9249

On the Solvent Isotope Effect in Hydrophobic Hydration

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It is a general result that the transfer of noble gases and aliphatic hydrocarbons from H_2O to D_2O is characterized by negative Gibbs energy changes, but positive heat capacity changes. These experimental evidences are difficult to reconcile with the classical view of hydrophobic hydration, which claims a reinforcement of H-bonds around nonpolar moieties. In contrast, according to a new emerging theory, the poor solubility of nonpolar compounds in water is determined by a balance between the excluded volume effect due to cavity creation for solute insertion and the attractive solute−water van der Waals interactions, whereas the reorganization of H-bonds is a compensating process. The hydration thermodynamics of argon, selected as suitable representative solute, in H_2O and D_2O, in the temperature range 5−100 °C, is analyzed by means of the new approach, which proves able to satisfactorily explain the experimental data. Since the strength of van der Waals interactions is the same in the two liquids, the slightly larger solubility of argon in D_2O, in the whole temperature range 5−100 °C, is due to the lower volume packing density of D_2O with respect to H_2O, which decreases the excluded volume effect for cavity creation. On the other hand, the positive transfer heat capacity change is related to the peculiar features of H-bond reorganization for H_2O and D_2O molecules constituting the hydration shell. By using the modified Muller's model to describe such H-bond reorganization, the positive heat capacity change is reproduced quite well in the temperature range 5−100 °C.

Introduction

A critical test for any theory which claims to explain the poor solubility of nonpolar compounds in water, hydrophobic hydration, is its capability to predict the magnitude of the thermodynamic quantities associated with the transfer of nonpolar solutes from H_2O to D_2O.[1,2] This is not a simple task since such a transfer process has peculiar features.

Recent and accurate calorimetric results have unequivocally pointed out that the transfer of nonpolar compounds from H_2O to D_2O is accompanied by a positive heat capacity change.[3] The same conclusion emerged from several previous investigations based on both calorimetric and solubility measurements.[4−6] A positive heat capacity change upon transfer of a nonpolar compound from phase A to phase B is usually considered a definite indication that the same nonpolar compound is less soluble in phase B than phase A.[7] Indeed, the transfer process between two phases of a nonpolar molecule that is accompanied by a positive heat capacity change has usually another characteristic thermodynamic property: also the Gibbs energy change is positive. Thus, the solubility of nonpolar compounds should be smaller in D_2O than H_2O. This expectation, however, is not correct. In fact, the Gibbs energy of transfer of noble gases and alkanes from H_2O to D_2O is negative, as unequivocally shown by the results from different research groups over the last forty years.[4,5,8−11] Therefore, the heat capacity increases upon transferring a nonpolar molecule from H_2O to D_2O, whereas the solubility of the same molecule is lower in H_2O than D_2O.

Theoretical approaches which try to rationalize hydrophobic hydration in terms of the reorganization of H-bonds around nonpolar moieties, following the original proposal by Frank and co-workers,[12] lead to the expectation of a smaller solubility in D_2O, because D_2O is generally considered to be more extensively H-bonded than H_2O, in view of its higher melting and boiling temperatures.[13] But this expectation contrasts with experimental data, leading to a serious failure.

Actually, even though a large and positive heat capacity change is often considered as the hallmark of hydrophobic hydration,[7] this reasoning is not correct. The large and positive Gibbs energy and heat capacity changes, characteristic of hydrophobic hydration, have distinct and different physical causes.[14] Therefore, since an emerging theory has proved able to satisfactorily explain most of the peculiar thermodynamic features of hydrophobic hydration,[14−16] we apply it to the analysis of the transfer of argon from H_2O to D_2O in the temperature range 5−100 °C. Argon is selected because it is one of the most extensively studied solutes and one for which there is good agreement among the experimental data from different laboratories.[8−11]

Theory of Hydration. Hydration of nonpolar molecules causes a change in thermodynamic functions given by the sum of two contributions: the direct perturbation of water owing to solute insertion, and the response of water as a consequence of perturbation (i.e., an alteration in the H-bonding state of water molecules). The hydration enthalpy change, in fact, is[17]

$$\Delta H^{\bullet} = E_a + \Delta H^h \tag{1}$$

where E_a is the average value of the solute−water van der Waals interaction energy and is the enthalpic part of the direct perturbation; ΔH^h is the contribution owing to the reorganization of H-bonds and represents the response of water to direct perturbation.

