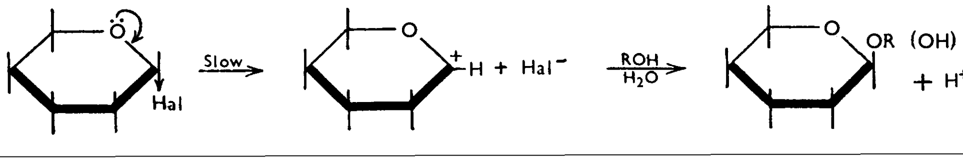
360. *The Reactivity of the* O-*Acylglycosyl Halides. Part IV.* The Solvolytic Reactions of* O-*Acetyl-α-*D*-glycosyl* 1-*Halides in the Presence of Electrophilic Catalysts.*

By G. L. Mattok and G. O. Phillips.

The rate of solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-halides in water–acetone and methanol–acetone in the presence of mercuric salts as catalyst, is proportional to the first power of both sugar halide and mercuric salt concentration. The mechanism postulated for the reaction involves the rate-determining formation of a carbonium-ion intermediate. In addition other features of this reaction such as salt effect, stereochemical form of the reaction, and solvent effects are similar to the uncatalysed S_N1 solvolysis of these compounds.

Hydrogen bromide can function as an electrophilic catalyst in a similar way to the mercuric salts, and this is discussed in relation to the autocatalysis by liberated hydrogen bromide which is a characteristic of non-catalysed solvolysis.

In earlier papers of this Series, the mechanism of solvolysis of the *O*-acetylglycosyl 1-halides in polar solvents was described. The reactions are of type S_N1 with the rate-determining ionisation facilitated by an electron-release mechanism operating from the lactol-ring oxygen atom :



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* Part III, *J.*, 1953, 2896.

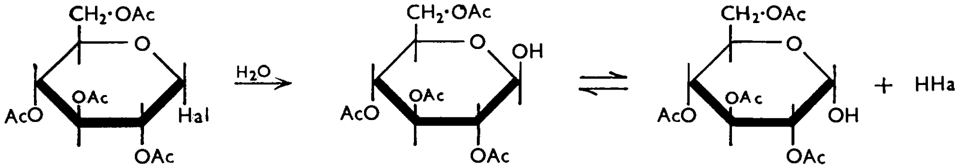
This view was opposed to that of Frush and Isbell,[1] who regarded the reactions as of the type S_N2. Lemieux and Huber,[2] however, support our results. They studied the solvolysis of 3 : 4 : 6-tri-*O*-acetyl-α- and -β-D-glucopyranosyl chloride in acetic acid, where the rate and stereochemical form of the reaction are unaffected by the addition of potassium acetate. Hassel and Ottar [3] examined the ring conformations necessary for the S_N2 mechanism in these compounds, and on this basis consider a bimolecular mechanism (S_N2) unlikely. In polar solvents, therefore, the S_N1 mechanism operating for the solvolytic reactions of tetra-*O*-acetyl-α-D-glucosyl 1-halides is the more probable. However, for certain reactions of these compounds where conditions are less favourable to the S_N1 mechanism, *e.g.*, low nucleophilic character of the reagent, low ionising power of the solvent, Chapman and Laird [4] report the incursion of bimolecular character, leading to an intermediate mechanism in some instances.

Considerable practical interest centres on the solvolytic reactions of *O*-acetylglycosyl 1-halides in polar media in the presence of electrophilic catalysts, and it was by this method that Koenigs and Knorr [5] first prepared glucosides. Under these conditions the reaction rates are considerably enhanced and the tendency for deacetylation of the molecule by the liberated halogen acid is decreased. In the present work mercuric salts were used as catalyst; here the medium is homogeneous throughout the reaction, thus eliminating the complications which arise when a precipitate is formed, *e.g.*, when silver salts are used as catalysts.

We have studied the mechanism of the catalysed solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-halides and compared this reaction with the uncatalysed unimolecular solvolysis of these compounds. The results suggest a close relation and enable also the autocatalysis by liberated hydrogen halides, characteristic of non-catalysed solvolyses, to be explained.

