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Thermodynamics of Aqueous Solutions of Alkyl p-Aminobenzoate

by

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Abstract

The solubilities of a series of alkyl p-aminobenzoates were determined in water at three temperatures. The solutes chosen were the methyl through the n-butyl p-aminobenzoates and the temperatures studied were 25°, 33° and 40°. These compounds present a chemically related series differing by methylene additions in incremental steps. The solubility determinations at various temperatures enabled calculation of thermodynamic elements in aqueous systems.

A recurrent non-linear pattern was obtained in the calculated and experimentally derived thermodynamic values of enthalpy, entropy, and free energy. However, an approximately linear relationship of chemical structure and the partial excess free energy for these solutes was found for these aqueous solutions.

Introduction

In this study, the solubilities of a homologous series of alkyl p-aminobenzoates were determined in water at various temperatures. In this manner, the values of thermodynamic parameters could be obtained. The heats of fusion were available from the literature (1) and were also determined in these laboratories by differential scanning calorimetry. With these values and the entropies of

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fusion values, a complete spectrum of thermodynamic values could be obtained. The relationship of the log of actual mole fraction solubilities with reciprocal temperature allowed for the determination of the heats of solution (ΔH_s) and the entropies of solution (ΔS_s) which are related to the slopes and intercepts of these types of plots.

The ideal mole fraction solubilities could be calculated from the heats of fusion and from these experimentally derived quantities, mixing and excess functions could also be calculated.

Activity coefficients can also be obtained from the ratio of the ideal mole fraction solubilities to the actual mole fraction solubilities. An additional thermodynamic parameter - the partial excess free energy of the solute could also be calculated from this data as well. The partial excess free energy of the solute is generally considered to be an overall property of the solution.

Some useful information about the overall solution process in terms of the various free energy functions might be anticipated from this study. It was felt that a relationship of the thermodynamic elements and the number of methylene groups in this short chemically related series might also be found.

Experimental

Chemicals - The following chemicals were used: methyl p-aminobenzoate[1], ethyl p-aminobenzoate[2], n-propyl p-aminobenzoate[3], n-butyl p-aminobenzoate[4] and water, distilled and deionized.

Equipment - The following equipment was used: a melting point apparatus[5], a spectrophotometer[6], a temperature control unit[7], a balance[8] and an electrobalance[9].

Heat of fusion values - by the method previously described (2).

Solubility determination - The solubility of the four aminobenzoate esters in water was determined by the following procedure. Each solute, in an amount in excess of its solubility, was placed in a screw capped vial[10] with water. The vials were sealed with adhesive tape. Vials were rotated at 28 rpm in a large constant temperature (± 0.2°) water bath and maintained successively at 25, 33 and 40 degrees.

After an equilibrium solubility was attained, at about 24 hours of continuous rotation[11], each of the six sample[12] vials were removed in succession for assay, with triplicate runs of each solute. The exterior of the vial was quickly dried, the sealing tape removed, and the cap was carefully removed to prevent water contamination. A filtered aliquot of the saturated solution was pipetted into tared containers, weighed and appropriately diluted for spectrophotometric assay with 95% ethanol to give a final concentration of the solute in the range of 1-5 μg/ml. All pipettes were prewarmed to prevent thermal precipitation and each had a pleget of fiber glass wrapped around its tip to act as a filter. The variation in solubility values was about 5% for the methyl derivitive and fell to about 3% for the butyl derivitive.

Spectrophotometric determinations - The spectrophotometer was calibrated for each aminobenzoate ester at its wavelength of maximum absorbance, at concentrations up to 15 g/ml. in 95% ethanol, in matched silica cells. A least squares method was used to determine the statistical significance ($\alpha = 0.0001$) of the linear relationship between absorbance and concentration, i.e., the Beer's law equation. The molar absorptivities were very close in value, varying from 2.05 for the methyl, ethyl and propyl ester to 2.07 for the butyl ester.

Results and Discussion

The experimental solubility for each of the solutes in this study are given in Table I in terms of mole fraction. The solubility of the methyl derivative was highest and solubility decreased with increasing carbon number for this series and increased with increasing temperature. Using the log of the determined mole fraction and plotting it as a function of reciprocal temperature gave linear relationships which are shown in Figure 1. From these plots, the slopes and the intercepts were obtained by least squares and which are related to the enthalpy of solution and the entropy of solution, respectively.

These plots show linearity for each solute but are not parallel to one another inciating the expected variations in the enthalpy and entropy of solution values.

