

Interfacial and Free Energy Effects in Aqueous Amide Cosolvents

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Abstract □ Data on the solubility of *p*-hydroxybenzoate in amide-water cosolvent system and surface tension of the binary amide-water cosolvents are analyzed in terms of the possible mechanism for cosolvency. The results of the study suggest that strong partitioning of the alkylated amides to the ester surface, thus reducing the hydrophobic interface within the system, may account for much of the cosolvency phenomena observed in these systems.

Keywords □ *p*-Hydroxybenzoate—solubility and surface tension in amide-water cosolvency—alkylated amides.

Cosolvency relates to the enhanced solvent properties of mixtures of polar organics in water over that of pure water. Characteristically, the organic component of the cosolvent is present in concentrations of up to 10~20%. This leads to the formation of solutions in which the solubility of a third, and usually very hydrophobic, component is raised significantly. The phenomenon has been the subject of much investigation over the years. However, no general agreement on a mechanism, or explanation has been reached.

Recently, Yalkowsky *et al.*¹⁾ have proposed the idea that a cosolvent system may function by reducing the interfacial tension between the

hydrophobic solute and its predominantly aqueous environment. Their view is that the events taking place are analagous to those in a binary, solute-single solvent system in which the decrease in free energy needed for solutions of the solute, ΔG , derives from the expression

$$\Delta G = c\Delta\gamma(\text{HSA})f_c \quad (1)$$

where $\Delta\gamma$ is the decrease in solute/solvent interfacial tension; (HSA) is the hydrophobic surface area presented by the solute; and c is a term to correct $\Delta\gamma$ for the extreme curvature of the interface at the solute surface. The term, f , is the volume fraction of polar organic in the cosolvent system, and reflects the Yalkowsky group contention that the composition at the solute interface is the same as that in the bulk.

Lindstrom *et al.*^{2,3)} have offered evidence that alkylated amides appear to be in excess in the region of a hydrophobic solute when compared to their expected distribution in cosolvent systems with water. Should this be the case, one would anticipate (a) that the amides in the aqueous cosolvents would exhibit surface activity proportional to their own amphiphilic character; and (b) that the solvent properties of these aqueous cosolvents should parallel the surface activity. The present study seeks to demonstrate that relationship.

EXPERIMENTAL RESULTS

Details of the experimental work have been given elsewhere.^{4,5} In general, the work entailed the measurement of the surface tensions of 0.01 mole fraction amide-in-water solutions of thirteen amides ranging in alkylated configuration from formamide through N,N-dipropylacetamide at 25°C. Data for the second part of the present analysis are free energy charges, ΔG° , accompanying the transfer of methyl p-hydroxybenzoate from 0.01 mole fraction formamide-in-water systems to the analogous cosolvents containing the various alkylated amides³. All of the data are assembled in Table I.

Included in the table, as well, are estimates of the hydrophobic surface area, HSA, for each of the alkylated amides. The values were calculated by summing the surface areas of methyl (85\AA^2), ethyl (128\AA^2) and/or propyl (160\AA^2) groups (6) as necessary to account for the characteristic alkylation of each amide. Thus, the HSA for N,N-diethylacetamide is obtained by adding the surface areas of two ethyl groups and one methyl group. For the latter case, recall that a methylene group is added to the carbonyl carbon in formamide to form acetamide.

DISCUSSION

Surface activity results from the partitioning of an amphiphile to the air/water interface. The process is said to be entropic⁶ since it is accompanied by a substantial reduction in the orderliness of the solution in the vicinity of the hydrocarbon, or hydrophobic segments of the

amphiphile.

Adsorption of an amphiphile to an oil/water or to a hydrocarbon solute/water interface is explained similarly. However, a difference in degree is possible since the free energy for the reaction is often further reduced through cooperative interactions between the hydrophobic moieties of the solute and amphiphile to exclude water. The interaction is commonly referred to as hydrophobic bonding.

One would anticipate that the extent of surface activity and adsorption for a given amphiphile family would vary with amounts of hydrophobic surface which the amphiphile presents to the water. This has been demonstrated frequently in the literature. Figure 1 shows this to be the case for relatively simple alkylated amides. In that figure, calculated hydrophobic surface, HSA, is plotted against the observed decrease in the surface tension of 0.01 mole fraction amide-in-water solution, $\Delta\gamma$, as the degree of amide alkylation is increased. Clearly, there is a cause and effect relationship. The effect is not nearly so dramatic as it is when surfactants are employed, but it is, nevertheless, analogous. Interestingly, the plot suggests that the surface tension may be lowered rather precipitously, with a further bit of alkylation on the amides. A limit on amide solubility and crowding of the amide polar function at the surface would undoubtedly preclude such an event.

Given the significant alkyl group-related surface activity of the amides in aqueous solution, it is interesting to speculate on a possible mechanism for the amides as a cosolvent. Since the amides partition to the

Table I: Thermodynamic data relating to 0.01 mole fraction amide-in-water cosolvent systems at 25°C

Amide	HSA ^a , Å ²	$\Delta\gamma^b$, dyne/ cm	ΔG_i^c , cal/ mole
Formamide	0	0	0
N-Methylformamide	85	2.4	-100
N-Ethylformamide	128	6.4	-155
N-Methylacetamide	170	3.1	-189
N-Ethylacetamide	213	7.9	-219
N-Methylpropionamide	213	7.2	-225
N,N-Dimethylformamide	170	5.8	-225
N,N-Diethylformamide	256	8.3	-390
N,N-Dimethylacetamide	255	7.3	-313
N,N-Diethylacetamide	341	18.6	-490
N,N-Dimethylpropionamide	298	12.1	-399
N,N-Dipropylacetamide	405	34.5	d
N,N-Diethylpropionamide	384	24.1	d

