

Depicted in Figure 7 are the total overlap populations between the neighboring first row atoms of furan, isoxazole, and oxazole anions in their "cyclic states" calculated by an EHT molecular orbital method.¹⁵ Depicted also in the figure are the LCAO descriptions of the semifilled molecular orbitals of these anions. It is immediately clear that, in each case, the orbital into which the extra electron enters possesses a strong antibonding character across the oxygen bonds, and the ring rupture of the anion occurs at the weakest bond. It should be pointed out that the bonds involving the

(15) R. Hoffmann, *J. Chem. Phys.*, **39**, 1307 (1963).

oxygen atom are the weakest bonds in the neutral state also. The additional electron of the anion makes them even weaker. Most interestingly, in the case of neutral oxazole, the calculation showed that the C₃-O bond is weaker than the C₂-O bond. As shown in the figure, the situation is reversed for the anion, predicting correctly the bond to be ruptured.

The ring-rupture processes observed in the present series of heterocycles thus can be understood as a manifestation of the electronegativity of oxygen and the weakness of the oxygen bonds, particularly in their anionic state.

Relation between Rate and Equilibrium Constants for Proton-Transfer Reactions^{1a}

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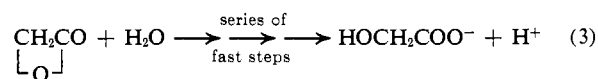
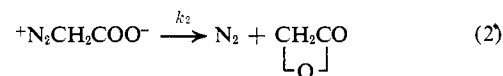
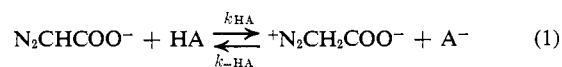
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Abstract: Considerable curvature is found in the Brønsted plot for the hydrolysis of diazoacetate ion by trialkylammonium salts. This curvature can be accounted for by Marcus' theory of atom transfer. The resultant parameters serve to separate from the free energy of activation that part which must be provided before the rate-determining proton transfer can take place and is, consequently, insensitive to the spontaneity of the overall reaction. The variation of the primary hydrogen isotope effect with structure in the same reactions is successfully correlated by the same parameters. A number of other reactions, for which data are taken from the literature, seem to follow similar patterns.

In the next few years it seems likely that the notion of a complete reaction mechanism will change from a series of equations identifying the starting state, the transition state, and any intermediates to a more or less complete description of the atomic motions leading from starting state to transition state and the potential energy hypersurface over which they occur.² There is presently no heterolytic, condensed phase, reaction for which such a complete mechanism can be said to be known, although such reactions are the subject of most current chemical and biochemical study. This lack can be traced to the fact that such reactions involve the repositioning and rebonding of large numbers of atoms (including those of solvent molecules). To many it has long seemed likely that the simplest of such reactions would be proton-transfer reactions.³ Among those it seems likely that the most readily understood will be homogeneous series in which those members which are strongly spontaneous reach large rate constants (10^4 – 10^8 $M^{-1} \text{ sec}^{-1}$) but do not become diffusion limited. The reason for that choice is that systematic changes in ΔF° of reaction can then be achieved which are of the order of the free energy of activation itself. Such changes should change the transition-state structure, as shown by changes in structure-reactivity re-

lationships (Hammett or Brønsted parameters) and isotope effects. From the sensitivity of the transition-state structure to changes in ΔF° , information about the original transition-state structure can be obtained.

General acid-catalyzed diazoacetate hydrolysis is a reaction of the desired type.⁴ The rate-determining proton transfer (eq 1) is followed by fast, irreversible steps (eq 2 and 3) which permit the reaction to be monitored by conventional techniques.



(The k 's are rate constants and follow previously established conventions.) When HA is $\text{H}^+(\text{aq})$ k_{HA} has a value of 6.5×10^4 $M^{-1} \text{ sec}^{-1}$.

We have previously reported⁵ that phenols and carboxylic acids generate quite different Brønsted α 's⁶ when used as catalysts for this reaction, but that the two sets of data combined generate a continuous curve of the

(1) (a) Supported, in part, by the National Science Foundation through Grants GP-7915, GP-13172, and GP-31360X. (b) Du Pont Summer Fellow, 1969; Mobil Oil Summer Fellow, 1970; Lubrizol Fellow, 1970–1971.

(2) L. Salem, *Accounts Chem. Res.*, **4**, 322 (1971).

(3) R. P. Bell, "Acid-Base Catalysis," Clarendon Press, Oxford, 1941, Chapter VIII.

(4) M. M. Kreevoy and D. E. Konasewich, *J. Phys. Chem.*, **74**, 4464 (1970).

(5) M. M. Kreevoy and D. E. Konasewich, *Advan. Chem. Phys.*, **21**, 241 (1972).

(6) J. N. Brønsted, *Chem. Rev.*, **5**, 231 (1928).

