QUARTERLY REVIEWS

THE RATES OF SIMPLE ACID–BASE REACTIONS

By R. P. BELL, F.R.S.
(BALLIOL COLLEGE, OXFORD)

IT is common experience that reactions between acids and bases in solution take place extremely rapidly, and would often be loosely described as "instantaneous". It might be thought that a reaction between a sufficiently weak acid and a sufficiently weak base would necessarily be slow, since the activation energy cannot be less than the endothermicity. However, in any direct kinetic observation the rate measured refers to the approach to equilibrium, and this involves the velocity constants of both the forward and the reverse reaction: for example, for two opposed first-order reactions the approach to equilibrium follows a first-order law with a velocity constant equal to the sum of the velocity constants for the forward and the reverse reaction. If the forward reaction is endothermic the reverse reaction will be exothermic, and the observed change is again likely to be a very fast one.* Moreover, if both the acid and the base are very weak the extent of their reaction at equilibrium will be small, and it may not be easy to follow the change in the system.

It is possible that the relatively high velocity of acid–base reactions is inherent in their nature as *proton-transfer processes*. The proton is a bare nucleus without any electrons attached to it, and in simple cases its transfer is attended by the minimum of disturbance in the rest of the molecule: in particular, it avoids the repulsion of unshared electrons which accompanies the transfer of other ions and groups, There are, however, a number of ways in which the velocities of acid–base reactions can be measured, either by indirect means or by making use of various techniques which have been developed recently for the study of fast reactions. This Review deals with the different techniques employed, and comments on some of the results obtained.

The ionisation of carbon acids

This subject will be treated briefly and separately, since the velocities involved are comparatively low and most of the measurements have been made by older techniques. The group $\geqslant$CH possesses no detectable acidic properties in simple hydrocarbons, and only very weak ones in acetylenic or aromatic molecules. However, if it is combined with certain

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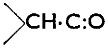
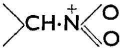
* In other words, in the reaction $A_1 + B_2 \rightleftharpoons B_1 + A_2$ if A_1 and B_2 are both very weak, the conjugate species B_1 and A_2 will be strong and the reverse reaction will be fast.

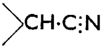
activating groups, of which the most important are $>C{=}O$, $-NO_2$, and $-CN$, the resulting molecules are acids of appreciable strength, usually having pK values in the range 7—20. This increased acidity arises because the negative charge in the anion can now reside on an oxygen or a nitrogen atom rather than on the carbon atom from which the proton has been detached. Thus the groups (*A*), (*B*), and (*C*)



(*A*)

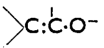


(*B*)

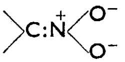


(*C*)

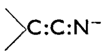
give respectively ions having the structures (*A1*), (*B1*), and (*C1*).



(*A1*)



(*B1*)



(*C1*)

When this type of acid reacts with the base there is, therefore, a considerable degree of electronic rearrangement, and it is not surprising that these reactions are much slower than those of simpler acids of the same strength.

There are a few systems in which the rate of reaction of a carbon acid with a base can be observed directly by conventional methods. The classical example is the reaction of nitro-paraffins with hydroxyl ions, first observed by Hantzsch,[1] and later studied by other workers.[2] The reactions can be readily followed by the change in electrical conductivity, and, more recently, a thermal method has been employed[3] to extend the range of investigation to half-times of only a few seconds. The conductivity method was also used to study the neutralisation of nitro-paraffins by solutions of ammonia and amines,[4] and it was found that the observed velocity cannot be attributed entirely to reaction with the hydroxyl ions present, but must also involve direct reaction with amine molecules, *e.g.*, $CH_3{\cdot}NO_2 + R{\cdot}NH_2 \rightarrow CH_2{:}NO_2^- + R{\cdot}NH_3^+$. This finding is of course analogous to general catalysis by acids or bases in catalysed reactions.

Similar behaviour is found with some other nitro-compounds provided that the reaction is slowed down by reducing the temperature. Thus tri-*p*-nitrophenylmethane reacts at a measurable rate with ethoxide ions in alcohol at —60°, the neutralisation being readily followed by the

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[1] A. Hantzsch and A. Veit, *Ber.*, 1899, **32**, 615. Hantzsch supposed that the observed rate represented the change of the normal form of nitromethane (a pseudo-acid) into its *aci*-isomer (a "true acid"), which then reacted rapidly with hydroxyl ions. It is not now believed that the *aci*- form plays any part in the change, which is regarded as a direct reaction between hydroxyl ions and the nitromethane molecule.

[2] W. F. K. Wynne-Jones, *J. Chem. Phys.*, 1934, **2**, 381; S. H. Maron and V. K. LaMer, *J. Amer. Chem. Soc.*, 1938, **60**, 2588; R. P. Bell and A. D. Norris, *J.*, 1941, 118.

[3] R. P. Bell and J. C. Clunie, *Proc. Roy. Soc.*, 1952, *A*, **212**, 16.

