Theoretical Studies of Proton-transfer Reactions

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A classical intersecting-state-model of harmonic oscillators was applied to the study of proton-transfer reactions. The activation free-energy barriers were found to be strongly dependent on the bond order of the transition state, $n^{\dagger}$, with this parameter ranging between 0.5 and 1.0. The carbon acids are closer to the first limit, HF is near to the second, and the nitrogen and oxygen acids are somewhere between. Such differences can be attributed to the polarity of the XH bonds. For a considerable number of reactions the distance between the minima of the harmonic oscillators is virtually independent of the reaction free energies, ΔG°, but for others such distance increases with an increase in $|\Delta G^{\circ}|$. The observed increase depends on the mixing entropy, λ. Non-linear Brönsted relationships and anomalous exponents could be interpreted by the model. The exponents are found to be related with the extent of proton transfer when the stretching force constants of the reactive bonds in reactants and products are the same, $n^{\dagger}$ is constant and λ is high. Isotope effects depend on ΔG°, but their maximum values seem to be related to $n^{\dagger}$, being higher when $n^{\dagger} = 0.5$ and close to 1 when $n^{\dagger} = 1.0$. Proton-transfer reactions in acid–base catalysis are also found to conform with the general picture provided by the model. Suggestions for the molecular parameters which dominated solvent effects are discussed.

Proton-transfer reactions are one of the most important classes of chemical reactions in solution which have been subjected to various theoretical analysis since the famous work of Brönsted and Pederson[1] in 1924. Many of those approaches are based on the transition-state theory and consequently have a significant empirical character. Nevertheless, all of them aim to elucidate transition-state structures, either through the interpretation of the Brönsted relation,[2–4] or more recently through the theory of Marcus.[5–7] In spite of such efforts, many unsolved problems still remain. The recent development of a theoretical model of chemical reaction rates,[8] which includes Marcus and BEBO models as particular cases, gives hope that a further step can be made in the understanding of proton-transfer reactions. Indications of the generality of the model come from the fact that its application has been extended from vapour-phase reactions[8,9] to electron-transfer,[9,10] nucleophilic,[9,11] and sigmatropic and cycloaddition[12] reactions in solution.

The present model assesses the role of several thermodynamic, geometric, and electronic factors on the energy barrier of a reaction, namely the free energy of the reaction, the force constants and bond length of the reactive bonds, the bond order at the transition state, and the so called 'mixing-entropy'.[13] It has been shown[8–12] that all these parameters are powerful instruments to elucidate mechanisms of chemical reactions. In this paper, after a short presentation of the theory, we will discuss the important role of the bond order at the transition state in characterizing the different types of proton-transfer reactions. Subsequently the role of reaction free energy and mixing entropy is presented, followed by an analysis of the Brönsted relation and the structural meaning of the Brönsted constants. Finally we analyse the solvent isotope effect and its dependence on the transition state bond order, and some other solvent effects.

Theory

The theory has been described in detail elsewhere,[8,9] but will be stated briefly here. Although the theoretical model is capable of estimating the reaction energy profile for a chemical reaction, we are only interested in the transition-state energy which can be estimated from the intersection of two parabolas representing the potential-energy curves of reactant and products. More complex curves, such as Morse oscillators, could have been considered,[8] but since the energy barriers of the proton-transfer reactions are much smaller than the relevant dissociation energies, the harmonic approach is adequate. One can write equation (1) where f_i are the harmonic force constants

$$\tfrac{1}{2}f_r x^2 = \tfrac{1}{2}f_p(d - x)^2 + \Delta G^{\circ} \qquad (1)$$

of reactant and product, ΔG° is the reaction free energy, x is the distension of the harmonic oscillator which represents the reactant state, and d is the sum of the bond distensions from reactant and product to the transition state. The parameter d is also the separation of the minima of the potential-energy curves of reactant and product.

The activation free energy of the reaction is given by (2) where

$$\Delta G^{\dagger} = \tfrac{1}{2}f_r x^2 \qquad (2)$$

x is estimated from equation (1), once d is known. This parameter d is proportional to the sum of the equilibrium bond lengths, l_i, of the harmonic oscillators of reactant and product [equation (3) where $l = l_r + l_p$] and the reduced bond distension is given by equation (4) where a' is a constant ($a' = 0.156$),

$$d = \eta l \qquad (3)$$

$$\eta = \frac{a'\ln 2}{n^{\dagger}} + \frac{a'}{2\lambda^2}(\Delta G^{\circ})^2 \qquad (4)$$

$n^{\dagger}$ is the bond order of the transition state and λ, which has dimensions of an energy, is the 'mixing entropy' or 'configuration entropy', defined by Agmon and Levine.[13]

