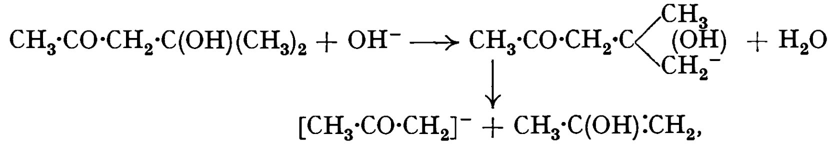
# 179. *Experiments with Heavy Water on the Acid Hydrolysis of Esters and the Alkaline Decomposition of Diacetone Alcohol.*

By W. E. NELSON and J. A. V. BUTLER.

Experiments have been made on the rates of hydrolysis of ethyl formate and methyl acetate in hydrochloric acid solutions in mixtures of water and deuterium oxide. The observations are in reasonable agreement with the calculated " thermodynamic " curves indicating that the reaction proceeds by way of an intermediate complex, probably $\mathrm{R{\cdot}CO{\cdot}\overset{H^+}{O}R'}$, which is in thermodynamic equilibrium with the medium. This reaction should not therefore be subject to general acid catalysis.

Similar experiments were made with the alkaline decomposition of diacetone alcohol, and the " thermodynamic " curve of an alkaline reaction has been calculated for comparison. The actual curve of the reaction rate against the deuterium content of the solution is more exactly linear than the calculated curve, but the difference is too small to be conclusive. The substitution of hydrogen by deuterium in the diacetone alcohol decreases the reaction rate, indicating that the rate-determining step is the transfer of a proton from the alcohol to $OH^-$ (or $OD^-$) :



$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}C(OH)(CH_3)_2 + OH^- \longrightarrow CH_3{\cdot}CO{\cdot}CH_2{\cdot}C\begin{cases}CH_3\\(OH)\\CH_2^-\end{cases} + H_2O$$

$$\downarrow$$

$$[CH_3{\cdot}CO{\cdot}CH_2]^- + CH_3{\cdot}C(OH){:}CH_2,$$

giving an ion which can immediately split into a molecule and ion of enolic acetone. This mechanism explains all the main features of the reaction.

THE use of deuterium compounds has provided a means of distinguishing in suitable cases the various mechanisms of acid- or base-catalysed reactions. It has been found that in some cases the reaction rate is increased and in others decreased by the substitution of deuterium oxide for water in the solvent. It was first suggested (Wynne-Jones, *Chem. Reviews*, 1935, **17**, 115) that, in reactions which are faster in light than in heavy water, the rate-determining step is a proton transfer, while in the reverse case there is an equilibrium between the substrate and hydrogen ions of the type $S + H_3O^+ \rightleftharpoons SH^+ + H_2O$, the concentration of the complex $SD^+$ being greater than that of $SH^+$ (Bonhoeffer and Moelwyn-Hughes, *Z. physikal. Chem.*, 1934, *B*, **26**, 272). In the latter case the complex should be in thermodynamic equilibrium with the medium, and the rate should be determined by the respective proton and deuteron activities of the solution. The former case thus corresponds to Brönsted's definition of general acid catalysis, and the latter to specific hydrogen-ion catalysis. The criterion is not, however, conclusive. Reitz has shown (*Z. physikal. Chem.*, 1937, *A*, **179**, 119) that in the bromination of light acetone, which was apparently a well-established case of general catalysis, the reaction is quicker in heavy than in light water and the variation of the rate with the deuterium content follows the equilibrium curve. The enolisation of acetone involves both acidic and basic catalysis, *viz.*,

$$CH_3{\cdot}CO{\cdot}CH_3 \underset{A^-}{\overset{AH}{\rightleftharpoons}} CH_3{\cdot}C(OH^+){\cdot}CH_3 \xrightarrow{B} CH_3{\cdot}C(OH){:}CH_2$$

and these observations indicate that equilibrium is established in the first stage but not in the second. This is confirmed by the fact that " heavy " acetone reacts more slowly than light in all media. It is clear that conclusions drawn from the relative rates in light and in heavy water should be controlled whenever possible by the use of reactants containing deuterium.