- a. Total hydrophobic surface area represented by the sum of the hydrophobic areas of the methyl, ethyl and propyl groups on the amides. See reference 1.
 b. The decrease in surface tension of 0.01 mole fraction amide-in-water solutions due to alkylation of the amides.
 c. Change in system free energy, ΔG_i^c , accompanying the transfer of methyl *p*-hydroxybenzoate from a 0.01 mole fraction formamide-in-water cosolvent to 0.01 mole fraction amide-in-water, cosolvents made using the alkylated amides indicated.
 d. Phase separation

air/water interface, it is not unreasonable to expect that they would adsorb to a hydrocarbon/water interface. In so doing, the hydrophobic surface of both the solute and the amide would be reduced, thus lowering the energy of the system. Alternatively, tension at the hydrophobe/water interfaces might drop to a lower value as the hydrophobic bonding at the interface leaves the polar, hydrophilic portions of the amide in contact with the water. The ability of the amide cosolvent to solubilize would then be some function of its own hydrophobicity. In the present work, the calculated

hydrophobic surface area, HSA, would seem to reflect that property, as seen in relationship to surface tension in Figure 1.

Figure 2 relates the calculated HSA of the amides considered in this study to the decrease in free energy, ΔG_i^c , of a solution system as methyl *p*-hydroxybenzoate is transferred from a cosolvent system containing formamide to those containing alkylated amides. In line with the speculation, one sees a continuing decrease in system energy as the degree of amide alkylation increases.

The very strong interactions between amides and water lessen the solubilizing effects of the amides in aqueous solution⁵). Nevertheless, the hydrophobic interaction can be substantial as the degree of alkylation increases. This is seen in the fact that a saturated solution of methyl *p*-hydroxybenzoate in 0.01 mole fraction cosolvents of either N,N-dipropylacetamide or N,N-diethylpropionamide separates into two phases.

The results of this study suggest a possible mechanism for cosolvency, at least as it applies to amides. It is one in which the amide adsorbs to the solute at its interface with water, thereby either reducing the hydrophobic surface or the solute/water interfacial tension. In so doing, the very soluble, hydrophilic portion of the amide cosolvent remains preferentially oriented toward the aqueous phase. It will be of interest to investigate further this possibility.

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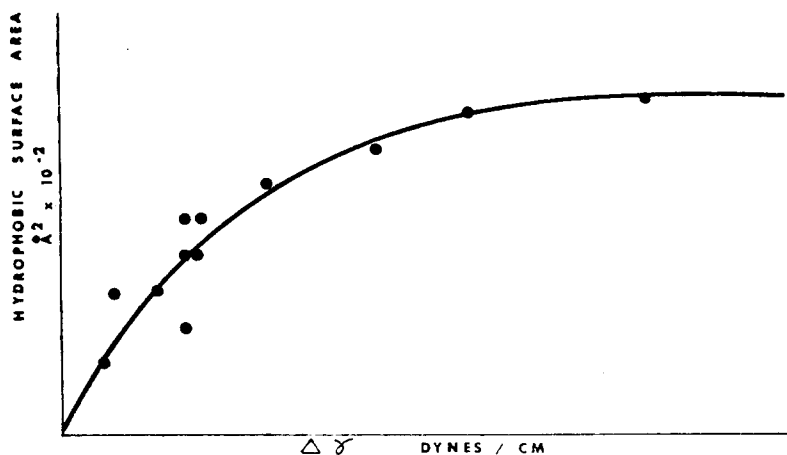


Fig. 1: The effect of the hydrophobic surface area presented by the alkyl groups of various amides on the surface tension of their respective 0.01 mole fraction amide-in-water solutions. At 25°C the effect is shown as the decrease in surface tension, $\Delta\gamma$, of the alkylsubstitutedamide solutions in contract with the surface tension of a 0.01 mole fraction formamide-in-water solution.

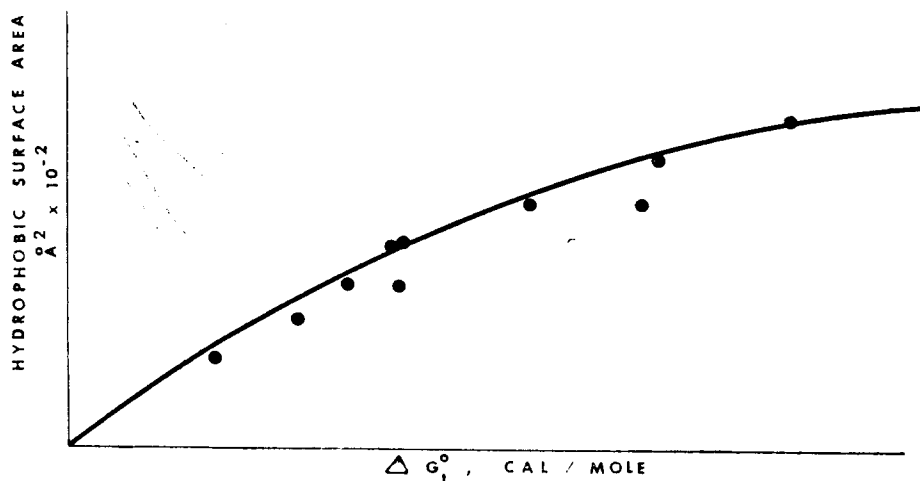


Fig. 2: The effect of the hydrophobic surface area presented by the alkyl groups of various amides on the free energy of transfer, ΔG_1^0 , of methyl *p*-hydroxybenzoate from 0.01 mole fraction formamide-in-water to 0.01 mole fraction amide-in-water solutions of the respective alkylated amides in water at 25°C.

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