and

$$\left|\frac{(k_4 - k_1)k_3}{k_4(k_2 + k_3)}\right| < 1 \qquad (38)$$

the summations in equations 35 and 36 converge and yield

$$x_{eq} = \frac{k_1k_4e_0s_0}{k_1k_4s_0 + k_1k_3 + k_2k_4} \qquad (39)$$

$$p_{eq} = \frac{k_1k_3s_0}{k_1k_3 + k_2k_4} \qquad (40)$$

Equations 39 and 40 are the correct equilibrium expressions when $s_0 >> e_0$. If $k_4 > k_1$ the inequalities 37 and 39 will always be satisfied and therefore the summations in equations 35 and 36 always converge to give the correct equilibrium expressions. However when $k_4 < k_1$ the inequalities will not *always* be satisfied and then the perturbation solution is not always applicable.

The first term in equation 35 is $(x_0)_{eq}$ and the first term in equation 36 is $(p_0)_{eq}$; the second terms are $(x_1)_{eq}$ and $(p_1)_{eq}$, etc. Thus by using particular values of the rate constants, s_0 and e_0 the number of perturbation terms needed to give any desired agreement with the correct value can be determined. In making the numerical calculations it appeared that this was also a good criterion for determining the number of perturbation terms needed to make the time course of the over-all reaction agree with the steady state solution.

Acknowledgments.—The authors are indebted to Miss Selma Hayman for many of the numerical calculations, to Dr. Wolfgang Wasow for suggesting the use of a perturbation solution and to Dr. Leonard Peller for suggestions concerning this research.

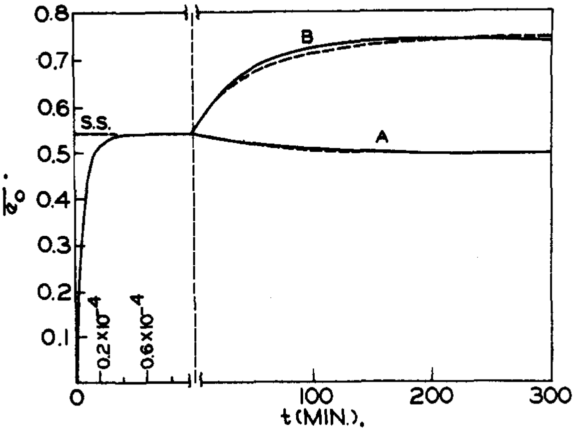

Fig. 4.—Plots of x/e_0 *vs.* t: Curve A was calculated using $k_1 = 7.9 \times 10^8\ M^{-1}$ min.$^{-1}$, $k_2 = 6.58 \times 10^4$ min.$^{-1}$, $k_3 = 1.49 \times 10^3$ min.$^{-1}$, $k_4 = 7.9 \times 10^7\ M^{-1}$ min.$^{-1}$, $s_0 = 10^{-4}\ M$ and $e_0 = 3 \times 10^{-10}\ M$. Curve B was calculated using the same values for k_1 and s_0 but with $k_2 = 2.07 \times 10^4$ min.$^{-1}$, $k_3 = 4.67 \times 10^4$ min.$^{-1}$, $k_4 = 7.9 \times 10^9\ M^{-1}$ min.$^{-1}$ and $e_0 = 10^{-11}\ M$. The first two perturbation terms were used in calculating the solid curve. The dashed curves were calculated using the steady-state assumption.

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Statistical Factors in the Correlation of Rate Constants and Equilibrium Constants

BY SIDNEY W. BENSON[1,2]

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It is shown that in comparisons of equilibrium constants with each other or of rate constants among a set of rate constants, it is the intrinsic or "chemical" constants which should be compared and not the observed constants. These chemical constants, K_{chem} (or k_{chem}), are related to the observed constants K (or k) by the relation: $K_{chem} = K/K_\sigma$; $k_{chem} = k/K^{\ddagger}{}_\sigma$ where K_σ and $K^{\ddagger}{}_\sigma$ are the ratios of symmetry numbers for reactant and product species in equilibrium and chemical reaction, respectively. This leads to some interesting changes in the "relative" base strengths of amines. The symmetry corrections are derivable from statistical mechanics and are equivalent to some of the more intuitive methods in current use. In the case of the Brönsted relation, correlating general acid–base catalytic behavior with acid strength, it leads to a consistent method of assigning symmetry corrections to both k and K_{ion}. The need for such corrections in other "linear free-energy relationships" is pointed out.

