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Anomerization of D-Glucopyranose Pentaacetate in Mixtures of Acetic Acid and Non-basic Solvents Catalyzed by Perchloric Acid[1]

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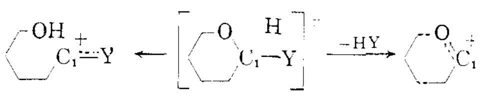
The acid-catalyzed anomerization of glucopyranose pentaacetate (SOAc) in acetic acid is a unimolecular substitution of a conjugate acid ion pair. When perchloric acid is the catalyst the ionic species is $SOAcH^+ClO_4^-$. The strength of the acid and basic properties of the substrate are influenced by solvent composition. Increasing substrate concentration and replacing part of the acetic acid by non-basic solvents gave rate increases. Non-basic solvents of low dielectric constant (they are also poor donors for hydrogen bonding) produced the largest initial rate increases. Over a wide range in composition the rate increase by non-basic solvents is just as large as that produced by acetic anhydride. The effect of solvents is in accord with Ingold's prediction for a reaction of the type: $RXH^+ \rightarrow R^{\delta+}—XH^{\delta+}$.

Kinetic[2] and stereochemical[3] evidence supports the conclusion of Ingold[4] that the acid hydrolysis of acetals is a unimolecular substitution of the acetal conjugate acid. We believe acid-catalyzed inversion at the anomeric carbon of glycosyl derivatives can best be explained in the same way.[5] Glycosides are the only glycosyl derivatives which are true acetals, but all of these compounds have a common structural feature. The acetal or anomeric carbon is bonded to two electronegative elements. One is always oxygen which can donate electrons to carbon when a bond is broken. The acetal example of catalysis by a proton donor illustrated with a glycosyl derivative (SY) can give two intermediates in the rate-determining step because SY compounds, unlike most acetals, contain two different displaceable groups.[6]



SHY⁺(III) SYH⁺(I) S⁺(II)

One factor which influences the site of cleavage is the relative ability of the ring oxygen or Y to donate electrons to carbon; S^+ would react with a solvent nucleophile to give substituted product; with SHY^+ the nucleophile can come from the solvent or it can be the C_5-alcohol. Anomerization can then

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

take place by reaction with a solvent nucleophile

$$SYH^+ \xrightarrow{-HY\ +\ HY} \text{inverted product}$$

or by a ring-opening, ring-closing process which does not require the solvent to be a source of the aglycon group.

$$\alpha\text{-SYH}^+ \longleftrightarrow SHY^+ \longleftrightarrow \beta\text{-SYH}^+$$

In the latter case a single molecule is involved in the inversion step, but the reaction must be classified the same as when the substitution is by a solvent nucleophile. In each case the rate-determining step is cleavage of a C_1–O or C_1–Y bond. With sugar derivatives the groups on the ring (not shown in I) influence both the steric course and rate of substitutions at the anomeric carbon so that in most cases the amounts of α- and β-products at equilibrium are far from equal.

Some acetylated glycosides in acetic acid–acetic anhydride with an acid catalyst give substituted products which show they may cleave at either anomeric carbon–oxygen bond.[7] Lemieux, Brice and Huber[8] labeled glucopyranose pentaacetate and showed anomerization in acetic acid–acetic anhydride is indeed a substitution process with cleavage at the C_1–OAc bond. No product expected when the ring oxygen cleaves[7] is obtained with SOAc so anomerization of this compound we believe is a substitution of II. The C_1–OAc bond is the one preferentially cleaved if the ring oxygen is a better electron donor than acetoxy.

In solutions of low dielectric constant such as acetic acid, electrolytes ionize to ion pairs. Even with strong electrolytes, dissociation constants[9–11] in acetic acid are in the range 10^{-5} to 10^{-6}. Aside from the fact the ion pair must be the major charged species of glycosyl derivatives dissolved in organic solvents when substitution due to acid catalysis takes place at C_1, experimental evidence which, although not decisive,[12] suggests the ion pair and not the dissociated ion is the reactive species. Bonner[13] found that lithium bisulfate did not suppress the rate of inversion of glucopyranose pentaacetate catalyzed by sulfuric acid in acetic acid–acetic anhydride. The perchloric acid-catalyzed rate is little affected by inorganic perchlorates. Kolthoff and Bruckenstein[9] find that inorganic perchlorates depress the dissociation of perchlorate indicator salts but do not affect the ratio of acid to alkaline species. Winstein and co-workers[12] give evidence

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[1] Some of these data were presented before the Division of Organic Chemistry, 123rd Meeting of Am. Chem. Soc., Los Angeles, Calif., 1953.

