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The Anomerization of Sugar Acetates. Glucose Pentaacetates in Acetic Acid–Acetic Anhydride Mixtures Catalyzed by Sulfuric and Perchloric Acids

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Perchloric acid behaves as a strong and sulfuric acid as a weak acid when compared by their catalysis of the anomerization of glucose pentaacetates in the solvent acetic acid–acetic anhydride. When perchloric acid is the catalyst the rate in approximately 98% acetic anhydride is about 600 times the rate in acetic acid. The suggested mechanism considers the anomerization a displacement process and the rate dependent upon the formation of sugar acetate carbonium ion. The formation of the carbonium ion from the conjugate acid of the sugar acetate [$SOAcH^+$] can account for the rate in acetic acid but not the rapid increase in concentrated solutions of acetic anhydride. If the species Ac^+ is present in acetic anhydride solutions, and a carbonium ion is formed by dissociation of $SOAc_2^+$, suggested equilibria can account for the rapid increase in rate. Calculated rates assuming the rate of anomerization will follow an expression of the type: rate = $k_a[SOAcH^+] + k_b[SOAc_2^+]$, agree quite well with experimental rates. The chief obstacle seems to be the uncertainty in the equilibria which involve acid species in the solvent system.

Introduction

Acid catalysts are commonly used in the preparation of sugar acetates. When a pure form of a sugar (α or β) is the starting material, it is possible with acid catalysts to obtain good yields of the acetate corresponding to the anomer used, providing the rate of esterification at the anomeric center greatly exceeds the rate of anomerization. If the reaction goes to completion, the composition is dependent upon the equilibrium

$$\alpha\text{-acetate} \rightleftarrows \beta\text{-acetate}$$

In many cases the equilibrium lies so far in favor of one of the anomers that it is the only one isolated.

Sulfuric acid has probably been used more than any other acid as a catalyst for acetylation and anomerization but Lewis acids are good catalysts in these reactions.

The first report on rates of isomerization was by Jungius[1] who used zinc chloride in acetic anhydride. Freudenberg and Soff[2] followed the changes in rotation when α- and β-forms of glucose acetates were dissolved in acetic acid–acetic anhydride mixtures containing sulfuric acid, but they did not calculate rates. Recently Bonner[3] reported on the kinetics of the anomerization of glucose pentaacetates by sulfuric acid in mixtures of acetic acid and acetic anhydride. In the present paper the rate of anomerization in acetic acid and in mixtures of acetic acid and acetic anhydride up to about 98% acetic anhydride is reported when the reaction is catalyzed by sulfuric and perchloric acids. Our interpretation of the kinetics, based on results with perchloric acid, differs from that suggested by Bonner, and a different mechanism of the anomerization is proposed.

Equilibrium of the Reaction.—When sulfuric or perchloric acid is added to either α- or β-1,2,3,4,6-pentaacetylglucose dissolved in mixtures of acetic acid and acetic anhydride the rotation changes to the same constant value. Typical curves are shown in Fig. 1.

The composition at equilibrium calculated from the rotations of the α- and β-forms was approximately 87% α and 13% β. This assumes the above α- and β-forms were the only products in the equilibrium mixture. Bonner[3] presented convincing evidence that this is so in acetates isolated from the anomerization. He found 83.5% α and 16.5% β in the product isolated. Jungius found approximately 90% α and 10% β at equilibrium and Freudenberg and Soff 88% α and 12% β. In nearly all solvent mixtures the rotation reached the same final equilibrium with either catalyst in our runs.

Rate Constants and Sugar Acetate Concentration.—The reversible reaction

$$\alpha\text{-acetate} \underset{k_2}{\overset{k_1}{\rightleftarrows}} \beta\text{-acetate} \qquad (1)$$

is analogous to the mutarotation of sugars. Solution of the equation

$$-\,d[\alpha]/dt = d[\beta]/dt = k_1[\alpha] - k_2[\beta] \qquad (2)$$

and expressing concentrations in terms of rotation gives the expression

$$k_1 + k_2 = \frac{1}{t}\,2.303 \log \frac{a_0 - a_\infty}{a_t - a_\infty} \qquad (3)$$

first applied by Hudson.[4]

Typical rate constants obtained in three runs using both acids in solvents of different compositions and calculated by equation 3 are shown in Table I.

Rate constants held up well throughout individual runs in nearly all cases. In the examples shown the calculations were continued until the rotation change was more than 90% completed. The last column shows that satisfactory constants can be obtained when the reaction is rapid. With perchloric acid there was no indication of a drift in rates during runs, except in some of the runs when the catalyst concentration was less than 0.001 *M* in nearly 100% acetic anhydride. Apparently some perchloric acid is lost due to the presence of a

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[1] C. L. Jungius, *Z. physik. Chem.*, **52**, 97 (1905).

[2] K. Freudenberg and K. Soff, *Ber.*, **69**, 1245 (1936).

[3] W. J. Bonner, THIS JOURNAL, **73**, 2059 (1951).

[4] C. S. Hudson, *Z. physik. Chem.*, **44**, 487 (1903).

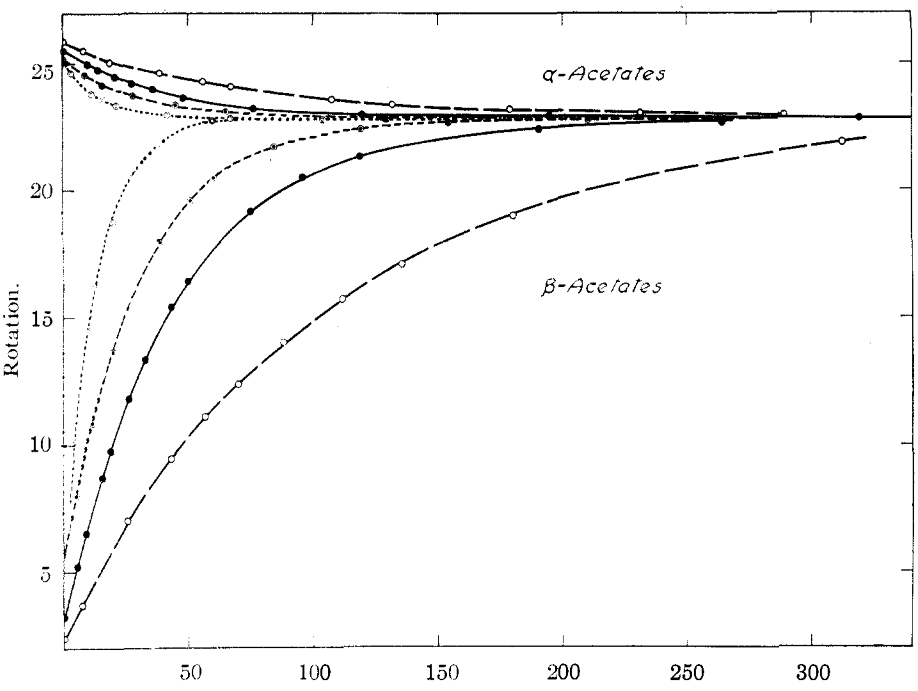

Fig. 1.—Mutarotation of α- and β-pentaacetates in acetic acid–acetic anhydride: —O—O—, 0.177 M H_2SO_4; —●—●—, 0.354 M H_2SO_4; - -○- -○- -, 0.178 M $HClO_4$; - -◎- -◎- -, 0.350 M $HClO_4$. Rotation is in arbitrary units; zero time is that of first reading.

small amount of oxidizable substance in the solvent. With sulfuric acid, however, rates dropped during a run as much as 50% when the anomerization was carried out in acetic acid and to a very slow rate when the solvent approached 100% acetic anhydride.

