Reduction of Heptanone-3-dicarboxylic Acid-1,5.—As before in the reduction of butyrofuronic acid, 9 g. of the acid was reduced by means of 1.8 g. of phosphorus and 60 cc. of hydriodic acid for eight hours at 190–200°. The product, extracted from the reduction mixture after decolorizing with sulfur dioxide and purifying by precipitation from hot water and benzene, consisted of 1 g. of colorless liquid which crystallized upon the introduction of a crystal of ethylpimelic acid. Analysis and melting point indicated that the reduction product was identical with that obtained from butyrofuronic acid, namely, ethylpimelic acid. The analysis of the silver salt gave the following results.

Anal. Subs. 0.5000: AgCl, 0.3601. Calcd. for $C_9H_{14}O_4Ag_2$: Ag, 53.73. Found: Ag, 54.20.

Summary

1. A method has been developed whereby furylangelic acid can be produced in yields of over 80% of the theoretical from furfural, sodium butyrate and butyric anhydride.
2. The structure of furylangelic acid and the course of the Perkin reaction when applied to furfural and butyric acid have been established through the isolation and identification of the products of oxidation of furylangelic acid.
3. Furylvaleric acid has been prepared and the ring opened by bromination and oxidation to yield heptene-1-one-3-dicarboxylic acid-1,5.
4. Butyrofuronic acid has been reduced to heptane-dicarboxylic acid-1,5 and heptanone-3-dicarboxylic acid-1,5.
5. The previously unprepared heptanone-3-dicarboxylic acid-1,5 and its ethyl ester have been prepared from furylangelic acid, and this product has been reduced to heptane-dicarboxylic acid-1,5.

WILMINGTON, DELAWARE

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE ACIDIC AND BASIC CATALYSIS OF ACETYLATION REACTIONS

BY JAMES B. CONANT AND GEORGE M. BRAMANN

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The acetylation of hydroxy compounds by means of acetic anhydride is frequently catalyzed by the addition of sulfuric acid, sodium acetate or pyridine. Since acetic acid is often the initial solvent and is always formed by the reaction, the behavior of these catalysts in this solvent may afford the clue to the explanation of their action. Sulfuric acid is obviously an acid catalyst which furnishes hydrogen ions in excess of those provided by acetic acid itself. Sodium acetate and pyridine are examples of basic catalysts, since it has been shown[1] that these substances are strong bases in acetic acid.

The development of methods of studying the hydrogen ion activity

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[1] Hall and Conant, THIS JOURNAL, **49**, 3047 (1927).

of glacial acetic acid solutions[1] makes possible a further investigation of the influence of the acidity or basicity of the medium on the rate of acetylation. The results presented in this paper are in the nature of a preliminary survey of the field. They are limited by the accuracy of the present methods of determining hydrogen ion activities in glacial acetic acid and, in their interpretation, by our inadequate knowledge of the physical chemistry of the behavior of acids, bases and salts in this solvent. Furthermore, it was not found possible to obtain precise measurements of the rate of any of the acetylation reactions we studied. In spite of these limitations the results clearly show the fundamental factors which affect the speed of acetylations with acetic anhydride. This suggests wide possibilities in regard to controlling such reactions for preparative and analytical purposes. We shall report experiments along these lines at another time.