In Table II, ideal mole fraction solubilities for these solutes are given at the three temperatures used in this study (2). The ideal mole fraction solubility values given would obtain for any solution with which an ideal solution forms. These ideal values would be expected to be far in excess of the actual solubilities in water, since aqueous solutions would be highly nonideal due to hydrogen and dipole interactions in the solvent. All of the values shown are greater than 0.1 with respect to mole fraction rising progressively to a value 0.66 for the n-butyl derivative at 40°C. The actual mole fraction solubilities that were determined were about 10^{-4} and the resultant activity coefficients would be expected to be large in magnitude. The activity coefficients were calculated and are given in Table III.

These "activity coefficients" values ran from about 600 to 29,000 for these solutes in water over the temperature range studied.

In Table IV, the thermodynamic elements for these solutes are given for the enthalpies of fusion, solution and mixing, the entropies of fusion, solution and mixing as well as the ideal, actual and excess free energy of these systems.

The heats of fusion of these compounds varied only slightly from each other having a magnitude of about 5 kcal./mole, however, there was no pattern observed with respect to the magnitude and carbon number. The enthalpy of solution and mixing showed dramatic changes in value for this short chemical series of substances. The enthalpy of solution for the first three members of this series decreased in a nonlinear fashion but the fourth in the series, the n-butyl derivative dramatically increased from the n-propyl derivative by about 7 Kcal./Mole. The heat of mixing likewise showed substantial differences in magnitude over this short series. The heat of enthalpy of mixing is derived from the enthalpy of solution, and in this case, it can be seen that the methyl and ethyl derivatives are close in value whereas the n-

Table I - Summary of the experimentally determined mole fraction solubility for the alkyl p-aminobenoates at various temperatures

Solute	Actual mole fraction solubility x 10^4		
	25^o	33^o	40^o
Methyl	1.93	2.52	3.32
Ethyl	1.12	1.47	1.86
n-Propyl	0.64	0.76	0.94
n-Butyl	0.15	0.25	0.40

Table II - Summary of the calculated mole fraction solubility for the alkyl p-aminobenzoates in water at the temperatures noted

Solute	Ideal mole fraction solubility		
	25^o	33^o	40^o
Methyl	0.1369	0.1722	0.2084
Ethyl	0.2195	0.2741	0.3299
n-Propyl	0.3100	0.3866	0.4648
n-Butyl	0.4319	0.5457	0.6632

Table III- Summary of the calculated activity coefficients for the alkyl p-aminobenzoates in water at the temperature noted.

Solute	Activity Coefficients		
	25^o	33^o	40^o
Methyl	709	683	628
Ethyl	1959	1864	1774
n-Propyl	4844	5087	4945
n-Butyl	28,660	21,826	16,533

Table IV - Summary of the thermodynamic values obtained for the Alkyl p-aminobenzoates in water

	Enthalpy (cal/mole)			Entropy (cal/deg-mole)			Free Energy (cal/mole)		
Solute	Fusion	Solution	Mixing	Fusion	Solution	Mixing	Ideal	Actual	Excess
Methyl p-aminobenzoate	5180	6620	1440	13.4	5.2	-8.3	1175	5070	3895
Ethyl p-aminobenzoate	5030	6260	1230	13.9	2.9	-11.0	895	5396	4501
n-Propyl p-aminobenzoate	5000	4720	-280	14.5	3.4	-11.1	691	3707	3016
n-Bentyl p-aminobenzoate	5290	11950	6660	16.1	18.0	+1.9	495	6584	6089

propyl derivative possesses a small negative enthalpy of mixing and the n-butyl derivative possesses a large positive enthalpy of mixing.

The entropy of fusion values shown in Table IV possess reasonable values and it can be seen that these increase with increasing carbon number in a nonlinear fashion. The entropy of solution values for the aqueous solutions of these substances vary from one another with the ethyl derivative possessing a minimum value of 2.9 cal./deg.-mole and the n-butyl derivative possessing a value of 18 cal./deg.-mole. The entropy of mixing also show quite variable results with negative values for the first three members of this series, whereas, the n-butyl derivative has a slight positive value. In order to view the overall thermodynamics, the free energy function must be considered, and these values are also given in Table IV. The ideal free energy values obtained from the enthalpy and entropy of fusion are seen to decrease with carbon number in a linear fashion. This would indicate that even when both the enthalpy and the entropy of fusion are nonlinear, the changes in the magnitude of these values leads to a linear relationship with respect to the overall free energy effect.

