Conclusion

It was hoped that the effect of different "bridging groups" between pentaammineruthenium(II) and pentaammineruthenium(III) groups could be ascertained by a study of the near-infrared spectra of the Ru(II)–Ru(III) complexes of 4,4′-bipyridine and 1,2-bis(4-pyridyl)ethylene. Neither chemical means nor electrochemical means (*via* cyclic voltammetry), however, could be shown to produce these complexes by oxidation of the analogous Ru(II)–Ru(II) complexes. It appeared evident from the cyclic voltammograms of the dipentaammineruthenium(II) complexes of 4,4′-bipyridine and 1,2-bis(4-pyridyl)ethylene that these complexes undergo reversible two-electron oxidation and reduction. The mechanism of the oxidation (*e.g.*, it could be simultaneous one-electron withdrawal from each end of the complex, or a two-electron withdrawal from one end, perhaps followed by an electronic reorganization) is not elucidated by the cyclic voltammetry results.

One of the puzzling and disappointing aspects of this study is the noninteraction between the metal ions in the dimers of 4,4′-bipyridine and 1,2-bis(4-pyridyl)ethylene as compared to the strong interaction found in the pyrazine dimer. We are now further investigating other pyrazine-like dimer systems in order to determine the particular feature of this system that leads to its rather interesting properties.

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Effects of Donor Nonideality on Molecular Complex Equilibria[1]

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Abstract: A treatment of molecular complex equilibrium is proposed that takes nonideality of the excess component into account by using activities from vapor pressure data. It is shown, using an nmr study of the benzene–caffeine complex in carbon tetrachloride as an example, how using donor activities removes the concentration scale dependence of the shift of the pure complex and brings equilibrium constants derived for mole fraction and molal scales into their proper infinite-dilution relationship. Traditional plots of the data using the usual ideal mixture of species approximation give good linear plots even for the molal scale, which artificially increases the nonideality. Thus, straight-line plots cannot be used as a criterion for the absence of nonideality effects.

In the last 20 years the experimental work devoted to studies of molecular complexes has been voluminous. It is summarized in numerous books and reviews.[2–9] There are good reasons for this work to be done. Besides understanding donor–acceptor complexes themselves, the basic interactions are of considerable importance in determining conformation of proteins and nucleic acids. Because of the significance of this work, it is important that the data obtained for simple molecular complexes rest on a secure theoretical foundation. Unfortunately, several groups of workers have pointed out that this foundation is far from secure.[10–13] It is the purpose of this paper to continue this discussion and to point out at least one way to strengthen this foundation.

A great deal of the effort mentioned above has been devoted to obtaining association constant data for large numbers of complexes as well as parameters relating to the structure of the complex such as absorbancy indices, dipole moments, nmr shifts, enthalpies of formation, etc. The problem is that there is coupling between the microscopic model which one uses to interpret the experimental data and the values of the association constant and structural parameters which one calculates. Thus, it is necessary to verify the model in order to assess the reliability of the results, and often it is impossible to do this because of the nature of the system.[13]

In what follows, we wish to use an nmr study of the benzene–caffeine complex in CCl_4 as an example of the kinds of difficulties which one runs into in studies of weak molecular complexes and to suggest a more adequate model than the one presently used.

Theory

Consider the case where there is only a 1:1 association equilibrium between a donor molecule, D, and an acceptor molecule, A, to form complex, AD

$$A + D = AD \qquad (1)$$

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[1] Supported in part by the National Science Foundation under Grant No. GP 11387.

[2] (a) G. Briegleb, "Electronen-Donator-Acceptor-Complexe," Springer-Verlag, Berlin, 1961; (b) L. J. Andrews and R. M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964.

[3] R. S. Mulliken and W. B. Person, "Molecular Complexes, A. Lecture and Reprint Volume," Wiley, New York, N. Y., 1969.

[4] R. Foster, "Organic Charge Transfer Complexes," Academic Press, New York, N. Y., 1969.