[2] (a) D. McIntyre and F. H. Long, THIS JOURNAL, **76**, 3240 (1954); (b) M. M. Kreevoy and R. W. Taft, Jr., *ibid.*, **77**, 3146 (1955).

[3] J. M. O'Gorman and H. J. Lucas, *ibid.*, **72**, 5489 (1950).

[4] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 334.

[5] E. P. Painter, THIS JOURNAL, **75**, 1137 (1953).

[6] Neighboring groups may participate in bond cleavage to give additional contributing forms with greater dispersal of cationic charge than in the forms illustrated. A well known example is when C_2 carries acetoxy *trans* to the bond cleaved. We use the symbol S to specifically designate 2,3,4,6-tetra-O-acetylglucopyranosyl but in the general case other sugar derivatives are not excluded. SY compounds extensively studied are those where the aglycon groups Y is alkoxy, acetoxy or halide.

[7] (a) E. M. Montgomery, R. M. Hann and C. S. Hudson, THIS JOURNAL, **59**, 1124 (1937); (b) B. Lindberg, *Acta Chem. Scand.*, **4**, 1153 (1949).

[8] R. U. Lemieux, C. Brice and G. Huber, *Can. J. Chem.*, **33**, 134 (1955).

[9] (a) I. M. Kolthoff and S. Bruckenstein, THIS JOURNAL, **78**, 1 (1956); (b) S. Bruckenstein and I. M. Kolthoff, *ibid.*, **78**, 10 (1956).

[10] T. L. Smith and J. H. Elliott, *ibid.*, **75**, 3566 (1953).

[11] M. M. Jones and E. Griswold, *ibid.*, **76**, 3247 (1954).

[12] S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *ibid.*, **78**, 328 (1956).

[13] W. A. Bonner, *ibid.*, **73**, 2659 (1951).

that the ion pair can be the reactive species in solvolysis. The ions I, II and III should then be considered cations of ion pairs in poor ionizing solvents.

From the evidence given the perchloric acid-catalyzed rate of anomerization of glucopyranose pentaacetate is given by

$$\text{rate} = k[\text{SOAcH}^+\text{ClO}_4^-] \qquad (1)$$

The concentration of reactive species ($\text{SOAcH}^+\text{ClO}_4^-$) depends upon the degree of ionization and relative basic strength of the sugar derivative and acetic acid.[14] The analytical concentration of perchloric acid is given by

$$[\text{HClO}_4]_0 = \text{HClO}_4 + (\text{AcOH})_2\text{H}^+\text{ClO}_4^- + \text{SOAcH}^+\text{ClO}_4^- + (\text{AcOH})_2\text{H}^+ + \text{SOAcH}^+ \qquad (2)$$

Strong electrolytes such as perchloric acid are usually considered nearly completely ionized in acetic acid. If this is the case and we neglect the small concentration of dissociated ions

$$[\text{HClO}_4]_0 \cong (\text{AcOH})_2\text{H}^+\text{ClO}_4^- + \text{SOAcH}^+\text{ClO}_4^- \qquad (2a)$$

we obtain from equation 2a and the equilibrium

$$(\text{AcOH})_2\text{H}^+\text{ClO}_4^- + \text{SOAc} \underset{}{\overset{K_1}{\rightleftarrows}} \text{SOAcH}^+\text{ClO}_4^- + (\text{AcOH})_2 \qquad (3)$$

the equation

$$\text{SOAcH}^+\text{ClO}_4^- = \frac{K_1[\text{HClO}_4]_0[\text{SOAc}]}{K_1[\text{SOAc}] + [(\text{AcOH})_2]} \qquad (4)$$

Recent data by Kolthoff and Bruckenstein[9] estimate perchloric acid to be half-ionized in acetic acid. In this case $\text{HClO}_4 = (\text{AcOH})_2\text{H}^+\text{ClO}_4^-$. Addition of the HClO_4 term to equation 2a and combining with 5 and 6

$$(\text{AcOH})_2 + \text{HClO}_4 \overset{K_2}{\rightleftarrows} (\text{AcOH})_2\text{H}^+\text{ClO}_4^- \qquad (5)$$

$$\text{SOAc} + \text{HClO}_4 \overset{K_3}{\rightleftarrows} \text{SOAcH}^+\text{ClO}_4^- \qquad (6)$$

gives

$$\text{SOAcH}^+\text{ClO}_4^- = \frac{K_3[\text{SOAc}]([\text{HClO}_4]_0 - [\text{HClO}_4])}{K_2[(\text{AcOH})_2] + K_3[\text{SOAc}]} \qquad (7)$$

Both equations 4 and 7 predict the rate in dilute solutions of sugar acetate in acetic acid to be first order in perchloric acid. This is confirmed experimentally.

