

The Brønsted Relation – Recent Developments

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1 Introduction

Fifty years ago, Brønsted and Pedersen reported¹ that a series of rate constants, k_B , which they had measured for the base-catalysed decomposition of nitramide, bore a simple relationship to the basicity constants, K_B , of the catalysts:

$$k_B = (6.2 \times 10^{-6}) (K_B)^{0.83} \quad (1)$$

They then suggested that similar correlations might be found for other proton transfer reactions. This hypothesis has been amply confirmed. In fact, it is now generally accepted that all reactions showing general acid–base catalysis will give relationships of the Brønsted type: $k_A = G_A(K_A)^\alpha$ for general acid catalysis and $k_B = G_B(K_B)^\beta = G'_B(K_A)^{-\beta}$ for general base catalysis. A large number of such correlations have been made, and the Brønsted relation has been used not only to summarize data and make predictions, but also for such diverse purposes as detecting changes in reaction mechanism, identifying nucleophile catalysis, and deducing transition-state structure. It should also be noted that the Brønsted relation is a linear free energy relationship, and that it antedates the better known Hammett equation by more than a decade; the already extensive but still rapidly growing area of chemistry which deals with free energy relationships can therefore be traced back directly to the Brønsted relation.²

Although the Brønsted relation is a linear correlation in the free energy sense, there are good reasons for expecting this linearity to hold only over a limited range. Brønsted and Pedersen recognized this themselves, and they predicted in their original paper¹ that $\log k_A$ would in the general situation be a curved rather than a linear function of pK_A . For many years, however, virtually all examples of the Brønsted relation proved to be accurately linear, even over extended ranges of pK_A . It therefore came as somewhat of a surprise when sharply curved relationships were produced recently by data made available through newly developed techniques for measuring the rates of very fast reactions.³ These sharply curved Brønsted plots use oxygen and nitrogen acids and bases as both the proton donor and the proton acceptor, whereas linear relations deal for the most part with proton transfer to or from carbon. It is nevertheless probable that the identity of the atoms between which the proton is being transferred is only

¹ J. N. Brønsted and K. Pedersen, *Z. phys. Chem.*, 1924, **108**, 185.

² L. P. Hammett, in Foreword to 'Advances in Linear Free Energy Relationships', ed. B. N. Chapman and J. Shorter, Plenum Press, London, 1972.

³ M. Eigen, *Angew. Chem. Internat. Edn.*, 1964, **3**, 1.

of secondary importance in determining whether a Brønsted relation will be linear or curved, and that the primary factor is the reactivity of the system; Marcus rate theory⁴ is especially useful in understanding this connection between reactivity and curvature.

Another recent development is the discovery of Brønsted exponents less than zero and greater than one. This is a phenomenon which Brønsted and Pedersen did not anticipate: they, as well as a number of subsequent authorities, expected α and β always to lie in the range zero to one. Marcus theory offers an explanation for anomalous Brønsted exponents such as these, and they may be understood also in terms of substituent effects, particularly those produced by interactions in the transition state.

Transition-state interactions have also been shown recently to be the origin of the dispersion according to charge type generally shown by the catalysts in a Brønsted correlation. Brønsted and Pedersen's own nitramide decomposition reaction provides what is probably the best known example of this phenomenon, but newly discovered cases serve to reinforce the explanation. The regular deviations from Brønsted relations commonly shown by the hydronium and hydroxide ions have also received recent attention and a new explanation.

These three phenomena, (i) curvature, (ii) anomalous exponents, and (iii) systematic deviations, together with their implications on certain uses to which Brønsted relations are often put, form the chief concern of this review.

2 Curvature

As Brønsted and Pedersen pointed out,¹ the rate of proton transfer from an acid to a base [equation (2)] cannot continue to increase in accordance with $k_A = G_A(K_{HA})^\alpha$ indefinitely. As the acid is made stronger and stronger, the rate will



become faster and faster until eventually reaction occurs at every encounter between the acid and base molecules. Once this limit is reached, further increases in acid strength will have no effect: k_A will then be constant and independent of K_{HA} , and α will therefore be equal to zero. In this situation, since $k_A/k_B = K$ and k_A is now constant, k_B will change in inverse proportion to K ; this, because $K = K_{HA}/K_{HB}$ and only K_{HA} is being varied, requires k_B to change as $(K_{HA})^{-1}$, *i.e.* it makes β equal to unity. If, on the other hand, the acid strength of HA is continually decreased, k_B will increase until the rate of reaction in this direction reaches its encounter-controlled limit. No further increase in rate will then be possible, and β will be equal to zero; under these conditions, α will have to be unity.

Arguments such as these led Brønsted and Pedersen to conclude that both α and β would have to change regularly between the limits zero and one. Neither exponent could be constant over any extended range of catalyst strength, and

⁴ R. A. Marcus, *J. Phys. Chem.*, 1968, 72, 891.

relationships such as that of equation (1) could therefore be valid only over limited intervals. They summarized these ideas in the form of a diagram (Figure 1), in which the solid lines represent a simple acid-base reaction [such as that of equation (2) with HA constant and B changing; the abscissa is then $\log K_{HB}$ and $k_D = k_B$], and the broken line refers to some other, more complex, base-catalysed process.

For many years after Brønsted and Pedersen's prediction there was little evidence for curvature in Brønsted relations. This was due in part to the fact that α and β often change only very slowly, and large differences in catalyst strength are therefore needed to produce detectable curvature; this requires considerable variation in catalyst structure, which itself is liable to produce deviations from the correlation. Some indication of curvature, however, was obtained from studies in which the substrate as well as the catalyst was varied. Bell and Lidwell^{5,6a} found that Brønsted relations for the base-catalysed halogenation of a series of ketones, though each accurately linear, gave values of β which decreased systematically with increasing substrate reactivity, and a plot of the pK_A 's of the substrates vs. $\log k$ for the reactions catalysed by a common base (water) was decidedly curved.^{6b}

Striking confirmation of Brønsted and Pedersen's prediction came about ten years ago when techniques for measuring rates of very fast reactions became

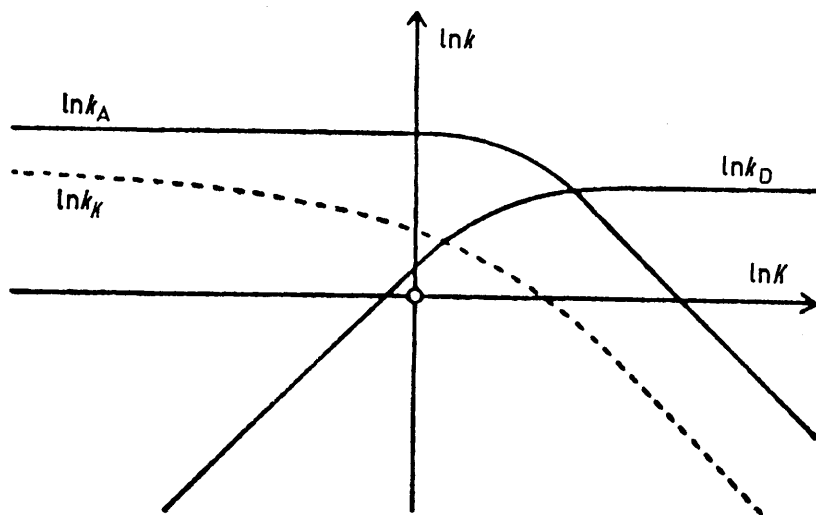


Figure 1 *Brønsted plot curvature predicted by Brønsted and Pedersen in 1924* (Reproduced by permission from *Z. phys. Chem.*, 1924, 108, 185)

⁵ R. B. Bell and O. M. Lidwell, *Proc. Roy. Soc.*, 1940, A176, 88.

⁶ R. P. Bell, 'The Proton in Chemistry', Cornell University Press, Ithaca, New York, 1959 (a) p. 171; (b) p. 163; (c) p. 172; (d) p. 173.

available. Eigen pioneered the application of these methods to acid–base reactions in solution; his data for a typical system, proton transfer to ammonia from a series of oxygen acids,³ are shown in Figure 2. In this diagram, X represents ammonia and HY the oxygen acids; the abscissa is equal to $pK_{HX} - pK_{HY}$ and the ordinate, $\log k$. It may be seen that the logarithm of the protonation rate constant changes from being almost directly proportional to $\log K_{HY}$ ($\alpha = 1$) for the weakest acids to being nearly independent of $\log K_{HY}$ ($\alpha = 0$) for the strongest acids. The reverse reaction gives corresponding behaviour, with β changing from 0 to 1; and the limiting rates agree well with those expected for encounter-controlled processes.

The sharp curvature shown by these Brønsted plots stands in marked contrast to the behaviour commonly found in other systems, where linear relations often extend over pK_a ranges comparable with, and sometimes even greater than, that of Figure 2. A possible cause of this striking difference is suggested by the fact that the curved relationships almost invariably use oxygen and nitrogen, and in a few cases sulphur, acids and bases as both the substrates and the catalysts. These substances are often inorganic, and they are in general species to which one would normally attach the label ‘acid’ or ‘base’. Eigen, in fact, classifies them as ‘normal’ acids and bases, and he calls the curved Brønsted plots which they generate, ‘normal’ behaviour.³ The systems giving linear plots, on the other hand, almost always involve proton transfer to or from carbon, *i.e.* although the catalysts may be oxygen and nitrogen acids or bases, the substrates are either carbon acids, such as nitro or carbonyl compounds, or carbon bases, such as

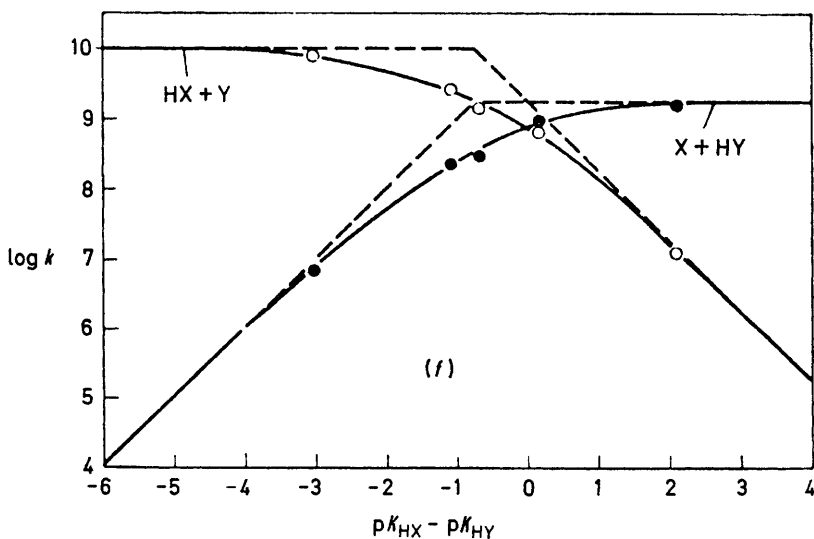


Figure 2 Brønsted plot curvature confirmed by Eigen in 1964
(Reproduced by permission from *Angew. Chem. Internat. Edn.*, 1964, 3, 1)

vinyl ethers or alkoxybenzenes. These are substances to which one does not normally attribute acidic or basic properties, and they are therefore often called 'pseudo' acids and bases.