The actual and the excess free energy, a composite of the solution enthalpy and entropy give values such the n-propyl derivative is at a minimum value with the n-butyl derivative spiking with a change of about 3 kcal. higher than the n-propyl ester.

In Figure 2, the enthalpies of fusion, mixing and solution are shown in terms of Kcal./mole versus the number of carbons in the n-alkyl ester substitution. The enthalpy of fusion is seen to be nonlinear with a minimum occurring for the n-propyl ester. The curves for the enthalpy of a solution and mixing give an irregular pattern with minimum also occurring for the three carbon propyl group with the butyl ester increasing substantially over the propyl ester.

In Figure 3 the entropy value in cal./deg.-mole for fusion, solution and mixing are given. The entropy of fusion is seen to increase in a nonlinear fashion with carbon number. In the manner similar to enthalpy a minimum is observed for the propyl derivative

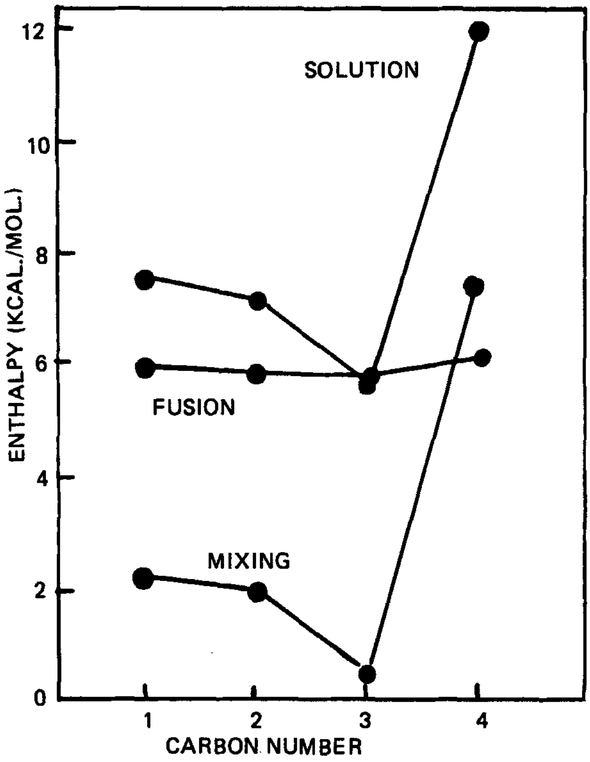

FIGURE 1: A plot of the mole fraction (log.) solubility as a function of reciprocal temperature for the noted alkyl p-aminobenzoates

followed by a large positive effect with the butyl derivative.

The overall effect of these two individual parameters upon free energy is shown in Figure 4 where the free energy in Kcal./mole has also been plotted as a function of the carbon number. Here it can be seen that the ideal free energy is a linear function decreasing with increasing carbon number. Both the actual and excess free energy curves possess a shape which is predicated on enthalpy and entropy values. The methyl and ethyl esters are similar in value, a sharp minimum occurring for the n-propyl derivative, then a large sharp positive rise for the n-butyl ester. These solutes in water do not show any pattern with respect to thermodynamic values and

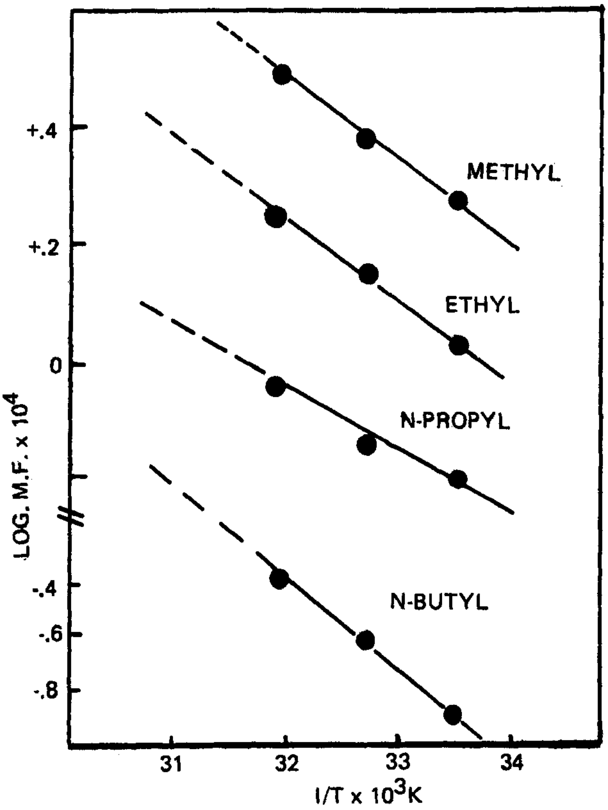

FIGURE 2: A plot of the various enthalpy values in Kcal./mole as a function of the carbon number of the n-alkyl group

chemical structure. The rather large values obtained for the actual and excess free energy probably imply these aqueous systems are highly nonideal and require energetic input such as temperature to just slightly increase the magnitude of solubility.