RESULTS

Catalysed Reactions.—During the solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-halides, inversion of configuration occurs, so formation of product can be followed polarimetrically. In aqueous solution, however, the over-all change of rotation is the result of two consecutive reactions. The initial solvolysis of the halide is followed by a slower mutarotation of the product,



which is most marked during the later stages of the reaction and in highly polar solvents. Fig. 1 shows the change in rotation with time for the hydrolysis of tetra-*O*-acetyl-α-D-glucosyl 1-bromide in acetone–water in the presence of mercuric bromide. The initial slope represents the formation of the β-tetra-*O*-acetylglucose. As the concentration of this compound builds up, the amount of mutarotation increases, and in the later stages this reaction predominates as shown by the final increase in rotation. Evaluation of the rate constant of the initial reaction by analysis of the curve is difficult because both reactions are catalysed by the liberated halogen acid. We have avoided these complications by extrapolating to zero time and calculating reaction rates from the initial slopes : this proved reliable and reproducible.

Order of the reaction. Measurement of the initial rates in acetone–water at 100°, in which the concentration of only one reactant was varied, showed the rate to be proportional to the first power of both halide and mercuric salt and independent of the concentration of water.

The results for tetra-*O*-acetyl-α-D-glucosyl 1-chloride are shown in Fig. 2 which gives the

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[1] Frush and Isbell, *J. Res. Nat. Bur. Stand.*, 1949, **43**, 161.
[2] Lemieux and Huber, *Canad. J. Chem.*, 1955, **33**, 128.
[3] Hassel and Ottar, *Acta Chem. Scand.*, 1941, **1**, 929.
[4] Chapman and Laird, *Chem. and Ind.*, 1954, 20.
[5] Koenigs and Knorr, *Ber.*, 1901, **34**, 95.

plots of log $(d\alpha/dt)_{t=0}$ against log $[HgCl_2]_{t=0}$ and log $[RCl]_{t=0}$. From the slope of the lines obtained it is seen that the rate is actually proportional to $[RCl]^{1\cdot04}$ and $[HgCl_2]^{1\cdot04}$. The rate was unaffected by the amount of water, in the range 1—4%, in aqueous acetone. We therefore calculated second-order rate constants by using the expression $(d\alpha/dt)_{t=0} = k_2[RCl][HgCl_2]$ and they are shown in Table 1.

For tetra-*O*-acetyl-α-D-glucosyl 1-bromide the results are similar (see Table 2).

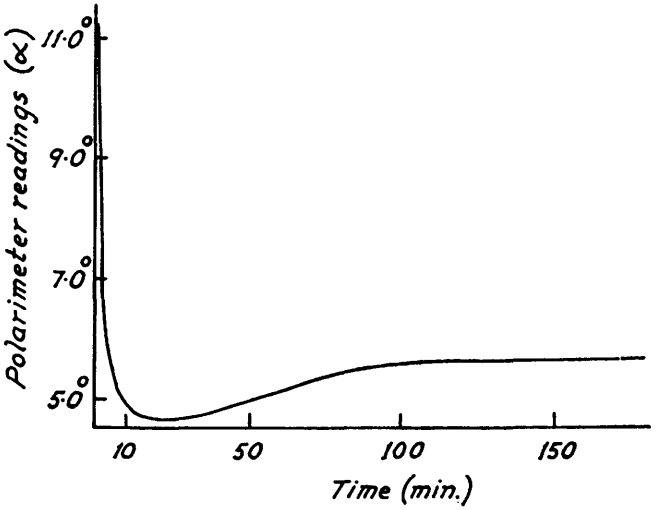

FIG. 1. *Hydrolysis of tetra-*O*-acetyl-α-glucosyl 1-bromide in 98% acetone–water, catalysed by mercuric bromide.*

[RBr] = 0·074M.
$[HgBr_2]$ = 0·062M.

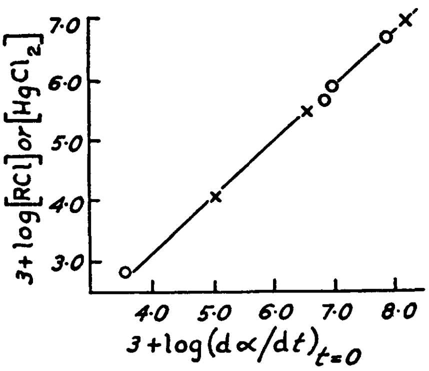

FIG. 2. *Solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-chloride in 98% acetone–water, catalysed by mercuric chloride. Order of the reaction.*

× [RCl]. ○ $[HgCl_2]$.

