**248.** *Acylation Reactions Catalysed by Strong Acids. Part I. Evidence for the Existence of Acetylium (the Acetyl Cation), $(CH_3 \cdot CO)^+$, in Solutions of Concentrated Aqueous Perchloric Acid in Acetic Anhydride.*
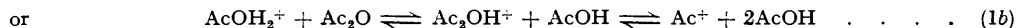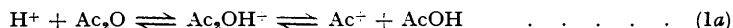
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Mixtures of perchloric and acetic acids which can contain hydrogen ion or solvated hydrogen ion, $AcOH_2^+$, are not *O*- or *C*-acetylating agents. Addition of acetic anhydride to such mixtures leads to the formation of acetylium (the acetyl cation), Ac^+, or the cation Ac_2OH^+; these ions, especially the former, are able to convert anisole into *p*-methoxyacetophenone. This "modified Friedel–Crafts reaction" can be carried out so that the yield of ketone exceeds that calculated on the amount of hydrogen ion (perchloric acid) originally used; an explanation for this is given.

Note on Nomenclature.—After consultation with the Editor, the cations referred to are named as follows : Ac^+, acetylium; $AcOH_2^+$, acetic acidium (compare nitric acidium for $H_2^+NO_3$); Ac_2OH^+, acetic anhydridium. The name "acetylium" appears preferable to acetyl cation, acetylonium, or acetonium.

The ready acetylation of hydroxy-compounds by an excess of acetic anhydride and a little concentrated aqueous perchloric acid appears to be simply explained if it is assumed that the perchloric acid (or hydrogen ion) first reacts with acetic anhydride to give acetylium :

$$H^+(+\ ClO_4^-) + Ac_2O \rightleftharpoons Ac^+(+\ ClO_4^-) + AcOH \quad . \quad . \quad . \quad . \quad (1)$$
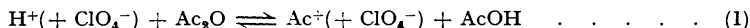
We consider that this overall reaction is best formulated, for reasons we shall discuss later, as

$$H^+ + Ac_2O \rightleftharpoons Ac_2OH^+ \rightleftharpoons Ac^+ + AcOH \quad . \quad . \quad . \quad . \quad (1a)$$

or

$$AcOH_2^+ + Ac_2O \rightleftharpoons Ac_2OH^+ + AcOH \rightleftharpoons Ac^+ + 2AcOH \quad . \quad . \quad . \quad (1b)$$

The resulting acetylium ions would then be expected to react as follows :

$$-OH + Ac^+ \longrightarrow -OAc + H^+ \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$
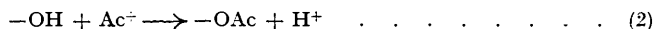
In turn, the regenerated hydrogen ion would then produce a further supply of acetylium by reaction (1) provided that acetic anhydride was present in the mixture (as is invariably the case using the above procedure). Concentrated (72%), aqueous perchloric acid contains a relatively high molecular proportion of water (2·2 mols. per mol. of $HClO_4$), which under the conditions of the acetylation reaction rapidly converts * the equivalent amount of acetic anhydride into twice the number of molecules of acetic acid. Thus, reagents made from 72% perchloric acid ($\equiv 1$ mol. of $HClO_4$) and acetic anhydride, even if reaction (1) did not occur, must contain a minimum of 4·4 mols. of acetic acid; accordingly more than 2·2 mols. of acetic anhydride must be used initially, if an excess of the anhydride is to be present. If reaction (1) is assumed to proceed exclusively to the right then a further molecule of acetic anhydride is converted into a further molecule of acetic acid. It is necessary to have a proper understanding of these molecular relationships in view of the work we now describe.

If the complete acetylation process obeys the sequence (1), (2), (1), (2), (1), etc., then clearly an excess of the anhydride is necessary, and, if it can be shown that the acetic acidium ion is not an acetylating agent, then the occurrence of the reaction, $H^+ + AcOH \rightleftharpoons AcOH_2^+$, is

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* This has been proved by Mackenzie and Winter (*Trans. Faraday Soc.*, 1948, **44**, 159, 171, 243), who appear to have been the first to suggest that reaction (1) or its equivalent takes place.

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of relatively little consequence in this connection. We have proved that a reagent containing only acetic and perchloric acids is not an acetylating agent, by showing that quinol is unaffected after 22 hours at room temperature; subsequent addition of acetic anhydride, however, causes immediate acetylation to take place.

It might appear to be immaterial in this *O*-acetylation process whether the equilibrium in reaction (1) lies to the right or to the left, provided that it is assumed that reactions (1) and (2) are both rapid. We are inclined to the view, however, that the equilibrium in (1) lies to the right, since we have recently shown (*J.*, 1950, 1062) that secondary alcohols of the type, $HO \cdot CHAr \cdot CH_2 \cdot NO_2$, can be smoothly acetylated by acetic anhydride and a little 72% perchloric acid without any tendency for dehydration to occur.

