C.—*Studies of Dynamic Isomerism.   Part XXI.   The Velocity of Mutarotation of Tetramethylglucose and of Tetra-acetylglucose in Aqueous Acetone.*

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ALTHOUGH it has long been known that water is an effective catalyst for the mutarotation of the sugars, even apart from the presence of basic or acidic impurities (see Part I, J., 1903, **83**, 1314), there was until recently no clear picture available as to the way in which the water intervenes in order to determine the changes of structure which give rise to the observed changes of rotatory power. In particular, although it was known that the formation of a hydrate does not bring about any marked alteration of the rotatory power of α-glucose, and cannot therefore be a direct cause of the muta-rotation of this sugar (Part III, J., 1904, **85**, 1551), there were no experimental data to show how the subsequent molecular rearrange-ment of the hydrate was effected. It was suggested, however, in a recent paper (Part XVIII, J., 1925, **127**, 1371) that there is a marked analogy between the conditions under which mutarotation occurs and those which are used to promote the hydrolysis of an ester, and that, since mixtures of acids and bases with water are even more efficient catalysts than water itself, the action of the water probably depends on its amphoteric properties. If this view were correct, any solvent which can accept a proton from the sugar, and return it to the sugar residue, might act as a complete catalyst for the mutarotation. This conclusion has been verified (Part XX, J., 1925, **127**, 2883) by the discovery that an anhydrous mixture of pyridine and cresol is an excellent catalyst for the mutarotation of tetramethylglucose.

The experiments now described were undertaken in order to secure information in reference to solvents which appear to diminish the catalytic activity of water instead of increasing it. The choice of acetone as a diluent was dictated by the fact that Irvine (J., 1913, **103**, 584) has found it to be a particularly easy solvent in which to effect an arrest of mutarotation in a methylated sugar. It was thought that this might be due to some restraining action of the

acetone upon the water or upon the other impurities which give rise to mutarotation in inert solvents. We therefore anticipated that, when mixed with water in various proportions, acetone would reduce the catalytic activity of the water more rapidly than its total concentration. The results recorded in Tables I and II show that this anticipation was amply fulfilled. Thus in a 50% mixture of acetone and water the velocity of mutarotation of tetramethyl-glucose is only about 20% of that in pure water. The water in this solution has therefore less than one-half of its normal activity in the free state.

We have also compared the velocity coefficients in Tables I and II with the partial vapour pressures of aqueous acetone at 30° as recorded by Makovetzki (*J. Russ. Phys. Chem. Soc.*, 1908, **40**, 226),

FIG. 1.
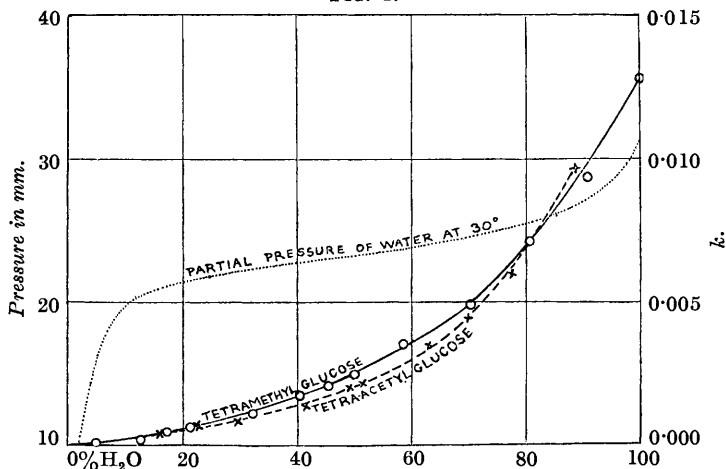
but can find no indication of any parallelism between them. In particular, the velocities shown in the figure appear to rise progressively from the origin at 0% H_2O, where the curves are perhaps tangential to the horizontal axis, whilst the dotted curve which shows the partial vapour pressure of water is inflected in the normal fashion for mixtures showing strong positive deviations from Raoult's law of lowering of vapour pressure. We therefore conclude that the catalytic activity of the water, which is obviously not proportional to its total concentration, is also not a simple linear function of its activity as measured by its partial vapour pressure above the solution.

EXPERIMENTAL.

