

On the Salting Out of Benzene by Alkali Chlorides[†]

Giuseppe Graziano*

Dipartimento di Scienze Biologiche ed Ambientali, Università del Sannio, Via Port'Arsa 11 — 82100 Benevento, Italy

At room temperature, the addition of alkali chlorides to water causes a decrease in the benzene solubility. This salting out effect is studied by calculating the reversible work of cavity creation in hard sphere mixtures with the scaled particle theory formula and the reversible work of turning on benzene–solvent attractive interactions. This approach, notwithstanding its simplicity, is able to provide a rationalization of experimental data, showing that two geometric features of aqueous salt solutions, the volume packing density and the average value of the effective hard sphere diameter, are the main determinants of benzene solubility.

Introduction

The low solubility of nonpolar species in water is further decreased by the addition of salts, a phenomenon called salting out.¹ It is described by the empirical Setchenow equation^{1,2}

$$\log[c_A(\text{water})/c_A(\text{salt})] = k_S c_S \quad (1)$$

where $c_A(\text{water})$ and $c_A(\text{salt})$ are the molarity of the species A in water and aqueous salt solutions, respectively; c_S is the molarity of the salt in the aqueous solution; and k_S is the corresponding salting out constant. In the case of benzene, the values of k_S at $t = 25\text{ }^\circ\text{C}$ and $p = 0.1\text{ MPa}$ for several salts were determined by McDevit and Long³ more than 50 years ago. This work focuses attention on the salting out of benzene caused by alkali chlorides, and the corresponding k_S values are listed in the fourth column of Table 1.

The chemical potential of the solute species A in water and aqueous salt solution, respectively, can be written as⁴

$$\mu_A(\text{water}) = \mu_A^\bullet(\text{water}) + RT \ln c_A(\text{water}) \quad (2)$$

$$\mu_A(\text{salt}) = \mu_A^\bullet(\text{salt}) + RT \ln c_A(\text{salt}) \quad (3)$$

where $\mu_A^\bullet(\text{water})$ and $\mu_A^\bullet(\text{salt})$ are the so-called Ben–Naim standard chemical potentials of A in water and aqueous salt solutions, respectively. In a thermodynamic system in which the momentum partition function can be separated from the configurational integral (i.e., a system in which the translational degrees of freedom can be treated classically), the Ben–Naim standard chemical potential corresponds to the reversible work necessary to transfer a solute molecule from a fixed position in the ideal gas phase to a fixed position in the liquid phase at constant temperature and pressure.⁴ Therefore, $\mu_A^\bullet(\text{water})$ represents the coupling work between an A molecule and the surrounding water molecules, while $\mu_A^\bullet(\text{salt})$ represents the coupling work between an A molecule and the surrounding water molecules and ions of the salt (i.e., there is no need to consider an unrealistic extrapolation to infinite dilution or to unit mole fraction). This means that $\mu_A^\bullet(\text{water})$ and $\mu_A^\bullet(\text{salt})$ are two distinct quantities and cannot be equal because they account for different interactions. The use of the Ben–Naim standard chemical potential is strongly recommended in studying

Table 1. Experimental Values, at $t = 25\text{ }^\circ\text{C}$ and $p = 0.1\text{ MPa}$, of the Density and Water Molarity for Water and the Aqueous 1 mol·L^{−1} Alkali Chloride Solutions, Experimental Values of the Salting out Constant, k_S , for Benzene at $t = 25\text{ }^\circ\text{C}$ and $p = 0.1\text{ MPa}$, and the Corresponding Ben–Naim Standard Gibbs Energy, μ^\bullet , for the Hydration of Benzene in Water and Aqueous 1 mol·L^{−1} Alkali Chloride Solutions^a

c_S mol·L ^{−1}	ρ g·L ^{−1}	$c_{\text{H}_2\text{O}}$ mol·L ^{−1}	k_S	μ^\bullet kJ·mol ^{−1}
0	997	55.3	–	−3.6
1 LiCl	1022	54.4	0.141	−2.8
1 NaCl	1037	54.3	0.195	−2.5
1 KCl	1044	53.8	0.166	−2.7
1 RbCl	1085	53.5	0.140	−2.8
1 CsCl	1125	53.1	0.088	−3.1

^a The latter are obtained by means of eq 5.

solvation phenomena because it has a well-defined physical meaning and it can be directly obtained from measurable quantities.⁴