The solute molecule is in a fixed position, adopting the Ben-Naim standard,[18] and the hydration entropy change is entirely

due to water reorganization. However, since a liquid is a condensed phase and each molecule possesses a finite volume, insertion of a solute molecule gives rise to an excluded volume effect for water molecules. This is the entropic part of the direct perturbation. In response to volume exclusion, water molecules undergo a further reorganization, due to an alteration in H-bonding states, providing another contribution to the entropy change. Therefore, the hydration entropy change can be split as follows:[16c,17]

$$\Delta S^{\bullet} = \Delta S_x + \Delta S^h \quad (2)$$

where ΔS_x is the contribution due to the excluded volume effect and ΔS^h is the contribution due to the reorganization of H-bonds. The term ΔS_x is simply calculated from the Gibbs energy cost of cavity creation as $\Delta S_x = -\Delta G_c/T$,[16c] because ΔG_c is an exact measure of the excluded volume effect.[19] Computer simulations confirmed that the excluded volume effect is geometric in nature, being independent of the presence of the H-bonding potential, but related to the size of solvent molecules.[20,21]

A fundamental point, demonstrated by several authors using different theoretical routes,[15,22] is that there is perfect compensation between the enthalpic and entropic contributions arising from H-bond reorganization at all temperatures:

$$\Delta H^h = T\Delta S^h \quad (3)$$

This means that the reorganization of H-bonds does not contribute at all to the hydration Gibbs energy change, which is simply given by

$$\Delta G^{\bullet} = E_a - T\Delta S_x = E_a + \Delta G_c \quad (4)$$

As a consequence, the poor solubility of nonpolar compounds in water is not due to the reorganization of H-bonds, but to the excluded volume effect, which, in liquid water, is amplified by the small size of water molecules themselves.[14–17,20,21,23]

The hydration heat capacity change, on the basis of eq 1, is given by the sum of the temperature derivatives of E_a and ΔH^h; however, $(\partial E_a/\partial T)$ is very small in water and $\Delta C_p^{\bullet}$ is dominated by the temperature dependence of H-bond reorganization:[14–17,24]

$$\Delta C_p^{\bullet} = (\partial \Delta H^h/\partial T) = \Delta C_p^h \quad (5)$$

By looking at eqs 4 and 5, it is evident that the large and positive Gibbs energy and heat capacity changes associated with the hydration of nonpolar compounds have distinct and different physical origins.[16c]

In the present work, we analyze the hydration thermodynamics of argon in both H_2O and D_2O, over the temperature range 5–100 °C, by means of this theoretical approach. In addition, we show that the thermodynamic contributions due to the reorganization of H-bonds, in both H_2O and D_2O, can be reproduced quite well using the modified Muller's model.[17]

Modified Muller's Model. Muller[25] developed a model of H-bond reorganization, by distinguishing the hydration shell from the bulk water and assuming that each H-bond has two accessible states: the lower energy state in which the H-bond is intact, and the upper energy state in which the H-bond is broken. The model, as modified by Lee and Graziano[17] to render it compensating, has seven parameters: $\Delta H_b°$ and $\Delta S_b°$ measure the enthalpy and entropy difference, respectively, between the two states of H-bonds in the bulk water; $\Delta H_{hs}°$ and $\Delta S_{hs}°$ have the same meaning for the H-bonds in the hydration shell water; n^h is the number of H-bonds in the hydration shell; ΔH_U and

ΔS_U measure the enthalpy and entropy difference, respectively, between the upper states of H-bonds in the hydration shell and in the bulk water. The physical reliability of the modified Muller's model has recently been pointed out in a theoretical investigation by Dill and colleagues.[26] Since Muller[27] extended the model to D_2O by a simple readjustment of the parameter values, we do the same thing in the present work.

For the two bulk phases the parameter values originally calculated by Muller[25,27] are retained; specifically, for H_2O: $\Delta H_b° = 9.80$ kJ mol^{-1} and $\Delta S_b° = 21.60$ J K^{-1} mol^{-1}; while, for D_2O: $\Delta H_b° = 10.76$ kJ mol^{-1} and $\Delta S_b° = 24.19$ J K^{-1} mol^{-1}. These values indicate that breaking H-bonds in D_2O requires a larger enthalpy cost, $\Delta\Delta H_b° = 0.96$ kJ mol^{-1}, and a larger entropy increase, $\Delta\Delta S_b° = 2.59$ J K^{-1} mol^{-1}, than breaking H-bonds in H_2O. This is in agreement with the largely accepted view that D_2O is a more extensively H-bonded liquid than H_2O.[13] In particular, it has recently been computed, by means of ab initio calculations,[28] that H-bonds involving deuterium are stronger than those involving protium by 0.84 kJ mol^{-1}, owing to a lower zero point vibrational energy, but their rupture affords a larger entropy gain, roughly amounting to 1.3 J K^{-1} mol^{-1}.