The product of the first-order constants $k_1 + k_2$ (see Experimental) and sugar acetate concentration should obey equations 4 or 7. Thus the amount anomerized from equation 4 is given by equation 8 and from 7 by equation 8a.

$$(k_1 + k_2)\ [\text{SOAc}]_0 = \frac{K_1[\text{HClO}_4]_0[\text{SOAc}]}{K_1[\text{SOAc}] + [(\text{AcOH})_2]} \qquad (8)$$

Effect of Sugar Acetate Concentration.—Providing the K[SOAc] term in the denominator of equations 4 and 7 is small compared to the $(\text{AcOH})_2$ term ($K_2 > K_1$ or K_3) the rate should increase when the acetic acid concentration is decreased. Since increasing the large sugar acetate molecule concentration markedly reduces acetic acid concentration, we can test equations 4 and 7. Not only should the amount of sugar acetate anomerized increase with SOAc concentration, but the first-order constant should increase as well. This was verified experimentally over the range of sugar acetate from 0.051 to 0.78 M (Table I).

TABLE I

EFFECT OF SUGAR ACETATE CONCENTRATION ON THE RATE OF ANOMERIZATION IN ACETIC ACID

SOAc, M	$(\text{AcOH})_2$, M	$k_1 + k_2$, min.$^{-1}$ at 0.1 M HClO_4	SOAc anomerized, mole/l. min. Found	Calcd. (1)[a]	(2)[b]
0.051	8.6	0.0070	0.00036		
.15	8.3	.0072	.0011	0.0011	0.0011
.26	8.1	.0078	.0020	.0019	.0018
.39	7.7	.0086	.0034	.0031	.0029
.53	7.3	.0091	.0048	.0044	.0041
.78	6.6	.0101	.0079	.0072	.0064

[a] For complete ionization of perchloric acid and the K_1[SOAc] term in denominator neglected (from equation 8). [b] For $K_2 = 1/8.6$ and the K_3[SOAc] term in the denominator neglected (from equation 8a).

The experimental rate increased slightly faster than rate increases calculated from equations 8 or 8a. This is not surprising. Acetic acid would solvate sugar acetate[14] so the true solvent composition is less than the concentrations given in Table I. This becomes more significant at high sugar acetate concentration. Any estimate of the number of moles of acetic acid solvating sugar acetate will increase the calculated rates. For this reason we attach no significance to the observation that rate increases by equation 8 are closer to experimental than those by equation 8a.

When acetic acid is held constant (at 0.103 M $(\text{AcOH})_2$) by the addition of methylene dichloride the amount of sugar acetate inverted increased with substrate concentration (Table II), but the relative increase was not as great as in Table I. The data in Table I were obtained in a solution where acetic acid was always in great excess; in Table II the substrate/acetic acid ratio changed from about 0.25 to 6.1. If we assume acetic acid is largely hydrogen bonded to the substrate at the higher substrate concentrations and not limiting the rate in the inversion step, the rate would approach a constant (first-order rate decreases) with K_3 large and increase (first-order rate constant) with substrate concentration with K_3 small. The observation that the last three first-order constants in Table II

TABLE II

EFFECT OF SUGAR ACETATE CONCENTRATION ON THE RATE OF ANOMERIZATION AT LOW ACETIC ACID CONCENTRATION[a]

SOAc, M	$(\text{AcOH})_2$, M	$k_1 + k_2$, min.$^{-1}$ at 0.1 M HClO_4	SOAc-anomerized, mole/l. min.
0.026	0.103	1.3	0.034
.051	.103	0.89	.045
.15	.103	.53	.079
.31	.103	.39	.12
.62	.103	.33	.20

[a] Exptl. HClO_4 was 0.0036 M; CH_2Cl_2 was the other solvent.

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(14) Solvent acetic acid is considered a dimer, but this is a troublesome point. Acetic acid is primarily a dimer in liquid and vapor but dissociates in the presence of oxygen-containing compounds [G. Allen and E. F. Caldin, *Quart. Revs.* (*London*), **7**, 255 (1953); C. P. Brown and A. R. Mathieson, *J. Phys. Chem.*, **58**, 1057 (1954)]. Allen and Caldin state that carboxylic acids dissociate in the presence of carbonyl compounds and Brown and Mathieson found acetic acid largely dissociated by oxygen compounds capable of forming hydrogen bonds. With the exception of a few runs at high sugar acetate concentration and when a second solvent was the major component the concentration of acetic acid greatly exceeded that of the sugar acetate.

appear to approach a constant value may be significant. The acetic acid concentration may be so low, particularly at the higher substrate concentrations, that it is limiting the rate in the substitution step.

