CXX.—*Acids as Accelerators in Acetylation. Part II.*

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IN our first paper (Trans., 1908, **98**, 1242), it was shown that anilines of a non-basic character, for example, anilines with two negative ortho-substituents, reacted with acetic anhydride with a far greater speed in the presence of mineral acids. Thus acetylation could be quickly effected at the ordinary temperature even with diluted acetic anhydride. Moreover, it was found that the acetylation of phenols was greatly hastened by many acids and not only by sulphuric acid; in fact, perchloric acid showed itself superior to a "dehydrating" material such as sulphuric acid, whilst phosphoric oxide (and phosphoric acid) are incomparably inferior to either acid.

In order to follow quantitatively the effect of the nature and concentration of acids on the speed of acetylation by acetic anhydride, we have been obliged to confine ourselves, owing to experimental difficulties, to the acetylation of *s*-tribromophenol and the use of sulphuric, perchloric, and orthophosphoric acids.

The results demonstrate that the speed of acetylation is

approximately proportional to the concentration of the acid. This relation is particularly well shown in the case of sulphuric acid, but is less well marked in the case of perchloric acid. For gram-molecular proportions, the rates of acetylation with these two acids are, at least when the concentration of the acid is small, in the ratio 2.5 : 1. Using orthophosphoric acid (or phosphoric oxide), acetylation was just perceptible under the same conditions of temperature and concentration after twenty-four hours, whilst in the presence of perchloric acid it was complete in 100 minutes. In the absence of any acid, no acetylation is detectable in six weeks.

It was suggested in a previous paper that the acetylation depends on the formation of a mixed anhydride of acetic acid and the mineral acid, for example, $\text{CH}_3\cdot\text{CO}\cdot\text{O}\cdot\text{ClO}_3$, a hypothesis which was supported by Franchimont, Skraup, and Thiele, and more recently by Stillich (*Ber.*, 1905, **39**, 1241), as accounting for the part played by sulphuric acid. An example of these mixed anhydrides has been obtained by Francis and Butler (*Ber.*, 1906, **39**, 3798, 3804), who isolated benzoyl nitrate, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{O}\cdot\text{NO}_2$, and showed that it gave with anilines a benzoyl derivative. Pictet and Khotinsky (*Compt. rend.*, 1907, **144**, 210) have prepared acetyl nitrate, the behaviour of which with anilines is quite similar. Since under the conditions of our experiments the phenol is attacked by nitric acid, a comparison of this acid as an accelerator with perchloric and phosphoric acids was impossible.*

Our results are in agreement with such a hypothesis. The speed of acetylation would be proportional to the concentration of this complex, which in its turn would be approximately proportional to the concentration of the acid, at least when the concentration

* In earlier papers (*Trans.*, 1902, **81**, 806 ; 1908, **93**, 727 ; *Ber.*, 1907, **40**, 370) we have shown that a mixture of acetic anhydride and nitric acid diluted with acetic acid makes an excellent nitrating mixture for anilines, converting them into nitroamines, $\text{Ar}\cdot\text{NH}\cdot\text{NO}_2$, the acetyl derivative only appearing as a by-product, although the proportion becomes greater with unsubstituted anilines. We have suggested (*Trans.*, 1908, **93**, 1242) that the acetyl nitrate reacts with the aniline mainly as follows :

whilst other acids yield mainly the acetyl derivative. In the light of the results or the authors cited above, it is obvious that acetyl nitrate, at least under certain conditions, yields only an acetyl derivative. Possibly the agent in nitration is a predecessor of the mixed anhydride, namely, an additive compound containing quadrivalent oxygen :

In any case, we find that the formation of nitroamine is a far more rapid process than acetylation.

of the anhydride was very large relative to that of the acid. Further, inasmuch as the amount of this complex produced at a given concentration, and its reactivity with the phenol, would depend on the nature of the acid, the speed of acetylation would vary with the acid used. In the case of phosphoric acid, both factors may play a part in rendering it so inefficient.

The possibility of the agent being an additive complex of the acetic anhydride and the acid, in which the oxygen had become quadrivalent, that is, the compound which might be supposed to precede the acetyl perchlorate, etc., is, on the other hand, rendered more remote, as in that case no great difference would be expected between the various acids.

Solvents.—The effect of solvents other than acetic acid has also been investigated. In chloroform, benzene, or acetone, *s*-tribromophenol is not acetylated at the ordinary temperature. In the presence of sulphuric acid, acetylation is complete in chloroform solution in twenty minutes (concentration, temperature, and ratio of acetic anhydride to phenol were the same as were used throughout these experiments: see Experimental Part; ratio of sulphuric acid to phenol = 0.5 : 1 gram-mol.). Although a reaction took place in benzene and acetone solution, it was very much slower, sufficient acetate for a melting-point determination being formed only after sixty minutes.

Acetylation of Phenols.—As a practical method of acetylating phenols, from which acetyl derivatives are difficult to obtain, our experiments show that acids are far superior to sodium acetate as catalysts. A comparison of acids with pyridine, which was recommended by Verley and Bölsing (*Ber.*, 1901, **34**, 3354) as a catalyst in acetylation by means of acetic anhydride, has been made.

