# Partial molal volumes of *n*-alkyl *p*-aminobenzoates in nonpolar solvents

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## Summary

The partial molal volumes of ethyl and *n*-butyl *p*-aminobenzoate were determined in seven solvents, including benzene, toluene, carbon tetrachloride, cyclohexane, *n*-dodecane, *n*-heptane and *n*-hexane. These *p*-aminobenzoates were found to have statistically larger partial molal volumes in the long-chain and cyclic alkanes than in the remaining five solvents. The higher partial molal volumes would contribute to deviations from ideal entropies of mixing in the form of excess volumes of mixing. Estimates of the solubility parameters for ethyl and *n*-butyl *p*-aminobenzoate were revised using the experimental partial molar volumes and solubility data for these two solutes in each of the seven solvents. The revised solubility parameters indicate that the experimental volumes do not reduce the previously reported variation in the solubility parameter when estimated from solubilities in these seven solvents. Consideration of the entropy of mixing in light of the experimental volumes showed no advantage over the assumption of an ideal entropy of mixing.

## Introduction

Regular solution theory has proved to describe adequately the solution behavior of nonelectrolytes in nonpolar solvents. In regular solution theory, interaction energies in solution are assumed to be independent of temperature, being dependent only on the orientation and the distance between molecules. The solute and solvent molecules should be similar in size, and distribution and orientation of the molecules in solution

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must be random for this theory to apply. There should be no change in volume at constant pressure upon mixing the species (Scatchard, 1934). At the heart of regular solution theory is the concept of the cohesive energy density. For the pure solute or solvent, the cohesive energy density is defined as the energy of vaporization divided by the molar volume. The cohesive energy density of the mixture of solute and solvent is not so easily assigned. Scatchard (1931, 1934) assumed that the cohesive energy density of a binary mixture meeting the basic assumptions cited above could be estimated by the geometric mean of the cohesive energy densities of the pure solute and solvent. In his 1956 review, Scott stated

that this theory fits the Gibbs free energy data on most binary systems of nonelectrolytes to within 10–20%. However, it is less successful for enthalpies and entropies of mixing (Scott, 1956).

Hildebrand et al. (1970) warn that the theory should not be applied when there is reason to believe that the molecules are not randomly distributed or the geometric mean assumption for the cohesive energy density of the mixture does not hold. In real solutions, even for simple mixtures, the assumptions of zero excess entropy and no volume change on mixing are often not valid. However, in the absence of polar or chemical interactions, there appears to be a considerable cancellation between enthalpic and entropic errors (Scatchard, 1934). As a first approximation, then, regular solution theory has a wider range of application to solutions of nonelectrolytes than does any other theory. A serious failure in the application of the theory implies that one or more of the fundamental assumptions does not hold (Scott, 1956).

A previous study examined the application of regular solution theory to $n$-alkyl $p$-aminobenzoates in nonpolar solvents, including $n$-hexane, $n$-heptane, $n$-dodecane, cyclohexane, carbon tetrachloride, toluene and benzene (Neau et al., 1989). Deviations, in the form of unexpectedly low solubilities, were seen with the $n$-dodecane and cyclohexane solutions. Solubilities in the five remaining solvents established a consistent, solvent-independent value for the solubility parameter of the solute. This value, in theory, could be used to predict the solubility of that solute in other nonpolar solvents which have a known solubility parameter. Predicted solubilities for these solutes in $n$-dodecane and cyclohexane, based on the solubility behavior in the five remaining solvents, were higher than experimental values.