[4] R. G. Pearson, *J. Amer. Chem. Soc.*, 1948, **70**, 204.

colour of the anion produced.[5] The charge distribution in this anion will be a complicated one, but no doubt most of the negative charge resides on the six oxygen atoms. If a weak acid is added to a solution of the sodium salt, the anion is reconverted into the hydrocarbon at a measurable rate, and the dependence of the reaction velocity upon the composition of the solution shows that most of the anions react with undissociated acid molecules rather than with hydrogen ions. This is again analogous to general acid-catalysis, and the rates of reaction with different acid molecules are closely related to their acidic strengths[6] just as in the well-known Brönsted relation for catalysed reactions. Other reactions of similar types have been studied over a wide temperature range by Caldin and his collaborators.[7]

By far the commonest method of measuring the rate of ionisation of carbon acids is the study of *base-catalysed reactions*. Since the anions of these acids differ considerably in electronic structure from the undissociated molecules they can often undergo rapid decomposition, rearrangement, or reaction with other species, and the rate of this reaction is then a measure of the rate at which the substrate reacts with the basic catalyst to form the anion. This field of investigation has been fully documented[8] and will not be dealt with here. The further reaction of the anion makes the ionisation process irreversible, so that the slow forward reaction can be measured without complication by the rapid reverse reaction. The reaction of the anion with halogens (kinetically of zero order with respect to the halogen) has been widely used for this purpose, and a compilation by Pearson and Dillon[9] gives the rates of the reaction $RH + H_2O \rightarrow R^- + H_3O^+$ for 37 carbon acids, mostly determined by this method. When the equilibrium constant of this reaction is known it is possible to deduce the velocity constant of the very fast reverse process.

Rates of hydrogen isotope exchange

If the ionisation of a weak acid takes place in deuterium oxide or a similar deuterated solvent, the reconversion of the anion into the acid will result in the introduction of deuterium into the molecule, and the initial rate of deuteration is equal to the rate of ionisation. This method is particularly suited to slow rates of ionisation, and in comparing it with other methods allowance must be made for the effect of isotopic substitution in the acid or the solvent upon the rate. Many substances which undergo exchange at a negligible rate in neutral solution do so more

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[5] G. N. Lewis and G. T. Seaborg, *J. Amer. Chem. Soc.*, 1939, **61**, 1894. These authors gave a more complex explanation of the observed phenomena, which seems very unlikely: cf. M. Kilpatrick, *ibid.*, 1940, **62**, 1094.

[6] M. Kilpatrick, ref. 5.

[7] E. F. Caldin and J. C. Trickett, *Trans. Faraday Soc.*, 1953, **49**, 772; E. F. Caldin and G. Long, *Proc. Roy. Soc.*, 1955, *A*, **228**, 263.

[8] See, *e.g.*, R. P. Bell, "Acid–Base Catalysis", Oxford, 1941; *Adv. Catalysis*, 1952, **4**, 151.

[9] R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, 1953, **75**, 2439.

rapidly in the presence of alkali, and the acid-base reaction involved is then $RH + OD^- \rightarrow R^- + HDO$. Rough measurements on a large number of carbon acids were made several years ago by Bonhoeffer,[10] and recent work is exemplified by the investigations of Hine and his collaborators[11] on the rates of ionisation of the haloforms. In this last work the deuterium compound CDXYZ (where X, Y, and Z are halogens) was dissolved in an aqueous alkaline solution, and the extent of conversion into CHXYZ determined from time to time by extraction with octane and examination of the infrared spectrum.

As might be expected, protons attached to oxygen undergo exchange with hydroxylic solvents too rapidly for measurement by isotopic exchange methods, but nitrogen is probably intermediate between carbon and oxygen in this respect, and measurable exchange rates have been observed with the cations of ammonia and some amines. In the first work on this subject[12] solutions of ND_4NO_3 in 54% aqueous nitric acid were precipitated after a short time by adding acetone and the isotopic composition of the precipitate was determined. At 0° C, the exchange had half-times of 1—10 minutes, and half-times up to 10 hours were observed in the later work[13] in which the rate of exchange of alkylammonium salts with butanol in chloroform solution was studied by a similar method. A more detailed study of the same kind has been carried out by Swain[14] on the rate of exchange of deuterium or tritium between alkylammonium ions and methanol or ethanol, both species being dissolved in the non-exchanging solvent dimethylformamide. The observed rate was proportional to the concentrations of alkylammonium ion and alcohol, and inversely proportional to the hydrogen-ion concentration, showing that a proton has been lost in the transition state. This cannot be caused by a rapid pre-equilibrium $NR_3H^+ \rightleftharpoons NR_3 + H^+$, since this would itself cause isotopic exchange. The simplest assumption is that the proton is lost from the alcohol molecule, the reactants being NR_3H^+ and MeO^- (or EtO^-); however, Swain produces some evidence that the free ions MeO^- and EtO^- are not present in kinetically significant amounts and prefers the mechanism

$$S + MeOH + NR_3H^+ \rightleftharpoons SH^+ + MeO\text{----}H\text{-----}NR_3 \text{ (Fast)}$$

$$MeO\text{-----}H\text{-----}NR_3 \rightarrow MeOH + NR_3 \text{ (Slow)}$$

where S is the solvent and the intermediate complex is held together by hydrogen-bonding. A mechanism of this kind receives some support from the studies of proton magnetic resonance described in a later section.

