1112 J. Am. Chem. Soc. 1983, 105, 1112-1117

Heat Capacities of Solution for Alcohols in Polar Solvents and the New View of Hydrophobic Effects

Dorla Mirejovsky and Edward M. Arnett*

Contribution from the Department of Chemistry, Duke University,
Durham, North Carolina 27706. *Received July 19, 1982*

Abstract: Heat capacities of solution ($\Delta C_{p_2}^\circ$) are presented for methanol, 1-butanol, and 1-pentanol in dimethyl sulfoxide, *N*,*N*-dimethylformamide, *N*-methylformamide, ethylene glycol, and ethylammonium nitrate, a low-melting fused salt. In all cases, $\Delta C_{p_2}^\circ$ values are negligible compared to those in water even though these solvents have high polarity, high cohesive energy, or a high degree of association. The unique heat capacity behavior of aqueous solutions persists even in concentrated solutions of urea. Water-like behavior was suggested by the heats, entropies, and free energies of solution for nonpolar gases in ethylammonium nitrate, by a nearly ideal heat of mixing with water, and by the ability of this solvent to produce micelles from surfactants. The failure of ethylammonium nitrate to exhibit water-like heat capacity behavior differentiates those properties of water which are due to fluctuations between forms of different geometry and density from those which are caused by its high cohesive energy. The results are considered with reference to the recent Benzinger–Frank–Lumry analysis of the thermodynamics for aqueous solutions.

Introduction

Recently, micelle formation of several surfactants has been reported in ethylammonium nitrate (EAN), a low-melting (~12 °C) fused salt.[1] The observed critical micelle concentrations were only 5 to 10 times larger than those found in water. Moreover, the magnitudes of the standard free energies, enthalpies, and entropies of solution for several nonpolar gases in this medium approach the magnitudes obtained for nonpolar gases in water, especially as the carbon number of the solute increases.[2] Since low solubility of nonpolar molecules and micellization are generally viewed as characteristic properties of aqueous solutions, the exciting possibility that EAN might exhibit other behavior peculiar to water appeared worth exploring.

The special interest in the physical study of water, a substance essential to animal and plant life, lies in its many anomalous properties (e.g., heat capacity, isothermal compressibility, thermal expansivity, density behavior, and negative volume of melting) not found in other solvents.[3] The pivotal biological role of water is attributed to its ability to promote the aggregation of nonpolar molecules. This so-called "hydrophobic effect", based upon the low solubility of nonpolar molecules in water, has been put forward as a major force for organizing proteins.[4]

Positive free energies of solution (ΔG_s°) resulting from negative entropies of solution (ΔS_s°), irrespective of the sign of ΔH_s°, are characteristic thermodynamic properties for the transfer of nonpolar solutes from organic solvents (or the gas phase) to water and are associated with the hydrophobic effect.[5] This loss of excess entropy led Frank and Evans to postulate in 1945 the existence of an enhanced water structure around apolar species.[6] Since the seminal paper of Frank and Evans, it has been widely accepted that the hydrophobic effect is "entropy driven".

Recently, H. S. Frank corrected this classical view of the hydrophobic effect by pointing out that by emphasizing the entropy anomaly Frank and Evans had underrated the significance of the equally striking enthalpy anomaly.[7] Frank referred to the peculiarity of ΔH_s° and ΔS_s° of nonpolar gases in water which, in contrast to nonaqueous solutions, change with temperature.[8] The similar way in which both enthalpy and entropy increase with increasing temperature suggests strongly that the dissolution of nonpolar solutes in water is accompanied by a process occurring close to its equilibrium temperature. This also implies that the abnormal part of the negative entropy of nonpolar solutes is compensation entropy, cancelling out a negative part of the enthalpy. Consequently, this suggests that the poor solubility of hydrophobic molecules in water is due to unfavorable enthalpy and not to unfavorable entropy.

The existence of a fluctuation process in cool bulk water is compatible with the present view that water molecules form a continuous hydrogen-bonded network containing predominantly four or five mutually associated molecules per cluster and many strained or broken hydrogen bonds.[9] The entire system undergoes continuous topological rearrangement resulting in the fluctuation of water molecules between cluster patterns, characterized by stronger hydrogen bonds with nearly tetrahedral angles, and the rest of the network which is more distorted, strained, and dense. This fluctuating system is affected by the temperature and by the addition of solutes. It appears that a lowering of the temperature as well as the addition of hydrophobic solutes both enhance cluster formation.[9]

Although it is clear that the unusual properties of water are related to its unique structural possibilities, we are still confronted by two questions: (1) To what extent is the molecular structure of water a prerequisite for its distinct properties as a solvent? (2) What solvent properties (if any) do truly distinguish water from all other highly polar solvents?

The first results obtained with EAN suggest that comparison of this solvent with cool water and other polar solvents could shed more light on these questions. EAN is a highly associated substance with a relatively large cohesive energy density.[10] Its equal number of potential donor and acceptor sites for hydrogen bonding suggests the possibility that a water-like,[2,10e] three-dimensional structure might be formed. In view of the first results showing a pattern reminiscent of the hydrophobic effect, we decided to test further the "hydrophobic behavior" observed in EAN by

---

[1] Evans, D. F.; Yamauchi, A.; Roman, R.; Casassa, E. Z. *J. Colloid Interface Sci.* **1982**, *88*, 89–96.

[2] Evans, D. F.; Chen, S.-H.; Schriver, G. W.; Arnett, E. M. *J. Am. Chem. Soc.* **1981**, *103*, 481–2.

[3] (a) Franks, F. "Water, A Comprehensive Treatise"; Franks, F., Ed.; Plenum Press: New York, 1972; Vol. 1, pp 1–20. (b) Franks, F. *Ibid.* 1973; Vol. 2, pp 1–54. (c) Franks, F.; Reid, D. S. *Ibid.* 1973; Vol. 2, pp 323–80. (d) Benson, S. W. *J. Am. Chem. Soc.* **1978**, *100*, 5640–4.

[4] Tanford, C. "The Hydrophobic Effect: Formation of Micelles and Biological Membranes"; Wiley: New York, 1980.

[5] Franks, F. "Water, A Comprehensive Treatise"; Franks, F., Ed.; Plenum Press: New York, 1975; Vol. 4, pp 1–94.

[6] Frank, H. S.; Evans, M. W. *J. Chem Phys.* **1945**, *13*, 507–32.

[7] Frank, H. S., private communication.