[5] J. Rose, "Molecular Complexes," Pergamon Press, Oxford, 1967.

[6] S. P. McGlynn, *Chem. Rev.*, **58**, 1113 (1958).

[7] J. N. Murrell, *Quart. Rev., Chem. Soc.*, **15**, 191 (1961).

[8] E. M. Kosower, *Progr. Phys. Org. Chem.*, 3, 81 (1965).

[9] R. Foster and C. A. Fyfe, *Progr. Nucl. Magn. Resonance Spectrosc.*, 4, 1 (1969).

[10] R. L. Scott, *Recl. Trav. Chim. Pays Bas*, **75**, 787 (1956).

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

[12] W. B. Person, *ibid.*, **87**, 167 (1965).

[13] D. A. Deranleau, *ibid.*, **91**, 4044, 4050 (1969).

The equilibrium constant for this reaction may be written in the standard way and may also be broken down into a product of an equilibrium *quotient*, Q, and an activity coefficient product according to

$$K = \frac{a_{\mathrm{AD}}}{a_{\mathrm{A}}a_{\mathrm{D}}} = \frac{[\mathrm{AD}]}{[\mathrm{A}][\mathrm{D}]}\frac{\gamma_{\mathrm{AD}}}{\gamma_{\mathrm{A}}\gamma_{\mathrm{D}}} = QK_{\gamma} \qquad (2)$$

In almost all experimental studies that have been done, activity coefficients have not been included and only equilibrium quotients have been measured. All discussions about complex strengths, donor or acceptor strengths, and other such properties have involved these equilibrium quotients. The assumption has been tacitly made that the equilibrium quotients Q and the equilibrium constants K are related. *This amounts to making the "ideal mixture of species"* approximation, which assumes either that $K_{\gamma} = 1$, in which case $Q = K$, or that K_{γ} is constant over the range of concentrations employed, in which case Q is proportional to K.

One now measures a property that depends on the concentration of complex—the absorbance in the optical spectrum, the shift of certain protons in the nmr, the dielectric constant, etc.—as a function of donor concentration, acceptor concentration, or both. We will only outline the procedure for nmr spectroscopy. The equations for the other types of measurements follow in a straightforward way.

The nmr chemical shift of acceptor protons for a rapidly exchanging system containing only complex and free acceptor is given by

$$\delta_{\mathrm{obsd}} = \frac{[\mathrm{AD}]}{A^0}\delta_{\mathrm{AD}} + \frac{A^0 - [\mathrm{AD}]}{A^0}\delta_{\mathrm{A}} \qquad (3)$$

where A^0 is the stoichiometric concentration of acceptor, δ_{AD} is the shift of the acceptor protons in the pure complex, and δ_{A} is the shift of the corresponding proton in isolated acceptor. Experimentally, it is usual to make the concentration of one component large compared with that of the other one. In this treatment we have assumed that $D^0 > A^0$, [AD]. Deranleau has discussed the error introduced by this assumption.[13] Following well-known procedures,[14] one can show that

$$\Delta_{\mathrm{obsd}} = Q\Delta_{\mathrm{AD}}D^0/(1 + QD^0) \qquad (4)$$

where $\Delta_{\mathrm{obsd}} \equiv \delta_{\mathrm{obsd}} - \delta_{\mathrm{A}}$ and $\Delta_{\mathrm{AD}} \equiv \delta_{\mathrm{AD}} - \delta_{\mathrm{A}}$ are the differences between observed and pure complex shifts and the shift of the corresponding protons on an isolated acceptor molecule. The problem is to use the available data to separate Q and Δ_{AD}.