[10] K. F. Bonhoeffer, *Trans. Faraday Soc.*, 1938, **34**, 252.

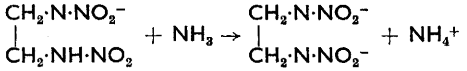
[11] J. Hine, N. W. Burske, M. Hine, and P. B. Lanford, *J. Amer. Chem. Soc.* 1957, **79**, 1406, and earlier papers.

[12] A. L. Brodskii and L. V. Sulima, *Doklady Akad. Nauk S.S.S.R.*, 1950, **74**, 513.

[13] L. Kaplan and K. E. Wilzbach, *J. Amer. Chem. Soc.*, 1954, **76**, 2593.

[14] C. G. Swain and M. M. Labes, *J. Amer. Chem. Soc.*, 1957, **79**, 1084; C. G. Swain, J. T. McKnight, and V. P. Kreiter, *ibid.*, p. 1088.

Slow acid–base reactions involving N–H bonds are presumably also responsible for the change of conductivity with time which is observed when amines are dissolved in alcohols,[15] though the interpretation of these results is not fully understood. The contrast between O–H, N–H, and C–H acids is illustrated by some investigations by Bell and Pearson.[16] With ethylenedinitramine the rate of the reaction



$$\begin{array}{l} CH_2\cdot N\cdot NO_2^- \\ | \\ CH_2\cdot NH\cdot NO_2 \end{array} + NH_3 \rightarrow \begin{array}{l} CH_2\cdot N\cdot NO_2^- \\ | \\ CH_2\cdot N\cdot NO_2^- \end{array} + NH_4^+$$

is just measurable by flow techniques, giving a velocity constant of about 10^5 l. mole^{-1}sec.$^{-1}$, compared with 7×10^{-3} l. mole^{-1}sec.$^{-1}$ for the corresponding reaction of nitroethane. On the other hand the neutralisation of the anion of *p*-nitrophenol by hydrogen ions was immeasurably fast ($t_{\frac{1}{2}} < 10^{-4}$ sec.) even at low temperatures, contradicting an earlier statement[17] which has been widely quoted.

The exchange of phosphine with deuterium oxide is a slow process which is catalysed by both hydrogen ions and hydroxyl ions.[18] Phosphine has extremely weak acidic and basic properties in aqueous solution, and there is little doubt that the velocities of two exchange processes are those of the reactions $PH_3 + D_3O^+ \rightarrow PH_3D^+ + D_2O$ and $PH_3 + OD^- \rightarrow PH_2^- + HDO$, since PH_2D will be formed when either of these reactions is reversed in a medium consisting mainly of D_2O. By making reasonable assumptions about the velocities of these reverse processes the authors were able to estimate values of 10^{-27} and 10^{-26} for the otherwise unobtainable acidic and basic dissociation constants of phosphine.

On the whole, isotopic exchange rates have not been used very extensively for measuring the rates of acid–base reactions, since more convenient and accurate methods are often available. The same applies to the use of *rates of racemisation*, because of the difficulty of preparing optically active compounds. On the other hand, a comparison of the rate of isotopic exchange with that of other processes such as racemisation or chemical reaction has often given information about the details of reaction mechanisms.[19]

The use of relaxation methods

This type of method has been applied recently to a number of acid–base reactions, especially by Eigen and his collaborators.[20] It is necessary that the system should contain a state of physical or chemical equilibrium the position of which can be shifted by a change in some external parameter

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[15] A. G. Ogston, *J.*, 1936, 1023; J. R. Schaefgen, M. S. Newman, and F. H. Verhoek, *J. Amer. Chem. Soc.*, 1944, **66**, 1847.

[16] R. P. Bell and R. G. Pearson, *J.*, 1953, 3443.

[17] G. E. K. Branch and J. Saxon-Deelman, *J. Amer. Chem. Soc.*, 1927, **49**, 1765.

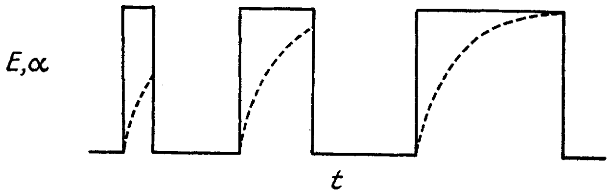
[18] R. W. Weston and J. Bigeleisen, *J. Amer. Chem. Soc.*, 1954, **76**, 3074.

[19] See, *e.g.*, C. K. Ingold, "Structure and Mechanism in Organic Chemistry", London, 1953, pp. 569—575.

[20] For a general account see M. Eigen, *Discuss. Faraday Soc.*, 1954, **17**, 194.

(electric field, pressure, or temperature). If the system is perturbed by a rapid change in this parameter the rate at which it changes to its new equilibrium state can be studied either by direct observation or by its interaction with the perturbing agent. Such systems are usually characterised by a *relaxation* time τ which is the time needed for the system to traverse a fraction 1/e of its path to the new equilibrium. For chemical changes τ is equal to the reciprocal of a first-order velocity constant, and is of the same order of magnitude as the half-time of the reaction.

