

Determination of Stability Constants from Optical Rotatory Dispersion Measurements

Camphor-Phenol System in Carbon Tetrachloride

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A spectropolarimetric method of determining stability constants of complexes formed through hydrogen bonding has been developed and applied to the camphor-phenol system. A variation of the Rossotti and Rossotti method modified to account for formation of complex species containing two molecules of phenol is shown to yield a stability constant in carbon tetrachloride of 12.2 L./mole at 25°.

ALTHOUGH it is generally recognized that such diverse factors as solubility behaviors of non-electrolytes in nonaqueous solvents, thermodynamic properties of organic solutes in organic solvents, rate of elution of sample components from GLC columns, melting points of organic solids, formation of molecular compounds and adducts, specific activities of drugs, etc., are usually strongly influenced by tendencies of polar centers in molecules to attract each other, relatively little quantitative information appears to be available in the literature. The present communication is concerned with preliminary results of an essentially little used but promising approach to this problem. Although stability constants of bonds formed between acidic hydrogen compounds and hydrogen accepting species can be determined by a number of different techniques including NMR, I.R., solubility studies, extraction studies, etc. (1), the feasibility of utilizing polarimetric methods seems not to have been thoroughly tested.

DISCUSSION

Theoretically, measurement of optical rotatory power appears to permit determination of physical constants with precision rarely possible with conventional commercial sensing instruments aside from gravimetric balances. Ultraviolet spectrophotometers, for example, can with only great care detect concentration differences of $\pm 0.1\%$. Corresponding infrared instruments are probably no better than $\pm 1\%$. NMR suffers from lack of both sensitivity and precision. Presently available commercial spectropolarimeters, on the other hand, appear to permit measurements of a few tenths of a millidegree in samples having rotations of several degrees corresponding to usable sensitivity approaching a few parts in 100,000.

For the computation of stability constants, a

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method given by Rossotti and Rossotti (2) is readily adaptable to polarimetric work and makes full use of experimental data. If complexes other than 1:1 can be neglected, the stability constant of the complex BA is given by:

$$\kappa_1 = \frac{[\text{BA}]}{b \cdot a} \quad (\text{Eq. 1})$$

with b and a representing the free concentration of the central group and of the ligand, respectively. If B and A denote total concentration.

$$a = A - [\text{BA}] \quad (\text{Eq. 2})$$

$$b = B - [\text{BA}] \quad (\text{Eq. 3})$$

and

$$[\text{BA}] = \kappa_1 (\text{AB} - \text{B} [\text{BA}] - \text{A} [\text{BA}] + [\text{BA}]^2) \quad (\text{Eq. 4})$$

Assuming that $[\text{BA}]^2 \ll \text{AB}$, we have

$$[\text{BA}] = \frac{\text{AB}}{\kappa_1^{-1} + \text{A} + \text{B}} \quad (\text{Eq. 5})$$

If r represents the molar rotation in a 1-cm. cell and if l is the pathlength in cm., the change in rotation arising from complexation is

$$\begin{aligned} R &= \{r_A \cdot l(\text{A} - [\text{BA}]) + r_B \cdot l(\text{B} - [\text{BA}]) + r_{\text{BA}} \cdot l[\text{BA}]\} - r_A l \text{A} - r_B l \text{B} \\ &= [\text{BA}] (r_{\text{BA}} - r_A - r_B) \cdot l = [\text{BA}] \cdot \Delta r \cdot l \quad (\text{Eq. 6}) \end{aligned}$$

Then

$$[\text{BA}] = \frac{R}{\Delta r \cdot l} \quad (\text{Eq. 7})$$

Equating Eqs. 5 and 7, one obtains

$$\frac{l \cdot \text{A} \cdot \text{B}}{R} = \frac{\text{A} + \text{B}}{\Delta r} + \frac{1}{\kappa_1 \cdot \Delta r} \quad (\text{Eq. 8})$$

A plot of the left-hand side of Eq. 8 versus $(\text{A} + \text{B})$ has a slope of $1/\Delta r$ and an intercept of $1/\kappa_1 \Delta r$.