There have been reports of unexpectedly low solubilities for simple aromatics in saturated long-chain alkane and cycloalkane solvents (Hildebrand et al., 1970; Funk and Prausnitz, 1970). The excess enthalpies and excess volumes of mixing associated with binary mixtures of aromatics and various organic compounds have also been reported (Oba et al., 1977; Kimura and Murakami, 1979; Cibulka and Holub, 1981; Barbosa and Lampreia, 1986). These reports indicate that, in long-chain and cyclic alkanes, aromatics experience an appreciable excess enthalpy and excess volume on mixing. If these excesses provide comparable contributions to the Gibbs free energy of the solution, a cancellation of errors can occur and the solubilities would still agree with theoretical values. In those cases where one contribution exceeds the other, deviations from theoretical solubilities exist. Efforts have been made to correct empirically for deviations from predicted solubilities by applying correction factors to the geometric mean (Funk and Prausnitz, 1970; Hildebrand et al., 1970; Preston and Prausnitz, 1970; Thomsen, 1971a,b, 1972; James et al., 1976; Oba et al., 1977; Martin et al., 1985a,b). The success of such factors indicates that the deviations are largely enthalpic in nature. The factors that are applied are not consistent enough, however, to provide a method for solubility prediction for all classes of nonpolar solutes and solvents (Neau, 1988).

In this report, the experimental partial molal volumes of $p$-aminobenzoates are presented. Measurement of thermodynamic equilibrium parameters can assist in describing and understanding molecular interactions of a solute with the solvent, other solutes or surfaces. Estimations of partial molal volumes are important to such fundamental concepts as solubility, partitioning into biophases and transport phenomena. However, in biological applications the medium may be complex and solution studies must begin with comparatively simple systems, such as these model nonpolar solvents.

The partial molal volume is defined as the instantaneous change in volume of a mixture with respect to a change in the number of moles of the component. The partial molal volumes of components in solutions that experience entropies of solution which agree with regular solution theory should confirm the molar volume of the solvent and provide a measure of the molar volume of a solid solute in its supercooled liquid state. The deviation from expected solubility behavior for the $p$-aminobenzoates in $n$-dodecane and cyclohexane may be due to a partial molal volume

greater than its partial molal volume in the other nonpolar solvents.

Liron and Cohen (1983) and Martin et al. (1985a) determined the partial molal volume of compounds by a densitometric method. A plot of the specific volume of the solution, $V_s$, which is the inverse of the density of the solution, as a function of the mass fraction of the solute, $y_2$, yields a curve. The tangent to the curve at a particular solute mass fraction can be used to calculate the partial specific volumes of the solute and the solvent in the solution defined by the solute mass fraction. The equation for the tangent to the curve at any $y_2$ gives the respective partial specific volume of the solute if $y_2$ is assigned the value of unity. By setting $y_2$ to zero, the tangent equation equals the respective partial specific volume of the solvent.

At mass fractions less than 0.01, the solution specific volume becomes linear with respect to the mass fraction (Martin et al., 1985a), presumably because the solvent partial specific volume does not appreciably change in these dilute solutions and in fact equals the specific volume of the solvent. The tangent to the curve in this linear portion has the same slope and intercept as the curve itself. When the tangent equation is a linear relation:

$$V_s = my_2 + b \tag{1}$$

the partial specific volume of the solvent, $V_{s1}$, is given by $b$, and the partial specific volume of the solute, $V_{s2}$, is the sum of $m$ and $b$. The partial molal volumes are the product of the molecular weight and the partial specific volume:

$$\bar{V}_1 = V_{s1}MW_1 \tag{2}$$

$$\bar{V}_2 = V_{s2}MW_2 \tag{3}$$

where MW is the molecular weight. Data generated by this technique have shown the variation in partial molal volume for organic solutes, both crystalline and liquid, in solvents of varying polarity (Martin et al., 1985a).

## Materials and Methods

### Chemicals and equipment

Ethyl $p$-aminobenzoate (Benzocaine) (99.9% pure by DSC) and $n$-butyl $p$-aminobenzoate (Butesin) (99.2% pure by DSC) were obtained from Sigma. Solvents were at least reagent grade purity. The temperature of the solution during density analysis was maintained at $25.00 \pm 0.01°C$ by a Neslab RTE 110 constant-temperature circulating bath. The densities of the solutions were determined to $\pm 0.00001$ g/cm$^3$ by a Mettler DA210 (Kyoto Electronics) densimeter which was standardized using dry air and degassed water.