TABLE I

RATE CONSTANTS FOR RUNS AT 25° WITH 0.0513 M GLUCOSE PENTAACETATE CATALYZED BY H_2SO_4 AND $HClO_4$

0.177 M H_2SO_4 in 4.07 M $(AcOH)_2$ plus 5.38 M Ac_2O		0.356 M $HClO_4$ in 100% $(AcOH)_2$		0.00178 M $HClO_4$ in 0.18 M $(AcOH)_2$ plus 10.15 M Ac_2O	
Time, min.	$k_1 + k_2$, min.$^{-1}$	Time, min.	$k_1 + k_2$, min.$^{-1}$	Time, min.	$k_1 + k_2$, min.$^{-1}$
7	0.0120	7	0.0232	2	0.0700
18	.0118	15	.0237	3	.0698
24	.0120	19	.0239	4	.0717
32	.0118	23	.0239	6	.0741
45	.0118	32	.0237	7	.0732
54	.0121	39	.0239	13	.0724
68	.0117	55	.0237	15	.0705
97	.0118	80	.0239	16	.0736
129	.0118			22	.0714
173	.0114				

Bonner[3] observed a downward drift in rate during runs when sulfuric acid was the catalyst in solvents high in acetic anhydride and he also found that sulfuric acid in solutions containing acetic anhydride lost their catalytic power when allowed to stand. He described the observation as "catalyst aging." The results are due to the formation of sulfoacetic acid by a reaction of sulfuric acid and acetic anhydride first described by Franchimont.[5]

The over-all reaction is usually written[6a]

$$Ac_2O + H_2SO_4 = HOSO_2CH_2COOH + AcOH \quad (4)$$

but in excess acetic anhydride an equilibrium mixture of sulfoacetic acid and its acetic acid anhydrides[6b] are the expected products. As sulfoacetic acid forms[7] the rate progressively decreases because the product formed in the solvent mixture is a weaker acid than sulfuric.

From the results in Table II it is clear that the rate of anomerization can be considered first order with respect to sugar acetate concentration over the range compared.

Effect of Concentration of Acid.—Anomerization rates plotted against perchloric acid concentration in three solvent mixtures are shown in Fig. 2.

The concentrations of perchloric acid in the solvent of 10.15 M acetic anhydride (curve I) are given in Table III.

The experimental rate in each solvent follows the expression

$$\text{rate} = k[\text{SOAc}][\text{H}^+] \quad (5)$$

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(5) A. P. N. Franchimont, *Compt. rend.*, **92**, 1054 (1881); *Rec. trav. chim.*, **7**, 27 (1888).

(6) (a) T. F. Murray and W. O. Kenyon, THIS JOURNAL, **62**, 1230 (1940); (b) T. F. Doumai and J. F. Cueno, U. S. Patent 2,550,141; *C. A.*, **45**, 9556 (1951).

(7) Murray and Kenyon[6a] found the rate of formation of sulfoacetic acid at 40° to increase about 100-fold in acetic acid-acetic anhydride mixtures when acetic anhydride was increased from 25 to 90%. In this range of solvent composition formation of sulfoacetic acid did not interfere with satisfactory measurement of the rate of anomerization because the rate of anomerization is much faster. Apparently the rate of sulfoacetic acid formation increases more rapidly than the rate of anomerization as acetic anhydride concentration is increased, so that when the solvent approached 100% acetic anhydride the anomerization rate drifts downward with time. We have found stock catalysts of sulfuric acid in equal volumes of acetic acid and acetic anhydride when stored in the refrigerator can be used over a period of several days without diminution of rates.

TABLE II

RATE CONSTANTS FOR THE ANOMERIZATION OF α- AND β-GLUCOSE PENTAACETATES IN EQUAL VOLUMES OF AcOH AND Ac_2O AT 25°

Form	Concn., %	Catalyst, M	$k_1 + k_2$, min.$^{-1}$
		H_2SO_4	
β	2	0.177	0.0110
α	2	.177	.0112
β	3	.177	.0109
α	5	.177	.0107
β	5	.177	.0104
		H_2SO_4	
β	1	0.354	0.0212
α	5	.354	.0212
β	5	.354	.0217
α	7	.354	.0213
		$HClO_4$	
β	2	0.089	0.0186
α	2	.089	.0189
β	3	.089	.0182
β	5	.356	.0801
α	5	.356	.0812

TABLE III

ANOMERIZATION OF β-GLUCOSE PENTAACETATE AT 25° BY $HClO_4$ IN A SOLUTION OF 10.15 M Ac_2O + 0.18 M $(AcOH)_2$

$HClO_4$, M	$k_1 + k_2$, min.$^{-1}$
0.000178	0.0069
.000534	.0207
.00089	.0368
.00142	.0575
.00178	.0719

where SOAc = sugar acetate, providing perchloric acid is completely dissociated. This is the behavior expected if the rate is dependent upon the formation of sugar acetate conjugate acid and perchloric is a strong acid in each solvent.

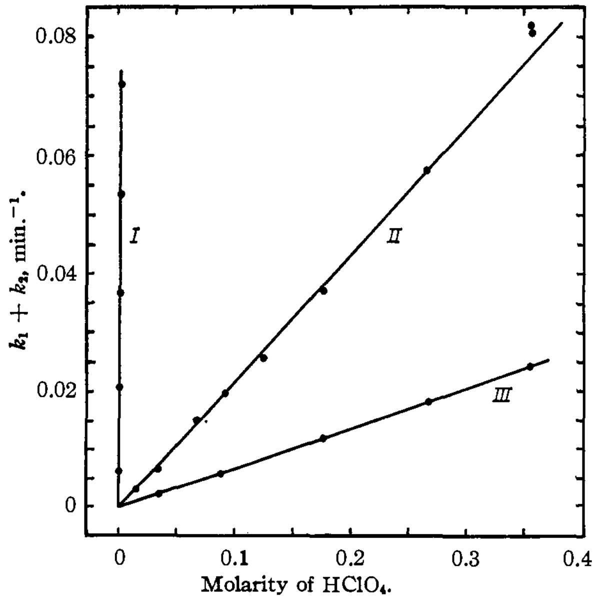

Fig. 2.—Relationship between rate and concentration of $HClO_4$: curve I at 10.15 M Ac_2O plus 0.18 M $(AcOH)_2$; curve II, 4.90 M Ac_2O plus 4.47 M $(AcOH)_2$ at 0.178 M $HClO_4$ with constant ratio of solvents at other concentrations of $HClO_4$, curve III, acetic acid only solvent.

While it is clear that sulfuric is a weak acid in the solvent used, the rate did not decrease when plotted against concentration of sulfuric (Fig. 3) as equation 5 predicts for a weak electrolyte. The plot is linear when measured in a solution of 4.85 M acetic anhydride + 4.50 M acetic acid dimer (curve II) except at low catalyst concentrations. Bonner[3] obtained essentially the same results in a solvent of similar composition. At a higher acetic acid concentration (curve III) the rate did not increase linearly as the concentration of sulfuric acid increased but fell off in the direction predicted by the dissociation of a weak electrolyte. When the rate was measured at high acetic anhydride concentration (curve I) the rate increased more rapidly

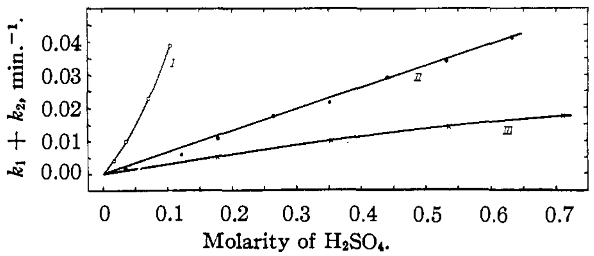

Fig. 3.—Relationship between rate and concentration of H_2SO_4: curve I, 9.52 M Ac_2O plus 0.68 M to 0.66 M $(AcOH)_2$; curve II, 4.84 M Ac_2O plus 4.51 M (AcOH) at 0.177 M H_2SO_4 with constant solvent ratio at other concentrations of H_2SO_4; curve III, 1.24 M Ac_2O plus 7.50 to 7.32 M $(AcOH)_2$.