Introduction

Since the early success of Brönsted and Pedersen[3] in correlating the catalytic rate constants of acids and bases with their ionization constants, it has become popular to extend this procedure to other reactions. Thus the Hammett[4] treatment of the acidities of substituted benzene derivatives and their correlation with rate constants is a further example of a correlation which is now come to be known more generally as the "linear free energy" relationship. It was early realized[3,5] that such correlations offer ambiguities when species of

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[2] The author wishes to acknowledge his appreciation to the National Science Foundation for a Senior Post-Doctoral Fellowship which made possible the present work.

[3] J. N. Brönsted and K. Pedersen, *Z. physik. Chem.*, **108**, 185 (1924).

[4] L. P. Hammett, *Chem. Revs.*, **17**, 125 (1935); *Trans. Faraday Soc.*, **34**, 156 (1938).

[5] J. N. Brönsted, *Chem. Revs.*, **5**, 322 (1928).

varying symmetry are compared. Thus a dibasic acid such as succinic should not be compared directly with a monobasic acid such as acetic. Rather it was proposed that the constants for the former should be divided by two to compensate for the purely statistical consideration of its possessing two acid groups. The extension of these considerations led to a somewhat elaborate method of correcting acid dissociation constants and rate constants for comparison purposes.[6]

It is the purpose of the present paper to show that the method of Brönsted is part of a more general scheme which can be used to correct rate and equilibrium constants for the statistical features of the reacting molecules without ambiguity.

Statistical Factors in Chemical Reactions.—The nomenclature "linear free energy relationship" is well chosen since a linear relation between the logarithms of equilibrium constants is indeed a linear relation between the corresponding standard free energy changes. This follows from the well known thermodynamic relation $\Delta F^0 = -RT \ln K$. If we are going to compare a series of equilibrium constants with each other, then the method of comparison is determined by the goal. If the aim is purely empirical for correlation or prediction purposes, perhaps no restraints are in order unless the correlation is unsuccessful. If, however, the goal is to relate the constants to molecular properties of the species, we should like to separate out from the constants any accidental elements such as symmetry (or statistics) not essential to the chemical properties. As an example we may consider the hypothetical gas phase equilibrium

$$\mathrm{RH} + \mathrm{Br_2} \rightleftarrows \mathrm{RBr} + \mathrm{HBr}$$

If we wished to compare a series of compounds of varying structure RH in an effort to relate their equilibrium constants to structural parameters, we would feel justified in removing contributions to K (or ΔF^0) due to symmetry. Thus in the case cited when RH = CH_4, there is a contribution of $-RT \ln 8 = 1.3$ kcal. (at 298°K.) to ΔF^0 just due to the lower symmetry of the products.[7]

The method of "correcting" the K_{eq} for these symmetry properties is provided by statistical mechanics. If we list the detailed partition functions Q_{i} for the species involved in an equilibrium

$$\mathrm{A} + \mathrm{B} \rightleftarrows \mathrm{C} + \mathrm{D} \qquad (1)$$

then factoring the symmetry number σ_{i} from Q_{i}

$$K_{\mathrm{eq}} = \frac{Q_{\mathrm{C}}Q_{\mathrm{D}}}{Q_{\mathrm{A}}Q_{\mathrm{B}}} = \frac{\sigma_{\mathrm{A}}\sigma_{\mathrm{B}}}{\sigma_{\mathrm{C}}\sigma_{\mathrm{D}}} \times \frac{Q'_{\mathrm{C}}Q'_{\mathrm{D}}}{Q'_{\mathrm{A}}Q'_{\mathrm{B}}} \qquad (2)$$

$$= K_\sigma \cdot K_{\mathrm{chem}} \qquad (3)$$

where σ_{i} represents the over-all symmetry number of the *i*th species and K_σ is the ratio of the products of the symmetry numbers. We see from eq. 3 that we can write any equilibrium constants as a product of two constants; one representing the symmetry features of the reaction, K_σ, and the other which we have called K_{chem} which reflects all of the remaining "chemical" properties. It would thus seem reasonable to say that in making comparisons of equilibrium constants it is not the observed K_{eq} but rather $K_{\mathrm{chem}} = K_{\mathrm{eq}}/K_\sigma$ which are to be compared. Since K_σ are in principle obtainable without ambiguity where the structures of reactants and products are known, this should at least lead to a consistent scheme without arbitrary rules.

