Influence of Self-Association on the Solubility of Phenol in Isooctane and Cyclohexane

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Received April 13, 1978

Abstract: The solubility of phenol at 25°C was found to be over ten times greater in cyclohexane (4.0 M) than in isooctane (0.3 M). This phenomenon has been rationalized with a study of the vapor pressures of phenol as a function of its concentration in the two solvents by invoking a self-association model. The data in both solvents at concentrations below 0.5 M can be accounted for by assuming that monomer–pentamer association predominates. Small solvent effects on monomer activity were found to be magnified exponentially by the self-association resulting in the dramatic increase in phenol solubility in cyclohexane.

Current approaches to predicting solubility often overlook the role of specific interactions in determining solubilities of organic solids in organic solvents. Far greater emphasis is often placed on the bulk properties of the pure components. One such approach which is commonly used is the application of solubility parameters[1] which were originally intended for regular solutions only. It has been shown that for systems involving polar nonelectrolytes in "interactive" solvents, solubility parameters or other bulk properties such as dielectric constant or polarities are unsuccessful in rationalizing the solubilities observed.[2] Rather, specific interactions such as hydrogen bonding appear to be a more important factor.

Data presented in this paper on the self-association of phenol in isooctane and cyclohexane serve to illustrate the importance of specific interactions on solubility. The surprising order of magnitude greater solubility of phenol in cyclohexane than in isooctane can be understood from a consideration of phenol's associative behavior in these two solvents and the concentration of monomer at saturation.

The nature and extent of self-association of phenol in these relatively "inert" solvents were determined by measuring the partial vapor pressure or phenol above solutions of known concentration by sampling a quantity of the head-space vapor in equilibrium with the solution and analyzing for its phenol concentration by gas chromatography.

Various models have been applied to the vapor pressure data by employing a least-squares computer fitting technique in an attempt to identify the associated species in solution. It has been found that (1) the "best" multiparameter model depends on whether deviation between experimental and calculated values of monomer concentration or formal phenol molarity is minimized but (2) when only a single polymeric species is allowed, a monomer–pentamer model fits the data within experimental error.

Experimental Section

Materials. Phenol was obtained from Aldrich Chemical Co. having a claimed purity of 99+%. Residual traces of water were removed by distillation of the benzene azeotrope under a nitrogen atmosphere. Following removal of benzene by further distillation, the liquid phenol was fractionally distilled under reduced pressure, recrystallized from the melt, and stored in a desiccator. Isooctane (99+ mol %) was obtained from Phillips Petroleum Co. and the cyclohexane was ACS reagent grade purchased from Fisher Scientific Co. Both solvents were stored over Linde 4 Å molecular sieves (Union Carbide Co.) to remove possible trace amounts of water.

Head-Space Technique. Samples of known phenol molarity ranging from less than 0.01 to 0.3 M in isooctane and to 1.0 M in cyclohexane were prepared in glass bottles with Teflon-lined screw caps. The bottles were immersed in a water bath at 25.0 °C and allowed to equilibrate at least 15 min prior to sampling the vapor.

Vapor samples were withdrawn from the head space in the bottles using a vapor sampling loop described previously[3] and analyzed for phenol concentration using a Varian 2100 gas chromatograph equipped with a flame ionization detector. The column used for phenol determinations was a 6 ft × 4 mm i.d. glass column packed with 3% Carbowax 20M on 80/100 mesh Chromosorb W H/P operated at a temperature of 125 °C.

The detector response vs. phenol concentration was found to be linear over the working range by injecting liquid samples of known concentration. Vapor concentrations in samples were obtained by comparing estimates of sample peak areas with those of the same volume of vapor over a saturated solution of phenol. Vapor pressures were then calculated by using as a reference the vapor pressure of pure phenol obtained from the literature.[4] The partial pressure of phenol over saturated solutions in isooctane or cyclohexane was equal, within experimental error, to the vapor pressure over solid phenol, indicating that solid solution formation does not occur.

Solubility Determinations. An amount of phenol well in excess of its solubility was allowed to equilibrate with approximately 5 mL of solvent in a sealed vial which was rotated in a water bath at 25 °C for at least 2 days. An aliquot of the saturated solution was then filtered through a Millipore filter (FHLP 01300) and diluted to an appropriate concentration in acidified methanol for spectrophotometric UV analysis.