TABLE IV

THE ANOMERIZATION OF GLUCOSE PENTAACETATE AT 25° IN ACETIC ACID–ACETIC ANHYDRIDE MIXTURES CATALYZED BY H_2SO_4

In the calculation a linear relationship between acid concentration and $k_1 + k_2$ was assumed

Molar concentrations			$k_1 + k_2$, min.$^{-1}$	
$(AcOH)_2$	Ac_2O	H_2SO_4	Detd.	Calcd. to 0.177 M H_2SO_4
8.52	0	0.177	0.00067	0.00067
8.42	0	.354	.0030	.0015
8.33	0	.708	.0076	.0019
8.29	0.20	.177	.00132	.0013
8.17	.41	.177	.0023	.0023
7.97	.60	.354	.0060	.0030
7.84	.82	.177	.0032	.0032
7.50	1.24	.177	.00555	.00555
6.82	2.01	.177	.00615	.00615
5.80	3.30	.177	.00875	.00875
5.42	3.59	.354	.0182	.0091
4.51	4.84	.177	.0115	.0115
4.08	5.37	.177	.0118	.0118
2.78	6.87	.354	.0410	.0205
2.67	7.07	.177	.0191	.0191
2.41	7.73	.106	.0127	.0212
1.69	8.29	.0708	.0101	.0253
1.44	8.54	.177	.0310	.0310
0.93	9.14	.177	.0416	.0416
.67	9.51	.106	.0392	.0655
.63	9.48	.177	.0755	.0755
.44	9.80	.0354	.0207	.104
.27	10.01	.0354	.0253	.127
.22	10.07	.0177	.0173	.173

with sulfuric acid concentration than if the relationship were linear. In pure acetic acid the change in rate from 0.177 to 0.708 *M* sulfuric was much more like curve I than curve III (see first three values in Table IV).

These data and those of Bonner suggest that in addition to H^+, molecular sulfuric acid and bisulfate ion may be catalysts in the anomerization. Bonner[3] added lithium bisulfate to a solution containing sulfuric acid and found the rate of anomerization essentially the same as with sulfuric acid alone. From this he concluded sulfuric acid was completely dissociated. In the absence of sulfuric acid, lithium bisulfate catalyzed the anomerization at a very slow rate. Kolthoff and Willman[8] found that lithium ion solvated in acetic acid to a greater extent than other univalent cations. Addition of lithium bisulfate would then give sulfuric acid and bisulfate ion in solution. In the presence of acetic anhydride bisulfate would likely form the weak acid sulfoacetic.[9] When Kolthoff and Willman measured the acid strength of several acids in acetic acid, they found them in the order: $HClO_4 > HBr > H_2SO_4 > HCl > HNO_3$. Only perchloric was considered a strong acid.

The Effect of Solvent Composition.—Data in Figs. 2 and 3 show that the rate of anomerization increases as the ratio acetic anhydride/acetic acid is increased. Rates were determined over the entire range from pure acetic acid to approximately 98% acetic anhydride with each catalyst. To facilitate comparisons all rates were calculated to the same concentration of acid.

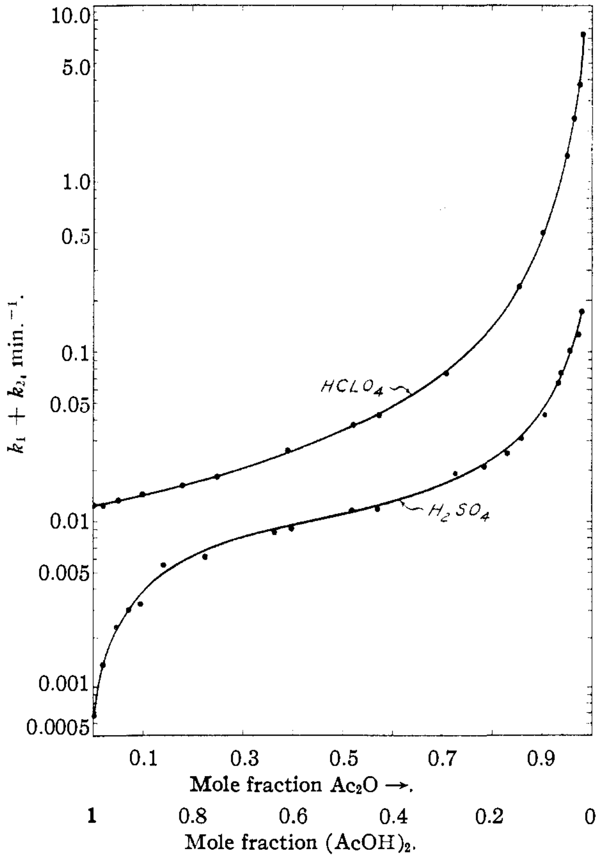

Fig. 4.—Dependence of rate upon solvent composition. All rates calculated to 0.177 *M* H_2SO_4 or 0.178 *M* $HClO_4$.

In only those cases where the anomerization was carried out at 0.177 *M* sulfuric acid is the comparison of rates strictly valid. At high concentrations of acetic anhydride, where more dilute sulfuric acid was used (last three runs Table IV) the rates calculated to 0.177 *M* acid are probably too low (Fig. 3). With perchloric acid calculation of rates to the same concentration of acid seems to give a true comparison over the entire range.

TABLE V

THE ANOMERIZATION OF GLUCOSE PENTAACETATE AT 25° IN ACETIC ACID–ACETIC ANHYDRIDE MIXTURES BY $HClO_4$

	Molar concentrations			$k_1 + k_2$, min.$^{-1}$	
Run	$(AcOH)_2$	Ac_2O	$HClO_4$	Detd.	Calcd. to 0.178 *M* $HClO_4$
1	8.55	0	0.178	0.0120	0.0120
2	8.40	0.21	.089	.00611	.0122
3	8.18	.45	.089	.00667	.0133
4	7.86	.87	.089	.00712	.0142
5	7.20	1.63	.089	.00805	.0161
6	6.68	2.27	.089	.00920	.0184
7	5.58	3.57	.148	.0221	.0265
8	4.47	4.90	.178	.0372	.0372
9	4.05	5.45	.0356	.00828	.0414
10	2.91	6.83	.0356	.0149	.0745
11	1.91	8.05	.0089	.00805	.161
12	1.50	8.56	.0178	.0242	.242
13	1.03	9.11	.0089	.0251	.502
14	0.53	9.73	.00178	.0143	1.43
15	.36	9.91	.00178	.0235	2.35
16	.27	10.02	.00178	.0375	3.75
17	.18	10.15	.00178	.0719	7.19

In order to show the extreme range of rates and the variation of rates with solvent composition, $k_1 + k_2$ was plotted against mole fraction of acetic anhydride (Fig. 4). Since the range in rates is approximately 10^4, it was necessary to plot $k_1 + k_2$ on a log scale.

The fit is not too good when sulfuric acid is the catalyst but the general trend is evident. Except for the lower rates in high acetic acid concentrations with sulfuric acid catalyst both curves are similar. Over the middle range the curves are nearly parallel, then the perchloric acid curve rises faster than the sulfuric acid curve as the solvent contains increasingly more acetic anhydride. The faster increase in rate with perchloric acid at high concentrations of acetic anhydride is the result expected if the rates are dependent upon an acid species formed by the dissociation of a strong and weak acid and acetic acid is a stronger base than acetic anhydride. While we believe acetic acid is the stronger base and part of the increase in rates going from acetic acid to almost 100% acetic anhydride can be explained on the basis of relative basic strength, the shape of the curves (Fig. 4) and magnitude of the increase (600 times with perchloric) cannot be explained on this basis alone.