The rate constants are related to $\Delta G^{\dagger}$ by equation (5) where c_o

$$k = \nu c_o^{1-m}\exp(-\Delta G^{\dagger}/RT) \qquad (5)$$

is the standard concentration ($c_o = 1$ mol dm^{-3}), m is the molecularity of the reaction ($m = 2$), and ν is the frequency of vibration which destroys the activated complexes. For reactions of acids with H_2O we take ν as given by the transition state theory, $\nu = k_BT/h$, *i.e.*, $\nu = 7 \times 10^{12}$ s^{-1} at room temperature. For reactions with H_3O^+ and OH^-, far from the diffusion-controlled limit[14] we have found that the free energies of

Table 1. Bond distensions for the ionization reactions $AH + H_2O \longrightarrow A^- + H_3O^+$ at 25 °C

AH	pK_{AH} [a]	k/mol^{-1} dm^3 s^{-1} [a]	$\Delta G^\dagger$/ kJ mol^{-1} [b]	ΔG°/ kJ mol^{-1}	$10^{-3}f$/kJ mol^{-1} Å^{-2} [c] reactant	product	l/Å [c]	d/Å	η	η(o)	$n^\dagger$
CH_3NO_2	10.22	7.7×10^{-10}	124.7	58.0	2.9	4.2	2.033	0.472	0.23		~0.55
$CH_3COCH_2CO_2C_2H_5$	9.0	2.2×10^{-5}	99.4	51.1	2.9	4.2	2.033	0.414	0.204	0.192	0.56
NH_4^+	9.25	4.4×10^{-1}	75.0	52.5	3.8	4.2	1.972	0.302	0.153	0.126	0.86
o-$O_2NC_6H_4OH$	7.17	1.8×10^{1}	65.8	40.7	4.2	4.2	1.93	0.286	0.148		~0.75
H_2S	7.24	7.8×10^{1}	62.2	41.1	2.2	4.2	2.295	0.338	0.147		~0.75
CH_3CO_2H	4.74	1.4×10^{4}	49.4	26.9	4.2	4.2	1.93	0.257	0.133	0.120	0.9
HF	3.15	1.25×10^{6}	38.3	17.9	5.8	4.2	1.88	0.214	0.144		~0.95

[a] Ref. 14*b*, pp. 210, 228; $[H_2O]$ 55.6 mol dm^{-3}. [b] ν 7×10^{12} s^{-1}. [c] Ref. 15.

Table 2. Rate constants for the reactions $A^- + H_3O^+ \longrightarrow AH + H_2O$

AH	k/mol^{-1} dm^3 s^{-1} [a] calc.	exp.
CH_3NO_2	7.2×10^{2}	6.8×10^{2}
$CH_3COCH_2CO_2C_2H_5$	1.3×10^{6}	5.8×10^{7}
NH_4^+	4.4×10^{10}	4.3×10^{10}
H_2S	7.7×10^{10}	7.5×10^{10}
CH_3CO_2H	4.4×10^{10}	4.5×10^{10}
HF	1.0×10^{11}	1×10^{11}

[a] ν 4×10^{14} s^{-1}.

activation for the forward and backward reactions, $\Delta G_f^\ddagger = \Delta G_b^\ddagger + \Delta G^\circ$, requires $\nu = 4 \times 10^{14}$ s^{-1} for both H_3O^+ and OH^-. This is probably a reflection of the role of Grotthuss mechanism in these reactions.[4]

The Role of Bond Order.—For a prototype reaction $A + BC \rightarrow AB + C$ the bond order of the molecular species can be conserved along the reaction co-ordinate. For single bonds, the bond order expressed in terms of the count of the elections is unity and one can write $m_{AB} + m_{BC} = 1$. At $\Delta G^\circ = 0$, the conservation of the total bond order leads to a transition-state bond order $m^\dagger = 0.5$. In this case the transition-state configuration can be dominated by the configuration of any intermediate state of lower energy and, consequently, of higher bond order ($m^\dagger > 0.5$). In such cases the total bond order is not conserved along the reaction co-ordinate.[8] Values of $m^\dagger > 0.5$ can be interpreted in terms of an electronic syphoning to the transition state of non-bonding or anti-bonding electrons of reactants or products,[8] electronic syphoning from election-rich substituents,[12] solvent effects,[9,11] and the polarity of the bonds in the activated complexes. Proton-transfer reactions are observed with many kinds of molecules, some of them classified as normal acids, and others are classified as 'pseudo acids'.[2,14] In the first case rates are diffusion controlled in basic media, whilst the second group have rates which are considerably slower. All these kinds of acids can be studied within the present model.