Figure 1 shows the optical rotatory dispersion curves observed for camphor and camphor and phenol solutions where approximately 24 and 39% of the camphor has been complexed. Because of the low stability constant, the fraction of camphor present as the complex is quite small even at moderate concentrations of phenol, and the rotational changes

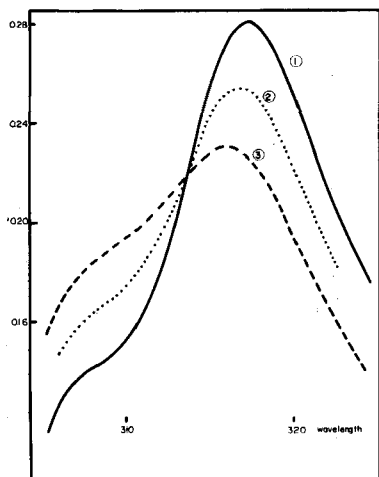


Fig. 1.—Optical rotatory dispersion spectra of camphor in carbon tetrachloride in presence and absence of phenol. ORD curves of camphor (1); complexed to the extent of 24% (2); and 39% (3). [Camphor] = $7.01 \cdot 10^{-3} m$.

reflecting complex formation represent only a small fraction of the total rotation. As a consequence of this situation, even a minute error in the camphor concentration would seriously affect the rotational changes measured. To reduce errors arising from small variations in the camphor concentration, the differential procedure which is explained below was adopted.

To determine the concentration of bound camphor [BA] in a solution containing phenol and $B = [BA] + b$ concentration of camphor, an ORD curve of the solution was recorded along with that of a solution containing the same amount of total camphor (*i.e.*, equal to B). Figure 2 shows schematically the two curves. The differences in rotation R' and R'' are then measured at the wavelengths λ_1 and λ_2 , which have been chosen such that the rotation of camphor is very closely the same. $R = R' + R''$ represents the value which is used in Eq. 8.

Let us now assume that the concentration of the uncomplexed solution is slightly in error and is $B + \beta$ instead of B . The rotational differences are then

$$\begin{aligned} \text{at } \lambda_1: R' &= l\{[BA](r_{BA,1} - r_{B,1}) - \beta r_{B,1}\} \\ \text{at } \lambda_2: R'' &= l\{[BA](r_{B,2} - r_{BA,2}) + \beta r_{B,2}\} \\ R' + R'' = R &= l\{[BA](r_{BA,1} - r_{BA,2}) + \\ & \quad ([BA] + \beta)(r_{B,2} - r_{B,1})\} \quad (\text{Eq. 9}) \end{aligned}$$

Since $(r_{B,2} - r_{B,1}) \ll (r_{BA,1} - r_{BA,2})$, the second term in the brackets is very small, so that R is essentially independent of the concentration error, β , and a function of [BA] only. From Eq. 9, it also follows that r_A and r_B in Eq. 6 are zero for the camphor-phenol system.

EXPERIMENTAL

Reagents.—The reagents used were either reagent grade or purified by recrystallization from appropriate solvents.

Instrumentation.—A Cary 60 spectropolarimeter was used for this study.

Procedure.—For each camphor concentration used, mixtures were made in carbon tetrachloride such that the phenol concentration was usually half, equal, and double the camphor concentration. In the regions around 308 and 328 $m\mu$, corresponding to λ_1 and λ_2 in Fig. 2, the rotation of the mixtures and of an uncomplexed camphor solution of equal concentration were recorded. Pathlength and scale expansion were adjusted such as to obtain the best precision and accuracy.

In view of the thermal expansion of carbon tetrachloride and of its tendency to produce schlieren effect when exposed to temperature changes, precautions were taken to assure essentially perfect temperature equilibrium of the solutions. In addition to keeping both the temperature of the room and the temperature of the internal thermostat of the polarimeter at 25° , the filled cells were left in the cell compartment of the instrument for 10 min. before the recordings were started.

RESULTS AND DISCUSSION

The experimental data obtained for the camphor-phenol system cannot be explained adequately only in terms of a 1:1 complex. These observations are, however, consistent if we assume, in addition, formation of the complex BA_2 . Such a complex can be thought to be formed either through binding of two phenol molecules to one camphor or through interaction between phenol dimer and camphor. The corresponding stability constants are

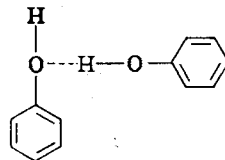
$$\kappa_2' = \frac{[BA_2]}{b \cdot (a_1)^2} \quad (\text{Eq. 10})$$

$$\kappa_2 = \frac{[BA_2]}{b \cdot a_2} \quad (\text{Eq. 11})$$

where a_1 and a_2 denote the concentration of free monomeric and dimeric phenol, respectively. If the dimerization constant of phenol is represented by κ_D , we have

$$\kappa_2' = \kappa_2 \cdot \kappa_D \quad (\text{Eq. 12})$$

The physical situation corresponding to Eq. 11,



appears to be more probable. Because of the smaller negative charge on the oxygen attached to the free hydrogen, dimerized phenol is expected to be more acidic than monomeric phenol. As a

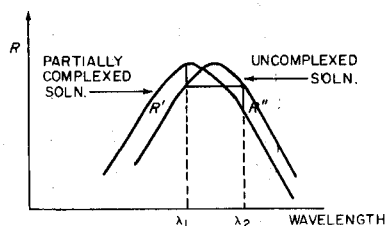


Figure 2

consequence, we would expect it to be a more effective hydrogen bonding species. As a matter of fact, the free hydrogen is so ready to form a hydrogen bond that, unless another partner is available, it forms a cyclic dimer. Equation 11 is preferable not only in that it probably gives a better description of the actual situation, but also in so far as it simplifies the calculations. It permits consideration of BA_2 as a 1:1 complex between B and A_2 and allows use of a plot similar to Eq. 8 for evaluation of κ_2 .