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[8] I. M. Kolthoff and A. Willman, THIS JOURNAL, **56**, 1007, 1014 (1934).

[9] H. A. E. Mackenzie, *J. S. African Chem. Inst. N. S.*, **3**, 1 (1950); *C. A.*, **45**, 3692 (1951).

Results obtained when sulfuric acid was the catalyst in pure acetic acid and in mixtures of low concentrations of acetic anhydride (Fig. 4) are difficult to interpret. Bonner was unable to isolate crystalline acetates from mutarotated β-glucose pentaacetate in acetic acid with sulfuric acid catalyst so concluded acetic anhydride was necessary for the anomerization. We find the equilibrium composition in acetic acid the same as in mixtures with acetic anhydride and when the anomerized solution with either catalyst was poured into ice cold sodium acetate solution, crystalline acetates readily precipitated. When a small amount of water is present the equilibrium rotation is different. This would be expected if some hemiacetal is formed by reaction with water. Since acetic anhydride was added equivalent to the calculated amount of water in the reagents, the presence of a trace of water or a trace of acetic anhydride is a difficult point to settle.

Kinetics and Mechanism of the Anomerization.—According to Bonner's mechanism of the anomerization[3] the rate is dependent upon the concentration of the sugar acetate and the conjugate acid of acetic anhydride. It now seems clear (Fig. 4) that if this mechanism is correct, the conjugate acid of acetic acid must also be considered a reacting species. The results when perchloric acid was the catalyst will be applied to inquire whether this mechanism can explain the rates. Since the sugar acetate must be considered one of the bases in the reaction mixture, the concentration of SOAc is dependent upon the equilibria

$$\text{SOAc} + \text{AcOH}_2^+ \overset{K_1}{\rightleftarrows} \text{SOAcH}^+ + \text{AcOH} \quad (6)$$

$$\text{SOAc} + \text{Ac}_2\text{OH}^+ \overset{K_2}{\rightleftarrows} \text{SOAcH}^+ + \text{Ac}_2\text{O} \quad (7)$$

and, if perchloric acid is completely dissociated

$$\text{SOAc} = \text{SOAc}_0 - \text{SOAcH}^+ = \text{SOAc}_0 - (\text{HClO}_4 - \text{AcOH}_2^+ - \text{Ac}_2\text{OH}^+) \quad (8)$$

where SOAc_0 = sugar acetate added; the following equations are obtained for the rate, R, in each of the two solvents.

$$R_{(\text{AcOH})} = k_3[\text{SOAc}][\text{AcOCH}_2^+] = \frac{k_3[\text{SOAc}][\text{HClO}_4][\text{AcOH}]}{K_1[\text{SOAc}] + [\text{AcOH}]} \quad (9)$$

$$R_{(\text{Ac}_2\text{O})} = k_4[\text{SOAc}][\text{Ac}_2\text{OH}^+] = \frac{k_4[\text{SOAc}][\text{HClO}_4][\text{Ac}_2\text{O}]}{K_2[\text{SOAc}] + [\text{Ac}_2\text{O}]} \quad (10)$$

We have no way of estimating K_1 and K_2, but, even if fairly large, the first term in the denominator can be neglected because the sugar acetate concentration is very small compared with acetic acid or acetic anhydride in each case so the rates should be given approximately by $k[\text{SOAc}_0][\text{HClO}_4]$. This is obeyed (Fig. 2 and Table II). If the anomerization follows equation 9, addition of an inert solvent should be without effect if K_1 is small and should retard the rate if K_1 is large. It was found, however, that dilution of acetic acid with carbon tetrachloride resulted in a sharp rise in rate. This result is strong evidence against equation 9 but the observed increase could be due to a solvent effect.

By use of the equilibrium

$$\text{AcOH}_2^+ + \text{Ac}_2\text{O} \overset{K_3}{\rightleftarrows} \text{Ac}_2\text{OH}^+ + \text{AcOH} \quad (11)$$

the following rate expression is obtained for the anomerization in a mixture of the two solvents

$$R_{(\text{mixture})} = \left\{\frac{[\text{SOAc}][\text{HClO}_4]}{K_1[\text{SOAc}] + [\text{AcOH}] + K_3[\text{Ac}_2\text{O}]}\right\} \times \{k_3[\text{AcOH}] + k_4K_3[\text{Ac}_2\text{O}]\} \quad (12)$$

Relative rates calculated from equation 12 can increase almost as rapidly as experimental rates when the concentration of acetic anhydride is increased providing we assume both K_1 and K_3 are so small the terms in which they appear in the denominator are negligible and SOAc does not change significantly; *i.e.*, $\text{AcOH}_2^+ \cong \text{HClO}_4$ and $\text{SOAc} \cong \text{SOAc}_0$. Equation 12 then reduces to

$$R = [\text{SOAc}][\text{HClO}_4]\left(k_3 + \frac{k_4K_3[\text{Ac}_2\text{O}]}{[\text{AcOH}]}\right) \quad (13)$$

Providing relative stoichiometric concentrations of the components can be calculated the rate increase by equation 13 can be calculated.

Up to now we have followed convention in writing equations 6, 7 and 11, but acetic acid is not best represented as a monomer. Numerous papers have appeared to show that acetic acid is a polymer both in solution and in vapor. Mackenzie and Winter[10] calculated freezing point data and believe that acetic acid can be best considered a dimer in mixtures with acetic anhydride until the latter exceeds 80%. At about 95% acetic anhydride they found the monomer present in greater concentration than the dimer. Acetic acid in solution is apparently best described by $(\text{AcOH})_n$, and if n = 2 we can include a dimerization constant

$$2\text{AcOH} \overset{K_4}{\rightleftarrows} (\text{AcOH})_2 \quad (14)$$

The equilibrium between the conjugate acids of the two solvents as expressed by equation 11 would then take the form

$$\text{AcOH}_2^+ + \text{Ac}_2\text{O} \overset{K_{3a}}{\rightleftarrows} \text{Ac}_2\text{OH}^+ + {}^1/_2(\text{AcOH})_2 \quad (15)$$

Another way to treat the situation is to write the equilibrium

$$(\text{AcOH})_2\text{H}^+ + \text{Ac}_2\text{O} \overset{K_{3b}}{\rightleftarrows} \text{Ac}_2\text{OH}^+ + (\text{AcOH})_2 \quad (16)$$

No doubt such an equilibrium exists but, whereas acetic acid dimer would be a stable species, addition of a proton would break a hydrogen bond so the conjugate acid would dissociate

$$(\text{AcOH})_2\text{H}^+ = \text{AcOH}_2^+ + {}^1/_2(\text{AcOH})_2$$

The increase in rates calculated by equation 13 from a selected base rate (run 5, Table V) using each of the three expressions for the equilibrium of solvent conjugate acids are in Table VI. The rate due to the first term was taken as the rate in pure acetic acid.

A plot of the calculated rates against mole fraction of acetic anhydride gives a curve similar in shape to the perchloric acid curve in Fig. 4, but even with assumptions to permit the maximum

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[10] H. A. E. Mackenzie and E. R. S. Winter, *Trans. Faraday Soc.*, **44**, 159 (1948).

TABLE VI

COMPARISON OF EXPERIMENTAL RATES WITH RATES CALCULATED BY EQUATION 13

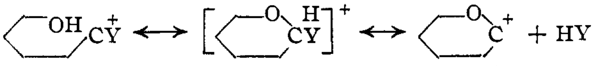
The expression for the concentration of acetic acid and acetic anhydride is in equations 11, 15 and 16 which define K_3, K_{3a} and K_{3b}, respectively. The units are the same as in Table V

Run	Exptl. rate minus rate in 100% AcOH	Rates calcd. from change of ratios $\frac{Ac_2O}{AcOH}$	$\frac{Ac_2O}{\sqrt{(AcOH)_2}}$	$\frac{Ac_2O}{(AcOH)_2}$
5	0.0041			
6	.0064	0.0062	0.0059	0.0062
7	.0145	.0116	.0102	.0116
9	.0294	.0246	.0184	.025
11	.149	.079	.040	.082
13	.490	.171	.063	.189
15	2.34	.65	.128	.973
16	3.74	1.03	.159	1.96

increase by equation 12, calculated rates do not increase as fast as experimental rates. The kinetic data do not fit the mechanism proposed by Bonner; therefore a mechanism which seems to best explain the hydrolysis of acetals will be applied to the anomerization of sugar acetates.

