**294.** *The Rates of Some Acid- and Base-catalysed Reactions, and the Dissociation Constants of Weak Acids in " Heavy " Water.*

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THE discovery of deuterium provided a new approach to the problems of acid and basic catalysis, and it appeared probable that it might provide a means of distinguishing the possible mechanisms. A number of reactions catalysed by acids or bases have been investigated, and in some cases the velocity constant is greater in deuterium oxide than in water (*e.g.*, inversion of cane sugar, Moelwyn-Hughes and Bonhoeffer, *Naturwiss.*, 1934, **22**, 174; *Z. physikal. Chem.*, 1934, **26**, B, 272; Gross, Steiner, and Suess, *Trans. Faraday Soc.*, 1936, **32**, 883; hydrolysis of methyl and ethyl acetates, Schwarz, *Anz. Akad. Wiss. Wien.*, 1934; decomposition of diazoacetic ester, Gross, Steiner, and Krauss, *Trans. Faraday Soc.*, 1936, **32**, 877), but in others it is smaller (*e.g.*, mutarotation of α-*d*-glucose catalysed by water and hydrogen ions, Moelwyn-Hughes, Klar, and Bonhoeffer, *Z. physikal. Chem.*, 1934, **26**, B, 278; ionisation reactions of nitromethane, Wynne-Jones, *J. Chem. Physics*, 1934, **2**, 381).

Moelwyn-Hughes and Bonhoeffer suggested that the enhanced rate of hydrolytic reactions in deuterium oxide was due to the greater stability of the complex with deuterium than of that with hydrogen, and the slower rate in the other reactions has been attributed to the rate-determining process being a proton (or deuteron) transfer. Wynne-Jones (*loc. cit.*, and *Chem. Reviews*, 1935, **17**, 115) has therefore suggested that the use of heavy water provides a means of distinguishing general catalysis [in which the rate-determining process is believed to be the proton (deuteron) transfer from the catalysing acid to the substrate] and specific catalysis by hydrogen ions, where the rate is determined by the concentration of the complex.

The relative rates of a number of other reactions have been investigated, and the temperature coefficients of the methyl acetate reaction determined. The acetal and orthoformate reactions have also been employed to determine the relative strengths of some weak acids in " light " and in " heavy " water. The chief difficulty in this work is the necessity of following the whole reaction with a small quantity of solution. Methods making use of the viscosity and refractive index changes have been devised for determining the velocity constants with about 1 ml. of solution.
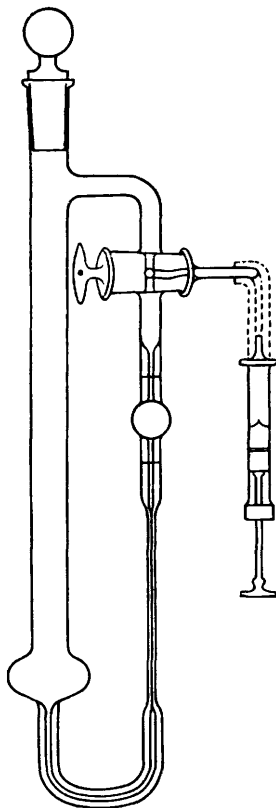
EXPERIMENTAL.

1. *Hydrolysis of Methyl Acetate.*—The reaction in $0.5M$-sulphuric acid was carried out in a viscosity tube, with parallel titrations, and it was found that the increase of viscosity (*ca.* 20%) in the reaction was proportional to the extent of hydrolysis. A small enclosed viscometer was constructed (see fig.) holding about 1 ml. of liquid. The capillary was about 10 cm. long, and the time of flow between the two marks on the upper bulb with water about 100 secs. The liquid was raised to the upper bulb by means of a hypodermic syringe, so that no air escaped. 1 Ml. of acid was placed in the dry viscometer in a thermostat, and its time of flow ($\pm$ 0.2 sec.) observed with a Venner stop watch. Then 0.1 ml. of methyl acetate was added, and the viscometer well shaken to ensure thorough mixing. It was then replaced in the thermostat, and readings of the time of flow taken every 3 mins., the time of the observation being taken to be the middle of the period of flow. If θ_t is the time of flow at the time t, and θ_∞ the final time when the reaction is complete, the amount of methyl acetate remaining is proportional to $\theta_\infty - \theta_t$, and the velocity constant is given by

$$k = (1/t) \cdot \log (\theta_\infty - \theta_0)/(\theta_\infty - \theta_t)$$

where θ_0 is the initial time of flow. Actually, k was determined by plotting log $(\theta_\infty - \theta_t)$ against t. Fairly good linear graphs were obtained, although occasionally trouble was experienced owing to the presence of minute particles of dust in the liquid, and a few experiments had to be abandoned for this reason.

