

CCCXXXIX.—*Studies of Dynamic Isomerism. Part XXIV. Neutral-salt Action in Mutarotation.*

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*Neutral Salt Action in Catalysis by Acids.*

THE idea of "neutral salt action" in catalysis by acids arose in the first instance from the observation of Arrhenius (*Z. physikal. Chem.*, 1889, 4, 226) that the rate of inversion of sucrose by weak acids was augmented by the addition of neutral salts of strong acids, such as potassium chloride, which, at a concentration of  $N/8$ , increases the catalytic activity of  $N/40$ -acetic acid by 12.6%. Since neutral salts are not themselves catalysts for the inversion of sucrose, this effect was attributed by Arrhenius to the indirect action of the salt in *increasing* the ionising power of the medium and therefore the ionisation of the weak acid; a similar increase of

the catalytic activity of hydroxyl ions by neutral salts has been postulated by Senter (J., 1907, **91**, 460), and by Osaka (*Z. physikal. Chem.*, 1900, **35**, 661). On the other hand, it has been suggested that neutral salts with a common ion may act by *decreasing* the ionisation of the acid, the undissociated molecules of which are assumed to be catalytically active, as well as the hydrogen ions derived from them. Thus, whereas Arrhenius supposed that only the hydrogen ions act as catalysts, Sneath (*Z. Elektrochem.*, 1912, **18**, 539; compare Goldschmidt, *Z. physikal. Chem.*, 1912, **81**, 30, and McBain, J., 1914, **105**, 1517) attributed a part of the catalytic activity of the acid to the undissociated molecules, the activity of the molecules and ions being in the ratio  $k_m:k_h = 0.06:1$  for picric acid, but about 2:1 for hydrochloric acid. On the other hand, Lapworth (J., 1908, **93**, 2163, 2187) and Dawson (J., 1911, **99**, 1; 1914, **105**, 1093), from a study of the influence of water in diminishing the catalytic activity of acids in alcoholic solutions, concluded that catalysis by acids, so far as it depends on the action of ions, is due to the presence of a mere trace of *free* hydrogen ions, the effect of the *hydrated* hydrogen ions (which are mainly responsible for the conductivity of the acid) being relatively unimportant. This conclusion is directly opposite to that of Kendall (*Proc. Nat. Acad. Sci.*, 1921, **7**, 56), who supposes that the hydrolysis of methyl acetate may be catalysed by compounds of anhydrous hydrogen ions with all the other components of the solution; but it was not intended to exclude catalysis by undissociated molecules of the acid, which was widely advocated by Dawson (J., 1915, **107**, 1426) as the "Dual Theory of Acid Catalysis." More recently, Dawson, who gave for the ratio  $k_m/k_h$  values ranging from 1.77 for hydrochloric acid to 0.0034 for acetic acid, has included the anion (but not the metallic kation) of the neutral salt as an independent catalyst, the acceleration produced by these anions being formulated as an inherent property of the ion, comparable with the independent catalytic activity of the hydrogen and hydroxyl ions.

The most important feature of Dawson's work is his repudiation of Arrhenius's hypothesis that the catalytic activity of the ions of a neutral salt is a secondary effect, which is produced only indirectly by stimulating the catalytic activity of some other ion. Each active component is therefore represented by an independent term in his equations. Moreover, Dawson found that he could make use of the *concentrations* of the various components, without attempting to convert them into *activities*. Finally, Dawson's results have attracted widespread attention by reason of their precise quantitative character, which can be illustrated by quoting the catalytic coefficients ( $\times 10^6$ ) deduced from a study of the

velocity of iodination of acetone in presence of sodium acetate and acetic acid, *viz.*,

$$\text{OH}' = 10^7; \text{H}' = 442; \text{Ac}' = 4.5; \text{HAc} = 1.5.$$

The authors of the present paper desire to put on record the fact that, whilst the theory set out in Part XXV (following paper) is a logical development of views advanced in previous papers of this series, the experiments now described were suggested directly by analogy with Dawson's observations on acetone. The analogies that have been detected afford confirmation of the view (which is still based on theory rather than on direct experiment) that the iodination of the ketone and the changes of rotatory power of the sugar are both dependent on a prototropic change, in marked contrast, for instance, to the isomeric change of *N*-chloroacetanilide, which has been shown to depend on a process of reversible chlorination (*Rep. Brit. Assoc.*, 1910, 85).