At thermodynamic equilibrium for the transfer of the solute species A between water and aqueous salt solution, the chemical potentials of A in the two liquid phases have to be equal, $\mu_A(\text{water}) = \mu_A(\text{salt})$, so that

$$\ln[c_A(\text{water})/c_A(\text{salt})] = [\mu_A^\bullet(\text{salt}) - \mu_A^\bullet(\text{water})]/RT \quad (4)$$

By combining eqs 1 and 4, one obtains

$$\mu_A^\bullet(\text{salt}) = \mu_A^\bullet(\text{water}) + 2.3RTk_S c_S \quad (5)$$

which implies that, from the experimental determination of $\mu_A^\bullet(\text{water})$ and k_S for a given salt, it is possible to calculate estimates of $\mu_A^\bullet(\text{salt})$ at the desired salt concentration.

Solubility data for benzene in water lead to $\mu^\bullet(\text{water}) = -3.6\text{ kJ}\cdot\text{mol}^{-1}$ at $t = 25\text{ }^\circ\text{C}$ and $p = 0.1\text{ MPa}$.⁵ By using the k_S values of alkali chlorides in eq 5, I have calculated μ^\bullet in aqueous 1 mol·L^{−1} salt solutions. The calculated values are listed in the fifth column of Table 1. It is evident that the $\mu^\bullet(\text{salt})$ values are negative in all 1 mol·L^{−1} alkali chloride solutions, but their magnitude is smaller than that in water, as a consequence of the salting out effect, even though the differences are not large. In particular, $\mu^\bullet = -2.8\text{ kJ}\cdot\text{mol}^{-1}$ in 1 mol·L^{−1} LiCl, $-2.5\text{ kJ}\cdot\text{mol}^{-1}$ in 1 mol·L^{−1} NaCl, $-2.7\text{ kJ}\cdot\text{mol}^{-1}$ in 1 mol·L^{−1} KCl, $-2.8\text{ kJ}\cdot\text{mol}^{-1}$ in 1 mol·L^{−1} RbCl, and $-3.1\text{ kJ}\cdot\text{mol}^{-1}$ in 1 mol·L^{−1} CsCl. These values reflect the trend of benzene

* Corresponding author. Phone: +39-0824-305133. Fax: +39-0824-23013. E-mail: graziano@unisannio.it.

[†] Part of the special issue “Robin H. Stokes Festschrift”.

solubility or the salting out ability of the different salts, which is a manifestation of the so-called Hofmeister effects.^{6,7} Actually, the alkali ions are normally quoted in the Hofmeister series in the order $\text{Li}^+ > \text{Na}^+ > \text{K}^+$ in terms of their salting out ability for hen egg white protein; according to benzene solubility data, the order is $\text{Na}^+ > \text{K}^+ > \text{Li}^+$, indicating that the solubility of globular proteins in aqueous solutions cannot be exactly described by that of benzene. The aim of the present study is to try to provide a molecular level rationalization of the benzene solubility trend in aqueous alkali chloride solutions.

Results

From the theoretical point of view,^{8–13} it is well established that hydration can be dissected in two subprocesses, cavity creation and turning on solute–solvent attractions, so that the Ben–Naim standard chemical potential of the solute species A is given by

$$\mu_A^\bullet = \Delta G_c + E_a \quad (6)$$

where ΔG_c is the reversible work spent to create a cavity in water or aqueous salt solution suitable to host the solute molecule and E_a is the energy gained by turning on solute–solvent attractive interactions. Note that the subscript A will be dropped in the following, and the symbol μ^\bullet will represent the Ben–Naim standard chemical potential of benzene in one of the considered liquid phases. Reliable values of ΔG_c are calculated by means of the scaled particle theory, SPT, formula for hard sphere mixtures¹⁴

$$\Delta G_c = RT\{-\ln(1 - \xi_3) + [3\xi_2/(1 - \xi_3)]\sigma_c + [3\xi_1/(1 - \xi_3)]\sigma_c^2 + [9\xi_2^2/2(1 - \xi_3)^2]\sigma_c^2\} \quad (7)$$

where $\xi_i = (\pi/6) \cdot \sum \rho_j \cdot \sigma_j^i$; ρ_j is the number density, in molecules per \AA^3 , of the species j ; and σ_j is the corresponding hard sphere diameter (i.e., the index j accounts for the components of the mixture, and in the present case, it goes from 1 to 3: 1 is water, 2 is the cation, and 3 is the anion). Note that: (a) $\xi_3 = (\pi/6) \cdot \sum \rho_j \cdot \sigma_j^3$ represents the volume packing density of the hard sphere mixture (i.e., of the solution); (b) σ_c is the diameter of the cavity, the spherical region from which all parts of the solvent molecules are excluded, and has to be equal to the diameter of the solute molecule (i.e., the diameter of the benzene molecule in the present case).