Dissociation Constants of Acids and Bases.—If we wish to make comparison of the strengths of a series of weak acids in a common solvent, we need to be able to write a stoichiometric equation for the reaction. This should in general involve the solvent, as for example with HCN and water

$$\mathrm{HCN} + \mathrm{H_2O} \rightleftarrows \mathrm{H_3O^+} + \mathrm{CN^{-1}} \qquad (4)$$

If, however, we are going to make use of a common solvent, then we can ignore the contribution of the solvent, conjugate acid–base pair to the equilibrium.[8] For the above example, K_σ is given by

$$K_\sigma = \frac{\sigma_{\mathrm{HCN}}\sigma_{\mathrm{H_2O}}}{\sigma_{\mathrm{CN^-}}\sigma_{\mathrm{H_3O^+}}} = K_\sigma(\mathrm{acid})K_\sigma(\mathrm{water}) \qquad (5)$$

In applying a symmetry correction to K_{ion} we shall use, instead of K_σ, the partial factor $K_\sigma(\mathrm{acid}) = \sigma_{\mathrm{HCN}}/\sigma_{\mathrm{CN^-}}$, the contribution due to the solvent being constant in the series. Table I gives the values of these partial factors and the corresponding symmetry numbers of the conjugate acid–base pairs for a few chosen acids.

TABLE I

SYMMETRY CORRECTION FACTORS FOR IONIZATION CONSTANTS OF SOME ACIDS[a]

Acid	σ_{HA}	σ_{B}	$K_\sigma' = \frac{\sigma_{\mathrm{HA}}}{\sigma_{\mathrm{B}}}$
H_3PO_4	3	2	1.5
$H_2PO_4^{-1}$	2	3	0.67
HPO_4^{-2}	3	12	0.25
HClO	1	1	1.00
$HClO_2$	1	2	0.50
$HClO_3$	1	3	.33
$HClO_4$	3	12	.25
H_3O^{+1}	3	2	1.5
HOH	2	1	2.0
C_6H_5OH	2	2	1.00
CH_3COOH	3	6	0.50
$HOOC{\cdot}CH_2{\cdot}COOH$	2	2	1.00
$HOOC{\cdot}CH_2{\cdot}COO^{-1}$	2	8	0.25
NH_4^{+1}	12	3	4.00
$CH_3NH_3^{+1}$	9	3	3.00
$(CH_3)_2NH_2^{+1}$	18	9	2.00
$(CH_3)_3NH^{+1}$	81	81	1.00

[a] An internal symmetry of 3 is included for each CH_3 and 2 for each CO_2^{-1}.

A number of interesting features can be seen. In the sequence of phosphoric acids the K_σ decreases regularly, meaning that K_{chem} (the quantity

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[6] R. P. Bell, "Acid-Base Catalysis," Oxford University Press, Oxford, England, 1941, Chap. V, has summarized the method and data and also some of the "apparent ambiguities."

[7] By way of comparison the result is $-RT \ln 12$ for RH = benzene; $-RT \ln 24$ for RH = neopentane and $+RT \ln 2$ for RH = $CHBr_3$. For the last two, the ratio of equilibrium constants arising from just symmetry changes is 48!

