Thermodynamics of Transfer of Nonelectrolytes from Light to Heavy Water. III. Transfer Free Energies of Tertiary Aromatic Amines

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The free energies of transfer from H_2O to D_2O for pyridine, eight substituted pyridines, quinoline, and acridine have been determined by distribution and solubility measurements. Correlations between the transfer free energy and different solvation properties are presented. The properties concerned here are the basicity, the so-called hydrophilic character, and the relative amount of hydrogen atoms in the solute molecule.

Studies of aqueous solutions by means of replacing H_2O by its isotopic form D_2O have been increasing lately. Two main approaches have been applied to explain the changes in solution properties between H_2O and D_2O. The first approach is based on a statistical model for the solute in the solvent water. The other treats the problem by trying to find correlations with various other solution properties in the transfer from H_2O to D_2O. These two methods of operation have a strong thermodynamical basis, although the latter also involves some extra-thermodynamic assumptions and correlations.

Recently Ben Naim [1] published a paper using the first approach. He applies statistical mechanics to relate the isotopic effect in the standard free energy in light and heavy water with the change in the average number of hydrogen bonds in the solvent. Although the model is simple, it is possible to classify some solutes as structure breakers and structure promoters.

With the second approach it is difficult to find universal correlations giving additional knowledge about water solutions. Several attempts, including the ones made by the present writers, have been made to solve the problem with the aid of the thermodynamic transfer properties from H_2O to D_2O.[3-5] The transfer free energy, which, in practice, is the only thermodynamic quantity that can be investigated without calorimetric measurements in this context, is very sensitive to many influences.

We have here determined the transfer free energies from H_2O to D_2O for a limited group of compounds, namely tertiary aromatic amines. These are slightly polar compounds with no exchangeable hydrogens. In pyridine the substituents are mainly at positions 2 and/or 6. The main focus of interest has been to study the substituent effect on the values of $\Delta G_t^{\ominus}$, the standard free energy of transfer from H_2O to D_2O. The solubilities of pyridines in water, in general, are of such magnitude that the distribution measurements were the only possible means for determining the transfer free energies. This, on the other hand, caused greater experimental errors than if the $\Delta G_t^{\ominus}$ values had been determined by some direct method, e.g. by solubility measurements. However, some distinct features are found in the correlations between $\Delta G_t^{\ominus}$ and other solution properties.

EXPERIMENTAL

Light and heavy water (Norsk Hydro, deuterium mol fraction 0.997) was treated as described earlier.[4] The pyridines were commercial products of *purissimum* grade. 2-Pentylpyridine was synthesized from 2-methylpyridine and 1-chlorobutane with sodamide in anhydrous

xylene.[6a] Quinoline was synthesized in the conventional way.[6b] Both the commercial and synthesized products were redistilled before use. Acridine was purified by recrystallizing twice from ethanol.

The free energies of transfer from H_2O to D_2O of 2-pentylpyridine and acridine were determined by solubility measurements. For the others the free energy values were determined by distribution measurements. The third solvent used in the partitioning of the solutes was 2,2,4-trimethylpentane (BDH, special for spectroscopy).

The analysis of the pyridines was carried out in either of the two following ways. In connection with the distribution measurements a titration method was used. Samples were taken from the organic phase and weighed and transferred to approximately 40 cm^3 of glacial acetic acid and titrated in a Metrohm Combi Titrator Type 3D with perchloric acid of known molarity. The second method of analysis was spectrophotometrical using a Beckman DK-2A Ratio Recording Spectrophotometer. A standard solution was first prepared in water and proper amounts of it were injected with an Agla micrometer syringe directly into the tared spectrophotometer cell filled with water. The absorbances were measured and plotted *versus* concentration to obtain a standard curve. The samples were taken from the aqueous phase and transferred with the Agla syringe to the spectrophotometer cell. The absorbances were then measured and the corresponding concentrations read on the standard curve.

In the distribution measurements the equilibrium was allowed to settle for at least three days. In the solubility measurements a longer time *viz.* one week was needed. The equilibration vessels were sealed flasks, which were kept in complete darkness to prevent a possible decomposition by light. These flasks were kept in a water bath of constant temperature of 298.15 ± 0.05 K. The contents of the flasks were mixed during the equilibration by a magnetic stirrer.