The principles of the relaxation method can be illustrated by the application of the *electric impulse* technique for measuring the rates of acid–base reactions. The equilibrium degree of dissociation of a weak electrolyte is increased by the application of a strong electric field. This phenomenon is known as the dissociation field effect or the second Wien effect: its magnitude can be calculated theoretically and has been confirmed by experiment. If the field is changed suddenly, the degree of dissociation α will not change immediately to its new value, and Fig. 1 shows how α will change during square-wave electric impulses of varying duration. If the duration of the impulse t is much smaller than the relaxation time τ the average value of α during the impulse will differ little from the low-field value, while if $t \gg \tau$, the average α is close to the high-field value. A measurement of α when $t \simeq \tau$ should therefore make it possible to estimate τ and hence the velocity constant of the dissociation process. Since the conductivity depends upon α, the method used is to measure the high-field conductivity as a function of t. In practice it is often convenient to use a sine-wave impulse instead of a square one, and the conductivity is measured by comparison with a strong electrolyte so as to eliminate that part of the Wien effect which is due to the ionic atmosphere. In order to obtain an appreciable change in α, fields of the order of 10^5 volt cm.$^{-1}$ must be used, together with impulse times of 10^{-5}–10^{-7} sec., which is comparable with the relaxation times involved. At such high field strengths it is in any case necessary to use very short impulses in order to avoid undue heating of the solution.



The electric-impulse method has been used to measure the rates of the reactions $Me{\cdot}CO_2H \rightleftharpoons Me{\cdot}CO_2^- + H^+$ and $NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$,[21] and also to the self-dissociation of water.[22] The results of these and

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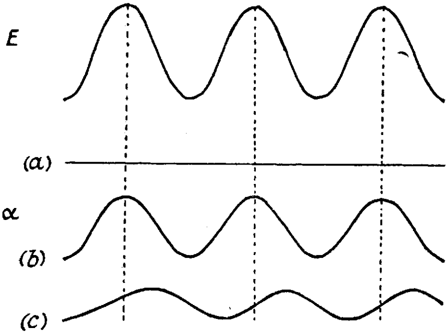
[21] M. Eigen and J. Schön, *Z. Elektrochem.*, 1955, **59**, 483.
[22] M. Eigen and L. de Maeyer, *Z. Elektrochem.*, 1955, **59**, 986.

other measurements are given in the last section of this article. Similarly, measurements of the high-field conductivity of very pure ice gave values for the equilibrium and rate constants of the process $H_2O \rightleftharpoons H^+ + OH^-$ in the solid phase.[23] Under these conditions the ions are removed so fast at high field strengths that the conductivity is determined by the rate at which fresh ions are formed by dissociation. Another application of high-field conductivities is to elucidate the state of carbon dioxide in aqueous solution.[24] In these solutions the equilibrium $H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$ will be affected by the field-strength, but not the equilibrium $H_2CO_3 \rightleftharpoons H_2O + CO_2$; moreover, during the short time of the impulse the second equilibrium does not have time to readjust itself, so that the observed effect relates solely to the dissociation of H_2CO_3. The magnitude of the field effect can be predicted theoretically in terms of the ionic mobilities and the dissociation constant, so that the observed effect leads to a value for the "true" dissociation constant of carbonic acid, $K(H_2CO_3) = [H^+][HCO_3^-]/[H_2CO_3] = 1{\cdot}3 \times 10^{-4}$ at 25°. Since the usual methods of measurement give the apparent constant

$$K(CO_2) = [H^+][HCO_3^-]/([CO_2] + [H_2CO_3]) = 4{\cdot}5 \times 10^{-7},$$

the ratio of the two constants is equal to $[H_2CO_3]/[CO_2] = 0{\cdot}0037$, in satisfactory agreement with earlier less accurate values.

Similar principles apply when a *high-frequency alternating field* is applied to a solution of a weak electrolyte. This is illustrated in Fig. 2,



where the upper curve represents the variation with time of the field strength, and the lower three plots the corresponding variation in the degree of dissociation α for different reaction velocities. Plot (*a*) represents a low velocity, so that α differs negligibly from the value corresponding to zero field, while for curve (*b*) the velocity is so high that α follows the instantaneous field strength and varies in phase with it. The case of most interest is when the half-time of the reaction is of the same order of

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[23] M. Eigen and L. de Maeyer, *Z. Elektrochem.*, 1956, **60**, 1037.

