Aqueous Solution Structure as Determined from Thermodynamic

Parameters of Transfer from H_2O to D_2O ^{1,2}

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ABSTRACT

The free energy and enthalpy of transfer from H_2O to D_2O at 25°C have been measured for several ketones and alcohols. Free energy of transfer is near zero for most substances studied. Exceptions to this occur for many cyclic compounds with side groups. Enthalpies of transfer range from -514 cal/mole for 3-pentanol to +70 cal/mole for 3,3-dimethylacetylacetone. These data combined with results from other laboratories have been interpreted in terms of solvent structure-breaking and making spheres of influence caused by polar and nonpolar groups of the solute and the interactions caused by the overlap of such spheres. Polar groups have been found to be structure-breakers, while methylene groups have been found to be structure-makers. Overlap of regions of structural influence decreases the capabilities of such groups to alter solvent structure. Ring compounds show unusually small enthalpies of transfer probably due to the inability of water to enter the interior area of

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the ring. Some ring solutes such as cyclohexanone, xylene, and naphthalene show relatively large free energies of transfer, but most nonelectrolytes show free energies of transfer near zero.

INTRODUCTION

For many years the lack of knowledge about water and solution structure has hindered the understanding of the role of the solvent in equilibria and reaction mechanisms for aqueous solutions. In some systems medium effects have been unjustly neglected. For example, the relative acidities of alcohols in aqueous solutions is a popular textbook justification for the belief that alkyl groups are electron donating. However, Brauman and Blair³ have recently

3) J. J. Brauman and L. K. Blair, J. Am. Chem. Soc. 92, 5986 (1970).

shown that the relative acidities of alcohols in water are reversed as compared to those in the gas phase, and that medium effects are responsible for the altered behavior. The medium effect is also very important in biological systems. Scheraga⁴ has stressed the importance of solvation in determining

4) H. A. Scheraga, Adv. in Phys. Org. Chem. 6, 103 (1968).

the conformation of proteins. It is of particular interest in that water is the "natural" solvent for proteins and enzymes. Jenks⁵ in discussing the

5) W. P. Jenks, Catalysis in Chemistry and Enzymology, McGraw-Hill, New York (1969).

role of hydrophobic interactions in equilibria and reactions in solution postulated that such effects are the result of attractive van der Waals-London dispersion forces, competing with the strong attraction of water molecules for each other; i.e., "water structure." A detailed quantitative model for such interactions is not yet available due to the numerous types of rather weak forces adding and competing with each other. It is for this reason that initial studies of water and solution structure have depended heavily on interpretation of thermodynamic parameters. Entropies, enthalpies, and free energies of hydration have been very valuable to such studies, but meaningful interpretation of data requires a gas phase standard state and thus very accurate values of such quantities as heats of vaporization combined with heats of solution. This is not possible for many relatively non-volatile solutes. The search for a more easily interpretable solvent had led Krishnan and Friedman⁶ to the use of propylene carbonate with some

6) C. V. Krishnan and H. L. Friedman, a) *J. Phys. Chem.*, 73, 1572 (1969);
 b). 73, 3934 (1969); and c) 74, 3900 (1970).

success. Such a solvent was chosen for its high dielectric constant, its lack of hydrogen-bonding capabilities and minimal basic and acidic tendencies. However, it is still quite difficult to correct for different subtle interaction between this solvent and various solutes. In a recent review, Arnett and McKelvey⁷ pointed out that if one is willing to accept the assumption that

7) E. M. Arnett and D. R. McKelvey, *Solute-Solvent Interactions*, ed. by J. F. Coetzee and C. D. Ritchie, Marcel Dekker, New York (1969), Ch. 6.

H_2O and D_2O have the same properties, differing only in degree, thermodynamic quantities of transfer can provide a great deal of information about aqueous solution structure without complication of large conformational changes of solutes and extraneous interactions in the standard state. Gurney⁸ and Frank and coworkers⁹ have presented similar models for the structure of the

8) R. W. Gurney, Ionic Processes in Solution, McGraw-Hill, New York (1953).