Table I. Acid-Dissociation Constants for $R_1R_2R_3NH^+$ and Their Catalytic Coefficients for Hydrolysis of Diazoacetate Ion

No.	R_1	R_2	R_3	pK_{HA}	$k_{HA}, M^{-1} sec^{-1}^a$
1	C_2H_5	C_2H_5	C_2H_5	10.66, 10.7 ^b	$2.7 \pm 0.8 \times 10^{-4}$
2	CH_3	CH_3	$n-C_4H_9$	10.02, 10.1 ^b	$2.89 \pm 0.16 \times 10^{-3}$
3	C_2H_5	C_2H_5	CH_2CH_2OH	9.87 ^b	$3.89 \pm 0.16 \times 10^{-3}$
4	CH_3	CH_3	CH_3	9.80 ^b	$8.75 \pm 0.32 \times 10^{-3}$
5	CH_3	CH_3	CH_2CH_2OH	9.31 ^c	$5.13 \pm 0.17 \times 10^{-2}$
6	CH_3	CH_2CH_2OH	CH_2CH_2OH	8.52 ^c	$2.14 \pm 0.07 \times 10^{-1}$
7	CH_2CH_2OH	CH_2CH_2OH	CH_2CH_2OH	7.74, 7.77 ^b	$6.43 \pm 0.07 \times 10^{-1}$
8	C_2H_5	C_2H_5	CH_2CH_2CN	7.63, 7.65 ^b	$3.64 \pm 0.12 \times 10^{-1}$
9	d			7.51	$4.55 \pm 0.15 \times 10^{-1}$
10	CH_3	CH_3	CH_2CH_2CN	7.03, 7.0 ^b	4.44 ± 0.14
11	CH_2CH_2OH	CH_2CH_2OH	CH_2CH_2CN	5.63	$2.11 \pm 0.07 \times 10$
12	C_2H_5	C_2H_5	CH_2CN	4.55	$1.11 \pm 0.04 \times 10^2$
13	C_2H_5	CH_2CH_2CN	CH_2CH_2CN	4.55	$2.88 \pm 0.15 \times 10$
14	CH_3	CH_2CH_2CN	CH_2CH_2CN	4.24, 4.34 ^e	$1.24 \pm 0.05 \times 10^2$
15	CH_2CH_2OH	CH_2CH_2CN	CH_2CH_2CN	3.46, 3.35 ^e	$1.67 \pm 0.12 \times 10^2$
16	CH_3	CH_2CH_2CN	CF_3CH_2	2.00	$<1 \times 10^3$

^a The reported uncertainties are probable errors (50% confidence limits). ^b D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butterworths, London, England, 1965. ^c D. E. Leyden and J. M. McCall, *Anal. Chim. Acta*, **49**, 77 (1970). ^d 1-(2-Cyanoethyl)piperidinium. ^e P. J. Steinwand, Ph.D. Thesis, University of Minnesota, 1965, pp 46-47.

form required by Marcus' theory of proton transfer.⁷ In the present paper catalytic coefficients are reported for the same reaction for a homogeneous series of trialkylammonium salts as acids. These are also shown to fit the Marcus formalism, removing any uncertainty about combining phenol and carboxylic acid data. The parameters obtained are shown to satisfactorily predict the relation between the primary hydrogen isotope effect, which was also measured, and the strength of the catalyzing acid.

Results

Rate Constants in H_2O . All rates were measured in water at $25.0 \pm 0.1^\circ$ by techniques which have been previously described.⁴ In all the cases discussed in the present paper k_{-HA} is a good deal smaller than k_2 , but where it was appropriate, suitable corrections were made⁴ in order to get accurate values of k_{HA} . These values are given in Table I. Relatively large uncertainties are associated with the catalytic coefficients of the strongest and the weakest acids, because the overall rate is dominated, in those cases, by hydronium-ion catalysis and water catalysis, respectively.⁴

Equilibrium Constants in H_2O . The pK_{HA} values of the various trialkylammonium salts are also given in Table I. A number of them were redetermined by pH titration using a carefully calibrated glass electrode.⁸ The dissociation constant of $(CH_3CH_2)_3NH^+$ was obtained by measuring the pH of several concentrations of the unbuffered base and that for $CF_3CH_2NH(CH_3)CH_2CH_2CN^+$ by measuring the pH of several concentrations of the unbuffered acid. In all cases measurements were made with at least three total concentrations of acid plus base in the range 0.1 to 0.0001 M and covering at least a factor of 10 for each compound. Activity coefficients of the trialkylammonium ions, γ_{HA} , were obtained for ionic strength, μ , by means of the Debye-Hückel limiting law, eq 5, using interionic distances, a ,

$$\log \gamma_{HA} = \frac{-0.511\mu^{1/2}}{1 + 0.33a\mu^{1/2}} \quad (5)$$

(7) R. A. Marcus, *J. Phys. Chem.*, **72**, 891 (1968).

(8) A. O. McDougall and F. A. Long, *J. Phys. Chem.*, **66**, 429 (1962).

between 4 and 7.5 Å, estimated from those given by Kielland.⁹

Activity coefficients of the neutral amines were assumed to be unity. Using these activity coefficients, the calculated infinite dilution dissociation constants were found not to exhibit any consistent variation under variation in concentrations. The pK_{HA} values showed a scatter ranging from about ± 0.01 , for those in the center of the range of measurement, to ± 0.05 , for the strongest and weakest acids. An additional uncertainty of 0.02 should probably be added to this to account for possible calibration errors, so that pK_{HA} values in the center of the range are considered uncertain by ± 0.03 and the weakest and strongest acids by ± 0.1 . Wherever previously reported values were redetermined, they were compared with the older values. The discrepancies did not, in general, exceed the sums of the anticipated uncertainties. In a number of cases available values seemed quite adequate for our purposes and were not redetermined.