The Rate of Acetylation of β-Naphthol

After some experimentation with a variety of substances, β-naphthol was chosen for the rate measurements. It is readily acetylated by acetic anhydride with the formation of a crystalline acetate which is insoluble in water and resistant to hydrolysis by cold water. The β-naphthol and a four-fold excess of acetic anhydride were allowed to interact in glacial acetic acid solutions of definite acidity. The extent of the reaction was determined by diluting with water, filtering off the mixture of β-naphthol and β-naphthyl acetate on a Gooch crucible, washing with water and saponifying the residue with standard sodium hydroxide. Experiments with mixtures of pure β-naphthyl acetate and β-naphthol showed that the precipitation by water was not complete. We, therefore, standardized our procedure by operating always with such volumes that the recovery of the acetate was 70 ± 5% as shown by numerous blank runs with varying proportions of β-naphthol and β-naphthyl acetate dissolved in acetic acid. In calculating the extent of the reaction, we corrected the actual titration figures on the assumption that only seven-tenths of the acetate was recovered. The correctness of this procedure was demonstrated by the fact that the final constant value for the amount of acetate formed in each buffer was 100 ± 10% on the corrected basis. The necessity for this correction as well as the difficulty of the uniform precipitation and washing make the method only an approximate one, as shown by the figures exhibited below. A qualitative check of some importance was afforded by the determination of the melting point of the product. The acetate melts at 68°, β-naphthol at 122°, while a 50–50 mixture when precipitated from acetic acid by water melts at 48–51°. The melting points of the products showed the general correctness of the results of the analytical procedure.

Analytical Procedure.—In starting each experiment, 5 cc. of a 0.5 molar solution of β-naphthol in glacial acetic acid was placed in a tube in a thermostat at 25°; 5 cc. of the buffer solution (see Table I) was then added. One cubic centimeter of acetic anhydride was added rapidly and the mixture shaken; the time was taken from this point (with a stop watch if necessary). The tube was closed by a cork or by sealing off the glass and allowed to stand in the thermostat for the allotted time. The contents were then added to 100 cc. of water and the mixture was shaken rapidly. The coagulated precipitate was filtered off on a Gooch crucible, pressed on the filter and washed with 100 cc. of water. The crucible was then transferred to a 250-cc. wide-mouthed flask, containing 25 cc. of alcohol and 25 cc. of 0.1 *N* sodium hydroxide. The mixture was heated for ten minutes on the steam-bath under a reflux condenser attached to a soda lime tube. The excess of sodium hydroxide was titrated with 0.1 *N* hydrochloric acid using phenolphthalein as the indicator; the end-point is difficult to ascertain because of the color of the solution. The following results, obtained with a 0.2 molar benzamide solution, 0.4 neutralized with sulfuric acid, as the buffer, are typical.

TABLE I

TYPICAL RESULTS

Time, minutes	Percentage reacted By titration	Corrected	$k \times 10^2$	Melting point of product, °C.
5	17	24	4.6	
10	25	35	4.4	
15	31	44	3.8	
20	36	51	3.5	55
25	52	74	5.4	
30	62	88	7.0	
40	68	97		63
50	68	97		
60	67	96		68
80	71	102		
140	70	100		

The results are summarized in Table II. The values of *k* given are the reaction velocity constants calculated from the monomolecular formula using natural logarithms and the time in minutes. Only experiments in which the extent of the reaction was between 10 and 85% were used in calculating *k*; the number of such experiments is given in the fourth column. In addition, there were always a number of experiments for longer periods of time to show that the reaction proceeded essentially to completion and thus to check our analytical procedure. The $P\text{H}^{(\text{HAc})}$ values were determined by means of the chloranil electrode as previously described; they agreed within 0.2 of a unit of the values predicted from the titration curves. Solutions 5 and 6 were intended to be identical but actually varied 0.3 in $P\text{H}^{(\text{HAc})}$; this slight difference was reflected in the rate measurements. The use of buffer solutions containing magnesium acetate partially neutralized with perchloric acid (Nos. 7, 9, 10) was suggested to us by Dr. N. F. Hall as a result of his further study of the behavior of acids and bases in glacial acetic acid.[2] Primary and secondary

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[2] To be published shortly.

amines and even urea were not suitable materials for preparing buffer solutions for our work since they are rapidly acetylated by acetic anhydride. Even benzamide and acetanilide are acted upon slowly, but not at a rate which seriously affects the validity of the results given in Table II.

