Short Communication

The Volume Change of an Intra-molecular Methyl — Methyl Group Interaction in Water

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The question of the volume change associated with hydrophobic interactions is still not quite settled. This is due to the inherent difficulty of measuring the volume of adjacent, but non-covalently bonded molecules or groups in an interacting state. Although quite a few investigations have been concerned with the measurement of related volume changes, no method has so far provided direct information.

A review of these investigations has recently been given by Ben-Naim.[1] Among all thermodynamic quantities associated with hydrophobic interactions, the volume change has probably received the last attention. I consider this very unfortunate, because the effect of pressure on several kinds of biological structures is directly related to this volume change. In the study of the response of living organisms to high pressures, the volume change in hydrophobic interactions, therefore, becomes of vital importance.

Earlier methods of measurements have been based on the volume difference between two singly dispersed monomers and one "dimer" simulating two interacting monomers, e.g. the monomer methane (Me) and the "dimer" ethane (Et).[1] This measure suffers from two weaknesses: (1) The distance between the interaction groups in the "dimer" is characteristic of a covalent bond, which is not a realistic distance between two interacting groups or molecules. (2) There are two hydrogen atoms less in the "dimer" than in the two monomers.

Both these factors probably lead to a smaller volume of the "dimer" than that of a real pair of interacting molecules. In a survey of partial molar volumes of simple organic molecules, a consistent division into group volume increments shows that a

CH_3 group and a CH_2 group requires 26 and 16 cm³ mol⁻¹, respectively.[2] This leads to a supposed volume of a hydrogen atom of about 10 cm³ mol⁻¹. It may be a coincidence that previous experiments very consistently have given the result,

$$\delta V^{HI} = -20 \text{ cm}^3 \text{ mol}^{-1}$$

However, a considerably better molecular system for direct measurement of intramolecular hydrophobic interactions has been suggested by Ben-Naim and Wilf.[3] This system may be two isomeric dialkylaromates, like the two species used in this work.

The idea is that when two a alkyl groups are in the 1,2 position on a benzene nucleus they are able to interact, while in the 1,3 or 1,4 position they are not able to interact. Basically these isomers are the same molecule, and when in the 1,2 position, the interaction distance between the alkyl groups is realistic. The difference in thermodynamic properties between e.g. the 1,2 and the 1,3 species in water is, therefore, assumed to be due to the hydrophobic interaction.

Ideally, the dialkylbenzenes would have been most suitable for this measurement, but their low solubility in water prohibited their use. Instead, the more soluble dimethylphenols were chosen under the assumption that the OH group would not make any significant disturbance.

Experimental. Pure 3,4- and 3,5-dimethylphenol were purchased from Koch-Light Lab. Ltd. and purified by recrystallization from ethanol — water mixtures. A near saturated solution of the 3,4-compound and a slightly supersaturated solution of the 3,5-compound in distilled water were obtained at 0.0285 and 0.0495 M, respectively. Measurements of the densities of dilution series of these solutions were made by means of a Paar DMA 02C precision density meter. The accuracy was of the order of 5×10^{-6} g cm⁻³.

The apparent molar volume of the solute was determined from eqn. (1), where d_0 is the density of water, d_s the density of a solution of molality m and M_s the molar mass of the solute. By extrapolation, the partial molar volume at infinite dilution was determined. Due to the relative uncertainty at the low concentrations, the partial molal volume was

determined to within ± 0.5 cm^3 mol^{-1}.

Theory. A thorough theoretical treatment of the method has been given by Ben-Naim and Wilf[3] as far as the free energy change in the hydrophobic interactions, δG^{HI}, is concerned. Adopting their notation, we denote the 3,4- and 3,5-dimethylphenols by ϕ_{34} and ϕ_{35}, respectively.

$$V = (d_o - d_s)/(md_o d_s) + M_s/d_s \tag{1}$$

$$\delta V^{HI} = \left(\frac{\partial \delta G^{HI}}{\partial p}\right)_T \tag{2}$$

Using the definition (2), we can obtain the equations for the volume relations from the equations for the free energy relations. The volume change associated with the hydriphobic interaction between the two methyl groups in the 3,4-position is then given by eqn. (3).