Effect of Non-basic Solvents.—Comparison of rates in Tables I and II confirm experimentally our prediction that the anomerization is much faster when acetic acid is replaced by a non-basic solvent. Several solvents representing a wide range in dielectric constant were then tested when mixed with acetic acid. Dilution of acetic acid by addition of a second solvent resulted in a rate increase in all cases. Only the ethers are considered bases to compete with sugar acetate and acetic acid as proton acceptors. While dioxane is a relatively weak base when measured by indicators in acetic acid,[15] it is a stronger base than diethyl ether.

In order to compare relative rate increases produced by the non-basic solvents some of the data from Table III, along with data on acetic acid–methylene dichloride mixtures, are plotted in Fig. 1.

TABLE III

ANOMERIZATION OF β-GLUCOPYRANOSE PENTAACETATE IN ACETIC ACID MIXED WITH A SECOND SOLVENT

Second solvent	Acetic acid, % by vol. added	$k_1 + k_2$, min.$^{-1}$ at 0.1 M $HClO_4$
Carbon tetrachloride	85.5	0.010
	73	.014
	60.5	.022
	49	.030
	42.5	.037
	33.5	.046
Benzene	85.5	.0097
	73	.013
	60	.017
	48	.024
	32.5	.055
Chloroform	90	.0078
	70	.011
	40.5	.021
Nitrobenzene	85.5	.0080
	71.5	.0095
	60.5	.011
	48	.017
	35.5	.024
	20	.067
Dimethyl sulfate	84.5	.0076
	53	.011
	48	.011
	31.5	.023
	17.5	.051
Cyclohexane	79	.013
Ethyl ether	43	.015
Dioxane	48	.011

The first-order rate goes up in each case as the non-basic solvent/acetic acid ratio increases. All curves in Fig. 1 are qualitatively much alike. Comparison of the position of each curve reveals the rate increases faster in solvents of low dielectric constant. The influence of the non-basic solvent is in the direction predicted by a unimolecular mechanism for a charged species giving a charged species in the transition step.[16] Hughes and Ingold conclude on going from the initial cation to the carbonium ion the rate should decrease in a more polar solvent because solvation in the transition state decreases with dispersal of charge.

Most solvents listed in Table III are not ideal to follow the rate up to very low concentrations of acetic acid. Miscibility limitations prevent measurements with high concentrations of carbon tetrachloride and benzene. High concentrations of dimethyl sulfate caused anomerization (presumably due to methyl hydrogen sulfate) without added perchloric acid. Methylene dichloride proved to be a suitable non-basic solvent to follow the rate to low acetic acid to see whether the rate continues to increase to near zero acetic acid as the increasing slopes of the curves in Fig. 1 suggest and as found with acetic acid–acetic anhydride mixtures.[5,13] The data obtained are in Table IV and plotted to compare with data on acetic acid–acetic anhydride mixtures, now extended to purified acetic anhydride, in Fig. 2.

TABLE IV

ANOMERIZATION OF 0.051 M GLUCOPYRANOSE PENTAACETATE IN ACETIC ACID AND METHYLENE DICHLORIDE

$(AcOH)_2$, M	$HClO_4$, M	$k_1 + k_2$, min.$^{-1}$	
		Found	Calcd. to 0.1 M $HClO_4$
8.6	0.045	0.0032	0.0070
8.6	.111	.0076	.0069
7.92	.045	.0035	.0078
7.05	.045	.0042	.0093
6.14	.053	.0059	.0111
4.38	.053	.0092	.0174
2.63	.053	.0194	.037
1.41	.0106	.0095	.090
0.895	.0106	.0153	.144
.361	.0106	.0423	.400
.103	.0036	.0321	.890
.093	.00088	.0086	.98
.0585	.00088	.0093	1.06
.0516	.0021	.023	1.10
.0231	.00088	.0101	1.15
.0069	.00088	.0085	0.97
.0034	.00044	.0019	.43

The rate in mixtures with methylene dichloride continued to increase (to about 160 times the acetic acid rate) up to less than 0.1 M acetic acid but finally decreased.[17] At very low acetic acid in methylene dichloride, acetic acid may be limiting the rate in the anomerization step. In mixtures of acetic acid and acetic anhydride the rate continues up to a maximum in "pure" acetic anhydride (Fig. 2). If plotted in Fig. 1 the curve for acetic acid–acetic anhydride mixtures would be close to that of acetic acid–methylene dichloride, so over

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(15) H. Lemaire and H. J. Lucas, THIS JOURNAL, **73**, 5198 (1951).

