Molecular Interactions and the Benesi–Hildebrand Equation

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Abstract: The thermodynamic and spectroscopic properties of weak complexes can contain large systematic errors when determined using the Benesi–Hildebrand method. The central issue is the choice of the proper concentration scale. The concentration scale appropriate to a given system can usually be determined experimentally. From the limited data available, molarity appears a better concentration unit than either mole fraction or molality.

There is a voluminous literature on the properties of weak complexes such as charge-transfer complexes and hydrogen-bonded species.[1,2] Not infrequently measurements on these complexes are made by spectroscopic methods, and the analysis of the data makes use of one of the variants of the Benesi-Hildebrand (BH) equation.[3–5] Several critical discussions of this treatment are available.[5–7] One matter of some concern to several authors is the rather startling observation that the thermodynamic and spectroscopic properties of the complexes are functions of the concentration units used to analyze the data.[5,6] The spectroscopic parameters (extinction coefficient in ultraviolet measurements, limiting chemical shifts in the nmr studies) should be properties of the pure molecular complex and should not depend upon the choice of a concentration scale. There have been reports of negative equilibrium constants as well.[8] The unusual results are in no way ascribable to experimental error, and the magnitude of the variations can be very large.[5,6] As a result there is a widespread feeling that the Benesi–Hildebrand methods contain a major ambiguity that potentially undercuts the utility of this approach. This paper resolves one source of these difficulties by showing that some of the ambiguities are artifacts resulting from an improper choice of concentration units. Given a proper choice of units, the BH equation *does* describe accurately the *average* properties of 1:1 complexes, in the absence of solvent competition.

Results

Consider a complex, AB, formed in the reaction

$$A + B = AB$$

in the presence of an inert solvent, S. Assume that A, B, AB, and S form an ideal solution on a suitable concentration scale when the reaction is taken into account. There are many ways to express an "equilibrium quotient" that relates the concentration of reactants and products. We will discuss two common ones (molar and mole fraction) and give results for a third (molal) We define

$$K_c = [AB]/[A][B] \tag{1a}$$

$$K_x = X_{AB}/X_A X_B \tag{1b}$$

where the symbols have their usual meanings. Activity coefficients are not needed because the solution is assumed to be ideal.[9] We neglect all other forms of further complexation including participation of the "inert" solvent. We assume that $n \gg n_A$, n_{AB} where n_i equals the number of moles of component i.

Equation 1 is easily solved for the fractional amount of A that is complexed. If P_0 is the magnitude of a property of the pure complex, then

$$P_{obsd} = \frac{K_c(\bar{B})P_0}{1 + K_c(\bar{B})} = \frac{K_x X_{\bar{B}} P_0}{1 + K_x X_{\bar{B}}} \tag{2}$$

where $(\bar{B})$ indicates the concentration of B before reaction and P_{obsd} is the observed magnitude of the property in any given solution. Inspection of eq 2 might lead one to believe that K_c and K_x are both equilibrium constants with values independent of concentration, but this conclusion cannot be generally true, as we now show (see also ref 5). Using eq 1 and the usual assumptions that there is no volume change on mixing and that A and AB are very dilute, we solve for K_x

$$K_x = \frac{K_c}{v_S + X_B(v_B - v_S)} \tag{3}$$

where v_B and v_S are the molar volumes of pure B and S. Equation 3 clearly shows that only if $v_B = v_S$ can *both* be equilibrium constants over any range of concentration. This is the crucial point, for we can readily show that the BH approach depends upon the equilibrium quotient being independent of concentration.

The BH method of analysis suggests that, given eq 2, P_{obsd} be measured as a function of $(\bar{B})$. Several different treatments of the data have been suggested.[3–5] We have selected the original method[3] for purposes of discussion, but the particular form chosen does not alter the conclusions. We rearrange eq 2

$$\frac{1}{P_{obsd}} = \frac{1}{Kf(\bar{B})P_0} + \frac{1}{P_0} \tag{4}$$

where K is a general equilibrium quotient and $f(\bar{B})$ is the concentration of B on an arbitrary concentration scale. We plot $1/P_{obsd}$ *vs.* $1/f(\bar{B})$. If K is not a function of $f(\bar{B})$ we can immediately identify the intercept

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[1] G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman & Co., San Francisco, Calif., 1960.