On this basis, the values of the fraction of broken H-bonds in the bulk liquid, f_b, are smaller in D_2O than in H_2O over most of the normal liquid range.[27] The difference, however, vanishes slightly below 100 °C. This is reasonable because, in the assumption that at the respective melting and boiling temperatures H_2O and D_2O have a similar content of intact H-bonds, one can state that the number of H-bonds in D_2O changes, in a range of 97.6 °C, to roughly the same extent as that of H_2O in a range of 100 °C (i.e., the melting and boiling temperatures are 3.8 and 101.4 °C for D_2O, and 0.0 and 100.0 °C for H_2O).[13] Other appealing properties of the parameter values selected for light and heavy water are[27] (a) the values of f_b are practically identical at the respective temperature of maximum density, $f_b[H_2O, 3.98 °C] = 0.1604$ and $f_b[D_2O, 11.23 °C] = 0.1622$; (b) the calculated values of the heat capacity for D_2O prove to be larger than those for H_2O, in agreement with experimental data.[13]

According to Muller,[25] $n^h = (3/2)N$, where N, the number of water molecules in the hydration shell, is equal to 16 for argon,[16c] regardless of which isotopic species of water is involved. This value of N, calculated from the ratio of cavity surface areas, agrees with the coordination number obtained from Monte Carlo simulations,[29] 16.8, and from a neutron diffraction study,[30] 16 ± 2. The remaining four parameters of the model are related to each other by three equations; i.e., eqs 13–15 in ref 16c. Since the model is underdetermined, ΔH_U can be used as an independent parameter to generate a set of models. Actually, in the previous work on the hydration thermodynamics of noble gases,[16c] we established that the best choice is $\Delta H_U = -0.50$ kJ mol^{-1}. This choice is retained in the present work for argon in both H_2O and D_2O.

Scaled Particle Theory Calculation. The Gibbs energy cost of cavity creation in the temperature range 5–100 °C for argon in both H_2O and D_2O, is also calculated by means of scaled particle theory,[31,32] SPT, using the following hard-sphere diameters: $\sigma = 3.41$ Å for argon and $\sigma = 2.75$ Å for both H_2O and D_2O.[16a] The latter value is close to the location of the first peak in the radial oxygen–oxygen distribution function of both H_2O and D_2O.[33] Indeed, crystallographic data indicated that the molecular dimensions and the H-bond length in H_2O and D_2O ice are identical within a few thousandths of an angstrom unit.[13] The temperature dependence of ΔG_c is solely due to the density

Solvent Isotope Effect in Hydrophobic Hydration

J. Phys. Chem. B, Vol. 104, No. 39, 2000 **9251**

TABLE 1: Ben-Naim Standard Thermodynamic Quantities Associated with the Transfer of Argon from Ideal Gas Phase into H_2O (a), and D_2O (b), in the Temperature Range 5−100 °C

	T °C	$\Delta C_p^\bullet$ J K^{-1} mol^{-1}	$\Delta H^\bullet$ kJ mol^{-1}	$\Delta S^\bullet$ J K^{-1} mol^{-1}	$\Delta G^\bullet$ kJ mol^{-1}
a	5	229	−13.84	−75.1	7.05
	25	195	−9.60	−60.4	8.40
	50	163	−5.13	−46.0	9.73
	75	144	−1.29	−34.6	10.76
	100	136	2.21	−24.9	11.50
b	5	250	−16.05	−81.7	6.67
	25	215	−11.40	−65.6	8.20
	50	180	−6.46	−49.7	9.60
	75	158	−2.24	−37.1	10.68
	100	147	1.57	−26.5	11.46

of light and heavy water, respectively, which are accurately known in a wide temperature range,[34] because the hard-sphere diameters are considered temperature independent.