(16) (a) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 352 (1953), Ref. 4, p. 347. (b) A. H. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons (1953), p. 135.

(17) The apparent decrease is deceptive. In the absence of any acetic acid the initial rate may be as fast, or faster, than the maximum in Table IV. While this portion of Fig. 2 was duplicated, attempts to approach the curve with sugar acetate in methylene dichloride and adding perchloric acid in nitromethane have been discouraging. The same rate will be obtained with either α- or β-acetate with most solvent mixtures in Table IV, but at very low acetic acid the equilibrium shifts to favor α. In the complete absence of acetic acid, $\beta \rightarrow \alpha$, but the reverse step is difficult to demonstrate.

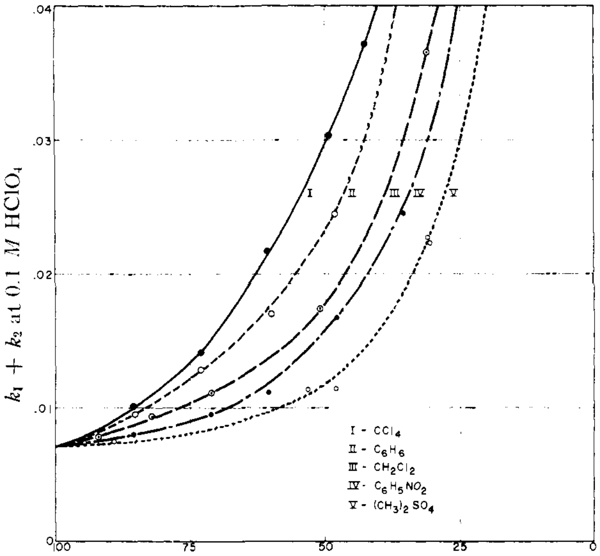

Fig. 1.—Effect of replacing acetic acid by non-basic solvents.

this range acetic anhydride behaves much like non-basic solvents listed in Table III.

Discussion

We believe the results are best interpreted by a unimolecular process which explains so admirably the behavior of acetals. The rate of anomerization is then dependent upon the dissociation

$$SOAcH^+ \longrightarrow S^+ + AcOH \qquad (9)$$

where now only the cation of the ion pair is included. The conjugate acid concentration is dependent upon an equilibrium between substrate and an acid species. Only strong acids catalyze the reaction in poor ionizing solvents; therefore, for proton acids, we believe we are dealing with specific acid catalysis. When acetic acid is replaced by a non-basic solvent the rate goes up as predicted. The increase on addition of those solvents of lower dielectric constant starts out slightly faster than predicted by equation 4 (Fig. 1) and the increase on addition of dimethyl sulfate is a little slower than predicted by equation 7. As the non-basic solvent becomes the major solvent component, where total ion pair concentration must be much less than added perchloric acid, the rates rise faster than equations given predict. The aprotic solvents give rate differences in line with Ingold's prediction for the transition state we propose, but the magnitude of the differences (Fig. 1) seems much too large to be explained on this basis alone.

If the rate-determining step is a first-order reaction of the conjugate acid, the rate is given by

$$\text{rate} = K^{\ddagger}(SOAcH^+)f_{SOAcH^+}/f_{\ddagger} \qquad (10)$$

For a large molecule like the protonated sugar acetate the transition state ($\ddagger$) must be much like the reactant so differences in the ratio $f_{SOAcH^+}/f_{\ddagger}$ due to solvent polarity would be small.

We can write

$$\text{rate} = K(SOAc)(HClO_4)f_{SOAc}f_{HClO_4}/f_{\ddagger} \qquad (11)$$

even though, in some solvents, the bulk of the transition intermediate does not arise by a reaction with molecular perchloric acid. The first-order constant takes the form