#### *Neutral-salt Action in Mutarotation.*

The influence of neutral salts on the mutarotation of the reducing sugars has received but little attention, perhaps because the changes of rotatory power proceed so rapidly, even in pure water, that a relatively small acceleration makes the velocities too great for accurate measurement. Ample evidence is available, however, to show that, whilst bases and acids (and even water) are powerful catalysts, no marked acceleration is produced by neutral salts of the type of sodium and potassium chlorides (Lowry, *J.*, 1903, **83**, 1317; Worley, *J. Physical Chem.*, 1927, **31**, 882). Kuhn and Jacob (*Z. physikal. Chem.*, 1924, **113**, 389) have indeed plotted a curve showing the influence of sodium chloride on the velocity of mutarotation of glucose at 25° over a range of acidity and alkalinity from  $p_{\text{H}}$  1 to 7.7. The influence of this salt is shown to be almost negligible throughout, although definite catalytic effects were attributed to the anions of the weak acids which were present in certain buffer solutions.

The experiments that have just been cited leave the impression that neutral salts in general exert only a negligible effect on mutarotation, and that the velocity of mutarotation is determined mainly, even if not quite exclusively, by the acidity or alkalinity of the solution, as represented by its "hydrogen-ion concentration." This view is expressed in a precise mathematical form in Hudson's well-known equation (*J. Amer. Chem. Soc.*, 1907, **29**, 1571), in which the velocity of mutarotation of glucose at 25° is given by

$$k^* = 0.0096 + 0.258[\overset{+}{\text{H}}] + 9750[\bar{\text{O}}\text{H}].$$

\* Calculated by the use of logarithms to the base 10.

This equation represents the observed velocities of mutarotation as depending on the sum of two variable terms, representing respectively the catalytic activity of *hydrogen ions* and of *hydroxyl ions*, together with a constant term which can be attributed to the action of *neutral water*. It has been adopted (with slightly different constants) by Kuhn and Jacob (*loc. cit.*), who write

$$k = 0.0104 + 0.334[\overset{+}{\text{H}}] + 9345[\bar{\text{O}}\text{H}],$$

and has been generally accepted as an adequate expression of all the relevant facts. This is made even more striking if the velocity of mutarotation is plotted against the  $p_{\text{H}}$  values of the solution, in the form of a "catalytic catenary" (Nelson and Beegle, *J. Amer. Chem. Soc.*, 1919, **41**, 559; Kuhn and Jacob, *loc. cit.*; Euler, *Z. anorg. Chem.*, 1925, **146**, 45; 1926, **152**, 113). The resulting curve falls to a shallow minimum at  $p_{\text{H}}$  5, and rises steeply on each side in order to show the rapid increase of velocity which is observed in acid or alkaline solutions for which  $p_{\text{H}} < 2$  or  $> 8$ , *i.e.*, at concentrations of acid or alkali greater than  $N/100$  or  $N/1,000,000$ , respectively. The purpose of the present paper is to prove by direct experiment that the algebraic and the geometric methods of representation are alike inadequate, unless the catalytic activity of at least three other possible components of the solution is also taken into account.

#### EXPERIMENTAL.

(a) *Materials*.—The glucose included a sample recently used in establishing a standard value for the velocity coefficient of the pure sugar (Richards, Faulkner, and Lowry, this vol., p. 113), together with a similar sample which had been purified and tested in the same way. The sodium acetate was thrice recrystallised from distilled water. Acetic acid was distilled from 2% chromic anhydride (Orton and Bradfield, *J.*, 1924, **125**, 960), and on redistillation the fraction of b. p. 116—118° was collected; after freezing, it melted at 16.2°, and therefore contained about 0.2% of water. Hydrochloric acid (approximately 0.2*N*) was standardised by estimating the chlorine gravimetrically, and was diluted to the required strength with conductivity water. The pyridine had been purified by Dr. I. J. Faulkner for experiments on mutarotation (*J.*, 1925, **127**, 2883). The phenol was colourless and melted at 40°. Sodium carbonate and bicarbonate of "A. R." quality were used without further purification.

(b) *Polarimetric and Electrometric Measurements*.—The velocities of mutarotation were determined in solutions containing 2 g. of glucose in 20 c.c. of the solution at 20°; the velocity coefficients

( $k_e$ ) are for time in minutes and for natural logarithms. After mutarotation was complete the  $p_H$  values of the solutions were determined by standard methods. When a hydrogen electrode was used, the gas was passed through alkaline permanganate and saturated mercuric chloride solutions, then over electrically-heated palladinised copper, through water, and finally through a solution identical with that under investigation before entering the electrode vessel; the values of the *E.M.F.* recorded for two electrodes in no case differed by more than 1 millivolt. These  $p_H$  values were checked by measurements with the quinhydrone electrode, or, when the concentration of electrolytes exceeded 0.1*M*, with the hydroquinhydrone electrode (Billmann, *Trans. Faraday Soc.*, 1924, 19, 676). The bicarbonate and carbonate solutions ( $p_H$  7—9) were examined by Dr. W. S. Hughes with a glass electrode, which had been standardised against a phosphate buffer ( $p_H$  6.80) and a borate buffer ( $p_H$  9.24, as determined by means of a hydrogen electrode).

