Rate and Equilibrium in the Addition of Bases to Electrophilic Carbon and in SN1 Reactions[1]

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Abstract: Rate constants (k_c) and equilibrium constants (K_c) for the addition of bases to a carbon atom of various electrophilic species are collected (or estimated) from the literature. Plots of log k_c *vs.* log K_c show linear relationships for various series of closely related reactions. For relatively unrelated reactions, however, there are enormous deviations from any straight line (or monotonic curve). Some of the lines for a given series of reactions in water at 25° are fit approximately by equations of the form shown in eq 4. The relative magnitudes of intrinsic barriers and variations in the slopes of the different lines are discussed in terms of steric hindrance, the principle of least motion, solvation, and other factors. It is shown that correlations between SN1 reactivity and carbonium ion stability may be very poor if there is much difference in the structures of the reactants being compared.

One of the first generalizations ordinarily applied by chemists to problems concerning structural effects on reaction rates may be referred to as the *product stability principle*, according to which structural modifications tend to change the rate constants for a given type of elementary reaction in the same direction that they change the equilibrium constants. This principle may be thought of as a basis for such quantitative correlations of rate and equilibrium constants as the Brønsted equation,[2] Evans and Polanyi's equation,[3] etc. Although there are many deviations from such equations known, the area of their validity is large enough to make them quite useful. Furthermore, the nature of the deviations has taught us much about the details of reaction mechanisms, and examination of the deviations has helped lead to new generalizations concerning structural effects on reaction rates. Simple proton transfer reactions, to which the Brønsted relation may be applied (with varying degrees of success), comprise a significant fraction of the individual steps that make up polar reactions. Another significant fraction of the individual steps in polar reactions is made up of simple Lewis acid–base reactions, by which are meant reactions in which some base uses a pair of its electrons to form a σ bond to some Lewis acid without simultaneously breaking any σ bond, or the reverse of such reactions. For such reactions, which include complexation between amines and boron or aluminum halides, attack of nucleophiles on aromatic rings and multiple bonds, SN1 reactions, etc., little attention has been given to quantitative correlations between rate and equilibrium constants,[4] perhaps largely because for most of the

appropriate elementary reactions for which the rate constants are known, the equilibrium constants are not known, and *vice versa*. On the basis of comparisons of rate and equilibrium constants for

$$Ar_3C^+ + H_2O \rightleftharpoons Ar_3COH + H^+ \qquad (1)$$

Diffenbach, Sano, and Taft concluded that there are important and severe structural limitations in linear relationships between cation stabilities (equilibria) and their reactivities (rates).[6] However, reaction 1 is probably a two-step process in which the products whose stabilities are measured by the equilibrium constant are not being formed in the step whose rate constant is being measured.[7] The present paper deals with *one-step* Lewis acid–base reactions in which the acidic atom of the Lewis acid is a carbon atom. For reactions of this type there are enough rate and equilibrium constants available or reliably estimable to provide valuable information concerning the range of validity of rate–equilibrium correlations for such reactions.

Results and Discussion

All the reactions to be discussed are of the type shown in eq 2, where B is a Lewis base and A is a Lewis

$$A + B \underset{k_d}{\overset{k_c}{\rightleftharpoons}} AB \qquad (2)$$

acid containing a carbon atom at the position at which it forms a bond to B. The equilibrium constant for the combination of A and B (K_c) is the quotient of the rate constants for combination and dissociation. The values of the rate and equilibrium constants will depend on four variables, the temperature, the solvent, and the nature of A and B. In order to examine the effect of changing each of the latter three variables one at a time, most of the data have been corrected to 25°. Since most of the available data referred to one solvent, water, most of our attention will be given to changes in the nature of A and B.

Rate and equilibrium constants in aqueous solution at 25° are listed in Table I. The rate constants are based

(1) (a) This investigation was supported in part by Grants GP-7629 and GP-14697 from the National Science Foundation; (b) part XIV in the series "Structural Effects on Rates and Equilibria." For part XIII under a narrower series title, see J. Hine and F. E. Rogers, *J. Amer. Chem. Soc.*, **90**, 6701 (1968).

(2) J. N. Brønsted and K. J. Pedersen, *Z. Phys. Chem.*, **108**, 185 (1924).

(3) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **32**, 1933 (1936); **34**, 22 (1938).

(4) Log–log plots have commonly been made of the rate constants for the reaction *vs.* the basicity constants of the nucleophiles (toward protons). However, these are equivalent to correlations of the rate constants and the equilibrium constants of the given reactions only when the proton basicities of the nucleophiles are linearly related to their carbon basicities in the reaction in question. Carbon basicity frequently does not parallel proton basicity. Deviations as large as 10^{10}-fold are common, and relative basicities toward one kind of carbon may differ from relative basicities toward another kind of carbon by equally large factors.[5]

(5) J. Hine and R. D. Weimar, Jr., *J. Amer. Chem. Soc.*, **87**, 3387 (1965).

(6) R. A. Diffenbach, K. Sano, and R. W. Taft, *ibid.*, **88**, 4747 (1966).

(7) When the data on reaction 1 are treated by methods analogous to those described in the present paper to obtain estimates of the equilibrium constants for the first step, the results add support to the conclusion stated in ref 6.