[2] (a) T. Rose, "Molecular Complexes," 1st ed, Pergamon Press, New York, N. Y., 1967; (b) L. J. Andrews and R. M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964.

[3] H. A. Benesi and J. H. Hildebrand, *J. Am. Chem. Soc.*, **71**, 2703 (1949).

[4] J. A. A. Ketelaar, C. van de Stople, A. Goudsmit, and W. Dzcubas, *Rec. Trav. Chim.*, **71**, 1104 (1952).

[5] R. L. Scott, *ibid.*, **75**, 787 (1956).

[6] P. J. Trotter and M. W. Hanna, *J. Am. Chem. Soc.*, **88**, 3724 (1966).

[7] L. E. Orgel and R. S. Mulliken, *ibid.*, **79**, 4839 (1957).

[8] M. W. Hanna and A. L. Ashbaugh, *J. Phys. Chem.*, **68**, 811 (1964).

[9] An ideal solution is not needed for what follows if all the activity coefficients are constant over the concentration range studied.

as $1/P_0$ and the slope as $1/KP_0$,[3] but, if K is a function of $f(\overline{B})$, the exact functional form is required to solve for S and I. A function such as given in eq 3 would alter both slope and intercept for the concentration-dependent K even though a good straight line would result (*vide infra*).

We come then to the vital question of which, if any, concentration scale supplies an equilibrium quotient which is independent of concentration. This is an experimental question. We require a test to determine for any given reaction which of the K's are constant. The most straightforward procedure would be to measure K as a function of $f(\overline{B})$. The method requires an independent determination of the concentration of both A and AB. Unfortunately, those times the BH equation is ordinarily useful are precisely those cases in which *independent* concentration measurements of both dilute components are most difficult.[10]

We propose that the constancy of K_c and K_x for a given reaction can be determined if there exist two inert solvents of differing molar volume, suitable for a BH dilution experiment. In practical terms the pair of inert solvents should be sufficiently close in properties so that one has reason to assume that K and P_0 of a molecular complex will be the same in both solvents. Then a simple comparison of P_{obsd} in solutions of the same molarity or mole fraction of active components will suffice. A constant K is demonstrated by the constancy of P_{obsd}. For illustrative purposes we report an experiment of this type performed on the chloroform–benzene complex, with heptane and hexadecane as the inert solvents. Table I reports the nmr solvent shift of the chloroform proton in two sets of benzene–heptane and benzene–hexadecane solutions. The first pair contains the same mole fraction of benzene; the second pair contains the same molarity of benzene. The results are clear-cut. The good agreement for constant molarity and poor agreement for constant mole fraction indicate K_c is the appropriate constant. These results are typical of many obtained in our laboratory on hydrogen-bonded or other weakly complexed systems. This type of experiment can be readily generalized for other concentration units.

Table I. Comparison of K_c and K_x for Chloroform–Benzene

Concn of benzene	Inert solvent	$-\delta_{\text{obsd}}$,[a] cps
For Constant Mole Fraction		
0.490 mole fraction	Heptane	31.3 ± 0.2
0.478 mole fraction	Hexadecane	22.9 ± 0.2[b]
For Constant Molarity		
5.11 moles/l.	Heptane	35.7 ± 0.2
5.11 moles/l.	Hexadecane	36.1 ± 0.2

[a] Nmr methods are described by F. Koenig, *J. Chem. Educ.*, **42**, 227 (1965). The δ_{obsd} is for the chemical shift of the $CHCl_3$ proton at high dilution in the benzene-alkane solution compared with the $CHCl_3$ chemical shift in neat heptane, at 60 Mcps. [b] If the mole fractions were both 0.490, this value would be increased by 0.3 cps.

We wish to anticipate the results of more systematic experiments of this type by advancing the *hypothesis* that K_c is the universally appropriate equilibrium expression for reacting systems. Both theoretical and experimental evidence can be cited. The theoretical arguments are persuasive but not rigorous. They include the following ideas. First, for the exactly soluble case of equilibria involving ideal gases, two equilibrium quotients are constant with respect to pressure and dilution with an inert gas: K_p (based on partial pressures) and K_c. K_x is *not* independent of pressure if the number of moles present changes during the course of the reaction (as it must for simple complexation).[11,12] Second, the law of mass action can be derived from statistical arguments, which leads directly to the pressure independence of K_p and K_c.[13] Reaction rates can also be related to equilibria for ideal cases.[14] Clearly it is inappropriate to employ mole fraction or molal units in the formulation of rate expressions.