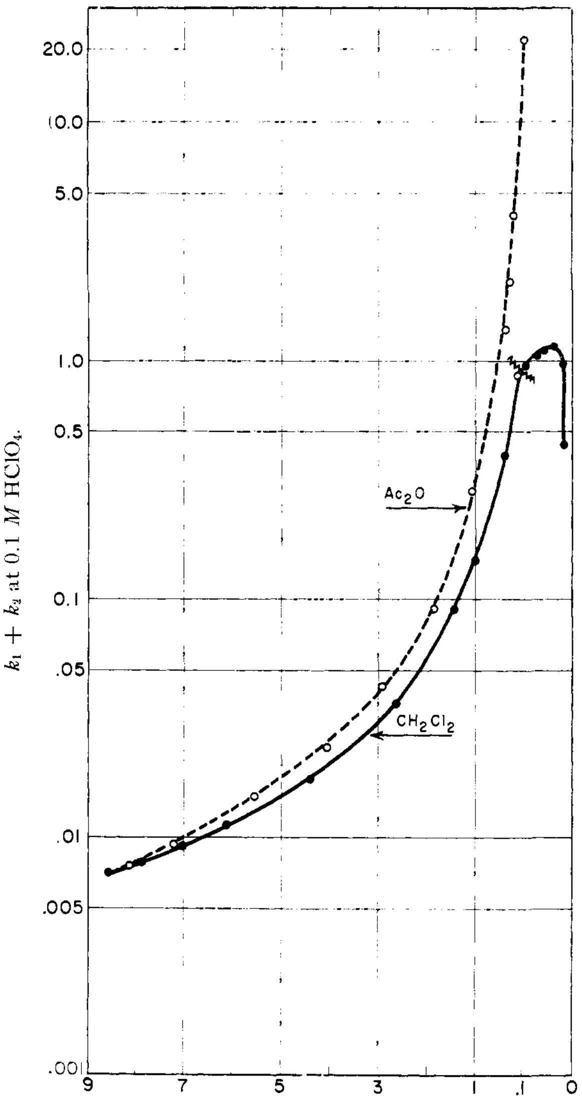

Fig. 2.—Rates in mixtures of acetic acid with methylene dichloride or acetic anhydride. The abscissa scale for the acetic anhydride curve is not changed. The peak is the experimental value for purified acetic anhydride.

$$k_1 + k_2 = Ka_{H^+}f_{SOAc}/f_{\ddagger} \qquad (12)$$

Acetic acid is a good solvent for both substrate and catalyst. Acetic acid hydrogen bonds with both. The activity of both sugar acetate and perchloric acid would increase when aprotic solvents replace acetic acid. We might expect the increase of f_{SOAc} to follow the ability of the second solvent to act as an electron donor for hydrogen bonding. When the second solvent is a poorer donor than acetic acid f_{HClO_4} should increase. The initial rate did increase much faster when the second solvent was carbon tetrachloride or benzene than when nitromethane or dimethyl sulfate. The latter are better solvents for perchloric acid than the former. The rate increase, when the weak bases (but donors for hydrogen bonding), dioxane and ethyl ether replaced acetic acid, was less than when solvents which are not considered basic to the system replaced acetic acid.

Measurements in acetic acid–acetic anhydride mixtures may be interpreted to indicate the rate change over the range shown in Fig. 1 is due mostly to an increase in a_{H^+}. The anomerization of sugar acetate[5] and acetylation of quinones[18] in acetic acid–acetic anhydride mixtures followed a measured acidity function[19] (indicator method) up to about 7 *M* acetic anhydride. Over this range Mackenzie and Winter[18] reported acetic acid to be mostly the dimer. Other evidence[14] led us to conclude acetic acid would dissociate when mixed with oxygen-containing solvents. At high concentrations of acetic anhydride, rates[5,18] increased faster than the acidity function. The deviation coincided with dissociation of acetic acid dimer.[18] The acetyl cation has been suggested to be the reactive species in solutions of acetic anhydride and a strong acid.[20] It is a product of anomerization (by our interpretation) when acetic anhydride is the source of the aglycon group. Even though some S^+ arises by the reaction of SOAc with Ac^+, to attribute the fast rate at high acetic anhydride to a property of the acetyl cation is not very satisfactory because the concentration of Ac^+ should be proportional to an acidity function. The experimental observation that the rate increases faster than a measured acidity function at high acetic anhydride may be explained just as well by an increase in the activity of sugar acetate as by a reaction with the acetyl cation.

If the inversion step is a reaction of S^+ with acetic acid from the environment[8] the rate should be limited by acetic acid at low concentration. Some of the data in Fig. 2 and in Table II suggest the rate may be limited by acetic acid in the anomerization step. Failure to obtain clear-cut evidence is not surprising because perchloric acid catalyzes the reaction

$$\beta\text{-SOAc} \longrightarrow \alpha\text{-SOAc} \qquad (13)$$

in aprotic solvents without added acetic acid. The reaction has previously been demonstrated in aprotic solvents with the catalyst a Lewis acid.[21] Anomerization of SOAc in the absence of added acetic acid must not go by the ring-opening ring-closing process proposed by Lindberg[7b] for acetylated glycosides, because Lemieux and Brice[21b] demonstrated that in this case the reaction is a substitution process. Exchange of labeled acetate occurred between the catalyst $SnCl_3OAc$ and substrate in the inversion step. The catalyst was a source of the aglycon group in the experiments of Lemieux and Brice; perchloric acid in our experiments was not. Lemieux[22] suggested that when β-SCl anomerized (no catalyst was added) the chloride did not completely dissociate. Extending this idea to our conditions we propose that acetic acid from the aglycon group solvates the anion of the ion pair (II is the cation) without complete dissociation from the substrate. A model shows that the solvated anion

$$\beta\text{-SOAcH}^+ClO_4^- \rightleftarrows S^+ClO_4^-HOAc \rightleftarrows \alpha\text{-SOAcH}^+ClO_4^- \qquad (14)$$

can move around the ring oxygen (as the oxonium cation of II) so the aglycon can become bonded to the anomeric carbon on either side of the ring. A model also shows why, with our substrate, more α may be present at equilibrium in aprotic solvents than when the solvent is a source of the substituting aglycon.