Rate and Equilibrium Constants in D_2O . Rate constants, k_{DA} , and acid-dissociation constants, K_{DA} , were also obtained for seven of the trialkylammonium ions, by the techniques already described, in D_2O .¹⁰ These results are given in Table II. The acid-dissociation constant in D_2O , K_{DA} , is given in the form of ΔpK , which is $pK_{DA} - pK_{HA}$. Slightly more accuracy can be attributed to ΔpK than to either pK_{HA} or pK_{DA} because some of the systematic errors, such as standardization errors and errors in activity coefficients, will be the same in both cases.

Isotope Effects on Product Ratios. In addition to the isotope effects measured kinetically, primary hydrogen isotope effects were also obtained from the radioactivity of products obtained in tritiated water. These were obtained by means of eq 6-9.¹¹ In these equations

$$k_{HA}/k_{DA} = (k_{HA}/k_{DA})\phi_{HA} \quad (6)$$

(9) J. Kielland, *J. Amer. Chem. Soc.*, **59**, 1675 (1937).

(10) After each such measurement the adventitious H concentration was estimated by the method of M. M. Kreevoy and T. S. Straub, *Anal. Chem.*, **41**, 214 (1969), and small corrections were applied, as necessary, to obtain results pertinent to 100% deuterated solutions.

(11) M. M. Kreevoy, R. Eliason, R. A. Landholm, T. S. Straub, and J. L. Melquist, *J. Phys. Chem.*, **76**, 2951 (1972).

Table II. Acid-Dissociation Constants for $R_1R_2R_3ND^+$ and Their Catalytic Coefficients for Hydrolysis of Diazoacetate Ion, All in D_2O

No. ^a	ΔpK	k_{DA} , $M^{-1} \text{ sec}^{-1}$	$k_{HA}/$ k_{DA}^b	$k_{HA}/$ k_{DA}^c
4	0.59, ^d 0.70 ^e	$6.13 \pm 0.20 \times 10^{-3}$	1.4	
5	0.66, ^f 0.64 ^{f,g}	$2.45 \pm 0.07 \times 10^{-2}$	2.1	2.6
6	0.61, ^f 0.62 ^{f,g}	$1.01 \pm 0.03 \times 10^{-1}$	2.1	2.9
7	0.59	$1.31 \pm 0.04 \times 10^{-1}$	4.9	4.8
10	0.61	1.02 ± 0.03	4.4	4.6
14	0.56	$1.90 \pm 0.07 \times 10$	6.5	8.5
15	0.56	$1.51 \pm 0.12 \times 10$	11.0	

^a The numbering follows that in Table I. ^b Obtained kinetically. ^c Obtained by competition. ^d G. Schwarzenbach, A. Epprecht, and H. Erlenmeyer, *Helv. Chim. Acta*, **19**, 1292 (1936). ^e R. J. Day and C. N. Reilly, *J. Phys. Chem.*, **71**, 1588 (1967). ^f D. E. Leyden and J. M. McCall, *Anal. Chim. Acta*, **39**, 77 (1970). ^g Obtained by direct determination of the isotopic composition of the acidic proton by nmr spectroscopy.

$$\log \phi_{HA} = \Delta pK - 0.48 \quad (7)$$

$$\log (k_{HA}/k_{DA}) = \log (k_{HA}/k_{TA})/1.44 \quad (8)$$

$$\frac{k_{HA}}{k_{TA}} =$$

$$\frac{k_{HA}(HA)A_{\text{solv}}}{A_{\text{prod}}\{k_H(H^+) + k_{HA}(HA)\} - k_H(H^+)A_{\text{solv}}(k_H/k_T)^{-1}} \quad (9)$$

A_{solv} is the radioactivity per gram atom of hydrogen in the solvent and A_{prod} is the radioactivity per mole of product. Equation 9 serves to separate the activity in the product into that due to H^+ catalysis and that due to catalysis by HA. Since the ΔpK values given in Table II do not seem to be a systematic function of structure, and since the variation in these values approximates their uncertainty, the average value of ΔpK , 0.60, was used throughout. The results are given in Table II. The tabulated uncertainties in k_{HA} and k_{DA} suggest that their ratio may be uncertain by 5–20% with the best values near the middle of the range. The scatter in the experimental values of k_{HA}/k_{DA} suggests a similar uncertainty in k_{HA}/k_{DA} as determined by competition. Within these limits the two sets of values are in substantial agreement, although one could wish for greater reliability.

Discussion

A plot of $\log k_{HA}$ against $\log K_{HA}$ is shown in Figure 1. It is plainly nonlinear, with a slope ranging from 1.0 or more for the weakest acids to something under 0.5 for the strongest.