The thermodynamic proton and deuteron activities in an aqueous solution may be expressed as

$$\alpha_{H^+} = \frac{\Sigma H_3O^+ \,.\, f^+[H_2O]^{\frac{1}{2}}}{Q'(n)}\ ; \quad \alpha_{D^+} = \frac{\Sigma H_3O^+ \,.\, f^+[D_2O]^{\frac{1}{2}}}{Q'(n)\sqrt{L}}$$

where $Q'(n)$ is a function, the nature of which has been established empirically by equilibrium measurements (Gross, Steiner, and Süss, *Trans. Faraday Soc.*, 1936, **32**, 883; Orr and Butler, J., 1937, 330). An assumption which permits its theoretical calculation has been suggested recently by Schwarzenbach (*Z. Elektrochem.*, 1938, **44**, 48). With the following equilibrium constants : *

$$\begin{aligned} k_1{}^{+H} &= [H_3O^+]/[H_2O]\alpha_{H^+} & 3k_1{}^{+D} &= [H_2DO^+]/[H_2O]\alpha_{D^+} \\ \tfrac{3}{2}k_2{}^{+H} &= [H_2DO^+]/[HOD]\alpha_{H^+} & \tfrac{3}{2}k_2{}^{+D} &= [HD_2O^+]/[HOD]\alpha_{D^+} \\ 3k_3{}^{+H} &= [HD_2O^+]/[D_2O]\alpha_{H^+} & k_3{}^{+D} &= [D_3O^+]/[D_2O]\alpha_{D^+} \end{aligned}$$

* The statistical factors 3 and $\frac{3}{2}$ are introduced here explicitly, whereas in Orr and Butler's paper they were contained in the constant; *i.e.*, $\frac{3}{2}k_2{}^{+H}$ is identical with Orr and Butler's $k_2{}^{+H}$.

Schwarzenbach's assumption is equivalent to

$$k_1{}^{+\mathrm{H}}/k_1{}^{+\mathrm{D}} = k_2{}^{+\mathrm{H}}/k_2{}^{+\mathrm{D}} = k_3{}^{+\mathrm{H}}/k_3{}^{+\mathrm{D}}$$

by which the equations connecting these constants can be solved, giving

$$\frac{k_2{}^{+\mathrm{H}}}{k_1{}^{+\mathrm{H}}} = \frac{k_2{}^{+\mathrm{D}}}{k_1{}^{+\mathrm{D}}} = \frac{2}{M^{\frac{1}{2}}K^{\frac{1}{2}}} \quad \text{and} \quad \frac{k_3{}^{+\mathrm{H}}}{k_1{}^{+\mathrm{H}}} = \frac{k_3{}^{+\mathrm{D}}}{k_1{}^{+\mathrm{D}}} = \frac{1}{M^{\frac{1}{2}}}$$

where $K = [\mathrm{HOD}]^2/[\mathrm{H_2O}][\mathrm{D_2O}]$ and $L = \alpha^2_{\mathrm{H}^+}[\mathrm{D_2O}]/\alpha^2_{\mathrm{D}^+}[\mathrm{H_2O}] = M(k_3{}^{+\mathrm{D}}/k_1{}^{+\mathrm{H}})^2$. If we define the proton and deuteron activities by putting $k_1{}^{+\mathrm{H}} = 1$, $k_3{}^{+\mathrm{D}} = 1$, and we take $K = 3{\cdot}27$, $M = 15{\cdot}3$, we find that $\frac{3}{2}k_2{}^{+\mathrm{H}} = 1{\cdot}05$ and $3k_3{}^{+\mathrm{H}} = 1{\cdot}21$, which are in reasonable agreement with the constants determined experimentally by Orr and Butler, *viz.*, $\frac{3}{2}k_2{}^{+\mathrm{H}} = 1{\cdot}05$, $3k_3{}^{+\mathrm{H}} = 1{\cdot}10$.