9) a) H. S. Frank and M. W. Evans, J. Chem. Phys., 13, 507 (1945).

b) H. S. Frank and Wen-Yang Wen, Disc. Far. Soc., 24, 133 (1957).

solvent water around both ions and nonelectrolytes. These models describe spheres of structure-making and breaking influence caused by various types of solutes. This paper presents new thermodynamic data for transfer of solutes from H_2O and D_2O and attempts to analyze the data in terms of an expanded version of the aforementioned model.

EXPERIMENTAL

A. Materials: Water was singly distilled and 99.8% A.R. heavy water was purchased from Mallinckrodt Chemical Works and was used without further purification. Cyclohexane was Fisher certified spectral grade as were acetone, benzene, toluene and isopropanol. Hexane-2,5-dione showed an unusually high U.V. extinction coefficient, which was not eliminated by distillation. Recrystallization of the diketone at $-60^\circ C$ in n-pentane yielded pure diketone with a reasonable extinction coefficient of 37.4 in cyclohexane at 275 m μ . All other compounds were distilled to at least a one-degree range.

B. Free Energy of Transfer from H_2O to D_2O : Slightly soluble solids and liquids were stirred separately with both H_2O and D_2O for at least 48 hours submerged in a $25.00 \pm 0.05^\circ C$ thermostated bath. The U.V. absorbance of a centrifuged sample of the aqueous phase was measured on a Cary 14. The ratio of the absorbance of the water and heavy water phases provided the ratio of solubilities, if it is assumed that extinction coefficients are the same in both mediums. This assumption was verified for acetone and 2-butanone.

For more soluble materials, a few drops of the solute was stirred for 48 hours at $25.00 \pm 0.05^\circ C$ in a flask containing 10 ml of light or heavy water. The U.V. absorbance of centrifuged samples of all phases were measured. Extinction coefficients were determined in H_2O and cyclohexane for the ketones to check purity and to calculate free energy of transfer from H_2O to cyclohexane. Concentrations of solutes were always less than 10^{-2} M. Using cyclohexane as a standard state yielded the free energy of transfer and the degenerate activity coefficients from H_2O to D_2O , as defined by

$$KH^{(D_2O)} \neq KH^{(H_2O)}, \gamma_{KH} \quad (1)$$

$$\gamma = \left[\frac{A_{KH}^{(H_2O)}}{A_{KH}^{(cyclohexane)}} \right] / \left[\frac{A_{KH}^{(D_2O)}}{A_{KH}^{(cyclohexane)}} \right] \quad (2)$$

$$\Delta \bar{G}_t^{25}(KH) = RT \ln \gamma_{KH} \quad (3)$$

where A is the observed absorbance of the solute KH in the indicated partitioned solvent.

C. Enthalpies of Transfer: Enthalpies of transfer from H_2O to D_2O were determined by dilution adiabatic calorimetry exactly as described by Scheraga

and coworkers.¹⁰ A typical experiment involves placing about 40 mg of carefully

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- 10) G. C. Kresheck, H. Schneider, and H. A. Scheraga, J. Phys. Chem., 69, 3123 (1965).
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weighed solute and about 3 ml of weighed H_2O in a small cell. After bringing the system to 25°C, a window in the cell was broken by an electrically controlled spring releasing the contents into a larger cell containing about 46 g of weighed D_2O . The temperature was monitored using thermocouples to within 1×10^{-4} °C. Similar measurements were done to determine the heat of dilution in pure H_2O . The heat of exchange of the H_2O and D_2O was determined by Scheraga.¹⁰ The heat change q_t due to the transfer of the solute is given by

$$q_t = q_{mix} - q_{H_2O} - q_{dil} \quad (4)$$

where q_{mix} represents the heat of dilution of the H_2O solution into D_2O , q_{H_2O} is the heat of exchange from mixing an equivalent amount of D_2O and q_{dil} is the heat of dilution of the H_2O solution into H_2O . Table I shows typical data for acetone. Table II shows the enthalpies of transfer obtained from the experiments performed in this laboratory. Since the final solutions after dilution contain about 7% protium, it is necessary to correct these values to 100% D_2O by dividing the determined molar enthalpy of transfer ΔH_t^0 values by the final mole fraction deuterium of the solvents. One experiment was performed at 15°C to determine the heat capacity of transfer for 2-butanone, which turned out to be near zero.