Experimental Data

Krause and Benson[35] determined the hydration thermodynamics of noble gases in the temperature range 0−60 °C, analyzing their solubility measurements by means of the procedure labeled Mark III (see Table VIII a−d of ref 35). Moreover, they analyzed both their measurements and experimental data at higher temperatures from other laboratories by means of the procedure labeled Mark II (see Table XI a−d of ref 35). By combining the two sets of values and performing the correction for the Ben-Naim standard, we obtain for the hydration of argon in H_2O the thermodynamic quantities listed in Table 1, part a. They are to be considered very reliable in view of the unsurpassed precision of the measurements by Krause and Benson. At 25 °C the results are $\Delta C_p^\bullet = 195$ J K^{-1} mol^{-1}, $\Delta H^\bullet = -9.60$ kJ mol^{-1}, $\Delta S^\bullet = -60.4$ J K^{-1} mol^{-1}, and $\Delta G^\bullet = 8.40$ kJ mol^{-1}.

For the hydration of argon in D_2O, there is good agreement between the $\Delta G^\bullet$ values at 25 °C obtained in different laboratories: $\Delta G^\bullet = 8.19$ kJ mol^{-1} in ref 8, 8.23 kJ mol^{-1} in ref 9, and 8.16 kJ mol^{-1} in ref 10. Therefore, we fix $\Delta G^\bullet = 8.20$ kJ mol^{-1} at 25 °C for argon in D_2O; so, the difference in $\Delta G^\bullet$ between D_2O and H_2O is equal to −0.20 kJ mol^{-1} at 25 °C, in good agreement with the value obtained by Ben-Naim[1a] in 1965. Moreover, we select for $\Delta H^\bullet$ and $\Delta S^\bullet$ at 25 °C the values reported in ref 8, −11.40 kJ mol^{-1} and −65.6 J K^{-1} mol^{-1}, respectively. Finally, since there is no reliable estimate for $\Delta C_p^\bullet$ associated with the hydration of argon in D_2O, but it is well established that it has to be larger than that in H_2O,[3,6] we fix the values reported in the second column, part b, of Table 1. The difference in $\Delta C_p^\bullet$ between D_2O and H_2O is always positive, and decreases from 21 J K^{-1} mol^{-1} at 5 °C to 11 J K^{-1} mol^{-1} at 100 °C. These values are reliable by considering both the experimental results for aliphatic alcohols and N-alkyl amides,[3,6] and the temperature dependence of the $\Delta\Delta H^\bullet$ values for argon quoted by Marcus and Ben-Naim,[11] and the estimates reported by Ben-Naim.[18] The other thermodynamic functions are calculated in the whole temperature range 5−100 °C, starting from their values at 25 °C and using the above estimates of $\Delta C_p^\bullet$; they are listed in part b of Table 1. The reliability of our $\Delta G^\bullet$ values for argon in D_2O, over the temperature range 5−100 °C, is confirmed by a comparison with those reported by Marcus and Ben-Naim,[11] and by Ben-Naim.[18]

Performing the difference between the values of the thermodynamic functions in D_2O and those in H_2O at each temperature, we obtain the values collected in Table 2. They emphasize the

TABLE 2: Transfer Thermodynamics of Argon from H_2O to D_2O, in the Temperature Range 5−100 °C

T °C	$\Delta\Delta C_p^\bullet$ J K^{-1} mol^{-1}	$\Delta\Delta H^\bullet$ kJ mol^{-1}	$\Delta\Delta S^\bullet$ J K^{-1} mol^{-1}	$\Delta\Delta G^\bullet$ kJ mol^{-1}
5	21	−2.21	−6.6	−0.38
25	20	−1.80	−5.2	−0.20
50	17	−1.33	−3.7	−0.13
75	14	−0.95	−2.5	−0.08
100	11	−0.64	−1.6	−0.04

following general features: (a) the values of $\Delta\Delta G^\bullet$ are negative and decrease, in absolute value, with temperature: argon is slightly more soluble in D_2O than H_2O, but the difference tends to vanish with temperature; (b) the values of $\Delta\Delta H^\bullet$ are negative and decrease, in absolute value, on raising temperature: the transfer of argon from H_2O to D_2O is exothermic; (c) the values of $\Delta\Delta S^\bullet$ are small and negative, slightly decreasing, in absolute value, with temperature; (d) the values of $\Delta\Delta C_p^\bullet$ are positive and decrease on raising temperature. The differences in thermodynamic functions for the hydration of argon in H_2O and D_2O are small, but this is expected in view of the close similarity of the two liquids. Nevertheless, such differences are systematic, because qualitatively similar results have been obtained for other nonpolar solutes;[4,8−11] therefore, they have to be properly addressed and rationalized. We will try to perform such a task by means of the theoretical approach reviewed above.