Our interpretation of the anomerization of SOAc is not identical with any of the generalized formulations for the anomerization of sugar derivatives given by Lemieux.[23] In three of the examples[23] a neutral molecule gave a cation and an anion. The transition step then belongs to the charge type

$$RX \longrightarrow R^{\delta+}\text{—}X^{\delta-} \qquad (15)$$

which gives a much faster rate in polar solvents.[16] Solvolysis rates of acetylated glycosyl halides when not catalyzed by acids[24] followed the prediction for the charge type illustrated by 15, but anomerization catalyzed by a proton acid does not. In another example[23] the aglycon group was displaced by the aglycon anion from the environment. Anions may displace the aglycon group of some sugar derivatives in a nucleophilic solvent, but SOAc is not anomerized in a solution of sodium acetate in acetic acid–acetic anhydride. Since a strong acid is required, the anion available to react with S^+ must come from the catalyst. A perchlorate (one species in equation 14 is the ion pair of $SClO_4$ solvated by acetic acid) is an expected intermediate in the absence of acetic acid in the solvent. Formation of a sugar perchlorate should depend upon the ClO_4^-/AcOH ratio. We do not believe that the concentration of $SClO_4$ is significant, so that a substitution of this species may influence the anomerization rate, in solutions where the $AcOH/HClO_4$ ratio is large. The experimental results over a wide acetic acid concentration range are in accord with Ingold's prediction for a transition step of the charge type

$$RXH^+ \longrightarrow R^{\delta+}\text{—}XH^{\delta+} \qquad (16)$$

Experimental

The procedure for following the rotation changes of glucose pentaacetates have been described[5] except that temperature (25 ± 0.2°) was controlled by circulating water through jacketed polarimeter tubes. First-order rate constants were calculated from the equation

$$k_1 + k_2 = \frac{2.3}{t} \log \frac{\gamma_0 - \gamma_\infty}{\gamma_t - \gamma_\infty}$$

Methylene dichloride, chloroform, carbon tetrachloride and benzene were dried over phosphorus pentoxide and the constant boiling fraction through a column of about fifteen plates used. Nitrobenzene and dimethyl sulfate were distilled, but not carefully purified. Acetic acid was first fractionated by distillation then further purified by partial freezing.

Dry acetic acid, free of acetic anhydride, was needed because Bonner[13] suggested acetic anhydride may be a necessary reagent for the anomerization of glucose pentaacetates. When dry acetic acid prepared by freezing was used and care taken to avoid moisture in the flasks and polarimeter tubes, satisfactory rates are obtained. When water is present the initial first-order constants during a run are high and the final equilibrium differs from that in dry solvents.

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

[19] H. A. E. Mackenzie and E. R. S. Winter, *ibid.*, **44**, 159 (1948).

[20] R. J. Gillespie, *J. Chem. Soc.*, 2957 (1950).

[21] (a) E. Pacsu, *Ber.*, **61**, 137 (1928); (b) R. U. Lemieux and C. Brice, *Can. J. Chem.*, **30**, 295 (1952).

[22] R. U. Lemieux, *Adv. in Carbohydrate Chem.*, **9**, 39 (1954).

[23] Reference 22, p. 24.

[24] F. H. Newth and G. O. Phillips, *J. Chem. Soc.*, 2896, 2904 (1953).

Table V shows the final equilibrium when β-glucose pentaacetate was anomerized in acetic acid purified by a single distillation. Rotations are in arbitrary units.

As a practical procedure one ml. of acetic anhydride was added to 100 ml. of purified acetic acid in most of the runs. The catalyst was prepared by dissolving anhydrous silver perchlorate in dry acetic acid and precipitating the silver with a stream of dry hydrogen chloride. A stream of dry nitrogen through the warmed solution removed the excess hydrogen chloride. Perchloric acid in acetic acid was determined by titration with potassium acid phthalate.[25]

TABLE V

EQUILIBRIUM ROTATION IN ACETIC ACID SOLUTIONS

H_2O added, ml./100 ml.	Acetic anhydride added, ml./100 ml.	Rotation
None		11.2
0.4		10.1
1.0		9.7
2.0		9.6
None	2	11.5
None	5	11.5

Most rates given at 0.1 *M* perchloric acid were calculated assuming the rate first order in acid as reported in acetic acid–acetic anhydride mixtures.[5] This has been found true by checking several solvent mixtures at two concentrations of acid. When the points were on a straight line through the origin it was assumed calculation to any concentration was justified. In Table VI results in a solvent low in acetic acid are given.