*Determination of the Catalytic Catenary for Glucose at 20°.*

Since the data of Kuhn and Jacob related to 25°, a fresh catalytic catenary was plotted for 20°, for comparison with the data of Euler (*Z. anorg. Chem.*, 1926, 152, 113). This was done (as in the experiments of the earlier workers) by using dilute hydrochloric acid and sodium bicarbonate or carbonate to produce the desired degrees of acidity or alkalinity. The electrometric and polarimetric data are set out in Table I, and the velocity coefficients from Table I have been plotted in Fig. 1 against the  $p_H$  values of the solutions.

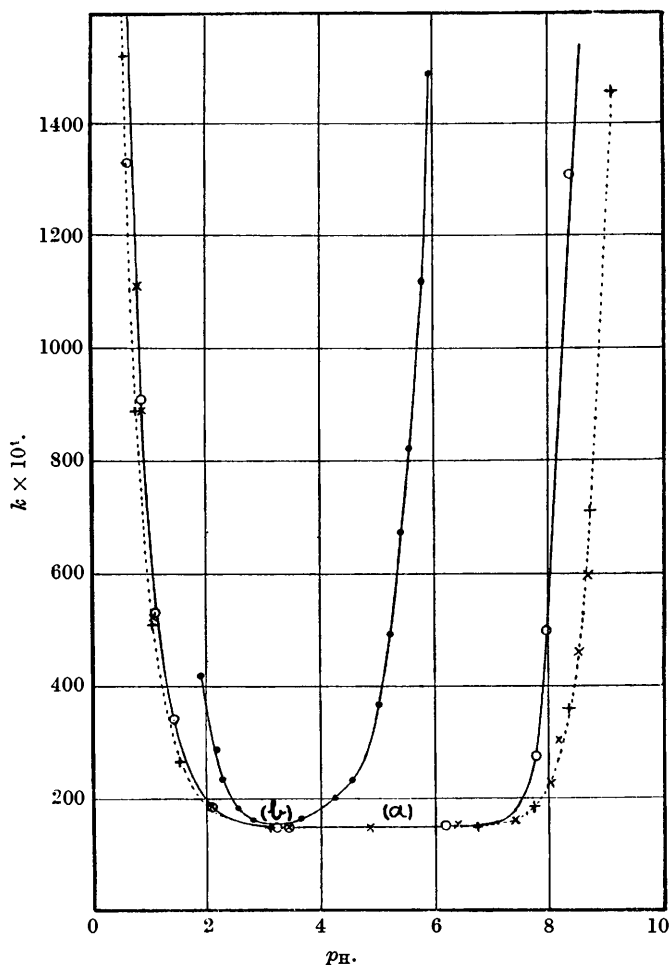
TABLE I.

*Mutarotation of glucose in acid and alkaline solutions.*

Solvent.	Hydrogen-ion concentration, $p_H$ .			$k_e$ .	$k_e -$ 0.0147.	$(k -$ 0.0147)/ $c$ .
	Hydro- gen electrode.	Quin- hydrone electrode.	Glass electrode.			
0.5 <i>N</i> -HCl	0.404	—	—	0.216	0.201	0.402
0.4062 <i>N</i> -HCl	0.483	—	—	0.174	0.159	0.391
0.3 <i>N</i> -HCl	0.619	—	—	0.133	0.118	0.393
0.198 <i>N</i> -HCl	0.900	0.88	—	0.0909	0.0762	0.385
0.1 <i>N</i> -HCl	1.09	1.09	—	0.0529	0.0382	0.382
ca. 0.05 <i>N</i> -HCl	1.44	1.44	—	0.0338		
0.05 <i>N</i> -HCl	1.40	—	—	0.0337	0.0190	0.380
0.01 <i>N</i> -HCl	2.08	2.10	—	0.0184	0.0037	[0.37]
ca. 0.001 <i>N</i> -HCl	3.23	—	—	0.0147		
ca. 0.0005 <i>N</i> -HCl	3.42	3.38	—	0.0147		
ca. 0.0001 <i>N</i> -HCl	6.18	—	—	0.0150		
0.01 <i>M</i> -NaHCO <sub>3</sub>	—	—	7.76	0.0274		
0.05 <i>M</i> -NaHCO <sub>3</sub>	—	—	7.92	0.0497		
0.001 <i>M</i> -Na <sub>2</sub> CO <sub>3</sub>	—	—	8.35	0.131		
0.002 <i>M</i> -Na <sub>2</sub> CO <sub>3</sub>	—	—	8.86	0.196		

The velocities measured by Euler at 20°, and by Kuhn and Jacob at 25°, have also been included in the figure, the latter being divided

