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SELF-ASSOCIATION OF PURINE BASES IN WATER-ORGANIC COMPONENT MIXTURES: 6-METHYLPURINE IN WATER-DIMETHYLSULFOXIDE SYSTEM

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Thermodynamic quantities of the self-association of 6-methylpurine in water(1)-dimethylsulfoxide(DMSO)(2)($x_2<0.1$) mixed solvent have been obtained at 25°C. They decreased remarkably with the mole fraction of DMSO up to about $x_2=0.012$ and then increased steeply. This behavior indicates that DMSO tends to stabilize the solvent structure at its very low content.

There have been numerous studies on the self-association of purine bases in water and in aqueous media, but only a few works[1,2] appeared to put emphasis on the solvent effects in aqueous solution containing organic component. Recently, thermodynamic studies of the self-association in aqueous organic solvents have been carried out by us through the measurement of heat of dilution and thereby some remarkable features of the thermodynamic quantities depending on organic cosolvent content were confirmed. From the determination of the thermodynamic quantities of the self-association of 6-methylpurine in water - 1,4-dioxane and - methanol solvents at 25°C, the standard enthalpy and entropy changes, ΔH^o and ΔS^o, of the association were found to exhibit characteristic behaviors.[3] That is, the values decreased remarkably with the organic content up to about $x_2=0.012$ for 1,4-dioxane and about $x_2=0.12$ for methanol, then increased steeply and finally approached relatively high values of the pure organic component. This behavior may be related to the structural changes of the solvent in an extremely sensitive way.

The solvent effect on the thermodynamic quantities in water-dimethylsulfoxide(DMSO) mixed solvent system will be shown here. At a water-rich composition, they were also affected largely by the organic component DMSO. In this system, the characteristic abrupt changes were found to be more distinguishing than in water - 1,4-dioxane system. This behavior is suggestive of the effect of solvent structure in association[3)] and of the denaturing action to proteins in aqueous DMSO solvent.[4)]

Thermodynamic quantities of the self-association of 6-methylpurine in various aqueous solvents were determined by the same method as Marenchic-Sturtevant's.[5)] They are obtained through the heat of dilution ΔH under a finite dilution condition, i.e., from initial molarity m_i to final molarity m_f,

$$\Delta H = \Delta H_\infty + \Delta H^o + (-\Delta H^o/K)^{1/2}[(\Delta H_\infty - \Delta H)/m_f]^{1/2}$$

where ΔH_∞ is the heat of dilution from m_i to zero concentration and K equilibrium constant. The values of ΔH were measured by using a LKB 8721 solution calorimeter and the thermodynamic quantities were determined by plotting ΔH against $[(\Delta H_\infty - \Delta H)/m_f]^{1/2}$. Evaluated thermodynamic quantities are listed in Table 1 and shown in Fig. 1 along with the values in the other systems. Investigations at higher organic contents than those indicated in the figure were impossible because of small solubility of the solute.

The thermodynamic values of the association depended on the structure of purine derivatives as well as organic solvent as shown in Fig. 1. The absolute values obtained for the case of 6-methylpurine are smaller than those for the other purines such as 6-dimethylaminopurine and actinomycin-deoxyguanosine. These decreased and

Table 1. Evaluated thermodynamic quantities of the self-association of 6-methylpurine in water-DMSO solvent system at 25°C.

DMSO in aq. solvent wt.%	x_2	K mol^{-1}	$-\Delta G^o$ kJ mol^{-1}	$-\Delta H^o$ kJ mol^{-1}	$-\Delta S^o$ J deg^{-1} mol^{-1}
0	0	9.8±0.2	5.7±0.1	22.5±0.4	56.4±1.1
5.00	0.0120	7.3±0.5	4.9±0.2	40.8±0.2	120 ±3.3
7.00	0.0171	8.4±0.6	5.3±0.2	35.7±0.7	102 ±3.0
15.0	0.0391	9.0±0.4	5.5±0.2	29.4±0.4	80.3±3.0
20.0	0.0545	9.6±1.4	5.6±0.4	25.8±1.0	67.9±1.8
30.0	0.0899	6.6±1.2	4.7±0.5	17.6±1.0	50.8±2.9

increased associations can be attributed mainly to the polarizabilities of π-electron system and the association in aqueous solvent systems is presumed to be partly attributed to hydrophobic interactions, which supposedly promote the stacking reactions of purine bases. In Fig. 1, some significant solvent effects on the hydrophobic interactions are indicated by the changes of thermodynamic values with the organic content.