The deuterium oxide contained more than 99·9% of D_2O, $d_{20°}^{20°} = 1.1079$. Solutions in both water and deuterium oxide were made by the addition of A.R. sulphuric acid (99·98%). This reduced the deuterium content of the D_2O to about 97%.

The results are given below, where w is the weight normality, d the density, and c the volume concentration (equivs./litre) of the acid, k the observed velocity constant, and E the apparent activation energy (in kg.-cals.) determined by the Arrhenius equation.

Velocity constants of hydrolysis of methyl acetate.

Solvent.	T.	w.	d.	c.	k (min.$^{-1}$).	k/c.	E.
H_2O	15°	1·381	1·042	1·439	0·00193	0·00134	
	25	1·381	1·039	1·431	0·00520	0·00364	17·0
D_2O	15	1·466	1·150	1·686	0·00408	0·00242	
(97%)	25	1·485	1·151	1·709	0·0104$_3$	0·00610	15·8

$$k_{D_2O}^°/k_{H_2O}^° = 1.85 \ (15°) \ ; \ = 1.68 \ (25°).$$

Alkaline Decomposition of Diacetone Alcohol.—The alkaline hydrolysis of methyl acetate is considerably more rapid than the above, and in solutions dilute enough to give a suitable rate the change of viscosity is too small for convenience. While this work was in progress, Wynne-Jones found by the conductivity method (*Chem. Reviews*, 1935, **17**, 115) that the alkaline electrolysis is more rapid in " heavy " than in " light " water in the ratio 1·33 : 1. Work on this reaction was therefore abandoned, but as an example of basic catalysis (though not strictly a hydrolytic reaction), we examined the reaction $CH_3 \cdot CO \cdot CH_2 \cdot CMe_2 \cdot OH \longrightarrow 2COMe_2$, which is catalysed by hydroxyl, but not at all by hydrogen ions (Koelichen, *Z. physikal. Chem.*, 1900, **33**, 129; Åkerlof, *J. Amer. Chem. Soc.*, 1926, **48**, 3046). These workers used a dilatometric method, which is very inconvenient, but it was found that there is an appreciable decrease of viscosity in the reaction, and the rate can easily be determined by the method described above. The alkaline solutions were made by dissolving A.R. sodium hydroxide in H_2O and in D_2O, a dry air-box being used. The aqueous solutions were carefully standardised independently. The diacetone alcohol was redistilled in a vacuum, and the fraction of b. p. 68°/14 mm. used. 1 Ml. of the alkaline solution was put in the viscometer, and 0·1 ml. of the alcohol added from a capillary pipette. A slight loss of acetone occurred, which made the final viscosity reading somewhat unreliable, but since numerous points are available it was possible to determine the end-point indirectly. If the equation of the unimolecular reaction is written as $d\theta/dt = k(\theta_\infty - \theta_t)$, it can be seen that θ_∞ can be obtained by plotting the values of $d\theta/dt$ against θ_t, which gives a straight line the extrapolation of which to $d\theta_t/dt = 0$ gives θ_∞. This procedure somewhat reduces the accuracy, and the determination of the temperature coefficient was not attempted. The results are given below.

Velocity constants for decomposition of diacetone alcohol.

Solvent.	T.	w.	d.	c.	k (min.$^{-1}$).	k/c.
H_2O	15·0°	0·090	1·004	0·090	0·0210	0·233
D_2O	15·0	0·120	1·111	0·133	0·0383	0·287
(99%)	15·0	0·082	1·109	0·0908	0·0258	0·284

$$k^\circ_{OD'}/k^\circ_{OH'} = 1 \cdot 22 \ (15°).$$

Acid Hydrolysis of Acetal and of Ethyl Orthoformate.—The hydrolysis of these compounds has been studied by Skrabal and by Brönsted and Wynne-Jones (*Trans. Faraday Soc.*, 1929, **25**, 59), who found that catalysis by acids other than hydrogen ions and by bases was undetectable.