[8] Note, however, in comparing the effects of different solvents on K_{eq} that it is the change in symmetry of the solvent, conjugate acid–base pair which is important.

to be compared) should be increased regularly over the observed K_{ion}, the over-all factor being 6 in the three successive stages of ionization. Similarly in the oxy-halogen acids, K_σ decreases regularly. In the methylammonium ion series the K_σ correction amounts to a factor of 8 going from NH_4^{+1} to $N(CH_3)_4^{+1}$. In comparing the base strength of the conjugate base, we should multiply K_B by K_σ(acid) to correct for the statistical factor. If we do this we find that the observed sequence: $K_B \times 10^5 = 1.8, 42, 59, 6.3$[9] (for NH_3 on down), changes to 7.2, 126, 118, 63. In particular the intrinsic (K_B(chem)) base strengths of methyl- and dimethylamine are inverted compared to K_B. Further K_B(chem) for NH_3 is now greater than K_B(chem) for $N(CH_3)_3$.

It is interesting to note that the intuitive Brönsted method of correcting K_{ion} by dividing K_{ion}(acid) by the number of equivalent protons and multiplying by the number of equivalent positions in the conjugate base where a proton may be added, is equivalent to this more formal scheme of symmetry numbers. The ambiguities discussed by Bell[6] in connection with H_2O and the amines are not real if the scheme is rigorously applied. The advantage of the present generalized procedure is that it permits comparison of systems of different structures which were previously considered equivocal.[6]

In the comparison of phenol with acetic acid, the twofold symmetry of the carboxylate ion acts as a statistical deterrent to the over-all ionization of acetic acid. There is also a big statistical barrier of 4 inhibiting the second ionization of dibasic acids.[10] Similar conclusions could be drawn from rigorous application of the Brönsted method.

Rate Constants.—The correction for rate constants is somewhat different than that for ionization constants. Let us restrict ourselves to metathesis reactions in the gas phase or to solution reactions for both of which transition state theories are valid.[11] In such cases the rate constant is proportional to an equilibrium constant for the formation of the transition state. For the reaction

$$A + B \underset{k_2}{\overset{k_1}{\rightleftarrows}} (A{\cdot}B)^{\ddagger} \xrightarrow{k_r} \text{products} \qquad (6)$$

where the decomposition of $(A{\cdot}B)^{\ddagger}$ is rate determining, we can write for the second-order rate constant k_0

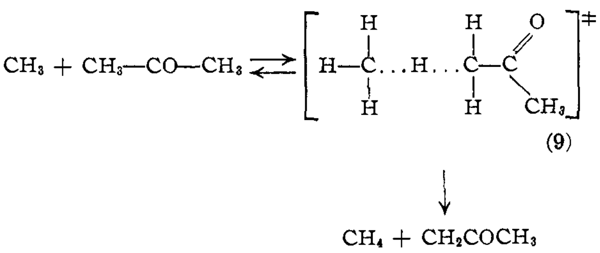
$$\ln k_0 = \ln K^{\ddagger} + C \qquad (7)$$

In the last equation C is usually independent or nearly independent[11] of any structural or molecular properties of the reaction so that changes in k_0 are almost completely a reflection of changes in $K^{\ddagger}$. If we set $K^{\ddagger} = K_\sigma^{\ddagger}/K^{\ddagger}_{\text{chem}}$ as we did for equilibrium constants, then we see that the correction to apply to K_σ is division by $K_\sigma^{\ddagger}$

$$k_{0(\text{chem})} = \frac{k_0}{K_\sigma^{\ddagger}} \qquad (8)$$

This correction is much more nebulous than that for equilibrium constants involving as it does the equilibrium properties of the non-observed, transition state complex. If, however, we are willing to make calibrated guesses at its structure, then we can also compute its symmetry.

If we take as example a metathesis reaction in the gas phase such as



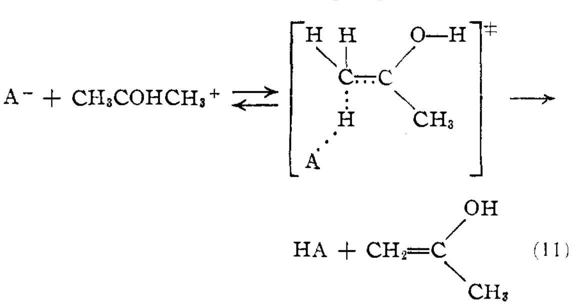
(9)

then

$$K_\sigma^{\ddagger} = \frac{\sigma_{CH_3}\sigma_{CH_3COCH_3}}{\sigma_{CH_3 \cdot CH_3COCH_3}} \qquad (10)$$

