Thermodynamics of aliphatic and aromatic hydrocarbons in water

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Abstract

Makhatadze and Privalov have analyzed the thermodynamics of transfer of aliphatic and aromatic hydrocarbons from the gas phase into water. Finding that the hydration free energy of aliphatic and aromatic hydrocarbons have different signs, they conclude that the mechanism causing hydrophobicity of these solutes is of a different nature. Here, we offer an alternative analysis of the dissolution of these non-polar compounds into water based on a recently published interpretation scheme for thermodynamic transfer functions. Our analysis shows that the hydrophobicity of aromatic and aliphatic hydrocarbons is qualitatively the same, i.e. its causes are the same namely the extremely high cohesive energy of water which overcomes the favorable solute–solute and solute–water interactions. However, both analyses conclude that the experimentally observed quantitative difference between the interactions of water with aliphatic and aromatic hydrocarbons, can be assigned to the formation of aromatic ring–water H-bonds. © 1998 Published by Elsevier Science B.V. All rights reserved.

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1. Introduction

Many aliphatic and aromatic groups are present in the interior of proteins. Upon unfolding of the native protein structure, these groups are exposed to water. Hence, the interactions between water and non-polar groups are of fundamental importance as they can be considered to be responsible for the maintenance of the native protein structure and to play a crucial role in the unfolding process. Studying the mechanism of interaction of aliphatic and aromatic hydrocarbons with water, Makhatadze and Privalov [1] have analyzed the transfer of these non-polar

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solutes from the gas phase into water. Their main conclusion was that the mechanism causing hydrophobicity of aliphatic and aromatic hydrocarbons has a different nature. Here, we disagree with this conclusion and, employing a recently published new interpretation scheme for the dissolution of non-polar substances into water [2], we offer an alternative analysis of the thermodynamic transfer functions.

2. The analysis by Makhatadze and Privalov

Makhatadze and Privalov based their analysis [1] in the so called hydration free energy $\Delta G_{hyd} = \Delta_g^w G$ where $\Delta_g^w G$ is the free energy of transfer of solute molecules from the gaseous state into aqueous solution. In Makhatadze and Privalov, $\Delta_g^w G$ data was obtained from the literature [3,4] using the molar concentration scale which, according to Ben-Naim [5–7], eliminates the volume effects (thermal roaming of the solute molecules) present when transferring molecules between phases with different densities. It was found that ΔG_{hyd} is negative for benzene and toluene for almost the whole range of temperature considered (278.15–398.15 K) while for ethane, propane and butane ΔG_{hyd} is positive. From these results, it was concluded that the mechanism causing hydrophobicity for aromatic and aliphatic hydrocarbons derives from interactions different in nature namely $\Delta G_{hyd} < 0$ for aromatics indicates that there is an additional interaction, which is absent in the aliphatic–water case. This additional interaction can be assigned to the formation of H-bonds between the π electrons of the aromatic ring and the hydrogen atoms in water. The existence of these H-bonds has been experimentally and theoretically substantiated in the literature [8–13]. The temperature-dependence of ΔG, ΔH and ΔS for these H-bonds was evaluated by Makhatadze and Privalov for benzene and toluene using hypothetical aliphatic hydrocarbons having the same water accessible surface area. The results of this calculation (Fig. 2 in Makhatadze and Privalov [1]) indicate that $\Delta G < 0$ with $\Delta H < 0$ and $\Delta S > 0$ both increasing in magnitude as the temperature increases. More specifically, according to Makhatadze and Privalov the

H-bonds between benzene or toluene and water become stronger as the temperature increases (from approx. -3 kJ/mol at 278.15 K to approx. -13 kJ/mol at 398.15 K) and the formation of these H-bonds have associated a positive entropy change at all temperatures. These are, in our opinion, unacceptable conclusions which have their roots in an erroneous interpretation and use of the thermodynamic transfer functions. This in turn is caused by the different ways to split the thermodynamic transfer functions into various contributions [14].