The foregoing viscosity method was laborious and exacting, so an attempt was made to find an alternative method. It was found that considerable changes of refractive index occurred in the hydrolysis, and the progress of the reaction could easily be followed by means of a Zeiss interferometer. The change of refractive index usually corresponded to *ca.* 60 drum divisions of the interferometer, and the accuracy of reading was $\pm$ 0·2 division. The reacting solution was placed in one of the cells with an " ether-proof " cover, and a similar solution containing no ester was placed in the other. During the winter months the temperature of the water-bath of the interferometer, which was well jacketted, remained practically constant, but in summer it was necessary to place the whole interferometer in a tunnel constructed in a thermostat. The reaction was followed by noting the drum reading required for the coincidences of the fringes in the upper and the lower part of the field. This method is extremely convenient for following the course of hydrolytic reactions in small quantities of solutions, and the curves obtained are very reproducible. The readings were treated in the same way as the viscosities above; *i.e.*, if η_t is the drum reading at time t, and η_∞ the final reading, the velocity constant is obtained by plotting log $(\eta_\infty - \eta_t)$ against t. Solutions of *ca.* 0·001N-hydrochloric acid were prepared by adding weighed quantities of accurately standardised 0·1M-acid in water to water and deuterium oxide severally. The deuterium content in the D_2O is thereby reduced by about 1%, which is not important.

The hydrolysis of ethyl orthoformate is so rapid that the reaction can only be followed in buffer solutions, for which we used half-neutralised solutions of weak acids. This introduces another factor, *viz.*, the relative dissociation of the weak acid in the two media. The observed ratio of the two rates is given by

$$k_{D_2O}/k_{H_2O} = (c_{D_2O'}/c_{H_2O'})(k^\circ_{D_2O'}/k^\circ_{H_2O'})$$

where $c_{D_2O'}$, $c_{H_2O'}$ are the concentrations of the ions in the two cases, and $k^\circ_{D_2O'}$, $k^\circ_{H_2O'}$ the specific constants for the two ions. In half-neutralised solutions of equal concentrations, the

ratio $c_{D_2O}/c_{H_2O} = K_D/K_H$, where K_D, K_H are the dissociation constants of the acid in D_2O and in H_2O. The value of $k^{\cdot}_{D_2O}/k^{\cdot}_{H_2O}$, which we may call the intrinsic catalytic ratio, is determined directly for acetal by measurements in the dilute hydrochloric acid solutions. The determination of the ratio k_{D_2O}/k_{H_2O} for acetal in the buffer solutions therefore gives a measure of the ratio K_D/K_H. Knowing this ratio for, say, acetic acid, we can now determine the intrinsic ratio of ethyl orthoformate from the observed rates in this buffer solution, and when this is known, this substance may be employed to determine the ratio K_D/K_H of other acids.

In preparing the buffer solutions, a fairly concentrated (1—2M) aqueous solution of the acid was made, and its titre against sodium hydroxide determined. The quantity of alkali required for half-neutralisation was then added, and the buffer solutions were made by adding such quantities of this solution to the two media as were required to give equal volume concentrations of *ca.* $M/100$. The percentage of deuterium in its oxide was thus lowered by 1—2%. The measurements made are summarised in following table.
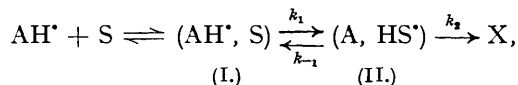
Rates of hydrolysis of acetal and of ethyl orthoformate in various buffer solutions.

Buffer acid.	Concn., mols./l.	K_H.	$k \times 10^3$, min.$^{-1}$.		k_{D_2O}/k_{H_2O}	$k^{\circ}_{D_2O}/k^{\circ}_{H_2O}$	c_{H_2O}/c_{D_2O}
			H_2O.	D_2O.			
			Acetal.				
Hydrochloric......	0·001	—	19·0	50·5	2·66	2·66	1·0
Oxalic...............	0·01	4×10^{-2}	33	84	2·56	2·66	1·0$_4$
Formic	0·0104	2×10^{-4}	4·55	4·49	0·99	2·66	2·6$_8$
Acetic...............	0·0096	$1·8 \times 10^{-5}$	0·67	0·64	0·96	2·66	2·7$_7$
			Ethyl orthoformate.				
Acetic...............	0·0096	$1·8 \times 10^{-5}$	370	280	0·74	2·05	2·7$_7$
Cacodylic	0·0096	4×10^{-7}	14·3	8·9	0·62	2·05	3·3$_0$

DISCUSSION.