Marcus' Theory. Marcus' formalism for a proton-transfer reaction is given in eq 10–12. In them ΔF_{HA}^*

$$\Delta F_{HA}^* = W^r + (1 + \Delta F_R^{\circ}/\lambda)^2 \lambda/4 \quad (10)$$

$$(1 > \Delta F_R^{\circ}/\lambda > -1)$$

$$\Delta F_{HA}^* = W^r \quad (11)$$

$$(-1 > \Delta F_R^{\circ}/\lambda)$$

$$\Delta F_{HA}^* = W^r + \Delta F_R^{\circ} \quad (12)$$

$$(\Delta F_R^{\circ}/\lambda > 1)$$

is the free energy of activation for the reaction catalyzed by HA, and ΔF_R° is the standard free energy of reaction within the reaction complex. The reaction com-

plex has sometimes been called an encounter complex, but the work described here makes it plain that considerably more than a simple encounter is required to generate a structure in which proton transfer will take place. The work required to form the reaction complex is W^r . Operationally it is that part of ΔF_{HA}^* which is insensitive to changes in pK_{HA} . For proton transfers from a homogeneous series of oxygen acids to a single substrate it has been suggested that W^r is made up of the entropy of localization and the free energy of desolvation of the acid.^{5,7} The free energy for desolvation of tertiary amines like those with which the present paper is concerned shows little systematic relation to their basicity.¹² It is reasonable to assume that the desolvation free energy of the ammonium salts will be unrelated to their acidity since that of the amines has been attributed mostly to van der Waals forces,¹² which would also operate in the solvated ions. Even hydrogen-bond energies have been shown to be only weakly related to acid strengths.^{13,14} Thus, to the extent that W^r is attributable to these causes, it should be approximately constant for a series of closely related acids like those presently under consideration.

The standard free energy for the reaction shown in eq 1, ΔF_R° , is the sum of W^r , $\Delta F_R^{\circ'}$, and W^p , where W^p is the analog of W^r for the reverse reaction, and expected to be approximately constant for the same reasons. Since ΔF_R° must vary with A in exactly the same way as ΔF_{HA}° , the standard free energy for the acid dissociation of HA, then, if W^r and W^p are constants, $\Delta F_R^{\circ'}$ must be given by ΔF_{HA}° plus a constant, C .

The intrinsic barrier, $\lambda/4$, is the free energy of activation within the reaction complex when ΔF_R° is zero. It is thought to be the mean of $\lambda_1/4$ and $\lambda_2/4$, where the latter are the analogous parameters for the two symmetrical processes. Since the barrier to proton transfer from a trialkylammonium ion to its conjugate base within a reaction complex, $\lambda_1/4$, is vanishingly small, and $\lambda_2/4$ must necessarily be constant as long as only one substrate is used, it is reasonable to believe that λ is constant in this series.¹⁵

Qualitatively W^r is the parameter which governs the ultimate rate which will be achieved by strongly spontaneous variants of the reaction in question, as shown by eq 10 and 11, and λ is the parameter which governs the curvature of the Brønsted plot. By twice differentiating ΔF_{HA}^* with respect to ΔF_{HA}° it can be shown that $\delta\alpha/\delta\Delta F_{HA}^{\circ}$ is $1/(2\lambda)$.⁵ It is obvious that the Marcus formalism can be regarded as a particular quantification of the "Hammond postulate."¹⁶

Application of Marcus' Formalism. With W^r and λ assumed to be constant, it is possible to use the data given in Table I to evaluate W^r , λ , and C , using $-RT \ln (hk_{HA}/kT)$ for ΔF_{HA}^* and $-RT \ln K_{HA}$ for ΔF_{HA}° .¹⁷ The parameters were adjusted so as to minimize the sum of the squares of the discrepancies between ob-

(12) E. Grunwald and E. L. Ralph, *Accounts Chem. Res.*, **4**, 107 (1971).

(13) R. W. Taft, D. Gurka, L. Joris, P. v. R. Schleyer, and J. W. Rakshys, *J. Amer. Chem. Soc.*, **91**, 4801 (1969).

(14) E. M. Arnett and E. J. Mitchell, *J. Amer. Chem. Soc.*, **93**, 4052 (1971).

(15) R. A. Marcus, *J. Amer. Chem. Soc.*, **91**, 7224 (1969).

(16) J. R. Murdoch, *J. Amer. Chem. Soc.*, **94**, 4410 (1972).

(17) S. Glasstone, K. J. Laidler, and H. Eyring, "Theory of Rate Processes," McGraw-Hill, New York, N. Y., 1941, p 190.

Table III. Parameters (kcal mol⁻¹) of Marcus Theory (eq 10)

Acids	Bases	$\lambda/4$	W^r	C	Ref
R ₁ R ₂ R ₃ NH ⁺	N ₂ CHCOO ⁻	1.4	13.8	-6.8	a
RCOOH and ArOH	N ₂ CHCOO ⁻	5.1	7.7	-3.5	b
Oxygen acids	CH ₃ COCHCOCH ₃ ⁻	3.3	9.0	-10.7	c
Oxygen anions	CH ₃ COCH ₂ COCH ₃	3.3	10.5		c
CH ₂ (CN) ₂ and (CH ₃) ₃ -CCH(CN) ₂	RCOO ⁻		7.0		d
H ⁺ (aq)	ArH	10	12		e
ArH ₂ ⁺	Aqueous solvent	10	8		e
RCOOH and H ⁺	CH ₃ COCN ₂ CH ₃	2	17		f
RCOOH and H ⁺	EtOCCN ₂ CH ₃	2	14		f

^a Present work. ^b Recalculated from the previously reported results⁵ to obtain the best overall fit. ^c Calculated from the values of ref 20; a variety of structural types were used. ^d Obtained from the results of ref 18, as described above. ^e Values taken from ref 19. ^f Values taken from ref 21.