General Analysis

The values of $\Delta G^\bullet$, according to eq 4, are solely determined by the direct perturbation, given by the balance between the solute−water van der Waals interaction energy, E_a, and the entropy decrease due to the excluded volume effect upon cavity creation for solute insertion, ΔG_c. We calculated $E_a = -10.90$ kJ mol^{-1} for argon in H_2O,[16a] and we consider this value correct also for argon in D_2O, owing to the close similarity of the dielectric constant, polarizability, and dipole moment of the two liquids.[13] For instance, the dielectric constant of D_2O is slightly smaller than that of H_2O at the same temperature, the difference being no more than 0.5 unit over the temperature range 4−100 °C.[36] Moreover, E_a is considered temperature independent; this assumption has a physical ground in the very slight temperature dependence of the density for both H_2O and D_2O: the density decreases by 3.8% for D_2O, and 4.2% for H_2O, passing from 5 to 100 °C.[34]

The values of the Gibbs energy cost for cavity creation, ΔG_c, are calculated in a hybrid manner, by means of eq 4, using the experimental data of $\Delta G^\bullet$ and the estimate of E_a. These values of ΔG_c, and the corresponding ones of $\Delta S_x = -\Delta G_c/T$, are reported in the second and fourth columns, respectively, of Table 3. What is important is the fact that ΔG_c is always slightly smaller in D_2O than H_2O: the excluded volume effect is smaller in D_2O. To confirm this finding, ΔG_c is also calculated, in the range 5−100 °C, by means of SPT, using the experimental density of light and heavy water at each temperature.[34] These estimates are reported in the third column of Table 3: they are in fair agreement with the values calculated via eq 4 at all temperatures. According to SPT, the magnitude of ΔG_c is determined by two geometrical properties of the liquid solvent:[14] the hard-sphere diameter of solvent molecules, σ; and its volume packing density, defined as the ratio of the physical volume of a mole of solvent molecules over the molar volume of the solvent (i.e., $\xi = \pi\sigma^3 N_{Av}/6v$, where v is the molar volume of the solvent, and N_{Av} is Avogadro's number), which is a measure of the void volume naturally existing in the pure liquid.

For the pair light water−heavy water, there is no difference in the hard-sphere diameter of the molecules, but there is a small

TABLE 3: Gibbs Energy Cost of Cavity Creation, ΔG_c, Calculated by Means of Both Equation 4 and Scaled Particle Theory; Entropic Contributions from the Excluded Volume, ΔS_x, and the H-bond Reorganization, ΔS^h; and Enthalpic Contribution from the H-bond Reorganization, ΔH^h, in H_2O (a), and D_2O (b), in the Temperature Range 5−100 °C[a]

	T °C	ΔG_c kJ mol^{-1}	ΔG_c(SPT) kJ mol^{-1}	ΔS_x J K^{-1} mol^{-1}	ΔS^h J K^{-1} mol^{-1}	ΔH^h kJ mol^{-1}
a	5	17.95	17.31	−64.5	−10.6	−2.94
	25	19.30	18.44	−64.7	4.3	1.30
	50	20.63	19.63	−63.8	17.8	5.77
	75	21.66	20.58	−62.2	27.6	9.61
	100	22.40	21.33	−60.0	35.1	13.11
b	5	17.57	17.13	−63.2	−18.5	−5.15
	25	19.10	18.32	−64.1	−1.5	−0.50
	50	20.50	19.53	−63.4	13.7	4.44
	75	21.58	20.51	−62.0	24.9	8.66
	100	22.36	21.27	−59.9	33.4	12.47

[a] Specifically, $\Delta G_c = \Delta G^{\bullet} - E_a$, where $E_a = -10.90$ kJ mol^{-1} for argon in both H_2O and D_2O; $\Delta S_x = -\Delta G_c/T$ and $\Delta S^h = \Delta S^{\bullet} - \Delta S_x$; $\Delta H^h = \Delta H^{\bullet} - E_a$.

TABLE 4: Experimental Density, Volume Packing Density, and Thermal Expansion Coefficient of H_2O (a), and D_2O (b), in the Temperature Range 5−100 °C; the Molar Volume Is Calculated at Each Temperature as $v = M_w/\rho$, Where $M_w = 18.02$ for H_2O, and 20.03 for D_2O[a]

	T °C	ρ g cm^{-3}	ξ	$\alpha \times 10^3$ K^{-1}
a	5	0.99996	0.3639	0.016
	25	0.99705	0.3628	0.257
	50	0.98804	0.3596	0.458
	75	0.97485	0.3548	0.613
	100	0.95836	0.3488	0.750
b	5	1.10562	0.3620	−0.067
	25	1.10445	0.3616	0.221
	50	1.09570	0.3587	0.440
	75	1.08158	0.3541	0.604
	100	1.06346	0.3482	0.746