In the three cases of acid hydrolysis studied, the reaction in deuterium oxide is considerably faster than that in water. The apparent activation energy of the methyl acetate hydrolysis is smaller in the former than in the latter by an amount which is of about the right order to account for the increase of rate, in agreement with Moelwyn-Hughes and Bonhoeffer's results with sucrose. It is thus clear that the explanation of the difference of rates is to be sought in the energetic factors rather than in the steric factors concerned.

The stages of a hydrolytic reaction catalysed by an acid $AH^{\cdot}$ may be formulated as

$$AH^{\cdot} + S \rightleftharpoons (AH^{\cdot}, S) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (A, HS^{\cdot}) \overset{k_2}{\longrightarrow} X,$$

(I.)   (II.)

where S represents the reacting molecule and X the products. If the concentration of the complex (I) which may be supposed to be in equilibrium with the reactants is $C[AH^{\cdot}][S]$, the reaction rate may be written (cf. Bell, *Proc. Roy. Soc.*, 1936, *A*, 154, 297)

$$- dS/dt = [k_2 k_1/(k_2 + k_{-1})] C[AH^{\cdot}][S]$$

When $k_2 \gg k_{-1}$, $- dS/dt = k_1 C[AH^{\cdot}][S]$, *i.e.*, the proton transfer (I)→(II) is the rate-determining step; but if $k_{-1} \gg k_2$,

$$- dS/dt = (k_1 k_2 C/k_{-1})[AH^{\cdot}][S] = (k_2/K)[AH^{\cdot}][S]$$

where K is the dissociation constant of the complex. In this case, the rate is determined by that of (II) → X, and hence by the equilibrium concentration of the complex (II).

It has been suggested that the increased rate of hydrolytic reactions in heavy water is due to the greater stability of the deuterium complex, *i.e.*, $K_D < K_H$. In Halpern's theory (see below) this is the case when the binding energy of a proton in the complex is greater than that in the $H_3O^{\cdot}$ ion, *i.e.*, when the complex ion has the properties of a *weak* acid. This seems to be impossible, for the addition of the ester to an acid solution would markedly reduce the p_H, and this would be observed without fail. It therefore appears that if the D-complex is more stable than the H-complex, it is on account of factors other than that suggested by Halpern.

Turning now to the relative dissociation constants of weak organic acids as measured by the reaction rates, it is clear that the ratio K_H/K_D increases as the acid becomes weaker. On the assumption that the energy changes of the reactions $HA + H_2O = H_3O^{\cdot} + A'$, $DA + D_2O = D_3O^{\cdot} + A'$, differ only by the respective zero-point energies, and the entropy changes are identical, Halpern (*J. Chem. Physics*, 1935, **3**, 459) obtained the expression

$$K_H/K_D = \exp. - Fh(v_H^W - v_H^A - v_D^W + v_D^A)/2kT,$$

where v_H^W and v_D^W are the fundamental vibration frequencies of the proton and deuteron in $H_3O^{\cdot}$ and $D_3O^{\cdot}$, v_H^A and v_D^A are those for HA and HD, F is the number of degrees of freedom of the oscillation, and h Planck's constant. Writing $v_H = \sqrt{2}v_D$, on account of the difference of mass, we have

$$K_H/K_D = \exp. - (1 - 1/\sqrt{2})Fh(v_H^W - v_H^A)/2kT \quad . \quad . \quad . \quad . \quad (1)$$

Since v_H increases with the binding energy, $v_H^A > v_H^W$ for all acids weaker than $H_3O^{\cdot}$, and K_H/K_D is positive and increases with increasing weakness of the acid.

A more quantitative development of this equation can be made in the following way. If the binding energy of a proton is expressed by Morse's equation

$$Q = Q^{\circ}[e^{-2a(r-r_0)} - 2e^{-a(r-r_0)}]$$

the fundamental frequency is $v = a/\pi . (Q^{\circ}/M)^{\frac{1}{2}}$, where M is the reduced mass of the vibrating system, and a the force constant. Let the values of these quantities for the systems $H^{\cdot}-H_2O$ and $H^{\cdot}-A'$ be a_W, a_A and Q_W, Q_A. Then (1) becomes

$$K_H/K_D = \exp. - (1 - 1/\sqrt{2})(hF/2kT\pi)\left(\frac{a_W Q_W^{\circ \frac{1}{2}}}{M_W^{\frac{1}{2}}} - \frac{a_A Q_A^{\circ \frac{1}{2}}}{M_A^{\frac{1}{2}}}\right) \quad . \quad . \quad (2)$$