RESULTS AND DISCUSSION

The free energy of transfer from H_2O to D_2O for solubility measurements can be evaluated in the way described earlier.[4] In the distribution measurements the simple calculations presented below are needed. Moderately low concentrations ($< 10^{-2}$ mol/dm^3) were used to assure the ideality of the system. The following equilibria prevail in the distribution experiments (the third solvent, 2,2,4-trimethylpentane, is denoted by S):

$$\text{solute}(m_H, \ H_2O) = \text{solute}(m_S, \ S) \quad (1)$$

$$\text{solute}(m_D, \ D_2O) = \text{solute}(m_S', \ S) \quad (2)$$

The partition coefficients are as follows

$$k_1 = m_S/m_H \quad (3)$$

$$k_2 = m_S'/m_D \quad (4)$$

If the solution in the third solvent is assumed to behave ideally, the partition coefficient (6) for the wanted equilibrium (5) is obtained.

$$\text{solute(hypoth. 1 m soln, } H_2O) = \text{solute(hypoth. 1 m soln, } D_2O) \quad (5)$$

$$K = k_1/k_2 = (m_S m_D)/(m_H m_S') \quad (6)$$

Table 1. Partition coefficients k_1 and k_2 and free energies of transfer from H_2O to D_2O of some tertiary aromatic amines.

Compound	$k_1{}^a$	$k_2{}^a$	$\Delta G_t{}^\ominus/\text{J mol}^{-1}$
1. Pyridine	41.79 ± 0.58	47.14 ± 1.76	306 ± 90
2. 2-Methyl-pyridine	157.7 ± 1.1	172.2 ± 1.4	218 ± 27
3. 2-Ethyl-	848.7 ± 2.2	896.0 ± 2.1	134 ± 11
4. 2-Pentyl- [b]	$(3.037 \pm 0.006)10^{-2}$	$(3.169 \pm 0.008)10^{-2}$	-104 ± 10
5. 2,6-Dimethyl-	544.8 ± 2.1	584.2 ± 2.1	174 ± 13
6. 2,4,6-Trimethyl-	1703 ± 19	1786 ± 25	118 ± 45
7. 2-Methoxy-	1344 ± 13	1536 ± 9	329 ± 28
8. 2,6-Dimethoxy-	15780 ± 107	17352 ± 71	235 ± 20
9. 2-Vinyl-	787.5 ± 8.9	903.4 ± 7.0	340 ± 35
10. Quinoline	1586 ± 9	1873 ± 17	412 ± 33
11. Acridine [b]	$(1.601 \pm 0.006)10^{-4}$	$(1.372 \pm 0.001)10^{-4}$	382 ± 18

[a] $(\pm)$-Values are standard errors. [b] Solubility values (aquamolal scale).

The free energy of transfer from H_2O to D_2O is then calculated from the well-known equation (7).

$$\Delta G_t^{\ominus} = -RT \ \ln \ (m_S m_D)/(m_H m_S') \qquad (7)$$

The measured partition coefficients and the free energies of transfer calculated therefrom are tabulated in Table 1. The values for m_H and m_D are expressed in aquamolal scale. The m_S values are for practical reasons expressed as mg/g, which has no effect on the $\Delta G_t^{\ominus}$ values being calculated in aquamolal scale.

The error limits reported in connection with the $\Delta G_t^{\ominus}$ values are based on standard deviations of the mean values. Therefore, the real absolute errors may be of greater magnitude. These data together with the previous results indicate that the values of standard free energies of transfer can be measured with an accuracy of $\pm 10 \%$.