A number of equations have been proposed to effect this separation. We will only mention three—the Benesi–Hildebrand or double-reciprocal equation (5),[15]

$$\frac{1}{\Delta_{\mathrm{obsd}}} = \frac{1}{Q\Delta_{\mathrm{AD}}}\frac{1}{D^0} + \frac{1}{\Delta_{\mathrm{AD}}} \qquad (5)$$

the Scott or half-reciprocal equation (6),[10] and the

$$\frac{D^0}{\Delta_{\mathrm{obsd}}} = \frac{1}{Q\Delta_{\mathrm{AD}}} + \frac{1}{\Delta_{\mathrm{AD}}}D^0 \qquad (6)$$

Scatchard equation (7).[16] Consideration of each of

$$\frac{\Delta_{\mathrm{obsd}}}{D^0} = -Q\Delta_{\mathrm{obsd}} + Q\Delta_{\mathrm{AD}} \qquad (7)$$

these equations shows that from the slope and the intercept one can calculate values of Q and Δ_{AD}. The usual procedure is to plot the data using one of the relations (5–7). If a straight line is obtained, the model is assumed to be correct and values of Q and Δ_{AD} are reported.

In 1969, Deranleau, following Person, published an extremely important piece of work in which he argued that this procedure was not justified.[13] We attempt to summarize his conclusions as follows. (1) To validate the assumed model, data must be taken over a wide range of the saturation fraction, $[\mathrm{AD}]/A^0$, since curvature may not show up on *any* plot for small ranges of the saturation fraction. He advocated at least 75% of the saturation fraction. (2) In Benesi–Hildebrand or Scott plots, it is impossible to tell what portion of the saturation fraction is being studied. The Scatchard plot does tell one how much is being covered if one begins the abcissa at zero. (3) The interpretation of the slope and intercept of straight-line plots is ambiguous unless higher order complexes have been shown *not to exist*. This has not been consistently done in molecular complexing studies and in fact the opposite has been shown to be true in at least one case.[17]

Unfortunately, many of the molecular complexes of interest to chemists and biochemists are relatively weak, and it is, therefore, impossible to study the complexes over a wide enough range of saturation to satisfy the Deranleau–Person criteria. Does this mean that we must give up work in this area? We think not.

One of the things that can be done to improve the situation is to examine the interpretive model using criteria from sources other than molecular complex studies. If we consider vapor pressure measurements, it is clear that the ideal mixture of species approximation *cannot be correct* for the experimental conditions usually employed in molecular complex studies. In Figure 1 is shown a graph of the Henry's law activity coefficients of benzene in carbon tetrachloride derived from accurate vapor pressure data at 40°.[18] There are two curves on this graph, one referring to a hypothetical mole fraction = 1 standard state and one referring to a hypothetical 1 *m* standard state. For both of these standard states, it is clear that the activity coefficient is not only varying, but is varying nonlinearly with concentration for mole fractions above 0.4 and for molalities over almost the entire scale. Similar results are obtained for the benzene–cyclohexane and the benzene–chloroform systems.

One point needs to be emphasized about the molal curve in Figure 1. Benzene in carbon tetrachloride forms almost ideal solutions, as evidenced by the small ΔH and ΔV of mixing. This is reflected by the mole fraction activity coefficient, which only drops to 0.9 at $X = 0.5$. The molal standard state makes the mixtures appear grossly nonideal, however. This is an artifact of using the molal standard states and indicates that molal concentration units should not be used in other than dilute solutions. A discussion of the molal standard state is included here for a pedagogical purpose,

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

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

[16] G. Scatchard, *Ann. N. Y. Acad. Sci.*, **51**, 660 (1949).

[17] P. J. Trotter and D. A. Yphantis, *J. Phys. Chem.*, **74**, 1399 (1970).

[18] G. Scatchard, S. E. Wood, and J. M. Mochel, *J. Amer. Chem. Soc.*, **62**, 712 (1940).

however, that of showing that the usual plots used to separate Q and Δ will not detect nonideality effects even if they are extremely large.