Results and Discussion

The solubilities of phenol in isooctane and cyclohexane at 25 °C are shown in Table I along with the solubilities of several other organic compounds obtained from the literature.[2] The solubility of phenol in the two alkane solvents differs by more than an order of magnitude. This large difference is a surprising result in view of the widely held supposition that aliphatic hydrocarbon solvents are quite similar in their interactive tendencies toward a given solute.[5] A comparison of the solubilities of several other organic compounds in these two solvents (Table I) generally shows only minor differences, suggesting that the phenol solubilities are an anomaly. It was hoped that a study of the self-association of phenol in isooctane and cyclohexane would shed light on the apparent anomalous solvent effect.

The partial vapor pressures of phenol vs. formal phenol molarity in isooctane and cyclohexane are shown in Figure 1. Values of Henry's law constants of 4.6 and 2.8 Torr L mol^{-1} in isooctane and cyclohexane, respectively, were obtained from the slopes of the vapor pressure vs. concentration plots at phenol molarities below 0.02 M using a literature value of 0.41 Torr for the vapor pressure of pure phenol.[4] The plots of vapor pressure vs. concentration were linear below 0.02 M within experimental error.

Calculation of Monomer Concentration from Vapor Pressure Data. The advantage of using vapor pressures to study self-association is that the partial vapor pressure of phenol is directly related to the concentration of phenol monomer in solution. Implicit in this statement are two assumptions: (1) The phenol in the vapor phase is totally monomeric. (2) The activity of phenol monomer in solution equals its concentration.

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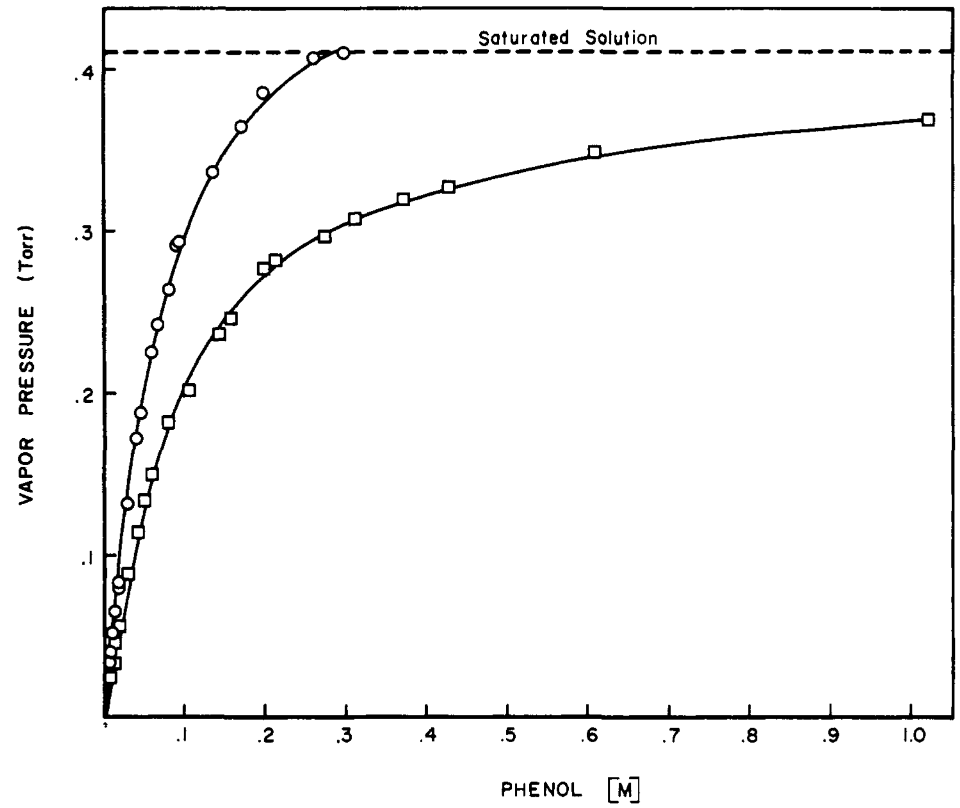

Figure 1. Vapor pressure of phenol vs. formal phenol molarity in isooctane (○) and in cyclohexane (□) at 25 °C.

Table I. Molar Solubilities of Several Polar Substances in Isooctane and Cyclohexane[a]

solute	cyclohexane	isooctane
carbazole	1.7×10^{-3}	1.1×10^{-3}
picric acid	4.1×10^{-4}	2.5×10^{-4}
salicylic acid	4.0×10^{-3}	2.3×10^{-3}
acetanilide	7.5×10^{-4}	9.3×10^{-4}
phthalic anhydride	6.4×10^{-3}	4.2×10^{-3}
phenol	4.0	0.30

[a] Phenol data were determined in this study. Other values were obtained from ref 2.