Effect of temperature and large variations of solvent. Although in the range 1—4% water in acetone, the rate is independent of the amount of water, larger proportions do affect the rate. Table 3 shows this for tetra-*O*-acetyl-α-D-glucosyl 1-chloride, and also the effect of temperature.

From the activation energies obtained we have calculated the thermodynamic constants of the reactions at the individual solvent concentrations (see Table 4).

Effect of addition of lithium chloride. Lithium chloride was added in the methanolysis of tetra-*O*-acetyl-α-D-glucosyl 1-chloride in acetone–methanol. The results are in Table 5.

Uncatalysed Solvolysis.—In the absence of mercuric chloride the solvolytic reactions of

TABLE 1. *Second-order rate constants for the solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-chloride in acetone–water catalysed by mercuric chloride, at 100°.*

[RCl] (10^2M)	$[HgCl_2]$ (10^2M)	H_2O (%)	10^3k_2 (l. mole^{-1} sec.$^{-1}$)	[RCl] (10^2M)	$[HgCl_2]$ (10^2M)	H_2O (%)	10^3k_2 (l. mole^{-1} sec.$^{-1}$)
5·005	3·875	2	3·70	4·985	1·915	2	3·31
5·00	3·695	2	3·79	4·97	6·40	1	3·75
5·00	4·72	2	3·71	5·10	4·57	4	3·85
3·57	4·965	2	3·73				

TABLE 2. *Second-order rate constants for the solvolysis of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-bromide in* 98% *acetone–water catalysed by mercuric bromide at* 25·2°.

[RBr] (10^2M)	5·045	7·415	4·98
[$HgBr_2$] (10^2M)	3·54	5·19	7·414
$10k_2$ (l. mole^{-1} sec.$^{-1}$)	1·24	1·27	1·20

TABLE 3. *Solvolysis of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-chloride in mixed solvents catalysed by mercuric salts.*

Acetone–water mixtures.				*Acetone–methanol mixtures.*			
Water (%)	Temp.	k_2 (l. mole^{-1} sec.$^{-1}$)	E (kcal. mole^{-1})	MeOH (%)	Temp.	k_2 (l. mole^{-1} sec.$^{-1}$)	E (kcal. mole^{-1})
2	100°	$3{\cdot}70 \times 10^{-3}$	17·5	10	133°	$1{\cdot}13 \times 10^{-2}$	13·2
	74·5	$7{\cdot}44 \times 10^{-4}$			100	$2{\cdot}87 \times 10^{-3}$	
	61·3	$2{\cdot}24 \times 10^{-4}$			77·7	$8{\cdot}44 \times 10^{-4}$	
10	100	$9{\cdot}35 \times 10^{-3}$	13·5		67·4	$4{\cdot}28 \times 10^{-4}$	
	76·4	$2{\cdot}74 \times 10^{-3}$		25	133	$1{\cdot}87 \times 10^{-2}$	13·3
	69·1	$1{\cdot}70 \times 10^{-3}$			100	$5{\cdot}10 \times 10^{-3}$	
	59·2	$9{\cdot}15 \times 10^{-4}$			77·3	$1{\cdot}71 \times 10^{-3}$	
20	100	$1{\cdot}11 \times 10^{-2}$	10·4		67·4	$8{\cdot}38 \times 10^{-4}$	
	74·5	$3{\cdot}76 \times 10^{-3}$		50	100	$5{\cdot}83 \times 10^{-3}$	12·9
	66·0	$2{\cdot}84 \times 10^{-3}$			77·8	$2{\cdot}21 \times 10^{-3}$	
	61·3	$2{\cdot}19 \times 10^{-3}$			67·4	$1{\cdot}20 \times 10^{-3}$	
30	100	$2{\cdot}50 \times 10^{-2}$	10·6	100	35·0	$2{\cdot}60 \times 10^{-4}$	13·8
	76·4	$9{\cdot}19 \times 10^{-3}$			31·5	$1{\cdot}91 \times 10^{-4}$	
	69·1	$6{\cdot}93 \times 10^{-3}$			26·8	$1{\cdot}35 \times 10^{-4}$	
40	100	$3{\cdot}43 \times 10^{-2}$	9·8		25·2	$1{\cdot}14 \times 10^{-4}$	
	69·6	$1{\cdot}05 \times 10^{-2}$					
	62·9	$7{\cdot}71 \times 10^{-3}$					
	58·5	$6{\cdot}54 \times 10^{-3}$					

TABLE 4. *Free energies, entropies, and heats of activation for the solvolysis of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-chloride in the presence of* 0·05M-$HgCl_2$, *at* 100°.