We therefore propose an alternate model to be used in studies of molecular complexing. In this model one uses vapor pressure or other thermodynamic data to evaluate the activity of the high concentration component. Rederiving the Scatchard equation for this case, one obtains

$$\Delta_{\text{obsd}}/a_{\text{D}} = -K'\Delta_{\text{obsd}} + K'\Delta_{\text{AD}} \tag{8}$$

where a_{D} is the donor activity and

$$K' = (\gamma_{\text{A}}/\gamma_{\text{AD}})K \tag{9}$$

If one now draws conclusions from an examination of K' values, one is making the assumption that the ratio $\gamma_{\text{A}}/\gamma_{\text{AD}}$ is either equal to 1, in which case $K' = K$, or constant over the concentration range of D employed, in which case K' is proportional to K. While these assumptions are still open to objection, they are certainly better than the ideal mixture of species approximation, since A and AD are both present as dilute components.

It was first pointed out by Professor Scott[10] and later emphasized by our group[11] that donor nonideality effects could be detected by observing a concentration scale dependence of the structural parameter determined for the complex. In what follows we will use nmr studies of the benzene–caffeine complex as an example of the effects that have been discussed in this section.

Experimental Section

The caffeine used was purified by sublimation. The benzene and carbon tetrachloride were gc spectrophotometric quality solvents and the cyclohexane, used as an internal reference compound, was spectroquality reagent.

Samples were prepared by weight in 10-ml volumetric flasks. In the preparation of caffeine–benzene solutions in carbon tetrachloride, the caffeine and cyclohexane concentrations were maintained at about 0.01 M. The solutions required heating on a steam bath to put the caffeine into solution.

The nmr spectra were recorded on the Varian A-60A spectrometer, making use of the side-band technique for the measurement of accurate chemical shifts.[19] Side bands were generated for the reference compound, cyclohexane, on the 50-Hz sweep by a Hewlett-Packard Model 200AB audiooscillator or a Hewlett-Packard Model 202A low-frequency function generator. The generated frequencies were measured by either the Hewlett-Packard Model 521C electronic counter or the Hewlett-Packard Model 5245M electronic counter. The cyclohexane side band was displayed at different frequencies, and an average of three or more passes through the peaks was obtained.

The 7-methyl peak of caffeine had a larger line width than the 3- or 1-methyl peaks because of the small coupling constant, about 1 Hz, between it and the 9-methine proton of caffeine.

Results and Discussion

Carbon Tetrachloride. Accurate vapor pressure data for the benzene–carbon tetrachloride system have been measured at 40.00 and 70.00°.[18] These data are given in Table I, and a graph showing Henry's law activity coefficients calculated from the 40° data has already been shown in Figure 1.

Measured chemical shifts for the 7-methyl protons in caffeine are given for a number of donor concentrations in Table II. A Benesi–Hildebrand plot of the 40° data using the ideal mixture of species approximation is shown in Figure 2.

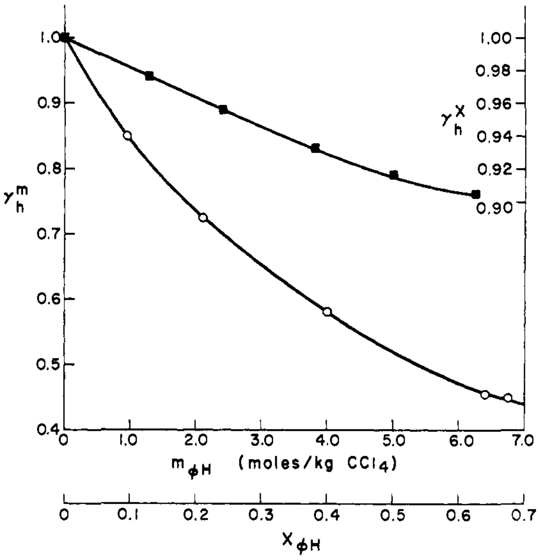

Figure 1. Henry's law activity coefficients for benzene in carbon tetrachloride at 40° with concentration in molal (○) and mole fraction (■) units. Note that not only are the solutions nonideal, but also the activity coefficient varies nonlinearly with concentration. Note also the artificial nonideality introduced by the molal standard state.