When we consider the transfer of a hydrogen atom or proton between two atoms, two extreme situations may be envisaged. The first corresponds to the transfer of a hydrogen atom, because the XH bond in the reactant is essentially covalent. For this situation the bond order at the transition state should be $n^\dagger = 0.5$, as found for the reactions with several hydrides in the vapour phase.[8,9] The other extreme corresponds to an XH bond which is purely ionic (X^-H^+) and the transition-state bond order is $n^\dagger = 1$, since there is virtually no breaking of the bond in the reactant. Following equation (4), for a thermoneutral reaction, the calculated reduced bond displacements for the two extreme situations are $\eta(o) = 0.216$ for $n^\dagger = 0.5$ and $\eta(o) = 0.108$ for $n^\dagger = 1$. For the proton-transfer reactions we expect, therefore, that $0.216 < \eta(o) < 0.108$ and $0.5 < n^\dagger < 1$. The 'pseudo-acids' are expected to be closer to the first limit (radical-type), and the normal acids closer to the second (ionic-type).

To investigate such expectations for ionization in water, we have employed in the calculation the stretching force constants and bond lengths for an XH bond in the reactant, and the one for an OH bond in the product.[15] Table 1 presents the results of the calculation of the bond distension parameters for several types of acids.

The results conform to the view previously given. We must point out that $n^\dagger$ values can only be obtained from equation (4) with $\Delta G^\circ = 0$, which is not the case for all the reactions studied. Nevertheless when this was possible, the values of the reduced bond distension at $\Delta G^\circ = 0$ [η(o)] are presented. Such values can be obtained from the extrapolation of η as a function of $(\Delta G^\circ)^2$ for a series of similar acids, as described in the next section. However for the majority of the cases such variation is not very important. The bond order at the transition states ranges between 0.5 and 1; the carbon acids are close to the first limit and HF is close to the second one. Somewhere in the middle are the nitrogen and oxygen acids. The hierarchy of $n^\dagger$ is the hierarchy of the rates of proton transfer (slowest at $n^\dagger = 0.5$, fastest at $n^\dagger = 1$) free from the effects of ΔG°, f, and l.

The reverse reaction of the ionization processes on Table 1 are estimated through equation (5), with $\Delta G_b^\ddagger = \Delta G_f^\ddagger - \Delta G^\circ$ and $\nu = 4 \times 10^{14}$ s^{-1}. Table 2 presents the calculated results. The agreement with experiment is good, even for reactions which are in the diffusion-controlled limit. The only exception is $CH_3COCH_2CO_2C_2H_5$ where the reverse reaction is probably not an elementary step.

Reaction Free Energy and the Brönsted Relation.—The effect of ΔG° on the reaction activation free energy can be analysed in two different ways. One is expressed in equation (1) and corresponds to a constant separation of the minima of the potential-energy curves of reactants and products. This is the situation considered by the theory of Marcus.[5] The other effect is the increase on the separation of the minima of the potential-energy curve with an increase in $|\Delta G^\circ|$, as expressed by equation (4). In order to study these effects we have considered the ionization in water of series of similar carbon acids, such that in each series $n^\dagger$ is a constant. Under these conditions the reduced bond distension, η, should be a linear function of $(\Delta G^\circ)^2$. The results are presented in Table 3 and Figure 1. The expected quadratic dependence of η on ΔG° is observed. The dependence is a moderate one (λ 300 kJ mol^{-1} for ketones and 127 kJ mol^{-1} for sulphones) when compared with the one observed in other kinds of reactions such as hydrogen-abstraction in gas-phase reactions, electron transfer, and nucleophilic substitutions,[9] which have considerably smaller mixing entropies.

The sulphone $(EtSO_2)_2CHPh$ does not conform to the observed linear relationship of Figure 1. This reveals that the

Table 3. Bond distensions for the ionization of carbon acids in water

HA	pK_{HA}[a]	k_1/dm^3 mol^{-1} s^{-1}[a]	$\Delta G^\dagger$/kJ mol^{-1}[b]	ΔG°/kJ mol^{-1}	d/Å[c]	η[c]	Values in the series η(o)	Values in the series $n^\dagger$
1 CH_3COCH_3	19.5	8.5×10^{-12}	135.7	110.7	0.415	0.202[d]	0.192	0.56
2 $CH_2(CO_2Et)_2$	13.3	4.5×10^{-7}	109.0	75.5	0.401	0.197		
3 $(CH_3CO)_2CH_2$	8.9	3×10^{-4}	92.9	50.5	0.395	0.194		
$Me_3CCH(CN)_2$	12.9	9.7×10^{-6}	101.4	73.2	0.38	0.187	0.168	0.64
$CH_2(CN)_2$	11.0	5.2×10^{-4}	91.6	62.5	0.369	0.182		
4,6-Dimethyl-3*H*-azulenium	0.48	1.5	71.9	2.7	0.403	0.199	0.199	0.54
2,4,6-Trimethoxybenzenium	−5.7	56	63.0	−32.4	0.418	0.205[e]		
4 $(PhSO_2)_2CH_2$	11.0	4×10^{-3}	86.6	62.5	0.352	0.173	0.154	0.70
5 $(EtSO_2)_2CHMe$	14.4	6.3×10^{-7}	108.0	81.8	0.385	0.189		
6 $(PhSO_2)_2CHMe$	13.76	1.2×10^{-5}	101	78.1	0.368	0.181		
7 $(EtSO_2)_2CHPh$	12.12	1.1×10^{-5}	101.2	68.8	0.388	0.191		
8 $(EtSO_2)_2CH_2$	12.2	3.1×10^{-4}	92.9	69.3	0.359	0.177		
9 $(MeSO_2)_2CHMe$	12.55	2.1×10^{-4}	93.9	71.3	0.359	0.177		