Catalysed hydrolysis (*in acetone–water mixtures*).

H_2O (%)	2	10	20	30	40
$\Delta G^{\ddagger}$ (kcal.)	26·3	25·6	25·6	24·9	24·7
$\Delta H^{\ddagger}$ (kcal.)	16·8	12·8	9·7	9·9	9·9
$\Delta S^{\ddagger}$ (e.u.)	−25·7	−34·6	−42·6	−40·3	−41·8

Catalysed methanolysis (*in acetone–methanol mixtures*).

% MeOH	10	25	50	100 *
$\Delta G^{\ddagger}$ (kcal.)	26·5	26·1	25·9	25·4
$\Delta H^{\ddagger}$ (kcal.)	12·5	12·6	12·2	13·0
$\Delta S^{\ddagger}$ (e.u.)	−37·7	−36·3	−36·9	−49·5

* Value obtained by extrapolation to 100°.

TABLE 5. *Effect of addition of lithium chloride: solvolysis of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-chloride in* 25% *methanol–acetone in presence of* 0·05M-$HgCl_2$ *at* 100°.

[LiCl] (10^2M)	0	2·16	2·53	4·95
10^3k_2 (l. mole^{-1} sec.$^{-1}$)	5·10	4·60	3·94	1·79

TABLE 6. *Effect of variation of temperature and solvent on the solvolysis of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-chloride in acetone–water.*

Temp.	10^6k_1 (sec.$^{-1}$)	E (kcal. mole^{-1})	Temp.	10^6k_1 (sec.$^{-1}$)	E (kcal. mole^{-1})	Temp.	10^6k_1 (sec.$^{-1}$)	E (kcal. mole^{-1})
	Water: 20%			Water: 30%			Water: 40%	
100°	59·7	20·0	100°	214·0	19·6	66·0	61·0	20·2
62·5	3·04		66·3	16·5		60·0	30·4	
55·2	1·50		55·2	5·72		50·1	13·1	
			50·1	4·64				

TABLE 7. *Free energies, entropies, and heats of activation for the solvolysis of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-chloride at* 100° *in acetone–water.*

Water (%)	20	30	40
$\Delta G^\ddagger$ (kcal.)	29·4	28·5	27·4
$\Delta H^\ddagger$ (kcal.)	19·3	18·9	19·5
$\Delta S^\ddagger$ (e.u.)	−27·2	−25·7	−21·4

TABLE 8. *Correlation of rates of solvolysis* (*extrapolated to* 25°) *of tetra-*O*-acetyl-α-*D*-glucosyl* 1*-chloride in acetone–water with* Y *values.*

Water (%)	20	30	40
Y value	−0·673	0·130	0·796
log k_1	−7·155	−6·635	−6·050

TABLE 9.

[HBr] (10^3M)	0	5·0	10·0	15·0	25·0
10^5k_1 (sec.$^{-1}$)	3·67	4·10	4·54	5·05	5·95

tetra-*O*-acetyl-α-D-glucosyl 1-chloride are of S_N1 type; for example, the reaction rate is unaffected by the addition of hydroxyl ions.[6]

We have extended previous studies on the uncatalysed solvolysis of this compound by measuring solvolysis rates in acetone–water at several temperatures. These and the activation energies are shown in Table 6. Winstein and Grunwald [7] correlated solvolysis rates with solvent properties by assigning to the solvent a characteristic constant (Y value). The authors are grateful to Professor Winstein for making available to them the Y values of acetone–water mixtures at 25°. On extrapolation of the results for tetra-*O*-acetyl-α-D-glucosyl 1-chloride to give the rates at 25°, the rate (k) can be correlated with the ionising power of the solvent. The plot of log k against Y is linear, which, represented by the relation $\log k = mY + \log k_0$, gives the characteristic constants $m = 0{\cdot}70$, $k_0 = -6{\cdot}69$ (Table 8).