The rate of a reaction in a mixed $\mathrm{H_2O}$–$\mathrm{D_2O}$ solution, which is determined by thermodynamic equilibrium, is given by

$$\kappa(n) = \alpha_{\mathrm{H}^+}k_{\mathrm{H}^+} + \alpha_{\mathrm{D}^+}k_{\mathrm{D}^+}$$

or

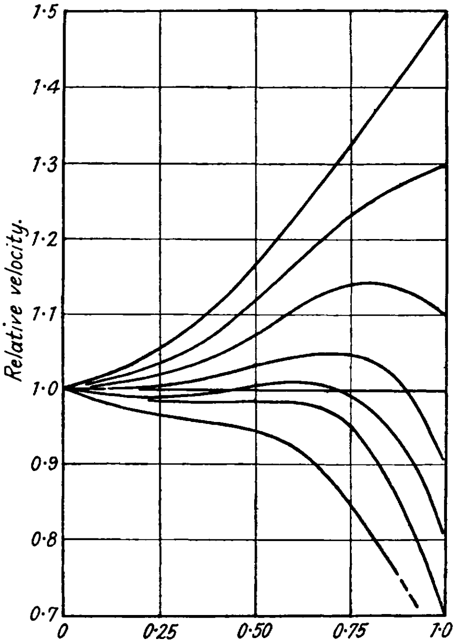
$$\kappa(n) = \Sigma\mathrm{H_3O^+} \,.\, f^+ \left\{\frac{k_1[\mathrm{H_2O}]^{\frac{1}{2}} + k_2[\mathrm{D_2O}]^{\frac{1}{2}}\sqrt{L}}{Q'(n)}\right\}$$

Values of $Q'(n)$, calculated from the theoretical constants given above, are as follows:

| | | | | | |
|---|---|---|---|---|---|
| $n$ | 0·00 | 0·25 | 0·50 | 0·75 | 1·00 |
| $Q'(n)$ | 1·00 | 0·816 | 0·612 | 0·421 | 0·26 |

The curves calculated for various ratios of $\kappa(1)$ from these constants are shown in Fig. 1.

FIG. 1.



*Calculated variation of velocity constant of acid-catalysed reactions, thermodynamic equilibrium between the complex and the solution being assumed.*

Acid-catalysed reactions which have been found to follow the thermodynamic relation are the decomposition of diazoacetic ester, hydrolysis of acetal, bromination of acetone, and (probably) the inversion of cane sugar; on the other hand, the mutarotation of α-glucose shows a large divergence. It is significant that so far as has been investigated all reactions which are faster in heavy water than in light water obey the thermodynamic relation, but no case has been found in which this holds for a slower reaction.

TABLE I.

Ethyl formate in 0·201N-H(D)Cl at 15·0° ± 0·05°.

| | | | | | | |
|---|---|---|---|---|---|---|
| $n$ | 0·00 | 0·27 | 0·72 | 0·82 | 0·96 | 1·00 |
| $n \times 10^3$ | 14·7 | 15·3 | 17·7 | 18·6 | 20·4 | (20·15)* |

$k_{D_2O^+}k/_{H_2O^+} = 1·37$

Methyl acetate in 1·317 N-H(D)Cl at 15·0° ± 0·05°.

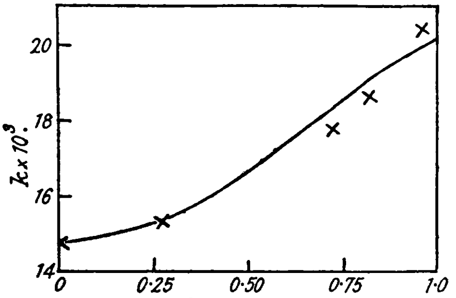
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $n$ | 0·00 | 0·214 | 0·265 | 0·512 | 0·703 | 0·713 | 0·984 | 1·000 |
| $k \times 10^3$ | 3·87 | 4·08 | 4·32 | 4·47 | 5·03 | 5·17 | 6·12 | (6·20)* |

$k_{D_2O^+}/k_{H_2O^+} = 1·60$

* Extrapolated from theoretical curve.