[a] Ref. 4, pp. 118 and 151. [b] $\nu = 7 \times 10^{12}$ s^{-1}. [c] $f_r = 2.9 \times 10^3$ kJ mol^{-1} Å^{-2}, $f_p = 4.9 \times 10^3$ kJ mol^{-1} Å^{-2}, $l = 2.033$ Å except where stated otherwise. [d] $l = 2.056$ Å. [e] $l = 2.044$ Å.

Table 4. Bond distensions for proton-transfer reactions of amines

Reaction		$\Delta G^\dagger$/kJ mol^{-1}	ΔG°/kJ mol^{-1}	d/Å[c]	η	$k_b/10^{10}$ mol^{-1} dm^3 s^{-1}[d] calc.	$k_b/10^{10}$ mol^{-1} dm^3 s^{-1}[d] exp.
$AH^+H_2O \rightarrow A + H_3O^+$[a]	AH^+						
1	NH_4^+	74.9	52.5	0.302	0.153	4.5	4.3
2	Trimethylamine	80.1	55.9	0.312	0.158	2.2	2.2
3	Dibenzylmethylamine	69.3	43.7	0.301	0.153	1.2	1.3
4	Imidazole	61.7	39.7	0.282	0.143	5.3	5
$A + H_2O \longrightarrow AH^+ + OH^-$[b]	A						
5	Methylamine	42.3	19.2	0.254	0.129	3.5	3.7
6	Trimethylamine	48.1	23.8	0.267	0.135	2.1	2.1
7	Piperidine	40.5	16.3	0.253	0.128	2.2	2.2
8	n-Octylamine	38.1	11.5	0.254	0.129	0.83	1.0

[a] Ref. 4, p. 232. [b] Ref. 4, p. 233. [c] $f_r = 3.8 \times 10^3$ kJ mol^{-1} Å^{-2}, $f_p = 4.2 \times 10^3$ kJ mol^{-1} Å^{-2}, $l = 1.972$ Å. [d] $\nu = 4 \times 10^{14}$ s^{-1}.

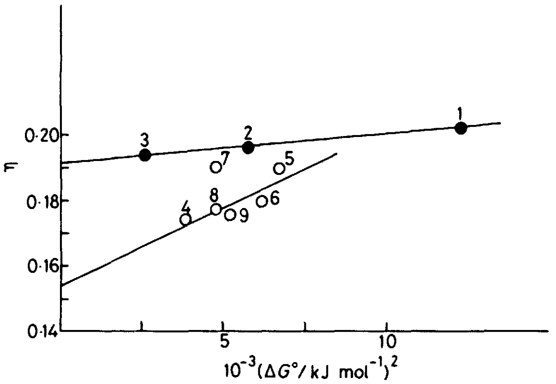

Figure 1. Reduced bond displacements, η, as a function of $(\Delta G^\circ)^2$ for the ionization of carbon acids: ● ketones; ○ sulphones. Legend for acids in Table 3

substituent phenyl group increases η by *ca.* 0.014 and consequently decreases the bond order at the transition state by $\Delta n^\dagger$ −0.045. We will come back to this point later.

The rates for ionization of protonated amines and for the hydrolyses of amines in water present the same features of the carbon acids as data of Table 4 and Figure 2 shows. The dependence of η on $(\Delta G^\circ)^2$ is more significant (λ 86.5 kJ mol^{-1}) than that observed with ketones and sulphones.

Table 4 also presents the calculated rates for the reverse reactions with H_3O^+ and OH^-. The calculated rates with ν 4×10^{14} s^{-1} are in good agreement with experiment. These results, associated with the ones of Table 2, show that the present model is also adequate to deal with proton transfer in general acid–base catalysis. Studies of the catalytic coefficients for diazoacetate hydrolysis (6)[16] whose rate is determined by a

$$N_2CHCO_2^- + H_2O \xrightarrow{HA} HOCH_2CO_2^- \qquad (6)$$

reaction such as (7) present the same features of the reaction

$$N_2CHCO_2^- + HA \longrightarrow N_2CH_2CO_2 + A^- \qquad (7)$$

with H_3O^+ and OH^-. A selection of the calculated data is presented in Table 5. As can be seen there is a small but significant effect of the acid nature on the bond order at the transition state; there are essentially three groups: H_2O and H_3O^+, phenols, and carboxylic acids. In spite of the fact that several acids which have reasonably high $n^\dagger$ for their ionization (*e.g.* CH_3CO_2H $n^\dagger$ *ca.* 0.9) were employed in the catalysis, the bond order at the transition state is dominated by that of the diazoacetate, $n^\dagger$ *ca.* 0.6, which reveals that the transition state is