Table I. Summary of Rate and Equilibrium Constants for Reactions between Lewis Acids and Bases in Water at 25°

Lewis acid	Lewis base	Log K_e, M^{-1}	Log k_e, M^{-1} sec^{-1}	Log k_d, sec^{-1}
Me$_2$CO	OH$^-$	-3.02	1.92	4.94
tert-BuCHO	OH$^-$	-0.58	3.57	4.15
i-PrCHO	OH$^-$	0.00	3.79	3.79
EtCHO	OH$^-$	0.27	4.09	3.82
MeCHO	OH$^-$	0.51	4.63	4.12
2-Pyridyl-CHO	OH$^-$	1.40	5.11	3.71
4-Pyridyl-CHO	OH$^-$	2.12	5.49	3.37
CH$_2$O	OH$^-$	3.99	6.45	2.46
CO$_2$	OH$^-$	7.68	3.92	-3.76
tert-BuCHO	MeOCH$_2$CH$_2$S$^-$	-4.11	5.06	9.17
tert-BuCHO	HOCH$_2$CH$_2$S$^-$	-4.16	5.11	9.27
MeCHO	MeOCOCH$_2$S$^-$	-3.96	5.37	9.33
MeCHO	MeOCH$_2$CH$_2$S$^-$	-2.80	5.67	8.47
MeCHO	EtS$^-$	-2.08	5.67	7.75
CH$_2$O	MeC(NO$_2$)$_2^-$	0.74	3.04	2.30
MeCHO	MeC(NO$_2$)$_2^-$	-5.58	-0.28	5.30
CH$_2$O	Me$_2$CNO$_2^-$	1.38	1.78	0.40
Me$_2$CO	CN$^-$	-1.21	0.52	1.77
MeCHO	CN$^-$	2.58	2.79	0.21
i-PrCHO	MeNH$_2$	-0.72	5.53	6.25
CH$_2$O	Me$_3$N	3.58	7.11	3.53
MeCHOH$^+$	H$_2$O	2.06	8.16	6.10
Me$_2$COH$^+$	H$_2$O	-1.66	5.93	7.59
i-PrCH=NHMe$^+$	OH$^-$	5.69	6.11	0.42
Me$_2$C=NHMe$^+$	OH$^-$	5.91	6.13	0.22
Me$_2$C=NHOH$^+$	OH$^-$	6.38	4.23	-2.15
1-n-Propyl-3-carbamoylpyridinium ion	CN$^-$	-0.73	-1.85	-1.12
1-Methyl-3-carbamoylpyridinium ion	CN$^-$	-0.62	-1.80	-1.18
1-β-Indolylethyl-3-carbamoylpyridinium ion	CN$^-$	-0.08	-1.38	-1.30
1-β-4'-Imidazolylethyl-3-carbamoylpyridinium ion	CN$^-$	0.03	-1.37	-1.40
1-Benzyl-3-carbamoylpyridinium ion	CN$^-$	0.48	-1.19	-1.67
1-(2,6-Dichlorobenzyl)-3-carbamoylpyridinium ion	CN$^-$	0.80	-1.01	-1.81
α-Nicotinamide adenine dinucleotide	CN$^-$	1.22	-1.12	-2.34
1-(p-Nitrobenzyl)-3-carbamoylpyridinium ion	CN$^-$	1.52	-0.64	-2.16
1-(2-Chloro-4-nitrobenzyl)-3-carbamoylpyridinium ion	CN$^-$	1.70	-0.48	-2.18
Nicotinamide mononucleotide	CN$^-$	1.83	-1.05	-2.88
β-Nicotinamide adenine dinucleotide	CN$^-$	2.21	-0.74	-2.95
2,4,6-(O$_2$N)$_3$C$_6$H$_2$Cl	OH$^-$	0.10	1.15	1.05
2,4,6-(O$_2$N)$_3$C$_6$H$_2$OMe	OH$^-$	0.00	1.11	1.11
1,3,5-(O$_2$N)$_3$C$_6$H$_3$	OH$^-$	0.33	1.61	1.28
2,4,6-(O$_2$N)$_3$C$_6$H$_2$CO$_2^-$	OH$^-$	0.28	1.52	1.24
2,4,6-(O$_2$N)$_3$C$_6$H$_2$NH$_2$	OH$^-$	1.53	1.65	0.12
(p-Me$_2$NC$_6$H$_4$)$_3$C$^+$	OH$^-$	4.64	-0.69	-5.33
(p-Me$_2$NC$_6$H$_4$)$_2$CPh$^+$	OH$^-$	7.16	0.32	-6.84
(p-Me$_2$NC$_6$H$_4$)$_2$CC$_6$H$_4$NO$_2$-p$^+$	OH$^-$	8.50	0.75	-7.75
(p-Me$_2$NC$_6$H$_4$)$_3$C$^+$	CN$^-$	>6	-1.06	<-7.06
(p-Me$_2$NC$_6$H$_4$)$_2$CPh$^+$	CN$^-$	>6	-0.16	<-6.16
(p-Me$_2$NC$_6$H$_4$)$_2$CC$_6$H$_4$NO$_2$-p	CN$^-$	>6	0.04	<-5.96

on assumptions concerning reaction mechanisms. For example, the rate constants listed for the combination of hydroxide ions with aldehydes and ketones are based on the assumption that this reaction is the rate-controlling step in the hydroxide ion catalyzed hydration of aldehydes and ketones. In some cases the equilibrium constants were not directly available. The equilibrium constant for addition of a hydroxide ion to an aldehyde, for example, may be calculated from the equilibrium constant for hydration of the aldehyde and the acidity constant of the aldehyde hydrate. However, the acidity constants of the hydrates of propionaldehyde and

pivaldehyde do not appear to have been reported, and they were therefore estimated from a Taft equation correlation of the acidities of aldehyde hydrates.[8] Details on the estimation of equilibrium constants and on the sources of the data used are in the Appendix.

A plot of log k_c vs. log K_c, which will be referred to as an *extended Brønsted plot*, is shown in Figure 1. As a whole, the plot shows little or no semblance of order. The same would be true of a similar plot for proton-transfer reactions. Analogy to the results that have

been obtained in applying the Brønsted equation leads us to expect that order will appear if comparisons are restricted to structurally similar reactants. If either reactant A or B in eq 2 is held constant and the other is varied among a group of closely related species the plot should come close to a straight line whose slope is between zero and one. Several sets of points that would describe such lines may be seen in Figure 1. For example, in the coordination of cyanide ions with the 4 position of 1-substituted 3-carbamoylpyridinium ions (solid square points) the points for primary 1-substituents lie on a straight line, but the three species with 1-ribosyl substituents react too slowly (by about threefold) to fall on this line.[9] When structural changes are made even nearer the reaction center, as when the Lewis acid is changed from a pyridinium ion to an aldehyde or ketone, deviations from linearity may become larger. The rates of attack of cyanide ions on acetone and acetaldehyde (open square points) are too large, by about 500-fold, to fall on the line for 1-RCH₂-3-carbamoyl-pyridinium ions, although they may be considered to form a second line of similar slope.