When a displacement of a glycosyl derivative gives a product with a different atom bonded to the anomeric carbon, *i.e.*, glycosyl chloride → glycoside, it is clear the bond between the anomeric carbon and aglucone is broken, but reactions of glucosides or glycosyl acetates which give back a product with a C_1–O bond the site of cleavage is by no means certain. Link and co-workers[11] have described displacements at the anomeric carbon of glycosides by methoxyl and hydroxyl ions (which probably follow S_N2 kinetics) and have demonstrated cleavage on either side of the glycosidic oxygen. Methoxide gave α-methyl glucoside with 3-phenyl-4-hydroxycoumarin β-glucoside and the methoxyaglucone with theobromine β-glucoside. Aromatic[11c] and a few other glycosides[12] are readily cleaved in alkaline solution but this can hardly be considered a general property of glycosides. Glycosyl derivatives are for the most part not readily displaced by anions or uncharged nucleophilic reagents unless an acid species is present. We have found that glucose acetates do not mutarotate when dissolved in acetic acid–acetic anhydride containing sodium acetate. Reactions which appear best interpreted as electrophilic displacements on oxygen with cleavage at the C_1–O bond are more common reactions of sugars. O'Gorman and Lucas[13] prepared acetals of optically active alcohols and obtained back after acid hydrolysis alcohols with no change in rotation. It seems likely that the reaction goes through a carbonium ion of the acetal carbon, as the above authors point out, and should follow S_N1 kinetics. We believe acid-catalyzed reactions of glycosyl derivatives are best interpreted by a similar carbonium ion mechanism.

If we represent the glycosyl radical by A, the derivative AY (a base where Y = OR, OCOR halogen) will react with an acid species. When the acid species is a proton doner, the conjugate acid AYH^+ can give two carbonium ion intermediates.[14]



B^+ AYH^+ A^+

Nucleophilic reagents (alcohols, organic acids, anions) can react with A^+ or B^+ to give a new glycosyl derivative. When the nucleophilic reagent, represented by ZH, reacts with A^+ the displacement product would be AZH^+. When the nucleophilic reagent reacts with B^+, the product BZH^+ must eliminate HY and recyclize to give the same displacement product AZH^+ produced from A^+. The products obtained at equilibrium would depend upon the abundance and nucleophilic character of the species reacting with the carbonium ions A^+ and B^+.

The anomerization of sugar acetates in the solvent acetic acid or acetic anhydride we consider to go primarily by a displacement process[15] through a carbonium ion intermediate. The ion corresponding to A^+ will be employed to illustrate the mechanism and in the equations but this choice is not intended to imply that the anomerization goes exclusively through this intermediate. Both B^+ and A^+ are expected intermediates and either will fit the mechanism proposed.

The conjugate acid of the sugar acetate $SOAcH^+$ is formed by a rapid equilibrium (equations 6 or 7) and dissociates to give the sugar acetate carbonium ion

$$SOAcH^+ \underset{k_{-6}}{\overset{k_6}{\rightleftarrows}} S^+ + AcOH \qquad (17)$$

Anomerization can occur in the rate expressed by $k_{-5}[S^+][AcOH]$ when the reaction goes in acetic acid. If the latter is very rapid compared with the rate of formation of the carbonium ion, the rate measured will be given by

$$R_{(AcOH)} = k_5[SOAcH^+] = k_5K_1[SOAc]([AcOH_2^+]/[AcOH]) \qquad (18)$$

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[11] (a) L. Spero, C. E. Ballou and K. P. Link, THIS JOURNAL, **71**, 3740 (1949); (b) C. E. Ballou and K. P. Link, *ibid.*, **71**, 3743 (1949); (c) J. A. Snyder and K. P. Link, *ibid.*, **74**, 1883 (1952).

[12] W. W. Pigman and R. M. Goepp, "Carbohydrate Chemistry," Academic Press, Inc., New York, N. Y., 1948, p. 199.

[13] J. M. O'Gorman and H. J. Lucas, THIS JOURNAL, **72**, 5489 (1950).

[14] A more complete picture would include additional contributing structures of the carbonium ions due to participation of neighboring groups such as acetoxy and hydroxy. These stabilize the carbonium ion and influence the steric course of each displacement. If the acid species reacting with AY is a carbonium ion or Lewis acid one carbonium ion would be the same as A^+ but the ones corresponding to B^+ would have the carbonium ion bonded to C_1-oxygen and the other would be a zwitterion.

[15] β → α transformations by acid catalysts have been described by Pacsu, Lindberg and others (summarized by Montgomery and Smith[16]) when acetylated glycosyl derivatives are dissolved in an inert solvent which does not contain the group attached to the anomeric center. This anomerization has been described as an intramolecular transformation. In the scheme now suggested inversion in this case appears most likely to occur in one of the steps $AYH^+ \rightarrow B^+ \rightarrow AYH^+$ (with necessary structural modifications when the acid catalyst is not a proton donor). Inversion could conceivably occur by bond formation with an anion from the catalyst with the anomeric carbon of species B^+ followed by elimination of the anion upon cyclization. The intermediate B^+ in acetylating solvents should lead to more products than α- and β-1,2,3,4,6-pentaacetylglucose. Other acetates may be present but in case the equilibrium greatly favors the two products considered in this paper (which must be true with glucose) these could escape detection.

[16] R. Montgomery and F. Smith, *Ann. Rev. Biochem.*, **21**, 84 (1952).

In acetic anhydride S^+ forms as in acetic acid but in the anomerization step acetic anhydride would react with the carbonium ion

$$S^+ + Ac_2O \underset{k_6}{\overset{k_{-6}}{\rightleftarrows}} SOAc_2^+ \qquad (19)$$

The rate expression is

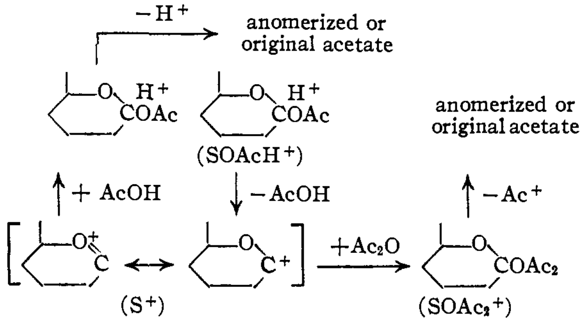
$$R_{(Ac_2O)} = k_6K_2[SOAc]\,\frac{[Ac_2OH^+]}{[Ac_2O]} + k_6[SOAc_2^+] \qquad (20)$$

In case $SOAc_2^+$ disappears by the reaction

$$SOAc_2^+ + AcOH \overset{1/K_5}{\rightleftarrows} SOAc + Ac_2OH^+ \qquad (21)$$

and the equilibrium lies far to the right so that the concentration of $SOAc_2^+$ is negligible compared to $SOAcH^+$, the second term in equation 20 can be dropped.

The following diagram is presented to clarify the picture in the two solvents.



If the anomerization goes by the mechanism proposed, acetyl ion (Ac^+) is a product of the anomerization step when the solvent is acetic anhydride.