The concept which connects these ideas is a simple one. Reactions generally involve energy changes which are directly related to intermolecular separations. Pressures, molarities, and volume fraction units are representative of these separations on an "absolute" basis. Mole fraction and molal units are not.

Further experimental evidence is also available. Buchowski, *et al.*,[15] studied heptyne-1-acetone hydrogen-bond formation using an infrared technique which permits the direct determination of K. K_c is convincingly independent of solvent in the series: cyclohexane, hexane, decane, tetradecane (0.44, 0.45, 0.43, 0.43 l./mole, respectively). K_x in the same series is 4.0, 3.4, 2.2, 1.6. Our own nmr work shows a similar result for the interaction of nitromethane with bromoalkanes.[16] These were studied under BH conditions. The nitromethane was in high dilution and its chemical shift was measured. Table II gives the results using both the mole fraction and the molarity of Br as the independent variable. Molarity is seen to be a far

Table II. Comparison of Mole Fraction and Molar Concentration Units for the System, Nitromethane–Alkyl Bromide[a]

$MeNO_2$ in	$(K_x)_{BH}$	$(\Delta_x)_{BH}$	$(K_c)_{BH}$	$(\Delta_c)_{BH}$
n-Propyl bromide	0.48	31	0.11	20
n-Pentyl bromide	0.72	20	0.13	16
n-Octyl bromide	0.90	17	0.11	22
1,6-Dibromohexane	1.52	21	0.11[b]	21

δ_{obsd} for $MeNO_2$ in Constant Molar or Constant Mole Fraction *n*-Propyl Bromide–Alkane Mixtures

Concn of *n*-propyl bromide	Inert solvent	$-\delta_{\text{obsd}}$,[c] cps
0.49 mole fraction	Heptane	6.5
0.46 mole fraction	Hexadecane	5.1
5.0 moles/l.	Heptane	7.3
5.0 moles/l.	Hexadecane	7.7

[a] Partial results of work reported in ref 16. Mole fractions were calculated from original data. Δ in cps, experimental uncertainty ±3 cps, K_x and K_c uncertainties ~±10%. [b] K_c Calculated per mole of Br. [c] See footnote *a*, Table I.

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[10] The experimental problem in uv measurements is that there is no simple way to use the acceptor absorption. In nmr only a single population weighted line is observed because of exchange processes.

[11] W. J. Moore, "Physical Chemistry," 3rd ed, Prentice-Hall, Inc., Englewood Cliffs, N. J., 1963, p 174.

[12] E. A. Moelwyn-Hughes, "Physical Chemistry," 2nd ed, Pergamon Press, New York, N. Y., 1961, p 1020 ff.

[13] N. Davidson, "Statistical Mechanics," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 7.

[14] F. Koenig, *J. Chem. Educ.*, **42**, 227 (1965).

[15] H. Buchowski, J. Devaure, P. B. Huong, and J. Lascombe, *Bull. Soc. Chim. France*, 2532 (1966).

[16] I. D. Kuntz and M. D. Johnston, *J. Am. Chem. Soc.*, **89**, 6008 (1967).

more appropriate variable in these systems because a single equilibrium constant and limiting chemical shift are sufficient to describe the chemical shift of nitromethane in any neat alkyl bromide (C_2 to C_{16}) or in any solutions of these alkyl bromides with heptane or cyclohexane. Even sufficiently separated 1,*n*-dibromides can be included. By contrast the equilibrium "constant" and limiting shifts obtained from a mole-fraction plot vary from compound to compound. The twofold variation in $(\Delta_x)_{BH}$ is particularly unsettling since it should be a property of the pure complex. The suggested procedure for deciding which concentration scale is correct confirms the choice of K_c (Table II). Surely these isolated examples and theoretical special cases are not conclusive proof that K_c is *always* the correct equilibrium constant, although we find it difficult to imagine a physical mechanism which would lead to the constancy of K_x or K_m. For the present we will proceed under the *assumption* that K_c is constant.[17]