TABLE I

Illustrative experimental data for acetone at 25°C for determination of enthalpy of transfer

Expt. #	wt. acetone (mg)	wt. H ₂ O (g)	wt. D ₂ O (g)	q _{mix} (cal)	q _{H₂O}	-q _{dil} (cal)
1	54.6	2.9882	46.96	4.696	4.841	0.018
2	48.0	2.9892	46.91	4.691	4.843	0.016

TABLE II

The enthalpies of transfer of various non-electrolytes from dilute
H₂O to dilute D₂O at 25.0°C

Compound	$-\bar{H}_t^\circ$ (cal/mole) to 93% D ₂ O	$-\bar{H}_t^\circ$ (cal/mole) to 100% D ₂ O	Average $-\bar{H}_t^\circ$ (cal/mole)
Ketones:			
acetone	135	144	160 ± 16
	164	176	
2-butanone	215	232	232 ± 0
	216	232	
	215 (15°C)	230 (15°C)	230 (15°C)
3-pentane	309	331	318 ± 12
	286	306	
3-hexanone	392	420	419 ± 1
	390	418	
cyclohexanone	157	168	186 ± 18
	190	203	
hexane-2,5-dione	8	9	18 ± 10
	26	28	
3,3-dimethyl acetylacetone	-66	-70	-70
Alcohols:			
isopropanol	357	383	384 ± 2*
	359	386	
3-pentanol	485	520	514 ± 6
	475	508	
cyclohexanol	408	437	449 ± 12
	429	460	

* Scheraga and coworkers¹⁰ determine $\bar{H}_t^\circ = -417 \pm 4$ cal/mole for isopropanol.

RESULTS

Enthalpy of Transfer: The molar enthalpies of transfer from H_2O to D_2O were determined in this laboratory for a homologous series of four monoketones plus two diketones, two secondary alcohols, cyclohexanone and cyclohexanol. From Table II it can be seen that all except 3,3-dimethylacetylacetone have negative enthalpies of transfer. Figure 1 contains these values as well as selected values obtained in other laboratories.¹¹ Arnett and McKelvey⁷

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- 11) The ΔH_t° 's for a) primary alcohols and amino acids, see ref. 10.
 b) Values for the sodium salts of carboxylic acids were obtained from H. Snell and J. Greyson, J. Phys. Chem., 74, 2148 (1970).
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have suggested that since D_2O is believed to be more structured than H_2O , it is more susceptible to structure-breaking and structure-making, the former being shown by a positive enthalpy of transfer and the latter by a negative enthalpy of transfer. This assignment was based on the fact that certain compounds and ions show structure-making and breaking qualities in water as measured by other techniques such as enthalpies and entropies of hydration, viscosity, diffusion, and conductivity. All of these methods give a rather consistent picture of the influence of certain types of solutes on water structure and correlate well with the enthalpies of transfer from H_2O to D_2O .