This suggests that the identity of the atoms between which the proton is being transferred is important in determining whether a Brønsted relation will be linear or curved, with linearity associated with carbon atoms and curvature a property of oxygen and nitrogen. Quite recently, however, sharply curved Brønsted relations were found for certain carbon acids. This development is due mainly to Long, who discovered that rates of proton transfer from cyanocarbons, such as malononitrile, to oxygen and nitrogen bases give Brønsted relations similar to that of Figure 2, *i.e.* they have linear portions of slope 1 and 0 which are connected by curved transition regions.⁷ Subsequent work shows that chloroform⁸ and phenylacetylene⁹ behave similarly.

These studies therefore negate the idea that the identity of the atoms between which the proton is transferred determines whether a Brønsted plot will be linear or curved, but they also point to another property, reactivity, which very probably is the controlling factor. Proton transfer between the oxygen and nitrogen acid-base pairs which give sharply curved Brønsted plots is very fast in the exothermic direction, and the same is true of the cyanocarbons, chloroform, and phenylacetylene. Proton transfer involving the carbon acids and bases which give linear Brønsted plots, on the other hand, is invariably slow, even when exothermic. This suggests, then, that rapid proton transfers, whether they involve carbon or not, will give curved Brønsted relations, and slow proton transfers, again irrespective of the identity of the atoms involved, will give linear relationships. Most proton transfers to or from carbon are of course slow, and this accounts for the preponderance of linear relations involving carbon. Moreover, since very few fast reaction rates were measured before the beginning of the past decade, all but the most recent history of the Brønsted relation is dominated by linear relationships.

Support for a connection between reactivity and Brønsted plot curvature comes from Marcus theory.⁴ This theory relates the free energy of activation for a proton transfer process, ΔG^\ddagger , to the standard free energy of reaction, ΔG° , through the free energy of activation when ΔG° is zero, ΔG_0^\ddagger [equation (3)]. The latter is the barrier to reaction when the process is free of any exothermic drive

$$\Delta G^\ddagger = (1 + \Delta G^\circ/4\Delta G_0^\ddagger)^2 \Delta G_0^\ddagger \quad (3)$$

or endothermic impediment; it is therefore a good measure of the intrinsic reactivity of the system, and Marcus in fact calls it the 'intrinsic barrier'. Since the Brønsted exponent α may be identified with the derivative $d\Delta G^\ddagger/d\Delta G^\circ$

⁷ (a) E. A. Walters and F. A. Long, *J. Amer. Chem. Soc.*, 1969, **91**, 3733; (b) F. Hibbert, F. A. Long, and E. A. Walters, *ibid.*, 1971, **93**, 2329; (c) F. Hibbert and F. A. Long, *ibid.*, 1972, **94**, 2647.

⁸ Z. Margolin and F. A. Long, *J. Amer. Chem. Soc.*, 1972, **94**, 5108; 1973, **95**, 2757.

⁹ A. J. Kresge and A. C. Lin, *J.C.S. Chem. Comm.*, 1973, 761.

[equation (4)],* and the curvature of a Brønsted plot, with the rate of change of α with ΔG° or second derivative of ΔG^\ddagger with respect to ΔG° [equation (5)], Marcus theory immediately provides a connection between curvature and reactivity. The resulting relationship predicts that intrinsically fast reactions (small ΔG_0^\ddagger) will show sharp curvature (large $d\alpha/d\Delta G^\circ$), and intrinsically slow reactions (large ΔG_0^\ddagger) will show little curvature (small $d\alpha/d\Delta G^\circ$).

$$\alpha = d\Delta G^\ddagger/3\Delta G^\circ = (1 + \Delta G^\circ/4\Delta G_0^\ddagger)/2 \quad (4)$$

$$d\alpha/d\Delta G^\circ = 1/8\Delta G_0^\ddagger \quad (5)$$

It is illuminating to evaluate equation (5) for some representative intrinsic barriers. When $\Delta G_0^\ddagger = 1$ kcal mol⁻¹, α changes from 0 to 1 over the interval $\Delta G^\circ = -4$ to $+4$ kcal mol⁻¹, which corresponds to a difference in catalytic strength of 5 pK units at 25 °C. With a barrier as small as this, the rate constant for a thermoneutral process at 25 °C is 1×10^{12} l mol⁻¹ s⁻¹; this is above the encounter-controlled limit, and such behaviour might therefore be typical of proton transfer between an oxygen or nitrogen acid-base pair, which is known to be a diffusion-controlled reaction. When $\Delta G_0^\ddagger = 10$ kcal mol⁻¹, on the other hand, a difference of 55 pK units is required to change α from 0 to 1, and when $\Delta G_0^\ddagger = 20$ kcal mol⁻¹, the range needed becomes 110 pK units. In the latter case, a change in catalyst strength of 5 pK units, a difference typically used in practice, would change α by slightly less than 0.05; a change as small as this would be difficult to detect experimentally and the Brønsted plot would therefore appear to be linear.

Marcus rate theory was first devised for outer-sphere electron transfer reactions in solution, where it has received considerable empirical support on a quantitative level.¹⁰ Its extension to proton transfer reactions in solution is more dubious, but the fundamental ideas of the theory seem at least to be qualitatively correct. For example, Marcus himself has applied equation (3) to literature data for a number of reaction series, most of which had previously been assigned linear Brønsted relations.¹¹ It is difficult to say in most cases whether curved relationships fit the data any better, but the intrinsic barriers which result from

* Although the Brønsted relation correlates specific rates of proton transfer between a substrate and a series of catalysts with the ionization constants of the catalysts, and it therefore relates rates and equilibria of two different processes, this is equivalent to correlating rates and equilibria of a single, *i.e.* the catalysed, reaction. This follows from the fact that the equilibrium constant for the substrate protonation reaction, $\text{HA} + \text{S} \rightarrow \text{A} + \text{HS}$, is equal to the acidity constant of the catalyst divided by the acidity constant of the protonated substrate: $K = (\text{A})(\text{HS})/(\text{HA})(\text{S}) = K_{\text{HA}}/K_{\text{HS}}$. Since the substrate, and therefore K_{HS} , remains constant along the reaction series, K and K_{HA} must vary in exactly the same way, and one may be substituted for the other in the correlation: $k_{\text{HA}} = G(K_{\text{HA}})^\alpha = G'(K)^\alpha$. In terms of free energies, then, the Brønsted relation correlates the free energy of activation of the proton transfer reaction, ΔG^\ddagger , with its standard free energy of reaction, ΔG° , and the Brønsted exponent measures the rate of change of the former with respect to the latter: $\alpha = \delta\Delta G^\ddagger/\delta\Delta G^\circ$, which, in the limit, is $d\Delta G^\ddagger/d\Delta G^\circ$.

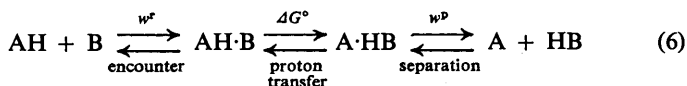
¹⁰ See, for example, R. E. Weston, jun., and H. A. Schwartz, 'Chemical Kinetics', Prentice Hall, New York, 1972, pp. 205–213.

¹¹ A. O. Cohen and R. A. Marcus, *J. Phys. Chem.*, 1968, 72, 4249.

this analysis do increase as factors known to slow proton transfer reactions, such as heavy atom reorganization and charge delocalization, come into prominence; the expected relationship between curvature and intrinsic reactivity is thus readily apparent.

There is also some independent theoretical support for Marcus theory. A relationship of the form of equation (3) can be obtained from a solvent polarization model for proton transfer,¹² and from the Leffler principle¹³ relating transition state to reactant and product free energies.¹⁴ Equation (3) may also be derived from the expression for an Eckart reaction barrier,¹⁵ and it follows as well from a simulation of the proton transfer process in terms of two intersecting parabolic potential energy functions.¹⁶ The latter model, however, as well as one based upon the BEBO method¹⁷ of predicting reaction barriers leads to important quantitative differences from equation (2) (see below).^{18,18}

Some difficulties also emerge from certain more detailed quantitative applications of Marcus theory to experimental data. These analyses use the extended description of proton transfer as a three-step process, upon which Marcus based his theory⁴ but which he did not himself use in his own analysis of experimental data.¹¹ This formulation, equation (6), treats the encounter of reactants and the



separation of products as distinct steps, separate from the actual proton transfer itself. Equation (3) is then taken to apply only to proton transfer within the encounter complex and not to the diffusion steps preceding and following it. This makes the observed free energy of activation, $(\Delta G^\ddagger)_{\text{obs}}$, equal to ΔG^\ddagger calculated by equation (3) plus w^r , the work expended in forming the encounter complex, or free energy of formation of $\text{AH}\cdot\text{B}$ from separated AH and B . The observed free energy of reaction, $(\Delta G^\circ)_{\text{obs}}$, is likewise equal to ΔG° , the free energy change for reaction within the encounter complex, plus w^r minus w^p , the latter being the free energy of formation of the product encounter complex from separated products. Recasting equation (3) in terms of observed quantities then leads to:

$$(\Delta G^\ddagger)_{\text{obs}} = w^r + \{1 + [(\Delta G^\circ)_{\text{obs}} - w^r + w^p]/4\Delta G_0^\ddagger\}^2 \Delta G_0^\ddagger \quad (7)$$

Experimental data are usually fitted to equation (7) on the assumption that w^r , w^p , and ΔG_0^\ddagger remain constant along a reaction series. This makes $(\Delta G^\ddagger)_{\text{obs}}$ a quadratic function of $(\Delta G^\circ)_{\text{obs}}$, whose three coefficients are themselves

¹² E. D. German, R. R. Dogonadze, A. M. Kuznetsov, V. G. Levich, and Y. I. Kharkats, *J. Res. Inst. Catalysis*, 1971, **99**, 115.

¹³ J. E. Leffler, *Science*, 1953, **117**, 340.

¹⁴ J. R. Murdoch, *J. Amer. Chem. Soc.*, 1972, **94**, 4410.

¹⁵ C. Eckart, *Phys. Rev.*, 1930, **35**, 1303.

¹⁶ G. W. Koepl and A. J. Kresge, *J.C.S. Chem. Comm.*, 1973, 371.

¹⁷ H. S. Johnston, 'Gas Phase Reaction Rate Theory', Ronald Press, New York, 1966.

