 1930.

[4] Gold and Riley, *J.*, 1960, 2973.

[5] Kastner in "Newer Methods of Preparative Organic Chemistry," Interscience Publ. Inc., New York and London, 1948, p. 281; Oelschläger, *Arch. Pharm.*, 1955, **288**, 102.

[6] Bien, Kraus, and Fuoss, *J. Amer. Chem. Soc.*, 1934, **56**, 1860.

[7] Noller and Adams, *J. Amer. Chem. Soc.*, **1924**, **46**, 1889.

containing *ca.* 19 g. of the trifluoride) in acetic acid (40 ml.). After being kept at 40° for 15 days, the solution was poured into ice-water. Ether-extraction, neutralisation, drying ($MgSO_4$) of the ether extract, and distillation under reduced pressure gave *ca.* 98% yield of 4-methoxyacetophenone, b. p. 143—144°/18 mm., identical with the specimen obtained by method (i). A vapour-phase chromatogram gave evidence of a single product only, indicating the absence of *ortho*- and *meta*-isomers. In method (iii) anisole (8 g.) and solutions of zinc chloride in acetic acid (53 ml. containing *ca.* 17 g. of zinc chloride) and of hydrogen chloride (*ca.* 3 g.) in acetic acid (50 ml.) were mixed and allowed to react at room temperature for 7 days. 4-Methoxyacetophenone indistinguishable from previous samples was isolated as before. The yield (4 g.) was 50%, based on the amount of acetic anhydride, but this figure is of doubtful significance in view of the possibility of acetylation by acetic acid. Method (i) was also used in the preparation of 2,4-dimethoxyacetophenone (80% yield) from *m*-dimethoxybenzene.

In kinetic experiments the reaction was initiated by addition of a measured amount of anisole to the catalyst solution at 40°. Samples of the mixture were quenched at timed intervals by running them into "AnalaR" ethanol and, after appropriate accurate dilution, analysed by spectrophotometry (Beckman DU instrument). Relevant blank measurements were performed and a small correction was applied for absorption due to the catalyst addition. The quenching of samples in ethanol (instead of acetic acid) was essential both in the present study and in that of the diphenylmethylation of anisole,[4] because the absorption spectra of anisole and boron trifluoride are not additive in acetic acid solution, whereas they are additive in ethanol solution. The non-additivity in acetic acid solution must be due to some interaction between the solutes which does not appear to be sufficiently extensive or profound (at least at lower concentrations of boron trifluoride) to affect the reactivity of anisole towards diphenylmethylation. It is possible that the ethanol–boron trifluoride interaction is stronger, so that any complex formation between anisole and boron trifluoride is effectively reversed on dilution of the sample in ethanol.

The reactions were of first order with respect to anisole, the acetylating agent (solvent) being in large excess. Rate constants are summarised in the Table.

First-order rate constants for acetylation of anisole by acetic acid at 40°.

(a) *Effect of catalyst concentration.* $[\text{Anisole}]_0 = 0{\cdot}192\text{M}$.

$[BF_3]$ (M)	4·98	5·26	5·88	6·12	6·46	6·74	7·05
10^6k_1 (sec.$^{-1}$)	3·75	4·94	10·9	13·5	23·0	28·7	39·2

(b) *Dependence on initial concentration of anisole.* $[BF_3] = 6{\cdot}74\text{M}$.

$10^2[\text{Anisole}]_0$ (M) ...	3·82	9·63	19·2
10^6k_1 (sec.$^{-1}$)	34·5	29·6	28·7

(c) *Effect of added water.* $[BF_3] = 6{\cdot}74\text{M}$. $[\text{Anisole}]_0 = 0{\cdot}0963\text{M}$.

$[H_2O]$ (M)	0	0·11	0·44
10^6k_1 (sec.$^{-1}$)	29·6	25·0	22·8

The progress of the reactions was attended by slow generation of an intense orange colour (due to the conjugate acid of the product) which was immediately discharged when a sample was quenched in ethanol. Quenched samples corresponding to long reaction times had an appreciable fluorescence. In some similar reactions such fluorescence has been attributed to the formation of pyrylium ions.[8] In view of the known conversion of acetophenone into pyrylium compounds in the presence of boron trifluoride,[9] this explanation appears very plausible in our reaction. At high acidities acetylation was complete before the fluorescence became noticeable, but at low acidities this subsequent reaction of the product interfered before completion of the acetylation, and infinity values of the optical densities had to be taken from the results for the faster reactions.