In acetic acid solution, pyridine was found to be nearly as effective as perchloric acid, and therefore considerably superior to sulphuric acid. When the pyridine and the phenol were in molecular proportions (the other conditions of concentration and temperature being identical with those which we have used throughout), only 10 per cent. of the phenol remained after thirty minutes. In chloroform solution, the reaction is more rapid, no phenol remaining after fifteen minutes. If pyridine is used as solvent, as in the usual method of acylation by acyl chlorides, the reaction is obviously still more speedy.

EXPERIMENTAL.

The measurements of the velocity of acetylation of *s*-tribromophenol by acetic anhydride in acetic acid solution in the presence of mineral acids were beset with many difficulties. In the first

place, it was impossible to avoid an initial rise of temperature on mixing, owing mainly to the reaction of the acetic anhydride with the water unavoidably present either in the acetic acid or in the mineral acid. We find that acids very greatly quicken this interaction of acetic anhydride and water. This source of error could be, however, reduced to a minimum by mixing in a certain order.

The phenyl acetate produced in a given time and the unchanged phenol were directly weighed, the weights being corrected for the solubility of each in the media from which they had separated. This correction was determined by estimations of the solubility, and by carrying out separations of mixtures of known quantities of the phenol and the acetate.

The perchloric and phosphoric acids were used in the form of 50 per cent. aqueous solutions, and the sulphuric as the ordinary concentrated acid.

The following procedure was adopted after many trials as giving the most consistent results:

Two grams ($1/16.5$ gram-molecule) of *s*-tribromophenol (crystallised from light petroleum, and melting constantly at 95°) were dissolved in 30 c.c. of glacial acetic acid (m. p. 16.4°), and placed in the bath kept at 15° ; 25 c.c. of redistilled acetic anhydride were mixed with 45 c.c. of acetic acid, and the mineral acid (measured in a standard burette graduated to 0.01 c.c.) added, whereupon a sharp rise of temperature took place. When the temperature of the latter mixture had fallen to 15° , the two solutions were mixed as rapidly as possible, the temperature rising $0.4-0.7^{\circ}$, but falling again to 15° within five minutes.

Ten c.c. of the mixture (that is, a volume containing 0.2 gram of the original phenol) were withdrawn at intervals, and added to 75 c.c. of warm ($40-50^{\circ}$) water. After keeping for several hours, the suspension in dilute acetic acid was placed in a water-bath for two hours, filtered through a large Gooch crucible (which was fitted with filter paper), and washed with 50 c.c. of water at 15° . The crucible containing the solid was dried in an evacuated desiccator over sulphuric acid and phosphoric oxide. The phenol was then extracted from the solid by treatment with 25 c.c. of 2 per cent. sodium hydroxide for ten minutes at 15° , and the undissolved acetate collected in a Gooch crucible, washed in 50 c.c. of water at 15° , dried, and weighed. The phenol was isolated from the alkaline solution.

A series of experiments showed that the loss of phenyl acetate was 5 milligrams, which must therefore be added to the weight found in order to determine the amount of phenol acetylated. The loss of phenol was greater, amounting to 0.0134 gram.

The quantities of the mineral acids, sulphuric and perchloric, relative to one gram-molecule of *s*-tribromophenol, used in the various experiments were respectively 1/8, 1/4, 1/2, and 1 gram-molecule. With the higher proportions of perchloric acid, the concentration was halved in order to bring the reaction to a measurable velocity.

The following table summarises the results of one of the measurements, using perchloric acid, 1/8 gram-molecule:

Time (in minutes).	Acetate (corrected).	Phenol changed.	Percentage of phenol changed.	K_1 .	K_2 .
15	0·0373	0·0331	16·55	0·012	—
30	0·0643	0·0570	28·53	0·0112	—
45	0·0855	0·0754	37·72	0·0105	0·0092
60	0·1043	0·0925	46·27	0·0103	0·0095
90	0·1358	0·1205	60·25	0·0102	0·0098
120	0·1594	0·1415	70·74	0·0102	0·0099
135	0·1684	0·1494	74·74	0·0102	0·0099

K_1 is calculated from the equation:

$$dx/dt = k \cdot c^{\text{phenol}} \times c^{\text{acetic anhydride}}.$$

The concentration of the acetic anhydride cannot be exactly determined, and since it is large relative to the phenol it may be taken as constant. Hence:

$$dx/dt = (k \cdot c^{\text{acetic anhydride}}) \times c^{\text{phenol}} = K_1 \cdot c^{\text{phenol}}.$$

Under K_2 we have values of K_1 calculated after the reaction has proceeded for thirty minutes, when the effect of the initial rise of temperature is no longer felt.

The following values of K_1 and K_2 were found in a series of measurements when sulphuric acid is used as the accelerator:

Proportion of sulphuric acid to 1 gram-mol. of <i>s</i> -tribromophenol.	Mean values of K_1 .	Mean values of K_2 .
1/8 gram-mol.	0·0042	0·00372
1/4 „	0·0069	0·0064
1/2 „	0·0159	0·01334

The following values of K_1 and K_2 were found when perchloric acid was used as an accelerator:

Proportion of perchloric acid to 1 gram-mol. of <i>s</i> -tribromophenol.	Mean values of K_1 .	Mean values of K_2 .
1/8 gram-mol.	0·0107	0·0097
1/4 „	0·0178	0·0165
1/2 „	0·0378	0·0375
1 „	0·0556	0·0484

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