In aqueous DMSO system, thermodynamic quantities, ΔH° and ΔS°, reach minimum values at about $x_2=0.012$. The tendency is quite similar in water - 1,4-dioxane system,3) where the minimum appears also at $x_2=0.012$. This sharp exothermic minimum of ΔH° should be substantially symmetrical3) to the sharp endothermic maximum of the heat of solution which has been studied by Arnett et al.5,6)

The values of ΔH° and ΔS° decreased remarkably with DMSO content up to about $x_2=0.012$. A possible explanation for the minimum would be that DMSO will stabilize the cooperative hydrogen bonded water structure7,8) around purine derivative molecules. They increased steeply after the minimum and still increased even after $x_2=0.07$(23 vol.%, 7 mol%) where they reached the corresponding values obtained in pure water. This fact suggests that DMSO reduces the hydrophobicity of purine bases responsible for promoting the solvent structurization. These explanation and suggestion should be reflected on the behavior of the standard free energy change ΔG° of association as

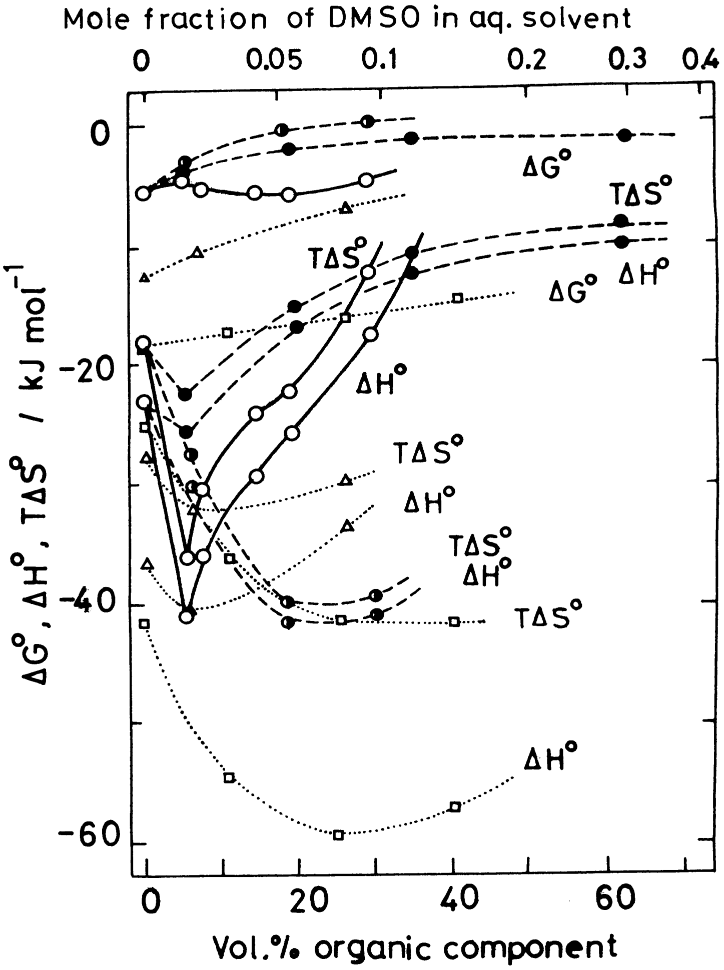

Fig. 1 Evaluated thermodynamic quantities of self-association plotted against organic contents in aqueous solvent: (—○—) 6-methylpurine in dimethylsulfoxide -, (--●--) 6-methylpurine in 1,4-dioxane3) -, (--◑--) 6-methylpurine in methanol3) -, (·····△·····) 6-dimethylaminopurine in acetonitrile2) - and (·····□·····) actinomycin-deoxyguanosine in methanol1) - water systems, at 25°C.

well. The behavior of ΔH^o or ΔS^o, however, provides better experimental evidence than that of ΔG^o. It can be concluded that DMSO tends to stabilize the water structure at very low DMSO mole fraction in this system. DMSO-induced destacking of purine bases will be consistent with the DMSO-induced breaking of the structure of solvent. It may be also concluded that destacking of 6-methylpurine takes place at higher DMSO content than 7 mol%.

In a plot of the heat of solution of tetraalkylammonium salts versus composition for water-DMSO binary solvent system, no maximum has been found9) and it has been indicated that DMSO tends to break down the structure of water.8-10) Nevertheless different results and conclusion were obtained in the present system at lower DMSO content than 7 mol%. It should be, therefore, emphasized that an appearance of this deep exothermic minimum of ΔH^o or ΔS^o at very low DMSO content is closely related to the large dimension of purine derivative molecule as hydrophobic solute.

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