Not enough data exist for a correlation similar to the one described in an earlier paper, i.e. the correlation of the transfer free energy from H_2O to D_2O versus the free energy of dissolution in water of the compounds in question.[4] Instead, the increments of the so-called intrinsic hydrophilic character, reported by Hine and Mookerjee have been applied.[7] In practice, this correlation (Fig. 1) is similar to that described in paper I in this series.[4] It shows that the increments of Hine and Mookerjee are useful at least within a certain group of compounds.
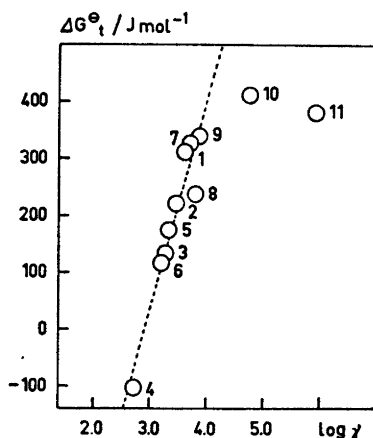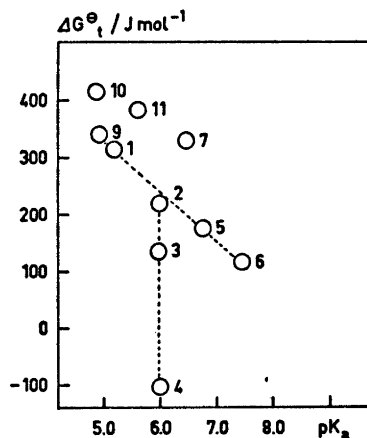

Fig. 2. Correlation between the free energy of transfer from H_2O to D_2O ($\Delta G_t^{\ominus}$) and the pK_a values of protonated tertiary aromatic amines.

Quinoline and acridine which deviate from the correlation line do not belong to the pyridine series.

Polar effects naturally play a marked role in the solvation of the solute in water. Therefore, one might expect that the basicity of the nitrogen atom would correlate with a quantity reflecting the dissolution phenomenon, viz. $\Delta G_t^{\ominus}$. Fig. 2 shows the plot of $\Delta G_t^{\ominus}$ versus pK_a the acidity constants of the conjugated acids having been taken from literature.[8] The cor-

Fig. 1. Correlation between the free energy of transfer from H_2O to D_2O ($\Delta G_t^{\ominus}$) and the so-called hydrophilic character of some tertiary amines.
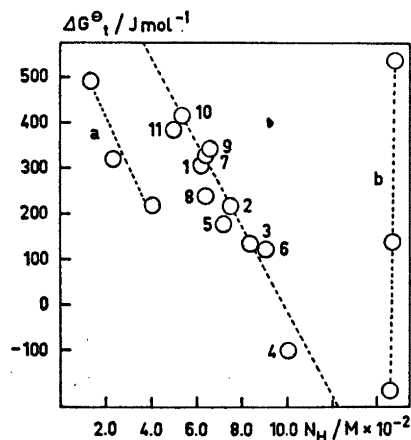

Fig. 3. Correlation between the free energy of transfer from H_2O to D_2O ($\Delta G_t^{\ominus}$) and the number of hydrogen atoms relative to molecular weights of solutes (a. the nitrobenzene group, b. the aliphatic amine group; Ref. 4.)

relation obtained is good especially for methyl-pyridines. Quinoline and acridine show small deviations which are to be expected considering their structures. There is, however, one striking feature in this plot, namely, the effect of the lengthening of the carbon chain of the substituent at position 2 in the pyridine ring (points 2, 3, and 4). A clear tendency towards lower free energies is observed when the length of the chain increases. This suggests that the polar effects, although important, are not the only ones operating in the dissolution phenomenon. We can call these additional effects hydrophobic or structure making. This same tendency is clearly observed in triethyl-, tripropyl-, and tributylamines. It can thus be said that in the dissolution of these compounds there exists a struggle between hydrophilic and hydrophobic characters.

One measure for the hydrophobic character is the number of hydrogen atoms in the solute molecule interacting with the solvent water. If this number is calculated on a relative basis, that is to say, if the number of hydrogen atoms divided by the molecular weight is chosen for this measure, the correlation in Fig. 3 is obtained. For this kind of limited group of compounds the correlation is satisfactory. No universal correlation is obtained on this basis. This can be seen in Fig. 3, where besides the pyridine group a nitrobenzene group and a tertiary aliphatic amine group are plotted as examples. These two last-mentioned groups deviate structurally from pyridines and also markedly from each other which is also indicated by the plots. This correlation can be used, however, as a good method of approximation for compounds whose structures closely resemble each other.

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