Most of the non-electrolytes and some of the sodium carboxylate salts are indicated in Fig. 1 to be structure-makers. In all cases, it is seen that the more carbons in a series of homologs, the more negative the enthalpy of transfer; which is consistent with the proposal that methylene groups are structure-makers. Also, it is noted that diketones have a much less negative enthalpy of transfer than do monoketones, indicating that the polar carbonyl groups are structure-breakers. It can be seen from Figure 1 that for a constant

number of carbons the order of increasing enthalpy of transfer is: primary alcohols < amino acids < monoketones < sodium carboxylates < diketones. With the exception of the amino acids this is the order of increased polarity and number of the functional groups. The unexpected low values for the amino acids are probably due to the three quickly exchangeable protons, which apparently create a more negative enthalpy of transfer. A similar result has been observed from the less accurate results of Krishnan and Friedman^{7c} for alkylammonium ions after correcting for the anion transfer. Arnett and McKelvey assumed that if the enthalpy of transfer of the lithium ion is zero, the sodium ion would take on a value of about +160 cal/mole. This would lower the values of the alkyl carboxylate ions by that amount making all, except formate structure-makers. This would not change the relative order of increasing enthalpies of transfer.

It should also be noted that the plot of ΔH_t° versus the number of carbons in the molecule is linear for the monoketones, while it is curved for small alcohols, amino acids and sodium carboxylates and fairly linear for the longer molecules. Finally, molecules with saturated or aromatic cyclic frameworks show much less negative enthalpies of transfer than linear molecules containing the same number of carbons and the same functional groups.

Free Energy of Transfer: The free energies of transfer from H_2O to D_2O ΔG_t° as obtained in this laboratory are listed in Table III. Arnett and McKelvey have summarized a few other values of ΔG_t° for nonelectrolytes and noted that in most cases enthalpies of transfers are 5 to 10 times the free energies of transfer. The ketones studied in this laboratory show zero free energies of transfer within experimental error, except for cyclohexanone.

TABLE III

The Free Energies of Transfer from
 H_2O to D_2O at $25.0^\circ C$

<u>Compound</u>	<u>$\Delta \bar{G}_t^0$ (cal/mole)</u> <u>mole fraction units</u>
Ketones:	
acetone	0 ± 15
2-butanone	7 ± 20
3-pentanone	-18 ± 20
3-hexanone	0 ± 15
cyclohexanone	$+52 \pm 10$
hexane-2,5-dione	0 ± 15
3,3-dimethylacetylacetone	$+41 \pm 40$
3-methylacetylacetone (keto)	$+25 \pm 40$
3-methylacetylacetone (enol)	$+200$
Aromatic:	
benzene	0 ± 15
toluene	$+25 \pm 15$
m-xylene	$+45 \pm 12$
o-xylene	$+84 \pm 20$
naphthalene	$+108 \pm 15$
benzyl alcohol	-9 ± 20
deuteroquinone ^a	$+110$
nitrobenzene ^b	$+157$
L-phenylalanine ^c	$+127 \pm 1$

a) Ref. 19

b) Ref. 20 determined at $30^\circ C$

c) Ref. 10

The free energy of transfer is also near zero for benzene, but slightly positive for toluene and much larger for the xylenes and naphthalene. Finally, from the keto-enol equilibrium of 3-methylacetylacetone the value of $\Delta\bar{G}_t^\circ$ for the cyclic enol is approximately 200 cal/mole, while for the keto form $\Delta\bar{G}_t^\circ = 25 \pm 40$ cal/mole.¹²

12) D. B. Dahlberg and F. A. Long, to be published.

DISCUSSION

Enthalpy of Transfer: In their recent review Arnett and McKelvey⁷ noted that $\Delta\bar{H}_t^\circ \approx T\Delta\bar{S}_t^\circ$ due to the extremely small values of $\Delta\bar{G}_t^\circ$ for such compounds as methyl halides, small alkanes, and amino acids. This relationship was also observed for most nonelectrolytes studied in this laboratory as seen from Table III. This is a special case of the "Vaslow-Doherty compensation" phenomenon as reviewed by Lumry and Rajender.¹³ When $\Delta\bar{H}_t^\circ$ is plotted against

13) R. Lumry and S. Rajender, *Biopolymers*, 9, 1125 (1970).

