Solvent effects on thermodynamic parameters for porphyrin–quinone interaction through multiple hydrogen bonding

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The enthalpy–entropy compensation plots for noncovalently linked porphyrin–quinone complexation exhibit a non-linear hook-shaped relationship between $\Delta H°$ and $T\Delta S°$ at various polarities in a toluene–ethanol binary solvent.

In general, water disrupts the formation of host–guest complexes linked by hydrogen bonding and complicates the binding mode in biological systems.[1,2] Thus, a simple host–guest model system would be very useful for evaluation of the effect of water on the thermodynamic parameters of the binding process. Recently, we have examined hydrogen-bonded porphyrin–quinone complexation,[3] in which ethanol was used as a co-solvent to simulate the behaviour of traces of water in a hydrophobic binding pocket in an enzyme. Here we report the solvent effects on the enthalpy and entropy changes upon binding between *meso*-α,α,α,α-tetrakis(2-hydroxy-1-naphthyl)porphyrin **1** and 2,3,5,6-tetramethoxy-*p*-benzoquinone **2** in a toluene–ethanol or toluene–butan-2-one binary solvent system (Fig. 1).[4,5]

Upon addition of ethanol or butan-2-one to the toluene solution, the affinity of **2** for **1** decreased with the increasing polarity of solvent.[6]§ Thermodynamic parameters ($\Delta H°$ and $\Delta S°$) for **1·2** complexation at various polarities were determined from van't Hoff plots obtained by UV–VIS titrimetric measurement. The van't Hoff plots show linearity in pure toluene and at >5.2 mol% of ethanol in toluene, whereas the plots at 0.36–3.5 mol% of ethanol in toluene gave a curved line, suggesting that $\Delta H°$ is a temperature-dependent parameter with non-zero heat capacity changes.¶ In contrast, a linear relationship was observed for the toluene–butan-2-one binary solvent system.

It is known that enthalpy–entropy diagrams for host–guest complexation generally display a linear relationship in a solvent system of varying polarity.[7] However, in this work, the $\Delta H°$ *vs.* $T\Delta S°$ compensation plots for **1·2** complexation in a toluene–ethanol binary system exhibit a unique hook-shaped line as shown in Fig. 2(*a*), with a turning point at approximately 3.5 mol% ethanol in toluene. One plausible interpretation is given in Fig. 3. In the presence of a polar solvent such as ethanol, we observe only the overall complexation comprised of solvent free complex **1·2** and various states of solvated complex **1·2**. Assuming that the affinity of ethanol molecules for complex free **1** and **2** is larger than that for complex **1·2**, $-\Delta H°$ drastically decreases upon addition of ethanol, since the functional sites of complex free **1** and **2** are saturated and stabilized by ethanol co-solvent even at low concentrations of ethanol ($|\Delta H°_a| > |\Delta H°_b|$ in Fig. 3). In contrast, the solvation of complex **1·2** gradually increases with the increasing number of ethanol molecules, and $\Delta H°$ becomes more negative in the presence of sufficient interactive ethanol to complex **1·2** ($|\Delta H°_b| < |\Delta H°_c|$ in Fig. 3). On the other hand, the entropy changes seem to depend on the behaviour of the ethanol molecules. At lower concentrations of ethanol, the desolvation of functional groups in **1** and **2** upon complexation contributes to entropy gain, whereas at higher concentrations of ethanol, the ethanol solvation of complex **1·2** and the formation of aggregated cluster of excess ethanol itself in apolar toluene