Table I. Vapor Pressure Data for the Benzene–Carbon Tetrachloride System[a]

40.00°			70.00°		
X_b	Y_b	P	X_b	Y_b	P
0.1282	0.1217	211.97	0.1250	0.1220	616.02
0.2415	0.2261	210.37	0.2376	0.2281	613.08
0.3799	0.3525	207.44	0.3776	0.3589	607.22
0.5014	0.4641	204.20	0.5061	0.4785	599.67
0.5081	0.4705	204.02	(0.5070)	(0.4796)	(600.77)
0.6265	0.5841	200.07	0.6209	0.5895	591.62
0.7622	0.7226	194.70	0.7606	0.7298	579.13
0.8602	0.8297	190.18	0.8572	0.8334	568.89

[a] X_b is the equilibrium mole fraction of benzene in the liquid, Y_b is the corresponding mole fraction in the gas phase, and P is the total pressure of the gas phase at equilibrium. Data are from ref 18.

Table II. Nmr Shifts as a Function of Donor Concentration for the 7-Methyl Proton in Caffeine at Two Temperatures[a]

		Δ_{obsd}	
X_b	m_b	40°	70°
0.08675	0.6188	8.5	7.1
0.11122	0.8154	10.8	8.9
0.15517	1.1971	14.5	11.9
0.21808	1.8179	19.3	16.1
0.27003	2.4116	22.8	19.1
0.33255	3.2491	26.8	22.6
0.41235	4.5772	31.2	26.7
0.46779	5.7360	34.1	29.2
0.54083	7.6900	37.5	32.4

[a] The caffeine concentration was maintained at 0.01 M. Shifts are in hertz from the position of free caffeine in CCl$_4$.

Three things need to be pointed out from this figure. (1) Excellent straight lines are obtained on both mole fraction and molal plots, in spite of the fact that the model used to arrive at the equation plotted is *known* to

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(19) A. A. Sandoval and M. W. Hanna, *J. Phys. Chem.*, 70, 1203 (1966).

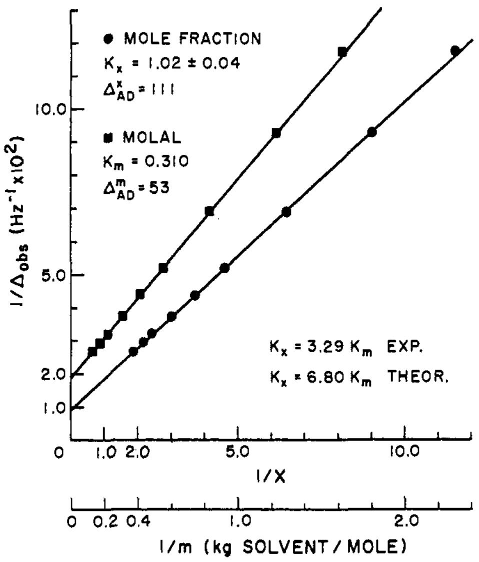

Figure 2. A Benesi–Hildebrand plot for chemical shift data for the benzene–caffeine system in carbon tetrachloride. Note the large concentration scale dependence of the Δ_{AD} values.

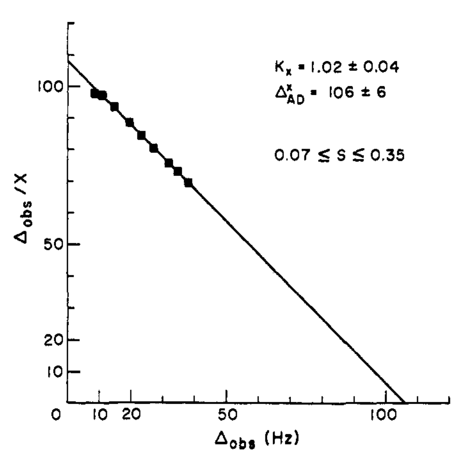

Figure 3. A Scatchard plot of the mole fraction data shown in Figure 2. Note that the range of saturation fraction is directly revealed along the abscissa.

be incorrect. Even the molal plot, which artificially magnifies the nonideality effects, gives a good straight line within the precision of the experimental points. (2) The values of Δ_{AD} are strongly concentration dependent. (3) The values of K_s and K_m (really Q_x and Q_m) are not related by the expected infinite-dilution relationships.