[24] D. Berg and A. Patterson, *J. Amer. Chem. Soc.*, 1953, **75**, 5197; D. M. French and A. Patterson, *J. Phys., Chem.*, 1954, **58**, 693.

magnitude as the periodic time of the field: we then obtain a curve such as (*c*), which has a smaller amplitude than (*b*) and is now out of phase with the applied field. As was first pointed out by Pearson,[25] the conductivity should vary with frequency in this region, but the effect will be a very small one, since only low field strengths can be employed if heating effects are to be avoided. A more promising experimental approach is to measure the dielectric loss, which arises from the phase difference between α and the applied field: this makes the process partially irreversible and leads to a dissipation of electrical energy as heat in excess of the normal power loss due to ionic migration. This method has recently been used to measure the rate constants for the reaction $H_3BO_3 \rightleftharpoons H_2BO_3^- + H^+$, and should be widely applicable.[26]

Analogous considerations apply to the effect of *ultrasonic vibrations* on a solution of an incompletely dissociated electrolyte. The primary effect here is due to the displacement of the equilibrium by the oscillating pressure of the sound wave according to the equation $\partial \ln K/\partial p = \Delta v/\boldsymbol{R}T$, but since the conditions are adiabatic, rather than isothermal, the temperature oscillations may also contribute to the observed effects. In principle it would be equally informative to study the frequency dependence of the velocity of sound (usually observed by determining the wavelength corresponding to a given frequency), of the heat produced, or of the attenuation of the sound-waves: in practice the last is the most convenient. It is of course important to eliminate other factors which can lead to ultrasonic dispersion, such as the finite rate of energy exchange between different degrees of freedom, which can be done in principle by investigating a sufficiently wide range of frequencies and concentrations. Not many acid–base systems have been studied, but the method has been used to obtain a value of 4×10^{10} l. mole^{-1}sec.$^{-1}$ for the velocity constant of the reaction $H^+ + SO_4^{2-} \rightarrow HSO_4^-$.[27] It is noteworthy that this reaction is much faster than reactions of the type $M^{2+} + SO_4^{2-} \rightarrow MSO_4$, where M is a metal, which have velocity constants in the range 10^4—10^6. This is probably because the association of the sulphate ion with a metal cation requires the removal of one or more water molecules from its hydration shell, while in the formation of HSO_4^- from SO_4^{2-} the proton is derived from one of the water molecules originally in contact with the anion, the charge being handed on by the same mechanism which is responsible for the abnormal mobility of the hydrogen ion in water.

Polarographic measurement of reaction rates

The polarograph can be used in some cases for the study of a variety of rate processes.[28] Under ordinary conditions the limiting current observed

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[25] R. G. Pearson, *Discuss. Faraday Soc.*, 1954, **17**, 187.

[26] W. R. Gilkerson, *J. Chem. Phys.*, 1957, **27**, 914.

[27] M. Eigen, G. Kurtze, and K. Tamm, *Z. Elektrochem.*, 1953, **57**, 103.

[28] For a general account of reaction kinetics in polarography, see P. Delahay, "New Instrumental Methods in Electrochemistry", New York, 1954, Chapter V.

at a dropping or rotating cathode (corresponding to the flat part of the polarographic curve) is controlled by the rate at which the reducible species can diffuse to the electrode, and is proportional to the concentration of this species. However, if a small quantity of a reducible species is in chemical equilibrium with a second species which is not reducible, then under suitable conditions of drop-rate, concentration, etc., the observed current may be controlled by the rate of the chemical process producing the reducible species. Because of the complicated diffusion conditions it is difficult to obtain an exact mathematical solution of the kinetic problem involved, but approximate absolute values of velocity constants can be easily obtained, and also fairly accurate relative values for a series of similar reactions. The first use of this method was for aqueous solutions of formaldehyde,[29] in which the equilibrium $CH_2(OH)_2 \rightleftharpoons CH_2O + H_2O$ is far over to the left and only the unhydrated formaldehyde is reducible.

It is usually found that only one member of an acid–base pair is reducible at the cathode: for example, undissociated pyruvic acid, $Me{\cdot}CO{\cdot}CO_2H$, is reducible, while its anion is not. Polarographic measurements[30,31] therefore make it possible to measure the velocity of the very fast reaction $Me{\cdot}CO{\cdot}CO_2^- + H^+ \rightarrow Me{\cdot}CO{\cdot}CO_2H$. Similar measurements have been made with phenylglyoxylic acid and its derivatives.[32] By working over a range of conditions, values were obtained for the rate of reaction of the anion with hydrogen ions, and also for its much slower reaction with weakly acidic species such as H_2O and H_3BO_3.

The above procedure is limited to the rather small class of reducible acids and bases, but the scope of the polarographic method can be greatly extended by using a somewhat different principle. For example, the cathodic reduction of azobenzene takes place according to the scheme $PhN{:}NPh + 2H^+ + 2e \rightarrow PhNH{\cdot}NHPh$, the hydrogen ions being commonly supplied by a buffer system $A \rightleftharpoons B + H^+$. Under suitable conditions the polarographic current is determined by the rate at which hydrogen ions are produced, and since the equilibrium constant is known the velocity constant of the reverse reaction $B + H^+ \rightarrow A$ can also be determined. In principle this method is applicable to any non-reducible buffer system A–B (though in practice there are quantitative limitations), but so far only formic and acetic acid have been studied.[33,34] Because of the low solubility of azobenzene in water, measurements were made in 50% alcohol, but presumably other reducible substances could be used.

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[29] R. Brdicka, *Coll. Trav. Czech. Chim.*, 1947, **12**, 213.