The accuracy of the densimeter was tested by calculating the excess volumes of mixing for binary mixtures of cyclohexane and benzene, a system that is a standard in the literature for excess volume measurements. These test solution excess volumes agreed with literature data (Oba et al., 1977; Kimura and Murakami, 1979; Cibulka and Holub, 1981).

A comparison of results was then made between those solutions with abnormal behavior and the remaining solutions to determine if the partial molal volume of the solute is greater when the solubility is lower than predicted by regular solution theory using the solubilities in other solvents. Partial molal volumes were submitted to a one-way analysis of variance at the 5% significance level to test the effect of the different solvents employed in this study. In addition, Duncan's multiple range test, also at the 5% level of significance, was conducted to establish the grouping among the partial molal volume means in each of the solvents. Calculations were performed with the aid of SAS/STAT, version 6.03.

Using the experimental data, the solvent volume fraction, $\phi_1$, was calculated using the equation:

$$\phi_1 = \frac{X_1\bar{V}_1}{X_1\bar{V}_1 + X_2\bar{V}_2} \tag{4}$$

to be used in the full equation relating the mole fraction solubility to the solubility parameters

(Hildebrand and Scott, 1950; Chertkoff and Martin, 1960):

$$\ln X_2 = \frac{-\Delta \overline{H}_f}{RT_m}\left(\frac{T_m - T}{T}\right) + \frac{\Delta C_P}{R}\left[\left(\frac{T_m - T}{T}\right)\right.$$

$$\left. + \ln\left(\frac{T}{T_m}\right)\right] - \frac{\overline{V}_2 \phi_1^2}{RT}(\delta_1 - \delta_2)^2 \qquad (5)$$

where $\Delta \overline{H}_f$ is the enthalpy of fusion (in cal/mol), $T_m$ the melting point (K), $T$ the solution temperature (K), $\Delta C_P$ the differential heat capacity in cal/mol per K, $R$ the ideal gas law constant, 1.987 cal/mol per K, and $\delta$ the solubility parameter in $(cal/cm^3)^{1/2}$.

In ideal and in regular solution theory, the solute molar contribution to the entropy of mixing is given by:

$$\Delta \overline{S}_{2,mix} = -R \ln X_2 \qquad (6)$$

This is reflected in the $\ln X_2$ on the left-hand side of Eqn 5. If the solute molar entropy contribution cannot be considered ideal, several other estimation methods are available. Two equations were drawn from the literature which take into account the volumes occupied by the solution components. The first was (Hildebrand, 1949):

$$\Delta \overline{S}_{2,mix} = -R\left[\ln \phi_2 + \phi_1\left(1 - \frac{\overline{V}_2}{\overline{V}_1}\right)\right] \qquad (7)$$

and the second (Huyskens and Haulait-Pirson, 1985):

$$\Delta \overline{S}_{2,mix} = -R\left[\ln \phi_2 - 0.5\left(\frac{\overline{V}_2}{\overline{V}_1} - 1\right)\phi_1\right.$$

$$\left. - 0.5 \ln\left(\phi_2 + \phi_1\frac{\overline{V}_2}{\overline{V}_1}\right)\right] \qquad (8)$$

With the experimental partial molal volumes, mole fraction solubilities and volume fractions, and using literature values for the solvent solubil-

ity parameter (Hoy, 1970) and for the enthalpies of fusion, melting points and differential heat capacities (Neau, 1988; Neau and Flynn, 1990), a 'best-fit' solubility parameter could be generated using SAS software and Eqn 5. As a semi-empirical method of incorporating the volume changes into the model given in Eqn 5, the Hildebrand and the Huyskens and Haulait-Pirson expressions were each substituted for the ideal partial molal entropy of mixing for the solute in Eqn 5 and the 'best-fit' solubility parameters were again generated using the experimental and literature data.