[8] Wilhelm, E.; Battino, R.; Wilcock, J. W. *Chem. Rev.* **1977**, *77*, 219–62.

[9] (a) Stillinger, F. H. *Science* **1980**, *209*, 451–57. (b) Stanley, H. E.; Teixeira, J. *J. Chem. Phys.* **1980**, *73*, 3404–22. (c) Jorgensen, W. L. *J. Chem. Phys.* **1982**, *77*, 4156–63. (d) Jonas, J. *Science* **1982**, *216*, 1179–84.

[10] (a) Walden, P. *Chem. Zentralbl.* **1914**, *1*, 1800–1. (b) Walden, P. *Z. Phys. Chem., Abt. A* **1931**, *157*, 389–421. (c) Sugden, S.; Wilkins, H. *J. Chem. Soc.* **1929**, 1291–8. (d) Gordon, J. E. "Techniques and Methods of Organic and Organometallic Chemistry"; Denney, D. B., Ed.; Marcel Dekker: New York, 1969; Vol. 1, pp 51–188. (e) Gordon, J. E. "The Organic Chemistry of Electrolyte Solutions"; Wiley: New York, 1975; pp 170–4.

0002-7863/83/1505-1112$01.50/0 © 1983 American Chemical Society

Table I. Enthalpies of Solution and Heat Capacities of Solution for Methanol, 1-Butanol, and 1-Pentanol in Various Solvents

	methanol		1-butanol		1-pentanol	
	$\Delta\bar{H}_S$ (25 °C), kcal mol^{-1}	$\Delta C_{p_2}°$, cal mol^{-1} K^{-1}	$\Delta\bar{H}_S$ (25 °C), kcal mol^{-1}	$\Delta C_{p_2}°$, cal mol^{-1} K^{-1}	$\Delta\bar{H}_S$ (25 °C), kcal mol^{-1}	$\Delta C_{p_2}°$, cal mol^{-1} K^{-1}
dimethyl sulfoxide	−0.33 ± 0.01	0.0 ± 0.5	0.98 ± 0.02	−7.1 ± 2.3	1.33 ± 0.02	−8.8 ± 3.0
N,*N*-dimethylformamide	−0.13 ± 0.01	0.0 ± 0.4	0.71 ± 0.01	−3.9 ± 0.8	0.91 ± 0.02	−4.0 ± 2.0
N-methylformamide	0.18 ± 0.01	0.0 ± 2.0	0.76 ± 0.01	−3.8 ± 2.0	0.89 ± 0.02	−3.4 ± 1.8
ethylene glycol	0.09 ± 0.01	0.0 ± 0.4	0.84 ± 0.01	0.0 ± 2.0	1.11 ± 0.01	0.0 ± 2.0
ethylammonium nitrate	−0.06 ± 0.01	0.0 ± 0.2	0.46 ± 0.01	−3.8 ± 1.3	0.62 ± 0.01	−4.6 ± 1.4
water[a]	−1.754 ± 0.007	23.1 ± 1.8	−2.249 ± 0.010	71.6 ± 3.8	−1.868 ± 0.011	83.5 ± 5.3
3 M aqueous urea	−1.35 ± 0.06	14.8 ± 6.7	−1.50 ± 0.02	44.3 ± 2.0	−1.11 ± 0.03	53.0 ± 2.2
6 M aqueous urea	−1.14 ± 0.06	7.9 ± 2.0	−1.03 ± 0.02	34.7 ± 1.8	−0.67 ± 0.02	41.9 ± 2.5

[a] Reference 11.

determining the heat capacities of solution at infinite dilution, $\Delta C_{p_2}°$, for several alcohols in the latter medium. Large and positive $\Delta C_{p_2}°$'s have been found for alcohols,[11-16] amides,[14,17] amines,[15-20] carboxylic acids,[15,17] ethers,[18,19,21] hydrocarbons,[22] amino acids,[23-26] peptides,[25-27] and tetraalkylammonium halides[28-35] in highly dilute aqueous solutions. In all cases the magnitude of $\Delta C_{p_2}°$ increases in direct proportion to the carbon number of the solute. The $\Delta C_{p_2}°$'s, derived from the temperature coefficients of partial molar heats of solution, are large and positive owing to gradually decreasing exothermicity of dissolution of nonpolar solutes as the temperature increases. This decrease in exothermicity as the temperature increases may be attributed to the reduced ability of hydrophobic molecules to enhance cluster formation at higher temperatures, i.e., temperatures at which a shift toward the more dense form of water takes place. This reduced ability to enhance cluster formation at higher temperature also accounts for the decreasing heat capacities of solution of hydrophobic molecules as the temperature is increased.[36]

One would therefore expect that any solvent lacking the fluctuations between forms of quite different geometry and density would show small heat capacities of solution. This is indeed suggested by several reports for $\Delta C_{p_2}°$ for tetraalkylammonium halides in ethanol,[28] methanol,[29,37] *N*,*N*-dimethylformamide, *N*-methylformamide, and *N*-methylacetamide,[31,32] ethane in *N*-methylacetamide,[38] alkanes in methanol,[39] *N*-alkylamides in methanol, ethanol, and carbon tetrachloride,[40] and alcohols in ethylene glycol.[41] $\Delta C_{p_2}°$ values were found to be small as compared to those for solution of the same compounds in water. Thus, the determination of $\Delta C_{p_2}°$'s of nonpolar solutes in EAN is important to the proper understanding of the classification of EAN in relation to water and other solvents.

In this article we report the $\Delta C_{p_2}°$'s of methanol, 1-butanol, and 1-pentanol in EAN. For comparison, the $\Delta C_{p_2}°$'s were also determined in dimethyl sulfoxide (DMSO), *N*,*N*-dimethylformamide (DMF), *N*-methylformamide (NMF), ethylene glycol, and 6 M and 3 M aqueous urea solutions.

The results which we shall present below reinforce the unique status of water as differential from all other solvents if $\Delta C_{p_2}°$ for solutes is used as the criterion. We shall discuss the discrepancy between the failure of EAN to exhibit water-like heat capacity behavior and its other "water-like" properties which prompted this research.