$\Delta\bar{S}_t^\circ$ for some equilibrium process of closely related compounds, a straight line is obtained, which has a slope of the order of 300°K and a relatively small intercept which is a measure of $\Delta\bar{G}_t^\circ$. Although this phenomenon is not unique to water solutions, it is believed to be related to the structural changes of the solvent. Lumry and Rajender have suggested that water acts as a "volume buffer" to counteract the changes of volume associated with certain structural changes of the solute and solvation shells. At least it is obvious that the binding of water by any mechanism, shown by a negative

$\Delta\bar{H}_t^\circ$, also restricts the degrees of freedom of that water, shown by a negative $\Delta\bar{S}_t^\circ$. Thus the enthalpies of transfer, which measure the energetics of solvent-solute and solute-solute interactions, are linearly related to the entropies of transfer, which is a measure of the order-disorder caused by such interactions. This allows at least qualitative discussion of solution structure in terms of enthalpies of transfer, when entropies of transfer are not available.

The Gurney,⁸ and Frank and Wen^{9b} models for the structure of the aqueous solvent near ionic solutes suggest that there is a region of highly structured water surrounding the ion due to the strong attractive forces between the ion and polar water. However, farther away from the ion the electrostatic forces are no longer strong enough to structure the water, but may be strong enough to break up some of the normal bulk water structure. Very far from the ion, the bulk solvent contains the normal unperturbed water structure. The observed entropy change is the sum of the changes for the two regions; i.e., ion structured, ion broken as compared with bulk water. For large ions, the charge is more diffuse and the region of highly structured water near the ion is smaller. Also, water is held away from the center of the charge by the physical size of the ion. This leads to a net structure breaking quality to most large ions. A similar picture can be applied to charged groups or even polar groups, explaining the structure-breaking influence seen here. The mechanism for the structure-making influence of methylene group is not understood, but the effect has been observed many times.^{7,9a}

Gurney⁸ has considered the problem of very concentrated solutions where various solute molecules or ions are forced so close together that their regions of structure-making or breaking influence overlap. This should cause

an overlap of effects with much duplication; i.e., the structure-breaking or making effects would be reduced due to the fact that in the regions of overlap of influence the structure effect of one molecule or ion makes no added contribution since the region has already been structured or destructured by another ion or molecule. This would lead to a decrease in the absolute value of the molar entropy and enthalpy of transfer with increased solute concentration for both structure-makers and structure-breakers.

Arnett and co-workers¹⁴ have observed this effect in the decrease of the

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- 14) E. M. Arnett, M. Ho, and L. L. Schaleger, J. Amer. Chem. Soc., 92, 7039 (1970).
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molar enthalpy of solution of benzene as the concentration of the benzene or tetrabutylammonium bromide (both structure-makers) is increased. Greyson and co-workers^{11b} have observed the same trend in the molar enthalpies of transfer from H_2O to D_2O of sodium salts of aliphatic acids as their concentration increased. Those with positive enthalpies of transfer, structure-breakers, yielded less positive values with increasing concentration, while those with negative enthalpies of transfer, structure-makers, yielded less negative values with increasing concentration.

Another example of the significance of overlap of spheres of influence was provided by Wetlaufer, et. al.¹⁵ who discovered that urea, a structure-

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- 15) D. B. Wetlaufer, S. K. Malik, L. Stoller, and R. I. Coffin, J. Amer. Chem. Soc., 86, 509 (1964).
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breaker, decreased the evolution of heat from dissolving several structure-making hydrocarbon gases in water. This seems to demonstrate that when a

sphere of structure-breaking influence is overlapped with a sphere of structure-making influence the result is at least partial cancellation of structure-making and breaking effects.

The concept of overlapping spheres of influence is applicable to molecules containing varying numbers of both polar and non-polar groups, in that the structure-breakers and makers are held closely together by chemical bonds. This idea was presented in a speculative way as early as 1957 by Everett,¹⁶

16) D. H. Everett, Disc. Faraday Soc., 24, 220 (1957).

but he did not analyze the specific nature of the solvent structure near various types of groups. The following is an analysis of the ΔH_t° data obtained in this and other laboratories in terms of the model of overlapping spheres of influence.