The simplest relation between the dissociation constant and the energy change in the dissociation is $Q_A - Q_W = - kT \log K_H$, and inserting this in (2), we get

$$\log K_H/K_D = - \frac{ba_W Q_W^{\circ \frac{1}{2}}}{M_W^{\frac{1}{2}}}\left\{1 - \frac{a_A}{a_W} . \frac{M_W^{\frac{1}{2}}}{M_A^{\frac{1}{2}}}\left(\frac{Q_W^{\circ} - kT \log K_H}{Q_W^{\circ}}\right)^{\frac{1}{2}}\right\}$$

where $b = (1 - 1/\sqrt{2})(hF/2kT\pi)$.
Since $kT \log K_H \ll Q_W$, this may be approximated to

$$\log K_H/K_D = - \frac{ba_W Q_W^{\circ \frac{1}{2}}}{M_W^{\frac{1}{2}}}\left\{1 - \frac{a_A}{a_W} . \frac{M_W^{\frac{1}{2}}}{M_A^{\frac{1}{2}}}\left(1 - \frac{kT \log K_H}{2Q_W^{\circ}}\right)\right\}$$

or

$$\log K_H/K_D = - (1 - 1/\sqrt{2})\frac{v_H^W h}{2kT}\left\{1 - \frac{a_A}{a_W} . \frac{M_W^{\frac{1}{2}}}{M_A^{\frac{1}{2}}}\left(1 - \frac{kT \log K_H}{2Q_W^{\circ}}\right)\right\}$$

Taking $v_H^W h/2$ (the zero-point energy of the proton in $H_3O^{\cdot}$) as 5·17 kg.-cals./g.-mol., and $Q_W^{\circ} = 180$ kg.-cals./g.-mol., and putting $M_W^{\frac{1}{2}} = M_A^{\frac{1}{2}}$, and $F = 1$, we thus obtain

$$\log_{10}(K_H/K_D) = - 2·2(1 - a_A/a_W) - 0·0042 (a_A/a_W) \log_{10}K_H * \quad . \quad . \quad (3)$$

That is, if the force constant a_A is supposed to be constant for a series of acids, the variation of K_H/K_D with K_H will be very small. The observed variation is of a much larger order of magnitude, and must be ascribed to variations of a_A. The acids chosen, except formic and acetic, are of different types, and it would not be surprising if a_A had different values. The following table shows the values of a_A/a_W required by (3) to account for the observed ratios.

Anion.	C_2O_4H'.	$H \cdot CO_2'$.	$CH_3 \cdot CO_2'$.	$(CH_3)_2AsO'$.
$\log_{10} K_H/K_D$	0·017	0·428	0·442	0·518
$-\log_{10} K_H$ †	2·9	5·3	6·3	8·1
a_A/a_W	1·01	1·18	1·18	1·22

* A more exact expression, which avoids the assumption that $Q_A - Q_W = - kT \log K_H$, is $\log_{10} (K_H/K_D) = - 2·2(1 - a_A/a_W) - 0·0042(a_A/a_W)(Q_W - Q_A/2·3kT)$. The conclusion to be drawn from this is the same.

† These are the true dissociation constants obtained by dividing the usual values by the molecular concentration of water.

It is thus possible, if $a_A > a_W$, for an acid to be as strong as or stronger than $H_3O^{\cdot}$, while $K_D/K_H > 1$. Such a circumstance would be sufficient to overcome the difficulty noted above, that if the greater rate of hydrolysis in deuterium oxide is due to a greater concentration of the complex, its dissociation constant in water must be greater than that in deuterium oxide, although it cannot have the properties of a weak acid.

SUMMARY.

1. The relative rates of hydrolysis in water and in deuterium oxide of methyl acetate, acetal, and ethyl orthoformate in acid solutions, and of the decomposition of diacetone alcohol in alkaline solutions, have been determined by micro-methods involving the viscosity or refractive index of the solution.

2. The acetal and orthoformate reactions have been used to determine the ratio of the dissociation constants of some weak acids in the two media. This increases as the dissociation constant of the acid decreases.

3. A modification of Halpern's theory of this effect is given, from which it appears that the ratio is determined mainly by the force constant between the proton and the acid anion rather than by the strength of the bond.

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