The assumption (1) that association in the vapor phase is negligible has been shown to be valid for alcohols at partial vapor pressures as high as 30-40 Torr[6,7] and should be a reasonable assumption for phenol at partial pressures below 0.41 Torr at 25 °C.

At equilibrium, the chemical potential of monomer must be the same in both phases and one can define the activity of phenol monomer in solution, a_1, as

$$a_1 = \gamma_1 c_1 = p_1/H \qquad (1)$$

where p_1 is the phenol vapor pressure in torr over a solution of known molarity, c_1, and H is the vapor pressure over the standard state, or simply the Henry's law constant. The standard state employed here is a hypothetical 1 M solution of monomer, the reference state being the solute at infinite dilution in isooctane or cyclohexane. γ_1 is the activity coefficient of monomer, which is assumed to equal 1 over the concentration range in which quantitative correlations are made. Nonlinearity in the vapor pressure curve is attributed to specific self-association interactions.

Monomer concentrations calculated from the vapor pressure data are plotted in Figure 2 vs. formal phenol molarity.

Models for Phenol Self-Association. The simplest association model which can be applied to these data is one in which the existence of a single polymeric species in equilibrium with monomer is assumed as characterized by the equilibrium constant, $K_{1,n}$:

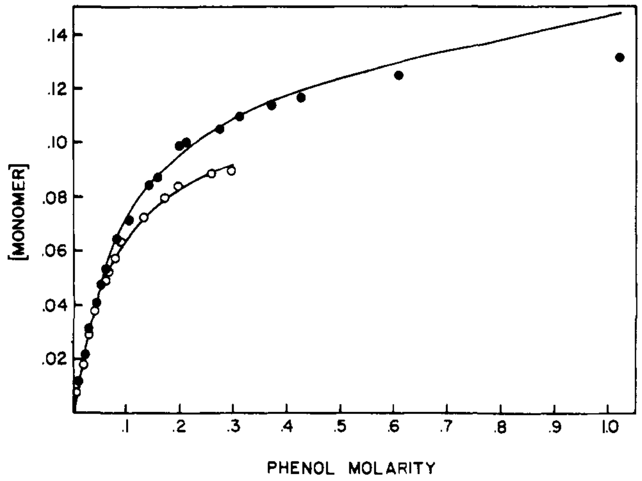

Figure 2. Monomer concentration (M) vs. formal phenol molarity in isooctane (○) and cyclohexane (●) at 25 °C.

$$K_{1,n} = \frac{(n\text{-mer})}{(\text{mon})^n} \qquad (2)$$

where n is the size of n-mer formed. The total phenol molarity, C_T, is then expressed by the relation

$$C_T = (\text{mon}) + nK_{1,n}(\text{mon})^n \qquad (3)$$

and

$$\log\,[C_T - (\text{mon})] = \log\,[nK_{1,n}] + n \log\,(\text{mon}) \qquad (4)$$

From eq 4 it can be seen that a plot of log (C_T − (mon)] vs. log (mon) should give a straight line with a slope of n if the initial assumption that a single polymer dominates is correct. Such

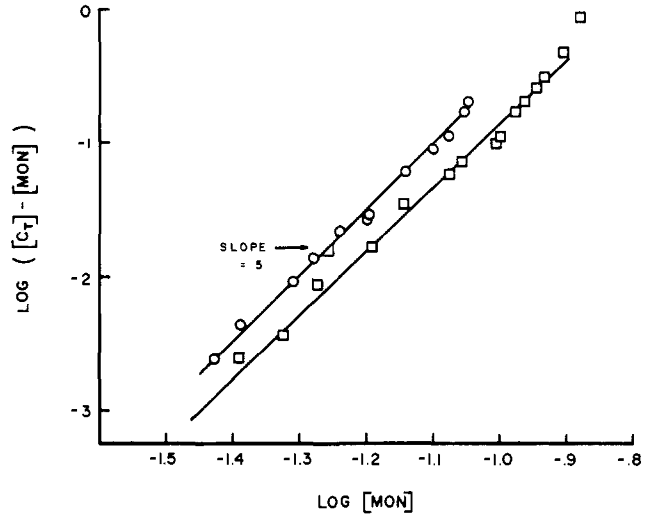

Figure 3. Log-log plots of phenol vapor pressure data in isooctane (○) and in cyclohexane (□) at 25 °C (see eq 4).

plots are shown in Figure 3. Any curvature existing in these plots is probably masked by the experimental error in the vapor pressure measurements (±2.6%). The lines are parallel in the two solvents with slopes of approximately 5 suggesting that pentamers may dominate.