Examination of Figure 1 shows that the structure-making effect of the methylene groups is dominant and is fairly constant per methylene group for any given series of homologs, except when there are only one or two carbons in the molecule, which are near part of the polar head group. Here the overlap of the structure-making and breaking spheres of influence cause a greatly reduced structure-making effect as seen by the upswing in the lines for shorter molecules. This effect is also apparent when comparing secondary alcohol with their primary isomers. Here the polar hydroxyl group is near three carbons; while for primary alcohols, it is near only two carbons. The influence seems to taper off quickly somewhere near the carbon alpha to the head group.

For the four monoketones the plot of ΔH_t° versus the number of carbons in the solute molecule is linear, because the polar group is always centrally

located as in the secondary alcohols. Acetone has a $\Delta\bar{H}_t^\circ = -160$ cal/mole, while hexane-2,5-dione as a $\Delta\bar{H}_t^\circ = -18$ cal/mole. If the diketone is looked upon as two acetones connected together, an enthalpy of transfer of a minus 320 cal/mole would be expected. The diketone has a $\Delta\bar{H}_t^\circ$ about 300 cal/mole higher than expected, and 3,3-dimethylacetylacetone is even higher. This suggests that the structure-making influence of the central carbons is greatly reduced by their overlap with each other in hexane-2,5-dione and that such overlap is enhanced even more by branching as in 3,3-dimethylacetylacetone.

Also of interest are the much less negative enthalpies of transfers of cyclic compounds. Both cyclohexanol and cyclohexanone are of the order of 200 cal/mole higher in $\Delta\bar{H}_t^\circ$ than their linear counterparts; and benzylalcohol and phenylalanine are about 270 cal/mole higher than expected values for their linear counterparts. A reasonable explanation is that there is no space for water in the interior of the ring and thus a great loss in water-structuring capability per methylene group. Aromaticity seems to further reduce the structure-making influence of the methylene groups, which is in line with the higher solubilities of aromatic compounds compared to saturated hydrocarbons. A final example of extreme overlap is observed for enthalpies of transfer for tetraalkylammonium salts.⁶ Even after correcting for the anion, the values are surprisingly high and the slope is very small (approximately 20 cal/mole per methylene group). The compact spherical geometry apparently greatly reduces the number of methylenes exposed to the water.

Attempts to make such a model quantitative are hampered by several problems. First, the so-called "spheres or structure influence" are probably neither spherical nor do they have a definite radius. Their shape and range of influence would depend on the shape and polarity of the functional groups

in question as well as the distance from the group. Also, there is no reason to believe that the mechanism of the structure-making influence of methylene groups is the same as the mechanism of structure-breaking influence of polar groups. Almost all solutes studied so far contain both polar and hydrophobic groups in close proximity, so there is no way of assigning values for the structure influence of either type alone. Finally, for the compounds studied so far, the overlap effects of polar groups seem to be so short-ranged as to affect only atoms one or two places removed. However, further study in this field would be greatly rewarding, because it would provide valuable information on the influence of water structure on the configuration of such molecules as proteins in water, as well as the interactions between molecules while involved in transition states of a reaction.

Free Energies of Transfer: As stated earlier, the free energies of transfer from H_2O to D_2O are near zero for most nonelectrolytes. However, some solutes do show significant free energies of transfer. It is apparent from the data of simple salts obtained by Salomaa and co-workers¹⁷ that anions are

17) P. Salomaa and V. Aalto, *Acta. Chem. Scand.*, 20, 2035 (1966).

characterized by positive ΔG_t° values, while those of cations are close to zero. They suggest that the difference arises because of a deuterium isotope effect for the H-bonding to the anions which is not present in aqueous solutions of cations. One would then expect to see the same effect with ketones, which are good H-bond recipients. However, the ketones show zero free energies of transfer. Reuben¹⁸ saw no difference in the oxygen-17 NMR chemical shifts of