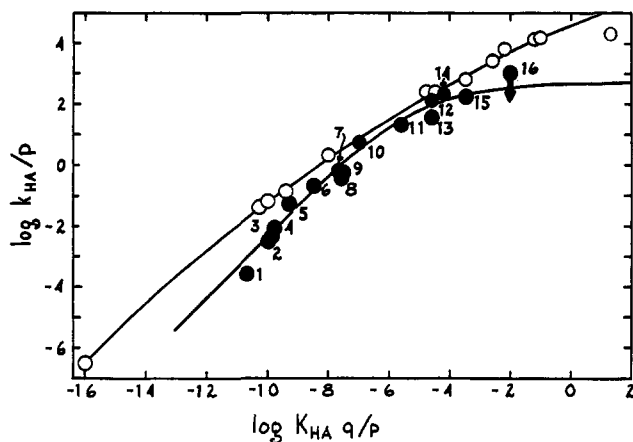


Figure 1. Predicted and experimental relations between $\log k_{HA}$ and $\log K_{HA}$. The closed points are the present results. The open points are the results of Kreevoy and Konasewich⁵ for oxygen acids. The solid lines are the predictions of eq 10 and 12 using the parameters given in Table III. The numbering of points follows Table I. Point number 16 is an upper limit only.

served and calculated values of ΔF_{HA}^* . The parameters obtained are given in Table III. Figure 1 shows the relation between $\log k_{HA}$ and $\log K_{HA}$ predicted by eq 10 and 12 with these parameters. Figure 1 also shows the fit of the rate constants for protonation of diazoacetate by oxygen acids⁵ to eq 10 using new, slightly different, parameters given in Table III, corresponding to the least-squares criterion of best fit.

Table III also shows values of W^r and λ obtained from a small number of other reaction series. The 2,4-pentanedione results were obtained from the data of Ahrens, *et al.*,²⁰ as described above. For the cyanocarbon acid deprotonations eq 11 was used. Equation 11 appears to be satisfied by the rate constants for deprotonation of malononitrile and *tert*-butylmalononitrile with carboxylate anions,¹⁸ permitting the evaluation of W^r but not λ . A treatment essentially equivalent to the present one has been applied by Kresge, *et al.*,¹⁹ to their results on the protonation of a variety of aromatic substances by the aquated proton. For such a series it is less certain that λ is constant¹⁵ but, as they have shown,¹⁹ these data also fit eq 10. The values for 3-diazo-2-butanone and ethyl diazopropionate were obtained by Alberly and coworkers²¹ from a

(18) F. Hibbert, F. A. Long, and E. A. Walters, *J. Amer. Chem. Soc.*, **93**, 2829 (1971).

(19) A. J. Kresge, S. G. Mylonakis, Y. Sato, and V. P. Vitullo, *J. Amer. Chem. Soc.*, **93**, 6167 (1971).

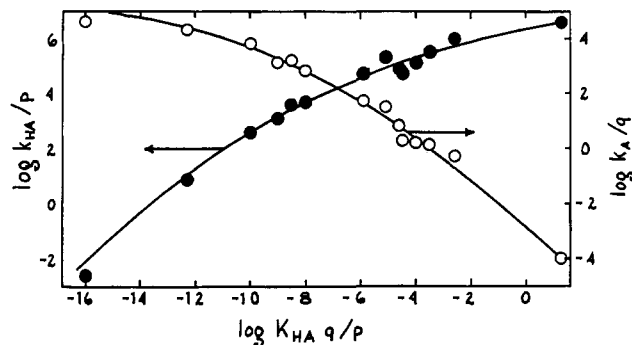


Figure 2. Predicted and experimental relations among k_{HA} , k_{A^-} , and K_{HA} for the acid-base reactions of acetylacetone.²⁰ The open points represent k_{A^-} , the rate constants for deprotonation of acetylacetone by oxygen anions, and the closed points represent k_{HA} , the rate constants for the reverse reaction. The value of the dissociation constant of H⁺ has been taken as 55 M and that for the dissociation constant of H₂O as (1/55) M to make them at least dimensionally consistent with those of the other acids. The solid lines are the predictions of eq 10 with the parameters given in Table III.

rather limited range of data, including the datum for H⁺, and required subsidiary assumptions, so that they are probably less quantitatively reliable, but other aspects of that work make them seem reasonable. The fit of eq 10 to the k_{HA} values for the protonation of acetylacetonate ion by a variety of oxygen acids is shown in Figure 2, along with the fit of the k_{A^-} values for the reverse reaction.^{20,21}

Except where otherwise specified the rate constants for the solvent and its derived ions acting as acids and bases have been omitted in obtaining W^r , λ , and C . Nevertheless, at least in the present cases, they seem to be reasonably well correlated.

In none of these cases does the average deviation of points from the curves exceed 0.2 log unit; thus the correlations are not substantially worse than linear Bronsted correlations which span large numbers of acids and long ranges of acid-base strength.^{6,22} The derived parameters given in Table III are thought to have an uncertainty of about ± 2 kcal mol⁻¹ except in the cases of the neutral diazo compounds, where they may be somewhat larger.²¹

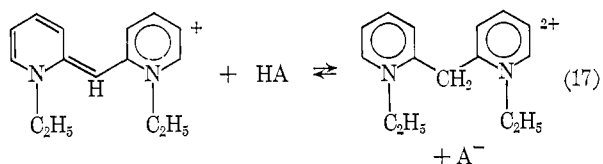
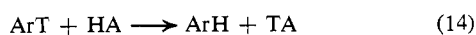
In addition to the reactions for which k_{HA} or K_{A}

(20) M.-L. Ahrens, M. Eigen, W. Kruse, and G. Maass, *Ber. Bunsenges. Phys. Chem.*, **74**, 280 (1970).