[a] Data are from ref 34.

difference in the volume packing density (see the values reported in the third column of Table 4): ξ is slightly lower in D_2O than H_2O, rendering ΔG_c smaller. The difference, however, tends to vanish as temperature rises. Clearly, in the assumption that E_a is the same in both light and heavy water, we can conclude that the solubility of argon is slightly larger in D_2O than H_2O because D_2O has a slightly lower volume packing density, and the excluded volume effect due to cavity creation proves to be smaller. It has to be noted that Jolicoeur, Fernandez-Prini, and their colleagues arrived at the same conclusion.[1c,5] In fact, ΔG_c(SPT, D_2O) − ΔG_c(SPT, H_2O), which is an estimate of $\Delta\Delta G^{\bullet}$, passes from −180 J mol^{-1} at 5 °C to −60 J mol^{-1} at 100 °C, in qualitative agreement with the experimental values reported in the fourth column of Table 2. It is also important to underscore that the Gibbs energy cost to create a cavity in both light and heavy water moderately increases as the temperature rises, in contrast to what happens in organic solvents. This important feature is related to the very small temperature dependence of water density, as already discussed and explained.[15,16]

Since SPT was originally devised for hard-sphere liquids,[31] its extension to water is questionable and some general comments are necessary. SPT is not a rigorous molecular theory because it does not provide the Gibbs energy as a function of the molecular properties of the system, from which the density of the liquid can be calculated.[37] Actually, the effective hard-sphere diameter of solvent molecules and the experimental

density of the liquid, at the specified temperature and pressure, are employed in SPT to calculate ΔG_c.[32] Therefore, structural information on the liquid is implicitly provided by the experimental density and the value selected for the hard-sphere diameter.[37] It is known by a long time that the creation of a cavity to accommodate the solute molecule is the process that distinguishes water from the other solvents.[38] The calculation of ΔG_c is a major achievement of SPT, and thus its application should give a physical insight into the special features of water. This is particularly true in performing a comparison between the solubility of nonpolar compounds in light and heavy water, because one can reliably assume that both the molecular size and the strength of van der Waals interactions are identical for such two liquids.

On the other hand, some authors claim that the work necessary to create a cavity in water is almost zero, because natural cavities are already present in the open three-dimensional H-bonded network of liquid water.[39] However, as stressed by Ben-Naim,[38] such an "argument is not valid for a liquid, where the natural holes cannot be taken for the cavities at fixed positions". This important topic has further been investigated and clarified by means of computer simulations, using different but very detailed models of liquid water; see, in particular, the works by Pratt and Pohorille.[40]

We turn now to the analysis of the enthalpy and entropy changes. The values of ΔS_x are large and negative in both H_2O and D_2O, but slightly smaller, in absolute value, in the latter, and are little dependent on temperature. They allow the calculation of ΔS^h by means of eq 2, using the experimental data of $\Delta S^{\bullet}$. These estimates of ΔS^h are reported in the fifth column of Table 3. They are negative for argon in H_2O only at 5 °C, and for argon in D_2O only at 5 and 25 °C; at all other temperatures in the range 5−100 °C, they are positive. This finding emphasizes that ΔS^h is strongly temperature dependent. Therefore, the large and negative entropy change associated with the hydration of argon is mainly due to the excluded volume effect; the reorganization of H-bonds provides a negative but small contribution only at low temperatures. This means that the reorganization of H-bonds cannot be described as iceberg or clathrate formation.

Similarly, having fixed E_a, we calculate ΔH^h by means of eq 1, using the experimental data of $\Delta H^{\bullet}$; these estimates of ΔH^h are listed in the sixth column of Table 3. They are negative for argon in H_2O only at 5 °C, and for argon in D_2O only at 5 and 25 °C; at all other temperatures in the range 5−100 °C, they are positive. This is expected owing to the validity of eq 3. In the assumption that E_a is identical for argon in both H_2O and D_2O, $\Delta\Delta H^{\bullet} = \Delta H^h(D_2O) - \Delta H^h(H_2O)$. Thus, the transfer of argon from H_2O to D_2O is exothermic as a consequence of the features of H-bond reorganization in the two solvents. In particular, $\Delta H^h(D_2O) = -5.15, -0.50,$ and 4.44 kJ mol^{-1} at 5, 25, and 50 °C, respectively, whereas $\Delta H^h(H_2O) = -2.94, 1.30,$ and 5.77 kJ mol^{-1} at 5, 25, and 50 °C, respectively.

