

CCXXV.—*Studies of Dynamic Isomerism. Part XXIII. Mutarotation in Aqueous Alcohols.*

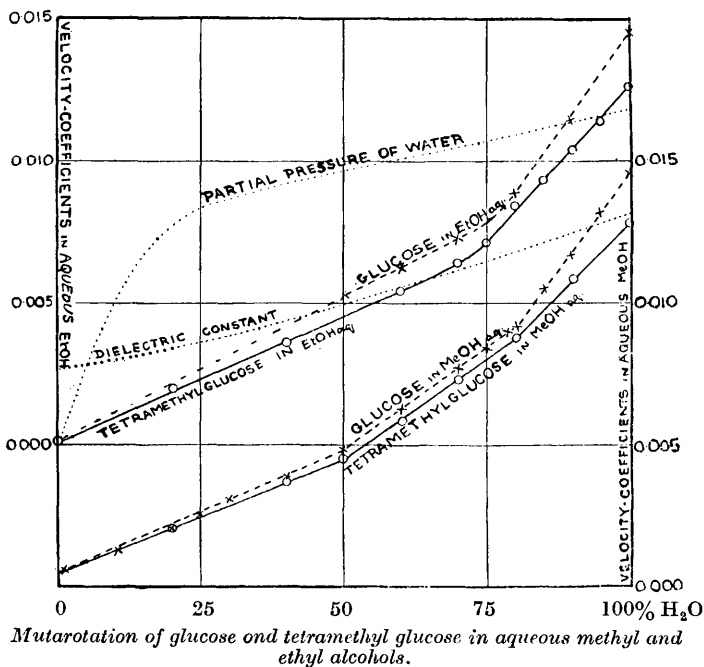
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THE present paper summarises the mutarotation data for some 80 solutions of glucose and of tetramethyl glucose in aqueous methyl and ethyl alcohols. These measurements formed part of a research on the influence of water concentration on velocity of mutarotation, and may therefore be regarded as a sequel to a recent investigation of the velocity of mutarotation of tetramethyl glucose and tetraacetyl glucose in aqueous acetone (Part XXI; J., 1926, 720). The results, however, were of an entirely different character from those recorded in the preceding papers of this series. Thus, whereas solutions in aqueous pyridine gave a curve with a strongly developed maximum (J., 1925, 127, 2883), and those in aqueous acetone gave a drooping curve approaching asymptotically to the axis of concentration (J., 1926, 721), the curves for solutions in aqueous alcohols show an approximate proportionality between water concentration and velocity, which persists up to 50% and up to about 70% of water in the case of methyl and ethyl alcohol, respectively.

It is not easy to give a precise interpretation of these facts. The direct proportionality between water content and velocity of mutarotation, which has been established by these present experiments, was regarded by Baker, Ingold, and Thorpe as a logical deduction from the hydrate theory of mutarotation, a conclusion that was illustrated by a diagram on which a line passing through the origin was labelled "Theoretical for Lowry and Armstrong's Mechanism" (J., 1924, 125, 281). Since, however, the lines which represent the influence of water concentration on the velocity of mutarotation in the two aqueous alcohols do not point towards the value for pure water, but to a velocity which is only about two-thirds as great, we cannot adopt the elementary view that mutarotation depends on a simple mass action, in which the catalytic activity of the water is proportional to its volume concentration and independent of all other factors. Moreover, we have already shown in the case of aqueous acetone that the velocity of mutarotation is not proportional to the "fugacity" of the water, since the partial vapour pressure of this component rises steeply in the region of small concentrations, whereas the velocity curves rise only very slowly from a horizontal asymptote. A similar conclusion can now be drawn in reference to aqueous ethyl alcohol, since the steep rise in the partial vapour pressure of the water, recently recorded by

Dobson (J., 1925, 127, 2872), is again in complete contrast with the slow progressive increase of velocity indicated by the straight lines of Fig. 1; nor does it appear likely that these unrelated curves could be brought into agreement by means of a correction based upon a hypothetical variation in the "fugacity" of the sugar. The new experimental evidence therefore provides ample confirmation of the view, which was already adopted in 1904 (J., 85, 1567), that the velocity of mutarotation of the sugars in aqueous solutions is not controlled by the initial hydration of the anhydrous sugar (which

FIG. 1.



can be regarded for this purpose as an instantaneous action) but by a much slower, and more fundamental, molecular rearrangement of the hydrate.