(21) W. J. Alberly, A. N. Campbell-Crawford, and J. S. Curran, *J. Chem. Soc. Perkin Trans. 2*, 2206 (1972).

(22) Reference 3, Chapter V.

values have been quantitatively fitted to the Marcus treatment, those shown in eq 13,^{23,24} 14,^{19,25} 15,²⁶ 16,²⁷ and 17²⁸ appear to be in qualitative agreement.



In eq 13 Ar can be either 2,4,6-trinitrophenyl²³ or 2,6-dinitrophenyl.²⁴ In eq 14 Ar is an azulene nucleus or an oxygen-substituted-benzene nucleus.^{19,25} In eq 15 $\text{Ar}_n\text{CH}_{4-n}$ is either a polyphenylmethane or a substituted fluorine.²⁶ A variety of cyanine dyes are actually represented in eq 17.²⁸ In eq 13 and 14 a variety of oxygen acids were used, while in eq 15 B^- is CH_3O^- in CH_3OH for the fluorenes and cesium cyclohexylamide for the polyphenylmethanes. In all cases the data seem too heterogeneous or too limited for quantitative fitting.

Only proton abstraction from nitroalkanes seems to give rate constants which cannot be fitted to eq 10–12 with constant W^\ddagger and λ .²⁹ When the Brønsted parameters α and β are obtained by varying the structure of the nitroalkane acid, they fall outside the limits of 0 and 1. It has been suggested that this is caused by the structure sensitivity of λ ^{15,30} due to the structure sensitivity of certain interactions in the reaction complex which do not exist when the reactants are separate. This explanation requires that α and β be normal when they are obtained by varying the structure of the oxygen or nitrogen base which abstracts the proton from the nitroalkane, while holding the latter constant, since λ must then be constant. The parameters obtained in this way are, indeed, around 0.5.²⁹ Another explanation has been offered by Alberty,²¹ who suggests that W^\ddagger may vary with substitution in the nitroalkanes.

Isotope Effects. The isotope effects shown in Table II are consistent with the physical interpretation given to W^\ddagger and λ . If this interpretation is correct, one might expect the kinetic isotope effect to be concentrated in λ , while W^\ddagger and $\Delta F_R^{\ddagger\ddagger}$ would be relatively insensitive to isotopic substitution. With these assumptions, eq 18 is readily obtained from eq 10.

$$\Delta F_{\text{DA}}^* - \Delta F_{\text{HA}}^* = \frac{1}{4}(\lambda_{\text{D}} - \lambda_{\text{H}}) + \frac{1}{4}(\Delta F_R^{\ddagger\ddagger})^2(1/\lambda_{\text{D}} - 1/\lambda_{\text{H}}) \quad (18)$$

(23) J. A. Blake, M. J. B. Evans, and K. E. Russell, *Can. J. Chem.*, **44**, 119 (1966).

(24) M. E. Langmuir, L. Dogliotti, E. D. Black, and G. Wettermark, *J. Amer. Chem. Soc.*, **91**, 2204 (1969).

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

(26) A. Streitwieser, Jr., W. B. Hollyhead, G. Sonnichsen, A. H. Pudjaatmaka, C. J. Chang, and T. L. Kruger, *J. Amer. Chem. Soc.*, **93**, 5096 (1971).

(27) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 172.

(28) P. J. Dynes, G. S. Chapman, E. Kebede, and F. W. Schneider, *J. Amer. Chem. Soc.*, **94**, 6356 (1972).

(29) F. G. Bordwell and W. J. Boyle, Jr., *J. Amer. Chem. Soc.*, **94**, 3907 (1972).

(30) A. J. Kresge, *J. Amer. Chem. Soc.*, **92**, 3210 (1970).

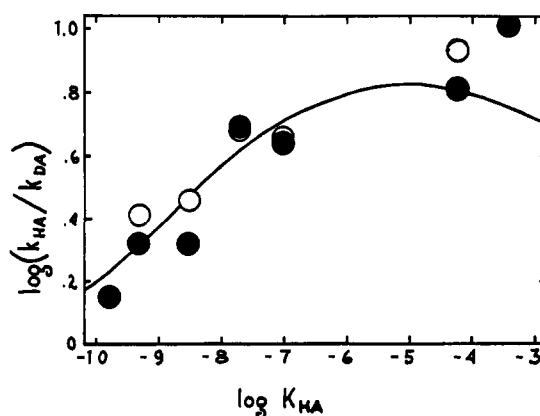


Figure 3. The primary hydrogen isotope effect as a function of the dissociation constant of the acid. The solid line is the prediction of theory, as outlined in the text. The closed points represent the kinetically determined isotope effects. The open points are the competitively determined values. The single parameter of the theory was adjusted to optimize the fit to the kinetically determined values.