Experimental Section

Ethylammonium Nitrate. EAN was prepared by dissolving a large excess of aqueous or gaseous ethylamine in 70% nitric acid in a three-neck round-bottom flask equipped with a stirrer, dropping funnel, and cold-finger condenser. The base was introduced under the surface. A dry ice–2-propanol slurry was used for cooling the flask during the reaction. Water was removed first in vacuo by rotary evaporation and then by prolonged high-vacuum pumping. Water removal was monitored by observing the disappearance of the H_2O resonance in the ^1H NMR spectra. Several weeks were needed to remove the residual water from a large batch of salt. The oily yellow salt was purified by fractional crystallization or by passing it through a column filled with charcoal. The resulting colorless liquid was kept for several days under high vacuum at room temperature to remove residual water. Subsequently, the solution was stored under a nitrogen atmosphere. The frozen solution yielded crystals melting from 11 to 13 °C. Anal. Calcd for $C_2H_8N_2O_3$: C, 22.22; H, 7.45; N, 25.92. Found: C, 22.21; H, 7.41; N, 26.03. We have attempted to detonate EAN by hammering and by exposure to a flame with no observable effect. However, we have been advised that under some conditions EAN is a powerful explosive.[42]

Materials. Methanol, 1-butanol, and 1-pentanol were refluxed with sodium for 2 h and then fractionally distilled. The water content, as determined by Karl Fischer titration, was below 0.005 v/v%. Ethylene glycol (Fisher, certified) was refluxed with sodium and then distilled. Neither the repetition of this procedure nor the passing of ethylene glycol

---

(11) Arnett, E. M.; Kover, W. B.; Carter, J. V. *J. Am. Chem. Soc.* **1969**, *91*, 4028–34.

(12) Alexander, D. M.; Hill, D. J. T. *Aust. J. Chem.* **1969**, *22*, 347–56.

(13) Jolicoeur, C.; Lacroix, G. *Can. J. Chem.* **1976**, *54*, 624–31.

(14) Sköld, R.; Suurkuusk, J.; Wadsö, I. *J. Chem. Thermodyn.* **1976**, *8*, 1075–80.

(15) Nichols, N.; Sköld, R.; Spink, C.; Wadsö, I. *J. Chem. Thermodyn.* **1976**, *8*, 993–9.

(16) Nichols, N.; Wadsö, I. *J. Chem. Thermodyn.* **1975**, *7*, 329–36.

(17) Konicek, J.; Wadsö, I. *Acta Chem. Scand.* **1971**, *25*, 1541–51.

(18) Cabani, S.; Conti, G.; Martinelli, A.; Matteoli, E. *J. Chem. Soc., Faraday Trans. 1* **1973**, *69*, 2112–23.

(19) Kiohara, O.; Perron, G.; Desnoyers, J. E. *Can. J. Chem.* **1975**, *53*, 2591–7.

(20) Bergström, S.; Olofsson, G. *J. Solution Chem.* **1975**, *4*, 535–55.

(21) Kusano, K.; Suurkuusk, J.; Wadsö, I. *J. Chem. Thermodyn.* **1973**, *5*, 757–67.

(22) Gill, S. J.; Nichols, N.; Wadsö, I. *J. Chem. Thermodyn.* **1976**, *8*, 445–52.

(23) Kresheck, G. C.; Benjamin, L. *J. Phys. Chem.* **1964**, *68*, 2476–86.

(24) Spink, C. H.; Wadsö, I. *J. Chem. Thermodyn.* **1975**, *7*, 561–72.

(25) Jolicoeur, C.; Boileau, J. *Can. J. Chem.* **1978**, *56*, 2707–13.

(26) Prasad, K. P.; Ahluwalia, J. C. *Biopolymers* **1980**, *19*, 263–72.

(27) Mishra, A. K.; Ahluwalia, J. C. *Int. J. Pept. Protein Res.* **1981**, *18*, 506–12.

(28) Arnett, E. M.; Campion, J. J. *J. Am. Chem. Soc.* **1970**, *92*, 7097–101, and references therein.

(29) Mastroianni, M. J.; Criss, C. M. *J. Chem. Thermodyn.* **1972**, *4*, 321–30.

(30) Mohanty, R. K.; Ahluwalia, J. C. *J. Chem. Thermodyn.* **1972**, *4*, 53–6.

(31) De Visser, C.; Somsen, G. *J. Chem. Thermodyn.* **1973**, *5*, 147–52.

(32) De Visser, C.; Somsen, G. *J. Chem. Soc., Faraday Trans. 1* **1973**, *69*, 1440–7.

(33) Shin, C.; Worsley, I.; Criss, C. M. *J. Solution Chem.* **1976**, *5*, 867–79.

(34) Perron, G.; Desrosiers, N.; Desnoyers, J. E. *Can. J. Chem.* **1976**, *54*, 2163–83.

(35) Castagnolo, M.; Sacco, A.; Petrella, G. *J. Chem. Soc., Faraday Trans. 1* **1981**, *77*, 9–13.

(36) Choudhury, N. R.; Ahluwalia, J. C. *J. Chem. Thermodyn.* **1982**, *14*, 281–9, and references therein.

(37) Shin, C.; Criss, C. M. *J. Solution Chem.* **1978**, *7*, 205–17.

(38) Wood, R. H.; DeLaney, D. E. *J. Phys. Chem.* **1968**, *72*, 4651–4.

(39) French, R. N.; Criss, C. M. *J. Solution Chem.* **1981**, *10*, 231–42.

(40) Öjelund, G.; Sköld, R.; Wadsö, I. *J. Chem. Thermodyn.* **1976**, *8*, 45–54.

(41) Nwankwo, S.; Wadsö, I. *J. Chem. Thermodyn.* **1980**, *12*, 881–4, 1167–70.

(42) Benson, S. W., private communication.

through a column of molecular sieves (Davison, 4A) brought the water content below 0.06 v/v%. *N,N*-Dimethylformamide (Fisher, certified) was stored over molecular sieves for 2 weeks and used without further purification. *N*-Methylformamide (Aldrich) was also stored over molecular sieves for 2 weeks and subsequently distilled under reduced pressure. The water content of these two solvents was approximately 0.02 v/v%. Highly purified dimethyl sulfoxide with a water content below 0.01 v/v% was available at this laboratory. After purification, all solvents were stored under nitrogen and used within a few days. Replicate thermochemical runs with different batches of solvents agreed within experimental error. Urea (Fisher, certified) was recrystallized from methanol and dried in vacuo overnight at 50 °C.