¹⁸ A. J. Kresge and G. W. Koepl, unpublished work.

functions of w^r , w^p , and ΔG_0^\ddagger . The latter three quantities may therefore be evaluated from these coefficients, determined, for example, by a least-squares fit of $(\Delta G^\ddagger)_{\text{obs}}$ to $(\Delta G^\circ)_{\text{obs}}$. Quite often, however, values of $(\Delta G^\circ)_{\text{obs}}$ are not available, for these require knowledge of the pK_A of the protonated substrate, pK_{SH^+} , as well as the pK_A 's of the catalysts. In such cases, ΔG_0^\ddagger and w^r may still be obtained from a fit of $(\Delta G^\ddagger)_{\text{obs}}$ to a quadratic expression in $\Delta G^\circ_{\text{HA}}$, the free energy of ionization of the catalyst, or from its equivalent, a fit of $\log k_{\text{obs}}$ to catalyst pK_A . The coefficient of the squared term in the relationship between these pairs of variables is a function of ΔG_0^\ddagger alone, and the constant term contains only ΔG_0^\ddagger and w^r ; both ΔG_0^\ddagger and w^r may therefore be evaluated. The coefficient of the linear term, however, is a function of pK_{SH^+} as well as w^p , ΔG_0^\ddagger , and w^r ; and, if pK_{SH^+} is unknown, w^p cannot be determined.

This kind of analysis was first applied by Kreevoy and Konasewich to the hydrolysis of diazoacetate ion catalysed by a series of phenols and carboxylic acids,¹⁹ and Kreevoy and Oh have since provided additional data for the same reaction using tertiary ammonium ion catalysts²⁰ (Table 1, Reactions 1 and 2). Proton transfer to other diazo-compounds has been investigated by Albery²¹ (Table 1, Reactions 4 and 5), and the protonation of a series of aromatic substances has been studied in the author's laboratory²² (Table 1, Reaction 3). Kreevoy²⁰ has also analysed literature data²³ for the enolization of acetylacetone catalysed by the anions of a group of oxygen acids, chiefly phenols and carboxylic acids but including also glucose and cacodylic acid (Table 1, Reaction 6), and Albery²¹ has done the same for Bell's data on the halogenation of various ketones catalysed by a common base (the anion of a hypothetical carboxylic acid with $pK_A = 4.00$)^{6c} (Table 1, Reaction 7). In addition to these examples already appearing in the literature, the author has carried out an analysis of the very extensive set of data due to Bell and Higginson for the acid-catalysed dehydration of acetaldehyde hydrate²⁴ (Table 1, Reaction 8).

Most of the Brønsted relations summarized in Table 1 are not very strongly curved, and in some cases the data fit a straight line as well as they do a quadratic expression. The uncertainty in the coefficient of the squared term, and consequently in ΔG_0^\ddagger , is therefore high. For example, standard statistical methods give $\Delta G_0^\ddagger = 9.8 \pm 2.0$ kcal mol⁻¹ for Reaction 3 and $\Delta G_0^\ddagger = 5.4 \pm 1.7$ kcal mol⁻¹ for Reaction 8; the standard deviations in the work terms, w^r and w^p , are comparable. These uncertainties, nevertheless, are not large enough to obscure the single most striking feature of these results, namely, that the intrinsic barriers are on the whole very small and the work terms are consequently large.

These work terms average 11 kcal mol⁻¹, which is far too much to represent simple encounter of the reactants: the energy needed to localize a catalyst mole-

¹⁹ M. M. Kreevoy and D. E. Konasewich, *Adv. Chem. Phys.*, 1971, **21**, 241.

²⁰ M. M. Kreevoy and S.-W. Oh, *J. Amer. Chem. Soc.*, 1973, **95**, 4805.

²¹ W. J. Albery, A. N. Campbell-Crawford, and J. S. Curran, *J. C. S. Perkin II*, 1972, 2206.

²² A. J. Kresge, S. G. Mylonakis, Y. Sato, and V. P. Vitullo, *J. Amer. Chem. Soc.*, 1971, **93**, 6181.

²³ M. L. Ahrens, M. Eigen, W. Kruse, and G. Maass, *Chem. Ber.*, 1970, **74**, 380.

²⁴ R. P. Bell and W. C. E. Higginson, *Proc. Roy. Soc.*, 1949, **A197**, 141.

Table 1 Results^a of analysis of some proton transfer reactions according to Marcus theory^b

Reaction	ΔG_0^\ddagger	w^r	w^p	Reference
1. RCO_2H or $\text{ArOH} + \text{CHN}_2\text{CO}_2^- \rightarrow \text{RCO}_2^-$ or $\text{ArO}^- + \text{CH}_2^+\text{N}_2\text{CO}_2^-$	5	8	—	19
2. $\text{R}_3\text{NH}^+ + \text{CHN}_2\text{CO}_2^- \rightarrow \text{R}_3\text{N} + \text{CH}_2^+\text{N}_2\text{CO}_2^-$	1	14	—	20
3. $\text{H}_3\text{O}^+ + \text{HAr} \rightarrow \text{H}_2\text{O} + \text{H}_2\text{Ar}^+$	10	10	8	22
4. $\text{RCO}_2\text{H} + \text{CH}_3\text{CN}_2\text{COCH}_3 \rightarrow \text{RCO}_2^- + \text{CH}_3\text{CHN}_2\text{COCH}_3$	2	16	—	21
5. $\text{RCO}_2\text{H} + \text{CH}_3\text{CN}_2\text{CO}_2\text{C}_2\text{H}_5 \rightarrow \text{RCO}_2^- + \text{CH}_3\text{CHN}_2\text{CO}_2\text{C}_2\text{H}_5$	2	14	—	21
6. Oxygen anions + $\text{CH}_3\text{COCH}_2\text{COCH}_3 \rightarrow$ Oxygen acids + $\text{CH}_3\text{COCHCOCH}_3^-$	3	11	9	20, 23
7. RCO_2^- ($\text{p}K_A = 4$) + ketones $\rightarrow \text{RCO}_2\text{H} +$ enolate anions	3	14	7	6c, 21
8. RCO_2H or $\text{ArOH} + \text{CH}_3\text{CH}(\text{OH})_2 \rightarrow \text{RCO}_2^-$ or $\text{ArO}^- + \text{CH}_3\text{CHO} + \text{H}_2\text{O}$	5	13	—	24

^aResults in kcal mol⁻¹.^bBased upon the definition $(\Delta G^\ddagger)_{\text{obs}} = -RT \ln (kh/kT)$ where k is a bimolecular rate constant expressed in units of l mol⁻¹ s⁻¹.

cule next to the substrate in aqueous solution is only about $2.5 \text{ kcal mol}^{-1}$ ($RT \ln 55.5$). It has been suggested, therefore, that work terms such as these should also include whatever energy is needed to orient the reactants properly within the encounter complex so that proton transfer may take place, *i.e.* to convert the encounter complex to a reaction complex.^{19,20} Reorganization of the solvent, which is known to contribute significantly to barriers for reactions in solution,²⁵ will be an important part of this orientation. In particular, for reactions between a carbon substrate and an oxygen or nitrogen catalyst in aqueous solution, where it is likely that proton transfer takes place directly with no solvent intervening between catalyst and substrate,²⁶ desolvation of the reactants will have to occur. Since the oxygen or nitrogen acid or base serving as the catalyst will very probably be hydrogen-bonded to the solvent, and since this hydrogen bond will not be replaced by another between the catalyst and carbon substrate when these two come into juxtaposition, desolvation will take place at the expense of, among other things, hydrogen-bond formation.

The strength of the hydrogen bond between a typical acid catalyst and solvent water has been estimated at about 6 kcal mol^{-1} .¹⁹ This, when added to the energy of reactant localization, gives a work term consistent with the smaller values of Table 1, and the difference between that and the larger results could easily be made up by further reorganizational effects.

Reaction 8 presents an apparent difficulty for this explanation, for its substrate is an oxygen base which can hydrogen bond to the acidic catalyst. Desolvation here should thus be less expensive energetically, but the work term is not reduced accordingly. There is evidence, however, that this reaction occurs through a cyclic transition state which immobilizes a water molecule in addition to the catalyst and the substrate.²⁷ Formation of such a reaction complex should be more difficult than usual, and it could well cost enough additional energy to offset that gained back through substrate-catalyst hydrogen-bond formation.

A more serious objection can be raised on the basis of whether or not it is correct to separate reagent positioning and solvent reorganization from proton transfer in this way, *i.e.* whether orientation and proton transfer do in fact occur in separate reaction steps.²⁸ A similar separation is in all probability valid for electron transfer, for which Marcus theory was first derived and where it appears to work well, for here the small mass of the electron ensures that electronic motion will be essentially uncoupled from whatever atomic rearrangements must take place. The mass of the proton, however, is much greater than that of the electron, and a similar kind of Born–Oppenheimer separation for proton transfer

¹⁹ C. D. Ritchie, in 'Solute–Solvent Interactions', ed. J. F. Coetzee and C. D. Ritchie, Marcel Dekker, New York, 1969, Chap. 4.

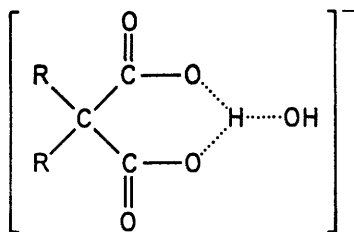
²⁶ D. M. Goodall and F. A. Long, *J. Amer. Chem. Soc.*, 1968, 90, 238; M. M. Kreevoy and J. M. Williams, *ibid.*, p. 6809.

²⁷ R. P. Bell, J. P. Millington, and J. M. Pink, *Proc. Roy. Soc.*, 1968, A303, 1; H. Dahn and J.-D. Aubert, *Helv. Chem. Acta*, 1968, 51, 1348; R. P. Bell and J. E. Critchlow, *Proc. Roy. Soc.*, 1971, A325, 35; R. P. Bell and P. E. Sorensen, *J. C. S. Perkin II*, 1972, 1740.

²⁸ R. P. Bell, personal communication.

might therefore be inappropriate. This argument may be countered,²⁹ however, by the observation that hydrogenic and heavy-atom motion remain largely uncoupled in molecular vibrations.

Some information bearing on the question of whether proton transfer and hydrogen-bond reorganization occur in a stepwise or concerted fashion comes from studies of the reaction of hydroxide ion with internally hydrogen-bonded acids, such as substituted hydrogen malonate ions. The strong internal hydrogen bonds in these systems are destroyed in these reactions, and the rates in the exothermic direction are consequently several orders of magnitude short of encounter-controlled, even though the proton is transferred between oxygen atoms. This retardation could operate through a stepwise mechanism, in which the internally hydrogen-bonded acid is first converted into an externally bound species with the acidic proton hydrogen-bonded to a solvent molecule; the hydroxide ion would then react with this low concentration intermediate in an encounter-controlled second step, much as it does with an ordinary carboxylic acid. Alternatively, hydrogen-bond breaking and proton transfer might occur simultaneously *via* a single, concerted transition state, such as that shown in (1); here the breaking and forming bonds are not collinear and the geometry is therefore not optimum for proton transfer.