TABLE VI

DEPENDENCE OF RATE ON $HClO_4$ CONCENTRATION AT LOW ACETIC ACID

$(AcOH)_2$, *M*	SOAc, *M*	$HClO_4$, *M*	$k_1 + k_1$, min.$^{-1}$ Found	$k_1 + k_1$, min.$^{-1}$ Calcd. to 0.1 *M* $HClO_4$
0.103	0.0513	0.0009	0.0083	0.92
.103	.0513	.0018	.0163	.91
.103	.0513	.0036	.0324	.90
.103	.0513	.0054	.0476	.88

Methylene dichloride was the other solvent.

When concentrations are given in % by volume, the measured volumes were mixed and the total volume assumed to be the sum. When concentrations are expressed as molar, solutions were made up to measured volumes.

DAVIS, CALIF.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Derivatives of D-Mannitol 1,2,3,5,6-Pentanitrate[1]

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The synthesis and reactions of several organic acid (acetic, propionic and benzoic) esters of D-mannitol 1,2,3,5,6-pentanitrate are described. Polymerization of 3-*O*-acryloyl-D-mannitol pentanitrate was effected only with considerable difficulty. The catalytic reduction of these materials under neutral or basic conditions promoted migration of the various acyl functions from carbon three to one; no migration was observed under acidic conditions. Several new ether derivatives, 1-*O*-methyl-D-mannitol pentanitrate, 3-*O*-*n*-propyl-D-mannitol and 3-*O*-allyl-D-mannitol pentanitrate, are described; polymerization of the last was not effected. The interesting conversion of 1,6-dichloro-1,6-dideoxy-D-mannitol, by the action of silver nitrate, to 1,4:3,6-dianhydro-D-mannitol 2,5-dinitrate has been discovered.

This Laboratory has been concerned with the synthesis of nitrated polymers through the direct addition polymerization of suitably substituted ethylenic monomers. The required nitrated monomers may be obtained by two routes. An unsaturated polyhydric substance may be nitrated under appropriate conditions to afford an unsaturated polynitrate.[2–4] The alternate route, of major importance in the current report, concerns the formation of unsaturated derivatives from a partially nitrated polyhydric alcohol.

Conversion of D-mannitol hexanitrate to D-mannitol 1,2,3,5,6-pentanitrate, in 70% yield, has been effected by treatment with pyridine[5] and ammonium carbonate in aqueous acetone.[6] We have found that the latter method was more convenient for conducting the denitration on a fairly large scale, since it did not require exhaustive drying of the explosive hexanitrate. Good reproducible yields (78%) were obtained when the reaction was carried out at 0 to 8°; at higher temperatures, considerable decomposition resulted. Reaction of allyl bromide with D-mannitol 1,2,3,5,6-pentanitrate in tetrahydrofuran, in the presence of silver oxide and anhydrous calcium sulfate, afforded a 3% yield of 3-*O*-allyl-D-mannitol pentanitrate. Larger amounts of this material were obtained (71% yield) by nitration of 3-*O*-allyl-D-mannitol with absolute nitric acid in acetic anhydride, following the general method described by Honeyman and Morgan.[7]

Good yields (72%) of crystalline 3-*O*-acryloyl-D-mannitol pentanitrate resulted from the reaction of acryloyl chloride with D-mannitol 1,2,3,5,6-pentanitrate dissolved in acetonitrile containing N,N-dimethylaniline. When the aniline derivative was replaced by pyridine, isolation of the product was not possible. Application of this method to the synthesis of 3-*O*-methacryloyl-D-mannitol pentanitrate resulted in a sirup which has not crystallized but readily afforded a hard polymer on exposure to light and air. Only low molecular weight, gummy polymers have been obtained from the action of dibenzoyl peroxide on 3-*O*-acryloyl-D-mannitol pentanitrate and under the same condi-

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(1) This work was carried out under Contract DA-33-019-ord-2025, between the Ballistic Research Laboratories of Aberdeen Proving Ground, Md., and The Ohio State University Research Foundation (Project 675). Preliminary communication: *Abstracts Papers Am. Chem. Soc.*, **135**, 8D (1959).

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