Table 5. Bond distensions for the catalytic coefficients of diazoacetate hydrolysis[a]

HA	$\Delta G^{\dagger}$/kJ mol^{-1}	ΔG°/kJ mol^{-1}	d	η
H_2O	107.9	74.4	0.36	0.177
H_3O^+	55.6	−24.9	0.368	0.181
p-$CH_3C_4H_6OH$	80.9	43.2	0.337	0.166
C_6H_5OH	79.5	41.6	0.336	0.166
p-BrC_4H_6OH	78.0	38.1	0.338	0.166
CH_3CO_2H	59.2	11.9	0.325	0.160
HCO_2H	57.3	6.3	0.329	0.162
$ClCH_2CO_2H$	53.7	1.2	0.326	0.160
F_2CHCO_2H	49.8	−6.7	0.327	0.161
Cl_2CHCO_2H	49.1	−7.9	0.326	0.160

[a] Experimental data from ref. 17. [b] Parameters employed in the calculation: $\nu = 7 \times 10^{12}$ s^{-1} except for H_3O^+ where $\nu = 4 \times 10^{14}$ s^{-1}, $f_r = 4.2 \times 10^3$ kJ mol^{-1} Å^{-2}, $f_p = 2.9 \times 10^3$ kJ mol^{-1} Å^{-2}, $l = 2.033$ Å.

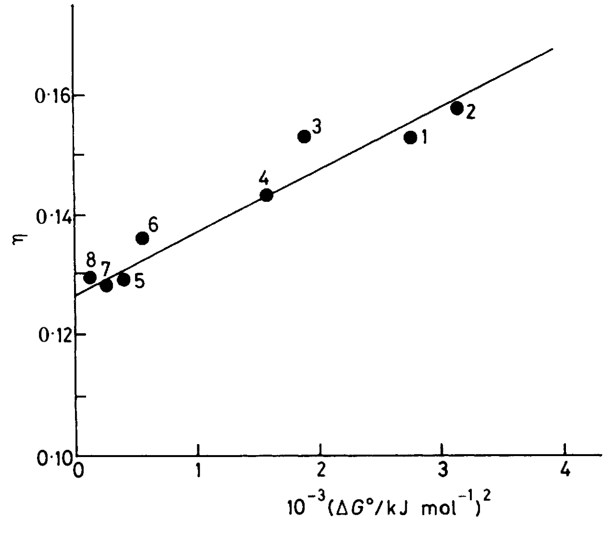

Figure 2. Reduced bond displacements, η, as a function of $(\Delta G^{\circ})^2$ for the ionization and hydrolysis of amines, Legend for compounds in Table 4

$$\alpha = \left(\frac{1}{2} + \frac{\Delta G^{\circ}}{fd^2}\right) \tag{8}$$

product-like (diazoacetate-like), which agrees with the fact that the reaction is endothermic or only weakly exothermic.

The relation proposed by Brönsted and Pederson[1] 60 years ago has dominated studies on proton-transfer reactions.[2–4] In general terms, for general catalysis $k = GK^{\alpha}$ where k is the rate constant of the catalysed reaction and K the equilibrium constant of the acid or base employed as catalyst. This relation has been extensively discussed,[3,17] because there are cases where curvatures have been observed and α has values outside the 0—1 range. In fact this contradicts the view that the Brönsted relation measures the extent of proton transfer at the transition state of the reaction being correlated, *i.e.* measures the product-like or reactant-like character of the transition state. Before we consider particular cases, let us analyse the relation in general terms.

The extent of proton transfer is given by the ratio of the bond distension in the reactant and the sum of the bond distensions in the reactant and product, *i.e.* x/d. When the stretching force constants are equal, in fact $x/d = \alpha$, we have equation (8) for all range of ΔG° values, as long as we neglect the quadratic dependence of η on $|\Delta G^{\circ}|$, as given by equation (4). Equation (8) shows that the Brönsted plots are curved since $\alpha = \frac{1}{2}$ only for $\Delta G^{\circ} = 0$, but assumes different values outside this range. As illustrated in Figure 3 the curvature is less pronounced when n^{+} is small, and this may explain why carbon acids generally give linear relationships whereas oxygen and nitrogen acid–base pairs show curved plots.[3] However when $f_r \neq f_p$ the Brönsted relation does not measure the extent of proton transfer, as Kresge has in fact pointed out in his excellent review article on the Brönsted relation.[3] In fact, even at $\Delta G^{\circ} = 0$, $x/d = (\sqrt{f_r f_p} - f_p)/(f_r - f_p)$ and $\alpha = f_r(\sqrt{f_r f_p} - f_p)/(f_r - f_p)(f_r f_p)$. Nevertheless the Brönsted relation close to $\Delta G^{\circ} = 0$ is useful to reveal the asymmetry of the force constants of reactant and product.