A least-squares computer fitting technique described previously[3] also yielded a smaller standard deviation for a monomer-pentamer model than for other monomer-single polymer models. The percent deviation between monomer concentration calculated from a monomer-pentamer model and experimental monomer concentration is generally less than 3%. Since the standard deviation for the determination of monomer concentration in a single phenol solution from vapor pressures is estimated to be ±2.6%, the simple model employed here fits the data within experimental error. Equilibrium constants for pentamer formation in isooctane and cyclohexane are shown in Table II.

The choice of the most appropriate model to describe phenol (and alcohol) self-association has been the subject of considerable controversy. In early studies, dimers were assumed to be important in the stepwise association process. More recently several investigators have suggested that dimer formation is negligible. Trimers were found to be the predominant phenol polymer in several NMR[9-11] and calorimetric[12,13] studies. Others have favored a 1-3-6 model[14] or a 1-3-∞ model for phenol association.[15]

Shown in Table II are the root mean square deviations in monomer concentration from computer fits of phenol vapor pressure data employing various one- and two-parameter models. As would be expected, fits are improved by the addition of more parameters to the model, but the confidence intervals for each parameter are generally quite large, making comparisons between systems difficult.

1-n-∞ models have been employed previously with $n = 2$ or 3.[7,8] It is assumed in applying this type of model that the first important associated species forms with a unique equilibrium constant, K_n, while the equilibrium constant for stepwise formation of higher polymers is K_∞. The general equation for application of the 1-n-∞ model is

$$C_T = (\text{mon}) + \frac{K_n(\text{mon})^n[n - (n-1)K_\infty(\text{mon})]}{[1 - K_\infty(\text{mon})]^2} \quad (5)$$

Extreme caution must be exercised in interpreting the results of fits of various models to self-association data. We do not believe that the evidence obtained in this study is sufficient to support any one model unequivocally. Nevertheless, models are useful for summarizing the data and for comparing phenol's associative behavior in different solvents.

Table II. Root Mean Square Deviations for Various Computer Fits of Phenol Vapor Pressures in Cyclohexane and Isooctane

model	cyclohexane[a] ($\times 10^3$)	isooctane[b] ($\times 10^3$)
1-4	2.4	2.2
1-5	1.5 ($K_{1,5}$ = 2660)	0.94 ($K_{1,5}$ = 6260)
1-6	2.4	1.4
1-2-5		0.94
1-3-5	1.4	
1-4-5	1.4	0.94
1-3-6	1.3	0.79
1-4-6	1.3	0.83
1-3-∞	2.2	1.5
1-4-∞	1.3	0.75
1-5-∞	1.5	0.90
1-6-∞	2.4	1.4

[a] Determined from vapor pressure data up to 0.43 M. [b] Determined from vapor pressure data up to 0.3 M.

As an example of why one should be cautious in drawing conclusions from computer fitting of data to various models, we have observed that the choice of the "best" model depends on whether variation in monomer or in formal phenol molarity is minimized. In this study variation between calculated and observed values of monomer was minimized because most of the experimental error is in monomer.

A recent study by Lin et al.[15] of phenol's self-association in cyclohexane favored a 1-3-∞ model. We have repeated the curve fitting of the data of Lin et al. for phenol in cyclohexane at 22.2 °C, modifying our program to minimize variation either in monomer concentration or formal phenol concentration. It was found that a 1-3-∞ model best fits their data when formal phenol molarity is treated as the dependent variable while a 1-5-∞ model is best when monomer molarity is treated as the dependent variable. The reason for this change in best model is probably a difference in weighting of individual data points in different concentration regions by the two methods.

Structural Effects on Self-Association. The self-association pattern observed for phenol in hydrocarbon solvents is quite similar to the associative behavior of primary alcohols.[3] Phenol is much more acidic than alcohols even in organic solvents as indicated by its strong hydrogen-donating ability compared to that of methanol, for instance.[16] Yet the $K_{1,5}$ value for phenol pentamer formation in isooctane is similar to the pentamer formation constants for primary alcohols ($K_{1,5}$ = 8700 L^4 mol^{-4} for 1-butanol in isooctane[3] and $K_{1,5}$ = 6300 L^4 mol^{-4} for phenol in isooctane). This suggests that self-association interactions are not extremely sensitive to the acidity of the hydroxyl group. Fluoro alcohols, which are better proton donors than alcohols,[17] are apparently less associated than the corresponding unsubstituted alcohols.[18] The steric effect of the fluoro group on self-association is unknown. Others have shown that 3- and 4-fluorophenol are less associated than phenol even though they are more acidic.[9] In a study of the self-association of para-substituted acetophenone oximes, it was suggested that the charge density on the proton acceptor atom is a more important factor than acidity of the proton donor; e.g., $CH_3OC_6H_4C(CH_3){=}NOH$ self-associates more strongly than $NO_2C_4H_4C(CH_3){=}NOH$.[19]