(1)

Internally hydrogen-bonded systems such as these have been examined in several laboratories, but the question of mechanism has been attacked most directly by Eyring. On the basis of medium effects,³⁰ isotope effects,³¹ the effect of changing the atoms involved in the hydrogen bond,³² and the non-zero slope of a Brønsted correlation based upon a group of different acids,³³ Eyring concluded that the concerted mechanism was operating. Very recently, however, the question was reopened by Fueno,³⁴ who pointed out that a non-zero Brønsted

²⁹ M. M. Kreevoy, personal communication.

³⁰ R. P. Jensen, E. M. Eyring, and W. M. Walsh, *J. Phys. Chem.*, 1966, **70**, 2264.

³¹ J. L. Haslam, E. M. Eyring, W. W. Epstein, R. P. Jensen, and C. W. Jaget, *J. Amer. Chem. Soc.*, 1965, **87**, 4247; E. M. Eyring and J. L. Haslam, *J. Phys. Chem.*, 1966, **70**, 293.

³² J. L. Haslam and E. M. Eyring, *J. Phys. Chem.*, 1967, **71**, 4470.

³³ M. H. Miles, E. M. Eyring, W. W. Epstein, and M. T. Anderson, *J. Phys. Chem.*, 1966, **70**, 3490.

³⁴ T. Fueno, O. Kajimoto, Y. Nishigaki, and T. Yoshioka, *J. C. S. Perkin II*, 1973, 738.

slope is really not inconsistent with the two-step mechanism, inasmuch as differences in strength between internal and external hydrogen bonds along the series of acids could produce regular changes in the first step and thus obscure the zero slope expected for the second. Eyring's evidence from isotope effects, moreover, is based upon a rather approximate separation of primary from secondary effects.

Some additional information on the timing of proton transfer and solvent reorganization comes from a comparison of Brønsted plots for the reaction of a group of hydrocarbon acids with anionic oxygen bases in methanol and in DMSO solution.³⁵ These reactions are faster in DMSO than in methanol, as expected on the basis of the well-known greater hydrogen-bond-donating ability of the latter solvent and its consequent stabilization of anions. But the data for DMSO also give a more curved Brønsted plot than do those obtained in methanol, which implies that the intrinsic barrier to proton transfer in these systems is lower in DMSO than in methanol. This suggests that there is a solvent effect on the proton transfer process, and that in turn requires solvent reorganization and proton transfer to occur simultaneously in a single step.

It is possible, however, to interpret this difference in behaviour between the two solvents in another way. The argument is based upon an interesting tendency, significant in its own right, which the diffusive steps of the three-stage mechanism for proton transfer [equation (6)] have of exaggerating Brønsted plot curvature. This effect was demonstrated by Murdoch,¹⁴ who carried out detailed calculations of overall specific rates using typical diffusion rate constants in combination with specific rates for the proton-transfer step governed by Marcus theory, *i.e.* by equation (3). The curvature of Brønsted plots in the regions near the limiting, *i.e.* zero and one, values of α , based upon such 'observed' rates was always greater than that provided by the proton transfer step alone, and these regions of exaggerated curvature pushed in toward the centre of the plot as the value of ΔG_0^\ddagger dropped. The effect may be traced to the fact that, unless ΔG_0^\ddagger is very large, diffusion and not proton transfer is rate-limiting at the ends of the range of ΔG° needed to change α from zero to one. Murdoch estimates that, even with ΔG_0^\ddagger as large as 10 kcal mol⁻¹, α based upon 'observed' rate constants is a reasonably accurate reflection of α for the proton-transfer step only over the middle third of the range zero to one. It is interesting in this connection that, in systems with intrinsic barriers as small as some of the lower values of Table 1 and a free energy of activation for diffusion of 2–3 kcal mol⁻¹, proton transfer can never be fully rate-determining; it can, at best, be only partly rate-controlling, and that only over a rather narrow interval a few kcal mol⁻¹ to either side of $\Delta G^\circ = 0$.

Exaggerated curvature of this kind depends not only on the magnitude of the intrinsic barrier but also upon the size of the barrier to diffusion, and making diffusion more difficult has the same effect as lowering the intrinsic barrier. Since DMSO is a more viscous solvent than methanol,³⁶ it is possible that the greater

³⁵ C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, 1968, **90**, 3415.

³⁶ A. J. Parker, *Chem. Rev.*, 1969, **69**, 1.

Brønsted plot curvature seen in DMSO solution for the reactions described above is simply a viscosity effect and is not caused by a difference in intrinsic barrier.

The timing of changes in solvent organization in proton transfer reactions has also been examined from a theoretical point of view recently, with the interesting conclusion that different kinds of behaviour should be observed for proton transfer between bases of different size.³⁷ When the bases involved are small, e.g. H₂O, changes in solvation should be coupled with proton transfer, and the mechanism should be synchronous. When the bases are large, on the other hand, a stepwise mechanism should be favoured, in which the solvent first reorganizes to a configuration appropriate for the transition state, the proton transfers, and the solvent then relaxes to its product configuration.

A general solvation rule proposed by Swain and Schowen several years ago³⁸ also has some bearing on this matter. This rule states that the proton will always be located in an entirely stable potential energy well at the transition state of a process in which proton transfer between electronegative atoms and heavy atom reorganization both occur; protonic motion here will therefore be uncoupled with heavy-atom movement. The situation, however, now appears to be more complex than was at first anticipated,³⁹ and some exceptions to this rule seem to have been uncovered.⁴⁰

Some additional information which bears upon the results listed in Table 1 comes from several theoretical studies of the proton transfer process itself. One of these¹⁶ is especially interesting in that it develops a familiar model for proton transfer and gives behaviour which reduces to Marcus theory under certain conditions. This model is shown schematically in Figure 3. It takes the reactant and product acids of the proton transfer process, $AH + B \rightarrow A + HB$, to be simple harmonic oscillators with intersecting potential energy functions; the point of intersection of the two parabolae is the energy of activation of the system, E_a , and their vertical displacement is its energy of reaction, ΔE . The model leads to an expression for E_a in terms of ΔE which contains three additional parameters: k_{AH} and k_{BH} , the harmonic force constants of the A—H and B—H bonds, and d , the horizontal distance between the bottoms of the two wells. When k_{AH} and k_{BH} are equal and constant, and when d is also constant, the relationship between E_a and ΔE assumes the simple quadratic form of equation (3), and the model conforms to Marcus theory.* This behaviour is conveniently summarized by the linear relationship between α and ΔE shown as curve A in Figure 4 [cf. equation (4)]; use of the reduced variable $\Delta E/E_{a,0}$ gives a single relationship for all values of the intrinsic barrier, $E_{a,0}$.

It is doubtful, however, whether the conditions which allow this model to

* Simple Marcus theory was in fact derived assuming intersecting parabolic potential-energy functions of constant curvature; the Reviewer thanks Professor R. P. Bell for bringing this to his attention.

³⁷ J. L. Kurz and L. C. Kurz, *J. Amer. Chem. Soc.*, 1972, **94**, 4451.

³⁸ C. G. Swain, D. A. Kuhn, and R. L. Schowen, *J. Amer. Chem. Soc.*, 1965, **87**, 1553.

³⁹ R. L. Schowen, *Progr. Phys. Org. Chem.*, 1972, **9**, 309.

⁴⁰ R. L. Schowen, H. Jayaraman, L. Kershner, and G. W. Zuorick, *J. Amer. Chem. Soc.*, 1966, **88**, 4008.

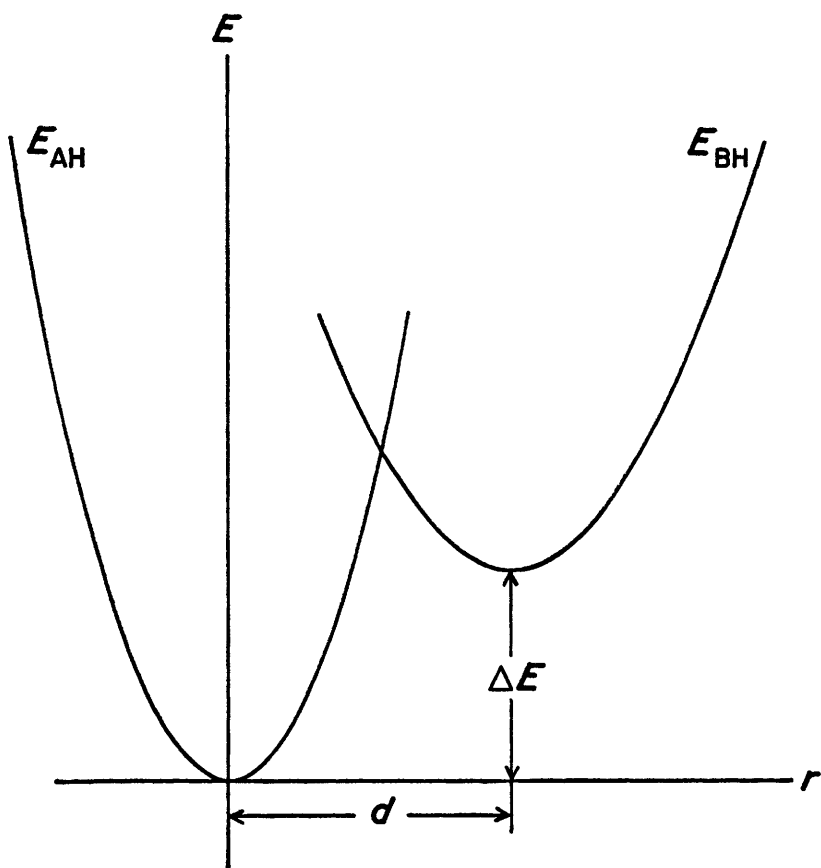


Figure 3 Intersecting oscillators model for proton transfer

reduce to Marcus theory behaviour will be met by real systems. Force constants are a measure of bond strength, and k_{AH} will therefore be equal to k_{BH} only when the strengths of the A—H and B—H bonds are the same, *i.e.* at $\Delta E = 0$. In the more general situation, as the A—H and B—H bond strengths are varied to produce changes in ΔE , k_{AH} and k_{BH} will change also. Similarly, the parameter d , which can be identified with the distance the proton must travel when it moves from donor to acceptor within the activated complex, can also be expected to change with ΔE . In particular, d is likely to be greater for the relatively loose activated complexes of strongly exothermic and strongly endothermic reactions than for the tight activated complexes of thermoneutral systems; this follows, for example, from the Pauling relation between bond length and bond order⁴¹

⁴¹ L. Pauling, *J. Amer. Chem. Soc.*, 1947, 69, 542.