Equation 18 is simpler than eq 5 and 6 of ref 5 and also more accurate. In deriving the latter $(1 + \Delta F_R^{\ddagger\ddagger}/\lambda_{\text{D}})$ is assumed to be equal to $(1 + \Delta F_R^{\ddagger\ddagger}/\lambda_{\text{H}})$. This approximation is both unnecessary and inaccurate. Since λ_{D} is larger than λ_{H} , there will be ranges of $\text{p}K_{\text{HA}}$ values for which the analog of eq 10 applies to ΔF_{DA}^* but eq 10 itself has given way to eq 11 or 12 for the calculation of ΔF_{HA}^* . For these ranges the two quantities can be calculated separately, each by the appropriate equation, and the isotope effect evaluated in the usual way from their difference. Figure 3 shows the success of this treatment in predicting the trend of $k_{\text{HA}}/k_{\text{DA}}$ with K_{HA} . The value of λ_{D} , 10.1 kcal mol⁻¹, the only new parameter, was adjusted so as to optimize the fit of the kinetically determined values of $k_{\text{HA}}/k_{\text{DA}}$.

The success of the treatment is particularly striking because the λ values obtained from the present set of data are considerably smaller than might have been anticipated. The fact that the isotope effect falls off rapidly from its maximum value, as required, testifies to the success of eq 10 in approximately separating the free energy of activation for the rate-determining process from the standard free energy of the preliminary reorganization.

Another consequence of the smallness of $\lambda_{\text{H}}/4$ and $\lambda_{\text{D}}/4$ (they are only 3–5 times RT) is that the zero-point energy theory of the isotope effect³¹ is very likely oversimplified, at least in this case. The energy barrier to the reversion of the reaction complex to starting materials must be even smaller if such a barrier exists at all. Thus, the transition state must occur on a fairly extended flat region of the potential energy hypersurface. Such a region would have an abundance of closely spaced energy levels, and considerable vibrational excitation would occur. This may be compensated by tunneling in some cases.³² In addition, since the reaction complex is so very short lived, a Boltzmann distribution over the energy levels may not be achieved.

Values of the Parameters. It has been suggested³

(31) L. Melander, "Isotope Effects on Reaction Rates," Ronald Press, New York, N. Y., 1960, p 20.

(32) R. P. Bell, *Trans. Faraday Soc.*, **54**, 1 (1952).

that, for oxygen acids, the principal contributions to W^r are the negative entropy associated with assembling the reaction complex out of the reactants and the positive free energy required to desolvate the acidic proton. An equivalent explanation for oxygen bases is readily available. These explanations suggest that W^r should be about the same for the same types of acids, regardless of the reaction type. Table III is not entirely in accord with the generalization, although the number of reactions is still small. It would appear, in fact, that for protonation of various diazoalkanes, changes in rates for the same acid are primarily due to changes in W^r . The values of W^r are also too large for the explanation previously given. Steric effects, steric inhibition of solvation, and a sort of Franck-Condon limitation on the efficiency of solvation²¹ may be responsible. More and better values of W^r , for a variety of substrates and for the same substrate in a variety of solvents, will be needed to disentangle these possibilities. In any event, the qualitative reality of the shifts in W^r and λ on going from the oxygen to the nitrogen acids with diazoacetate as substrate is strongly supported by Figures 1 and 3.

Conclusion

The major conclusion of this work is that rate constants are systematically, though not linearly, related to equilibrium constants for many reactions, and that these relations can be used to separate the overall energy of activation into that part required in the rate-determining step and that part required in preliminary steps. This separation now appears to show that much, and perhaps most, of the heavy atom and solvent reorganization that accompanies a proton transfer precedes or follows the rate-determining step. There can be no other explanation for the large values of W^r consistently observed. This observation should considerably simplify the construction of the required potential surface for the rate-determining step.

Experimental Section

Materials and Solutions. Potassium diazoacetate was prepared by the method of Muller³³ and recrystallized by dissolving it in 95% ethanol, then adding ether.³⁴ Standard hydrochloric acid solutions were prepared from constant boiling HCl in the usual manner.³⁵ Standard potassium hydroxide, sodium hydroxide, and sodium deuterioxide were prepared and standardized as described previously.⁴ Standard DCl solutions were prepared from 20% DCl obtained from Diaprep, Inc. Deuterium oxide was obtained from Aldrich Chemical Co. and had a nominal isotopic purity of 99.7%. Tritiated water was purchased from International Chemical and Nuclear Corp.

Triethylamine, diethyl-2-hydroxyethylamine, tris(2-hydroxyethyl)amine, and diethyl-2-cyanoethylamine were purchased from Aldrich Chemical Co. and purified in the form of their hydrochlorides. The amines were dissolved in ether and treated with decolorizing carbon; the hydrochloride was precipitated by adding anhydrous HCl. The hydrochlorides were recrystallized from acetone-ether or acetone-methanol mixtures.

The amines $(\text{CH}_3)_2\text{NCH}_2\text{CH}_2\text{OH}$ (5) and $\text{CH}_3\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$ (6) were purchased from Aldrich Chemical Co. and were twice distilled. $(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CN}$ (12) was prepared by the method of