3. An alternative analysis

The hydration free energy can be written as

$$\Delta G_{hyd} = \Delta_g^w G = \Delta_l^w G - \Delta_l^g G \qquad (1)$$

where $\Delta_l^g G$ is the liquid to gas transfer or vaporization free energy of the pure solute and $\Delta_l^w G$ is the free energy of transfer from the pure liquid solute into water. Using $\Delta_g^w G$ data, as in Makhatadze and Privalov, has the disadvantage that in the gas to water transfer the solute molecule undergoes a drastic decrease in degrees of freedom which are not fully taken into account when using the molar concentration scale. It is more convenient to use experimental $\Delta_l^w G$ data provided they are corrected for the combinatorial effects arising from the mixing process [2,15]. The need for such corrections, usually called 'volume effects' or 'different molecular size' corrections, has been clearly demonstrated [16] on thermodynamics grounds and is widely accepted. Amongst the several alternatives to make this correction, that given by the Flory–Huggins (FH) theory is often used [17]. The applicability of FH theory to the analysis of the solubilities of non-polar solutes in water has been recently discussed in detail [18] concluding that it is a good first-order approximation for obtaining size independent transfer free energies. In Costas et al. [2] and Silveston and Kronberg [15], we used the FH theory employing the partial molar volumes of the solutes in water instead of their molar volumes, as usually done due to the lack of data. It was found [2,15] that the non-combinatorial

free energy of transfer $\Delta_l^w G'$ is the relevant quantity to analyze the dissolution of non-polar compounds into water. A clear indication of this is that a unique or master curve is obtained [2] when $\Delta_l^w G'$, expressed per solute surface area, is plotted against temperature for a series of alkylbenzenes. Unique curves for the pure liquid to water enthalpies and heat capacities of transfer had been found previously for non-polar solutes [19–22] but, in contrast, for the free energies and entropies of transfer, whose examination is complicated by standard-state choices, common curves for a series of solutes had never been found until $\Delta_l^w G'$ was employed. It is then our contention that if one wishes to use ΔG_{hyd} as a basis for examining hydrophobicity, then $\Delta_l^w G'$ should be used in Eq. (1). Table 1 displays ΔG_{hyd} for benzene and toluene at 298.15 K using $\Delta_l^w G'$ and contrasts the results with those from Makhatadze and Privalov. Here, we limit ourselves to consider only benzene and toluene, since only these are considered in Makhatadze and Privalov. It can be seen that for both aromatic solutes $\Delta G_{hyd} > 0$ and hence unfavorable: given [2,15] $\Delta_l^w G' > \Delta_l^w G$ for the aliphatic hydrocarbons, ΔG_{hyd} will also be positive. We conclude that for both types of solutes, i.e. aromatics and aliphatics, the mechanism causing hydrophobicity is not qualitatively different. It should be pointed out that if $\Delta_g^w G$ for benzene and toluene are calculated following the scheme presented in Sharp et al. [16] for the transfer energies of n-alkanes to water, the results are also that $\Delta G_{hyd} > 0$.

In Costas et al., we presented a new interpretation scheme for the thermodynamic transfer functions. In this scheme the pure liquid (l) to water (w) transfer was used (rather than the gas to water transfer) and only non-combinatorial quantities were employed. The l to w transfer was divided into two steps introducing an intermediate hypothetical state termed unrelaxed water (urw). The urw to w step is characteristic of water as a solvent and is only proportional to the surface area of the solute while the l to urw step contains all the solute–solute, solute–water and water–water interactions; a detailed description of the molecular level components assigned to each of these two steps is given in Costas et al. It was found that $\Delta_l^{urw} G = \Delta_l^{urw} H$ are different for aromatic and aliphatic hydrocarbons, their values being 63.1 mJ/m^2 and 67.3 mJ/m^2 for any alkylbenzene and any n-alkane, respectively. $\Delta_l^{urw} G$ is a purely interactional free energy, liberated from the combinatorial or different-size effects and hence the smaller value for the alkylbenzenes implies a more favorable interaction with water and explains the larger solubilities of the aromatics in water. Assuming as in Makhatadze and Privalov that the difference $\Delta_l^{urw} X$ (alkylbenzenes) $- \Delta_l^{urw} X$ (n-alkanes) with $X = G = H$ is a measure of the contribution to the free energy and enthalpy due to the formation of the aromatic ring–water H-bonds, one obtains a value of -2.6 kJ/mol using a benzene surface area of 101 Å^2 (as in Costas et al. [2]) or a value of -5.8 kJ/mol using a surface area of 228 Å^2 (as in Makhatadze and Privalov [1] and Sharp et al. [16]). Both values correspond to weak H-bonds as