The free energies, entropies, and heats of activation for the reaction were calculated and are shown in Table 7.

Autocatalysis by liberated hydrogen halides : addition of hydrogen bromide. Addition of anhydrous hydrogen bromide in the methanolysis of tetra-*O*-acetyl-α-D-glucosyl 1-bromide (at 25°) increases the initial rate of reaction. The first-order solvolytic constants increase linearly with the concentration of added hydrogen bromide within the range 0—2·5 × 10^{-2}M (Table 9).

DISCUSSION

The solvolysis of alkyl halides in aqueous solvents, or alcohols, catalysed by metal salts has been extensively studied.[8, 9, 10] When silver salts are the catalysts in such reactions, the mechanism shows features similar to those of an S_N1 reaction; for example, Hughes and Ingold and their co-workers and others [9-12] have shown that the effect of constitutional changes, stereochemical form of the reaction, and nature of the products are closely related in the two instances. These results indicate that the reaction catalysed by silver salts and the S_N1 solvolysis proceed by way of the same intermediate carbonium ion; silver ions are the main catalytic agent, but there is also a rather indefinite contribution by the surface of the precipitated silver halides. As noted on p. 1837, this complication is avoided without altering the general course of the reaction, by use of mercuric salts as catalysts. Benfey,[13] and Hammett and Roberts,[14] found that, for the solvolysis of several organic

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[6] Newth and Phillips, *J.*, 1953, 2896.

[7] Winstein and Grunwald, *J. Amer. Chem. Soc.*, 1948, **70**, 846.

[8] Senter, *J.*, 1910, **97**, 346; 1911, **99**, 95; Baker, *J.*, 1934, 987; Kappanna, *Proc. Indian Acad. Sci.*, 1935, **2**, 512.

[9] Hughes, Ingold, and Masterman, *J.*, 1937, 1236.

[10] Cowdrey, Hughes, and Ingold, *J.*, 1937, 1243.

[11] Whitmore, Whittle, and Popkin, *J. Amer. Chem. Soc.*, 1939, **61**, 1586.

[12] Dostrovsky and Hughes, *J.*, 1946, 169.

[13] Benfey, *J. Amer. Chem. Soc.*, 1948, **70**, 2165.

[14] Roberts and Hammett, *ibid.*, 1937, **59**, 1063.

bromides catalysed by mercuric nitrate, the rate is determined by formation of a carbonium-ion intermediate, the catalytic agent being mercuric ions : $Hg^{2+} + RX \longrightarrow HgX^+ + R^+$. Ingold [15] made a brief reference to unpublished work by Bunter, Hughes, and Ingold on the mercuric chloride-catalysed hydrolysis of 1-phenylethyl chloride; similarities to the S_N1 reaction are again evident, but catalysis here is by un-ionised mercuric salt. Our results on the kinetics of solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-halides catalysed by mercuric salts show that the rate-determining stage is dependent on the first power of the concentration of the halide and of the mercuric salt. The rate is independent of the reagent provided it is present only in low concentration and does not appreciably affect the dielectric properties of the medium. In the solvents used, acetone and alcohol, it is unlikely that the mercuric halides are dissociated, and catalysis will therefore be by the un-ionised salt. The mechanism may therefore be represented :

$$\begin{array}{c} RX + HgX_2 \xrightarrow{\text{Slow}} R^+ + HgX_3^- \\ R^+ + \underset{(HOH)}{R'OH} \xrightarrow{\text{Fast}} \underset{(ROH)}{ROR'} + H^+ \end{array}$$

The catalyst facilitates the removal of the halide ion, and the rate of the catalysed reaction is considerably faster than that of the uncatalysed ionisation. The existence of the complex ion HgX_3^- is well established. Bayles, Bentley, A. G. Evans, and Jones [16] recently showed that when triphenylmethyl chloride and mercuric chloride are mixed in nitromethane the following equilibria are set up :

$$\begin{array}{c} Ph_3C{\cdot}Cl + HgCl_2 \rightleftharpoons PhC_3^+\,HgCl_3^- \\ Ph_3C^+\,HgCl_3^- \rightleftharpoons Ph_3C^+ + HgCl_3^- \end{array}$$

The concentrations of these ions were also measured.