The physical constants of the tetramethylglucose used in these experiments have already been given (J., 1925, **127**, 1387, footnote);

they are in close agreement with those recorded by Irvine. The purity of the sample is, however, guaranteed even more effectively by the arrest of mutarotation observed in several inert solvents; moreover, the mutarotation constants of the sugar were not altered appreciably by three further crystallisations from ether and from petrol :

	Specific rotation, $[a]_{5461}$.			
	Initial.	Final.	Ratio.	Vel. coeff.
Before recrystallisation	117°	95°	1·23	0·0128
After „	115	94	1·23	0·0124

The tetra-acetylglucose was prepared for us by Messrs. Boots Pure Drug Co., Nottingham, to whom we wish to express our thanks for their generous gift. The substantial purity of the specimen was established by analysis, but we have not been able to find any trustworthy figures for the physical constants of the compound. The melting point, 118°, given by Fischer and Delbrück (*Ber.*, 1909, **42**, 2779) has no clear significance, since prototropic compounds have two different melting points, according as time is allowed for isomeric change to take place or not. In the case of tetra-acetyl-glucose we find that the true melting point, at which the compound melts in about 10 seconds when plunged into a bath heated to a known temperature, is 123°, as recorded by a standardised Anschütz thermometer graduated to 0·2°; and that the "equilibrium tem-perature" (Lowry, J., 1899, **75**, 233), at which the compound melts or re-melts when heated slowly, is 110°. Since a small specimen of tetra-acetylglucose given to us by Professor Haworth melted at the same temperatures, within less than a degree in each case, we feel justified in putting forward these temperatures as provisional standards, which can be verified by comparison with values recorded in the future for other specimens of the purified sugar. The rotatory powers given by Fischer and Delbrück, $[\alpha]_D^{22°} = + 2\cdot19°$ to $+ 82\cdot7°$, were apparently determined at room temperature, with unpurified sodium light, and in alcohol of unspecified water content. We have not attempted to make any exact comparison with these uncertain data, but in our opinion the value $[\alpha]_{5461} = + 6°$ for a 5% solution of tetra-acetylglucose in pure anhydrous acetone at 20° can be accepted provisionally as a characteristic constant of the unchanged sugar, since this value is permanent over a period of several hours. As in the case of tetramethylglucose, the purity of the sample used in our experiments was established most satisfactorily by the complete arrest of mutarotation which we have observed repeatedly in solutions of the sugar in an inert solvent. Since the suggestion has been made that the mutarotation of tetra-acetylglucose in aqueous acetone may be due in part to hydrolysis instead of to isomeric change, we have made direct experiments to test this point, but could

not detect any hydrolysis after a week at a temperature of about 18°; after 10 days, the proportion of sugar hydrolysed was only of the order of 0·5%. After 7 months, the residues from the original experiments were hydrolysed to the extent of only 5%. The hydrolysis of the sugar can therefore have had no perceptible influence on the velocity of mutarotation, a conclusion which we had already anticipated from the steadiness of the observed end-points, since it was incredible that hydrolysis (as well as isomeric change) could be complete in the course of a few hours or days.

The acetone had been purified through the compound with sodium iodide (J., 1913, **103**, 1255). The solutions were prepared by dissolving about 1 g. of tetramethylglucose, or 0·5 g. of tetra-acetylglucose, in 20 c.c. of an aqueous acetone made up by weighing. Tetramethylglucose was examined over the whole range of concentrations from 0 to 95% of acetone, but tetra-acetylglucose is almost insoluble in water and only slightly soluble in water containing 5% of acetone. A solution of the latter concentration was prepared by dissolving the sugar in acetone and adding the necessary quantity of water; but the constants of the mutarotation curve were unsatisfactory, and the values for this solution have not been included in the table. The very slow mutarotations in acetone containing only traces of water were not included in the present research. In order to economise space, all the individual readings have been omitted, but the unimolecular velocity coefficients for the various solutions are set out in Tables I and II, and are shown graphically in the figure.

TABLE I.			TABLE II.		
Mutarotation of Tetramethylglucose in Aqueous Acetone at 20°.			Mutarotation of Tetra-acetylglucose in Aqueous Acetone at 20°.		
Acetone %.	Acetone, mols. %.	$k \times 10^5$.	Acetone %.	Acetone, mols. %.	$k \times 10^5$.
0	0	1280	11·5	3·7	965
9·25	3·08	934	22·6	8·0	596
19·20	6·9	710	30·0	11·6	441
29·7	11·8	487	36·8	15·0	346
41·4	18·0	351	48·4	23·5	217
50·0	23·7	246	50·7	24·6	200
54·6	27·3	206	58·5	30·6	129
59·6	31·4	177	70·3	42·1	80
67·7	39·4	110	77·3	50·7	60
78·7	53·4	60	83·9	61·8	28
82·8	59·5	45			
87·3	69·8	18·4			
95·1	85·7	3·0			

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