The pressure–volume work has been neglected in eq 7 because it is a negligible quantity by fixing $p = 0.1$ MPa, as recommended for the application of the SPT formula to real liquid solutions.⁸ The experimental density values of water and aqueous alkali chloride solutions at $t = 25$ °C and $p = 0.1$ MPa,^{15,16} listed in the second column of Table 1, have been used in performing calculations. A fundamental and critical point is the selection of the effective hard sphere diameter of the involved molecules and ions.¹⁷ I have selected: (a) $\sigma(\text{H}_2\text{O}) = 2.80$ \AA , which is close to the position of the first peak of the oxygen–oxygen radial distribution function of water¹⁸ and allows a satisfactory description of the cavity size distribution function of water by means of SPT;^{19,20} (b) $\sigma(\text{C}_6\text{H}_6) = 5.26$ \AA , that is the effective hard sphere diameter of benzene determined from the analysis of gas solubility data²¹ and is close to the first peak of the ring center–ring center radial distribution function of liquid benzene at room temperature, as determined from X-ray and neutron scattering measurements and computer simulations.^{22–24} The shape of this radial distribution function supports the approximation of treating a benzene molecule as spherical.

Table 2. Effective Hard Sphere Diameters Assigned to Alkali Cations, Volume Packing Density, at $t = 25$ °C and $p = 0.1$ MPa, of Water and Aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ Alkali Chloride Solutions, SPT Estimates of the Gibbs Energy of Cavity Creation ΔG_c , and Estimates of the Benzene–Solvent Interaction Energy E_a ^a

c_s $\text{mol} \cdot \text{L}^{-1}$	$\sigma(\text{M}^+)$ \AA	ξ_3	ΔG_c $\text{kJ} \cdot \text{mol}^{-1}$	E_a $\text{kJ} \cdot \text{mol}^{-1}$	$\Delta G_c + E_a$ $\text{kJ} \cdot \text{mol}^{-1}$	μ^\bullet $\text{kJ} \cdot \text{mol}^{-1}$
0	–	0.3830	41.3	–44.9	–3.6	–3.6
1 LiCl	1.52	0.3926	43.3	–46.0	–2.7	–2.8
1 NaCl	2.02	0.3934	43.5	–46.1	–2.6	–2.5
1 KCl	2.66	0.3933	43.3	–46.1	–2.8	–2.7
1 RbCl	2.96	0.3934	43.2	–46.1	–2.9	–2.8
1 CsCl	3.32	0.3940	43.1	–46.2	–3.1	–3.1

^a In the last two columns, the values of the $\Delta G_c + E_a$ sum are compared to the experimental values of the Ben–Naim standard Gibbs energy μ^\bullet for the hydration of benzene in water and aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions. See text for further details.

The hard sphere radii of the various alkali cations have been obtained by performing the difference between the M^+Cl^- distance observed in the crystals with the sodium chloride structure (as reported in Table 13-6 of Pauling's book²⁵) and the radius, 1.81 \AA , assigned to the Cl^- ion by Pauling himself. In this manner, the effective diameters are: $\sigma(\text{Li}^+) = 1.52$ \AA , $\sigma(\text{Na}^+) = 2.02$ \AA , $\sigma(\text{K}^+) = 2.66$ \AA , $\sigma(\text{Rb}^+) = 2.96$ \AA , $\sigma(\text{Cs}^+) = 3.32$ \AA , and $\sigma(\text{Cl}^-) = 3.62$ \AA (these values are listed in the second column of Table 2). These diameters are significantly smaller than the Lennard-Jones diameters selected to construct computer simulation models of aqueous salt solutions.²⁶ Actually, in computer simulation models, the ions possess charges to interact among each other and with water molecules. These strong electrostatic interactions lead to a decrease in their size so that their effective diameters prove to be close to the present ones, as emphasized by the location of the first peak in the relevant radial distribution functions.²⁶