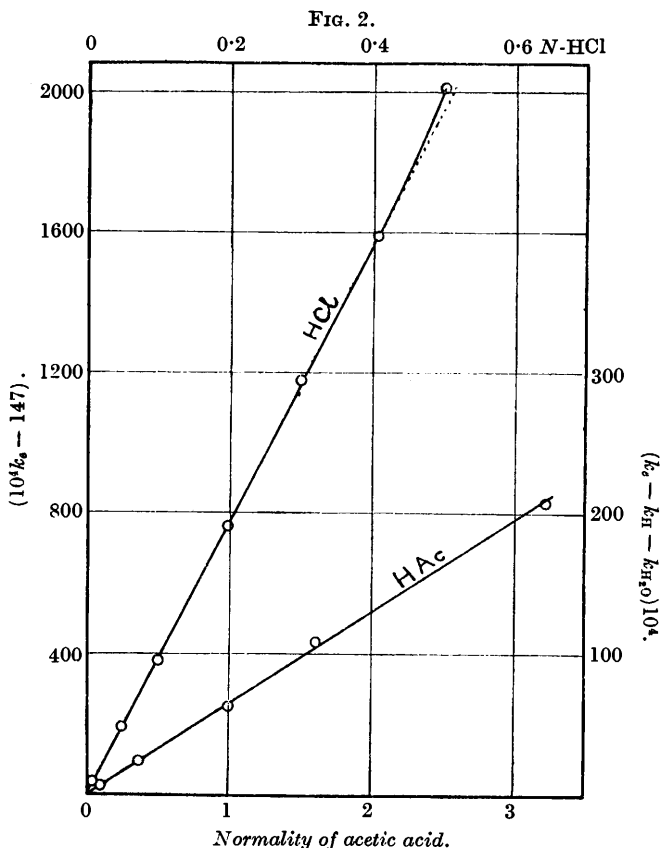
FIG. 1.



Velocity of mutarotation of glucose at 20° in acid and alkaline solutions: (a) the hollow circles are for solutions made acid with hydrochloric acid or alkaline with sodium carbonate or bicarbonate. The crosses (+) on a dotted curve represent Euler's data for 20°. The diagonal crosses (×) represent Kuhn and Jacob's data for 25° reduced to 20° by dividing the velocity coefficients by 1.65; (b) the black circles are for solutions containing (i) various proportions of acetic acid (L.H.), (ii) N/10-acetic acid with various proportions of sodium acetate (R.H.).

by 1.65 to allow for the difference of 5° in temperature (Hudson and Dale, *J. Amer. Chem. Soc.*, 1917, **39**, 320).

(a) *Acid solutions.* The velocity coefficients and hydrogen-ion concentrations were measured in 10% solutions of glucose in aqueous hydrochloric acid over a range from 0.0001 to 0.5*N*-acid. The  $p_H$  values, which were determined with a hydrogen electrode and checked in some cases with a hydroquinhydrone electrode, agree closely in this part of the catenary with those given by the



Velocity of mutarotation of glucose at 20° in presence of hydrochloric and acetic acids.

earlier workers; but these electrometric data do not give a very satisfactory constant for the catalytic coefficient of the ion. On the other hand, Fig. 2, in which the increment produced by the acid in the velocity coefficient of the sugar is plotted against the volumetric concentration of the acid, shows a linear relation between these two quantities which persists up to about 0.4*N*, but is then followed by a definite upward curvature. The values of the ratio

$(k_e - 0.0147)/c$ , which are given in the last column of Table I, show a small progressive increase with increasing concentration, from 0.38 at 0.05*N* to 0.40 at 0.5*N*. This increase can be explained quite readily by accepting Sneath's view that the catalytic coefficient of the undissociated molecules of hydrochloric acid is greater than that of the hydrogen ions derived from them. Since the degree of dissociation of hydrochloric acid in water is about 83% at *N*/2 and 93% at *N*/20, a rough extrapolation to zero concentration would give a limiting value of 0.36 for the catalytic coefficient of the hydrogen ion at 20°. This agrees closely with the coefficient given by Hudson, which is about 0.36, when reduced to base *e* and divided by 1.65 to correct for the difference of 5° in temperature. A much rougher estimate shows that, since the catalytic coefficient of the acid is increased in the ratio of 19 : 20 when the ionisation is decreased from 93 to 83%, that of the undissociated molecules of the acid must be about half as great again (1.53 : 1) as that of the hydrogen ions derived from them, in close agreement with the ratio 1.55 : 1 deduced by Dawson in 1915.