We have referred (p. 1203, footnote) to the postulation by Mackenzie and Winter (*loc. cit.*) of acetylium as a reactive species in mixtures of acetic anhydride and perchloric acid. This view was put forward in order to account satisfactorily for the results obtained in a kinetic study of the perchloric acid-catalysed, Thiele acetylation of quinones. We consider that this reaction does in fact involve acetylium, and we have shown (*Chem. and Ind.*, 1950, 92) that, whereas 2-methyl-1 : 4-naphthaquinone is unaffected by acetic anhydride–sulphuric acid (Anderson and Newman, *J. Biol. Chem.*, 1933, **103**, 405), the perchloric acid–acetic anhydride reaction leads, under suitable conditions, to reasonably good yields of 1 : 3 : 4-triacetoxy-2-methylnaphthalene. We shall be discussing the Thiele acetylation reaction in a subsequent paper, but in the mean-time we desire to draw attention to what we consider to be a serious defect in the mechanism put forward by Mackenzie and Winter, namely, the postulation of free phenols. From what we have already shown, we consider that any intermediate hydroxy-compound, in the presence of acetylium, could not have more than a transitory existence and would accordingly be acetylated rather than undergo dehydrogenation by unchanged quinone.

We have referred above to the fact that a reagent containing acetic and perchloric acids only is not an acetylating agent. As a precautionary measure we have also shown that this reagent is without effect on anisole during 72 hours at room temperature. We selected anisole for this purpose since if acetylium ions are formed as we have suggested, then the anisole would be expected to be readily converted into *p*-methoxyacetophenone :

$$PhOMe + Ac^+ \longrightarrow OMe \cdot C_6H_4 \cdot COMe + H^+ \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad (3)$$
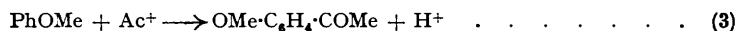
It is clearly possible to devise experiments to show whether or not the hydrogen ion thus liberated in reaction (3) would react further with acetic anhydride (reaction 1), and so acetylate more anisole than is stoicheiometrically possible on the amount of perchloric acid (hydrogen ion) originally used and *assumed to be all converted* by reaction (1) into acetylium ions. That such an operation can be carried out is illustrated by experiments 2, 7, and 8 (see Table) and proves conclusively that reaction (3) is followed by reaction (1). We cannot give precise details as to the relative speeds of these reactions, but it would appear (see experiments 5—7) that (3) is fast, and probably also that (1) is fast.

We can offer some evidence that the initial phases of reactions (1) and (3) are probably both fast since we have shown that by adding 0·05 mol. of perchloric acid (as 72%) to a mixture of anisole (0·1 mol.) and acetic anhydride (0·1 mol.) (diluted with an equal weight of acetic acid), the anhydride thus being used in an amount deficient to react with all the water ultimately present [in other words, the reaction mixture, provided that neither reaction (1) nor (3) occurred, contains anisole, perchloric and acetic acids, and a little (approximately 0·01 mol.) water], some acylation occurs. The fact that 0·012—0·014 mol. of *p*-methoxyacetophenone was isolated from reaction mixtures (Expt. 11 and 12) appears to prove beyond doubt that as soon as the first drop of perchloric acid is added reaction (1) begins and that this is followed immediately or fairly rapidly by reaction (3). The only possible alternative explanation is that the acetylium ions formed, of necessity to a limited extent, are stable in acetic acid containing a little water. We cannot conceive that this is so. We are of the opinion, however, that acetylium has " some stability in acetic acid," a statement which is meant to denote that acetic anhydridium ions (see 1*a* and 1*b*) are capable of acetylating anisole. Some evidence on this point appears to be available from a comparison of Expts. 1 and 2 and also from Expts. 8 and 9.

It will be apparent from Expts. 1, 11, and 12 that the order of mixing the reagents is of some importance and we have accordingly used two techniques.

The results detailed in the table give clear indications of four factors, namely, time, temperature, and the amounts of acetic acid and anhydride present. Expts. 5 and 6 emphasise that even at 0° the reactions (1) and (3) are both relatively fast and that the longer reaction

time leads to a higher yield of ketone; it is therefore certain that reaction (3) is the rate-determining stage in these cases.   Prolonged reaction times have, in fact, led to the production of tars both at 0° and at 15°; we are of the opinion that in such case the *p*-methoxyacetophenone first formed undergoes some further reaction.

The overall reaction occurs, as expected, more rapidly at 15° than at 0°; we did not consider it essential to do strictly comparative experiments to prove this point.