By using the SPT eq 7, the estimates of the reversible work to create a cavity suitable to host C_6H_6 prove to be: $\Delta G_c = 41.3 \text{ kJ} \cdot \text{mol}^{-1}$ in water, $43.3 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ LiCl, $43.5 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ NaCl, $43.3 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ KCl, $43.2 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ RbCl, and $43.1 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ CsCl (see the fourth column of Table 2). It is worth noting that the ΔG_c estimate from SPT in water is reliable. At room temperature and $p = 0.1$ MPa, for a cavity suitable to host benzene, van Gunsteren and colleagues²⁷ found $\Delta G_c = 43.0 \text{ kJ} \cdot \text{mol}^{-1}$, and Schravendijk and van der Vegt²⁸ obtained $\Delta G_c = 41.8 \text{ kJ} \cdot \text{mol}^{-1}$. The fact that ΔG_c is always larger in aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions than in water is in line with both the increase in surface tension^{1,29} and the decrease in isothermal compressibility^{30,31} caused by the addition of these salts to water. On the other hand, ΔG_c increases on passing from $1 \text{ mol} \cdot \text{L}^{-1}$ LiCl to $1 \text{ mol} \cdot \text{L}^{-1}$ NaCl and then decreases in a continuous manner (the differences are always small), even though the volume packing density slightly increases, $\xi_3 = 0.3934$ for $1 \text{ mol} \cdot \text{L}^{-1}$ NaCl versus 0.3940 for $1 \text{ mol} \cdot \text{L}^{-1}$ CsCl.

In a pure liquid, according to SPT, the ΔG_c magnitude depends on two geometric properties:^{32,33} the molecular hard sphere diameter and the volume packing density of the liquid. Fixed the molecular size, ΔG_c increases on increasing ξ_3 : the void volume in the liquid decreases, so that the probability of finding a molecular-sized cavity decreases, leading to a ΔG_c increase. Fixed the volume packing density, ΔG_c increases on decreasing σ : the void volume is partitioned in smaller pieces so that the probability of finding a molecular-sized cavity decreases, leading to a ΔG_c increase. This analysis, with a small but conceptual change, can be applied also in the case of aqueous alkali chloride solutions. For the latter, an average value

of the effective hard sphere diameter should be defined and calculated according to the following relationship^{34,35}

$$\langle \sigma \rangle = \chi(\text{H}_2\text{O}) \cdot \sigma(\text{H}_2\text{O}) + \chi(\text{M}^+) \cdot \sigma(\text{M}^+) + \chi(\text{Cl}^-) \cdot \sigma(\text{Cl}^-) \quad (8)$$

where the χ_i are the molar fractions of the various species in the aqueous MCl solutions. It is readily verified, using data in Table 1, that $\langle \sigma \rangle = 2.80 \text{ \AA}$ for both $1 \text{ mol} \cdot \text{L}^{-1}$ LiCl and $1 \text{ mol} \cdot \text{L}^{-1}$ NaCl solutions, 2.813 \AA for $1 \text{ mol} \cdot \text{L}^{-1}$ KCl, 2.818 \AA for $1 \text{ mol} \cdot \text{L}^{-1}$ RbCl, and 2.825 \AA for $1 \text{ mol} \cdot \text{L}^{-1}$ CsCl. These numbers, together with the ξ_3 ones, allow a rationalization of the ΔG_c magnitude in the various aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions.

In the assumption that the $\Delta G_c(\text{SPT})$ estimate is quantitatively right in water, the E_a value for benzene in water can be determined in a hybrid manner by performing the difference

$$E_a(\text{water}) = \mu^*(\text{water}) - \Delta G_c(\text{SPT}, \text{water}) \quad (9)$$

The obtained number $E_a(\text{water}) = -3.6 - 41.3 = -44.9 \text{ kJ} \cdot \text{mol}^{-1}$ is physically reliable because it is *in between* the estimates of the interaction energy of van der Waals models of benzene (i.e., a benzene model in which all partial charges were removed) with water. In fact, for a van der Waals model of benzene: (a) Linse,³⁶ by performing molecular dynamics simulations in TIP4P water at room temperature and $p = 0.1 \text{ MPa}$, found $E_a(\text{water}) = -42.6 \text{ kJ} \cdot \text{mol}^{-1}$; (b) Schravendijk and van der Vegt,²⁸ by performing molecular dynamics simulations in SPC water, found $E_a(\text{water}) = -45.6 \text{ kJ} \cdot \text{mol}^{-1}$. It is worth noting that more realistic benzene models, harboring partial charges that allow the formation of the weak H-bonds with water molecules over the two faces of the aromatic ring,^{37,38} showed $E_a(\text{water})$ values significantly larger in magnitude. Linse³⁶ found $E_a(\text{real benzene-water}) = -61.6 \text{ kJ} \cdot \text{mol}^{-1}$, and Schravendijk and van der Vegt²⁸ found $E_a(\text{real benzene-water}) = -59.4 \text{ kJ} \cdot \text{mol}^{-1}$. If one would insert the latter numbers in eq 6 together with the SPT estimate of ΔG_c , the calculated μ^* values would be markedly larger in magnitude than the experimental one (i.e., the solubility of benzene in water would be largely overestimated). This supports the original claims by Graziano and Lee^{11,39} that: (a) the weak H-bonds between water and the aromatic ring do not play an effective role to enhance the solubility of benzene in water and (b) the van der Waals energy of attraction between a benzene molecule and surrounding water molecules is larger than ΔG_c because the large polarizability of the aromatic ring, arising from the delocalized π -electrons, strengthens the dispersion interactions with water molecules.