As Brønsted and Pedersen pointed out for the case of proton transfer reactions, straight lines observed in logarithmic rate-equilibrium plots must be just portions of longer curved lines.[2] After all, structural changes can increase or decrease equilibrium constants practically without limit, but bimolecular reactions can proceed no faster than bimolecular collisions and unimolecular reactions can proceed no faster than molecular vibrations. The nature of the curvature in Brønsted and extended Brønsted plots has been treated by a number of workers.[2,3,10-16] The parameter referred to by Marcus as the "intrinsic barrier" would be useful for classifying the reactions in Table I. However, since the reactions for which intrinsic barriers were calculated[15] are bimolecular processes in both the forward and reverse directions, their equilibrium constants are dimensionless and the values of the free energy change used to calculate the barriers do not depend on the choice of standard state used, whereas our K_c has dimensions so that the values calculated for the free energy change in reaction 2 depend on the choice of standard state. To avoid this complication K_c has been factored into two components, K_e, the equilibrium constant for the association of the reactants to give an intimate encounter complex, and K_r, the dimensionless equilibrium constant for transformation of this encounter complex to the reaction product. For maximum simplicity K_e has been given the same value for all the reactions. This value, 0.017 M^{-1}, was calculated by arbitrarily defining the encounter complex as having the nucleus of the basic atom in B within either of two spherical regions of radius 1.5 Å (the van der Waals radius of oxygen) on either side of the acidic carbon atom of A and then assuming that this basic atom was

(9) R. N. Lindquist and E. H. Cordes, J. Amer. Chem. Soc., 90, 1269 (1968).

(10) J. Horiuti and M. Polanyi, Acta Physicochim. USSR, 2, 505 (1935).

(11) R. P. Bell, Proc. Roy. Soc., Ser. A, 154, 414 (1936).

(12) R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941, Chapter VIII.

(13) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963, pp 156-161.

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

(15) A. O. Cohen and R. A. Marcus, ibid., 72, 4249 (1968).
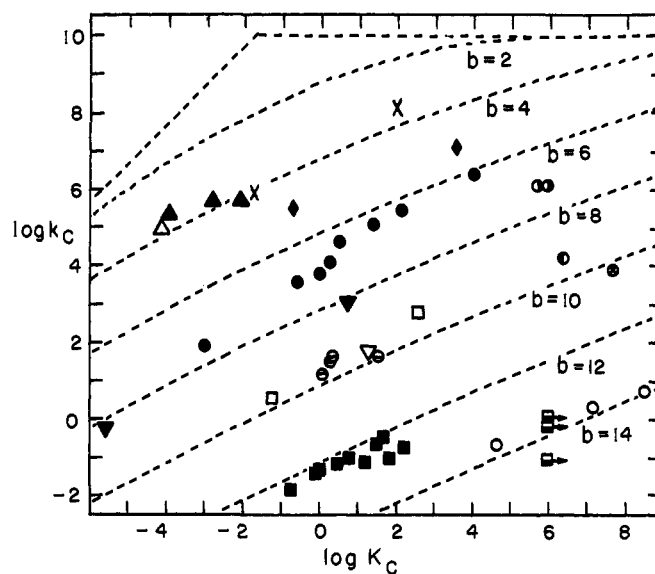
(16) R. A. Marcus, J. Amer. Chem. Soc., 91, 7224 (1969).

Figure 1. Log-log plot of rate constants vs. equilibrium constants for Lewis acid-base reactions in water at 25°: ●, OH⁻ + >C=O; ○, OH⁻ + Ar₃C⁺; ◐, OH⁻ + >C=N⁺HMe; ⊖, OH⁻ + 2,4,6-(O₂N)₃C₆H₂X; ⊗, OH⁻ + CO₂; ◖, OH⁻ + >C=N⁺HOH; ■, CN⁻ + 1-(R)-3-CONH₂-pyridinium ions; □, CN⁻ + MeC=O; ■→, CN⁻ + Ar₃C⁺ (points lie an unknown distance to the right); ▲, R S⁻ + MeCHO; △, RS⁻ + tert-BuCHO; ▼, MeC(NO₂)₂⁻ + -CH=O; ▽, Me₂CNO₂⁻ + CH₂O; ◆, amines + >C=O; X, H₂O + MeC=OH⁺.

just as likely to be at any one point in the solution as another. It follows that K_r is equal to $K_c/0.017$. The collision rate for species in aqueous solution at 25° is taken as 10^{10} M^{-1} sec⁻¹.[17] Substitution into the simplest equation used by Marcus[16] gives eq 3, if we use statistically corrected rate and equilibrium constants

$$RT \ln \frac{10^{10}}{k_c} = \Lambda\left(1 - \frac{RT \ln K_r}{4\Lambda}\right)^2 \qquad (3)$$

Substitution and rearrangement in eq 3 gives

$$\log k_c = 10 - b\left(1 - \frac{\log K_c + 1.77}{4b}\right)^2 \qquad (4)$$

if $|\log K_c + 1.77| \le 4b$

$$\log k_c = 10 \qquad (5)$$

if $\log K_c + 1.77 > 4b$

$$\log k_c = \log K_c + 11.77 \qquad (6)$$

if $\log K_c + 1.77 < -4b$

where, in each equation, b, the log k equivalent of the Marcus intrinsic barrier Λ, is equal to $\Lambda/2.3RT$. At sufficiently large values of log K_c, eq 4 gives way to eq 5, corresponding to reaction at the maximum possible (diffusion-controlled) rate. At sufficiently small values of log K_c, eq 4 gives way to eq 6, corresponding to the reverse rate constant k_d having the maximum value ($10^{11.77}$ sec⁻¹) permissible by the treatment. These two limits, $k_c = 10^{10}$ and $k_c = 10^{11.77}K_c$, are indicated in Figure 1 by dashed lines of slope zero and 1.0, respectively.