The factors which determine the velocity of this fundamental change of structure have not yet been fully disclosed. On general grounds it might be supposed that the velocity of the change would be proportional to the dielectric constant of the solution. The data for the dielectric constant of aqueous ethyl alcohol, which are plotted in Fig. 1, show that this property is related to the water content of the solutions according to a nearly linear law, which

extends (with a "sag" of 3 or 4 units in the centre of the curve) over the whole range of concentrations from 0 to 100%. Whilst, however, the dielectric constants for water and for ethyl alcohol are in the ratio $80 : 26 = 3 : 1$, the velocities of mutarotation in the two solvents are in a ratio which cannot be less than $80 : 1$, since the velocity coefficient for tetramethyl glucose falls from 0.0128 in water to a figure which is certainly less than 0.00016 in alcohol. The velocity of mutarotation in pure alcohol is indeed so small as to be almost negligible, whereas the dielectric constant of the medium is quite high enough to give to it the normal properties of an ionising solvent. Again, the curve showing the variation of the dielectric constant with the water content of the solution (like that which expresses the partial vapour pressure of the water) gives no indication whatever of the abrupt change of direction in the velocity curve, which is more than twice as steep for solutions containing from 75 to 100% H_2O as for solutions containing 0 to 70% H_2O .

Since none of these suggested relationships can be verified, the theory which links the velocity of mutarotation with the acid and basic properties of the medium (J., 1925, **127**, 1382) is at the present time the only one for which any experimental justification can be found. In the case of aqueous solutions, detailed evidence of this relationship is given by Euler's precise quantitative determination of the influence of hydrogen-ion concentration on the velocity of mutarotation of α - and β -glucose (*Z. anorg. Chem.*, 1925, **146**, 45; compare Hudson, *J. Amer. Chem. Soc.*, 1907, **29**, 1572, and Kuhn and Jacob, *Z. physikal. Chem.*, 1924, **113**, 389). In the case of solvents which are either wholly or partly non-aqueous, the hydrogen-ion concentrations are not known; but, since mutarotation can be arrested in media which possess only acid or only basic properties (as well as in media which possess neither), there can be little doubt that in these cases also the velocity of mutarotation must be a fairly simple function of these two properties.

EXPERIMENTAL.

The first experiments were made with samples of purified glucose and glucose hydrate supplied by Messrs. British Drug Houses, Limited. The suitability of these two samples for experiments on mutarotation was established by the fact that they gave normal values for the velocity coefficient in aqueous solutions, namely, $k_e = 0.0146$ for the anhydrous sample and $k_e = 0.0147$ for the hydrated sample at 20° .* We are indebted to Mr. G. F. Smith

* The values recorded here and in the preceding papers (Parts XIX to XXII) are for $k_e = 1/t\{\log_e(a_0 - a_\infty) - \log_e(a_t - a_\infty)\}$ and not for $k_{10} = 1/t\{\log_{10}(a_0 - a_\infty) - \log_{10}(a_t - a_\infty)\}$.

for a detailed investigation of this point. His observations showed that a commercial sample of glucose, which gave $k_e = [0.0160]$, 0.0142, 0.0145, 0.0144 and 0.0144, after precipitation with alcohol gave $k_e = 0.0153$, 0.0146. After crystallisation of the original sample from alcohol the product gave $k_e = 0.0146$, 0.0146, whilst after a second crystallisation from alcohol it gave $k_e = 0.0145$. The average, $k_e = 0.0146$, of these very concordant data may be taken as a standard velocity coefficient in future tests of the purity of glucose. Values recorded by other workers are set out below for comparison.

Velocity of mutarotation of glucose in water.