Calorimetry. Heats of solution were determined with a Tronac 450 titration calorimeter using a 40-mL reaction Dewar, following the general procedure described previously.[43] The partial molar heats of solution at infinite dilution were measured at 18, 25, 33, and 42 °C, and $\Delta C_{p_2}°$'s were calculated from the temperature coefficients of partial molar heats of solution as in our previous work.[11]

Usually, three successive injections of the solute were made for each run. For every addition, the final solute concentration ranged from 0.5×10^{-2} to 1.5×10^{-2} M. No concentration dependence of the enthalpies of solution was detectable. Moreover, every measurement was repeated on different days and with different batches of solvents. The scatter of the latter results is reflected by the reported standard deviations.

Results

Partial Molar Heats of Solution of Alcohols in Various Solvents. Partial molar heats of solution at infinite dilution, $\Delta \bar{H}_s$, of methanol, 1-butanol, and 1-pentanol in the various solvents at 25 °C are given in Table I. A number of published values can be compared with our data. Heats of solution of MeOH reported in the literature are −0.34,[44,45] −0.27 kcal mol^{-1} [46] in DMSO, −0.14,[45,47] −0.15 kcal mol^{-1} [46] in DMF, and 0.091 kcal mol^{-1} in ethylene glycol.[41] Published enthalpies of solution of 1-butanol are 0.99,[44] 0.95,[45] and 0.985 kcal mol^{-1} [47] in DMSO, 0.70[45] and 0.724 kcal mol^{-1} [47] in DMF, 0.746 kcal mol^{-1} in NMF,[47] and 0.84 kcal mol^{-1} in ethylene glycol.[41] Finally, the values reported for 1-pentanol are 1.29 kcal mol^{-1} in DMSO[45] and 0.90[45] and 0.91 kcal mol^{-1} [47] in DMF. Thus, our results agree quite well with those obtained in other laboratories.

The heats of solution of alcohols in EAN were measured in the purified liquid salt. However, in order to determine the effect of impurities, and especially of water, enthalpies of solution of 1-butanol were also measured in EAN with 2 mol % of water added (mp ~8–10.5 °C) and in a sample of EAN taken while the removal of residual water was still in progress (~6 mol % of H_2O, mp ~6–10 °C). The $\Delta \bar{H}_s$ values were exactly the same as those measured in the dried and purified salt. Thus, the heats of solution of alcohols in EAN are not very sensitive to the presence of small amounts of water.

Table I shows that $\Delta \bar{H}_s$'s for the alcohols in ethylammonium nitrate are closer to those obtained in dipolar solvents than to those obtained in water. The presence of urea in water depresses the exothermicity of the reaction. However, the enthalpies of solution for the alcohols in concentrated aqueous solutions of urea are still more exothermic than any enthalpies obtained in dipolar protic and aprotic solvents.

Heat Capacities of Solution for Alcohols in Various Solvents. $\Delta C_{p_2}°$'s of methanol, 1-butanol, and 1-pentanol in various solvents at 25 °C are shown in Table I. They represent the difference between the heat capacity of the pure solute and the solute at infinite dilution in the given solution, $\Delta C_{p_2}° = \bar{C}_{p_2} - C_{p_2}{}^*$, and are derived from the temperature coefficients of partial molar heats of solution.[11] Recently, small positive heat capacity changes of methanol (0.48 cal mol^{-1} K^{-1}), ethanol (1.20 cal mol^{-1} K^{-1}), propanol (1.67 cal mol^{-1} K^{-1}), and butanol (2.39 cal mol^{-1} K^{-1}) in ethylene glycol were reported by Nwankwo and Wadsö.[41] Their results agree with ours within the combined experimental error.

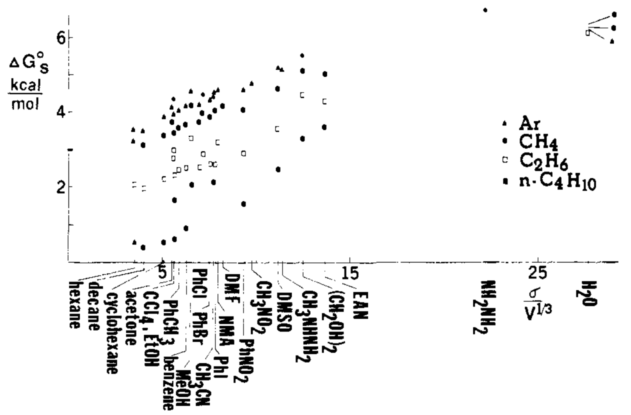

Figure 1. Solvation enthalpies for alcohols in various solvents expressed as a function of the number of carbon atoms.

Table II. Heats of Solution and Heat Capacities of Solution for Water in Ethylammonium Nitrate and for Ethylammonium Nitrate in Water and in 1 N HCl

	$\Delta \bar{H}_s$ (25 °C), kcal mol^{-1}	$\Delta C_{p_2}°$, cal mol K^{-1}
$H_2O \rightarrow EtNH_3NO_3$	0.32 ± 0.01	−2.6 ± 1.2
$EtNH_3NO_3 \rightarrow H_2O$	0.62 ± 0.03	−1.7 ± 3.0
$EtNH_3NO_3 \rightarrow$1 N HCl	0.69 ± 0.02	0.0 ± 3.1

It follows from Table I that the $\Delta C_{p_2}°$ values of alcohols in EAN are small and not significantly different from those obtained in the other polar solvents. Moreover, the difference between the heat capacity changes of 1-butanol and 1-pentanol is negligible while the difference of 12 cal mol^{-1} K^{-1} in water is typical of the large and nearly constant CH_2 increment for $\Delta C_{p_2}°$'s in that solvent. Heat capacities of solution in aqueous urea decrease as the concentration of urea increases. The $\Delta C_{p_2}°$ decrease for 1-butanol is as large as that for 1-pentanol.

$\Delta \bar{H}_s$ and $\Delta C_{p_2}°$ of Water in EAN and of EAN in Water and 1 N HCl. The heats of solution and the heat capacities of solution of water in EAN as well as of EAN in water and 1 N HCl are shown in Table II and are seen to be nearly identical. Also, the $\Delta C_{p_2}°$ values of water in EAN and EAN in water are the same. This implies that, at low concentration, EAN and water form almost ideal solutions.

Discussion

Enthalpies of Solvation. Heats of solution of alcohols in various solvents determined at 25 °C are referred to the gas phase following Krishnan and Friedman by combining the heat of solution at infinite dilution with the heat of vaporization of the pure alcohol.[45,48] This allows a comparison of the behavior of EAN with a number of other solvents of known properties. The solvation enthalpies of methanol, 1-butanol, and 1-pentanol in various solvents, expressed as a function of the number of carbon atoms, are shown in Figure 1.