Lindberg [17] also found that the solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-bromide in the presence of mercuric bromide was of the second order. This evidence is based on the analysis of the complete hydrolysis curve (Fig. 1), by allowing for the accompanying mutarotation. At best, this procedure can only be very approximate, especially when no allowance was made for catalysis of the main reaction by the liberated halogen acid. The method we have described is not dependent on Lindberg's assumptions regarding the mutarotation, and our rate constants are not in exact agreement with his; nevertheless, we are in accord with his general conclusion that the rate-determining step is the removal of the halogen to form the carbonium ion.

When lithium chloride is added in the catalysed solvolysis of tetra-*O*-α-D-glucosyl 1-chloride, the reaction velocity is decreased (Table 5). This behaviour may be interpreted in a similar manner to the salt effects for S_N1 reactions :

$$RCl + HgCl_2 \underset{\text{Fast}}{\overset{\text{Slow}}{\rightleftharpoons}} R^+ + HgCl_3^- \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

$$R^+ + H_2O \xrightarrow{} ROH \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (2)$$

$$HgCl_3^- \overset{\text{Fast}}{\rightleftharpoons} HgCl_2 + Cl^- \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (3)$$

The formation of the carbonium-ion is the slow rate-determining stage, the back-reaction being much faster and comparable with the formation of the product by reaction (2). Addition of chloride ions suppresses the dissociation of the mercuric complex ion, and the bimolecular back reaction between R^+ and $HgCl_3^-$ would therefore gain in importance by comparison with reaction (2). It is not possible to study salt effects where the added salt has no common ion, *e.g.*, lithium bromide, because under these conditions exchange of the halogens predominates.

The acetyl-glycosyl 1-halides are therefore suitable compounds by which to compare

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[15] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, Ltd., London, 1953, p. 359.

[16] Bayles, Bentley, A. G. Evans, and Jones, *J.*, 1955, 206; *Research*, 1952, **5**, 535.

[17] Lindberg, *Acta Chem. Scand.*, 1947, **1**, 710.

the uncatalysed solvolysis, which is an established S_N1 reaction, with the formation of the carbonium ion catalysed by mercuric salt. The stereochemical form is identical in the two cases, with almost complete inversion of configuration accompanying replacement of the halogen group. Such a definite stereochemical result is not normally associated with an S_N1 mechanism and it is this which led Isbell and Frush [1] to suggest an S_N2 mechanism. Inversion of configuration is probable, however, because the 2-acetyl group hinders entry of the reactant molecule at position 1 on the side leading to retention of configuration. The direction of departure of the replaced halogen group would also contribute to this tendency.

Our experiments also provide a comparison, based on the effect of solvent variation, for the catalysed and the uncatalysed mechanism; the general behaviour is similar but there are particular differences. Brown and Hudson [18] studied the effect of variation of solvent on the thermodynamics of S_N1 reactions. They investigated the variation in activation energy E and rate constant k, with changes in the solvent composition for several chlorides, and compared the behaviour with established S_N1 reactions. Fig. 3 shows results they quote for *tert.*-butyl chloride in comparison with our results for the catalysed and uncatalysed solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-chloride. The three instances are characterised by the constancy of the activation energy at high water contents. Brown and Hudson discussed the nature of the solvation process for the S_N1 reaction, where it is probable that the change in reaction velocity on increasing the polarity of the solvent is due entirely to variation in the entropy of activation, with little or no contribution from activation energy. Table 7 confirms this for the uncatalysed S_N1 solvolysis. When the proportion of water is increased, $\Delta S^\ddagger$ becomes less negative, but $\Delta H^\ddagger$ remains constant.

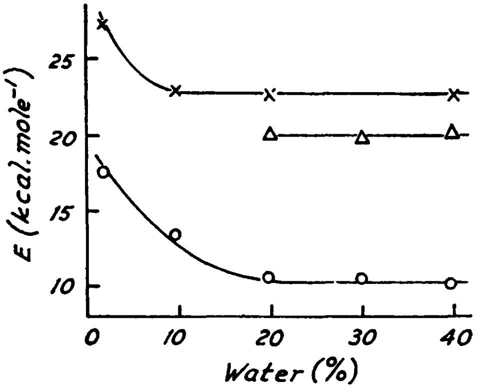

FIG. 3. *Variation of activation energy with solvent composition in acetone–water mixtures.*

× Bu^tCl.
△ Tetra-*O*-acetyl-α-D-glucosyl 1-chloride, uncatalysed.
○ Tetra-*O*-acetyl-α-D-glucosyl 1-chloride, catalysed.