Equations like (4), (5), and (6) can be made to fit any data. They become useful only if something can be said in advance about the magnitude of the intrinsic

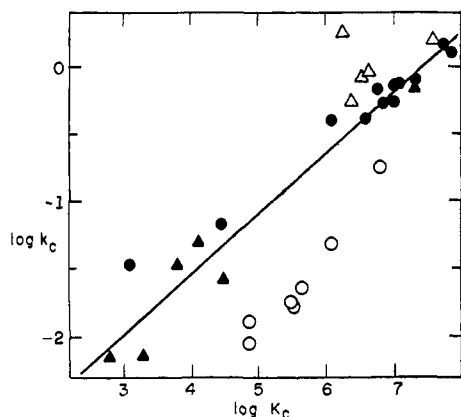(17) Cf. M. Eigen, Angew. Chem., Int. Ed. Engl., 3, 1 (1964).

Figure 2. Log–log plot of rate constants $vs.$ equilibrium constants for combination of hydroxide ions with derivatives and analogs of malachite green and benzaurin: ●, m- and p-$XC_6H_4C^+(C_6H_4NMe_2-p)_2$; ○, o-$XC_6H_4C^-(C_6H_4NMe_2-p)_2$; ▲, meta- and para-substituted $C_6H_5C^+(C_6H_4O^--p)_2$; △, $HetC^+(C_6H_4NMe_2-p)_2$, where Het is a furan, pyridine, or thiophene radical.

barrier b. If b is constant for a series of related reactions, a plot of $\log k$ $vs.$ $\log K$ gives a curve of which a moderate-sized segment may approximate a straight line, such as a Bronsted line. Dashed curves, calculated from eq 4 for various values of b, are shown in Figure 1. Outside the limits of applicability of eq 4, these curves merge with the maximum rate constants indicated by straight dashed lines.

To the extent to which the points for a given reaction series do not run parallel to the curves calculated from eq 4 that are shown in Figure 1, the data on that series cannot be described simply in terms of the intrinsic barrier b. Nevertheless, average values of b for the 14 different series into which the reactions in Table I have been divided are listed in Table II. If some of the as-

Table II. Intrinsic Barriers and Extended Bronsted Slopes for Various Series of Lewis Acid–Base Reactions in Water at 25° [a]

Acid	Base	Average b	Slope Calcd	Slope Exptl
RCHO	RCH_2S^-	3.7	0.56	$\sim$0.3[b]
R_2COH^+	H_2O	3.8	0.44	0.60
R_2CO	R_2NX	5.1	0.42	0.37
R_2CO	OH^-	6.7	0.46	0.67
$R_2C=NHMe^-$	OH^-	7.2		
RCHO	$MeC(NO_2)_2^-$ [c]	8.2	0.51	0.53
$Me_2C=NHOH^+$	OH^-	9.4		
RCOMe	CN^-	9.5	0.47	0.60
CH_2O	$Me_2CNO_2^-$ [c]	9.7		
$2,4,6-(O_2N)_3C_6H_2X$ [d]	OH^-	9.7	0.47	$\sim$0.4[b]
CO_2	OH^-	10.3		
$1-RCH_2-3-CONH_2-$ pyridinium ion[e]	CN^-	12.3	0.48	0.54
$(p-Me_2NC_6H_4)_2C^+Ar$	OH^-	13.8	0.42	0.38
$(p-Me_2NC_6H_4)_2C^+Ar$	CN^-	>14		

[a] R is either hydrogen or an organic radical attached via a carbon atom, Ar is a meta- or para-substituted phenyl group, and X may be anything. [b] The experimental points give poor agreement with any straight line. [c] Forming a bond via its carbon atom. [d] There is some uncertainty as to which position is attached by the base. [e] The cyanide ion attacks the 4 position.

sumptions used by Marcus in treating electron-, atom-, and ion-transfer reactions[14] may be applied to reaction 2, the b values should be approximately equal to the sum

of contributions from each of the two reactants. Tables I and II do not provide enough data to test this possibility quantitatively, but they do give some qualitative support for it. For example, the intrinsic barrier for the cyanide ion is greater than that for the hydroxide ion, not only toward aldehydes and ketones but also toward derivatives of the malachite green [bis(p-dimethylamino)triphenylmethyl] cation (and toward the formation of Meisenheimer complexes, if $1-RCH_2-2-CONH_2-$ pyridinium ions and $2,4,6-(O_2N)_3C_6H_2X$'s are sufficiently similar to make a comparison permissible). Similarly, the malachite green cations have a higher barrier than aldehydes and ketones for reaction with hydroxide ions as well as with cyanide ions. Some regularities may also be seen in comparing the intrinsic barriers in Table II with those that could be calculated by an analogous treatment of data on proton transfer reactions. For example, the 2-nitropropyl anion has a higher barrier than the 1,1-dinitroethyl anion for reaction with formaldehyde just as it does for reaction with protons.[18]

Some of the relative magnitudes of the barriers may be rationalized qualitatively in terms of commonly used generalizations. The higher intrinsic barrier for reaction of hydroxide ions with carbon dioxide than for reaction with aldehydes and ketones might be expected from the principle of least nuclear motion, one of the two logical subdivisions of the principle of least motion.[19,21] The OCO bond angle in carbon dioxide changes by about 60°, whereas the angles around the carbonyl carbon atom of an aldehyde or ketone change by only about 10.5° on combination with a base. There also seems to be clear evidence that the intrinsic barrier may be increased by steric hindrance. Figure 2 is an extended Bronsted plot for the reaction of hydroxide ions with derivatives and analogs of malachite green[22-26] and benzaurin[27] in water at 20° and ionic strength 0.5 M. The points for meta- and para-substituted compounds lie fairly near a straight line of slope 0.45 (although some of the deviations seem large enough to be significant). All the ortho-substituted compounds react too slowly (by three- to eightfold) for their points to fall on this line. The points for heterocyclic analogs of malachite green are in general slightly above the line. Even without ortho substituents the propeller-shaped triarylmethyl cations must have a hindered electrophilic carbon atom. This probably contributes to making the intrinsic barriers for their reactions higher than those for the analogous reactions of aldehydes and ketones.