An additional thermodynamic parameter was investigated for its utility to see if a relationship of the thermodynamic values and chemical nature could be obtained. The partial excess free energy of the solute, $\overline{F}_2^E$ (3, 4) can be considered as an overall property of the solution and was also used since these values could be calculated from these results.

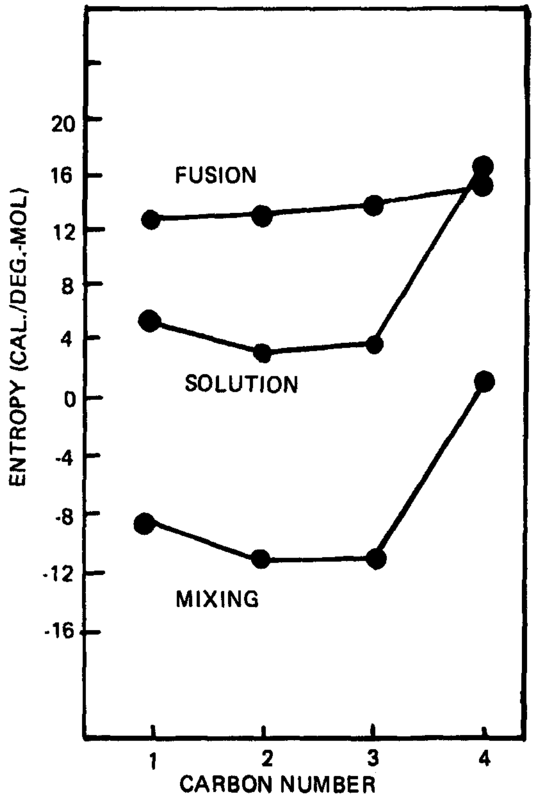

FIGURE 3: A plot of the various entropy values in cal./deg.-mole as a function of the carbon number

The partial excess free energies are obtained from activity coefficients, although previously shown to be very large in magnitude, still lead to reasonable results for this thermodynamic function. These values were calculated and are shown in Table V. Relatively large positive values were obtained indicating a positive deviation from Raoult's Law implying the highly non-ideal nature of these dilute solutions.

In Figure 5, the values of the excess partial free energy at each temperature for the solutes has been plotted as a function of the carbon number of the alkyl ester group. In this case, an approximately linear relationship is observed with a slope of about

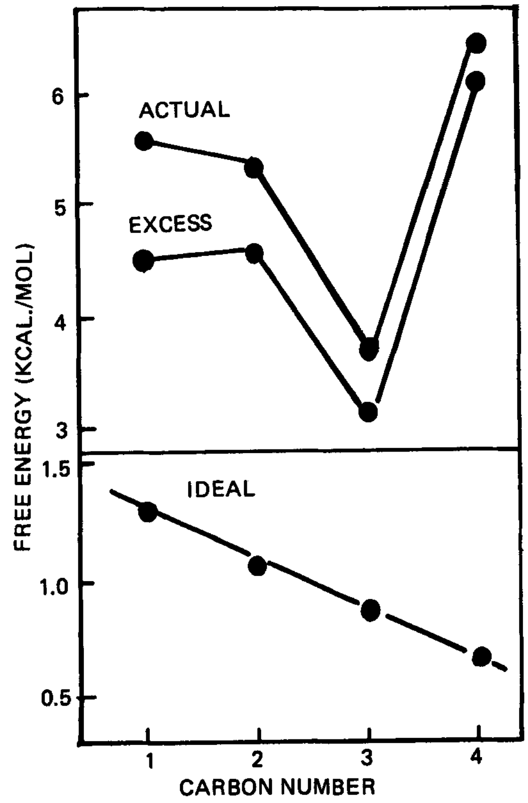

FIGURE 4: A plot of the various free energy values in Kcal./mole as a function of carbon number

Table V - Summary of the Solute Partial Free Energy for the Alkyl p-Aminobenzoates in water at the temperatures noted