The plot of $k_1 + k_2$ against perchloric acid concentration (Fig. 2) is a straight line as required by equation 18. This is true provided $AcOH_2^+ \cong HClO_4$. While K_1 (equation 6) may be quite large, $SOAcH^+$ must be small compared to $AcOH_2^+$ because $SOAc_0$ was 0.0513 M and $(AcOH)_2$ about 8.5 M. From the relation in equation 8 the rate is given by

$$R_{(AcOH)} = \frac{k_5K_1[HClO_4][SOAc]}{K_1[SOAc] + [AcOH]} \qquad (22)$$

This gives a straight line providing K_1[SOAc] is very small compared to AcOH. If K_1[SOAc] is appreciable it should have shown up when the concentration of sugar acetate was varied. We will assume from now on that the concentration of $SOAcH^+$ is negligible and the concentration of solvent conjugate acids is equal to the concentration of perchloric acid.

When the value for Ac_2OH^+ from equation 11 is substituted into equation 20 and, making use of the relation $K_1 = K_2K_3$, we obtain equation 18. This then gives the predicted rate in a mixture of two solvents differing in basic strength if the rate is dependent upon the formation of $SOAcH^+$. The results cannot, however, be adequately explained on the basis of relative basic strength. Unreasonable values for the equilibrium of solvent conjugate acids (such as $K_{3b} = 8.5 \times 10^{-5}$) are required to give the range in rates in Table V. Calculated rates using this value do not follow experimental rates over much of the range. Evidence that acetic anhydride is a weaker base than acetic acid has been presented. If acetic anhydride is the stronger base it should slow down the rate as Bonner found when the bases, dioxane and butyl ether, were added to the anomerization mixture.

Hammett[17a] has found the acidity function (H_0) to follow a simple relation to the rate of many acid-catalyzed reactions. If the rate-determining step in the anomerization of sugar acetates is the formation of S^+ from $SOAcH^+$ the acidity function should apply. Hammett and Paul[17b] pictured the hydrolysis of sucrose to go by a mechanism similar to that now proposed for the anomerization of glucose acetates and the rate followed the acidity function for all acids except trichloroacetic. The advantage of H_0 lies in the fact that changes in activity coefficients, which we have not considered up to now, appear to cancel out.

From equations given we can write

$$R = k[SOAcH^+]\,(\gamma_{SOAcH^+}/\gamma_{X^+}) \qquad (23)$$

where γ_{X^+} is the activity coefficient of the activated complex. By employing equilibria for the formation of $SOAcH^+$, setting $a_{AcOH_2^+} + a_{Ac_2OH^+} = a_{H^+}$ and the activity of the solvent $N_{AcOH} + N_{Ac_2O} = 1$, equation 23 takes the form

$$R = kKa_{H^+}(\gamma_{SOAc}/\gamma_{X^+}) \qquad (24)$$

and by definition of H_0[17a] we obtain

$$-\log R = -\log kK + H_0 \qquad (25)$$

Providing the ratio of the activity coefficient of the activated complex to the sugar acetate is affected by the medium in the same way as the indicator ratio γ_{BH^+}/γ_B found in the experimental determination of H_0, a plot of log ($k_1 + k_2$) against H_0 should give a straight line of slope = −1.

Mackenzie and Winter[10] have measured apparent H_0 values in solutions of 0.0778 M perchloric acid in mixtures of acetic acid and acetic anhydride. The rates in Table V calculated to 0.0778 M perchloric plotted against H_0 values of Mackenzie and Winter[18] are shown in Fig. 5.

While the first five points which covered the range 2.27 to 6.8 M acetic anhydride (runs 6–10, Table V) come very close to a straight line of slope −0.95, at higher concentrations the rate increases much too fast. The rate of acetylation of quinones[19] followed H_0 up to about 7 M acetic anhydride then increased in about the same manner as the data in Fig. 5. The reason suggested for the failure of the rate to follow H_0 in high concentrations of acetic anhydride[19] is this solvent contains acetyl ions in the presence of a strong acid such as perchloric.

We have already seen that if the anomerization

(17a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 267.

(17b) L. P. Hammett and M. A. Paul, THIS JOURNAL, **56**, 830 (1934).

(18) The H_0 values plotted in Fig. 5 correspond to those for the acetic anhydride concentrations in our solutions and in those of Mackenzie and Winter. The ratio acetic acid/acetic anhydride differed because the volume occupied by the sugar acetate and catalyst was greater than the reactants in the solutions of Mackenzie and Winter. The difference in composition was, however, small. The values Mackenzie and Winter reported from measurements with the indicator 2,6-dimethoxybenzoquinone may not be identical with Hammett's H_0.

(19) H. A. E. Mackenzie and E. R. S. Winter, *Trans. Faraday Soc.*, **44**, 171, 243 (1948).

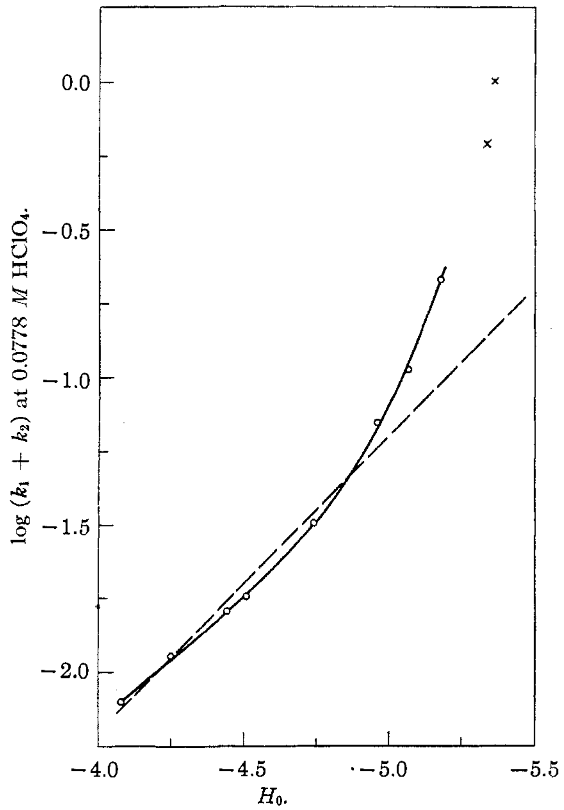
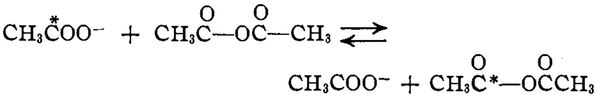


Fig. 5.—Relationship between rate and acidity function: ----, has slope = −1. The points indicated by X are extrapolated H_0 values.

proceeds through a carbonium ion mechanism the species Ac$^+$ is a product of the process when the solvent is acetic anhydride. Acetyl ion is not new as it has been suggested in the Friedel–Crafts and other reactions. Mackenzie and Winter[19] and Burton and Praill,[20] who prepared p-methoxyacetophenone from anisole in acetic anhydride with perchloric acid, zinc chloride, acetyl chloride and acetyl perchlorate (silver perchlorate dissolved in acetyl chloride), have presented a case for the presence of acetyl ions in solutions of acetic anhydride. Part of the evidence cited was the fact that the specific conductance of acetic anhydride is much greater than that of acetic acid and an exchange reaction between acetate containing radioactive carbon readily occurred with acetic anhydride.[21] Apparently the reaction goes as



$$\mathrm{CH_3\overset{*}{C}OO^- + CH_3\overset{O}{C}{-}O\overset{O}{C}{-}CH_3 \rightleftarrows CH_3COO^- + CH_3\overset{O}{C}{}^*{-}O\overset{O}{C}CH_3}$$

The species Ac$^+$ is an attractive one since it leads to a simple mechanism for many reactions. If the reaction

$$\mathrm{ROA + Ac^+ = ROAc + A^+} \qquad (26)$$

where A$^+$ = H$^+$ or a carbonium ion, is a general one, it would explain many reactions of acetic anhydride. In the case studied by Burton and Praill the reaction appears to be

$$\mathrm{RH + Ac^+ = RAc + H^+} \qquad (27)$$

so reactions of Ac$^+$ are not limited to atoms bonded to oxygen.