Scaled particle theory indicates that the thermodynamics of the purely structural solvent reorganization is correlated to the thermal expansion coefficient α of the solvent;[32] specifically, in the notation of the present work, $\Delta H^h \propto \alpha$ and $\Delta C_p^h \propto (\partial\alpha/\partial T)$. The experimental values of α for H_2O and D_2O, in the temperature range 5−100 °C, are listed in the fourth column of Table 4; at low temperature α is smaller in D_2O than H_2O, but at 100 °C, the difference practically vanishes. These data agree qualitatively with the finding that $\Delta\Delta H^{\bullet} = \Delta H^h(D_2O) - \Delta H^h(H_2O)$ is negative and decreases, in absolute value, on raising temperature. Moreover, the stronger temperature dependence

Solvent Isotope Effect in Hydrophobic Hydration

J. Phys. Chem. B, Vol. 104, No. 39, 2000 **9253**

TABLE 5: Thermodynamic Contributions Arising from H-bond Reorganization upon Hydration of Argon in H_2O (a) and D_2O (b), Calculated with the Modified Muller's Model, by Fixing $\Delta H_U = -0.50$ kJ mol^{-1} and Assuming Perfect Compensation at Any Temperature^a

	T °C	f_b %	f_{hs} %	ΔC_p^h J K^{-1} mol^{-1}	ΔH^h kJ mol^{-1}	ΔS^h J K^{-1} mol^{-1}	ΔS_U J K^{-1} mol^{-1}
a	5	16.3	23.5	214	-2.81	-10.1	1.27
	25	20.5	29.3	195	1.30	4.4	1.28
	50	25.9	36.3	159	5.74	17.8	1.24
	75	31.3	42.8	119	9.21	26.4	1.17
	100	36.3	48.7	81	11.69	31.3	1.09
b	5	14.9	20.9	228	-4.96	-17.8	1.03
	25	19.3	26.8	215	-0.50	-1.7	1.06
	50	25.1	34.2	180	4.47	13.8	1.03
	75	30.8	41.2	137	8.44	24.3	0.97
	100	36.4	47.6	94	11.32	30.3	0.90

^{a} Parameter values: $N = 16$ in both solvents; $\Delta H_{hs}° = 10.23$ kJ mol^{-1} and $\Delta S_{hs}° = 26.97$ J K^{-1} mol^{-1} for argon in H_2O; $\Delta H_{hs}° = 11.21$ kJ mol^{-1} and $\Delta S_{hs}° = 29.24$ J K^{-1} mol^{-1} for argon in D_2O.

of α in D_2O than H_2O accounts qualitatively for the positive values of $\Delta\Delta C_p^\bullet$ experimentally found. Since $(\partial\alpha/\partial T)$ is proportional to the ensemble correlation between volume fluctuations and the fluctuation in the breath of the enthalpy fluctuations,[14] the strong temperature dependence of α for both H_2O and D_2O reflects the unique features of the tetrahedral H-bonded network of liquid water.

Application of the Modified Muller's Model. Now we try to gain further insight into the reorganization of H-bonds in both H_2O and D_2O by means of the modified Muller's model. By fixing $N = 16$ and $\Delta H_U = -0.50$ kJ mol^{-1}, and by using the values at 25 °C of $\Delta H^h = 1.30$ kJ mol^{-1}, $\Delta S^h = \Delta H^h/T = 4.4$ J K^{-1} mol^{-1}, and $\Delta C_p^\bullet = 195$ J K^{-1} mol^{-1} for argon in H_2O, we obtained[16c] $\Delta H_{hs}° = 10.23$ kJ mol^{-1} and $\Delta S_{hs}° = 26.97$ J K^{-1} mol^{-1}. Similarly, by fixing $N = 16$ and $\Delta H_U = -0.50$ kJ mol^{-1}, and by using the values at 25 °C of $\Delta H^h = -0.50$ kJ mol^{-1}, $\Delta S^h = \Delta H^h/T = -1.7$ J K^{-1} mol^{-1}, and $\Delta C_p^\bullet = 215$ J K^{-1} mol^{-1} for argon in D_2O, we obtain $\Delta H_{hs}° = 11.21$ kJ mol^{-1} and $\Delta S_{hs}° = 29.24$ J K^{-1} mol^{-1}. These values indicate that, also in the hydration shell, breaking H-bonds among D_2O molecules requires a larger enthalpy cost, $\Delta\Delta H_{hs}° = 0.98$ kJ mol^{-1}, and a larger entropy increase, $\Delta\Delta S_{hs}° = 2.27$ J K^{-1} mol^{-1}, than breaking H-bonds among H_2O molecules.