In applying the principle of least nuclear motion, the solvation shell of an ion, especially one with a concen-

(18) V. M. Belikov, Yu. N. Belokon, N. G. Falcev, and Ts. B. Korchemnaya, $Izv. Akad. Nauk SSSR, Ser. Khim.$, 1477 (1968); $Bull. Acad. Sci. USSR, Div. Chem. Sci.$, 1391 (1968).

(19) ". . . those elementary reactions will be favored that involve the least change in atomic position and electronic configuration. . ." [20]

(20) F. O. Rice and E. Teller, $J. Chem. Phys.$, 6, 489 (1938).

(21) The other subdivision will be called the $principle of least change in electronic configuration$.

(22) R. Cigen, $Acta Chem. Scand.$, 12, 1456 (1958); 13, 1113 (1959); 14, 979 (1960); 15, 1892 (1961); 16, 192 (1962).

(23) R. Cigen and C. G. Ekström, $ibid.$, 17, 1843, 2083 (1963); 18, 157 (1964).

(24) R. Cigen and G. Bengtsson, $ibid.$, 17, 2091 (1963).

(25) G. Bengtsson, $ibid.$, 17, 2165 (1963).

(26) C. G. Ekström, $ibid.$, 19, 1381 (1965); 20, 444 (1966).

(27) H. G. Hansson, $ibid.$, 13, 1309 (1959); 14, 407, 2021 (1960); 17, 2155 (1963).

trated exposed charge, should be considered as part of the structure of the ion. Convincing evidence for the contribution of solvation effects to intrinsic barriers has been provided by Ritchie, Skinner, and Badding, who found that both k_c and k_d in the reactions of bases with malachite green cations were increased by going from water to methanol or from methanol to dimethyl sulfoxide as the solvent.[28] These observations were explained by the postulate that solvent reorganization is a significant contributor to the activation process. It may be that strong hydrogen bonding of solvent to a base has an opposite effect on its reactivity (in reactions with a given equilibrium constant) in Lewis acid–base reactions and in proton-transfer reactions between oxygen and nitrogen atoms. In the proton-transfer reactions, when the solvated base has formed a solvent-separated encounter complex with the acid, it can proceed to the intimate complex with little loss in stability, or perhaps even a gain in stability, because the acid replaces a molecule of solvent in stabilizing the base by hydrogen bonding. Within such an intimate encounter complex reaction can take place by movement of the proton along the hydrogen bond, whose length depends on the hydrogen-bonding abilities of the acid and the base, and reorganization of the surrounding solvent. In the intimate encounter complex of a Lewis acid–base reaction, the Lewis acid may be much poorer at stabilizing the base than the molecule of solvent whose place it has taken. Thus the hydroxide ion, which ordinarily removes oxygen- and nitrogen-bound protons from acids at essentially every collision if they are more acidic than a proton of water, encounters higher barriers in its reactions with Lewis acids, in which it must shed part of its solvation shell and in which it is not brought particularly close to the atom to which it must form a bond. In contrast, mercaptide anions, which appear to encounter significant barriers in proton transfer reactions,[29] have smaller barriers than hydroxide ions in attacking aldehydes, perhaps because the mercaptide anions are so much more weakly solvated that less energy is required to shed part of the solvation shell and form the intimate encounter complex, and less solvent reorganization has to accompany the covalent bond formation.

The strong solvation of ions with relatively concentrated charges does not seem to explain the relatively large intrinsic barriers found in the reactions of cyanide ions with Lewis acids. The basicity of the cyanide ion increases on going from water to dimethyl sulfoxide by only about the same amount as does that of the azide ion,[28] whose reaction with the p-nitro malachite green cation has a smaller intrinsic barrier than that of methoxide ions.[30] In contrast, the same solvent change increases the basicity of hydroxide and alkoxide ions enormously.[31]

The barrier for the reaction of hydroxide ions with the conjugate acid of acetoxime is higher than for the reaction with N-methyliminium ions. The former reaction destroys the conjugation between the hydroxy group and

the double bond to which it was attached and in this respect is similar to the attack of a methoxide ion on the 1 position of 2,4,6-trinitroanisole,[32] 2,4,6-dinitrocyanoanisoles,[33] or 2,4,6-dicyanonitroanisoles,[34] which has a larger equilibrium constant than attack in the 3 position but a smaller rate constant. The preferential protonation of the cyclohexadienyl anion to give 1,4-cyclohexadiene and many analogous observations[35] show that the reaction in which conjugation is destroyed does not always have the highest barrier, however.