[30] P. Rüetschi and G. Trümpler, *Helv. Chim. Acta.* 1952, **35**, 1957.

[31] P. Delahay and T. J. Adams, *J. Amer. Chem. Soc.*, 1952, **74**, 1437.

[32] K. Wiesner, M. S. Wheatley, and J. M. Los, *J. Amer. Chem. Soc.*, 1954, **76**, 4858; M. S. Wheatley, *Experientia*, 1956, **12**, 339.

[33] P. Delahay and W. Vielstich, *J. Amer. Chem. Soc.*, 1955, **77**, 4955.

[34] P. Ruetschi, *Z. phys. Chem. (Frankfurt)*, 1956, **5**, 323.

Nuclear magnetic resonance[35]

This method of investigation depends essentially on measuring the frequency of the radiation absorbed in transitions between different orientations in a magnetic field of a nucleus possessing a magnetic moment, for example, the proton. The exact frequency absorbed, and also the fine structure of the absorption line, depend upon the environment of the nucleus, and although the differences are extremely small the resolving power in the radio-frequency range is ample for detecting and measuring them. If a solution contains two sets of protons in different environments the observed spectrum depends upon the rate at which the two sets can interchange. If the interchange is slow compared with the frequency used for making measurements two distinct peaks will be observed in the spectrum, but if it is fast there will be only a single peak at a position between the two. If either the rate of interchange or the observing frequency is varied continuously there will be an intermediate range in which the two separate peaks broaden and coalesce, and in this range the mean life of the proton in one of its situations is of the same order of magnitude as $1/\nu$, where ν is the observing frequency. Similarly, the splitting of the lines into a number of components (which is due to the interactions between the observed nucleus and other magnetic nuclei) is lost if the mean life-time is much smaller than $1/\nu$, and will be restored if either the life-time or the frequency is increased. In principle, therefore, the velocity of the interchange can be determined by observing the changes in the spectrum of a given solution when the frequency is progressively varied, or (which is experimentally more convenient) when the frequency is held constant and the reaction velocity varied by altering some property of the solution such as the pH or the concentration.

This method offers great possibilities for measuring the velocities of rapid acid–base reactions, and in particular makes it possible to determine the rate of symmetrical proton-transfers such as $NH_4^+ + NH_3 \rightleftharpoons NH_3 + NH_4^+$. So far, however, most of the kinetic information obtained has been qualitative or semiquantitative in nature. This is partly because of experimental difficulties, but also because the relation between the observed pattern and the velocity constants involved is complicated to derive and difficult to apply in practice. A recent paper by McConnell[36] gives a simple derivation which should be useful in interpreting future observations.

Some of the earliest applications to acid–base kinetics are due to Ogg.[37] He showed that in very pure liquid ammonia the proton-resonance line shows a triplet structure due to interaction with the nucleus ^{14}N, but that this structure disappears on introducing very small amounts of the ions NH_2^- or NH_4^+, the latter by adding a trace of water. This is undoubtedly

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[35] For a general account of this technique, see J. A. S. Smith, *Quart. Rev.*, 1953, **7**, 279; R. E. Richards, *ibid.*, 1956, **10**, 480.

[36] H. M. McConnell, *J. Chem. Phys.*, 1958, **28**, 430.

[37] R. A. Ogg, *J. Chem. Phys.*, 1954, **22**, 560; *Discuss Faraday Soc.*, 1954, **17**, 215.

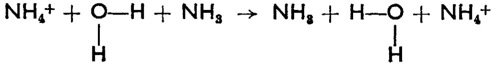
due to the exchange reactions $NH_3 + NH_2^- \rightleftharpoons NH_2^- + NH_3$ and $NH_3 + NH_4^+ \rightleftharpoons NH_4^+ + NH_3$, but only a very rough estimate of the velocity constants could be obtained, partly because the very low ionic concentrations were not well defined. Similar results were obtained by observing the nuclear resonance of the ^{14}N nucleus rather than of the proton. Ogg also showed that an acid solution of an ammonium salt gave a triplet due to $^{14}NH_4^+$ and a singlet due to H_2O, but that in neutral solution these were merged into a single peak by the occurrence of exchange reactions with NH_3 or OH^-.

A quantitative study of the last system has been recently carried out by Meiboom, Loewenstein, and their collaborators, who observed the proton magnetic resonance spectra of solutions of ammonium salts over a range of pH and concentration.[38] The reactions considered (after excluding some improbable ones) were the following:

(1) $NH_4^+ + H_2O \rightarrow NH_3 + H_3O^+$ k_1

(2) $NH_4^+ + OH^- \rightarrow NH_3 + H_2O$ k_2

(3) $NH_4^+ + NH_3 \rightarrow NH_3 + NH_4^+$ k_3

(4)

$$NH_4^+ + \underset{\displaystyle H}{\overset{|}{O}}\!-\!H + NH_3 \rightarrow NH_3 + H\!-\!\underset{\displaystyle H}{\overset{|}{O}} + NH_4^+$$
k_4