We have found the heterogeneous acetylation of sugars goes much more rapidly when the solid is suspended in acetic anhydride than when in a mixture of acetic acid–acetic anhydride with perchloric acid catalyst and that perchloric acid is a better catalyst than sulfuric acid or zinc chloride. Reaction 26 suggests a simple explanation for the relative rates.

In the anomerization of sugar acetates Ac$^+$ would be an acid and, consistent with the mechanism proposed, the rate would depend upon the formation of S$^+$ as

$$\mathrm{SOAc_2{}^+ \underset{k_{-6}}{\overset{k_6}{\rightleftarrows}} S^+ + Ac_2O} \qquad (28)$$

By making the same assumptions regarding the rate-determining step as with SOAcH$^+$, the rate due to SOAc$_2{}^+$ is given by

$$R_{(\mathrm{SOAc_2{}^+})} = k_6[\mathrm{SOAc_2{}^+}] \qquad (29)$$

This is the second term in equation 20.

Mackenzie and Winter preferred to assume Ac$^+$ free in solution but it must be solvated since it would be a strong electrophilic species. It could arise from the conjugate acids of acetic anhydride (this may be considered Ac$^+$ solvated by acetic acid) or acetic acid.

$$\mathrm{AcOH_2{}^+ + 2Ac_2O \overset{K_6}{\rightleftarrows} Ac_2OAc^+ + 2AcOH} \qquad (30)$$

Treffers and Hammett[22] have convincing evidence that diortho substituted benzoic acid gives a carbonium ion in sulfuric acid. The postulated rate-determining species (SOAc$_2{}^+$) would be formed by equation 21, and

$$\mathrm{Ac_2OAc^+ + SOAc \overset{K_7}{\rightleftarrows} SOAc_2{}^+ + Ac_2O} \qquad (31)$$

By combining equations 29 and 21 the rate expression for the term now being considered becomes

$$R_{(\mathrm{SOAc_2{}^+})} = k_6K_5[\mathrm{SOAc}]\frac{[\mathrm{Ac_2OH^+}]}{[\mathrm{AcOH}]} \qquad (32)$$

Combining equations 31 and 30 with 29 and utilizing equations 11, 15 or 16 gives equations of the same form as 32 except with different constants.

The rate of anomerization by the mechanism suggested is dependent upon a first order dissociation of SOAcH$^+$ and SOAc$_2{}^+$ to give S$^+$. The SOAcH$^+$ rate in the two solvents is given by

$$\frac{\mathrm{SOAcH^+\ rate\ in\ Ac_2O}}{\mathrm{SOAcH^+\ rate\ in\ AcOH}} = \frac{K_2[\mathrm{Ac_2OH^+}]}{K_1[\mathrm{Ac_2O}]} \times \frac{[\mathrm{AcOH}]}{[\mathrm{AcOH_2{}^+}]} = \frac{[\mathrm{AcOH}]}{K_3[\mathrm{Ac_2O}]} \qquad (33)$$

and in a mixture by

$$\frac{\mathrm{SOAcH^+\ rate\ in\ mixture}}{\mathrm{SOAcH^+\ rate\ in\ AcOH}} = \frac{[\mathrm{AcOH_2{}^+}]}{[\mathrm{AcOH}]}(\mathrm{mixture}) \times \frac{[\mathrm{AcOH}]}{[\mathrm{AcOH_2{}^+}]}(\mathrm{AcOH}) \qquad (34)$$

These equations assume the SOAcH$^+$ rates depend upon relative basic strength only (no solvent ef-

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[20] H. Burton and P. F. G. Praill, *J. Chem. Soc.*, 1203, 2034 (1950); 726 (1951).

[21] S. Ruben, M. G. Allen and P. Nahinsky, This Journal, **64**, 3050 (1942).

[22] H. P. Treffers and L. P. Hammett, *ibid.*, **59**, 1708 (1937).

TABLE VII

COMPARISON OF RATES CALCULATED BY EQUATIONS 34 AND 32 WITH EXPERIMENTAL RATES

		Calcd. for K_{3a} = 0.02			Calcd. for K_3 = 0.2			Calcd. for K_3 = 0.4		
Run	Exptl. rate	$SOAcH^+$ rate	$SOAc^+$ rate	Sum	$SOAcH^+$ rate	$SOAc_2$ rate	Sum	$SOAcH^+$ rate	$SOAc_2^+$ rate	Sum
3	0.0133	0.0122	(0.0011)[a]		0.0125	(0.0008)[a]		0.0124	(0.0009)[a]	
4	.0142	.0125	.0022	0.0147	.0129	.0016	0.0145	.0128	.0017	0.0145
5	.0161	.0132	.0044	.0176	.0139	.0036	.0175	.0135	.0039	.0174
6	.0184	.0139	.0067	.0206	.0149	.0060	.0209	.0144	.0060	.0204
8	.0372	.0157	.0242	.0399	.021	.028	.049	.019	.027	.046
10	.0745	.0194	.0429	.0623	.028	.081	.109	.023	.076	.099
12	.242	.0281	.099	.127	.044	.301	.345	.030	.234	.264
13	.502				.057	.560	.617	.036	.416	.452
14	1.43				.069	1.55	1.62	.041	1.02	1.06
16	3.75	.056	.616	.67	.085	3.78	3.87	.046	2.19	2.24

[a] Difference between experimental and calculated $SOAcH^+$ rate. The units are the same as in Table V.

fects) and that the concentration of solvent conjugate acids $\cong HClO_4$.

The total rate in acetic acid is due to $SOAcH^+$ so the $SOAcH^+$ rate in a mixture can be calculated by equation 34 for any assumed value for the equilibrium between solvent conjugate acids as defined by K_3 or K_{3a}. The experimental rate minus the $SOAcH^+$ rate gives the $SOAc_2^+$ rate. By selecting a small $SOAc_2^+$ base rate from a run with the solvent high in acetic acid a $SOAc_2^+$ rate can be calculated over a wide solvent concentration range from equation 32. Calculated $SOAcH^+$ and $SOAc_2^+$ rates[23] are shown for three values for the equilibrium constants in Table VII.

K_{3a} which treats acetic acid as a dimer gives calculated rates very close to experimental rates at high acetic acid concentration but when acetic anhydride becomes the major solvent component calculated rates fall behind. K_3 which treats acetic acid as a monomer gives calculated rates which increase as rapidly as experimental rates even in high acetic anhydride. This is the expected result from what is known of the behavior of acetic acid in solution with carbonyl compounds.[10,24] Acetic acid at high concentrations may be considered a dimer but here the $SOAcH^+$ rate accounts for most of the anomerization and this rate is relatively insensitive to changes in concentration. Whether acetic acid is treated as a dimer or monomer does not greatly affect the calculated $SOAcH^+$ rate over a short range where acetic is the major solvent component. When acetic anhydride becomes appreciable the $SOAc_2^+$ rate increases rapidly so nearly all of the anomerization goes through this species. With increasing acetic anhydride a larger proportion of acetic acid is present as a monomer. Thus in high concentrations of acetic anhydride only by treating acetic acid as a monomer can calculated $SOAc_2^+$ rates increase as fast as experimental rates. The sum of calculated rates at $K_3 = 0.2$ comes surprisingly close to experimental rates over a wide range.

By assuming acetyl ions in solutions of acetic anhydride the rapid increase in rate as acetic anhydride replaces acetic acid can be readily explained. The test of the equations is only qualitative as data on the equilibrium in the solvent system are inadequate to permit a more rigid test. The calculated rates are about those expected and the constants used appear reasonable where applicable.