The reactions of hydroxide ions with N-methyliminium ions may seem anomolous in that both the rate and equilibrium constants are about the same for the isobutyraldehyde derivative and the acetone derivative, whereas K_c and k_c are considerably larger and k_d smaller in the reaction of hydroxide ions with isobutyraldehyde than in the reaction with acetone. Steric strain in the N-methyliminium ion of acetone is probably an important factor in bringing about this difference in rate–equilibrium patterns. The nitrogen-bound methyl group in the iminium ion presumably interacts with the carbon-bound methyl group that is cis to it in a destabilizing fashion. Such an interaction has been suggested to explain the fact that the N-alkylimines derived from isobutyraldehyde are, within the experimental uncertainty, completely trans.[36]

For nine of the reaction series listed in Table II there are at least two points with significantly different K_c values. The slope of the best straight line through each of the sets of points is listed in the table. It is interesting to compare these experimental extended Brønsted slopes with the values that would be expected from eq 4 (taking b as a constant), which can be calculated from eq 7. The calculated slopes listed in Table II were ob-

$$\frac{d\ (\log\ k_c)}{d\ (\log\ K_c)} = 0.5\left(1 - \frac{\log K_c + 1.77}{4b}\right) \quad (7)$$

tained using the average values of log K_c and b for the reaction series in question. Comparison of the two slopes is probably not meaningful in the two series in which there was no good straight line through the points[37] nor in the reactions of the type $R_2CO + R_2NX$, in which neither reactant was kept constant. The other six reaction series include two, the reactions of pyridinium ions with cyanide ions and the reactions of malachite green cations with hydroxide ions, in which steric effects are kept relatively constant. The experimental slopes for each of these series is within 0.06 of the calculated value.[38,39] The other four series all in-

(28) C. D. Ritchie, G. A. Skinner, and V. G. Badding, J. Amer. Chem. Soc., **89**, 2063 (1967).

(29) Cf. M. M. Kreevoy, D. S. Sappenfield, and W. Schwabacher, J. Phys. Chem., **69**, 2287 (1965).

(30) This conclusion follows from an extended Brønsted plot of the data of Ritchie and coworkers.[24]

(31) Cf. E. C. Steiner and J. M. Gilbert, J. Amer. Chem. Soc., **85**, 3054 (1963).

(32) K. L. Servis, ibid., **89**, 1508 (1967).

(33) J. H. Fendler, E. J. Fendler, and C. E. Griffin, J. Org. Chem., **34**, 689 (1969).

(34) E. J. Fendler, J. H. Fendler, C. E. Griffin, and J. W. Larsen, ibid., **35**, 287 (1970).

(35) J. Hine, ibid., **31**, 1236 (1966).

(36) J. Hine and C. Y. Yeh, J. Amer. Chem. Soc., **89**, 2669 (1967).

(37) A fairly good line of slope ∼0.1 may be obtained if the first series in the table is restricted to reactions of the type MeCHO + RCH₂S⁻. I do not understand why the slope of this line is so small.

(38) The agreement of the calculated slope with the experimental slope in the reaction of triarylmethyl cations with hydroxide ions is even better if the data of Figure 2 are used.

(39) This fact is a justification of the choice of 0.017 M^{-1} as the value of K_c. A narrower definition (with spheres of 0.4 Å radius) could have been used to obtain a value of $10^{-3.5}$ M^{-1} for K_c, which would then have yielded a maximum k_d value of $10^{13.5}$ sec⁻¹, about the vibrational frequency of the bonds undergoing cleavage. However, then the calculated slopes would be further from the experimental values, a defect that could be cured in several ways such as using a more complicated

volve aldehydes and ketones or their conjugate acids and have experimental slopes that range from slightly larger to considerably larger than the calculated slopes. Steric effects on the intrinsic barriers may contribute to these deviations (although experimental error may also be significant). In the series in which formaldehyde appears it has the largest values of k_c and K_c; in those in which acetone (or its conjugate acid) appears it is the only ketone and has the smallest values of k_c and K_c. If the intrinsic barriers for formaldehyde are lowered and those for acetone raised (relative to those for ordinary aldehydes) by steric effects, the result will be larger experimental extended Brønsted slopes than would be found if steric effects were kept constant.

The extent to which the rate constants (k_d) for the reverse of reaction 2 are correlated with the equilibrium constants ($1/K_c$) is precisely the same as for the forward reaction, of course. Hence, the data in Table I show that unless the reactant structures being compared are quite similar, there may be very poor correlations between rate constants and equilibrium constants for SN1 reactions. The largest deviation from such a correlation is found in comparing the loss of cyanide ion from its β-nicotinamide adenine dinucleotide adduct with the loss of water from the conjugate acid of acetaldehyde hydrate, which is about a billion times as fast even though it has about the same equilibrium constant.

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Appendix

Many of the data in Table I come from studies of carbonyl addition reactions. If K_{ad} is the equilibrium constant for addition of HB to a carbonyl compound (eq 8) and K_{aa} is the acidity constant of the adduct (eq 9), K_c for the combination of B with the carbonyl compound may be expressed by eq 10, where K_{hb} is the acidity constant of HB. In the case where HB is water,

$$K_{ad} = \frac{[R_2C(B)OH]}{[R_2CO][HB]} \tag{8}$$

$$K_{aa} = \frac{[H^+][R_2C(B)O^-]}{[R_2C(B)OH]} \tag{9}$$

$$K_c = K_{aa}K_{ad}/K_{hb} \tag{10}$$

values of K_{ad} for propionaldehyde,[40] pivaldehyde,[40] 2-pyridinecarboxaldehyde,[41] 4-pyridinecarboxaldehyde,[41] isobutyraldehyde,[42] and carbon dioxide[43] at 25° were obtained from the literature. The value of K_{ad} for formaldehyde was determined at 20°[44] and corrected to 25°,[45] and the value for acetaldehyde (0.022 M^{-1}) came from a survey of data on the hydration of acetaldehyde,[46] most of which are listed by Bell.[45] Since the

entropy changes for several reactions in which two molecules combine to give one, including hydrations of aldehydes and ketones,[45] average around −25 eu, this value was used to correct the K_{ad} value for acetone determined at an nmr probe temperature of about 33[47] to 25°. Values of K_{aa} have been determined for the hydrates of formaldehyde,[45] acetaldehyde,[46] isobutyraldehyde,[42] and carbon dioxide[43] at 25°, and the values determined for 2-pyridinecarboxaldehyde and 4-pyridinecarboxaldehyde at 20°[48] were assumed to be applicable at 25°. From a Taft equation correlation of the acidity of 1,1-diols that is rather precise for diols of the type $RCH(OH)_2$ but is not as reliable for the hydrates of formaldehyde and ketones,[8] pK_{aa} values of 13.68, 13.94, and 14.19 were calculated for the hydrates of propionaldehyde, pivaldehyde, and acetone. When HB is water, K_{hb} is 1.8×10^{-16} M.