Obviously, the reliability of curves constructed from only three points (Figure 1) is questionable. However, the solvation enthalpies of alcohols in water, DMSO, and DMF published by Krishnan and Friedman match these curves closely. Moreover, the heats of solution of alcohols in ethylene glycol reported by Nwankwo and Wadsö also fit on the respective curves in Figure 1.[41] Thus, in our opinion, these curves indicate with sufficient accuracy that the behavior of EAN as a solvent is similar to that of DMSO, DMF, NMF, and ethylene glycol. This behavior sharply distinguishes EAN and other dipolar solvents from water and also from aqueous solutions of urea. Even a 6 M urea solution

---

(43) (a) Arnett, E. M.; Chawla, B. *J. Am. Chem. Soc.* **1978**, *100*, 217–21. (b) Arnett, E. M.; Chawla, B.; Hornung, N. J. *J. Solution Chem.* **1977**, *6*, 781–818.

(44) Arnett, E. M.; McKelvey, D. R. *J. Am. Chem. Soc.* **1966**, *88*, 2598–9.

(45) Krishnan, C. V.; Friedman, H. L. *J. Phys. Chem.* **1971**, *75*, 3598–606.

(46) Cox, B. G.; Parker, A. J.; Waghorne, W. E. *J. Am. Chem. Soc.* **1973**, *95*, 1010–4.

(47) Rouw, A. C.; Somsen, G. *J. Chem. Thermodyn.* **1981**, *13*, 67–76.

(48) (a) Krishnan, C. V.; Friedman, H. L. "Solute-Solvent Interactions"; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1976; Vol. 2, pp 1–103. (b) Krishnan, C. V.; Friedman, H. L. *J. Phys. Chem.* **1969**, *73*, 1572–80.

behaves much more like water than do any of the dipolar solvents. The "structural effects" characteristic of aqueous solutions are clearly absent in EAN as well as in other polar and structured solvents and remain unique to water.

Krishnan and Friedman divided the enthalpy of solvation of alcohols into two components: that for the solvation of head groups and that for the solvation of the hydrocarbon portion.[45,48] The former, given by the intercept of the lines shown in Figure 1, reflects the ability of a given solvent to interact with hydroxyl groups. Krishnan and Friedman have shown that such ordering of solvents according to their basicities correlates well with other measures of base strengths. According to this analysis, the basicity of EAN is similar to that of ethylene glycol or DMF. The question of whether this basicity of EAN can also be confirmed by other probes remains open.

The slopes of the lines in Figure 1 indicate the ability of each solvent to solvate alkyl chains in terms of solvation enthalpies per methylene group. Krishnan and Friedman arranged several polar solvents into a "lipophilic series" where 1-butanol was the most lipophilic solvent and nitromethane the least. By this criterion, EAN appears to be rather lipophilic, falling between NMF and methanol. This position indicates a behavior contrasting sharply with the water-like behavior suggested by our measurements of solubilities of nonpolar gases in EAN. Thus, we are confronting two different types of behavior in the solute–solvent interactions, one based on the free energies of solution and the other on enthalpies of solution.

Solubility of Nonpolar Gases. The standard free energies of solution for nonpolar gases in EAN are more positive than those in any other nonaqueous solvent. However, they become less positive as the molar volume of the alkane increases.[2] Generally, the solubility of nonpolar solutes in nonaqueous solvents increases as the molecular volume of the solute increases.[49,50] On the other hand, in water $\Delta G_s°$ values remain nearly constant for small molecules. For larger alkanes, the solubility decreases ($\Delta G_s°$ becomes more positive) as the carbon number increases.[8] This implies that despite the relatively positive $\Delta G_s°$ values for nonpolar solutes in EAN, the behavior of EAN is similar to that of nonaqueous solvents.

Since we aim at comparing the behavior of EAN with that of a large series of solvents, including water, the $\Delta G_s°$ values of solution of alkanes in various solvents are shown as a function of $\sigma/V^{1/3}$ (Figure 2). This alternative measure of cohesive energy density, where σ is the surface tension and V the molar volume, was proposed by Gordon to estimate the cohesive energies of molten salts in relation to polar liquids.[51] The free energies of solution of gaseous solutes in a series of nonaqueous solvents were taken from data tabulated by Abraham[50] and those by Wilhelm and Battino.[49] The latter work supplied also the values of molar volumes and surface tensions. Figure 2 shows a fairly good correlation between the $\Delta G_s°$ values and the cohesive energy densities for small solutes. For larger solutes more scattered results were obtained. Several other correlations for gas solubilities were reported in the literature.[49] Most often, solubility was plotted against the Hildebrand solubility parameter.[52] Because the energy of vaporization is not accessible for ionic liquids, an alternative measure of cohesion must be used.[51] Both methods yield comparable results.

Figure 2 suggests that the puzzling insolubility of nonpolar solutes in *cold* water is due to the high cohesive energy of this liquid. This fact is being increasingly recognized.[50,53] Actually, the solubilities of argon, methane, ethane, and *n*-butane in water are greater ($\Delta G_s°$ less positive) than would be expected by extrapolation from the $\Delta G_s°$ values for other solvents. This increased solubility of nonpolar species in *cold* water due to "hydrophobic hydration" has been noted previously.[54]

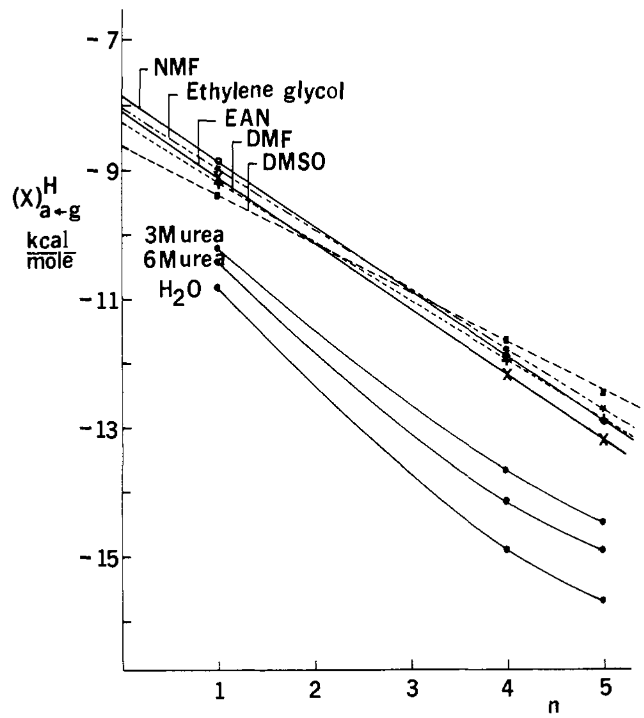

Figure 2. Standard free energies of solution of argon, methane, ethane, and *n*-butane as a function of cohesive energy density of various solvents.