	k_{10} .	k_e .	Observer.
(a) At 20°	0.0065	0.0150	Trey (<i>Z. physikal. Chem.</i> , 1895, 18 , 205).
	0.0059	0.0136	Parcus and Tollens (<i>Annalen</i> , 1890, 257 , 160).
	0.0061	0.0140	Levy (<i>Z. physikal. Chem.</i> , 1895, 17 , 307).
	0.00635	0.0146	Hudson and Dale (<i>J. Amer. Chem. Soc.</i> , 1917, 39 , 320).
	0.00627	0.0144	Mackenzie and Ghosh (<i>Proc. Roy. Soc. Edin.</i> , 1914, 35 , 22).
(b) At 25°	0.0104	0.0239	Osaka (<i>Z. physikal. Chem.</i> , 1900, 35 , 702).
	0.0074	0.0170	Trey (<i>ibid.</i> , 1897, 22 , 427).
	0.0100	0.0230	J. Meyer (<i>ibid.</i> , 1908, 62 , 59).
	0.0106	0.0244	Hudson (<i>J. Amer. Chem. Soc.</i> , 1907, 29 , 1573).
	0.0103	0.0237	Böeseken (<i>Ber.</i> , 1913, 46 , 2626).
	0.0104	0.0239	Kuhn and Jacob (<i>Z. physikal. Chem.</i> , 1924, 113 , 387).
	0.0095	0.0219	Worley and Andrews (<i>J. Physical Chem.</i> , 1927, 31 , 744).

When dissolved in methyl alcohol (purified as described in Part XIX and containing about 99.5% MeOH), the anhydrous glucose gave a velocity coefficient $k_e = 0.0006$. The corresponding value for tetramethyl glucose in a sample of methyl alcohol containing 99.1% MeOH was 0.0004, but this was subsequently reduced to 0.0002 by further purification of the alcohol, and even lower values have since been recorded by Worley and Andrews (*J. Physical Chem.*, 1927, **31**, 742) for the velocity coefficient of glucose in anhydrous methyl alcohol. The minimum velocity, however, represents a standard of purity which cannot be maintained in practice, since it corresponds with the conditions required to produce a complete arrest of mutarotation in a hydrocarbon solvent; Worley's velocities, as well as our own, are therefore a little too high at the alcohol end, but not to such an extent as to affect the general form of the velocity curves.

On account of the limited solubility of glucose in ethyl alcohol, suitable solutions could not be prepared in the higher ranges of concentration, and, even when methyl alcohol was used, it was

found convenient to prepare many of the solutions by filtering off an excess of the sugar, instead of by weighing out an exact percentage. Since identical velocity coefficients were obtained for these filtered solutions of glucose in 40% alcohol, and for solutions containing 4% of sugar, it appears that the velocity is not affected by the corresponding changes of sugar concentration; but, since filtration introduces an additional risk of contamination by catalytically active impurities, the difficulty of securing concordant velocities was increased considerably by the sparing solubility of the sugar, and in several cases the experiment had to be repeated more than once before a trustworthy minimum velocity could be recorded. It was therefore decided to regard all the data for glucose as preliminary determinations only, and to confirm the whole of the observations by duplicate experiments with tetramethyl glucose. This procedure had the double advantage that the sugar was of undoubted purity (compare J., 1925, 127, 1387, footnote; 1926, 721), and that solutions of any desired strength could be prepared in an aqueous alcohol of any desired concentration and examined under comparable conditions. Moreover, it was found in practice that much less difficulty was experienced in securing consistent values for the velocity coefficients. Nevertheless, the complete concordance of the velocity curves for tetramethyl glucose with those already plotted for the parent sugar shows that the velocity coefficients finally recorded for glucose must have been substantially correct.

Results.—In order to economise space, all the direct readings of rotatory power have been omitted, but the unimolecular velocity coefficients deduced from them are set out in Tables I to IV below, and are represented graphically in Fig. 1. In general there is no great difference between the velocity of mutarotation in methyl and ethyl alcohols of a given water content, as is seen in the following summary of the data for glucose:

Water (%)	90	80	70	60	50	40	30	20	10
10,000 k_a (EtOH)	114	89	73	61	52	38	—	16	—
10,000 k_a (MeOH)	117	91	76	62	48	39	31	20	13

The two curves must cross, however, on either side of the 50% point, since the velocities at this concentration are slightly less in methyl than in ethyl alcohol, whereas they are slightly greater in the ranges outside 40 to 60% H_2O .

In Fig. 1, the full lines are for tetramethyl glucose, whilst the dotted lines refer to the less trustworthy experiments with glucose. Curves have also been added to show the dielectric constant, and the partial pressure of water vapour, in mixtures of ethyl alcohol and water. The experimental points have been represented as lying

TABLE I.