If eq 3 describes the concentration variation of K_x, substitution for K_x in eq 2 gives the following form of eq 4 (see also ref 2b and 5).

$$\frac{1}{P_{\text{obsd}}} = \frac{v_S}{K_c P_0}\frac{1}{X_B} + \left(1 + \frac{v_B - v_S}{K_c}\right)\frac{1}{P_0} \tag{5}$$

Although eq 5 accurately describes a straight line on a BH plot, the concentration dependence of K_x has introduced additional factors multiplying the normal slope and intercept terms. If we define $(K_x)_{BH}$ and $(P_{0,x})_{BH}$ as the *experimentally* determined parameters obtained from a BH mole fraction plot, we see

$$(K_x)_{BH} = \frac{I}{S} = \frac{K_c}{v_S} + \frac{v_B - v_S}{v_S} \tag{6a}$$

$$(P_{0,x})_{BH} = \frac{1}{I} = \left(\frac{K_c}{v_B - v_S + K_c}\right)P_0 \tag{6b}$$

where I and S are the experimental intercept and slope respectively, and the other symbols have been previously defined. Equation 6 indicates that a concentration-dependent equilibrium quotient can have several implications for the BH method. First, the measured quantities, $(K_x)_{BH}$ and $(P_{0,x})_{BH}$, cannot be construed as representing molecular properties unless $v_B = v_S$. Second, it is easy to see that reasonable values of K_c, v_B, v_S can result in zero or negative values of $(K_x)_{BH}$. Third, $(P_{0,x})_{BH}$ will vary from solvent to solvent even if P_0 itself does not. Fourth, we emphasize again the point raised by Trotter and Hanna[6] that simple inspection of eq 5 and 6 cannot reveal whether a proper concentration scale has been selected since the "goodness-of-fit" of given data to any of the common concentration scales will be the same.

An analogous set of calculations has been performed for molal BH plots under the assumption that K_c is constant. The experimentally determined parameters are related to the molar values by

$$(K_m)_{BH} = \rho_S(K_c + V_B) \tag{7a}$$

$$(P_{0,m})_{BH} = P_0\left(\frac{K_c}{K_c + V_B}\right) \tag{7b}$$

where ρ_S is the density of the inert solvent in g/ml· Equations 6 and 7 can be rearranged to solve for K_c and P_0 which are the "true" parameters if the reaction is correctly described by a molar equilibrium constant.

The same arguments indicate that $(K_x)_{BH}$ and $(K_m)_{BH}$ would surely not be suitable for direct use in ΔH determinations. Even K_x and K_m must be corrected for such purposes to account for the change in the appropriate volume and density terms as the temperature changes. For weak interactions with K_c's of order 0.1–1.0 l./mole and $-\Delta H$'s of 1–5 kcal/mole, discrepancies in excess of 100% are readily obtainable.

Discussion

We strongly endorse the conclusion of other workers that the choice of concentration units is crucial in determining the properties of weak complexes by the Benesi–Hildebrand equations.[5,6] We emphasize the importance of a concentration-independent equilibrium quotient because the BH method is based upon the assumption that the entire concentration dependence of an observable can be ascribed to changes in the concentration of the complex. If *any* other terms have an intrinsic concentration dependence there is no single BH experiment that can accurately determine K and P_0. In contrast to earlier workers we feel it is possible to decide experimentally which concentration scale is most likely to be correct, at least for simple equilibria. The experiment involving a change in inert solvent should have general applicability whenever the straight-chain alkanes can be used.[18]

Our suggestion that a concentration scale can be considered "correct" or "incorrect" should be explained. Thermodynamic arguments alone could never justify such a contention precisely because thermodynamic results are independent of the details of molecular interactions. However, the study of weak complexes rarely stops at the level of measuring thermodynamic properties. The major impetus of essentially all such studies is the *interpretation* of the thermodynamics in terms of molecular models. In this case, one is permitted to employ all the usual tests of the "correctness" of a scientific theory. One of these tests suggests that, if several theories are equally successful for predictative purposes, one is to choose the theory with the fewest *ad hoc* hypotheses. In terms of the specific problem before us, *any* concentration scale can be made to yield quantitatively correct physical predictions by the use of suitable "activity coefficients." Elaborate theories could be advanced to explain the ordering of these coefficients, but, at least in the work described in ref 15 and 16, the only function of the activity coefficients is to compensate for the concentration effects introduced by the differing molar volumes of the solvents. The fact that the common concentration scales are all proportional to one another in dilute solutions is not evidence that they are actually "interchangeable" in any general sense. The proportionality constants between the concentration scales are dependent on the solvents and can lead to major ambiguities, even in infinitely dilute solu-

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(17) If this assumption proves incorrect for some reaction, the same mathematical procedure can be carried through with the entire concentration dependence assigned to K_c instead of K_x or K_m.