Figure 2 shows that $\Delta G_s°$ values for nonpolar solutes in EAN correlate well with those obtained in other nonaqueous solvents and implies that the relatively large positive $\Delta G_s°$'s obtained in EAN are simply due to its large cohesive energy, as compared with any other nonaqueous solvent studied so far. Thus, EAN and other molten salts with high cohesive energy densities may occupy a useful intermediate position between ordinary nonaqueous solvents and water.

Entropies of Solution in Ethylammonium Nitrate. Entropies of solution for several nonpolar gases in EAN show an interesting pattern. The $\Delta S_s°$ of Ar in EAN is similar to that obtained in ethylene glycol,[55] and $\Delta S_s°$ of CH_4 in EAN is similar to that in MeOH.[2,50] On the other hand, the $\Delta S_s°$'s for Kr, C_2H_6, and n-C_4H_{10} (−22.08, −26.62, and −31.27 cal K^{-1} mol^{-1}, respectively)[2] are more negative in EAN than in any organic solvent studied so far.[49,50] For comparison, the $\Delta S_s°$ of n-C_4H_{10} in MeOH is −22.0 cal K^{-1} mol^{-1} [50] and in water −42.13 cal K^{-1} mol^{-1}.[8]

So far, large negative entropies of solution for nonpolar solutes have only been found in water and, therefore, are considered as a part of the unique behavior of this medium.[49,50,56] As pointed out in the Introduction, the insertion of nonpolar molecules into *cold* water is a compensated process characterized by negative entropy and enthalpy changes. Compensated entropy and enthalpy do therefore not contribute to the free energy. We shall say more about this subject in the final part of the Discussion. At this point we would like to stress only that every $\Delta S_s°$ for a nonpolar solute in water contains a portion which does not affect the solubility and which actually leads to a misleadingly large negative entropy of solution. Subtraction of the compensated entropy would result in a much less negative entropy of solution, comparable to those found in organic solvents. Supporting evidence for this reasoning is that the $\Delta S_s°$ values become gradually less negative at elevated temperatures where water behaves increasingly like other solvents.[8]

The small heat capacities of solution for alcohols in EAN as well as the linear van't Hoff plots obtained for nonpolar gases in EAN indicate that, in contrast to water, the fluctuation process is absent in this medium. Hence, the relatively large negative

---

(49) Wilhelm, E.; Battino, R. *Chem. Rev.* **1973**, *73*, 1-9.

(50) Abraham, M. H. *J. Am. Chem. Soc.* **1982**, *104*, 2085-94.

(51) Reference 10e, pp 158-162.

(52) Hildebrand, J. H.; Prausnitz, J. M.; Scott, R. L. "Regular and Related Solutions"; Van Nostrand-Reinhold: New York, 1970.

(53) Tanford, C. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 4175-6.

(54) Shinoda, K. *J. Phys. Chem.* **1977**, *81*, 1300-2.

(55) Lumry, R., private communication.

(56) (a) Abraham, M. H.; Nasehzadeh, A. *J. Chem. Thermodyn.* **1981**, *13*, 549-56. (b) Abraham, M. H.; Nasehzadeh, A. *J. Chem. Soc., Faraday Trans. 1* **1981**, *77*, 321-40.

entropies of solution obtained for larger solute molecules in EAN must have a different origin than those found in water. Although there are few published values of ΔS_s°'s for large solutes in associated and highly cohesive liquids, the solubility data of nonpolar gases in alkali nitrates[57] suggest that the large negative ΔS_s° values for large nonpolar solutes in EAN cannot be attributed entirely to its high cohesion energy. In spite of the fact that the cohesion energy of KNO_3 at 334 °C is only slightly lower than that of EAN at 25 °C,[51] the ΔS_s° of Ar in KNO_3 at 367 °C was found to be -5.3 cal K^{-1} mol^{-1}. Besides, the ΔH_s° of Ar in KNO_3 at 367 °C is more positive than for nonpolar gases in EAN, indicating much weaker solute–solvent interactions in the first medium. Hence, the unusual ΔS_s° and ΔH_s° quantities obtained in EAN must be determined by the character of the EAN molecule itself. EAN provides the first known case in which large negative entropies of solution for nonpolar gases are found in a solvent other than water and therefore demonstrates that the magnitude of ΔS_s° is not an adequate criterion of water-like behavior.

Mutual Heats of Solution of EAN and H_2O. The nearly identical heats of solution of water in EAN and of EAN in water deserve comment since by this classical criterion of ideality EAN is indeed water-like. The small $\Delta C_{p_2}^\circ$'s of both EAN in water and water in EAN show that, at low concentrations, the effect of temperature on the interactions of these two species is low. Moreover, the small $\Delta C_{p_2}^\circ$ for EAN in water indicates that although EAN contains an ethyl group it does not show a pattern characteristic of a "structure maker". Similarly, although EAN is an electrolyte it does not show a pattern characteristic of a "structure breaker".

An ideal heat of mixing with water was, however, also established for several nonelectrolytes. For example, urea is known for its low heat of mixing with water, and its heat capacity of solution is only 3 to 6 cal mol^{-1} K^{-1}.[58] The heat of solution of formamide in water is only 0.49 kcal mol^{-1} and that of water in formamide 0.32 kcal mol^{-1}.[46] The ΔC_p° of formamide in water is -4 to -6 cal mol^{-1} K^{-1}.[14,59] The results obtained for urea were attributed to the fact that urea lacks the ability to participate in tetrahedrally coordinated water because of its geometry, although it can form hydrogen bonds.[60] Similarly, the solubility data for nonpolar solutes in water–ethylene glycol and water–hydrazine mixtures indicate that hydrazine and ethylene glycol at low concentrations restrict fluctuations of water by decreasing the probability of cluster formation.[41,61]

It is surprising that a liquid electrolyte should dissolve in a highly polar solvent with negligible heat change since ionic hydration energy must be involved and the usual energy to break up the crystal lattice of the salt is lacking. At this time the very small heat of mixing of these two liquids simply seems to imply that the heat required for them to disrupt each other's structure is compensated by the heat of hydration of this salt which must involve both hydrophobic and ionic hydration. However, it is clear that the ideal mixing of a given species with water is again not an adequate criterion of the water-like behavior of that species.