(b) *Alkaline solutions.* On the alkaline side, the quinhydrone electrode is no longer trustworthy, and the hydrogen electrode is subject to error as a result of the displacement of carbon dioxide from the solutions by hydrogen. We have therefore based our calculations on a series of determinations by Dr. W. S. Hughes, in which a glass electrode was used. The alkaline arm of our catenary is therefore notably different from that of the catenaries plotted by Kuhn and Jacob, and by Euler, which are practically coincident when allowance is made for the different temperatures at which their measurements were made. We believe, however, that the velocities now recorded for the mutarotation of glucose in alkaline solutions ( $p_H > 7$ ) are free from a source of error that was previously present, and are therefore more trustworthy than those published hitherto. Whilst, however, it is possible to deduce a satisfactory value for the catalytic activity of the *hydrogen ion* from measurements of the velocity of change in a dilute solution of a strong acid, this cannot be done in the same simple way in the case of the *hydroxyl ion* of an alkali because (i) the concentrations of alkali that are required to produce a given velocity are about 30,000 times smaller than in the case of an acid, and (ii) a very dilute solution of a free alkali inevitably becomes carbonated, and to an unknown extent, by the carbon dioxide of the atmosphere. The required degree of alkalinity can therefore only be maintained by using a "buffer solution"; and, as Kuhn and Jacob have shown, the anion of the buffer solution may have a catalytic activity which is comparable in magnitude with that of the trace of hydroxyl



ions which the solution contains. Since precisely the same considerations must apply to a carbonate or bicarbonate as to a phosphate or citrate, it is clear that solutions that have been made alkaline with sodium carbonate or bicarbonate cannot be used to give an exact value for the catalytic activity of the hydroxyl ion, unless a correction is made for the catalytic activity of the carbonate and bicarbonate ions, of which the concentrations are uncertain and the specific catalytic activities unknown. We therefore merely put on record the fact that the catalytic coefficient of the hydroxyl ion is probably less than  $k_e = 20,000$ , since this number includes the catalytic activity of the bicarbonate ions as well as of the hydroxyl ions; but we are not yet prepared to put forward a more definite value.

(c) *Neutral solutions.* The concentrations of the hydrogen and hydroxyl ions at the isoelectric point are so small that their effect on the velocity of mutarotation of the sugar (as calculated from the effects produced by higher concentrations of acid or alkali) is only of the order of  $1 \times 10^{-5}$ , and is therefore quite inappreciable. This is true, not only at the isoelectric point, but over a considerable range on either side, so that the central part of the catalytic catenary is almost horizontal over the range  $p_H$  3—7. The actual velocity of mutarotation at the isoelectric point, however, so far from being inappreciable, is only a little less than it is in neutral water, where the influence of the ions should be about 100 times greater than at the isoelectric point. Thus Hudson's equation gives a velocity coefficient  $k = 0.0106$  for glucose in neutral water at  $25^\circ$ , falling to a minimum value of  $k = 0.0097$  at the isoelectric point; the velocity at the isoelectric point is therefore 91.5% of that in neutral water. In the same way, the minimum velocity,  $k = 0.01041$ , calculated from the equation of Kuhn and Jacob is 92% of the velocity,  $k = 0.01133$ , in neutral water. These authors therefore concur in postulating a diminution of about 8% in the velocity of mutarotation of glucose in feebly acid solutions. On the other hand, this effect was not observed by Andrews and Worley (*J. Physical Chem.*, 1927, **31**, 882). In the present series of experiments, our own measurements have given a velocity coefficient  $k_e = 0.0147$  at  $p_H$  3.23 and 3.42, and  $k_e = 0.0150$  at  $p_H$  6.18; as contrasted with the standard value  $k_e = 0.0146$  in neutral water at  $20^\circ$ . These measurements therefore afford no experimental confirmation for the very plausible theoretical view that the velocity coefficient in feebly acid solutions should be rather less than in pure water; and it is noteworthy that Euler also does not record any value less than 0.0146 for the velocity coefficient of glucose at  $20^\circ$ , although his measurements at  $5.2^\circ$  show a well-marked minimum.

*Determination of the Catalytic Coefficient of an Undissociated Acid.*

The catalytic coefficient of the undissociated molecules of a strong acid is difficult to detect, because this component only becomes important at high concentrations, when the velocity of mutarotation is too great for accurate measurement. We can, therefore, only put on record a general statement to the effect that the catalytic coefficient of the undissociated molecules of hydrochloric acid is apparently about 1.5 times as great as that of its ions. In the case of a weak acid, such as acetic acid, however, a fairly accurate value for the catalytic coefficient of the undissociated acid can be deduced from the measured velocities of mutarotation of glucose in solutions of the acid. The data for 10% solutions of glucose in acetic acid over the range 0.1—3.22*N* are set out in Table II and plotted in Fig. 2.

TABLE II.

*Mutarotation of glucose in dilute acetic acid at 20°.*

Conc. of acetic acid, <i>N</i> .	$p_H$ .	$k_o$ .	$k_A$ .	$k_o - k_A$ .	$(k_o - k_A)/c$ .
3.22	1.87	0.0416	0.0208	0.0208	0.0065
1.61	2.17	0.0284	0.0175	0.0109	0.0068
1.00	2.26	0.0233	0.0170	0.0063	0.0063
0.370	2.54	0.0182	0.0158	0.0024	0.0065
0.100	2.78	0.0158	0.0152	0.0006	—

In Fig. 2 the velocity coefficients have been diminished by an amount equal to the value of the coefficient in dilute hydrochloric acid of equal electrometric activity, and the differences have been plotted against the normality of the acetic acid. The relation between these two quantities is linear over the whole range of concentrations. This difference is a measure of the catalytic activity of the acid, after allowing for the catalytic activity of the hydrogen ions and of the water in the solution. Since the acid is ionised only to a very small extent (about 1%) even in the most dilute solutions, the constant ratio shown in the last column of Table II gives the catalytic coefficient of the undissociated acid,  $k_c = 0.0065[\text{HAc}]$ .