In strongly acid solution there is a sharp triplet due to NH_4^+ and a singlet due to H_2O, and the width of these lines gives a maximum value $k_1 < 6 \times 10^{-3}$ l. mole^{-1}sec.$^{-1}$: this is consistent with the approximate values obtained from isotopic exchange experiments. In the range pH = 1·5—2·5 the triplet broadens and coalesces, and the dependence of the broadening upon the ammonia concentration shows that this must be caused by reactions (3) or (4) rather than by $NH_4^+ + OH^-$. The concentration of hydroxyl ions is actually so low that the last reaction would not be detected unless k_2 were greater than 10^{12} l. mole^{-1}sec.$^{-1}$: this is greater than the maximum value expected theoretically, and the electrical impulse method (ref. 21) gives $k_2 = 3 \times 10^{10}$ l. mole^{-1}sec.$^{-1}$. Most of the NH_4^+ broadening is attributed to reaction (3), for which $k_3 = 1{\cdot}1 \times 10^9$, but since it is accompanied by some broadening of the water line, reaction (4) is believed to occur simultaneously with about one-tenth of the velocity.

The same authors have studied the three methylamines in the same way,[39] and for these systems confirmatory evidence is obtained by observing the splitting of the peak from the CH_3 protons, which is due to the protons attached to the nitrogen atom.* The results obtained are similar to those for ammonia, but there are some interesting quantitative differences. Thus the relative importance of reaction (4), involving a water molecule,

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[38] S. Meiboom, A. Loewenstein, and S. Alexander, *J. Chem. Phys.*, 1958, **29**, 969.

[39] E. Grunwald, A. Loewenstein, and S. Meiboom, *J. Chem. Phys.*, 1957, **27**, 630; A. Loewenstein and S. Meiboom, *ibid.*, p. 1067.

* It is not immediately obvious why the CH_3 peak is not further split by the ^{14}N nucleus, but a quantitative theoretical treatment shows that this further splitting should not be detectable.

increases with methyl substitution, and for trimethylamine the direct exchange reaction (3) is undetectable. It seems likely that solvent molecules may take part in many other acid–base reactions, but this cannot be detected by any of the usual means of observation. Trimethylamine also differs from ammonia and the other methylamines in that reaction (1) now makes a detectable contribution, with $k_1 = 6 \times 10^{-2}$ l. mole^{-1}sec.$^{-1}$.

A small amount of information has also been obtained about the exchange of protons attached to oxygen. Thus Arnold[40] found that in "pure" ethyl alcohol the life-time of the –OH proton was about 1 sec., but that this was reduced to about 0·01 sec. in either 10^{-5}M-acid or 10^{-4}M-alkali. This suggests velocity constants in the range 10^6–10^7 l. mole^{-1}sec.$^{-1}$ for exchange reactions such as $\mathrm{EtOH + EtOH_2^+ \rightleftharpoons EtOH_2^+ + EtOH}$ and $\mathrm{EtOH + EtO^- \rightleftharpoons EtO^- + EtOH}$. More quantitative information has been obtained by Loewenstein and Meiboom for aqueous solutions of hydrogen peroxide,[41] in which the main process leading to exchange is a reaction between HO_2^- and H_2O, probably also involving a second water molecule. The study of nuclear magnetic resonance clearly offers great possibilities in acid–base kinetics, as it does in so many other fields, and only a small fraction of these have been explored.

Acid–base reactions of excited species

The fast acid–base reactions of electronically excited species have been recently investigated by Weller,[42] using measurements of fluorescence. Most of these measurements relate to β-naphthol, which is a weak acid (pK 10) but is converted into a much stronger acid (pK 3) on absorbing ultraviolet radiation. Both the excited naphthol molecule and the anion formed from it can lose energy as fluorescent radiation, and the relative intensities of the two types of fluorescence depend upon the rate at which the molecule is converted into the anion. If A–B is any acid–base pair present in solution, the complete kinetic scheme is as follows:

(i) $\mathrm{ROH} + h\nu \rightarrow \mathrm{ROH}^*$
(ii) $\mathrm{ROH}^* + \mathrm{B} \rightleftharpoons \mathrm{RO}^{-*} + \mathrm{A}$
(iii) $\mathrm{ROH}^* \rightarrow \mathrm{ROH} + h\nu'$ (Ultraviolet fluorescence)
(iv) $\mathrm{RO}^{-*} \rightarrow \mathrm{RO}^- + h\nu$ (Blue fluorescence)
(v) $\mathrm{ROH}^* \rightarrow \mathrm{ROH}$ } Quenching
(vi) $\mathrm{RO}^{-*} \rightarrow \mathrm{RO}^-$ }

In practice the reverse of reaction (ii) can be neglected, and the velocity constant for $\mathrm{ROH}^* + \mathrm{B}$ can be evaluated in terms of the observed intensities of the two kinds of fluorescence and the mean life-times of the excited species. The latter are of the order 10^{-8} sec., and are either obtained

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[40] J. T. Arnold, *Phys. Rev.*, 1956, **102**, 136.

[41] M. Anbar, A. Loewenstein, and S. Meiboom, *J. Amer. Chem. Soc.*, 1958, **80**, 2630.