Although for the present purpose the observed deviations from simple assumption of a 1:1 complex were entirely attributed to contributions from complexation by phenol dimers, it is apparent that other more or less equivalent and equally satisfactory physical models are possible. Since the exact mode of association adopted by phenol in solution is still, however, open to question, a more elaborate hypothesis is probably premature and unproductive.

Calculation of the Stability Constants κ_1 and κ_2 .—With the type of experimental data available from ORD measurements, it is not possible to solve for κ_1 and κ_2 simultaneously. Instead, separate calculations have to be used for the evaluation of the monomeric and of the dimeric parts of the system, and it is necessary to go through a number of step-wise approximations in approaching the true values of the stability constants.

The species present in the camphor-phenol system add up to the total concentrations in the following manner:

$$B = b + [BA] + [BA_2] \quad (\text{Eq. 13})$$

$$A = a_1 + 2a_2 + [BA] + 2[BA_2] \quad (\text{Eq. 14})$$

$[BA_2]$ is rather small, and for the investigation of the monomeric part, it is treated as a constant. If

$$B^0 = B - [BA_2] \quad (\text{Eq. 15})$$

$$A^0 = A - 2[BA_2] \quad (\text{Eq. 16})$$

then

$$b = B^0 - [BA] \quad (\text{Eq. 17})$$

It is convenient to express the concentration of free monomeric phenol as the fraction m of the total free phenol concentration:

$$a_1 = m(A^0 - [BA]) \quad (\text{Eq. 18})$$

Values for m are available in Mecke's work (3). From Eqs. 1, 17, and 18

$$[BA]^2 - [BA] \left(\frac{1}{\kappa_1 m} + A^0 + B^0 \right) + A^0 B^0 = 0 \quad (\text{Eq. 19})$$

and

$$[BA] = \frac{\{A^0 + B^0 + (1/\kappa_1 m) - \sqrt{[A^0 + B^0 + (1/\kappa_1 m)]^2 - 4A^0 B^0}\}}{2} \quad (\text{Eq. 20})$$

Application of Eq. 20 to the experimental data shows that $[BA]^2$ in Eq. 19 is not quite small enough to be entirely neglected as was done in the derivation of Eq. 8. It is sufficiently small, however, that

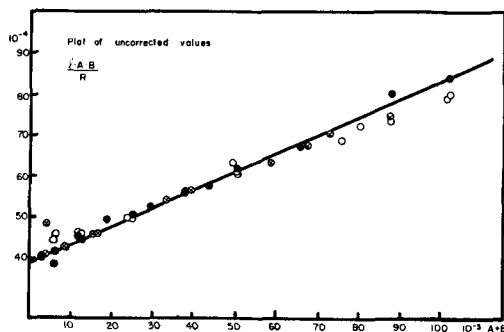


Fig. 3.—Plots based on Eq. 23 neglecting $[BA]^2$ and BA_2 and assuming $m = 1$, $R = R_1$ for the camphor-phenol system. Key: ●, $A < B$; ○, $A = B$; ⊙, $A > B$.

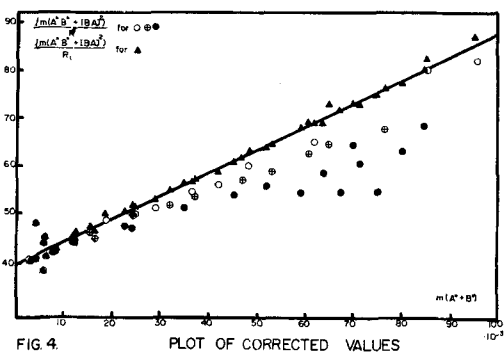


FIG. 4. PLOT OF CORRECTED VALUES

Fig. 4.—Plots based on Eq. 23. The triangular points represent the ordinate value after correction for contribution from the species [camphor:2 phenol]. Key: ○, $A < B$; ⊙, $A = B$; ●, $A > B$; ▲, after correction for R_2 .

approximating $[BA]^2$ and treating it subsequently as a constant represents a satisfactory approach:

$$[BA] = \frac{A^0 B^0 + [BA]^2}{(1/\kappa_1 m) + A^0 + B^0} \quad (\text{Eq. 21})$$

The observed rotation R represents the sum of the contribution R_1 associated with the formation of BA and of R_2 associated with the formation of BA_2 . Corresponding to Eq. 7

$$[BA] = \frac{R_1}{l \cdot \Delta r_1} \quad (\text{Eq. 22})$$

and from Eqs. 21 and 22

$$\frac{l m (A^0 B^0 + [BA]^2)}{R_1} = \frac{1}{\kappa_1 \cdot \Delta r_1} + \frac{m(A^0 + B^0)}{\Delta r_1} \quad (\text{Eq. 23})$$

From a plot of the left-hand side of Eq. 23 versus $m(A^0 + B^0)$, κ_1 and Δr_1 can be found.