On the basis of a simple formula proposed by Pierotti⁸ to calculate E_a , it is reliable to assume that the fundamental variable on passing from water to aqueous MCl solutions is the difference in volume packing density. In addition, according to neutron scattering data,⁴⁰ there should be no need to consider the direct interaction of the benzene molecule with the M^+ and Cl^- ions that are individually entirely surrounded by water molecules. Since according to Pierotti's formula the E_a magnitude is directly proportional to the volume packing density of the liquid phase,⁸ it is reliable to fix

$$E_a(\text{MCl}) = E_a(\text{water}) \cdot \xi_3(\text{MCl}) / \xi_3(\text{water}) \quad (10)$$

where $\xi_3(\text{MCl})$ indicates the volume packing density of aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions. By inserting the $E_a(\text{water})$ estimate and the relevant ξ_3 numbers into eq 10, one obtains $E_a = -46.0 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ LiCl, $-46.1 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ NaCl, $1 \text{ mol} \cdot \text{L}^{-1}$ KCl, and $1 \text{ mol} \cdot \text{L}^{-1}$ RbCl, and

$-46.2 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1}$ CsCl. These values, listed in the fifth column of Table 2, are very close to each other and slightly larger in magnitude than $E_a(\text{water})$. More importantly, when summed to the $\Delta G_c(\text{SPT})$ estimates, they produce the numbers reported in the sixth column of Table 2 that prove to be very close to the experimental μ^* values (see the last column of Table 2). The calculated salting out constants, $k_s = 0.158$ in $1 \text{ mol} \cdot \text{L}^{-1}$ LiCl, 0.175 in $1 \text{ mol} \cdot \text{L}^{-1}$ NaCl, 0.140 in $1 \text{ mol} \cdot \text{L}^{-1}$ KCl, 0.123 in $1 \text{ mol} \cdot \text{L}^{-1}$ RbCl, and 0.088 in $1 \text{ mol} \cdot \text{L}^{-1}$ CsCl, are in satisfactory agreement with the experimental values listed in the fourth column of Table 1. These results support the validity of the simple calculation procedure devised and suggest that it is not necessary to invoke a role for the weak benzene–water H-bonds or for a structural reorganization of water molecules to rationalize the benzene salting out by alkali chlorides. It is worth noting that I have analyzed the solubility of water in benzene and other nonpolar organic solvents by means of a similar theoretical approach in a previous article.⁴¹

Discussion

The performed analysis shows that the benzene salting out by alkali chlorides is mainly due to the increase in the volume packing density ξ_3 of aqueous MCl solutions with respect to water. The ξ_3 increase is a direct consequence of the density increase on adding MCl to water that, in turn, reflects the strength of the M^+ –water and Cl^- –water attractive interactions (i.e., the strong electrostatic interactions of ions toward the dipolar water molecules affect the 3D tetrahedral H-bonding network of water). Therefore, the use of the experimental density values in performing calculations is a fundamental point, as noticed by Paschek.⁴²

Leberman and Soper,⁴³ by comparing the hydrogen–hydrogen pair correlation function for pure water and some aqueous salt solutions, determined by neutron scattering measurements, pointed out that: (a) there is a marked increase of water density around the ions compared to pure water at the same temperature; (b) this density increase can be regarded as equivalent to that occurring when the pressure applied on water is markedly increased at constant temperature; and (c) this density increase is related to a partial disruption of the 3D tetrahedral H-bonding network of water. All these statements should be right for aqueous MCl solutions, even though neutron scattering measurements have been performed solely on aqueous NaCl and KCl solutions.^{40,43}