TABLE II

RATE OF ACETYLATION OF β-NAPHTHOL IN GLACIAL ACETIC ACID BUFFER SOLUTIONS AT 25°

Concn. of β-Naphthol, 0.22 molar; of acetic anhydride, 0.88 molar

Soln. no.	Composition of buffer solution	P_H(HAc)	No. of expts.	Range of values of $k \times 10^2$	Average value of $k \times 10^2$	$k \times 10^2$ calcd. from Eq. 2
1	0.2 *M* $HClO_4$	−4.5	2	Too fast to measure	*ca.* 5000	2800
2	0.2 *M* H_2SO_4	−3.3	4	100–200	160	200
3	0.2 *M* $C_{10}H_7SO_3H(\beta)$	−2.3	9	10–30	21	20
4	0.2 *M* $C_6H_5CONH_2$, 0.4 neut. with H_2SO_4	−1.8	5	3.5–5.0	4.2	6.3
5	0.2 *M* CH_3CONH_2, 0.55 neut. with H_2SO_4	−1.3	7	1.5–1.9	1.6	2.0
6	0.2 *M* CH_3CONH_2, 0.55 neut. with H_2SO_4	−1.0	6	0.9–1.5	1.1	1.0
7	0.05 *N* $Mg(OCOCH_3)_2$, 0.9 neut. with $HClO_4$	−0.6	5	0.06–0.15	0.12	0.4
8	0.2 *M* H_3PO_4	−0.2	3	0.13–0.17	0.12	0.16
9	0.05 *N* $Mg(OCOCH_3)_2$, 0.5 neut. with $HClO_4$	+0.5	5	0.029–0.050	0.039	0.037
10	0.05 *N* $Mg(OCOCH_3)_2$, 0.1 neut. with $HClO_4$	+1.5	11	0.007–0.031	0.017	0.0084
11	0.05 *M* CH_3COONa, 0.5 neut. with $HClO_4$	+2.9	5	0.006–0.011	0.009	0.013
12	0.2 *M* CH_3COONa	+3.3	5	0.017–0.040	0.028	0.025
13	0.77 *M* Pyridine	+4.0	6	1.0–1.5	1.3	1.6
14	2 *M* CH_3COOK	+4.5	7	0.10–0.18	0.13	0.32
15	3 *M* Pyridine	+4.8	3	7–10	8.0	6.2

The most detailed recent studies of acid and base catalysis in aqueous solutions have been carried out by Lowry[3] and by Brönsted[4] in connection with the investigation of the mutarotation of glucose. The results of these two investigators show that in this process both an acid and a base (in Brönsted sense of the terms) are involved. If the acetylation of β-naphthol by acetic anhydride is subject to the same fundamental laws, the catalysts which would be effective would be the solvated hydrogen ion (the acetonium ion $CH_3COOH_2^+$), undissociated acid molecules, the acetate ion (or other ion of a weak acid) and relatively strong basic molecules such as pyridine. Just as the hydrated hydrogen ion and the hydroxyl ion are usually the most effective catalysts in aqueous solution, so in glacial acetic acid the solvated hydrogen ion and the acetate ion would

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[3] Lowry, *J. Chem. Soc.*, **1927**, 2554.

[4] Brönsted and Guggenheim, THIS JOURNAL, **49**, 2554 (1927).

be expected to be of predominant influence. The molecules of acetic acid, like those of water, may act as either acid or basic catalysts by virtue of their ability to donate or receive a proton with the formation of the acetate and acetonium ions, respectively. The effectiveness of these catalysts would be expected to be expressed by an equation such as the following

$$k = k_o + k_{\mathrm{H}^+} C_{\mathrm{H}^+} + k_{\mathrm{Ac}^-} C_{\mathrm{Ac}^-} + k_{\mathrm{B}} C_{\mathrm{B}} \qquad (1)$$

In this equation, k is the specific reaction constant as measured, k_o the constant in pure acetic acid, k_{H^+}, k_{Ac^-}, k_{B}, the constants characteristic of the solvated hydrogen ion, the acetate ion and any strongly basic ion and C_{H^+}, C_{Ac^-}, C_{B} the concentrations of these acids and bases. The effect of very weak acids and bases has been neglected since the recent work of Brönsted shows that, at least in certain cases, the value of each catalytic constant is closely related to the strength of the acid or base.