When the distance between the minima of the potential-energy curves increases with $|\Delta G^{\circ}|$, even stronger curvatures are observed, and $\alpha > 1$ in the acid region and $\alpha < 0$ (normally called β) in the basic region are observed on a pK range of *ca.* 9 in each region (Figure 4).

Table 6. Bond distensions for the rates of reaction of 1-arylnitroalkanes with OH^- in water

	Substituent	$\Delta G^{\dagger}$/kJ mol^{-1} [a]	ΔG°/kJ mol^{-1} [a]	d/Å [c]	η
Arylnitromethane		70.2	−40.4	0.450	0.221
	o-CH_3	71.4	−36.3	0.449	0.221
	m-CH_3	70.8	−39.6	0.450	0.221
	m-Cl	67.5	−41.8	0.444	0.218
	p-NO_2	63.6	−46.0	0.438	0.215
Arylnitroethane		78.6	−37.5	0.468	0.230
	m-CH_3	78.7	−37.0	0.468	0.230
	p-NO_2	72.7	−42.5	0.459	0.226
	m,m'-$(NO_2)_2$	68.6	−45.7	0.451	0.222
CH_3NO_2 [b]		124.7	57.9	0.471	0.229
$C_2H_5NO_2$ [b]		125.0	48.8	0.485	0.239

[a] Data from ref. 18 with $\nu = 4 \times 10^{14}$ s^{-1}. [b] Ionization in water. [c] $f_r = 2.9 \times 10^3$ kJ mol^{-1} Å^{-2}, $f_p = 4.2 \times 10^3$ kJ mol^{-1} Å^{-2}, $l = 2.033$ Å.

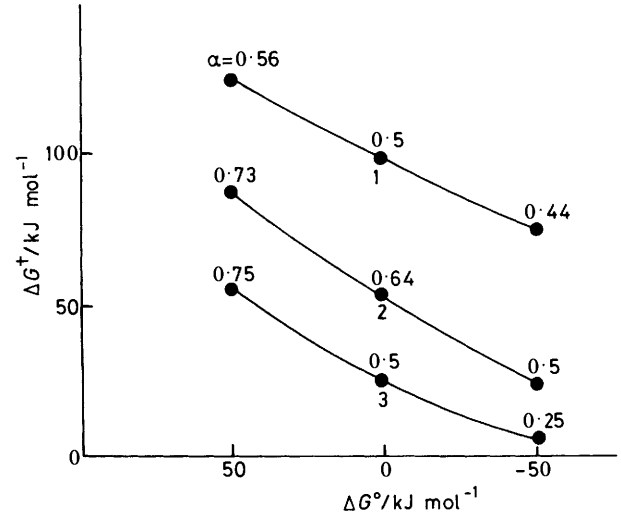

Figure 3. Calculated Brönsted plots for different conditions of $n^{\dagger}$ and f: 1, $f_r = f_p = 4.2 \times 10^3$ kJ mol^{-1} Å^{-2}, $n^{\dagger} = 0.5$; 2, $f_r = 4.2 \times 10^3$ kJ mol^{-1} Å^{-2}, $f_p = 1.4 \times 10^3$, $n^{\dagger} = 0.5$; 3, $f_r = f_p = 4.2 \times 10^3$, $n^{\dagger} = 1$; $l = 2$ Å for all cases. The values of α ($\alpha = \delta\Delta G^{\dagger}/\delta\Delta G^{\circ}$) are shown at several points (●) on each curve

Table 7. Bond distension parameters for proton exchange between NH_3 and NH_4^+

	k/mol^{-1} dm^3 s^{-1}	$\Delta G^\dagger$/kJ mol$^{-1\,a}$	ΔG°/kJ mol^{-1}	d^b	η	$n^\dagger$
NH_3–NH_4^+	12.7×10^8	21.0	0	0.212	0.105	1.0
NH_3–H_2O–NH_4^+	5×10^7	29.2	0	0.248	0.123	0.88

[a] Ref. 4 p. 234. [b] $f_r = f_p = 3.8 \times 10^3$ kJ mol^{-1}, $l = 2.024$ Å.