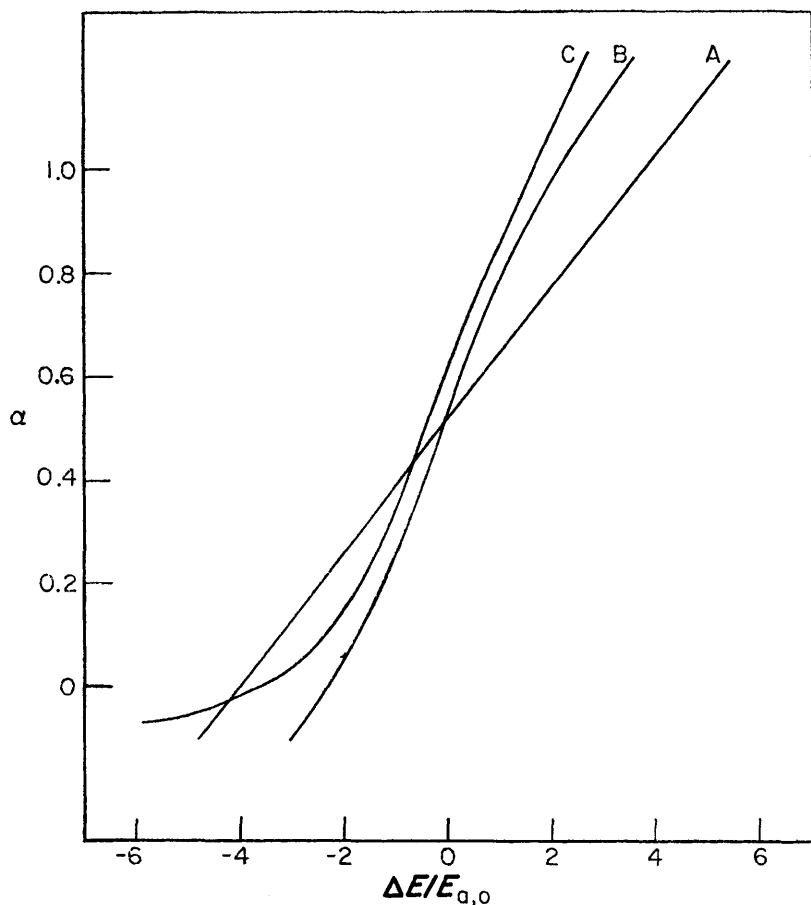


Figure 4 Relationship between α and ΔE : curve A, simple Marcus theory; curve B, intersecting oscillators model with both E_{AH} and E_{BH} varied; curve C, intersecting oscillators model with E_{AH} varied and E_{BH} held constant

upon which the highly successful BEBO method of predicting reaction barriers is based.

When these features are incorporated into the model, the simple linear dependence of α upon ΔE gives way to more complex sigmoid relationships, such as that shown by line B of Figure 4. The central regions of these curves, however, are nearly linear over appreciable ranges, and data conforming to this model in these regions could easily be fitted to Marcus theory. But the slopes of these central linear portions are considerably greater than that predicted by Marcus theory, *i.e.* by equation (5); for the example given in Figure 4, for instance, the

difference amounts to a factor of two. An analysis of such data by Marcus theory would therefore produce an intrinsic barrier only half the true value.

Theoretical examination of proton transfer using the BEBO method for generating reaction barriers leads to a similar conclusion.¹⁸ Marcus has derived an extended version of his theory starting with BEBO premises,⁴ and this too gives a sigmoid dependence of α upon ΔE whose central linear region has a slope some 50% greater than the slope predicted by the simple theory. Another model study which uses a modified Sato potential energy surface to describe the proton transfer process⁴² gives the same result, *i.e.* it too suggests that intrinsic barriers obtained by applying simple Marcus theory to experimental data are apt to be somewhat lower than true values.

It should be emphasized, however, that these theoretical studies all give Brønsted relations which are curved. They are also in unanimous agreement with Marcus theory in predicting that the degree of curvature will change with the intrinsic reactivity of the system, and that faster reactions will show more curvature than more slowly reacting systems. These model studies thus support the important qualitative deductions about Brønsted plot curvature which can be made using simple Marcus theory.

It is likely, moreover, that the relative values of parameters obtained using simple Marcus theory are valid even if these quantities themselves are misleading in an absolute sense. It is interesting, therefore, that the greatest intrinsic barrier listed in Table 1 is for aromatic protonation; this reaction destroys a resonance-stabilized ring, and it is therefore certain to be accompanied by much structural reorganization, a feature known to make proton transfer slow. The second greatest barrier is for the dehydration of acetaldehyde hydrate, a reaction with a cyclic transition state which contains a molecule of solvent water in addition to the catalyst and the substrate;²⁷ here again, therefore, considerable heavy-atom motion will occur as the reaction takes place. Another interesting system is diazoacetate ion hydrolysis, where the barrier for catalysis by phenols and carboxylic acids is somewhat greater than that for catalysis by ammonium ions; this difference is consistent with the hypothesis that charge delocalization, which occurs in carboxylate and phenoxide but not ammonium ions, makes proton transfer kinetically more difficult.^{6d,43}

These model studies also have an interesting bearing on the generally held belief that α will be one-half when the proton transfer is between bases of equal strength and therefore $\Delta G^\circ = 0$. This idea is implicit in simple Marcus theory; it follows, for example, from equation (4). The model studies, however, suggest that α will be one-half at $\Delta G^\circ = 0$ only when the system is symmetrical. For the intersecting oscillators model, this means that the relationship between force constants and bond strength must be the same for AH as for BH, and that changes in ΔE along the reaction series must be made up of equal changes (in opposite directions) in the strengths of both AH and BH bonds. It is difficult

⁴² G. W. Koepl, unpublished work.

⁴³ A. J. Kresge and Y. Chiang, *J. Amer. Chem. Soc.*, 1973, **95**, 803.

to say whether the first of these conditions will be met in general, but the second is certainly contrary to the way Brønsted relations are commonly set up: the usual practice is to keep one of the reaction partners (the substrate) constant and to vary only the other (the catalyst). When this feature is included in the model, the kind of skewed behaviour illustrated by line C of Figure 4 results; in this case, the value of α at $\Delta E = 0$ is 0.6 rather than 0.5.¹⁶

Symmetry for the BEBO model also means that both reaction partners must contribute equally to changes in ΔE , and it requires further that the bond-energy–bond-order relationships which this method uses¹⁷ be the same for the forming as for the breaking bond.¹⁸ These BEBO relationships, however, are sensitive to the identity of the atoms bonded,¹⁷ and there is also some evidence that they depend upon the structure of the molecule in which the bond happens to be located.⁴⁴ In particular, they seem to change regularly with factors such as charge delocalization and heavy-atom rearrangement, which implies that they may be different for bonds to hydrogen in pseudo acids than for bonds to hydrogen in oxygen and nitrogen species. This suggests that α is especially likely to deviate from being one-half at $\Delta E = 0$ for Brønsted relations generated by proton transfer between pseudo acid substrates and oxygen or nitrogen catalysts.

3 Anomalous Exponents

During very nearly all of the long history of the Brønsted relation, it was taken for granted that Brønsted exponents would never be less than zero nor greater than one. Brønsted and Pedersen said as much in their original paper,¹ and the statement was repeated in many discussions of acid–base catalysis.

It is logical, in a sense, to limit Brønsted exponents to the range zero to one, for it is only then that proton transfer reactions can be acid-catalysed in one direction and base-catalysed in the other. Consider, for example, proton transfer from an acid to a substrate [equation (9)], with Brønsted relations for forward



and reverse reactions: $k_{\text{A}} = G_{\text{A}}(K_{\text{HA}})^{\alpha}$ and $k_{\text{B}} = G_{\text{B}}(1/K_{\text{HA}})^{\beta}$. When α exceeds unity, the forward reaction still behaves normally in the sense that k_{A} increases with increasing acidity of the proton donor, *i.e.* it is acid-catalysed. But now, since the sum of α and β must be unity,^{*} β will be negative and $k_{\text{B}} = G_{\text{B}}(1/K_{\text{HA}})^{-\beta} = G_{\text{B}}(K_{\text{HA}})^{\beta}$. Thus the rate of the reverse reaction also increases with the acid strength of the catalyst, *i.e.* the reverse reaction is acid-catalysed as well. When α is less than zero, similar arguments lead to base catalysis in both directions.

* This may be seen by comparing the expression for the equilibrium constant of equation (9),

$$K = \frac{(\text{A}^-)(\text{HS}^+)}{(\text{HA})(\text{S})} = K_{\text{HA}}/K_{\text{HS}^+},$$

with the ratio of the Brønsted relations for the forward and the reverse reactions, $K = k_{\text{A}}/k_{\text{B}} = G_{\text{A}}(K_{\text{HA}})^{\alpha}/G_{\text{B}}(K_{\text{HA}})^{-\beta} = (G_{\text{A}}/G_{\text{B}})(K_{\text{HA}})^{\alpha+\beta}$. Since K_{HA} is the only quantity varied, its exponent must be the same in both expressions for K , and $\alpha + \beta = 1$.

⁴⁴ A. V. Willi, *Helv. Chim. Acta*, 1971, 54, 1220.

Brønsted exponents outside the range zero to one are also incompatible with the practice of equating the exponent with the fractional extent of proton transfer at the transition state of the reaction being correlated: less than no transfer ($\alpha < 0$) and more than complete transfer ($\alpha > 1$) clearly have no meaning.

Certain expected relationships between the free energies of initial, final, and transition states of the same reaction also require Brønsted exponents to lie in the range zero to one.^{43,46} This follows from the fact that structural changes occur smoothly and continuously as a system moves from reactants through transition state to products; the transition state thus has a structure intermediate between reactants and products. A perturbation made upon the system, such as the substituent change in the catalyst commonly used to produce variation along a Brønsted correlation reaction series, must therefore affect the free energy of the transition state by an amount which is also intermediate between its effects on the initial and final states. This requires the substituent effect on the change in free energy between initial and transition states, $\delta_R \Delta G^\ddagger$, to be in the same direction as, but not greater than, the substituent effect on the free energy change between initial and final states, $\delta_R \Delta G^\circ$; and that, since $\delta_R \Delta G^\ddagger / \delta_R \Delta G^\circ = \alpha$ (see footnote, p. 480), limits α to the range zero to one.

Despite all of this, a number of Brønsted exponents less than zero, and others greater than one, have been discovered during the past few years. The first of these were found almost simultaneously by Bordwell⁴⁶ and Schechter⁴⁷ in the reaction of substituted 1-phenyl-1-nitroethanes with hydroxide ion, and by Bordwell⁴⁶ in the analogous reaction of substituted 1-phenyl-2-nitropropanes. Bordwell later provided additional examples using substituted phenylnitromethanes reacting with hydroxide ion and with several different amine bases.⁴⁸ Both Bordwell and Schechter, moreover, pointed out that data which had been in the literature for some time on the acidity constants of nitromethane,⁴⁹ nitroethane,⁴⁹ and 2-nitropropane⁵⁰ and the specific rates of reaction of these substances with hydroxide ion,⁵¹ when combined gave a negative value of α . These reactions all use nitro-compound pseudo acids as the proton donor, but Stuehr has recently found that proton transfer from a series of internally hydrogen-bonded phenols to hydroxide ion also gives a Brønsted plot with α greater than one.⁵² These examples are summarized in Table 2.