Unfortunately we have no certain information in regard to the concentrations of the ions in the case at hand so we cannot substitute the proper values in Equation 1. However, we have found that our experimental results may be formulated in terms of the hydrogen ion activity of our solutions by means of an equation similar to Equation 1. This empirical equation is as follows:

$$k \times 10^2 = 0.005 + 0.1\, a_{\mathrm{H}^+} + \frac{10^{-5}}{a_{\mathrm{H}^+}} + 2.0\, C_{\mathrm{Pyridine}} \qquad (2)$$

In this equation a_{H^+} denotes the hydrogen ion activity referred to an aqueous solution of $P_{\mathrm{H}} = 0$ as the reference state as in the previous work; it is defined experimentally as $\log a_{\mathrm{H}^+} = -P_{\mathrm{H}}^{(\mathrm{HAc})}$.

The values of k calculated according to Equation 2 are given in the last column of Table II. In Fig. 1, where log k is plotted against $P_{\mathrm{H}}^{(\mathrm{HAc})}$, the curve of Equation 2 omitting the last term is shown. For solutions 1 to 8 only the second term of Equation 2 is involved and there is, therefore, a straight line relationship between log k and a_{H^+}. With solution 14 only the third term is significant and the factor of 10^{-5} was obtained by a consideration of this point. The value of k_0 (0.005) was found empirically as that necessary to give the proper values with those solutions in which both the second and third terms are small. The introduction of the last term in the cases of the solutions containing pyridine is necessary to correspond to the increased catalytic activity; that such a term should appear would be expected from Brönsted's theory.

It is obvious that the factors 0.1 and 10^{-5} in the second and third terms of Equation 2 are *not* k_{H^+} and k_{Ac^-}, but include also a factor which relates the activity of the hydrogen ion, in the one case to the concentration of the acetonium ion ($CH_3COOH_2^+$) and in the other case to the concentration of the acetate ion. If in a 0.2 *M* solution of perchloric acid $C_{\mathrm{H}^+} = 0.2$, k_{H^+} is about 10^4 and if in a 0.2 *M* solution of sodium acetate $C_{\mathrm{Ac}^-} = 0.2$,

$k_{Ac^-} = 0.1$. It is extremely unlikely that such a simple state of affairs is actually the case even in the strong acid and basic solutions in glacial acetic acid; the assumption, however, may not be very greatly in error. It is interesting that k_B for pyridine (2.0) was found to be only about twenty times the value of k_{Ac^-} (0.1) derived on this simple assumption. It is impossible to estimate, at present, the concentration of the solvated hydrogen ion in solutions 2–15 except on the simple assumption that there is a direct proportionality between C_{H^+} and a_{H^+}, as has been done in writing Equation 2. To evaluate the catalytic activity of the other components of these buffer solutions will require work of a greater accuracy than that presented in this paper.