*Determination of the Catalytic Coefficients of Anions and Kations.*

Although the equations of Hudson and of Kuhn and Jacob contain a "neutral water" term (which is not present in Dawson's equation), there is nothing in their equations to correspond with Dawson's "anion" term. This omission is all the more remarkable in view of the observations made by Kuhn and Jacob on the catalytic activity of buffer solutions. A most important feature

of the present experiments, therefore, was an attempt to discover the existence of an "anion" term in mutarotation, and to determine its magnitude in some particular case. It was already clear from earlier observations that the ions of sodium and potassium chlorides had no marked catalytic properties; but we anticipated on theoretical grounds that the anion of a weak acid might possess appreciable catalytic activity. A difficulty immediately arises, however, from the fact that the salts of a weak acid are hydrolysed to an extent which increases as the dissociation constant of the acid diminishes; moreover, the catalytic activity of the hydroxyl ions resulting from this hydrolysis is so enormous that it would entirely mask any small catalytic activity due to the anion of the acid, unless the latter were present at relatively enormous concentrations. For this reason we adopted the device of adding to the neutral salt (*N*-sodium acetate solution) a quantity of the free acid (*N*/10-acetic acid) sufficient to make the reaction of the solution definitely *acid* instead of *alkaline*. The ideal condition would, of course, be to work at the isoelectric point, where the velocity of mutarotation (in the absence of some catalytically active ion other than hydrogen and hydroxyl) would be, if anything, rather less than in pure water.

(a) *Catalytic coefficient of the acetate ion.* Our first experiment showed that a solution of glucose in *N*-sodium acetate gave a velocity coefficient,  $k_e = 0.0982$  at  $20^\circ$ , which was nearly *seven* times as great as in neutral water ( $k_e = 0.0146$  at  $20^\circ$ ). In this case an acceleration was inevitable in view of the alkaline character of the salt; but this explanation was no longer possible in a second experiment in which the velocity coefficient for 0.961*N*-sodium acetate, *in a solution acidified with N/10-acetic acid to  $p_H$  5.54*, was found to be  $k_e = 0.0822$ , or about *six* times as great as in water. In this experiment, if hydrogen and hydroxyl ions and neutral water had been the only catalysts in the solution, the velocity coefficient would have been  $k_e = 0.0147$ ; and a correction for the catalytic activity of the undissociated molecules of acetic acid would have increased this only to  $k_e = 0.0153$ . This number is rather less than one-fifth of the velocity coefficient actually observed, and, since the sodium ion is known to be inactive, the other four-fifths of the observed velocity must have been due to the *acetate ion*, which was thus shown to be an active catalyst for the mutarotation of the sugar.

Table III gives the velocity coefficients and  $p_H$  values for a series of solutions containing *N*/10-acetic acid, with various proportions of sodium acetate. The velocity coefficients of these solutions are plotted against the  $p_H$  values in the form of a catalytic catenary

TABLE III.

Mutarotation of 10% glucose in 0.1N-acetic acid + sodium acetate at 20°.

NaAc, <i>N</i> .	$p_H$ .	$k_e$ .	$k_e - 0.0153$ .	$(k_e - 0.0153)/c$ .
0.0096	3.64	0.0164	0.0011	—
0.0480	4.25	0.0200	0.0047	—
0.100	4.52	0.0230	0.0077	—
0.300	5.00	0.0365	0.0212	0.071
0.480	5.21	0.0491	0.0338	0.070
0.750	5.41	0.0672	0.0519	0.069
0.961	5.54	0.0822	0.0669	0.070
1.50	5.75	0.119	0.104	0.069
2.00	5.89	0.149	0.134	0.067

in Fig. 1, whilst in Fig. 3 the  $p_H$  values are plotted against the concentrations of sodium acetate.