## Results

Tables 1 and 2 report the number of data points which defined the linear portion, $n$; the correlation coefficient for the linear relation, $r$; and the solute partial molal volume, $\overline{V}_2$. The results of the Duncan's multiple range test are included in Tables 1 and 2.

Table 3 lists solubility parameters for ethyl and $n$-butyl $p$-aminobenzoate estimated by five different methods. The first are estimates based on additivity properties (Hoy, 1970). The second are previously reported best-fit solubility parameter for these esters, generated from the solubility data in the seven solvents of this study and an estimated molar volume at 25°C of 136.2 and 168.6 $cm^3$/mol for the supercooled liquid form of ethyl and $n$-butyl $p$-aminobenzoate, respectively (Neau et al., 1989). The third set of solubility parameters were calculated using a Gauss iterative method and Eqn 5 with literature values and the revised values for the partial molal volumes and the solvent volume fractions. The fourth and fifth sets were generated by substituting the Hildebrand and the Huyskens and Haulait-Pirson expressions for the partial entropy of mixing for the solute.

Table 4 presents the estimates of the solute contribution to the entropy of mixing using the ideal, Hildebrand and Huyskens and Haulait-Pirson equations and the experimental parameters.

TABLE 1

*Partial molal volumes of ethyl p-aminobenzoate*

| Solvent | $n$ | $r$ | $\bar{V}_2$ (cm$^3$/mol) |
|---|---|---|---|
| Benzene | 5 | 0.9992 | 141.5 |
|  | 9 | 0.9999 | 143.3 |
|  | 8 | 0.9998 | 146.1 |
|  | 8 | 0.9999 | 143.1 |
|  |  |  | 143.5 ± 1.9 [a] |
| Toluene | 8 | 0.9999 | 142.7 |
|  | 5 | 0.9980 | 144.1 |
|  | 8 | 0.9973 | 143.6 |
|  | 6 | 0.9996 | 142.8 |
|  |  |  | 143.3 ± 0.7 [a] |
| Carbon tetrachloride | 5 | 0.9995 | 144.2 |
|  | 8 | 0.9978 | 142.5 |
|  | 8 | 0.9999 | 143.4 |
|  |  |  | 143.4 ± 0.9 [a] |
| *n*-Dodecane | 6 | 0.9975 | 152.2 |
|  | 7 | 0.9997 | 152.1 |
|  | 9 | 0.9989 | 152.1 |
|  | 7 | 0.9958 | 152.9 |
|  | 6 | 0.9978 | 154.6 |
|  |  |  | 152.8 ± 1.1 [b] |
| Cyclohexane | 7 | 0.9976 | 151.1 |
|  | 10 | 0.9957 | 153.4 |
|  | 10 | 0.9973 | 152.2 |
|  | 7 | 0.9975 | 154.1 |
|  | 10 | 0.9957 | 153.3 |
|  |  |  | 152.8 ± 1.2 [b] |
| *n*-Heptane | 7 | 0.9975 | 149.3 |
|  | 5 | 0.9964 | 145.9 |
|  | 8 | 0.9979 | 150.1 |
|  | 7 | 0.9980 | 148.9 |
|  | 7 | 0.9996 | 151.5 |
|  |  |  | 149.1 ± 2.0 [c] |
| *n*-Hexane | 7 | 0.9960 | 144.2 |
|  | 6 | 0.9989 | 144.9 |
|  | 7 | 0.9960 | 144.2 |
|  | 5 | 0.9973 | 146.0 |
|  | 8 | 0.9983 | 144.3 |
|  |  |  | 144.7 ± 0.8 [a] |

[a,b,c] Mean values ± S.D. shown with the same letter are not significantly different (Duncan's multiple range test, $\alpha = 0.05$).