Sterically, a phenyl group is similar to a secondary alkyl.[20] Secondary alcohols have been shown to be less strongly associated than the corresponding primary alcohols[21] and are also associated to a lesser extent than phenol under the same conditions. Apparently the phenyl ring is less effective in hindering self-association than would be expected from steric considerations, possibly because of the planarity of the ring.

The Dramatic Difference in Phenol's Solubility in Two Hydrocarbon Solvents. The greater than tenfold enhancement in the solubility of phenol in cyclohexane over that in isooctane serves to demonstrate the important but often overlooked role specific interactions such as hydrogen bonding play in determining solubility. The direct solvent effect on solubility, which reflects solvation differences, is manifested in the ratio of phenol's Henry's law constants in the two solvents. This ratio is 1.6 with the vapor pressure of phenol monomer being higher in isooctane than in cyclohexane. The inverse of this ratio would represent the solubility ratio if no solute-solute interactions occurred in solution. Table III shows the amount of phenol in monomeric and polymeric states, neglecting changes in activity coefficients of the individual species, in saturated phenol solutions at 25 °C. The ratio of monomeric phenol in the two solvents at saturation (1.6) is similar to the solubility ratios observed for other organic compounds in the two solvents shown earlier in Table I. (The acetanilide solubilities are an apparent exception.) This agreement suggests that the solute-solvent interactions between phenol and cyclohexane or isooctane are similar and cannot alone explain the large disparity in solubility. The order of magnitude difference in solubility is possible because phenol is largely self-associated at saturation, and is due to differences in polymer concentration at saturation in the two solvents.

Phenol's tendency to form polymers at low concentration is quite similar in the two solvents, being slightly less in cyclohexane as reflected by the constants in Table II and Figure 2. Apparently, both polymer and monomer are stabilized in cyclohexane so the equilibrium constant for association is not changed significantly. Assuming a monomer-pentamer association model, the much higher polymer concentration at saturation in cyclohexane reflects primarily a small increase in the allowed monomer concentration raised to the fifth power. Of course, other factors such as deviations of the individual species activity coefficients from unity with increasing phenol concentration may also contribute to the enhanced solubility in cyclohexane, but it is the fact that phenol self-associates which results in the apparent anomaly.[22]

Conclusion

In summary, it is shown that changes in the thermodynamic activity of phenol as a function of its concentration in alkane solvents can be rationalized by assuming that phenol molecules self-associate at increasing formal molarities to form new chemically distinct species which do not contribute significantly to the partial vapor pressure. The data suggest that the dominant polymeric species are larger than dimers—possibly pentamers. We have also shown that a consideration of the specific interactions occurring in solution can explain the solubility differences observed for phenol in cyclohexane when compared to its solubility in isooctane.

Knowledge obtained in this study of the thermodynamic activity of phenol as a function of its concentration in isooctane will be used in a later publication reporting the results of a current study in this laboratory on the effect of specific intermolecular interactions on the diffusional mass transfer of solute species.

Table III. Concentrations of Phenol Existing in Monomeric and Polymeric States in Saturated Phenol Solutions at 25 °C

solvent	phenol in monomeric state, M	phenol in polymeric state, M
isooctane	0.09	0.21
cyclohexane	0.15	3.9

Acknowledgments. This work was supported by the University of Kansas General Research Fund and Grant 1 PO1 GM 22357 from the National Institutes of Health. B. D. Anderson received partial support from an American Foundation for Pharmaceutical Education Fellowship. We express appreciation to Dr. Wesley White for his assistance with the computer programming.

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(22) Because the points at high concentration in cyclohexane diverge from the simple 1–5 model, a reviewer has pointed out that to fit the saturated solution in cyclohexane one needs a $K_{1,5}$ even greater than in isooctane, making suspect the statement that the solubility in cyclohexane is so much larger even though $K_{1,5}$ is less. A more revealing comparison can be made at 0.3 M, where both systems follow the 1–5 model. At 0.3 M the isooctane solution is saturated with respect to phenol but the cyclohexane solution is well below saturation even though $K_{1,5}$ is less in cyclohexane. The observed difference in self-association *K*'s cannot account for this observation.