The Arrhenius rate equation and a value of 12 for log A were used to correct k_c values determined at other temperatures to 25°. This value was chosen because it is intermediate between the value (13.2) that may be calculated for the attack of hydroxide ion on acetaldehyde from the best data at 0 and 25°[46] and the value (9.7) obtained from data on isobutyraldehyde at 0[40] and 35°,[49] and because such a value of log A gives a diffusion-controlled rate constant (10^{10} M^{-1} sec^{-1}) at 25° when the Arrhenius activation energy is 2.7 kcal/mol, a value in the vicinity (2.3 kcal/mol for the reaction of hydrogen ions with trimethylamine and 3.5 kcal/mol for the reaction of hydrogen ions with hydroxide ions, according to data listed by Grunwald[50]) of those for reactions known to be diffusion controlled. Values of k_c have been reported for propionaldehyde,[40] pivaldehyde,[40,51] 2-pyridinecarboxaldehyde,[52] and 4-pyridinecarboxaldehyde[52] at 0°, for acetone[53] at 28.5°, and for carbon dioxide[54] at 25°. The value for isobutyraldehyde was interpolated[40,49] and the value for formaldehyde was obtained from kinetic studies on the dehydration of formaldehyde hydrate.[55]

Values of K_{ad}, K_{hb}, and k_c relating to the attack of mercaptide ions on acetaldehyde and pivaldehyde are available.[56a] Corrections for hydration had already been made in the case of acetaldehyde; the pivaldehyde data were corrected for hydration by use of the observations referred to earlier.[40] There is some uncertainty in the value of k_c for the attack of the conjugate base of methyl mercaptoacetate on acetaldehyde because of a possible change in the rate-determining step.[56b] A Taft correlation (eq 11)[46] of the acidities of alcohols of

$$pK_a = 16.56 - 1.38(\sigma_R{}^* + \sigma_{R'}{}^* + \sigma_{R''}{}^*) \tag{11}$$

the type RR'R''COH, in which the value 0.29 is used

equation instead of eq 4. This was not done because it was felt that the present experimental evidence as to the proper form of the equation was not substantial enough to support further complications.

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(51) It was assumed that the value 6.3 × 10³ listed[40] should have been 6.3 × 10² as indicated by certain statements in the text and particularly by Figure 1.
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for $\sigma_H{}^*$, and the assumption that $\sigma_{MeOCH_2}{}^* - \sigma_{EtSCH_2}{}^*$ is equal to $\sigma_{FCH_2}{}^* - \sigma_{ClCH_2}{}^*$ and that $\sigma_X{}^*$ is equal to $2.8\sigma_{XCH_2}{}^*$ give a pK_{aa} of 13.88 for $MeCH(SEt)OH$. It was then assumed that since the substituents that make the acidities of the thiols differ are two atoms further from the hydroxylic hydrogen atoms in the hemithioacetals than they are from the acidic hydrogen atoms in the thiols, they will affect the pK_a's of the hemithioacetals by $(1/2.8)^2$ as much.

Values of K_{ad} for the addition of hydrogen cyanide to acetone[57,58] and acetaldehyde[59] at 25° are available. The assumption that the ionization constant of acetic acid[60] is 28,800 times as large as that of hydrogen cyanide[61] in the acetate buffers in which kinetic runs were made,[57] just as it is at infinite dilution, leads to the k_c values shown in Table I for the combination of cyanide ions with acetone and acetaldehyde. Values of K_{aa} were calculated from eq 11 using 3.64 as the value of $\sigma_{CN}{}^*$.

Equilibrium[62] and rate[63] data were used to calculate K_{ad} and k_c for combination of the 1,1-dinitroethyl anion with formaldehyde. To estimate K_{aa} for 2,2-dinitro-1-propanol the σ^* value for the 3,3-dinitrobutyl group[64] was multiplied by 2.8^2 to get 2.76 as σ^* for the 1,1-dinitroethyl group, which was then used in eq 11. Allowance for the extent of hydration of the aldehyde at equilibrium was made in these calculations and in the calculation of k_c and K_{ad} for the addition of the 1,1-dinitroethyl anion to acetaldehyde[65] and for the addition of the 2-nitro-2-propyl anion to formaldehyde.[18] The value of K_{aa} for the latter case was calculated from eq 11 using a σ^* for the 2-nitro-2-propyl group of 1.21, which was obtained by multiplying σ^* for 2-nitroethyl by 2.8 to get σ^* for nitromethyl and then subtracting 0.19 (the difference between σ^* for methyl and 2-propyl).

Equilibrium measurements on the addition of trimethylamine to formaldehyde at $30 \pm 5°$ were taken as the values at 25° and combined with rate data at 25° to give the data[66] listed in Table I. The values listed for the reaction of methylamine with isobutyraldehyde and for the reaction of hydroxide ions with N-isobutylidenemethylammonium ions come from a study of the formation and hydrolysis of N-isobutylidenemethylamine at 35°[67] and are based on some estimates as well as experimental data. Allowing for the tendency of charge formation to lead to a decrease in entropy in aqueous solution,[68] an entropy change of -35 eu was estimated for K_c for addition of amines to carbonyl compounds in water, a reaction in which two electrically neutral molecules combine to give a zwitterion, and an entropy change of zero was estimated for combination of the oppositely charged hydroxide and iminium ions to

give a neutral molecule. These entropies of addition were used to correct the K_c values to 25° and a log A value of 12 was used to correct the k_c values.