For the catalysed reaction the consequences of increasing the polarity of the solvent differ in some respects (Table 4). Increasing the proportion of water or methanol accelerates the rate of the reaction, but this is not so pronounced as for the S_N1 reaction (Table 7). For the catalysed reaction, varying the solvent from 80 to 60% acetone–water results in a three-fold increase in reaction rate, as compared with a ten-fold variation for the uncatalysed reaction. Nevertheless, the general variation in activation energy with solvent composition remains characteristic of the S_N1 process (Fig. 3), E becoming constant at high water or methanol concentrations. In reactions where Brown and Hudson [18] encountered S_N2 reactions, *e.g.*, the hydrolysis of *p*-nitrobenzoyl chloride in acetone–water, E showed a gradual increase with increasing solvent polarity, and this is no doubt related to the more diffuse charge distribution in the transition state of the bimolecular reaction. This difference in behaviour may thus be applied as a criterion for distinguishing between S_N1 and S_N2 reactions. The corresponding changes in entropy of activation with solvent composition for the catalysed reaction differ somewhat from those of the S_N1 reaction. As the solvent is varied from 2 to 20% of water in acetone, $\Delta S^\ddagger$ becomes much more negative. Further addition of water results in much smaller rate changes, giving almost constant values for

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[18] Brown and Hudson, *J.*, 1953, 3352.

$\Delta S^\ddagger$. In methanol–acetone there is very little change in $\Delta S^\ddagger$ throughout the whole range of solvent variation. The large difference in activation energy between the uncatalysed and the catalysed reaction is noteworthy; the entropy factor is also less favourable in the latter.

The plot of log k_{25} against Y value of the solvent for the solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-chloride in acetone–water is linear and consistent with an S_N1 reaction. The significance of these results will be discussed later.

There is a strong autocatalytic influence [6] of liberated hydrogen bromide during the solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-bromide in methanol which is greater than in aqueous media. Salomaa [19] finds this behaviour a characteristic feature of 1-halogeno-ether solvolysis, and he observed that autocatalysis was more pronounced for solvents in which the liberated hydrogen halide is only slightly dissociated. He therefore regards the catalysis as arising from a positive salt effect rather than simple acid catalysis. Previously we [6] had also regarded this as a positive salt effect. Experiments where hydrogen bromide was added initially show that the initial rate is of the first order with respect to hydrogen bromide (Table 9). It appears therefore that hydrogen bromide functions as an electrophilic catalyst in a manner similar to the mercuric salts, giving rise to autocatalysis in non-solvolytic reactions: $RBr + HBr \longrightarrow R^+ + HBr_2^-$. This mechanism is supported by the evidence from the sugar halides and the 1-halogeno-ethers that un-ionised hydrogen halides are more effective catalysts than are ions formed in aqueous solution. The ions increase the reaction rate only in so far as they increase the polarity of the solvent and make conditions more conducive to the S_N1 reaction.

EXPERIMENTAL

Solvents.—Methanol and acetone were purified as described in earlier papers.

The term $x\%$ aqueous acetone refers throughout to a medium obtained by mixing at room temperature x volumes of dry solvent with $(100 - x)$ volumes of distilled water. Similarly $x\%$ methanol–acetone refers to a mixture of x volumes of methanol with $(100 - x)$ volumes of acetone.

*Tetra-*O*-acetyl-α-D-glucosyl 1-Bromide.*—This was prepared from β-penta-*O*-acetylglucose by treatment with hydrogen bromide in glacial acetic acid: the m. p. was 88—89°, and $[\alpha]_D^{20}$ +198° (*c*, 2·0 in $CHCl_3$).

*Tetra-*O*-acetyl-α-D-glucosyl 1-Chloride.*—This was prepared by treating β-penta-*O*-acetyl-glucose with titanium tetrachloride in chloroform and had m. p. 75—76°, $[\alpha]_D^{20}$ +166° (*c*, 2·1 in $CHCl_3$).