Actually, the ξ_3 increase is not the whole story because it is the average effective hard sphere diameter $\langle \sigma \rangle$ which accounts for the different benzene solubility in the aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions. If the $\langle \sigma \rangle$ value would become too large, notwithstanding the ξ_3 increase, the salt should *salt in* benzene due to a decrease in the ΔG_c magnitude.^{32,33} To test the validity of this analysis, I have applied it to describe the salting in of benzene caused by the tetramethylammonium bromide, $\text{N}(\text{CH}_3)_4^+\text{Br}^-$. It was experimentally determined that $k_s = -0.24$ for benzene in $\text{N}(\text{CH}_3)_4^+\text{Br}^-$ aqueous solutions at room temperature.³ Such a k_s value, inserted in eq 5, leads to $\mu^* = -5.0 \text{ kJ} \cdot \text{mol}^{-1}$ for the hydration of benzene in $1 \text{ mol} \cdot \text{L}^{-1}$ $\text{N}(\text{CH}_3)_4^+\text{Br}^-$ at $t = 25 \text{ }^\circ\text{C}$. This means that the addition of $\text{N}(\text{CH}_3)_4^+\text{Br}^-$ to water causes an increase of benzene solubility.

In performing calculations, I have used: (a) the experimental density of an aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ $\text{N}(\text{CH}_3)_4^+\text{Br}^-$ solution, $\rho = 1040 \text{ g} \cdot \text{L}^{-1}$ at $t = 25 \text{ }^\circ\text{C}$ and $p = 0.1 \text{ MPa}$;¹⁶ (b) $\sigma(\text{Br}^-) = 3.90 \text{ \AA}$, as fixed by Pauling,²⁵ and $\sigma[\text{N}(\text{CH}_3)_4^+] = 5.02 \text{ \AA}$, as fixed by Masterton and co-workers⁴⁴ (the latter is markedly smaller than the diameter obtained by Robinson and Stokes, 6.94 \AA , measuring

on atomic models the distance from the center of the nitrogen atom to the most distant hydrogen atom in methyl groups;⁴⁵ it seems reliable that the effective hard sphere diameter of the $\text{N}(\text{CH}_3)_4^+$ ion in aqueous solution should be smaller than that obtained by Robinson and Stokes). In this manner, the volume packing density $\xi_3 = 0.3991$ for an aqueous $1 \text{ mol} \cdot \text{L}^{-1} \text{ N}(\text{CH}_3)_4^+ \text{Br}^-$ solution. The reversible work of cavity creation was calculated by means of eq 7, $\Delta G_c = 41.3 \text{ kJ} \cdot \text{mol}^{-1}$, the same estimate obtained in water, and smaller than the values in aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions. This happens because, even though ξ_3 in $1 \text{ mol} \cdot \text{L}^{-1} \text{ N}(\text{CH}_3)_4^+ \text{Br}^-$ is larger than in aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions, the average effective hard sphere diameter $\langle \sigma \rangle = 2.865 \text{ \AA}$ is larger, causing a decrease in the ΔG_c magnitude. On the other hand, by using eq 10, one obtains $E_a = -46.8 \text{ kJ} \cdot \text{mol}^{-1}$ in $1 \text{ mol} \cdot \text{L}^{-1} \text{ N}(\text{CH}_3)_4^+ \text{Br}^-$, a number close to those determined in the case of aqueous $1 \text{ mol} \cdot \text{L}^{-1}$ alkali chloride solutions. The fundamental point is that the sum $\Delta G_c + E_a = -5.5 \text{ kJ} \cdot \text{mol}^{-1}$ is in satisfactory agreement with the experimental datum $\mu^* = -5.0 \text{ kJ} \cdot \text{mol}^{-1}$. From these very simple calculations, it emerges that the salting in action of $\text{N}(\text{CH}_3)_4^+ \text{Br}^-$ on benzene solubility is determined by a tradeoff effect of a ξ_3 increase and $\langle \sigma \rangle$ increase on the magnitude of both ΔG_c and E_a . The E_a magnitude increases linearly with ξ_3 according to eq 10; instead, the ΔG_c magnitude, notwithstanding the ξ_3 increase, is dominated by the $\langle \sigma \rangle$ increase.

Conclusion

The performed analysis shows that the salting out of benzene by alkali chlorides can be rationalized by means of an approach grounded on SPT calculations and a simple formula for the benzene–solvent attractive energy. It emerges that two geometric features of aqueous salt solutions, the volume packing density and the average value of the effective hard sphere diameter, are the main determinants of benzene solubility.