18) J. Reuben, *J. Amer. Chem. Soc.*, 91, 5725 (1969).

acetone in H_2O and D_2O , indicating that there is no difference between the strengths of the H-bond and D-bond to the carbonyl. This may not be the case for the much stronger H-bonds to anions. Large positive value of $\Delta\bar{G}_t^\circ$ also occurs with some nonelectrolytes too. Scheraga and co-workers¹⁰ pointed out that the $\Delta\bar{G}_t^\circ$ for L-phenylalanine was +127 cal/mole, while values for amino acids not containing rings ranged from -28 cal/mole for glycine to +13 cal/mole for DL-norleucine. Deuteroquinone¹⁹ and nitrobenzene²⁰ show unusually high

19) B. Hayes, Thesis, M.I.T., Cambridge (1964).

20) H. E. Vermillion, et. al., J. Amer. Chem. Soc., 63, 1346 (1941), determined at 30°C.

$\Delta\bar{G}_t^\circ$ of +100 cal/mole and +157 cal/mole respectively. The ring alone is not the cause of such high $\Delta\bar{G}_t^\circ$ as demonstrated by the near zero values for benzene and benzylalcohol; however, the addition of certain side chains often causes significantly larger increases in $\Delta\bar{G}_t^\circ$ as shown by toluene, the xylenes, naphthalene, and cyclohexanone. The importance of shape is seen from the keto-enol isomer equilibrium of 3-methylacetylacetone,¹² where the keto form acts as most ketones, while the enol, which with its intramolecular H-bonded ring structure looks very much like trimethylbenzene, shows a very high $\Delta\bar{G}_t^\circ$. Even quite subtle differences like ortho and meta-xylene causes relatively substantial changes in $\Delta\bar{G}_t^\circ$.

With only limited data it is difficult to interpret these results in terms of water structure. The low solubility of alkyl substituted cyclohexanones and of benzene prevents the study of $\Delta\bar{H}_t^\circ$ for these compounds. F. Franks, et. al.²¹ have, however, studied the heats of hydration $\Delta\bar{H}_h^\circ$ of several

21) F. Franks, M. A. S. Quickenden, D. S. Reid and B. Watson, Trans. Far. Soc., 66, 582 (1970).

cyclic ether derivatives in H_2O . They noted that little net change in total interactions occurs when the tetrahydrofuran ring is enlarged. They also concluded that the addition of a $-CH_2OH$ group causes $\Delta\bar{H}_n^0$ to be markedly more exothermic. It appeared to them that side groups of cyclic compounds determine the $\Delta\bar{H}_n^0$ value, which was only slightly modified by the ring. This agrees with the observation made here that the $\Delta\bar{H}_t^0$ is affected very little by methylene groups involved in a ring structure. Clemmentt and co-workers²² studies cyclic ethers in H_2O by NMR and diffusion techniques

22) C. J. Clemmentt, et. al., J. Chem. Soc. A, 455 (1969).

concluded that such ring compounds in water rich mixtures are closely enveloped by water molecules, but do not interact strongly with them. Whether or not this "envelope" is different from the structure-making region of linear alkyl groups, and how sensitive this structure is to the shape of the solute, as well as size, remains to be seen. The fact that for anions and a few nonelectrolytes, especially rings with branches, the enthalpies of transfers are not completely compensated for by the entropies of transfer indicates that special solvent-solute and solute-solute interactions occur with these solutes, that are not present with simple cations and most nonelectrolytes. The lack of understanding of the nature of these interactions and the resulting non-zero free energies of transfer stands in the way of truly understanding medium effects on equilibria and kinetics in aqueous solutions.

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FIGURE I

The Enthalpy of Transfer from Light to Heavy Water vs.
the Number of Carbons in the Solute Molecule

- Primary Alcohols
- Secondary Alcohols
- Amino Acids
- Monoketones
- Diketones
- Sodium Salts of Carboxylic Acids