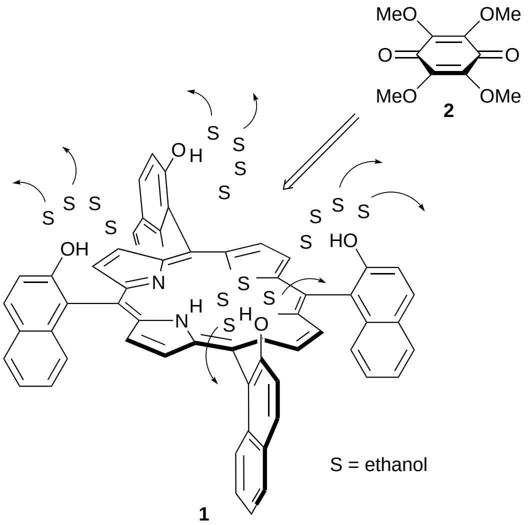

Fig. 1

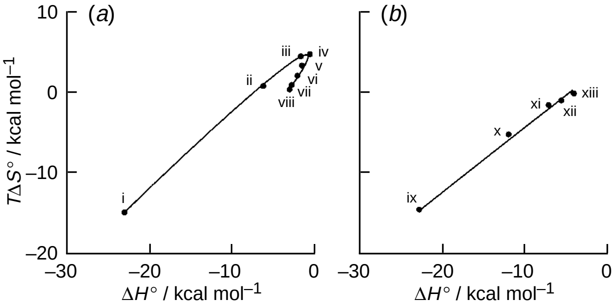

Fig. 2 Plots of the apparent $\Delta H°$ *vs.* $T\Delta S°$ for the binding of quinone **2** to porphyrin **1** at 298 K in (*a*) toluene–ethanol and (*b*) toluene–butan-2-one mixtures: (i) 0, (ii) 0.9, (iii) 1.8, (iv) 3.5, (v) 5.2, (vi) 8.3, (vii) 13 and (viii) 15 mol% EtOH in toluene, and (ix) 0, (x) 3.4, (xi) 11, (xii) 19 and (xiii) 28 mol% butan-2-one in toluene

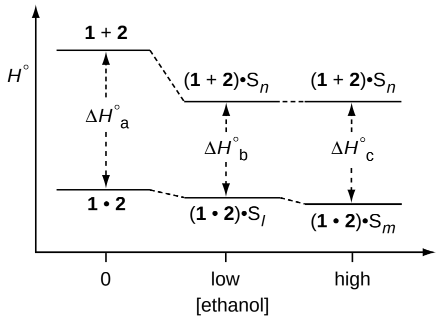

Fig. 3 Variation of $H°$ with concentration of EtOH; (**1** + **2**)·S = solvated **1** and **2**, (**1·2**)·S = solvated complex of **1·2**, S = ethanol molecule(s), *l*, *m* and *n* represent the number of ethanol molecules

gives rise to entropy loss.[8] In contrast, the same compensation plots in the toluene–butan-2-one binary solvent system show a linear relationship [Fig. 2(*b*)], suggesting that the solvation of functional groups in **1** and **2** in toluene–butan-2-one is weaker than that in the toluene–ethanol binary solvent system.

To the best of our knowledge, this is the first example of a hook-shaped ΔH° *vs.* ΔS° relationship in host–guest complexation *via* hydrogen-bonding interaction. Eftink has reported the simulation of the hook-shaped enthalpy–entropy relationship due to the protonation of a protein–ligand complex in a variety of pH conditions.[9,10][‖] Thus, our present results derived from the solvation of recognition sites at a variety of polarities is consistent with previous results from the literature that focused on the protonation of each component in protein–ligand binding.

In conclusion, this work indicates that the enthalpy and entropy changes for binding processes *via* hydrogen-bonding recognition are strongly influenced by solvation in a compensating manner.

T. M. is grateful for a Research Fellowship from the Japan Society for the Promotion of Science for Young Scientists.

Footnotes and References

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[§] In the ^{1}H NMR spectrum of **1**, the OH proton at δ 4.97 in pure toluene was shifted downfield with increasing concentration of ethanol or butan-2-one. The downfield shift in toluene–ethanol is approximately twice that in toluene–butan-2-one.

[¶] The discussion of heat capacity changes has been previously reported [ref. 3(*c*)]. We calculated the thermodynamic parameters from non-linear van't Hoff plots by use of following equation:

$$\begin{aligned} R\ln K(T) &= -[\Delta H^\circ(T)/T] + \Delta S^\circ(T) \\ &= -[\Delta H^\circ(T_0) + (T - T_0)\Delta C_p^\circ]/T + \Delta C_p^\circ\ln(T/T_o) + \Delta S^\circ(T_0) \end{aligned}$$

where $K(T)$, $\Delta H^\circ(T)$ and $\Delta S^\circ(T)$ are temperature-dependent parameters and $\Delta H^\circ(T_0)$ and $\Delta S^\circ(T_0)$ are constants with $T = T_0$.

[‖] It has been suggested that hook-shaped ΔH° *vs.* ΔS° compensation plots in ligand binding could be caused by a change in pH, ionic strength, solvent composition or macromolecule concentration (ref. 10).

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Received in Cambridge, UK, 12th June 1997; 7/04107A