Figure 3 shows a Scatchard plot of the mole fraction data. The parameters are the same within experimental error, but now it can be seen that only about 35% of the saturation fraction is being covered in these experiments. The long extrapolation also helps evaluate errors in the intercept on the X axis. A Scatchard plot of the data using the molal scale gives the same values of the parameters as were obtained using the Benesi–Hildebrand equations. Thus, the concentration scale dependence remains regardless of plot. It is important to emphasize that the effects of an incorrect model cannot be removed simply by using different equations (derived from that model) to plot the data.

In Figure 4 are shown plots of the data using benzene activities calculated from the vapor pressure data and

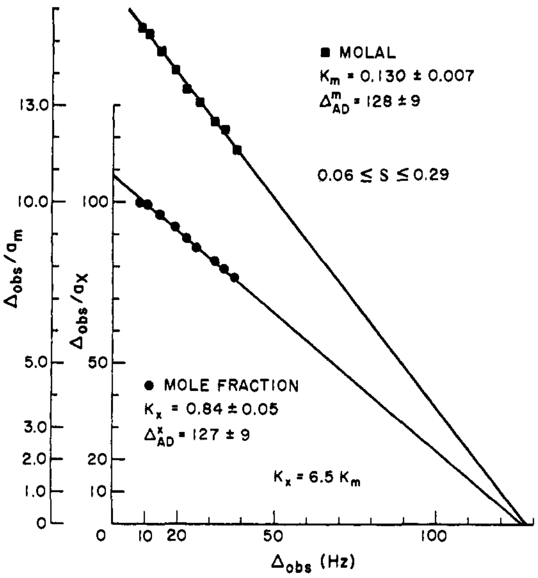

Figure 4. Scatchard plots of molal and mole fraction data on the benzene–caffeine complex using donor activities derived from vapor pressure measurements.

eq 8. Four things also need to be emphasized from this graph. (1) The concentration scale dependence of the Δ_{AD}'s has disappeared. (2) The value of Δ_{AD} is *different* from either of those obtained using the ideal mixture of species approximation. (3) The K_x and K_m values have their proper relationship. This does not necessarily mean that the K values so derived are completely unambiguous, since a large part of the disagreement using the ideal mixture of species approximation was brought about by the artificial nonideality introduced by using the molal standard state. It is a necessary condition that should be checked, however. (4) The amount of the saturation fraction covered is *different* than for the ideal mixture of species approximation.

Table III summarizes the values of the parameters obtained using the different models at both 40 and 70°.

The enthalpy of formation of a molecular complex is always of great interest, and this parameter, too, will depend upon nonideality effects, since activity coefficients are temperature dependent. Table IV gives values of enthalpies and entropies of formation using different models and different concentration scales. Also shown in Table IV are enthalpies obtained from Benesi–Hildebrand plots using the ideal mixture assumption and the ratio of slopes at two temperatures. This latter procedure does not depend on a separation of K and Δ_{AD} and only assumes the Δ_{AD} is not temperature dependent.