The effect of increasing the amount of acetic acid is apparent from a comparison of Expts. 8 and 9; the extremely vigorous reaction with the smaller quantity of acetic acid has been " slowed down " by adding more acetic acid and, even if the equilibria of the reactions $Ac_2OH^+ \rightleftharpoons Ac^+ + AcOH$ (1a) or $Ac_2OH^+ + AcOH \rightleftharpoons Ac^+ + 2AcOH$ (1b) are substantially to the left in Expt. 8, a clear indication that the acetic anhydridium ion might be an acetylating agent is apparent.

In all the experiments 0·1 g.-mol. of anisole, and 72% perchloric acid $\equiv$ 0·05 g.-mol., were used. In experiments 1—7, the anisole was added last : in experiments 8—12 the perchloric acid was added last.   The figures quoted in columns 2, 3, 6, and 7 refer to g.-mols.

Expt.	AcOH initially present.	" Free " * Ac_2O.	Reaction time.	Temp.	$MeO \cdot C_6H_4 \cdot COMe$ isolated.	PhOMe recovered.	Residue from distillation.
1	0·44	0	72 hours	15°	0	0·085	0·1 g.
2	0·44	0·2	2 hours	5—15	0·066	0·015	1·2 g.
3	0·22	0·05	45 mins.	0	0·02	0·07	0·2 g.
4	0·22	0·1	45 mins.	0	0·033	0·049	0·3 g.
5	0·22	0·2	45 mins.	0	0·049	0·035	0·4 g.
6	0·22	0·2	23 mins.	0	0·038	0·05	0·4 g.
7	0·22	0·3	45 mins.	0	0·056	0·03	0·3 g.
8	0·94	0·315	2 hours	15	0·072	0·007	1·1 g.
9	0·22	0·315	2 hours	15	†	†	†
10	0·22	0·015	48 hours	15	0·027	0·04	1 g.
11	0·392	0	48 hours	15	0·012	0·064	0·2 g.
12	0·392	0	2 hours	15	0·014	0·069	0·2 g.

* Based on the assumption that reaction (1) has *not* taken place.
† The majority of the reaction product was a tar which subsequently solidified; some ether-soluble material was obtained but was not examined further.

The effect of increasing the concentration of acetic anhydride has been studied most, and it is clear from Expts. 3, 4, 5, and 7 that, for a given time at 0°, the yield of ketone increases steadily to a limiting value.   There is a notable increase in the yield of ketone with increasing amount of acetic anhydride up to and including four mols. for each mol. of perchloric acid; beyond this the effect is not very marked.   All these results appear to us to show that our original suggestion that the equilibrium in (1) lies to the right, is true for acetylating reagents containing a large excess of acetic anhydride.   We can offer no quantitative evidence on this point, since we have not attempted to study the kinetics of any of the reactions formulated. We must emphasise that all the work so far done by us is of a purely qualitative or preparative nature; in fact no precautions whatever (*e.g.*, exclusion of moisture) have been taken nor were they considered essential for our purpose.

In all the experiments detailed we have, with one exception, been able to account for 80—90% of the anisole used, either as unchanged anisole or as *p*-methoxyacetophenone actually isolated.   The exception was Expt. 9 where excessive production of tar was observed.

In all the experiments carried out with anisole little development of colour occurred in the reaction mixtures provided that " free " acetic anhydride was absent.   It was noted, however, that in mixtures containing even a small amount of " free " acetic anhydride, a brownish-orange colour developed immediately.   This colour may indicate formation of the oxonium ion, PhO^+MeAc, or $[PhOMe,Ac_2OH]^+$, but the amount so produced must have been very small, since clearly such an ion could not be expected to undergo a Friedel–Crafts type of reaction with acetylium ions.   We should also expect that such an ion would undergo " acetolysis " to phenyl acetate; examination of the alkaline washings of ethereal extracts of the reaction products did occasionally reveal traces of phenol, especially when the reaction mixtures had been kept for relatively long times.   It appears clear that if the colour is due to formation of an oxonium ion then this cannot possibly have the structure, PhO^+HMe.

We suggest that mixtures of acetic anhydride and concentrated sulphuric acid may react similarly to give acetylium ions :

$$H^+ + HSO_4^- + Ac_2O \rightleftharpoons Ac^+ + HSO_4^- + AcOH$$
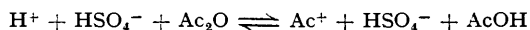
We decided not to investigate this sytem in the first place, because it is well known that such mixtures can act as sulphonating agents (including mutual reaction to produce sulphoacetic acid).

<div align="center">EXPERIMENTAL.</div>

Materials.—Acetic anhydride and 72% perchloric acid were AnalaR reagents. Acetic acid was purified by the method of Orton and Bradfield (*J.*, 1924, 960). Redistilled anisole was used in all the experiments.