In each of these reaction series, the substance held constant, and therefore the one taken to be the substrate, is either the hydroxide ion or an amine. Amines

⁴³ J. E. Leffler and E. Grunwald, 'Rates and Equilibria of Organic Reactions', Wiley, New York, 1963, p. 156, 235.

⁴⁶ F. G. Bordwell, W. J. Boyle, jun., J. A. Hautala, and K. C. Yee, *J. Amer. Chem. Soc.*, 1969, **91**, 4002; F. G. Bordwell, W. J. Boyle, jun., and K. C. Yee, *ibid.*, 1970, **92**, 5926.

⁴⁷ M. Fukuyama, P. W. K. Flanagan, F. T. Williams, jun., L. Frainier, S. A. Miller, and H. Schechter, *J. Amer. Chem. Soc.*, 1970, **92**, 4689.

⁴⁸ F. G. Bordwell and W. J. Boyle, jun., *J. Amer. Chem. Soc.*, 1971, **93**, 511; 1972, **94**, 3907.

⁴⁹ R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, 1953, **75**, 2439.

⁵⁰ D. Turnbull and S. H. Maron, *J. Amer. Chem. Soc.*, 1943, **65**, 212; G. W. Wheland and J. Farr, *J. Amer. Chem. Soc.*, 1943, **65**, 1433.

⁵¹ S. H. Maron and V. K. La Mer, *J. Amer. Chem. Soc.*, 1938, **60**, 2588.

⁵² M. C. Rose and J. Stuehr, *J. Amer. Chem. Soc.*, 1971, **93**, 4350; 1970, **94**, 5332.

Table 2 Anomalous Brønsted relations

Reaction	α	Reference
1. $R_2CHNO_2 + HO^- \xrightarrow{H_2O} R_2CNO_2^- + H_2O$ (R = H or CH ₃)	-0.48 ± 0.13	49, 50, 51
2. $ArCH_2NO_2 + HO^- \xrightarrow{H_2O} ArCHNO_2^- + H_2O$	1.54 ± 0.10	48
3. $ArCH_2NO_2 + B \xrightarrow{H_2O} ArCHNO_2^- + BH^+$ (B = morpholine)	1.29 ± 0.10	48
4. $ArCH_2NO_2 + B \xrightarrow{H_2O} ArCHNO_2^- + BH^+$ (B = 2,6-lutidine)	1.30 ± 0.09	48
5. $ArCHMeNO_2 + HO^- \xrightarrow{H_2O} ArCMeNO_2^- + H_2O$	1.14 ± 0.04	48
6. $ArCHMeNO_2 + HO^- \xrightarrow{50\% H_2O-dioxan} ArCMeNO_2^- + H_2O$	1.17 — 1.20 ± 0.05 — 0.06	47
7. $ArCHMeNO_2 + RO^- \xrightarrow{50\% H_2O-MeOH} ArCMeNO_2^- + ROH$	1.37 ± 0.07	46
8. $ArCH_2CHMeNO_2 + RO^- \xrightarrow{50\% H_2O-MeOH} ArCH_2CMeNO_2^- + ROH$	1.61 ± 0.11	46
9. $ArOH + HO^- \xrightarrow{H_2O} ArO^- + H_2O$ (Phenolic hydroxy-group internally hydrogen-bonded to azo or carboxylate function)	1.21 ± 0.09	52

and the hydroxide ion, however, are normally used as catalysts rather than substrates in Brønsted correlations. In all but the last example, moreover, the catalysts are pseudo acids, but pseudo acids generally serve as substrates rather than catalysts. In these anomalous relations, therefore, the catalyst and substrate roles are the reverse of normal practice. It is in a sense somewhat arbitrary, however, which partner in a proton-transfer reaction is taken to be the catalyst and which the substrate, and in that respect this reversal of roles is of no consequence. Marcus theory, on the other hand, takes the view that it does make a difference, and the theory in fact predicts that anomalous relations are more likely to be found when the substance varied is a pseudo acid than when it is an oxygen or nitrogen species.⁵³

The argument is based upon an expression for α which is more complete than that given in equation (4). The latter was derived on the assumption that the intrinsic barrier does not change along a reaction series; however, this will not be necessarily true, and, when that possibility is taken into account, equation (10)

$$\alpha = d\Delta G^\ddagger/dG^\circ = [(1 + \Delta G^\circ/4\Delta G_0^\ddagger)/2] + [1 - (\Delta G^\circ/4\Delta G_0^\ddagger)^2]d\Delta G_0^\ddagger/d\Delta G^\circ \quad (10)$$

results. For a series with a constant intrinsic barrier, $d\Delta G_0^\ddagger/d\Delta G^\circ = 0$; the second term of equation (10) then drops out, leaving equation (4). This, when limited to the range of ΔG° over which simple Marcus theory is valid: $-4\Delta G_0^\ddagger < \Delta G^\circ < +4\Delta G_0^\ddagger$,* confines α to the range zero to one. When the intrinsic barrier is not constant, on the other hand, the second term of equation (10) contributes, and for suitable values of $d\Delta G_0^\ddagger/d\Delta G^\circ$ it may make α less than zero or greater than one.

Some insight into the conditions under which $d\Delta G_0^\ddagger/d\Delta G^\circ$ will be significant may be gained from the Marcus theory expression, equation (11), which gives the intrinsic barrier to proton transfer between two different bases, equation (12), as the mean of the barriers for the two identity reactions, equations (13) and (14). This makes the intrinsic barrier for proton transfer between a pseudo acid and

$$(\Delta G_0^\ddagger)_{AB} = [(\Delta G^\ddagger)_{AA} + (\Delta G^\ddagger)_{BB}]/2 \quad (11)$$



an oxygen or nitrogen base the mean of the barriers for the identity reactions between the pseudo acid–base pair and the oxygen or nitrogen acid–base pair. Inasmuch as proton transfer between oxygen or nitrogen acids and bases is usually very fast whereas that between pseudo acids and bases is slow, one of these identity reactions, that between the oxygen or nitrogen acid–base pair, will

* This is the range over which ΔG^\ddagger is a single-valued function of ΔG° and therefore the range over which the theory is physically realistic.

⁵³ R. A. Marcus, *J. Amer. Chem. Soc.*, 1969, **91**, 7224.

have a much lower barrier than the other and will consequently contribute little to the intrinsic barrier for the mixed reaction. Changes in the pseudo acid are therefore likely to have a much greater effect on ΔG_0^\ddagger than changes in the oxygen or nitrogen base, and $d\Delta G_0^\ddagger/d\Delta G^\circ$ may consequently be appreciable in the former case but negligible in the latter.

Rates of identity reactions for nitro-compounds have not been measured, but it is likely that they would be both slow and variable. It is known, for example, that nitroalkanes react only slowly with oxygen and nitrogen bases even when the base is as strong as the hydroxide ion, and that the rates of these reactions are sensitive to the structure of the nitro-compound.^{46-49,51} This slowness and variability are likely to be accentuated when both reaction partners become pseudo acids or bases. Nitro-compounds, for instance, are poor catalysts for the dehydration of acetaldehyde hydrate when compared with oxygen and nitrogen acids of the same pK_A ,²⁴ and nitronate ions are likewise poor catalysts in the decomposition of nitramide.¹ It seems likely, therefore, that barriers for the identity reactions of the nitro-compounds listed in Table 2 will be large and variable, and that intrinsic barriers will thus not remain constant within the reaction series. Marcus has analysed the data for the first reaction in this Table and has found $d\Delta G_0^\ddagger/d\Delta G^\circ$ to be 1.1.⁵³

Reaction 9 has also been treated in this way with the result $d\Delta G_0^\ddagger/d\Delta G^\circ = 0.8$.⁵² It is superficially less obvious why the intrinsic barrier should change significantly along this series, for the proton transfer here is between a group of phenols and hydroxide ion, and both reaction partners are therefore substances whose identity reactions should be fast. The phenols, however, are internally hydrogen-bonded, and their rates of reaction are accordingly slowed. Provided, then, that internal hydrogen-bond breaking is concerted with proton transfer in these systems, *i.e.* that the synchronous mechanism described above in the discussion of internally hydrogen-bonded systems is operative, the intrinsic barrier for this series could be large and variable. It should be mentioned, however, that some of the phenols used here are rather different from the others, and that a group which makes a structurally more homogeneous subset gives an entirely normal Brønsted relation with $\alpha = 0.3 \pm 0.4$.

A somewhat different approach to understanding Brønsted relations with anomalous exponents examines the problem in terms of substituent effects.⁵⁴ It begins with the definition $\alpha = \delta_R\Delta G^\ddagger/\delta_R\Delta G^\circ$, and points out that this requires the exponent to lie in the range zero to one only if the substituent interacts with the reaction zone in just one way. When two or more interaction mechanisms are operative, and when these differ in sign and some lead or lag behind others, their effects may then combine to make $\delta_R\Delta G^\ddagger$ greater than $\delta_R\Delta G^\circ$ or to give these two quantities opposite signs; the first of these conditions would, of course, make α greater than one and the second would make it less than zero. Situations could also exist in which substituent effects contribute to $\delta_R\Delta G^\ddagger$ without affecting $\delta_R\Delta G^\circ$, as a result of interactions which develop in the transition state

⁵⁴ A. J. Kresge, *J. Amer. Chem. Soc.*, 1970, 92, 3210.

but are absent from initial and final states. This could happen, for example, in bimolecular reactions where two reagents separated by large distances in the initial and final states come together in the transition state.