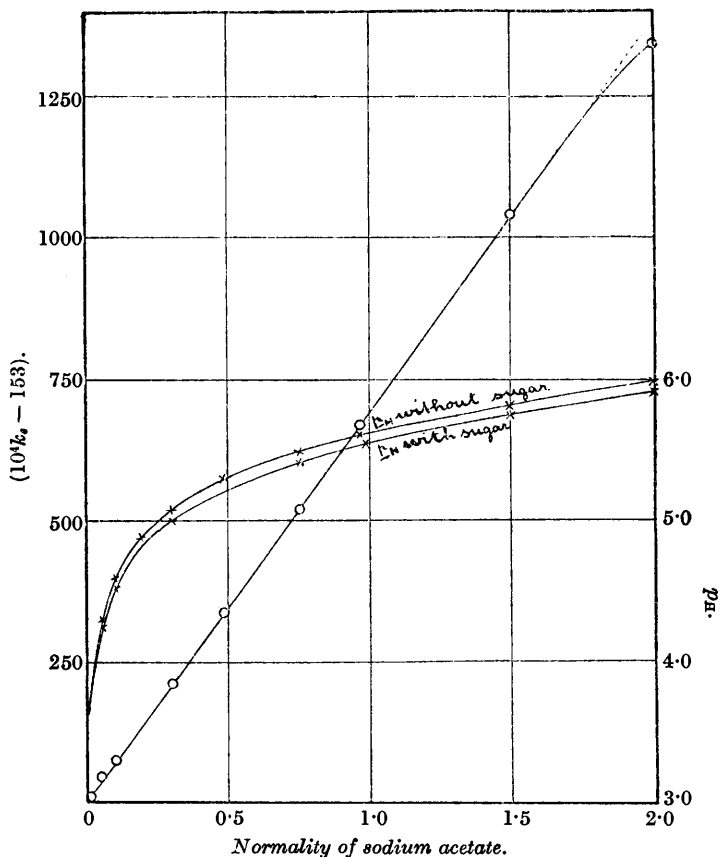
The  $p_H$  values plotted in the upper curve of Fig. 3 for solutions which did not contain any sugar agree closely with those given by Dawson, but these values were lowered when determined in presence of 10% of glucose by an amount which varied from 0.02 to 0.06 as the concentration of the sodium acetate increased from 0.0096 to 0.3*N*, and then remained almost constant up to 2*N*.

The solutions now under consideration were too near to the isoelectric point to exhibit any marked catalysis by hydrogen or hydroxyl ions, but they all contained, in addition to the acetate ion, the catalytically active molecules of water (which would give a partial velocity coefficient of 0.0147) as well as active molecules of *N*/10-acetic acid (which would give a partial velocity coefficient of 0.0006). Fig. 3 shows that, when the difference between the observed velocity coefficients and a constant partial velocity coefficient of 0.0153 is plotted against the volumetric composition of the sodium acetate, these two quantities are proportional to one another over the range from 0.0096*N* to 1.5*N*. The ratio  $(k_e - 0.0153)/c$ , which is given in the last column of Table III, tends to increase in the most dilute solutions; but, over the range from 0.3*N* to 2.0*N*, it gives an average value for the catalytic coefficient of the acetate ion,  $k_e = 0.069$ . In Dawson's experiments on the iodination of acetone, the catalytic coefficient of the acetate ion was about 3 times as great as that of the undissociated molecule of acetic acid, but the ratio of the two coefficients, when deduced from a study of their influence on the mutarotation of glucose, is rather greater than 10 to 1.

(b) *Catalytic coefficient of the ammonium ion.* Theoretical reasons led us to suppose that catalytic activity need not be confined to the *anion* of a salt, but that a *kation* might possess similar catalytic powers, provided that it could be classed as a proton donator. We therefore determined the velocity of mutarotation of glucose

in a *N*-solution of ammonium chloride, and found that, although the hydrogen-ion concentration of the solution ( $p_H$  4.7) coincided almost exactly with the isoelectric point, the velocity coefficient,  $k_e = 0.0159$  at  $20^\circ$ , was actually 8% greater than in neutral water. The catalytic coefficient of the ammonium ion as deduced from

FIG. 3.



Velocity of mutarotation and  $p_H$  values for solutions of glucose in *N*/10-acetic acid with various concentrations of sodium acetate.

this experiment is approximately 0.0012. This is about one-fifth as great as the coefficient for undissociated acetic acid, but sixty times smaller than that of the acetate ion.

#### Catalytic Coefficients of Neutral Salts.

A comparison of the "acetate" catenary of Fig. 1 with the "carbonate" catenaries previously deduced from the behaviour of

carbonate and bicarbonate solutions is very instructive, since it shows the relatively small part that is played by the feeble acidity or alkalinity ( $p_H$  2 to 8) of a buffer solution in determining the velocity of mutarotation of the sugar, and the enormous influence of the neutral or saline components of the solution. In order, however, to dissipate finally the idea that the velocity of mutarotation is determined predominantly by the acidity or alkalinity of the solution, or by its hydrogen-ion concentration, a number of measurements were made with aqueous solutions of glucose containing a salt of a weak acid and a weak base, under conditions which ensured that the hydrogen-ion concentrations were either approximately equal to that of neutral water or intermediate between that of neutral water and the isoelectric point. Since the velocity coefficients calculated from the equations of Hudson or of Kuhn and Jacob are substantially constant from  $p_H$  3 to  $p_H$  7, any solution in this range might be expected, on the basis of these equations, to give a velocity coefficient equal to, or slightly less than, that observed in neutral water; on the other hand, if our theoretical views were well-founded, it appeared likely that a neutral solution containing the neutral salt of a weak acid and base would change much faster than a neutral solution in pure water, or than a neutral solution containing only a neutral salt of a strong acid and base.