Table 1
Free energies of transfer (in kJ/mol) for benzene and toluene at 298 K

| | Makhatadze and Privalov [1] | | | This work | |
	Benzene	Toluene		Benzene	Toluene
$\Delta_l^w G$	15.46[a]	17.95[a]	$\Delta_l^w G'$	24.5[c]	29.5[c]
$\Delta_l^g W$	19.06[b]	21.61[b]	$\Delta_g^l G$	19.06[b]	21.61[b]
$\Delta G_{hyd} = \Delta_g^w G$	-3.60	-3.66	$\Delta G_{hyd} = \Delta_g^w G$	5.44	7.89

[a] Calculated from $\Delta_l^w G = \Delta_g^w G + \Delta_l^g G$ with $\Delta_g^w G$ from Wauchope and Haque [4] and corrected for volume effects in Makhatadze and Privalov [1] and $\Delta_l^g G$ from Ben-Naim [6].
[b] From Ben-Naim [6].
[c] From Silveston and Kronberg [15].

expected for a π–proton interaction and are smaller than the theoretical calculations (-7.5 kJ/mol in Suzuki et al. [8]; -6.3 to -8.4 kJ/mol in Bredas and Street [13]) and the experimental estimates (-6.8 to -11.6 kJ/mol in Gotch and Zweir [23] and -6.0 kJ/mol in Wanna et al. [24]). It appears then that the interpretation scheme in Costas et al. is also able to distinguish, without resorting to the concept of hydration free energy, between aromatics and aliphatics in water, the energetic difference between them being attributable to aromatic–water H-bonds.

There are two important differences between the scheme in Costas et al. [2] and that in Makhatadze and Privalov [1]. The first is that in Costas et al. $\Delta_l^{urw}S = 0$ since the combinatorial contributions were subtracted from the experimental $\Delta_l^{w}G$ results and all the temperature-dependence of the $\Delta_l^{w}S$ transfer was attributed to the $\Delta_{urw}^{w}S$ step; hence, in this scheme the entropy change associated with the formation of the aromatic–water H-bonds is zero. This result must be understood in the following terms: since the combinatorial entropy has been eliminated from the analysis, the molecules, i.e. for example benzene and water are already 'positioned' to form H-bonds without any extra entropy loss; this contrasts with the unexplained entropy gain reported in Makhatadze and Privalov. The second difference is that since $\Delta_l^{urw}S = 0$, $\Delta_l^{urw}G = \Delta_l^{urw}H$ and they were assumed in Costas et al. to be temperature-independent. Hence, the enthalpy and free energy of the aromatic–water H-bond are also temperature-independent; this is certainly an approximate result but closer to reality than the fourfold increase for the enthalpy of H-bonding reported in Makhatadze and Privalov. Note that there is nothing in the interpretation scheme in Costas et al. that hinders a separate temperature-dependence to be allocated to the aromatic–water H-bonding; in such case, however, the simplicity would be diminished.

4. Conclusions

The hydrophobicity of aromatic and aliphatic hydrocarbons is qualitatively the same, i.e. its causes are the same, namely the extremely high cohesive energy of water which overcomes the favorable solute–solute and solute–water interactions [2]. The quantitative difference indicates a more favorable interaction for the aromatics which can be assigned to aromatic ring–water H-bonds; in turn, this interaction explains the larger solubilities of aromatics in water as compared with the aliphatic solutes.

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