These ideas are well illustrated by the first reaction series listed in Table 2, where a proton is transferred to hydroxide ion from the successively methyl-substituted nitro-compounds CH_3NO_2 , $\text{CH}_3\text{CH}_2\text{NO}_2$, and $(\text{CH}_3)_3\text{CHNO}_2$. The experimental data give $\delta_R\Delta G^\ddagger = +1.0 \text{ kcal mol}^{-1}$ and $\delta_R\Delta G^\circ = -2.0 \text{ kcal mol}^{-1}$ as the average effects of methyl substitution. Since these quantities are different in sign, α is negative. The change in ΔG° , moreover, is opposite from that expected on the basis of the acid-weakening polar (inductive) effect commonly shown by methyl groups in acid ionization equilibria, and that suggests that a second interaction is operating. This additional interaction has in fact been identified recently, through the use of secondary isotope effects, as hyperconjugative stabilization of the carbon–nitrogen double bond in nitronate ions.⁵⁵

In addition to these two effects, each of which contributes to $\delta_R\Delta G^\ddagger$ as well as to $\delta_R\Delta G^\circ$, two others will operate in the transition state alone and thus will add to $\delta_R\Delta G^\ddagger$ without affecting $\delta_R\Delta G^\circ$. One of these is a polar (electrostatic) interaction between the hydroxide ion and the methyl group dipole; this is absent from the initial state because the hydroxide ion and the nitro-compound have not yet come together, and it does not exist in the final state because the hydroxide ion has now been converted into a water molecule. The other effect without an initial-state or a final-state counterpart is the polar interaction of the methyl group with the negative charge which builds up on the α -carbon atom. Although the negative charge of fully formed nitronate ions is very probably largely delocalized on to the nitro-group, this is less likely to be the case in a nitronate-ion-producing transition state where the carbon–nitrogen double bond, through which delocalization must take place, is only partly formed; electrostatic attraction between the departing proton and the electron pair of the breaking bond will further inhibit the flow of negative charge away from the α -carbon atom.

It is possible, on the basis of reasonable assumptions concerning the structure of the transition state, to make rough quantitative estimates of each of these effects. These lead to a value of α which is negative, in agreement with the experimental result. The model, moreover, may be applied to the other nitro-compound reaction series listed in Table 2 by leaving out the hyperconjugative interaction, inasmuch as this effect will be either absent from or constant along each of the other series. The result now is a positive value of α , which is again consistent with the experimental finding.

An important feature of this model is the incomplete delocalization of charge on to the nitro-group in the transition state, and its consequent build-up on the α -carbon atom. This places the charge considerably closer to the substituent in the transition state than in the final state, and that permits a disproportionately large transition-state interaction. It follows from this that removing the sub-

⁵⁵ A. J. Kresge, D. A. Drake, and Y. Chiang, *Canad. J. Chem.*, in the press.

stituent to some more remote part of the system might restore normal behaviour, and it is significant, therefore, that Brønsted relations constructed by keeping the nitro-compound constant and changing substituents in the base have completely normal exponents ranging from 0.50 to 0.65.^{48,56} Marcus theory, of course, also predicts that moving the site of substitution away from the pseudo acid part of the system and into the oxygen or nitrogen base in this way should restore normal behaviour.

Proton transfer from pseudo acids is usually accompanied by considerable charge delocalization and redistribution, whereas that from oxygen or nitrogen species ordinarily involves little or none. The unusual charge distributions which lead to disproportionate transition state interactions are therefore more likely to occur in pseudo acids and bases. Analysis in terms of substituent effects thus leads to the same general conclusion as Marcus theory, *viz.* that, in proton transfer between a pseudo acid and an oxygen or nitrogen base, anomalous Brønsted relations are less likely to occur if the pseudo acid is held constant and the oxygen or nitrogen species is varied than if the pseudo acid is varied and the other species held constant.

4 Systematic Deviations

A. Electrostatic.—It is well known that the catalysts in a Brønsted relation must be structurally similar if the correlation is to be a good one. Differences in charge type are especially likely to produce deviations, as is illustrated, for example, by the base-catalysed decomposition of nitramide: here dipositive, neutral, negative, and dinegative catalysts define four parallel lines separated by more than two orders of magnitude in reactivity.^{1,57a} A more recent example of the effect of charge is provided by the hydrolysis of ethyl vinyl ether, where neutral carboxylic acids and positively charged amino-acids give good parallel correlations separated by a factor of two in rate, and individual negatively charged acids show deviations from the neutral carboxylic acid line which approach a factor of ten in reactivity.⁵⁸ These data for ethyl vinyl ether hydrolysis illustrate quite dramatically what may happen when a small number of structurally dissimilar catalysts are used in a Brønsted relation: taking the catalysts in pairs gives values of α which range from -3 to $+15$!

Systematic deviations such as these may be understood in terms of transition-state interactions not unlike those used above to account for anomalous Brønsted relations. For example, in the transition state for decomposition of nitramide, the base is removing a proton from a neutral substrate, and the substrate is therefore taking on negative charge. A positive charge initially situated on the base

⁵⁶ (a) R. G. Pearson and F. V. Williams, *J. Amer. Chem. Soc.*, 1954, **76**, 258; M. J. Gregory and T. C. Bruice, *ibid.*, 1967, **89**, 2327; J. E. Dixon and T. C. Bruice, *ibid.*, 1970, **92**, 905; (b) D. J. Barnes and R. P. Bell, *Proc. Roy. Soc.*, 1970, **A318**, 421.

⁵⁷ R. B. Bell, 'Acid-Base Catalysis', Oxford University Press, London, 1941, (a) p. 86; (b) p. 92; (c) p. 89.

⁵⁸ A. J. Kresge and Y. Chiang, *J. Amer. Chem. Soc.*, 1973, **95**, 803.

will undergo an attractive interaction with this negative charge, and that will lower the free energy of the transition state and increase the rate of reaction. A negative charge initially on the base will have the opposite effect, and reactivity should therefore increase as the charge on the catalyst changes from dinegative to negative to neutral or dipositive, just as observed. In the hydrolysis of ethyl vinyl ether, on the other hand, a proton is being transferred from an acid to a neutral substrate, and the substrate is therefore taking on positive charge, which gives a situation just the opposite of that in nitramide decomposition. The effect of charge on reactivity should therefore also be reversed, *i.e.* positive charge on the catalyst should now slow the rate while negative charge accelerates, which again is just as observed.

Dipolar groups in the catalyst might be expected to show similar but smaller effects. Some evidence that this is so comes from the hydrolysis of eight different vinyl ethers catalysed by the same set of seven neutral carboxylic acids.⁵⁹ A few of the acids which contain strongly dipolar groups, such as cyano or methoxy, show small but consistent, *i.e.* always positive or always negative, deviations from Brønsted correlations based upon all of the data. These deviations, moreover, are more pronounced at the strong acid ends of the correlations than at the weak acid ends, and they might therefore influence the slopes of these plots. It is thus significant that those of these hydrolyses which show maximum isotope effects, and in whose transition states the proton is therefore presumably half-transferred,⁶⁰ give Brønsted α 's greater than 0.5, *i.e.* of the order of 0.60–0.65. Further differences of this sort may be found in the hydrolysis of ethyl vinyl ether where $\alpha = 0.70$,^{59a} but isotope effects in H₂O–D₂O mixtures suggest only 0.6 proton transfer,⁶¹ and comparison of kinetically with competitively determined isotope effects implies the value 0.56.⁶²

It is possible, on the other hand, that these differences may be due to the fact that the isotope effects are for hydronium ion catalysis whereas the Brønsted correlations are based upon considerably weaker carboxylic acid catalysts: the degree of proton transfer at the transition state should of course decrease with increasing catalyst strength. The Brønsted plot curvature which this implies corresponds, on the basis of simple Marcus theory, to an intrinsic barrier of *ca.* 10 kcal mol⁻¹. This is not an unreasonable value, and it is in fact in good agreement with an estimate of 12 kcal mol⁻¹ which can be made using the measured free energy of activation of the hydrogen ion catalysed reaction, $\Delta G^\ddagger = 17$ kcal mol⁻¹,^{59a} and a value of its standard free energy of reaction, $\Delta G^\circ = 10$ kcal mol⁻¹, based upon an estimate of the pK_A of carbon-protonated ethyl vinyl ether.⁶³

It is interesting that the second of these calculations of the intrinsic barrier for

⁵⁹ (a) A. J. Kresge, H. L. Chen, E. Murrill, M. A. Payne, and D. S. Sagatys, *J. Amer. Chem. Soc.*, 1971, **93**, 413; (b) A. J. Kresge, and H. J. Chen, *ibid.*, 1972, **94**, 2818.

⁶⁰ A. J. Kresge, D. S. Sagatys, and H. L. Chen, *J. Amer. Chem. Soc.*, 1968, **90**, 4174.

⁶¹ A. J. Kresge and Y. Chiang, *J. Chem. Soc. (B)*, 1967, 58.

⁶² M. M. Kreevoy and R. E. Eliason, *J. Phys. Chem.*, 1968, **72**, 1313.

⁶³ P. Salomaa and A. Kankaanpera, *Acta Chem. Scand.*, 1966, **20**, 1802.

ethyl vinyl ether hydrolysis assumes the work term, w^r , to be zero whereas the first does not. The good agreement between the two estimates might thus be taken as evidence that w^r is in fact small and cannot therefore represent reagent positioning or solvent reorganization in addition to reactant encounter. This argument, however, presumes that carboxylic acids and the hydronium ion constitute a homogeneous set of catalysts correlated by a single Brønsted relation, but that, as will be seen in the section below, is probably not the case.

B. Hydronium and Hydroxide Ions.—It has been recognized for some time that the hydronium and hydroxide ions usually do not conform to Brønsted relations based upon other, non-solvent-derived, catalytic species. In 1941, for example, Bell^{67b} listed seven reactions for which the hydroxide ion catalytic coefficient had been measured and for which Brønsted relations were also available. In only one of these systems, the mutarotation of glucose, was the rate constant calculated from the correlation as close as a factor of five to the observed result; in all of the other cases the discrepancy amounted to at least two, but more often three or four, orders of magnitude. Less information was available at that time for hydronium ion catalysis, but what few data did exist suggested that this species was also in general an anomalous catalyst.

Table 3 lists these early examples together with some more recent results. Many more data are now available for hydronium ion catalysis, principally because of the recent positive identification⁷⁹ and subsequent detailed investigation of slow proton transfer from acid to substrate, a reaction type not available before 1959. Very few of the reactions listed in this Table show good agreement between observed and calculated hydronium and hydroxide ion catalytic coefficients. Both ions are in most cases anomalously poor catalysts, but, significantly, in a few systems they are better than predicted.

There is a difficulty in assigning exact acid and base strengths to the hydronium and hydroxide ions in aqueous solution which is not unrelated to this anomalous behaviour. The conventional acidity constant of an acid which ionizes in water according to equation (15) is given as $K_{HA} = (H_3O^+)(A^-)/(HA)$; it

⁶⁴ C. A. Marlies and V. K. La Mer, *J. Amer. Chem. Soc.*, 1935, **57**, 1812.

⁶⁵ J. N. Brønsted and E. A. Guggenheim, *J. Amer. Chem. Soc.*, 1927, **49**, 2554.

⁶⁶ T. M. Lowry and G. L. Wilson, *Trans. Faraday Soc.*, 1928, **24**, 683.

⁶⁷ R. P. Bell, M. H. Rand, and K. M. A. Wynne-Jones, *Trans. Faraday Soc.*, 1956, **52**, 1093.

⁶⁸ R. P. Bell and P. G. Evans, *Proc. Roy. Soc.*, 1966, **A291**, 297.

⁶⁹ A. J. Kresge, S. Slæe, and D. W. Taylor, *J. Amer. Chem. Soc.*, 1970, **92**, 6309.