Solute	Partial Excess Free Energy, $\bar{F}_2^E$ (cal/mole)		
	25°	33°	40°
Methyl	3873	3952	4002
Ethyl	4473	4557	4647
n-Propyl	5008	5168	5284
n-Butyl	6060	6050	6036

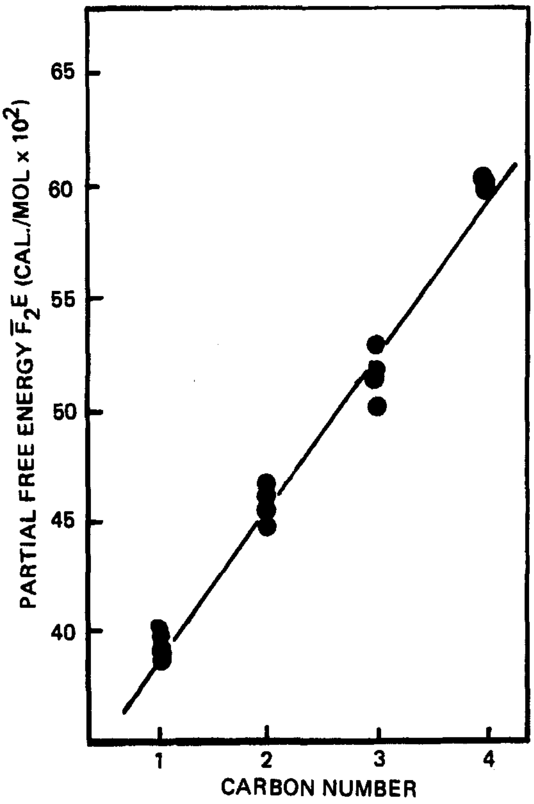

FIGURE 5: A plot of the partial excess free energy of the solute, $\bar{F}_2^E$ in cal./mol. as a function of the carbon number.

500 calories/carbon atom. This linear relationship then allows for a definitive relationship of a thermodynamic parameter and molecular structure. Specifically, the change in the partial excess free energy is linearly related to the incremental increase of the alkyl group assuming the remainder of the molecule has a constant effect. This linear relationship has previously been obtained for aqueous solutions of parabens as well (5).

Conclusions

The thermodynamic elements for aqueous solutions of alkyl p-aminobenzoates has been determined from experimentally determined solubilities at various temperatures and heat of fusion data.

A wide spectrum of thermodynamic values were considered in attempting to find a relationship with the molecular structure of these esters. A linear relationship of the partial excess free energy of the solute with carbon number of the alkyl group was found possessing a slope of 500 calories per carbon atom.

Specifically, an approach to highly non-ideal solubility behavior or dilute semi-polar nonelectrolytes in aqueous systems relative to their thermodynamics has been given.

Finally, a spectrum of thermodynamic values can be readily obtained for any chemical series by determining solubility as a function of temperature once the heat of fusion is available or has been determined.

FOOTNOTES

1. Lot 3403 Eastman Chemical Co., Rochester, NY
2. Lot EX 305 Matheson, Coleman and Bell, Norwood, Ohio
3. Lot 3, City Chemical Co., supplied through courtesy of Astra Pharmaceutical Products, Worcester, MA.
4. Lot 7, Matheson, Coleman and Bell, Norwood, Ohio
5. Thomas-Hoover, 6404, A.H. Thomas Co., Philadelphia, PA
6. Cary Model 16, Cary Instruments, Monrovia, CA
7. Porta-Temp, Precision Scientific Co., Chicago, IL
8. Mettler H6T, Mettler Insturment Corp., Princeton, NJ
9. Cahn Electrobalance Model 18, Cahn Instruments, Paramount, CA
10. Lined with Teflon
11. Previous studies showed that this time was sufficient to attain saturated solutions at 25°.
12. Only 3 samples in triplicate of propyl p-aminobenzoate were used because of its scarcity

References

(1) S. H. Yalkowsky, G. L. Flynn and T. G. Slonick, J. Pharm. Sci. 61, 853 (1972)

(2) P. A. Schwartz and A. N. Paruta, J. Pharm. Sci. 65, 252 (1976)

(3) J. H. Hilderbrand and R. L. Scott, "The Solubility of Nonclectrolytes", 3rd Ed., Reinhold, N. Y., 1949, p. 44

(4) Ibid, P. 14.

(5) A. N. Paruta, K. S. Alexander, B. Laprade, J. W. Mauger; J. Pharm. Sci., 67, 624 (1978)