TABLE 2

*Partial molal volumes of n-butyl p-aminobenzoate*

| Solvent | $n$ | $r$ | $\bar{V}_2$ (cm$^3$/mol) |
|---|---|---|---|
| Benzene | 6 | 0.9999 | 177.3 |
|  | 8 | 0.9986 | 175.4 |
|  | 5 | 0.9999 | 177.8 |
|  |  |  | 177.0 ± 1.4 [a] |
| Toluene | 5 | 0.9999 | 177.1 |
|  | 6 | 0.9988 | 176.7 |
|  | 8 | 0.9984 | 176.2 |
|  | 10 | 0.9995 | 178.3 |
|  |  |  | 177.1 ± 0.9 [a] |
| Carbon tetrachloride | 5 | 0.9997 | 174.6 |
|  | 6 | 0.9994 | 177.7 |
|  | 8 | 0.9991 | 177.5 |
|  |  |  | 176.6 ± 1.7 [a] |
| *n*-Dodecane | 9 | 0.9990 | 183.3 |
|  | 10 | 0.9993 | 183.8 |
|  | 9 | 0.9992 | 186.1 |
|  | 7 | 0.9967 | 184.1 |
|  | 8 | 0.9996 | 183.1 |
|  | 8 | 0.9999 | 183.8 |
|  |  |  | 184.0 ± 1.1 [b] |
| Cyclohexane | 13 | 0.9996 | 184.5 |
|  | 14 | 0.9998 | 184.9 |
|  | 8 | 0.9979 | 180.0 |
|  | 9 | 0.9993 | 184.4 |
|  | 8 | 0.9992 | 183.2 |
|  |  |  | 183.4 ± 2.0 [b] |
| *n*-Heptane | 5 | 0.9967 | 180.7 |
|  | 8 | 0.9997 | 179.0 |
|  | 7 | 0.9994 | 177.9 |
|  | 7 | 0.9985 | 178.1 |
|  | 8 | 0.9967 | 180.5 |
|  |  |  | 179.2 ± 1.3 [c] |
| *n*-Hexane | 10 | 0.9995 | 175.3 |
|  | 12 | 0.9996 | 178.5 |
|  | 6 | 0.9999 | 174.3 |
|  | 6 | 0.9973 | 176.2 |
|  | 5 | 0.9986 | 179.3 |
|  |  |  | 176.7 ± 2.1 [a] |

[a,b,c] Mean values ± S.D. shown with the same letter are not significantly different (Duncan's multiple range test, $\alpha = 0.05$).

## Discussion

The partial molal volumes of the solvents were consistent and agreed with literature values for the molar volumes (Hoy, 1970). The correlation coefficients indicated that the solution specific volumes were linear with respect to the solute mass fraction at the concentrations of interest. The linearity of the data indicates that the microenvironment of the solute in solution is consistent as the solution is diluted. The data yielded mean values for the solute partial molal volume with a standard deviation in the range of 0.4–1.3% of the mean.

Tables 1 and 2 show that four of the solvents, benzene, toluene, carbon tetrachloride and n-hexane, provided a consistent value for the partial molal volume of the p-aminobenzoate. Partial molal volumes in n-heptane were both larger than in n-hexane. In n-dodecane and cyclohexane the solute partial molal volumes proved to be significantly larger than in the five remaining solvents. These larger volumes would result in excess volumes of mixing that were not anticipated in the regular solution theory treatment of the previous report.

In Table 3, the best-fit solubility parameters calculated using the experimental partial molal volumes and Eqn 5 agree with the previous solubility parameters which were estimated from the solubility data. The standard errors indicate that

the experimental partial molal volumes barely reduced the variation in the estimated parameter. Therefore, these larger partial molal volumes of ethyl and n-butyl p-aminobenzoate in n-dodecane and cyclohexane do not account for the deviations. The mean and standard error were not substantially different when calculated using either of the literature estimates for the solute contribution to the entropy of mixing given in Eqns 7 and 8. An examination of Table 4 reveals that these alternate expressions do not substantially alter the solute partial entropy of mixing for n-dodecane and cyclohexane solutions. It was expected that entropy contributions to mixing in these two solvents would be most affected by the larger solute partial molal volumes.