[42] A. Weller, *Z. Elektrochem.*, 1952, **56**, 662; 1954, **58**, 849; 1956, **60**, 1144; 1957, **61**, 956; *Z. phys. Chem.* (*Frankfurt*), 1955, **3**, 238.

from other experiments or estimated theoretically from the extinction coefficients. The base B can be either a water molecule or a constituent of a buffer solution (*e.g.*, acetate ion) and the velocity constants are about 10^9 l. mole^{-1}sec.$^{-1}$. Similar measurements were made for excited acridine and its cation.

Some experimental results

In contrast to the wealth of information for carbon acids (ref. 9) our knowledge of the more rapid reactions of nitrogen and oxygen acids is still fragmentary, and the accuracy of the results is not high. Some of the values are given in the Table, together with a few results for carbon acids for comparison. The first part of the Table shows that, although the strengths of the acids vary over 14 powers of ten, the velocity constant k_2 for the reverse reaction $B + H_3O^+$ remains almost constant at about 3×10^{10} l. mole^{-1}sec.$^{-1}$. (It may be significant that the largest deviations from this mean value are shown by the polarographic data, for which there is the largest uncertainty in the absolute values of the constants.) This suggests strongly that none of these reverse reactions possesses any appreciable energy of activation, the rate being determined by the rate at which the reacting species can come together. The value of 3×10^{10} is in fact in good agreement with theoretical expressions for the rate of a diffusion-controlled reaction between two ions.[43]

Velocities of acid–base reactions (*aqueous solutions at* 18–25° C)

$$A\ (+\ H_2O) \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B + H_3O^+$$

Acid	Method	Ref.	p*K*	log k_1	log k_2
H_2O	Electric impulse	22	15·7	−4·6	11·1
Me_3NH^+	Proton magnetic resonance	39	9·8	1·0	10·8
H_3BO_3	Dielectric loss	26	9·1	1·0	10·1
$Me{\cdot}CO_2H$	Polarography	33, 34	5·4*	5·4*	10·8*
	Electric impulse	21	4·8	5·9	10·7
$H{\cdot}CO_2H$	Polarography	33	4·3*	4·7*	9·0*
$C_{10}H_8{\cdot}OH$*	Fluorescence	42	3·1	7·6	10·7
$Me{\cdot}CO{\cdot}CO_2H$	Polarography	30, 31	2·6	6·3	8·9
HSO_4^-	Ultrasonic	27	1·6	9·0	10·6
$Ph{\cdot}CO{\cdot}CO_2H$	Polarography	32	1·4	10·2	11·6
$Me{\cdot}COMe$	Bromination	9	20	−9·3	10·7
$CH_2(CO_2Et)_2$	„	9	13·3	−4·6	8·7
$CH_2(CN)_2$	„	9	11.2	−1·8	9·4
$Me{\cdot}CO{\cdot}CH_2{\cdot}COMe$	„	9	9·0	−1·8	7·2
$EtNO_2$	„	9	8·6	−7·4	1·2
$Me{\cdot}CO{\cdot}CH_2{\cdot}NO_2$	„	9	5·1	−1·4	3·7
$CH_2(NO_2)_2$	„	9	3·6	−0·1	3·5

k_1 in sec.$^{-1}$, k_2 in l. mole^{-1}sec.$^{-1}$

* Denotes value in 50% alcohol.

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[43] P. Debye, *Trans. Electrochem. Soc.*, 1942, **82**, 265; L. Onsager, *J. Chem. Phys.*, 1934, **2**, 599.

Since k_2 is roughly independent of the acid–base strength of the pair A–B, the forward rate k_1 must be approximately proportional to the acid dissociation constant of A. These two types of behaviour correspond respectively to $\beta = 0$ and $\alpha = 1$ in the equations of the type $k_a = G_a K^{\alpha}$, $k_b = G_b(1/K)^{\beta}$ which relate reaction velocity to acid–base strength in reactions catalysed by acids and bases. It is noteworthy that when these relations were first put forward in 1924 Brönsted and Pedersen predicted that these extreme values would occur in very fast reactions, although it is only recently that experimental evidence has been forthcoming.[44]

The position is different for the carbon acids in the second half of the Table. Although k_2 approaches the maximum value for the very weakest acids, it is usually at least several powers of ten below this, and its value depends not only on the pK of the system but also on the chemical nature of the activating groups in the molecule. This is undoubtedly because of the considerable and varied electronic rearrangements which occur in the ionisation of this type of acid, in contrast to the simple processes involved in the first half of the Table. It would be of interest to extend rate measurements for acid–base reactions to a wider range of chemical types, especially since there has recently been renewed interest in the theory of diffusion-controlled reactions.[45]

[44] J. N. Brönsted and K. J. Pedersen, *Z. phys. Chem.*, 1924, **108**, 185.

[45] See, *e.g.*, R. M. Noyes, *J. Chem. Phys.*, 1954, **22**, 1349; *J. Amer. Chem. Soc.*, 1956, **78**, 5486; A. Weller, *Z. phys. Chem. (Frankfurt)*,1957, **13**, 335.