The dimeric system is treated similarly with

$$B^* = B - [BA] \quad (\text{Eq. 24})$$

$$A^* = A - [BA] \quad (\text{Eq. 25})$$

we obtain:

$$b = B^* - [BA_2] \quad (\text{Eq. 26})$$

$$a_2 = [(1 - m)/2] (A^* - 2[BA_2]) \quad (\text{Eq. 27})$$

In the case of the dimeric system, it is safe to assume $[BA_2]^2 \ll A^*B^*$, so that

$$[BA_2] = \frac{A^*B^*}{[2/(1 - m)\kappa_2] + A^* + 2B^*} \quad (\text{Eq. 28})$$

and since

$$[BA_2] = \frac{R_2}{l \cdot \Delta r_2} \quad (\text{Eq. 29})$$

$$\frac{l(1 - m)A^*B^*}{R_2} = \frac{2}{\kappa_2 \Delta r_2} + \frac{(1 - m)(A^* + 2B^*)}{\Delta r_2} \quad (\text{Eq. 30})$$

From a plot of the left-hand side of Eq. 30 versus $(1 - m)(A^* + 2B^*)$, κ_2 and Δr_2 can thus be determined.

From the experimental data, only A, B, and R are known. Values for m , $[BA]$, $[BA_2]$, R_1 and R_2 have to be approximated and the approximations improved by reiteration. A preliminary value of κ_1 can be obtained if one assumes that at low phenol concentrations the dimeric species BA_2 , a_2 can be neglected, so that $m = 1$ and $R \approx R_1$. If, furthermore, $[BA]^2$ is neglected, a plot according to Eq. 23 leads to a preliminary value for κ_1 . This plot is represented in Fig. 3, and it is quite surprising to find that experimental values obtained even at high phenol concentrations fall fairly well on a straight line together with the others. Apparently the influence of dimerization on the plotting function is balanced by the formation of BA_2 .

The preliminary value for κ_1 thus obtained is used for calculating $[BA]$ (Eq. 20) and m . Based on these values, an improved plot (Eq. 23) can be constructed. If the system consisted of a_1 , a_2 , b , and $[BA]$ only, all the points should fall on a straight line. Since this is not the case, the actual distribution of the points represented by circles in Fig. 4 is nonlinear. The deviations from the straight line are largest for solutions whose composition would favor the formation of BA_2 .

From the plot, an estimate of R_1 and R_2 can be obtained as follows. If we abandon the assumption $R_2 = 0$ but maintain $A = A^0$, then the ordinate

represents

$$\frac{l \cdot m(AB + [BA]^2)}{R_1 + R_2}$$

With no BA_2 present, R_2 would be zero and the points would fall on the straight line. Increasing amounts of BA_2 would entail a proportionate increase in R_2 , which in turn would make the corresponding points fall below the straight line. From the ordinate values that would make every point fall on the line, therefore, an approximate R_1 can be calculated, and the difference between this and the measured value R is R_2 . It must be borne in mind, however, that reasonably accurate values can be expected for R_2 only at high concentrations of phenol. On the basis of approximate values for $[BA]$, m , R_2 , a plot according to Eq. 30 can be constructed to yield a preliminary value for κ_2 .

The position of the tentatively drawn straight line in the monomeric plot can now be improved by inserting individual values for $[BA_2]$ at each point. With Eq. 29, R_2 is calculated, and with $R_1 = R - R_2$ a strictly monomeric plot according to Eq. 23 is constructed. From the straight line thus obtained, an improved value for κ_1 is calculated. Making use of this improved value and of $[BA_2]$, all the steps described are repeated. Figure 4 is a plot of the final values according to Eq. 23, the circles representing the situation before, the triangles after making corrections for the contributions R_2 . The fact that all the points, even those with extreme proportions of B:A fall reasonably well on a straight line is evidence that the concepts used lead to an adequate description of the behavior of the camphor-phenol system.

The best value for the stability constant of BA estimated in this manner was found to be 12.2 L./mole at 25°. Gramstad (4) has previously reported $\kappa_1 = 9.53$ L./mole at 20° from measurements of the OH-overtone band at 7052 cm^{-1} . The stability constant κ_2 of the complex BA_2 was found to be 33 ± 7 L./mole at 25°.

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