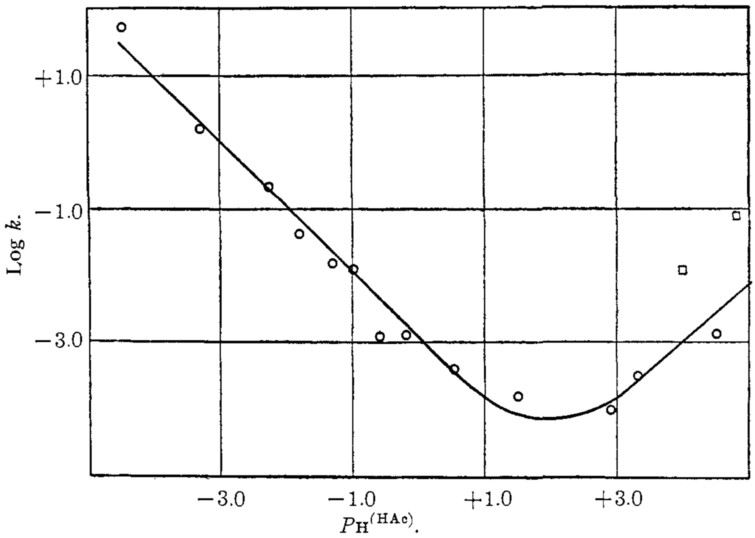

Fig. 1.—The rate of acetylation of β-naphthol in glacial acetic acid solutions. The smooth curve corresponds to Equation 2 with the omission of the last term. The experimental values are shown by the circles; the squares indicate the experiments using pyridine.

From the preparative point of view, it should be noted that the results reported in Table II cover a very wide range in the rates of reaction. Thus, in the perchloric acid solution (No. 1) the time required for 50% reaction is less than six seconds as compared with five days in the slowest reaction (No. 11) and ten minutes with a 3 molar pyridine solution. It is thus possible by choosing the proper buffer solution to regulate quite closely the rate of the reaction between acetic anhydride and hydroxy compounds.

Summary

Measurements have been made of the rate of acetylation of β-naphthol by acetic anhydride in glacial acetic acid solutions of definite hydrogen ion

activity. The rate varies nearly a million-fold and is dependent on the acidity or basicity of the medium. The maximum rate is at $P_H^{(HAc)}$ -4.5, the minimum at about $P_H^{(HAc)}$ $+2.0$; over this range the rate is approximately proportional to the hydrogen ion activity. Between $+2.0$ and $+5.0$ the rate increases again showing that the process is one which is subject to both acid and basic catalysis.

CAMBRIDGE 38, MASSACHUSETTS

NOTE

A Simpler Derivation of the Cook Formula for the Determination of the Acetyl Value of Fats and Oils.—It is now generally conceded that the André–Cook[1] method of determining the acetyl number is more accurate and more rapid than the older method of Lewkowitsch.[2] The André–Cook method consists merely in determining the saponification value of the oil before and after acetylation. The acetyl value is then calculated by means of the formula

$$A = \frac{S' - S}{1 - 0.00075S}$$

where A is the acetyl value, and S and S' are the saponification values before and after acetylation. The derivations of this formula given by André and by Cook are rather involved.

In this note the same formula is derived by a simpler method. Let x represent the weight of acetylated oil which will contain 1 mole (59 g.) of *acetate* radical. Then x g. of acetylated oil will yield one mole of acetic acid on hydrolysis, and this quantity of acetic acid will require 1 mole or 56,000 mg. of potassium hydroxide for neutralization. Therefore, the acetic acid from 1 g. of acetylated oil will require $56{,}000/x$ mg. of potassium hydroxide, and

$$A = \frac{56{,}000}{x} \text{ or } x = \frac{56{,}000}{A} \qquad (1)$$

By definition of x it is obvious that x g. of acetylated oil was derived from a quantity of original oil which contained 1 mole (17 g.) of hydroxyl radical. The gain in weight during the acetylation of this quantity of oil was $59-17$ or 42 g. Therefore x g. of acetylated oil was derived from (x-42) g. of original oil.

Since A is equal to the number of mg. of potassium hydroxide needed to neutralize the acetic acid from 1 g. of acetylated oil, Ax mg. of potassium hydroxide will be needed for the acetic acid from x g. of acetylated oil. Similarly $S'x$ mg. of potassium hydroxide will be needed to saponify x g. of acetylated oil; and $S(x-42)$ mg. will be needed to saponify $(x-42)$ g. of

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[1] André, *Bull. soc. chim.*, [4] **29**, 745 (1921); Cook, THIS JOURNAL, **44**, 392 (1922).

[2] Lewkowitsch, *J. Soc. Chem. Ind.*, **16**, 503 (1897).