Significance of These Results to the New View of Hydrophobic Phenomena. Our most important finding is the apparent contradiction between the small heat capacities of solution for alcohols in EAN as compared with those found in water and the other "water-like" properties observed in EAN. However, as stated in the Discussion, the magnitudes of ΔG_s° and ΔS_s° of nonpolar species in a given solvent are inadequate criteria of water-like behavior because the magnitude of ΔG_s° is mainly determined by the cohesive energy of the solvent, and the magnitude of ΔS_s° can be due to effects other than those operating in water. Similarly, the results of micellization and of heat capacities of solution obtained in EAN are not in mutual contradiction, and the cmc measurements in EAN cannot by themselves establish the water-like character of this salt. This can be supported by the following facts. As is apparent from our work and from the literature, $\Delta C_{p_2}^\circ$'s of nonpolar solutes in aqueous urea solutions are lower than those in water.[34,62] On the other hand, the presence of urea in water does not affect cmc's substantially.[63] Furthermore, micelle formation has also been observed in nonaqueous solvents such as ethylene glycol, glycerol,[63a,64] or another organic fused salt, pyridinium chloride.[65] Hence, it appears that the heat capacities of solution for nonpolar solutes and cmc's reflect two different processes caused by different water properties.

In order to answer the question of which solvent properties do indeed distinguish water from all other highly polar solvents, we must go back to Frank and Lumry and their recent reexamination of the hydrophobic effect.[7,66] A suggestion by Benzinger that enthalpy as well as entropy consists of two components formed a point of departure for Frank and Lumry's reasoning.[67] According to Benzinger, the first components, intrinsic enthalpy and motive entropy, contribute to the free energy while the second components, enthalpy and entropy of fluctuation, cancel one another and, therefore, do not contribute to the free energy. Indeed, it has become clear that the abnormal thermodynamic behavior of *cold* water is entirely due to fluctuations. This also means that other solvents with properties nearly identical with those of water, except the fluctuations, can mimic "inhibited water".

Frank suggested hydrazine and showed that the ΔG_t° for transfer of Ar from cyclohexane to hydrazine is even larger than that for transfer from cyclohexane to water, whereas ΔH_t° is large and positive and ΔS_t° nearly zero. As a result, the ΔG_t° value for the transfer of Ar from hydrazine to water is small because of the cancellation of a large negative ΔH_t° by a large negative ΔS_t°.[7,66] This demonstrates that the large negative entropy of solution for nonpolar molecules in water is used incorrectly in explanations of their low solubility which is solely due to the high cohesive energy of water and the energy required for cavity formation. However, the dissolution of nonpolar species is coupled with a process which shifts the fluctuation equilibrium toward cluster formation. This restructuring of water around nonpolar species, demonstrated in several studies,[68] is characterized not only by a loss of entropy but also by a loss of enthalpy and is thus a spontaneous process. The solubility of nonpolar solutes in *cold* water is indeed enhanced by hydrophobic hydration.[54]

From the vantage point of this paper, we would like to stress again that only those properties which are due to the effects of solute or temperature on the fluctuations of cold water between forms of different geometry and density distinguish water from other associated liquids. The uniqueness of water lies solely in these properties. On the other hand, the properties which reflect its high cohesive energy may also be found in other liquids.

It appears from this work that the $\Delta C_{p_2}^\circ$'s for nonpolar solutes remain as a property which clearly distinguishes water from other

---

(57) Green, W. J.; Field, P. E. *J. Phys. Chem.* **1980**, *84*, 3111–4.

(58) (a) Subramanian, S.; Balasubramanian, D.; Ahluwalia, J. C. *J. Phys. Chem.* **1969**, *73*, 266–9. (b) Subramanian, S.; Sarma, T. S.; Balasubramanian, D.; Ahluwalia, J. C. *Ibid.* **1971**, *75*, 815–20. (c) Bonner, O. D.; Bednarek, J. M.; Arisman, R. K. *J. Am. Chem. Soc.* **1977**, *99*, 2898–902.

(59) Bonner, O. D.; Cerutti, P. J. *J. Chem. Thermodyn.* **1976**, *8*, 105–12.

(60) Frank, H. S.; Franks, F. *J. Chem. Phys.* **1968**, *48*, 4746–57.

(61) (a) Ben-Naim, A. *J. Phys. Chem.* **1968**, *72*, 2998–3001. (b) Lumry, R.; Battistel, E.; Jolicoeur, C. *Symp. Faraday Soc.*, in press.

(62) (a) Kresheck, G. C. *J. Chem. Phys.* **1970**, *52*, 5966–7. (b) Sarma, T. S.; Ahluwalia, J. C. *J. Phys. Chem.* **1972**, *76*, 1366. (c) Chawla, B.; Sunder, S.; Ahluwalia, J. C. *Ibid.* **1973**, *77*, 2335. (d) Prasad, K. P.; Ahluwalia, J. C. *Biopolymers* **1980**, *19*, 273–84.

(63) (a) Kresheck, G. C. In ref 5, pp 95–167. (b) Mukerjee, P.; Mysels, K. J. "Critical Micelle Concentrations of Aqueous Surfactant Systems"; U.S. Government Printing Office, Washington, D.C.; *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand.* No. 36. (c) Fendler, J. H.; Fendler, E. J. "Catalysis in Micellar and Macromolecular Systems"; Academic Press: New York, 1975; pp 306–10.

(64) (a) Reference 63c; pp 320–5. (b) Ionescu, L. G.; Fung, D. S. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2503–6.

(65) Reinsborough, V. C. *Aust. J. Chem.* **1970**, *23*, 1473–5.

(66) Lumry, R. "Bioenergetics and Thermodynamics: Model Systems"; Braibanti, A., Ed.; Reidel Publishing Co.: Dordrecht, Holland, 1980; pp 405–23.

(67) Benzinger, T. H. *Nature (London)*, **1971**, *229*, 100–2.

(68) (a) Hallenga, K.; Grigera, J. R.; Berendsen, H. J. C. *J. Phys. Chem.* **1980**, *84*, 2381–90, and references therein. (b) Rossky, P. J.; Karplus, M. *J. Am. Chem. Soc.*, **1979**, *101*, 1913–37. (c) Rapaport, D. C.; Scheraga, H. A. *J. Phys. Chem.* **1982**, *86*, 873–80.

solvents. However, the properties which are usually considered as characteristic of the hydrophobic effect (i.e., low solubility of nonpolar molecules and association of nonpolar species in water) are unrelated to the unique fluctuational situation in water.