In this case, using the values of 6 for CH_3, 18 for CH_3COCH_3 and 9 for the complex, we find $K_\sigma^{\ddagger} = 12$, a rather large "driving force" for the association reaction. If we were comparing the rate constants for the reactions of a series of compounds RH with CH_3 radicals, then we would want to use only a partial $K'^{\ddagger}_\sigma = K_\sigma^{\ddagger}/\sigma_{CH_3}$ since the σ_{CH_3} would be constant for the series. This leads to results identical with those from the procedure of dividing k_0 by the number of reactive H atoms per RH.

In the analysis of catalytic constants for general, acid- and base-catalyzed reactions, the correction will hinge very sharply on knowing the correct structure and the transition state, **including** solvent, if that is of importance. Suppose we consider the acid-catalyzed iodination of acetone which has been so extensively studied.[6] If we represent the rate-determining step as the removal of a proton from the conjugate acid of acetone, to form the enol the process might perhaps be



(11)

In this case the partial symmetry correction to k_{HA}, the catalytic rate constant for the A^-, would be $\sigma_{A^-}/\sigma^{\ddagger} = K'^{\ddagger}_\sigma$ the omitted factor for $CH_3COHCH_3^+$ being a constant in the series. For NH_3, $K'^{\ddagger}_\sigma$ becomes 1 while for acetate ion it is 2.

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[9] K data from compilation by R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworth Scientific Publications, London, England, 1955.

[10] Despite appearances this is the same for the unsymmetrical dibasic acids (such as methylsuccinic acid) unless the lack of symmetry is such as to produce appreciably different K_{ion} for the two COOH groups.

[11] S. W. Benson and A. E. Axworthy, Jr., *J. Chem. Phys.*, **21**, 428 (1953).

Expressed in terms of the acid catalysis as is more usual,[12] these become 4 and 1, respectively.

In these more general terms we see that the Brönsted relation for generalized acid-catalysis can be written as

$$\frac{k_{\mathrm{HA}}}{K_{\sigma}^{\ddagger}} = G_{\mathrm{A}}\left(\frac{K_{\mathrm{HA}}}{K_{\sigma}(\mathrm{HA})}\right)^{\alpha} \qquad (12)$$

A similar equation can be written for basic catalysis.

It is clear that for any comparison of rate constants with equilibrium constants such as is being done today in the field of displacement reactions, similar corrections should be made. For the treatments used by Hammett originally, the corrections turn out to be self-cancelling. However, for some of the more extended treatments and particularly for the comparisons of substituent effects, symmetry factors should be introduced as corrections.

It is not the intention of the present paper to make an ardent defense for the linear free energy relationships that have been introduced. Actually a great deal more scrutiny should be made of other "accidental" contributions to free energy changes such as molecular weight, moments of inertia, choices of solvent[13] and temperature. This would certainly be required before "molecular" interpretation can be justified. The correction for symmetry is merely one of the more obvious of this set for which a consistent approach is possible.

Acknowledgments.—The author wishes to express his appreciation to his temporary colleague at Cal Tech, Dr. Edward L. King of the University of Wisconsin for his patient interest and sage counsel in matters pertaining to the subject of this paper.

PASADENA, CALIFORNIA

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[12] If the transition state were AH. . .OC$(CH_3)_2$, there would be a different $K_{\sigma}^{\ddagger}$, written in terms now, of (HA) and $(CH_3)_2CO$ instead of their conjugates. However, the rate constant for the latter, $k_{\mathrm{HA}} = k_{\mathrm{A}^-} X K_{\mathrm{HOC(CH_3)_2^+}}/K_{\mathrm{HA}}$ so that when we correct for the ionization constants, we find the two states equivalent.

[13] The nature of solvent interactions, particularly in ionic systems. is by no means trivial since a good part of the free energy changes in such systems is attributable to changes in ion–solvent interaction. Thus our interpretation of the H^+ behavior will depend on whether we will represent it as H^{+1}, H_3O^{+1}, $H_5O_2^{+1}$, etc. Similarly for HO^{-1} we may write $H_3O_2^{-1}$, etc.