(a) *Ammonium acetate*. This prediction was tested by measuring the velocity of mutarotation of glucose in presence of *N*-sodium acetate and *N*-ammonium chloride. Since sodium chloride produces no important changes of velocity, this solution was equivalent to one containing *N*-ammonium acetate. As we anticipated, the sugar in this neutral solution changed even more rapidly than in a solution containing only *N*-sodium acetate, which has a strongly alkaline reaction, or in a solution of ammonium chloride, which is definitely acid in its reaction. The velocity coefficient,  $k_e = 0.106$  at  $p_H$  6.66, was found to be more than seven times as great as in neutral water. It is also about 25% greater than the value,  $0.0147 + 0.0012 + 0.069 = 0.085$ , calculated by adding together the catalytic coefficients of neutral water and of the ammonium and acetate ions. This acceleration, which can be attributed to the "hydrolysis" of the salt to free ammonia and free acetic acid, was in accord with the expectations which we had formed in view of the increase in the amphoteric properties of the solution, which would result from the simultaneous presence of the weak acid and the weak base. The approximate value of the catalytic coefficient of the salt in its various forms is 0.091.

(b) *Pyridine and phenol*. The neutral-salt effect described in the preceding paragraph (which is of a totally different character

from that postulated by Arrhenius, since the increment of velocity produced by the neutral salt was 626% instead of only 12.6%) would obviously become negligible if the acid and base were so weak as no longer to exhibit any appreciable acid or basic properties; it is also known to be negligible when the acid and base are both strong. The effect must therefore rise to a maximum at some intermediate value of the dissociation constants. For this reason, the experiment was repeated, but with phenol and pyridine as the acid and base in place of acetic acid and ammonia. The relevant dissociation constants are set out below, whilst the velocity coefficients and  $p_H$  values are included in Table IV.

Acid dissociation constant, $K_a$ .	Basic dissociation constant, $K_b$ .
Phenol: $1.1 \times 10^{-10}$ at 18° or 25°	Pyridine: $1.6 \times 10^{-9}$ at 18° $2.3 \times 10^{-9}$ at 25°
Acetic acid: $1.8 \times 10^{-5}$ at 18° or 25°	Ammonia: $1.75 \times 10^{-5}$ at 18° $1.8 \times 10^{-5}$ at 25°

TABLE IV.

*Mutarotation of glucose in presence of a weak acid and base.*

Solvent.	$p_H$ .	Velocity coefficient at 20°.
<i>N</i> -Sodium acetate .....	—	0.0982
<i>N</i> -Ammonium chloride .....	4.7	0.0159
<i>N</i> -Sodium acetate } .....	6.66	0.106
<i>N</i> -Ammonium chloride } .....		
0.5 <i>N</i> -Phenol .....	5.8	0.0146
0.1 <i>N</i> -Phenol .....	6.21	0.0147
0.1 <i>N</i> -Pyridine } .....	7.48	0.0447
0.1 <i>N</i> -Phenol } .....		

Since phenol is not sufficiently soluble to give a *N*-solution, the acid and base were used at *N*/10-concentrations, and gave a velocity coefficient,  $k_e = 0.0447$  at 20° for  $p_H$  7.48. The velocity coefficient was therefore 3 times as great as in water, although the  $p_H$  was changed by less than 0.5 unit from that of neutral water. If the slight alkalinity of the solution had been produced by a trace of sodium bicarbonate, the velocity coefficient would have been about 0.0175, or about 40% of that actually observed; the other 60% must therefore be due to the *N*/10-pyridinium phenoxide. The catalytic coefficient of the pyridinium salt as deduced from these data is roughly 0.272. It is noteworthy that the catalytic coefficient of the pyridinium salt in *N*/10-solution is about 3 times as great as that of ammonium acetate in *N*-solution, and is very nearly as large as that of the hydrogen ion, although it is still not so great as that of the undissociated molecules of a strong acid.

*Summary.*

(a) Although the mutarotation of glucose is catalysed by acids and bases, as well as by water, it is not affected appreciably by neutral salts of the type of sodium chloride.

(b) Definite catalytic activity has been detected, however, in (i) the undissociated molecules of a strong or weak acid, (ii) the anion of a weak acid, and (iii) the kation of a weak nitrogenous base.

(c) The catalytic coefficients of these components are

$$[\text{HCl}] \text{ about } 0.5; [\overset{+}{\text{N}}\text{H}_4] = 0.0012;$$

$$[\text{HAc}] = 0.0065; [\overset{-}{\text{A}}\text{c}] = 0.069.$$

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