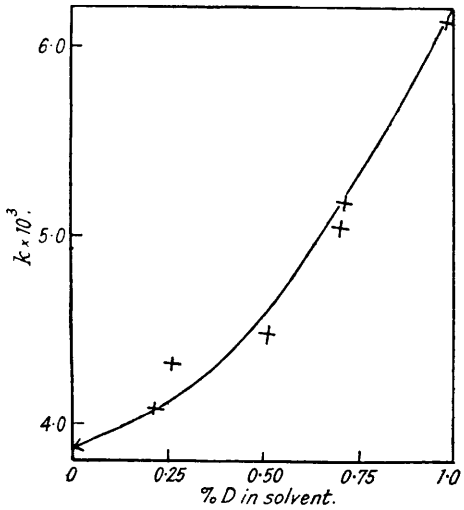
A case of some interest is the hydrolysis of simple esters, in which general catalysis by undissociated acids has been reported (Dawson, J., 1927, 2107, 2444). In this case there does not appear to be any possibility of a pre-equilibrium followed by general basic catalysis, as in the case of acetone, so that the shape of the curve should give conclusive evidence as to the existence of general acid catalysis. Measurements were made with ethyl formate and methyl acetate, and the results are shown in Table I, and Figs. 2 and 3 show the comparison with the calculated curves. The ethyl formate reaction was followed by observation of the refractive-index change in an interferometer. Considerable difficulty was experienced in obtaining stable final readings and the accuracy of the series is not great. For the methyl acetate reaction a direct micro-titration method was employed and the results are in close agreement with the thermodynamic relation. It must be concluded that the complex is in thermodynamic equilibrium with the medium, and general catalysis by acids is therefore improbable.

FIG. 2.



*Variation of velocity of hydrolysis of ethyl formate in* H(D)Cl *solutions with deuterium content of solution.*

FIG. 3.



*Variation of hydrolysis rate of methyl acetate in* H(D)Cl *solutions with deuterium content of solution.*

*Alkaline Catalysis of the Decomposition of Diacetone Alcohol.*—The variation with the deuterium content of the water of a reaction catalysed by alkalis has not previously been investigated. The variation of the activities of the hydroxyl and deuteroxyl ions with the composition of the water could be established by determinations of the dissociation constants of a weak base, or alternatively by calculation from the constants given above, together with the dissociation constants of $H_2O$ and $D_2O$. Since those constants account successfully for the course of the hydrogen-ion catalysis, the latter method has been adopted. The relative concentrations of $OH^-$ and $OD^-$ are determined by the equation

$$2OD^- + H_2O = 2OH^- + D_2O.$$

Writing $N = [OH^-]^2[D_2O]/[OD^-]^2[H_2O]$

and $k_1{}^{-H} = [OH^-]\alpha_{H^+}/[H_2O]; \quad k_3{}^{-D} = [OD^-]\alpha_{D^+}/[D_2O]$

we find that $N = \frac{1}{M}\left(\frac{k_1{}^{+H}k_1{}^{-H}}{k_3{}^{+D}k_3{}^{-D}}\right)^2 = \frac{1}{M}\left(\frac{K_{H_2O}}{K_{D_2O}}\right)^2$

where $K_{H_2O} = [H_3O^+][OH^-], \quad K_{D_2O} = [D_3O^+][OD^-].$

Taking $K_{D_2O}/K_{H_2O}$ as 0·184 at 15° (Wynne-Jones, *Trans. Faraday Soc.*, 1936, **32**, 1397) and $M = 15{\cdot}3$, we have $N = 1{\cdot}93$.

Writing $\Sigma OH^- = [OH^-] + [OD^-]$ and $[OD^-]/[OH^-] = \sqrt{[D_2O]/N[H_2O]} = R(n)$,

we have $[OH^-] = \Sigma OH^-/[1 + R(n)]$

and $[OD^-] = \Sigma OH^-/[1 + 1/R(n)]$

Therefore, if the reaction rate is determined by the hydroxyl- and the deuteroxyl-ion activities, we have

$$\kappa(n) = k_1[OH^-] + k_2[OD^-]$$
$$= \Sigma OH^-[k_1 + k_2R(n)]/[1 + R(n)]$$

and the ratio of the rate in a given solution to that in similar circumstances in light water is

$$\zeta(n) = [1 + (k_2/k_1)R(n)]/[1 + R(n)]$$

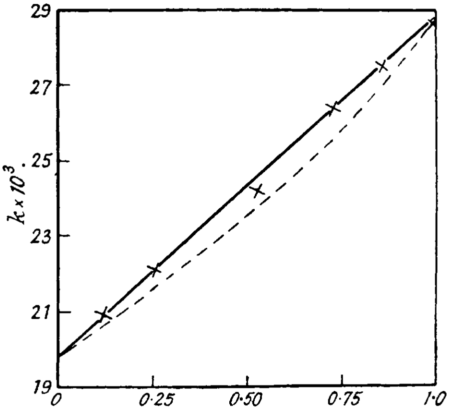
TABLE II.