DISCUSSION

The discussion of the mechanism of acetylation by boron trifluoride in acetic acid is intimately connected with the chemical equilibria in this system. In earlier work[4] it

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[8] Burton and Praill, *J.*, 1951, 726; Lombard and Stéphan, *Compt. rend.*, 1953, **237**, 333.

[9] Dovey and Robinson, *J.*, 1935, 1389.

was shown that the solutions produced have a marked power to promote ionisation in the sense

$$\mathrm{ROAc} + (\mathrm{H}^+) \longrightarrow \mathrm{R}^+ + \mathrm{AcOH} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

but it was not necessary—in that context—to consider the processes which led to the high level of acidity and low activity of acetic acid whose combined effect gives rise to the favourable equilibrium concentration of R^+ cations. In view of the general existence of complexes $BF_3,2AcOH$, boron trifluoride in acetic acid solution is plausibly considered [10] to be mainly in the form $[AcOH_2]^+[BF_3{\cdot}OAc]^-$. On this basis we can understand the observation [11] that solutions of boron trifluoride and of sulphuric acid in acetic acid have almost the same high acidity (since they both contain the same Brønsted acid species $AcOH_2^+$) and that boron trifluoride should be slightly superior to sulphuric acid in the promotion of equilibrium (1) by virtue of the formation of the ion $[BF_3{\cdot}OAc]^-$.[4]

There is evidence that the acetic acidium ion $AcOH_2^+$ is not a strong acetylating agent.[12] However, it is not certain that this evidence would exclude the possibility that high concentrations of the ion—such as are probably formed in the solutions of the present study—might be effective. Nevertheless, it seems unlikely that $AcOH_2^+$ is the species concerned in the attack on anisole for, if it were, one would expect the reaction rate to be proportional to the concentration of boron trifluoride. In fact, the reaction velocity shows a steeper dependence on catalyst concentration [see section (a) of the Table], and this points to the formation of an active acetylating species—most plausibly the acetyl cation $CH_3{\cdot}CO^+$—by a more complicated pre-equilibrium. (As the reaction is of first order with respect to anisole, the production of the acetylating agent cannot be rate-controlling.)

The formation of the acetyl cation from the conjugate acid of acetic acid is a dehydration which would be thermodynamically favoured by a low activity of water in the medium. It may be that this activity is particularly low in the boron trifluoride–acetic acid solutions because of an equilibrium $[BF_3{\cdot}OAc]^- + H_2O \rightleftharpoons [BF_3{\cdot}OH]^- + AcOH$ which tends to lie largely over to the right-hand side and thus effectively removes water from the medium. On the basis of this hypothesis the formation of acetyl cations would be represented by the reaction $[AcOH_2]^+[BF_3{\cdot}OAc]^- \longrightarrow [Ac]^+[BF_3{\cdot}OH]^- + AcOH$.

An explanation along these (or similar) lines finds support in the small effect of added water on the reaction velocity [section (c) of Table] and also in our earlier observation [4] that the ionisation of diarylmethyl acetate indicators in boron trifluoride–acetic acid solutions is only slightly changed when some of the acetic acid in the solvent is replaced by water, a result which seems to imply that the added water does not cause the replacement of acetic acidium ions by hydroxonium ions, but is removed by a process which has little effect on the acidity of the medium.[13]

King's College, Strand, W.C.2.

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[10] Greenwood and Martin, *Quart. Rev.*, 1954, **8**, 1.

[11] Meerwein, *Annalen*, 1927, **455**, 227.

[12] *E.g.*, Burton and Praill, *J.*, 1950, 1203.

[13] Cf. Wichterle, Laita, and Pazlar, *Chem. Listy*, 1955, **49**, 1612.