Several things should be emphasized from the results in Table IV. First, ΔH values determined when Q and Δ are separated and the ideal mixture approximation is used are strongly concentration scale dependent and, therefore, unreliable. This concentration dependence disappears when donor activity is taken into account. It also disappears when the slope ratio method is used, and the value of ΔH obtained using the slope ratio method is quite close to that obtained using the donor nonideality model. It therefore appears that ΔH's determined using the slope ratio method compensate for temperature-dependent activity effects and are, there-

Table III. A Comparison of Molecular Complex Parameters Obtained Using the Ideal Mixture of Species Model and the Donor Nonideality Model[a]

Model	40.0° Q, K'	40.0° Δ_{AD}	70.0° Q, K'	70.0° Δ_{AD}
Ideal mixing, X	1.02 ± 0.04	106 ± 5	0.86 ± 0.03	102 ± 5
Ideal mixing, m	0.310 ± 0.006	53 ± 2	0.285 ± 0.005	47 ± 1
Donor nonideality, X	0.84 ± 0.05	127 ± 9	0.70 ± 0.03	126 ± 5
Donor nonideality, m	0.130 ± 0.007	128 ± 9	0.108 ± 0.004	125 ± 5

[a] Notice the extreme concentration scale dependence of Δ_{AD} using the ideal mixture of species model. The difference between Q and K' is discussed in the text.

Table IV. A Comparison of ΔH Values Calculated from van't Hoff Plots for Various Approximations and from the Slope Ratio Method[a]

Model	ΔH, kcal/mol	ΔS, eu
Ideal mixing, X	−1.2 ± 0.5	−3.8 ± 1.6
Ideal mixing, m	−0.60 ± 0.25	−4.2 ± 0.8
Ideal mixing, slope ratio, X, m	−1.4 ± ?	
Donor nonideality, X	−1.3 ± 0.7	−4.5 ± 2.2
Donor nonideality, m	−1.3 ± 0.6	−8.3 ± 1.9

[a] ΔS value for the slope ratio method was not calculated because of the uncertaintities in K for the ideal mixing model.

fore, much more reliable even when the ideal mixture approximation is made.

Since there has been considerable discussion of the relative merits of various concentration scales,[10,11,20] it might be tempting to look at the above data and conclude that the mole fraction scale is "best," since parameter values derived from this scale using the ideal mixture approximation are closest to those from the donor nonideality model. This conclusion would not be warranted, however. For all binary systems exhibiting positive deviation from Raoult's law, the molal activity coefficients for a dilute solution standard state will always be less than the mole fraction activity coefficients.[21] Both will, of course, be less than one. Therefore, for these cases the system will always be "more ideal" on the mole fraction or molar scale than on the molal scale. We have remarked in the Theory section how the molal scale artificially makes an ideal mixture appear nonideal at high concentrations. For systems with negative deviations from Raoult's law, no conclusion about which scale will have activity coefficients closer to unity can be rendered without a detailed consideration of the vapor pressure data.

It is instructive to inquire as to why gross nonideality effects do not cause curvature in plots of the Benesi–Hildebrand type. This can be seen by writing the expression for the activity coefficient of donor as a series expansion in powers of the donor concentration. Some straightforward algebra shows that if only the linear term is kept, an equation for a straight line is still obtained but the *intercept no longer has the simple interpretation given in eq 5.* The separation of Q and Δ then gives incorrect values of both.

In summary, this work confirms and extends earlier conclusions that many of the equilibrium constant data on weak molecular complexes need to be reevaluated. It will at least be necessary to obtain activity coefficient data on common donor–solvent systems. The reliability of K' values obtained from treatments in which donor nonideality effects are included will not be completely free from question, but at least these values will form a better basis for comparison of complex properties than the present ones based on the ideal mixture of species approximation. It is important to do this, because many people interested in the structure of donor–acceptor complexes are interested in properties such as complex dipole moments, shifts of protons in the pure complex, molar absorbancy indices, etc. All of these complex parameters require the separation of the equilibrium constant and will be strongly affected by donor nonideality.

Acknowledgment. The authors are grateful to Professor Sherrill Christian for a perceptive and helpful critique of this work.

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(20) I. D. Kuntz, F. P. Gasparro, M. D. Johnson, and R. P. Taylor, *J. Amer. Chem. Soc.*, **90**, 4778 (1968).

(21) D. G. Rose, M. S. Thesis, University of Colorado, 1970.