Literature Cited

- (1) Baldwin, R. L. How Hofmeister Ion Interactions Affect Protein Stability. *Biophys. J.* **1996**, *71*, 2056–2063.
- (2) Setchenow, M. Action de l'Acide Carbonique sur les Solutions des Sels a Acides Forts. *Ann. Chim. Phys.* **1892**, *25*, 226–270.
- (3) McDevitt, W. F.; Long, F. A. The Activity Coefficient of Benzene in Aqueous Salt Solutions. *J. Am. Chem. Soc.* **1952**, *74*, 1773–1777.
- (4) Ben-Naim, A. *Solvation Thermodynamics*; Plenum Press: New York, 1987.
- (5) Graziano, G. Hydrophobicity of Benzene. *Biophys. Chem.* **1999**, *82*, 69–79.
- (6) Hofmeister, F. Zur Lehre von der Wirkung der Salze. *Zweite Mittheilung. Arc. Exp. Path. Pharmacol.* **1888**, *24*, 247–260.
- (7) Collins, K. D.; Washabaugh, M. W. The Hofmeister Effect and the Behavior of Water at Interfaces. *Q. Rev. Biophys.* **1985**, *18*, 323–422.
- (8) Pierotti, R. A. A Scaled Particle Theory of Aqueous and Nonaqueous Solutions. *Chem. Rev.* **1976**, *76*, 717–726.
- (9) Pratt, L. R.; Chandler, D. Theory of the Hydrophobic Effect. *J. Chem. Phys.* **1977**, *67*, 3683–3704.
- (10) Lee, B. Solvent Reorganization Contribution to the Transfer Thermodynamics of Small Nonpolar Molecules. *Biopolymers* **1991**, *31*, 993–1008.
- (11) Graziano, G.; Lee, B. Hydration of Aromatic Hydrocarbons. *J. Phys. Chem. B* **2001**, *105*, 10367–10372.
- (12) Guillot, B.; Guissani, Y. A Computer Simulation Study of the Temperature Dependence of the Hydrophobic Hydration. *J. Chem. Phys.* **1993**, *99*, 8075–8094.
- (13) de Souza, L. E. S.; Ben-Amotz, D. Hard Fluid Model for Molecular Solvation Free Energies. *J. Chem. Phys.* **1994**, *101*, 9858–9863.
- (14) Lebowitz, J. L.; Helfand, E.; Praestgaard, E. Scaled Particle Theory of Fluid Mixtures. *J. Chem. Phys.* **1965**, *43*, 774–779.
- (15) Kell, G. S. Density, Thermal Expansivity, and Compressibility of Liquid Water from 0 to 150 °C: Correlations and Tables for Atmospheric Pressure and Saturation Reviewed and Expressed on 1968 Temperature Scale. *J. Chem. Eng. Data* **1975**, *20*, 97–105.
- (16) Weast, R. C., Ed. *Handbook of Chemistry and Physics*, 53rd ed.; Chemical Rubber Co.: Cleveland, OH, 1972.
- (17) Tang, K. E. S.; Bloomfield, V. A. Excluded Volume in Solvation: Sensitivity of Scaled Particle Theory to Solvent Size and Density. *Biophys. J.* **2000**, *79*, 2222–2234.
- (18) Sorenson, J. M.; Hura, G.; Glaeser, R. M.; Head-Gordon, T. What Can X-Ray Scattering Tell Us about the Radial Distribution Functions of Water. *J. Chem. Phys.* **2000**, *113*, 9149–9161.
- (19) Graziano, G. On the Cavity Size Distribution in Water and n-Hexane. *Biophys. Chem.* **2003**, *104*, 393–405.
- (20) Graziano, G. Water: Cavity Size Distribution and Hydrogen Bonds. *Chem. Phys. Lett.* **2004**, *396*, 226–231.
- (21) Wilhelm, E.; Battino, R. Estimation of Lennard-Jones (6,12) Pair Potential Parameters from Gas Solubility Data. *J. Chem. Phys.* **1971**, *55*, 4012–4017.
- (22) Narten, A. H. X-ray Diffraction Pattern and Models of Liquid Benzene. *J. Chem. Phys.* **1977**, *67*, 2102–2108.
- (23) Linse, P. Thermodynamic and Structural Aspects on Liquid and Solid Benzene. Monte Carlo Study. *J. Am. Chem. Soc.* **1984**, *106*, 5425–5430.
- (24) Cabaco, M. I.; Danten, Y.; Besnard, M.; Guissani, Y.; Guillot, B. Neutron Diffraction and Molecular Dynamics Study of Liquid Benzene and Its Fluorinated Derivatives as a Function of Temperature. *J. Phys. Chem. B* **1997**, *101*, 6977–6987.