⁷⁰ R. J. Thomas and F. A. Long, *J. Amer. Chem. Soc.*, 1964, **86**, 4770.

⁷¹ V. Gold and D. C. A. Waterman, *J. Chem. Soc. (B)*, 1968, 849.

⁷² T. S. Straub, Ph.D. Thesis, Illinois Institute of Technology, Chicago, Ill., 1970.

⁷³ V. Gold and D. C. A. Waterman, *J. Chem. Soc. (B)*, 1968, 839.

⁷⁴ A. J. Kresge, Y. Chiang, and J. R. Wiseman, to be published.

⁷⁵ M. M. Kreevoy, T. S. Straub, W. V. Kayser, and J. L. Melquist, *J. Amer. Chem. Soc.*, 1967, **89**, 1201.

⁷⁶ M. M. Kreevoy and R. A. Landholm, *Internat. J. Chem. Kinetics*, 1969, **1**, 157.

⁷⁷ R. E. Barnett and W. P. Jencks, *J. Amer. Chem. Soc.*, 1969, **91**, 2358.

⁷⁸ M. E. Aldersley, A. J. Kirby, and P. W. Lancaster, *J. C. S. Chem. Comm.*, 1972, 570.

⁷⁹ A. J. Kresge and Y. Chiang, *J. Amer. Chem. Soc.*, 1959, **81**, 5509.

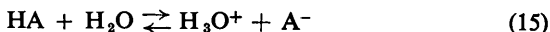
Table 3 Catalysis by hydroxide and hydronium ions

Reaction	$k_{\text{obs}}/\text{l mol}^{-1} \text{s}^{-1}$	$\log \frac{k_{\text{obs}}}{k_{\text{catc}}}$	Reference
Hydroxide Ion			
1. Decomposition of nitramide	2×10^4	-3.0	57b, 64
2. Iodination of acetone	2.5×10^{-1}	-3.54	5, 57b
3. Iodination of acetylacetone	1.7	-3.74	5, 57b
4. Iodination of monochloroacetone	9.3	-3.43	5, 57b
5. Iodination of monobromoacetone	2.0×10^2	-2.92	5, 57b
6. Bromination of 1,1-dichloroacetone	4.5×10^2	-2.71	5, 57b
7. Detritiation of phenyl[2- ³ H]acetylene	2.3×10^2	-2.10	9
8. Ionization of ethyl nitroacetate	1.5×10^5	-2.57	56b
9. Detritiation of 1,4-dicyano[1- ³ H]but-2-ene	2.1×10^{-1}	-3.0	7a
10. Detritiation of <i>p</i> -nitro[α - ³ H]benzyl cyanide	2.6×10	-1.65	7c
11. Mutarotation of glucose	6.4×10	+0.71	57b, 65, 66
12. Hydration of acetaldehyde	8×10^4	+1.31	67
13. Dehydration of methylene glycol	1.6×10^3	+0.90	68
Hydronium Ion			
1. Iodination of acetone	7.4×10^{-4}	-1.29	57c
2. Detritiation of 1,3,5-trimethoxy[2- ³ H]benzene	6.2×10^{-3}	-1.53	69
3. Detritiation of [1- ³ H]azulene	1.8×10^{-1}	-1.63	70
4. Detritiation of [3- ³ H]guaiazulene	6.1	-1.60	70
5. Hydrolysis of ethyl isopropenyl ether	5.8×10^2	-1.57	59a
6. Hydrolysis of ethyl cyclopentenyl ether	4.5×10^2	-1.35	59a
7. Hydrolysis of ethyl cyclohexenyl ether	8.0×10	-0.89	59a
8. Hydrolysis of methyl cyclohexenyl ether	4.2×10	-1.24	59a

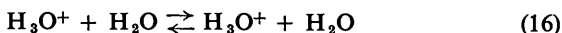
9. Hydrolysis of phenyl isopropenyl ether	6.0	-0.99	59a
10. Hydrolysis of ethyl vinyl ether	1.8	-1.35	59a
11. Hydrolysis of β -methoxy- <i>trans</i> - β -methylstyrene	1.7	-1.34	59b
12. Hydrolysis of phenyl vinyl ether	3.3×10^{-8}	-1.84	59a
13. Hydrolysis of 2-dichloromethylene-1,3-dioxolan	1.0×10^8	-1.81	71
14. Hydrolysis of dimethylketen dimethyl acetal	2.9×10	-1.01	72
15. Hydrolysis of cyanoketen dimethyl acetal	2.4×10	-2.07	73
16. Hydrolysis of methylbromoketen diethyl acetal	6.5	-1.12	72
17. Hydrolysis of dichloroketen dimethyl acetal	5.2	-1.12	72
18. Hydrolysis of dichloroketen diethyl acetal	3.4	-1.39	72
19. Hydration of bicyclo[3,3,1]non-1-ene	3.2×10	-1.33	74
20. Acid cleavage of allylmercuric iodide	1.4×10^{-8}	-1.53	75
21. Acid cleavage of isobutenylmercuric bromide	2.4×10^{-8}	-1.60	76
22. Mutarotation of glucose	2.4×10^{-8}	+0.24	65
23. Hydration of acetaldehyde	9.3×10^8	+0.22	67
24. Dehydration of methylene glycol	2.7	+0.08	68
25. Intramolecular aminolysis of <i>S</i> -acetylmercaptoethylamine	6.5×10^{10}	+1.36	77
26. Intramolecular aminolysis of <i>S</i> -chloroacetylmercaptoethylamine	6.5×10^{10}	+1.40	77
27. Hydrolysis of di-isopropyl- <i>N</i> - <i>n</i> -propylmaleamic acid	6.5×10^8	+1.38	78

For footnote references in Table, see page 499.

is therefore equal to the equilibrium constant for equation (15), $K_{15} = (\text{H}_3\text{O}^+)(\text{A}^-)/(\text{HA})(\text{H}_2\text{O})$, times the concentration of water: $K_{15}(\text{H}_2\text{O}) = (\text{H}_3\text{O}^+)(\text{A}^-)/(\text{HA}) = K_{\text{HA}}$. The particular case of equation (15) for $\text{HA} = \text{H}_3\text{O}^+$



is given by equation (16), whose equilibrium constant is of course unity. The



acidity constant of the hydronium ion must therefore be unity times the concentration of water, which is 55 on the molar scale; thus $K_{\text{H}_3\text{O}^+}$, according to this convention, is 55. A similar argument applied to the conjugate acid of the hydroxide ion, water, leads to $10^{-14}/55 = 1.8 \times 10^{-16}$ as the acidity constant of this species.

Although these are the values commonly used in fitting hydronium and hydroxide ion points to Brønsted relations, it is not at all certain that they should be mixed in with more conventional acidity constants, inasmuch as they involve the concentration of the solvent whereas the other constants refer only to dilute solution solute species. It has been pointed out⁸⁰ that this difficulty would be relieved to a considerable extent if the appropriate species to be used in equation (16), and its analogue for H_2O acting as an acid, were monomeric water. Since liquid water has an extensively hydrogen-bonded polymeric structure, the fraction of monomeric molecules is small, and monomeric water is therefore in a sense in relatively dilute solution in the rest of the solvent. The effect of using $[\text{H}_2\text{O}] < 55 \text{ mol l}^{-1}$ would be to lower $K_{\text{H}_3\text{O}^+}$ and to raise $K_{\text{H}_2\text{O}}$. These changes are in the directions required to reduce negative rate deviations for both ions, and negative deviations in both cases make up the bulk of the anomalous behaviour.

Several estimates of the acidity constants of H_3O^+ and H_2O have been made on this basis,^{80,81} even though the concentration of monomeric molecules in liquid water is not very well known. The idea has more often been applied in the opposite sense, to calculate acidity constants for H_3O^+ and H_2O by putting the catalytic coefficients for these species on Brønsted lines defined by other catalysts.^{59,73} The values obtained, however, scatter widely, and the hypothesis at any rate can account only for negative and not for positive rate deviations.

The anomalous behaviour of hydronium and hydroxide ions has also been discussed in terms of Brønsted plot curvature⁷⁰ and electrostatic interactions,⁵⁸ but these explanations again cannot account for both positive and negative deviations. A somewhat different approach has been taken in connection with the reversible ionization of carbon acids.⁸ This explanation focuses its attention on the reverse reaction, which it describes as occurring *via* a hydrogen-bonded complex between the carbanion and the protonated proton acceptor. It requires solvent water, which will be the protonating agent in the reverse reaction when

⁸⁰ R. P. Bell, *Trans. Faraday Soc.*, 1943, 39, 253.

⁸¹ A. J. Kresge, Y. Chiang, and Y. Sato, *J. Amer. Chem. Soc.*, 1967, 89, 4418.

proton transfer in the forward direction is to hydroxide ion, to be relatively ineffective at forming such a hydrogen-bonded complex; this will impede the reverse reaction, which, *via* the equilibrium, will slow the forward process as well. It is not clear, however, why water should be a poor hydrogen-bond donor relative to its pK_A , and the explanation also does not allow for cases where the reverse reaction does not occur but the anomaly still exists, such as the halogenation of ketones.

An explanation⁹ which is free of these objections makes use of the well-known fact that hydronium and hydroxide ions enter into the hydrogen-bonded structure of liquid water unusually well and are consequently more strongly solvated than most other acids and bases. Desolvation of the catalyst will therefore require the input of more energy, and will make a greater contribution to the reaction barrier, when the proton transfer involves hydronium or hydroxide ion than when it involves other acids or bases. It is likely, however, that this rate-retarding effect will operate only when the substrate itself cannot hydrogen-bond to the solvent, for, when it can, proton transfer by the Grotthuss chain mechanism becomes possible and desolvation is not necessary. The Grotthuss chain mechanism, moreover, gives a special advantage to hydronium and hydroxide ions, and positive deviations might therefore be observed in some cases.

This hypothesis is supported by the fact that in all but one of the 31 reactions of Table 3 which show negative deviations, the proton transfer is to or from carbon. Carbon acids and bases, of course, form hydrogen bonds to water reluctantly if at all; the Grotthuss chain mechanism will therefore not be available here, and negative deviations will occur. The single exception to this generalization is the nitrogen acid nitramide, whose decomposition catalysed by hydroxide ion gives a strong negative deviation despite the fact that the proton is transferred from an N—H bond which is presumably capable of hydrogen-bonding to the solvent. The deviation here, however, is based upon a linear Brønsted relation, and a curved correlation,³ which erases the anomaly, fits the data equally well.

All of the nine reactions listed in Table 3 which show positive deviations, on the other hand, are systems in which the catalyst operates on a hydroxy- or an amino-group. In each of these cases the substrate will be hydrogen-bonded to the solvent at the reaction site, and in each case, therefore, proton transfer can proceed by the Grotthuss chain mechanism. That, of course, gives positive deviations.

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