The equilibrium constant for the formation of acetoxime from acetone and hydroxylamine is said to be 1.06×10^6 M^{-1} at about 19°.[69–71] If the entropy change is zero for the dimensionless equilibrium constant obtained by multiplying by the water concentration, then ΔH is -10.3 kcal/mol and the equilibrium constant as ordinarily written is 7.4×10^5 M^{-1} at 25°. This value may be combined with the equilibrium constant for the addition of hydroxylamine to acetone (1.0 M^{-1})[69] and the pK_a (1.75) for the conjugate acid of acetoxime[72] to give the value of K_c listed in Table I for the combination of hydroxide ion with the conjugate acid of acetoxime. The process referred to as the water-catalyzed dehydration of $Me_2C(OH)NHOH$ is taken to be the ionization of the species by heterolysis of the carbon–oxygen bond, and therefore k_d is obtained by multiplying the reported second-order rate constant[73] by the water concentration. Values of K_c, k_c, and k_d for the combination of hydroxide ions with N-isopropylidenemethylammonium ions may be calculated analogously. The equilibrium constant for imine formation from methylamine and acetone at 25° is reported[73] to be 0.22 M^{-1}. The assumption that log K for the addition of methylamine to acetone gives agreement with the best straight line through a plot of such constants for additions to acetone vs. the corresponding constants for additions to 4-pyridinecarboxaldehyde[47] gives a value of log K (-1.32) at 35° that was corrected to 25° by use of an entropy of addition of -25 eu. N-Isopropylidenemethylamine is probably a stronger base than N-isobutylidenemethylamine for the same reason that acetophenone is a stronger base (by about tenfold)[74] than benzaldehyde. However, in an iminium ion the positive charge on the sp^2 carbon atom must be smaller than it is in the case of a protonated aldehyde or ketone. Hence the pK_a of the ketiminium ion has been assumed to be only 0.5 higher than that of the aldiminium ion,[67] which has a pK_a of 7.09 when corrected to 25° by the method of Perrin.[75] Kinetic measurements give 0.114 M^{-1} sec^{-1} for the product of the equilibrium constant for addition of methylamine to acetone and the rate constant for uncatalyzed transformation of $Me_2C(OH)NHMe$ to the imine,[73] which we assume consists simply of an ionization to hydroxide and iminium ions. This rate constant is listed as k_d, and with K_c was used to calculate k_c.

In calculating rate and equilibrium constants for the combination of water with the conjugate acids of acetaldehyde and acetone, it was assumed that this combination is the rate-determining step in the hydrogen-ion catalyzed hydration of these compounds.[46,76] Application of the method of Bunnett and Olsen[77] to literature data[78] gives -6.2 ± 0.2 for the pK_a of the conjugate acid of acetone.[46] The conjugate acid of acet-

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aldehyde is assumed to be ten times as strong an acid, just as the conjugate acid of benzaldehyde is about ten times as strong as that of acetophenone.[74] A pK_a of -10.2 has recently been reported for the conjugate acid of acetaldehyde from measurements in CF_3CO_2H–CF_3SO_3H[79] but a plot of log ($[HA^+]/[A]$) vs. H_0 in this case gives a slope of about -0.6, showing that acetaldehyde is not a Hammett base. Methods like that of Bunnett and Olsen could be applied to such data, but since the solvent mixture does not approach pure water with increasing H_0 we did not use these data. Plots of log ($[ROH_2^+]/[ROH]$) from Raman studies[80] vs. $-H_0$ have slopes of about 0.3 in the H_0 range (around -4) where measurements can be made. These slopes must become 1.0 by the time that H_0 has increased to the point (around $H_0 = 1$) that it becomes essentially identical with pH. The assumption that this increase occurs monotonically gives pK_a's of -2.2 ± 1.2 and -1.7 ± 1.3 for the conjugate acids of methanol and 2-propanol, respectively.[46] The conjugate acid of ethanol was assumed to have the intermediate value -1.9 and the α-hydroxy substituent was assumed to decrease pK_a by 1.88, just as it does in the case of ammonium ions, and to increase it by a statistical factor of 0.3. The resulting estimated pK_a values for the conjugate acids of the hydrates of acetaldehyde and acetone may be combined with equilibrium constants for the hydration of acetaldehyde[45,46] and acetone[47] (as corrected to $25°$) to give the values of K_c listed. Studies of the hydrogen-ion catalyzed [17]O exchange of acetone at $27°$ [53] and of the hydrogen-ion catalyzed hydration of acetaldehyde at several temperatures using several techniques[45,46]

gave the k_c values shown. The hydration of the conjugate acids of acetone and acetaldehyde thus gives products whose expected rate constants for heterolysis (k_d) are considerably smaller than their expected rate constants for deprotonation ($>10^{10}$ sec^{-1}). This supports the assumption made concerning the rate-determining step of the reaction.

Data on the addition of cyanide ions to certain pyridinium ions[9] were used without modification. Stopped-flow measurements on the coordination of hydroxide ions with compounds of the type $2,4,6\text{-}(O_2N)_3\text{-}C_6H_2X$ were made at $20°$.[81] These results were corrected to $25°$ by use of an entropy of -20 eu for the equilibrium and a log A value of 12 in the Arrhenius equation for k_c. The complexes formed with picryl chloride and methyl picrate were stated to have the hydroxide ion attached to the same carbon atom as the chlorine or methoxy group.[81] However, the fact (which was recognized) that this requires hydroxide ions to be lost from the intermediate much more rapidly than X anions makes this structure for the intermediate quite implausible, especially in the case of the chloride.

The data on the reactions of triarylmethyl cations reported by Ritchie and coworkers[28] are listed in Table I because they were determined at $25°$ and extrapolated to infinite dilution and were therefore more directly comparable to the other data. Since these data suffice to compare triarylmethyl cations with other types of Lewis acids, the much more extensive data of the Lund school,[22–27] which were used to illustrate another point, were not corrected to $25°$. In the reactions of triarylmethyl cations with cyanide ions, only limits on the equilibrium constants were obtained.[28]

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