Decomposition of diacetone alcohol in 0·1185N-NaOH(D) at 15° ± 0·05°.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| $n$ .................. | 0·00 | 0·121 | 0·259 | 0·529 | 0·725 | 0·853 | 0·990 | 0·996 | 1·000 |
| $k \times 10^3$ ......... | 19·8 | 20·9 | 22·1 | 24·2 | 26·4 | 27·5 | 28·6 | 28·7 | (28·7) |

$k_{OD^-}/k_{OH^-} = 1{\cdot}45.$

FIG. 4.



*Alkaline decomposition of diacetone alcohol in* NaOH(D) *solutions.*
– – – *Calculated curve.*

Measurements were made of the rates of decomposition of diacetone alcohol in alkaline solutions of constant alkalinity; the results are given in Table II and the comparison with the calculated curve is shown in Fig. 4. The observed variation is practically linear, whereas the calculated curve has a slight but definite sag. This certainly favours the view that the reaction does not proceed by way of an equilibrium complex, but the difference is too small to be conclusive.

In order to obtain more definite evidence, some " heavy " diacetone alcohol was prepared, containing 60·4% of deuterium, and its rate of decomposition in alkaline solutions in light and heavy water determined. In both cases it reacts appreciably more slowly than the " light " compound :

| | 0·1185N-NaOH in $H_2O$. | 0·1166N-NaOD in $D_2O$. |
|---|---|---|
| " Light " diacetone alcohol | 19·8 | 29·2 |
| " Heavy " diacetone alcohol | 15·8 (17·0) * | 26·6 |

* Original product prior to distillation.

The linearity of the rate with the deuterium content of the alcohol being assumed, the rate of decomposition of the heavy alcohol would be about 0·7 of that of the light compound. This is considerably greater than that observed in comparable cases, *e.g.*, in the neutralisation of heavy and light nitroethane, where the ratio is about 0·1, but the difference from unity seems too great to be ascribed merely to the effect of the additional mass of the deuterium atoms in the molecule.

It is therefore concluded that the rate-determining step is a proton (or deuteron) transfer from the compound to the hydroxyl (deuteroxyl) ion, and the mechanism given in the summary (p. **958**) is indicated. The proton would most naturally be lost from one of the terminal methyl groups adjacent to the hydroxylic oxygen. This half of the molecule is thus converted into enolic acetone, and the molecule would then split into an enolic acetone molecule and the corresponding ion. This accounts for all the main features of the reaction : (1) The " heavy " alcohol reacts more slowly because the transfer of $D^+$ from the compound to $OH^-$ or $OD^-$ is slower than the corresponding transfer of $H^+$. (2) The " light " alcohol reacts more quickly in $D_2O$ than in $H_2O$, because the rate of transfer of a proton to the deuteroxyl ion is more rapid than to a hydroxyl ion; *e.g.*, Wynne-Jones (*J. Chem. Physics*, 1934, **2**, 281) found that the rates of neutralisation of nitroethane in alkaline solutions in light and in heavy water were in the ratio 39 : 60. (3) The reaction is not catalysed by acids. The enolisation of the terminal acetone cannot be effected by acid catalysis because the oxygen is already in the hydroxylic form.

## EXPERIMENTAL.

The diacetone alcohol reaction gives rise to a marked change of refractive index and its progress could easily be followed by the interferometric method previously described. The temperature control in the interferometer was considerably improved by filling all the space inside the water jacket not occupied by the cell or required for the beams of light by massive blocks of metal. The concentration of the alcohol was kept constant throughout the series of solutions, which were made by adding 0·025 c.c. of alcohol to 1 c.c. of solution.

The heavy diacetone alcohol was prepared as follows. Acetone was mixed with an equal volume of " heavy " water (actually the residues from kinetic experiments and containing acetone and alkali) and heated in a sealed vessel at about 70° for 2 days. The acetone was then recovered by fractional distillation and treated with a further quantity of heavy water in the same way. The resulting " heavy " acetone was condensed by refluxing in a small Soxhlet extractor, the condensate running through a thimble of heavy baryta (Conant and Tuttle, " Organic Syntheses," Vol. I, 45). After 3 days the product was fractionated and a good yield of the alcohol obtained.

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KING'S BUILDINGS, WEST MAINS ROAD, EDINBURGH.

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