- (25) Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960.
- (26) Weerasinghe, S.; Smith, P. E. A Kirkwood-Buff Derived Force Field for Sodium Chloride in Water. *J. Chem. Phys.* **2003**, *119*, 11342–11349.
- (27) Beutler, T. C.; Beguelin, D. R.; van Gunsteren, W. F. Free Energy of Cavity Formation in Solvent: Computational, Methodological, and Physical Aspects. *J. Chem. Phys.* **1995**, *102*, 3787–3793.
- (28) Schravendijk, P.; van der Vegt, N. F. A. From Hydrophobic to Hydrophilic Solvation: An Application to Hydration of Benzene. *J. Chem. Theory Comput.* **2005**, *1*, 643–652.
- (29) Jarvis, N. L.; Scheiman, M. A. Surface Potentials of Aqueous Electrolyte Solutions. *J. Phys. Chem.* **1968**, *72*, 74–78.
- (30) Hummer, G.; Garde, S.; Garcia, A. E.; Paulaitis, M. E.; Pratt, L. R. Hydrophobic Effects on a Molecular Scale. *J. Phys. Chem. B* **1998**, *102*, 10469–10482.
- (31) Islam, S.; Waris, B. N. Intermolecular/Interionic Interactions in Leucine-, NaCl-, and KCl-aqueous urea systems. *Thermochim. Acta* **2004**, *424*, 165–174.
- (32) Lee, B. The Physical Origin of the Low Solubility of Nonpolar Solutes in Water. *Biopolymers* **1985**, *24*, 813–823.
- (33) Graziano, G. Comment on Reevaluation in Interpretation of Hydrophobicity by Scaled Particle Theory. *J. Phys. Chem. B* **2002**, *106*, 7713–7716.
- (34) Graziano, G. On the Solubility of Aliphatic Hydrocarbons in 7 M Aqueous Urea. *J. Phys. Chem. B* **2001**, *105*, 2632–2637.
- (35) Graziano, G. Size and Temperature Dependence of Hydrocarbon Solubility in Concentrated Aqueous Solutions of Urea and Guanidine Hydrochloride. *Can. J. Chem.* **2002**, *80*, 388–400.
- (36) Linse, P. Molecular Dynamics Simulation of a Dilute Aqueous Solution of Benzene. *J. Am. Chem. Soc.* **1990**, *112*, 1744–1750.
- (37) Levitt, M.; Perutz, M. Aromatic Rings Act as Hydrogen Bond Acceptors. *J. Mol. Biol.* **1988**, *201*, 751–754.
- (38) Suzuki, S.; Green, P. G.; Bumgarner, R. E.; Dasgupta, S.; Goddard, W. A.; Blake, G. A. Benzene Forms Hydrogen Bonds with Water. *Science* **1992**, *257*, 942–945.
- (39) Graziano, G. Benzene Solubility in Water: A Reassessment. *Chem. Phys. Lett.* **2006**, *429*, 114–118.
- (40) Mancinelli, R.; Botti, A.; Bruni, F.; Ricci, M. A.; Soper, A. K. Hydration of Sodium, Potassium, and Chloride Ions in Solution and the Concept of Structure Maker/Breaker. *J. Phys. Chem. B* **2007**, *111*, 13570–13577.
- (41) Graziano, G. Solvation Thermodynamics of Water in Nonpolar Organic Solvents Indicate the Occurrence of Nontraditional Hydrogen Bonds. *J. Phys. Chem. B* **2005**, *109*, 981–985.
- (42) Paschek, D. Temperature Dependence of the Hydrophobic Hydration and Interaction of Simple Solutes: An Examination of Five Popular Water Models. *J. Chem. Phys.* **2004**, *120*, 6674–6690.
- (43) Leberman, R.; Soper, A. K. Effect of High Salt Concentrations on Water Structure. *Nature* **1995**, *378*, 364–366.
- (44) Masterton, W. L.; Bolocofsky, D.; Lee, T. P. Ionic Radii from Scaled Particle Theory of the Salt Effect. *J. Phys. Chem.* **1971**, *75*, 2809–2815.
- (45) Robinson, R. A.; Stokes, R. H. *Electrolyte Solutions*, 2nd ed.; Butterworths: London, 1959.

Received for review June 26, 2008. Accepted August 19, 2008.

JE8004722