As mentioned above, the studies in EAN suggest that the fluctuation behavior is not a prerequisite for micellization at least as far as cmc's are concerned. Recent work of Evans and Wightman on micelle formations above 100 °C in water provides further supporting evidence.[69] Cmc's determined for tetradecyltrimethylammonium bromide in water from 25 to 166 °C increased only 10-fold over this temperature range. The peculiar behavior of water, however, gradually disappears as the temperature is increased, and water begins to behave more like a regular liquid. Hence, the interesting question of how the restructuring of water around the hydrocarbon chains influences the cmc's as well as their aggregation numbers remains open.

Conclusion

In view of the crucial role of water to terrestrial processes, especially biological ones, it is of great importance to separate those of its properties which are essential to hydrophobic interactions from those which are correlated, but largely irrelevant. The Benzinger-Frank-Lumry analysis preserves most of the Frank-Evans picture of water structure but removes the emphasis on entropies and heat capacities of solution as factors of commanding importance to the hydrophobic behavior of water as a solvent. The recent studies of Evans and his associates and the results presented here are the first tests of this change in viewpoint and strongly confirm it through thermodynamic properties for solution of nonpolar gases in EAN, and through its ability to produce micelles from surfactants. Its failure to demonstrate water-like heat capacity behavior serves to differentiate those properties of water which are due to fluctuations between different isomeric states, from those which are caused by its high cohesive energy.

Acknowledgment. This work was supported by NSF Grant CHE-8006202 to E.M.A. We appreciate the help of Mr. Andrew Maynard supported by the NSF Undergraduate Research Program. We are much indebted to Professors D. F. Evans, R. Lumry, and H. S. Frank for sharing viewpoints and results prior to publication.

Registry No. H_2O, 7732-18-5; methanol, 67-56-1; 1-butanol, 71-36-3; 1-pentanol, 71-41-0; DMSO, 67-68-5; DMF, 68-12-2; NMF, 123-39-7; ethylene glycol, 107-21-1; EAN, 22113-86-6; urea, 57-13-6.

---

(69) Evans, D. F.; Wightman, P. J. *J. Colloid Interface Sci.* **1982**, *86*, 515-24.

Novel Photoreversible Cyclization of Acyl-Substituted 2,4,6-Triisopropylbenzophenones[1]

Yoshikatsu Ito,* Brij Pal Giri, Masaaki Nakasuji, Toshiya Hagiwara, and Teruo Matsuura

Contribution from the Department of Synthetic Chemistry, Faculty of Engineering, Kyoto University, Kyoto 606, Japan. *Received July 19, 1982*

Abstract: A photoreversible cyclization of 3′(or 4′)-X-2,4,6-triisopropylbenzophenones **1** (X = C_6H_5CO, 2,4,6-(i-Pr)$_3C_6H_2CO$, CH_3CO) into the corresponding **2** was investigated in benzene at 313 nm. When the meta (2,4,6-(i-Pr)$_3C_6H_2CO$) derivative **1d** was photolyzed, an additional product, 1,1′-(*m*-phenylene)bis(benzocyclobutenol) (**3d**), arising from further photocyclization was also obtained. On the contrary, the para (2,4,6-(i-Pr)$_3C_6H_2CO$) derivative **1c** did not further photocyclize. Diene-quenching experiments of the back-photoreaction **2** → **1** revealed that cleavage of the C_1-C_2 single bond in the benzocyclobutenol ring occurred much faster with para (4′-X) substituents ($>10^{10}$ s^{-1}) than with meta (3′-X) substituents ($\sim 10^8$ s^{-1}). These results were explained by the difference in spin densities at the para and meta positions. The reaction **2** → **1**, where X is benzoyl group, can be categorized into a novel π^*-orbital-initiated photoreaction of simple substituted benzophenones.

Introduction

The excited states of simple aromatic ketones are characterized by extremely rapid and quantitative intersystem crossling ($k_{ST} > 10^{10}$ s^{-1}, $\phi_{ST} = 1.0$).[2] Hence, benzophenone and acetophenone are frequently used as typical triplet sensitizers completely free from complications due to singlet sensitization. The photoreactions of these ketones, e.g., hydrogen abstraction,[2] oxetane formation,[2] α-cleavage,[2] and others,[3] are usually interpreted in terms of singly occupied n-orbital initiation, explicitly considering in certain cases a bimolecular interaction of charge-transfer nature which occurs prior to actual bond formation (or rupture).[4] Indeed, π^*-orbital-initiated photoreactions of simple substituted benzophenones with $T_1(n,\pi^*)$ states appear so far to be unknown.[5]

Table I. Products and Isolation Yields from Photolyses of Acyl-Substituted 2,4,6-Triisopropylbenzophenones 1a-f in Benzene

starting material	irradiation time, h	photolyses products (isolation yields, %)
1a	3	2a (24), 1a (73)
1b	3	2b (63), 1b (30)
1c	7	2c (23), 1c (74)
1d	0.7	2d (25), 3d (60), 1d (7.5)
1e	2.5	2e (62), 1e (31)
1f	3	2f (73), 1f (13)

---

(1) Photoinduced reactions, part 141.

(2) See any standard textbook on photochemistry: for example, Turro, N. J. "Modern Molecular Photochemistry"; Benjamin/Cummings: Menlo Park, CA, 1978.

(3) For example: (a) Barwise, A. J. G.; Gorman, A. A.; Leyland, R. L.; Parekh, C. T.; Smith, P. G. *Tetrahedron* **1980**, *36*, 397. (b) Fox, M. A. *J. Am. Chem. Soc.* **1979**, *101*, 5339. (c) Nowada, K.; Hisaoka, M.; Sakuragi, H.; Tokumaru, K.; Yoshida, M. *Tetrahedron Lett.* **1978**, 137. (d) Davis, D. D.; Ahmed, F. U. *J. Am. Chem. Soc.* **1981**, *103*, 7653.

(4) For example, photoreduction by amines (Cohen, S. G.; Parola, A.; Parsons, G. H. *Chem. Rev.* **1973**, *73*, 141) and by phenols (Das, P. K.; Encinas, M. V.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 4154).

0002-7863/83/1505-1117$01.50/0 © 1983 American Chemical Society