(18) On occasion halogenated solvents are required. By nmr standards these are not "inert."[16,19] Nonetheless, careful pairing might be successful. Possibilities include carbon tetrachloride and tetrachloroethylene, chloroform and pentachloroethane, etc.

(19) A. D. Buckingham, T. Schaefer, and W. G. Schneider, *J. Chem. Phys.*, 32, 1227 (1960).

tions. The data from Table II, for example, might be used to suggest that nitromethane interacts twice as strongly with octyl bromide as with propyl bromide if mole fraction units are used, yet molar units suggest the interaction is the same in both cases. Only one of these interpretations can be correct. Thus the choice of concentration units, which led to the differing interpretations, cannot be considered an arbitrary one.

The vast majority of the systems described in the weak complex literature can be tested by changing the inert solvent or by using active and inert solvents of very similar molar volumes. Thus we can hope that the use of these procedures will bring a direct resolution of the question of the proper choice of concentration scale. If it should turn out that one of the common K's is universally applicable, the equations derived here, or similar ones, can be applied directly to the data on hand without the need of repeating earlier work.

In the view of the experiments and discussion presented in this paper that advocate the use of K_c, eq 6 and 7 can provide estimates of K_c and P_0 for previous studies using mole fraction and molal units. We have collected a few examples in Table III. A considerable proportion of the differences between heptane and carbon tetrachloride solvents are removed when K_c and P_0 are calculated. Note that the K_c's indicate the greater inertness of heptane compared to CCl_4.

Throughout this discussion we have focused on simple equilibria. We can generalize our results. In those reactions where the number of moles changes, the arguments advanced so far would apply, although the detailed formulas would differ. For reactions in which the number of moles is conserved (*i.e.*, $A + B = C + D$), the equilibrium quotients K_c, K_x, and K_m do not differ in their concentration dependence. Cases where the "inert" solvent is actually an active participant can fall into this category. Solvent participation can readily yield simple BH plots which nonetheless have unreasonable K's and P_0's.[6,20] If other solvents are available, it is usually possible to isolate the participating equilibria. Such checks should be made whenever possible.

Table III. Literature Data for Iodine Charge-Transfer Complexes

System (solvent)	$(K_x)_{BH}$	$(\epsilon_x)_{BH}$	K_c	ϵ_c	Ref
I_2–benzene (CCl_4)	1.72	15,400	0.176	14,600	3
I_2–benzene (hexane)	1.21	...	0.202	...	*a*
I_2–benzene (heptane)	1.15	18,000	0.229	13,400	3
I_2–mesitylene (CCl_4)	7.2	9,300	0.66	9,900	3
I_2–mesitylene (heptane)	5.3	9,900	0.77	10,000	3
I_2–MeOH (CCl_4)	4.65	...	0.51	...	*b*
I_2–EtOH (CCl_4)	4.00	...	0.43	...	*b*
I_2–Et_2O (CCl_4)	8.7	...	0.84	...	*b*
I_2–Et_2O (heptane)	5.9	...	0.92	...	*b*

[a] G. Körtum and W. M. Vogel, *Z. Elektrochem.*, **59**, 16 (1955).
[b] P. deMaine, *J. Chem. Phys.*, **26**, 1192 (1957).

Conclusions

Very substantial errors can be made using the Benesi–Hildebrand equation for weak complexes if the improper choice of concentration units is made. The proper concentration scale can be determined experimentally if two inert solvents are available. The proper scale cannot be determined by simple inspection of the BH plots. Considerable evidence points to molarity as the proper unit for these equilibria, particularly if the properties of the complexes are to be discussed at the molecular level.

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(20) S. Carter, J. N. Murrell, and E. J. Rosch, *J. Chem. Soc.*, 2048 (1965).