Allen and VanAllen;³⁶ bp 61–63° (14 mm). $\text{CH}_3\text{N}(\text{CH}_2\text{CH}_2\text{CN})_2$ (14) was prepared as previously described by Steinwand;³⁷ bp 158° (4 mm) (lit. 110–112° (0.06 mm)³⁷ and 148° (3 mm)³⁸). $(\text{CH}_3)_2\text{NCH}_2\text{CH}_2\text{CN}$ (10) was obtained according to the method of Colouge, *et al.*;³⁸ bp 45° (3 mm) (lit. 39 172° (760 mm)). $\text{C}_5\text{H}_5\text{N}(\text{CH}_2\text{CH}_2\text{CN})_2$ (13), $(\text{HOCH}_2\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{CN}$ (11), and $\text{C}_5\text{H}_{10}\text{NCH}_2\text{CN}$ (9) were prepared after the general method of Oda, *et al.*³⁹ (13): bp 154° (2.5 mm); n_D^{25} 1.4588 (lit. 39 bp 200–202° (30 mm); n_D^{20} 1.4591). (9): bp 74° (0.55 mm); n_D^{25} 1.4682 (lit. 39 bp 129–130° (30 mm); n_D^{20} 1.4697). (11): n_D^{25} 1.4793 (lit. 40 n_D^{25} 1.4793). $(\text{CH}_3)_2\text{N}-n\text{-Bu}$ (2) was prepared by the method of Clark, *et al.*;⁴¹ bp 92–93° (lit. 41 bp 94°). $\text{HOCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{CN})_2$ (15) was prepared as by Steinwand.³⁷ Acrylonitrile (159 g; 2.9 mol) was added slowly to ethanalamine (31 g; 0.51 mol), maintaining the temperature below 30°. After the addition the mixture was refluxed at 80° for 4 hr and was then allowed to stand 10 days at room temperature. The volatile substances were removed under high vacuum. A quantitative yield of the amine 15 was obtained. It was undistillable. Titration indicated a purity of 98%, and no secondary amine could be detected.

Amine 16, $\text{CF}_3\text{CH}_2\text{N}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CN}$, appears to be a new preparation. Trifluoroacetic acid (100 g; 0.88 mol) and urea (53 g; 0.88 mol) were heated together in a Claisen flask at 160°. After about 50 g of NH_3 and CO_2 gas had escaped, the mixture was distilled. The distillate was collected at 179–181° and was immediately mixed with methylamine hydrochloride (34 g; 0.5 mol).⁴² The reaction mixture was warmed for several minutes. Chloroform was added to precipitate ammonium chloride which was removed by filtration. The mixture was distilled, and $\text{CF}_3\text{CONHCH}_3$ was collected at 154°. To a solution of LiAlH_4 (20 g; 0.53 mol) in 750 ml of ether was added dropwise a solution of the amide (50 g; 0.43 mol) in 500 ml of ether.⁴⁴ During the addition the solution was stirred vigorously. The mixture was allowed to stand for a day after which time water was added to decompose any unreacted LiAlH_4 . The amine was extracted with dilute sulfuric acid solution which was then made strongly basic with 10 N NaOH. The free amine was extracted from the aqueous alkaline solution with ether. The ethereal solution was saturated with dry HCl gas, and the crude salt was collected. A mixture of water (26 g), Na_2CO_3 (11 g), acrylonitrile (11 g), and crude amine salt (30 g) was refluxed for an hour and allowed to stand at room temperature for 10 days. The amine was extracted with CHCl_3 . The solvent was removed and the amine distilled: bp 102–104° (0.3 mm); n_D^{25} 1.3834.

Anal. Calcd for $\text{C}_6\text{H}_9\text{N}_2\text{F}_3$: C, 43.37; H, 5.46; N, 16.86. Found: C, 43.20; H, 5.28; N, 16.98.

All of these amines were converted to their hydrochlorides by saturating an ethereal solution of the amine with gaseous HCl. The hydrochlorides were dried under vacuum and their identity and purity confirmed by titration with standard base. (For the weaker acids a pH titration was performed. The stronger ones were titrated to a phenolphthalein end point.) In no case did the experimental titer differ from the calculated by more than 1%.

Trimethylamine hydrochloride (4) was purchased from Aldrich Chemical Co. and used without further purification.

Rates and Product Collection. The kinetic and product collection techniques used have been previously described.⁴ The amine solutions were prepared gravimetrically. The ionic strength of the reaction media was maintained at 0.1 M by the addition of appropriate amounts of 1.0 M KCl. Calculated amounts of KOH or HCl were added to solutions of the amines or their hydrochlorides to produce the appropriate buffer for the reaction media.

(36) C. F. Allen and J. A. VanAllen, "Organic Synthesis," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 275.

(37) P. J. Steinwand, Ph.D. Thesis, University of Minnesota, 1965.

(38) J. Colouge, G. Descotes, and G. Frency, *Bull. Soc. Chim. Fr.*, 10, 2264 (1963).

(39) R. Oda, Z. Yoshida, and E. Osawa, *Kogyo Kagaku Zasshi*, 63, 1593 (1960).

(40) F. C. Whitmore, *et al.*, *J. Amer. Chem. Soc.*, 66, 725 (1944).

(41) H. T. Clark, H. B. Gillespie, and S. Z. Weisshaus, *J. Amer. Chem. Soc.*, 55, 4571 (1933).

(42) G. H. Coleman and A. M. Alvarado, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 3.

(43) A. Galat and G. Elion, *J. Amer. Chem. Soc.*, 65, 1566 (1943).

(44) A. von Uffer and E. Schittler, *Helv. Chim. Acta*, 31, 1397 (1948).

(33) K. Muller, *Ber.*, 41, 3136 (1908).

(34) C. N. King and E. D. Bolinger, *J. Amer. Chem. Soc.*, 58, 1533 (1936).

(35) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," Macmillan, New York, N. Y., 1943.