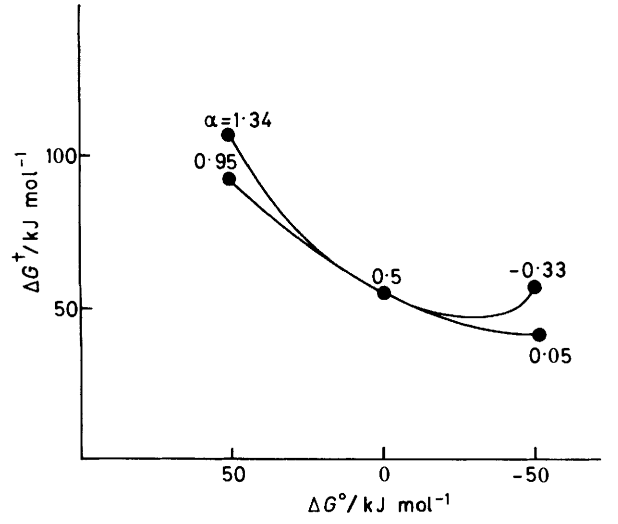

Figure 4. Calculated Brönsted plots including the effect of the mixing entropy parameter λ. Parameters employed in the calculation: $f_r = f_p = 4.2 \times 10^3$ kJ mol^{-1} Å^{-2}, $l = 2$ Å, $n^\dagger = 0.67$; bottom curve $\lambda = 88$ kJ mol^{-1}, top curve $\lambda = 62.5$ kJ mol^{-1}. The values of α are shown at several points (●) on each curve

It will now be useful to analyse some particular cases where anomalous Brönsted coefficients have been found. A typical case is the reactions of 1-arylnitroalkanes with OH^-, where α *ca.* 1.5.[18] The calculations are presented in Table 6. Substituents such as Cl and NO_2, instead of increasing d with a decrease in ΔG°, as predicted by equation (4), decrease η, *i.e.*, increase $n^\dagger$. This is also evident with the ionization in water of some nitroalkanes (Table 6). The Brönsted relation is a linear free-energy relationship and we have shown that such relationships are only valid when $n^\dagger$ is constant.[19] This is not the case with some substituents and consequently such a relationship is not strictly valid. However since the change in $n^\dagger$ is not very large, the relationship apparently holds, but with anomalous α exponents. As Kresge[3] has pointed out if we ignore that in a Brönsted relation only structurally similar catalysts have to be considered, even much larger (α = 15!) coefficients can be found. Although anomalous α seem to be related with moderate changes in $n^\dagger$, we cannot exclude the other possibility shown in Figure 4, valid for a constant $n^\dagger$, but with relatively low mixing entropies or, in equivalent terms,[9,10] quite negative activation entropies.

In conclusion the Brönsted coefficients only represent the extent of proton transfer when $f_r = f_p$, $n^\dagger$ is constant, and λ is high ($\lambda > 90$ kJ mol^{-1}). In any other conditions α has a very dubious physical meaning. Brönsted coefficients have also been interpreted as a measure of the effective charge for reactions in solution.[20] In the appropriate conditions this is only a measure of the extent of the reaction, but is not related with the bond order of the transition state. The Brönsted coefficients are in fact independent of $n^\dagger$.

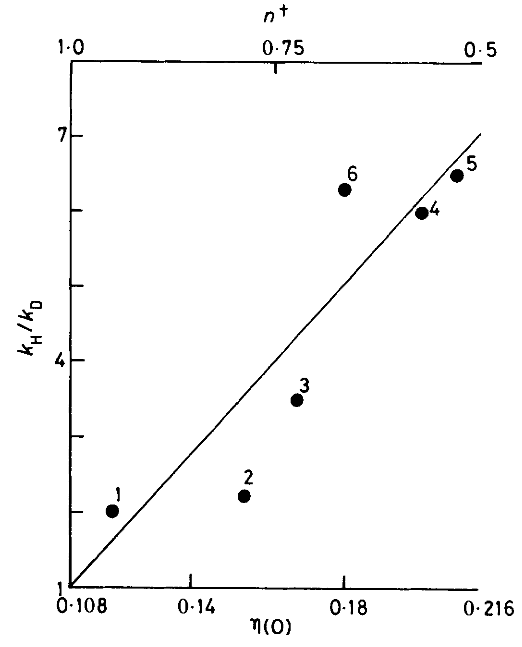

Figure 5. Maximum kinetic isotope effects as a function of the reduced bond displacement η(o) or the bond order at the transition state; theoretical line and experimental data: 1, $CH_2(Me)O^-$ + AH;[a] 2, disulphone in water;[b] 3, 1,4-dicyanobut-2-ene + OH^-;[c] 4, $\Rightarrow CCH_2$ + A^-;[a] 5, NO_2CH_3 + ^-O_2CCH;[d] 6, hydrolysis of diazoacetate with $RR'R''NH^+$.[e] (*a*) A. F. Hegart and W. P. Jencks, *J. Am. Chem. Soc.*, 1975, **97**, 7188. (*b*) Ref. 4, p. 185. (*c*) Ref. 4, p. 136. (*d*) Ref. 4, p. 28. (*e*) Ref. 22.

Isotope and Solvent Effects.—Primary isotope effects on proton-transfer reactions have also been extensively studied[2,4,6,21] to provide information on the transition-state structure. Consequently many correlations of isotope effects and Brönsted exponents have been made. However, such correlations have no physical basis, as we will see.