Reaction Product.—Tetra-*O*-acetyl-α-D-glucosyl 1-bromide (6 g.) and mercuric bromide (5·2 g.) were dissolved in methanol (250 ml.) and kept at 30°. After 24 hr. the solvent was removed under reduced pressure (at <50°) and the resulting mixture of syrup and mercuric bromide extracted with chloroform. The mercuric bromide was filtered off, the solution dried (Na_2SO_4), and the solvent removed under reduced pressure. The syrup crystallised only with great difficulty, giving methyl 2 : 3 : 4 : 6-tetra-*O*-acetyl-β-D-glucoside, m. p. 103—105° (after 3 recrystallisations), $[\alpha]_D^{20}$ −17·5° (in $CHCl_3$).

Rate Measurements.—The solvolysis of the halide was followed in a 2·2 dm. polarimeter tube, fitted with a jacket through which water from a thermostat was circulated. The thermostat temperature was constant within ±0·1°.

(a) *Reactions catalysed by mercuric salts.* The experiments with tetra-*O*-acetyl-α-D-glucosyl 1-bromide were carried out at approx. room temperature. The mixture was prepared from a known quantity of the halide in acetone and a known quantity of mercuric salt dissolved in a suitable medium, and was transferred quickly to the polarimeter tube. The solutions were pre-heated to the reaction temperature in the thermostat.

Solvolysis of tetra-*O*-acetyl-α-D-glucosyl 1-chloride was studied from 50° to 100°, necessitating the use of a sealed-ampoule technique. The mixture was prepared at room temperature as above, heated in a thermostat at the required temperature for varying intervals in the ampoule, cooled in ice, and then transferred to the polarimeter tube for measurement.

The rate constants were evaluated from the initial rates of the reaction.

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[19] Salomaa, "The Kinetics of 1-Halogenoether Alcoholysis," Annales Universitatis Turkuensis, Turku, 1953.

(b) *Uncatalysed reactions.* For the tetra-*O*-acetyl-α-D-glucosyl 1-bromide the technique was that recorded in previous publications. For the chloride the sealed-ampoule technique was necessary.

Tables 10—12 show typical runs, only a part of the experimental observations being given. In general, the calculated values of the activation energy are accurate to ± 0·3 kcal.

TABLE 10. *Solvolysis of tetra-O-acetyl-α-D-glucosyl 1-bromide in 98% acetone–water at 25·2° catalysed by mercuric bromide.*

[RBr] = 0·05M. [$HgBr_2$] = 0·074M.

t (min.)	0	2	3	4	5	6	8	10	12	20	45	1200
α	7·59°	4·52°	3·46°	2·61°	2·41°	2·14°	1·72°	1·58°	1·34°	1·10°	1·50°	3·13°

$(d\alpha/dt)_{t=0}$ = 4·1 degree min.$^{-1}$. k_2 = 1·2 × 10^{-1} l. mole^{-1} sec.$^{-1}$.

TABLE 11. *Solvolysis of tetra-O-acetyl-α-D-glucosyl 1-chloride in 70% acetone–water at 100°.*

[RCl] = 0·05M.

t (min.)	0	4	8	12	16	41	71	101	175	265	600	660
α	6·34°	5·99°	5·69°	5·40°	5·10°	3·60°	2·93°	2·49°	1·74°	1·55°	1·23°	1·27°

$(d\alpha/dt)_{t=0}$ = 7·9 × 10^{-2} degree min.$^{-1}$. k_1 = 2·14 × 10^{-4} sec.$^{-1}$.

TABLE 12. *Solvolysis of tetra-O-acetyl-α-D-glucosyl 1-chloride in absolute methanol at 25·2°, catalysed by mercuric chloride.*

[RCl] = 0·049M. [$HgCl_2$] = 0·067M.

t (hr.)	0·1	0·5	1·0	1·5	2·0	3·0	5·0	22	25	29	45	70	∞
α	6·42°	6·31°	6·23°	6·12°	6·04°	5·84°	5·43°	2·64°	2·10°	1·54°	0·35°	−0·13°	−0·38°

$(d\alpha/dt)_{t=0}$ = 3·25 × 10^{-3} degree min.$^{-1}$. k_2 = 1·14 × 10^{-4} l. mole^{-1} sec.$^{-1}$.

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