The solubility parameters calculated using Eqn 5 and the experimental parameters still possess a standard error comparable to that of the previously reported values even though the larger partial molal volumes were considered here. Substituting the solute partial entropy of mixing calculated by Eqn 7 or 8 for $-R \ln X_2$ does not substantially alter either the mean or the standard error of the solubility parameters. Nevertheless, it should be noted that the long-chain and cyclic alkane solutions again presented larger partial molal volumes for aromatic solutes. Cyclohexane, in particular, is employed as a model nonpolar solvent in solubility studies and in solubility parameter and partial molal volume deter-

TABLE 3

*Solubility parameters of ethyl and n-butyl p-aminobenzoate from solubility data*

| Ester | Estimated [a] | Previous [b] | Estimated | | |
|---|---|---|---|---|---|
| | $\delta$ | $\delta$ | $\delta$ [c] | $\delta$ [d] | $\delta$ [e] |
| Ethyl | 12.3 | 12.39 ± 0.16 [f] | 12.21 ± 0.13 | 12.23 ± 0.13 | 12.22 ± 0.13 |
| n-Butyl | 11.5 | 11.50 ± 0.23 | 11.40 ± 0.21 | 11.44 ± 0.18 | 11.40 ± 0.19 |

[a] Solubility parameter estimated from additive properties (Hoy, 1970).
[b] Solubility parameter estimated from solubilities in seven solvents using an estimated solute molar volume (Neau, 1988; Neau et al., 1989).
[c] Solubility parameter estimated from solubility in seven solvents accounting for the experimental solute partial molal volumes.
[d] Solubility parameter estimated from experimental data using the Hildebrand (1949) estimate of the entropy of mixing with respect to the solute.
[e] Solubility parameter estimated from experimental data using the Huyskens and Haulait-Pirson (1985) estimate of the entropy of mixing with respect to the solute.
[f] Mean ± asymptotic standard error calculated by a Gauss iterative method using SAS.

TABLE 4

*Calculated entropies of mixing for ethyl and n-butyl p-aminobenzoate*

| Ester | Solvent | Entropy of mixing (cal/mol per K) | | |
|---|---|---|---|---|
| | | Ideal [a] | Estimated [b] | Estimated [c] |
| Ethyl | *n*-Hexane | 14.0 | 14.1 | 14.1 |
| | *n*-Heptane | 13.9 | 13.9 | 13.8 |
| | *n*-Dodecane | 13.2 | 13.3 | 13.3 |
| | Cyclohexane | 13.7 | 13.9 | 13.8 |
| | Carbon tetrachloride | 9.30 | 9.38 | 9.36 |
| | Toluene | 6.22 | 6.28 | 6.24 |
| | Benzene | 5.40 | 5.54 | 5.42 |
| *n*-Butyl | *n*-Hexane | 12.0 | 12.1 | 12.0 |
| | *n*-Heptane | 11.7 | 11.8 | 11.8 |
| | *n*-Dodecane | 11.1 | 11.1 | 11.1 |
| | Cyclohexane | 11.1 | 11.5 | 11.3 |
| | Carbon tetrachloride | 2.98 | 3.24 | 3.14 |
| | Toluene | 2.38 | 2.54 | 2.48 |
| | Benzene | 2.23 | 2.48 | 2.38 |

[a] Entropy of mixing estimated from $-R \ln X_{2,\text{experimental}}$ (Neau et al., 1989).

[b] Entropy of mixing estimated by Eqn 7 (Hildebrand, 1949).

[c] Entropy of mixing estimated by Eqn 8 (Huyskens and Haulait-Pirson, 1985).

minations. These results should discourage an investigator from the use of cyclic or long-chain alkanes as model solvents in those studies involving aromatic solutes. Further studies are necessary to determine the underlying molecular level or thermodynamic causes for the reduced solubilities of the *p*-aminobenzoates in long-chain and cyclic alkanes.

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