Isotope effects vary with the free energy of the reaction, presenting a maximum normally at $\Delta G^\circ = 0$. This is well explained in terms of Marcus theory, considering slightly different $\Delta G^\dagger$ at $\Delta G^\circ = 0$ in H_2O and D_2O.[22,23] Although this implies slightly different force constants, according to the present model, this is reasonable in liquid solutions if the force constant for the reaction are also slightly dependent on hydrogen bonds. We will not be further concerned with this effect here. We simply point out that differences in pK have also been observed in both solvents, *ca.* 0.6,[22] and this can upset the normal isotope effect by further increasing k_H/k_D by about two times. Here we will be concerned with the structural factors which affect k_H/k_D, free from any differences in ΔG°.

Winey and Thornton[24] have suggested that isotope effects should be related with chemical bond orders, and in fact we have verified that the ratio of secondary isotope effects and the corresponding equilibrium constant in sigmatropic shift reactions are related to the bond order at the transition state.[12] In

Figure 5 we investigate if the same is valid for $(k_H/k_D)_{max.}$ in proton-transfer reactions. The isotope effect is expected to be a maximum (*ca.* 7) for a purely XH covalent bond, *i.e.* η(o) 0.216 and $n^\dagger$ 0.5, and nonexistent for a purely ionic bond, *i.e.* η(o) 0.108 and $n^\dagger$ 1. Although we have looked for $(k_H/k_D)_{max.}$ for several reactions, in many of them we are not sure that they are completely free from the effect of ΔG°. Although the scatter is considerable in Figure 5, the points tend to follow the theoretical line and suggest that the kinetic isotope effect is related to the bond order of the transition state. Since the Brönsted coefficient, α, does not depend on $n^\dagger$, it is now obvious that $(k_H/k_D)_{max.}$ is not correlated with α.

Another feature which comes out from the isotope effects is that tunnelling does not play a significant role on proton-transfer reactions at room temperature. In fact the maximum isotope effect predicted from theory is 7.0 (6.2 for CH and 7.9 for OH bonds[21]) and will be considerably higher when tunnelling of hydrogen atoms or protons occurs. However there are few cases where $7 < k_H/k_D < 10$ and even the highest values can be caused by small differences in p*K* in H_2O and D_2O. If we consider tunnelling of hydrogen in the potential-energy curves of our model we find rates a few orders of magnitude higher than the ones for thermal activation. However these potential-energy curves are not appropriate for hydrogen tunnelling because they are estimated with ΔG° values which include solvent reorientation after proton transfer. Tunnelling of hydrogen atoms can be considered for a frozen solvent, but then ΔG° is higher, and consequently the same happens to the barrier height; furthermore the distance between the minima of the potential-energy curves is the actual distance which must be travelled by the hydrogen atom and this is at least three times higher than *d*. Under these conditions tunnelling does not compete with thermal activation at room temperature.

Finally we will discuss some aspects of solvent effects on proton-transfer reactions. The evidence that we have been presenting so far suggests that the proton motion is coupled with that of solvent, probably restricted to the first or even the first two shells of solvent molecules close to the reactive species. Further evidence for such effects can be found in the proton exchange between NH_3 and NH_4^+, either directly or through on H_2O bridge.[25] Whereas the direct proton transfer has $n^\dagger$ = 1.0 (Table 7), the process through an H_2O bridge has a smaller bond order at the transition state. A value of $n^\dagger$ = 1.0 can be understood if in the transition state the nonbonding pair of NH_3 acquires a bonding character.[8,9] However, the value $n^\dagger$ = 0.88 for the water bridge reaction, identical to the one found for ionization of amines at ΔG° 0 (Figure 2) suggests there is some O–H bond-breaking–bond-forming process from the water molecule. This resembles the effect of an associative mechanism on $n^\dagger$ for solvent-exchange processes.[9,11] Such a mechanism may interpret the increase on proton transfer rates in dimethyl sulphoxide[14,26] which for solvent-exchange processes was found to increase $n^\dagger$.[11] However, the present data on these solvents are insufficient for a more rigorous theoretical analysis.

Conclusions

We have shown that it is possible to interpret proton-transfer reactions of different kinds of acids within the same theoretical formalism. The high energy barriers for carbon acids seem to derive from a low bond order of the transition state, $n^\dagger$, due to the lower polar character of the CH bonds. Nitrogen and oxygen acids have lower barriers, which are interpreted in terms of higher $n^\dagger$, due to the more polar character of such bonds. The effect of reaction free energy is well accounted for by the model, and the Brönsted coefficient can only be related with the extent of proton transfer for reactions with a common stretching force constant for the reactive bonds in reactant and product, with high activation entropies and constant $n^\dagger$. The isotope effects are affected by several parameters, but its maximum values can be related with $n^\dagger$, but not with the Brönsted exponent. Acid–base catalysis was found to be interpretable within the present model.

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