The knowledge of $\Delta H_{hs}°$ and $\Delta S_{hs}°$ allows the calculation of the contribution to thermodynamic functions arising from H-bond reorganization at any temperature (for more details see ref 16c). The calculated values of f_{hs}, ΔC_p^h, ΔH^h, and ΔS^h in the temperature range 5−100 °C are listed in Table 5, part a for argon in H_2O, and part b for argon in D_2O. A comparison between the calculated ΔC_p^h values and the experimental $\Delta C_p^\bullet$ data, in the whole temperature range considered, confirms that the model characterized by $\Delta H_U = -0.50$ kJ mol^{-1} works well for both H_2O and D_2O. In particular, at any temperature, the calculated values of ΔC_p^h are larger in D_2O, as experimentally found. This means that the enthalpy fluctuations associated with the two-state equilibrium of H-bonds are larger in D_2O than H_2O, because the values of $\Delta H_{hs}°$ and $\Delta S_{hs}°$ prove to be larger. Therefore, according to the modified Muller's model, the positive values of $\Delta\Delta C_p^\bullet$ are a consequence of the fact that the H-bonds are slightly stronger in D_2O than H_2O, and their rupture provides a slightly larger entropy gain in D_2O than H_2O.

Clearly, also the calculated values of ΔH^h and ΔS^h, in both H_2O and D_2O, are in agreement with the estimates obtained via eqs 1 and 2 and listed in the last two columns of Table 3. The fact that ΔH^h and ΔS^h are both negative for argon in D_2O

at low temperatures is correctly reproduced by the modified Muller's model without the need of additional assumptions or parameters. A simple shift of the equilibrium between broken and intact H-bonds in the hydration shell can generate both positive and negative values of ΔH^h and ΔS^h. Thus, the modified Muller's model is able to give a better-than-qualitative explanation of the differences in thermodynamic functions arising from H-bond reorganization in both H_2O and D_2O.

It is important to note that, at each temperature, the values of f_{hs}, the fraction of broken H-bonds in the hydration shell, are larger than those of f_b in both H_2O and D_2O (see Table 5). Even though the H-bonds in the hydration shell are energetically slightly stronger than those in the bulk water, since $\Delta H_{hs}° > \Delta H_b°$, they are, on average, more broken at all temperatures, $f_{hs} > f_b$, because the rupture of a H-bond in the hydration shell affords a larger entropy gain than the same process in the bulk water, $\Delta S_{hs}° > \Delta S_b°$. In this regard, it is worth noting that the entropy change plays a decisive role in the two-state equilibrium.[16c,d] These statements are entirely true for both H_2O and D_2O, and confirm that the hydration shell is by no means more ordered than the bulk. This conclusion is in clash with the claims originated from the classical approaches to hydrophobic hydration;[12] but it proves to be of general validity for the hydration of noble gases, aliphatic hydrocarbons, benzene, and aliphatic alcohols,[14–17] and is in line with computer simulation results[41,42] and, more importantly, with direct structural determinations.[43,44]

Clathrate- or iceberg-like structures around nonpolar moieties have not been detected in several computer simulation studies;[41] in addition, molecular dynamics simulations of some hydrocarbons in different water models have confirmed that $f_{hs} > f_b$ at all temperatures,[42] as originally claimed by Muller.[25,27]

Neutron scattering studies have pointed out the existence of a hydration shell around nonpolar compounds,[43] including argon,[30] but the degree of disorder is large. X-ray absorption spectroscopy measurements of the hydration shell of krypton lead to similar conclusions.[44] In addition, Finney and colleagues[44b] have clearly detected the increase in the structural disorder of the hydration shell as temperature rises. This structural evidence is in complete agreeement with the strong temperature dependence of ΔH^h and ΔS^h, and reproduced quite well by the modified Muller's model.

In conclusion, the solubility of argon is slightly larger in D_2O than H_2O because D_2O has a lower volume packing density and the Gibbs energy cost for cavity creation proves to be slightly smaller. On the other hand, the heat capacity change associated with the transfer of argon from H_2O to D_2O is positive because the enthalpy fluctuations due to the reorganization of H-bonds prove to be larger in D_2O. It is important to note that these results should be of general validity for nonpolar compounds.

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