Experiments with Quinol.—(a) Acetic anhydride (11·2 g., 0·11 mol.) was added dropwise to a cooled mixture of 72% perchloric acid (7·0 g. ≡ 0·05 mol. of $HClO_4$) and acetic acid (10·8 g., 0·18 mol.), so that the temperature of the mixture did not exceed 30—35°. After 8—10 minutes, quinol (5·5 g., 0·05 mol.) was added, with shaking, in small portions, and the orange-coloured mixture kept at room temperature. At intervals during the following 18 hours, 2—3 drops of the soluble portion of the reaction mixture, which still contained a little undissolved solid, were added to water (*ca.* 5 c.c.), clear solutions being obtained (in the later stages, seeding with quinol diacetate caused no separation of solid material). After 18 hours the mixture was warmed to effect complete dissolution, and the resulting deep-orange liquid kept at room temperature for a further 2—3 hours; test portions added to water gave on indication of acetylation. Acetic anhydride (10·2 g., 0·1 mol.) was then added at such a rate that the temperature of the reaction mixture did not exceed 30° (a test portion taken after the addition of half of the acetic anhydride gave an immediate crystalline precipitate). After 30 minutes at room temperature, much crystalline material had separated; decomposition with ice gave 7·2 g. (75%) of nearly pure quinol diacetate, m. p. 120°, raised to 123° by one crystallisation from alcohol. The 75% yield does not take into account the 11 test portions removed during the experiment.

(b) A mixture of quinol (5·5 g.), acetic acid (10·8 g.), and acetic anhydride (10·2 g.) was treated with 2 drops of 72% perchloric acid, whereupon the temperature of the mixture rose to 64° and then began to fall fairly rapidly, and complete dissolution occurred. The mixture was poured, after less than 1 minute, on ice. The resulting quinol diacetate (7·7 g., 80%) had m. p. 121—122°.

Experiments with Anisole.—(a) *Method* 1 (Table : Experiments 1—7). 7·0 G. of 72% perchloric acid were added dropwise to the appropriate amount of acetic anhydride or mixture of acetic anhydride and acetic acid cooled in ice, at such a rate that the temperature was kept below 35°. After cooling to 15° (room temperature) or 0°, the anisole (0·1 g.-mol.) was added fairly rapidly, only a slight increase in temperature being observed. After being kept for the times stated, the mixture was poured on crushed ice.

(b) *Method* 2 (Table : Experiments 8—12). Anisole (0·1 g.-mol.), dissolved in the acetic anhydride or acetic anhydride–acetic acid, was cooled in ice and treated dropwise with the 72% perchloric acid (7·0 g.) so that the temperature of the reaction mixture did not exceed 30°. The resulting orange-red solution was cooled rapidly to the appropriate temperature and after being kept for the times stated was decomposed with ice.

The oil which separated in both methods was extracted with ether; in some experiments a varying but small amount of a bright yellowish-orange solid (*A*) began to separate in the aqueous phase; this was filtered off before continuing with the extraction. The ethereal extract was washed with aqueous sodium carbonate until free from acid, then with 2N-sodium hydroxide (repeated if acidification gave an opalescence), and finally with water. The dried (Na_2SO_4) extract was then evaporated and the residue fractionated at about 4 mm., whereby a sharp separation of unchanged anisole from *p*-methoxy-acetophenone, b. p. 110—115°/3·8—4 mm., was achieved. The *p*-methoxyacetophenone solidified, on cooling, to a crystalline mass, m. p. 34—37°, which when redistilled gave material, m. p. 39—40° (Found : C, 72·3; H, 6·7. Calc. for $C_9H_{10}O_2$: C, 72·0; H, 6·7%).

The phenylhydrazone crystallised from alcohol in pale yellow needles, m. p. 135°, and the 2 : 4-di-nitrophenylhydrazone separated from alcohol in bright red needles, m. p. 223°. Vogel (" Practical Organic Chemistry," Longmans, Green and Co., 1948, p. 706) gives m. p. 142° and 220°, respectively.

By-products.—Formation of the bright yellowish-orange solid (*A*) (above) was most noticeable in experiments which had been carried out for the longer reaction periods. It did not melt but inflamed when heated on a spatula. Solutions in alcohol exhibit a vivid green fluorescence similar in intensity and colour to that shown by fluorescein. The compound probably contains chlorine (copper wire test) and may be an organic perchlorate.

The opalescence noticed on acidification of some of the sodium hydroxide extracts of the ethereal solutions of the reaction product appeared to be caused by the separation of a phenolic substance. Attempted isolation of this from some of the experiments by extraction with ether gave small amounts (0·2 g. or less) of a dark oil which smelled strongly of phenol but did not solidify.

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