If acetyl ions catalyze the anomerization it is not possible to deduce a simple relationship between H_0 and the rate. In the measurement of H_0 the indicator ratio would be represented by $B/(BH^+ + BAc^+)$ and Mackenzie and Winter[19] could not differentiate between the two. They did give evidence that BAc^+ was a colored compound as well as BH^+. The concentration of $SOAc_2^+$ must be much lower than $SOAcH^+$ but the first order dissociation of $SOAc_2^+$ to give S^+ must be faster.

Experimental

α- and β-1,2,3,4,6-pentaacetyl-D-glucose were prepared by standard procedures. Each was recrystallized five times from 96% ethanol.

Stock solutions of glucose acetates were prepared by dissolving 10 g. in one of the solvents and making the volume of 100 ml. The solvents were 100% acetic acid, a 1:1 mixture of acetic acid and acetic anhydride, and acetic anhydride. Analytical reagents were used. The impurity in acetic acid was assumed to be water and in acetic anhydride acetic acid.

Stock catalysts of 1.77 *M* sulfuric acid and 0.89 *M* perchloric acid in 100% acetic and in a 1:1 mixture were prepared by cooling the solvent in a Dry Ice-bath and adding the aqueous acids at a rate so acetic acid crystals were present in the solvent. The calculated amount of acetic anhydride was added to react with the water in the acids to give the desired concentration. For runs in high acetic anhydride the perchloric acid catalyst was diluted with acetic anhydride. Near 98% acetic anhydride at concentrations of about 0.001 *M* perchloric acid the catalyst was not stable.

All solutions and solvents were placed in a constant temperature bath before the solutions were made up for runs. In most cases 10 ml. of sugar acetate solution was pipetted into 50-ml. volumetric flasks, a measured volume of the desired solvent added, the catalyst added and the solution made to volume by addition of the desired solvent. The entire contents were immediately poured into 200-ml. glass stoppered flasks set in the constant temperature bath. The flasks were shaken to ensure mixing and the solutions poured into polarimeter tubes and the rotation changes followed. Water-jacketed polarimeter tubes at the temperature of the bath were used. They were removed from the bath and short time necessary to take readings. The temperature of the bath was 25 ± 0.02°.

When sulfuric acid was the catalyst in high concentrations of acetic anhydride, individual rate constants were plotted

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[23] Several sources of errors can influence calculated rates. The assumption regarding solvent effects is probably not true. The calculation of the concentration of solvent components where each is low may cause the ratios upon which relative rates depend to drift from the true value. The success of the calculation of the $SOAc_2^+$ rate depends upon selecting correct base rates. The difference between the experimental rate and calculated rate can vary greatly percentagewise even though the experimental rates (runs 1 and 3) were determined with a high degree of precision.

[24] (a) F. A. Landee and I. B. Johns, THIS JOURNAL, 63, 2891 (1941); (b) J. J. Kipling, *J. Chem. Soc.*, 2861 (1952).

against time and the initial rate estimated from the curve. With the same catalyst in acetic acid the values which were constant over most of the run were averaged.

Density measurements were made on the solvents, the catalyst and the sugar acetate in several solvents to aid in the calculation of solvent composition.

Acknowledgment.—The author expresses his appreciation to Professor R. M. Keefer for many useful suggestions in the preparation of this manuscript.

DAVIS, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Condensations by Sodium. XXXIV. The Effect of Sodium Reagents on Indicators[1]

BY AVERY A. MORTON AND FRANK H. BOLTON

RECEIVED JANUARY 19, 1951

Organosodium reagents, potassium and sodium hydroxide, will cause indicators of the type of benzeneazodiphenylamine to change to the same color as is produced by strong acids. Water helps produce the color when *n*-butyllithium and ethylmagnesium bromide are used.

The behavior of indicators with alkali metal reagents, particularly solids, is interesting because the colors produced imply a *p*H value. Similar tests have already been applied by Walling[2] to copper sulfate, calcium chloride, magnesium perchlorate and other solids which show little chemical reactivity with organic compounds, and the color changes suggest acidity. Also measurements with indicators have been made of alumina–silica surfaces.[2,3] The present study consists of tests with a wide range of indicators on representative sodium reagents, an Alfin catalyst, triphenylmethylsodium, 9-fluorenylsodium, potassium hydroxide, sodium hydroxide and others, all as solids suspended in some medium or, where possible, dissolved in ether. As might be expected, these reagents cause trinitrobenzene, ethyl bis-(2,4-dinitrophenyl)-acetate, and *m*-nitrophenol to show color on the basic side. However, they also had the unique feature of producing at once the color which certifies acidity with benzeneazodiphenylamine and 2-amino-5-azotoluene.

TABLE I

COLORS INITIALLY PRODUCED ON VARIOUS INDICATORS BY ALKALI METAL REAGENTS

Indicators[a]		I	II	III	IV	V	VI	VII
*p*H		1.2-2.9		1.4-2.8	2.8-4.4	6.8-8.6	8-10	2-14
Acid color[b]		Violet	Red-vio.	Red	Red	Colorless	Colorless	Colorless
Basic color[c]		Yellow	Yellow	Yellow	Yellow	Yel.-or.	Blue	Red-br.
Reagent[d]	Sol.[d]*							
$C_3H_5Na^c$	PP	V	V	R	d	O	d	R-B
C_3H_5Na	P	V						
$(C_6H_5)_3CNa$	E	V	Y					
$C_{13}H_9Na$	P	V		R	N	R	C	C
$C_{13}H_9Na$	E	V	Y	R	N	R	Bl	Bl
$(CH_3)_3CONa$	T	Y	Y	Y	Y			
$(CH_3)_2CHOK$	P	Y	Y	Y	Y			
KOH (t)	P	V	N	R	N	Y-O	B	R
KOH (t)	B	V		R	N	O	B	R
KOH (t)	E	R-V		Y	N	O	B	R
KOH (t)	W	Y		Y	Y	O	B	R
KOH (p)	P	V	N	R	N	Y-O	B-Bl	R
NaOH (t)	P	V						
NaOH (p)	P	Y		Y	N	O-R	B	R-B
LiOH	P	Y		Y	Y	O	B	R
$B(OH)_2$	P	Y		Y	Y	Y	B	C
NaCl	P	N		N	N	N	N	N

[a] In the order of numbering the indicators are benzeneazodiphenylamine, *p*-(phenylmethylamino)-azobenzene, 3,2'-dimethyl-4-aminoazobenzene, *p*-dimethylaminoazobenzene, *m*-nitrophenol, ethyl bis-(2,4-dinitrophenyl)-acetate and 1,3,5-trinitrobenzene. [b] The abbreviations used for the colors are obvious from the colors listed for acid and base. Bl means black. In addition, "d" indicates the solution and solid reagent were decolorized, "N" means no absorption occurred. [c] For the hydrocarbon residues, C_3H_5, C_6H_5 and $C_{13}H_9$ refer, respectively, to allyl, phenyl and fluorenyl. The letters "c," "t," and "p" in parentheses, after some formulas, refer, respectively, to catalyst (Alfin), technical grade and prepared from the metal and water in pentane suspension. [d] The abbreviation for solvents are the first letters for pentane, ether, toluene, benzene and water.

Table I lists the results from test-tube experiments. The first and third indicators have the general structure RN=NR'NHR″ where R and R' are aromatic nuclei and R″ is hydrogen or phenyl. All organosodium reagents, solid potassium hydroxide and the commercial solid sodium hydroxide (but not one prepared from sodium and water suspended in pentane) caused the acid color

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[1] The authors are indebted to the Office of Synthetic Rubber, Reconstruction Finance Corporation, for financial support of this work.

[2] C. Walling, THIS JOURNAL, **72**, 1164 (1950).

[3] M. W. Tamele, *Far. Soc., Discussions No. 8*, 270 (1950); T. H. Milliken, Jr., G. A. Mills and A. G. Oblad, *ibid.*, 279 (1950).