Mutarotation of Glucose in Aqueous Methyl Alcohol at 20°

Water %.	Sugar %.	Length of tube (cm.).	Vel. coeff., $k_s \times 10^4$.	Water %.	Sugar %.	Length of tube (cm.).	Vel. coeff., $k_s \times 10^4$.
100.0	5	20	146	60	5	20	63
95.2	3	"	131	60	5	"	62
90	5	"	117	49.4	Sat.	60	48
"	3	"	118	49.2	3	20	48
85	"	"	105	40	1	60	39
82.6	"	"	100	30	1	"	31
80.2	"	"	93	25.2	Sat.	"	25
80.1	"	"	91	19.8	"	"	20
77.6	"	"	90	10	1	"	13
75.3	"	"	84	1.5	Sat.	20	11
70.2	"	"	77	0.3	"	60	8
70.0	5	"	76	0.5	"	"	6

TABLE II.

Mutarotation of Glucose in Aqueous Ethyl Alcohol at 20°.

First series.			Second series.		
Water %.	Sugar %.	Vel. coeff., $k_s \times 10^4$.	Water %.	Sugar.	Vel. coeff., $k_s \times 10^4$.
100	5	146	74.7	Sat.	83
90	"	114	"	"	83
80	"	89	70.0	"	72
70	"	73	"	"	74
60	4	62	65.1	"	70
"	Sat.	63	"	"	68
50	"	54	59.5	"	61
			50.2	"	52

TABLE III.

Mutarotation of Tetramethyl Glucose in Aqueous Methyl Alcohol at 20°.

Water %.	Sugar %.	Length of tube (cm.).	Vel. coeff., $k_s \times 10^4$.
100	5	20	127
"	4	60	129
90.1	"	"	108
80.2	"	"	87
70.3	"	"	72
60.1	"	"	58
49.3	"	"	45
40.3	"	"	37
30.1	"	"	32
19.9	"	"	20
0.9	10	"	4

TABLE IV.

Mutarotation of Tetramethyl Glucose in Aqueous Ethyl Alcohol at 20°.

Water %.	Sugar %.	Length of tube (cm.).	Vel. coeff., $k_s \times 10^4$.
100	5	20	127
"	"	"	114
90	"	"	104
85	"	"	93
80	"	"	84
75	"	"	71
70	"	"	61
60	"	"	54
40	"	"	36
20	"	"	20
0	"	"	2

on or near two straight lines for each of the series of observations in aqueous ethyl alcohol, and three straight lines in the case of methyl alcohol. It is probable that the points might be represented equally well as lying on a continuous curve, like Worley's data for

aqueous methyl alcohol at 25°; but for this purpose it would be essential that the curve should be indistinguishable from a straight line at concentrations up to 50% MeOH or 70% EtOH. Whilst, therefore, we do not suggest that there are any real "kinks" in the velocity curves, we have plotted the data on a linear framework, on the ground that they probably belong to the type, of which the real existence was demonstrated many years ago by Pickering (see especially *Phil. Mag.*, 1892, **33**, 134), which can be represented more closely by a pair of intersecting lines than by a single parabolic curve. Discontinuities of an even more striking character than those discovered by Pickering have been recorded by McCombie and his colleagues (J., 1921, **119**, 970; 1923, **123**, 2688) in the data for the velocity of saponification of esters in aqueous alcohols, where "breaks" were observed at 79, 64, 48, and 37% MeOH, and at 80, 62.5 or 59, 46, and 30% EtOH. Since their observations did not include the most dilute alcohols, it is not possible to make a direct comparison of these "breaks" with the rapid changes of curvature which are shown by our data at about 20% MeOH and 25% EtOH; but the change of curvature at 48 to 50% MeOH which is indicated by our data occurs at a concentration agreeing closely with that of their "break" at 48% MeOH. A "break" at this concentration has also been recorded in the viscosity, dielectric constant, and heat of dilution of this series of aqueous alcohols (McCombie, *loc. cit.*, p. 2690).

Summary.

(a) Data are given for the velocity of mutarotation of glucose and of tetramethyl glucose in aqueous methyl and ethyl alcohols.

(b) When the velocity coefficients are plotted against the water content of the solution, a linear relation is seen to extend up to about 50% H₂O in aqueous methyl alcohol and 70% H₂O in aqueous ethyl alcohol.

(c) No parallelism can be traced between the velocity of mutarotation and the partial pressure of the water, or the dielectric constant of the water-alcohol mixtures; but attention is directed to certain analogies with data recorded by McCombie and his colleagues for the velocity of saponification of esters dissolved in aqueous alcohols.

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