$$\delta V^{HI}\{(3,5) \rightarrow (3,4)\} = \Delta V^\circ(\phi_{34}) - \Delta V^\circ(\phi_{35}) \tag{3}$$

The lh's represent the volume change associated with the process of transferring a methyl group from position 5 to position 4. On the rh's we have the standard volumes of transfer for the two dimethylphenols. These quantities are related to the measurable partial molal volumes $\bar{V}^\circ(\phi_i)$ by (4),[1]

$$\Delta V^\circ(\phi_i) = \bar{V}^\circ(\phi_i) - RT\beta_T \tag{4}$$

where β_T is the isothermal compressibility of water. Since we do not here work on the "dimer"

— monomer basis, the compressibility factors cancel, and measurements of the partial molar volumes immediately give us the quantity δV^{HI} by difference.

Results and discussion. The concentration dependence of the apparent molar volumes of 3,4- and 3,5-dimethylphenol is shown in Fig. 1. At infinite dilution, the partial molar volumes were found to be

$$\bar{V}(\phi_{34}) = 118.8 \pm 0.5 \text{ cm}^3 \text{ mol}^{-1}$$
$$\bar{V}^\circ(\phi_{35}) = 120.6 \pm 0.5 \text{ cm}^3 \text{ mol}^{-1}$$

Accordingly, subtraction gives

$$\delta V^{HI} = -1.8 \pm 0.5 \text{ cm}^3 \text{ mol}^{-1}$$

which is a volume change a magnitude smaller than calculated on the "dimer" — monomer basis. Now, this interaction situation may be a special case because the two methyl groups do not extend far from the benzene nucleus. This is to be expected from the hydrophobic interaction energies measured by Ben-Naim and Wilf.[3] They found that δG^{HI} was doubled in going from methyl to ethyl groups. However, the decreasing solubility of compounds with increasing chain length makes density measurements of larger molecules difficult.

It is interesting to compare the present result with similar results in a nonpolar liquid like CCl$_4$. Shahidi et al.[4] have investigated relations between partial molar volumes and steric effects of organic compounds in carbon tetrachloride. This solvent, of course, does not show hydrophobic effects. Anyhow, the *m*- and *p*-xylene have exactly the same partial
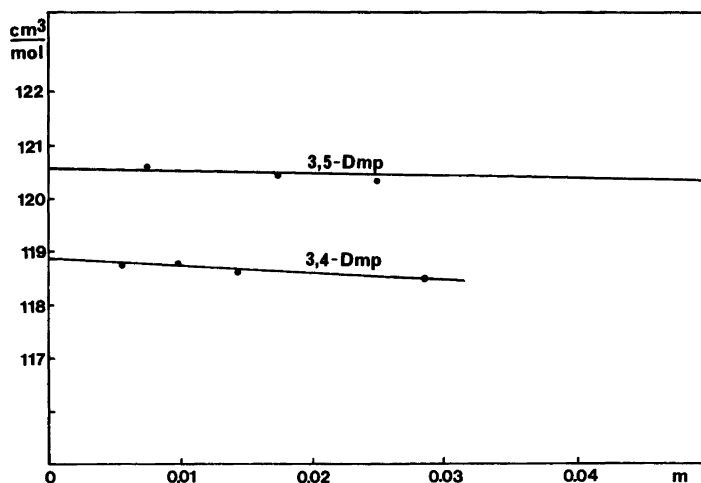

Fig. 1. Plot of apparent molar volume of the 3,4- and 3,5-dimethylphenols as functions of their molality m in water.

molar volumes, 124.4 cm^3 mol^{-1}, while the o-xylene have the volume 121.2 cm^3 mol^{-1}. Likewise, for m- and p-diethylbenzene, the partial molar volumes were found to be 152.2 and 151.9 cm^3 mol^{-1}, respectively, while the o-diethylbenzene volume was 148.4 cm^3 mol^{-1}. Thus in these intramolecular interactions there seems to be a general volume decrease regardless of solvent.[5] It can accordingly be questioned whether the volume decrease in water involves changes in water structure typical of hydrophobic interactions. It may be that most solvents create a more open structure around small groups, and that this structure is slightly disrupted by interaction. The interesting observation is, however, that the volume change in water is negative and smaller than previously believed.

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