CH3F5 Worked Examples - answers

1. Estimate the change in free energy upon association, $\Delta\Delta G$ of molecules 1 and 2 in:

(a) chloroform $\alpha = 2.2$, $\beta = 0.8$ (b) DMSO, $\alpha = 0.8$, $\beta = 8.9$

You will need the following data:

Pyridine $\alpha = 1.4$, $\beta = 7.0$ (Carboxylic acid) $\alpha = 3.6$, $\beta = 5.3$ R = 0.008314 kJK⁻¹mol⁻¹

Note units!



a) First draw the supramolecular structure identifying the hydrogen bond donor(s) and acceptor(s).



 $\Delta\Delta G = -(\alpha - \alpha_s)(\beta - \beta_s) + 6 \text{ kJ mol}^{-1} \text{ (add } + 6 \text{ once per complex to account for entropic cost of non$ $covalent bond formation)}$

For the HB donor (carboxylic acid) and HB acceptor (pyridine):

 $\Delta\Delta G = -(3.6-2.2)(7.0-0.8) + 6$ $\Delta\Delta G = -8.68 + 6 \text{ kJmol}^{-1} = -2.68 \text{ kJmol}^{-1}$

 $\ln K = -(\Delta G)/\mathrm{RT}$

hence $K = \ln^{-1} - (-2.68)/0.008314*298$ $K = \ln^{-1} 1.08$

 $K_{\rm a} = 3.0 \ {\rm M}^{-1}$

Which is low, but within the range expected for a hydrogen bond of this type in chloroform.

(b) DMSO $\Delta\Delta G = -(\alpha - \alpha_s)(\beta - \beta_s) + 6$ $\Delta\Delta G = -(3.6 - 0.8)(7.0 - 8.9) + 6$ $\Delta\Delta G = 5.32 + 6 \text{ kJ mol}^{-1} = + 11.32 \text{ kJ mol}^{-1}$ hence $K = \ln^{-1} -((11.32))/0.008314*298$ $K = 0.01 \text{ M}^{-1}$ Showing how weak HB interactions are in DMSO, which is a potent HB acceptor.

2. Estimate the change in free energy upon association, $\Delta\Delta G$ of molecules **3** and **4** in (a) chloroform $\alpha = 2.2$, $\beta = 0.8$ (b) DMSO, $\alpha = 0.8$, $\beta = 8.9$



In molecule **3** there are two amide HB donors and 1 pyridyl HB acceptor. In molecule **4** there are two amide-like carbonyl HB acceptors and one "amide-like" HB donor (actually an imide: better values of α and β could be estimated by a semi-empirical calculation if required). Hence using data from **Table 3 (Hunter** *ACIEE* review) in the complex formed, the change in free energy upon complexation in chloroform at 298 K is:

 $\Delta\Delta G = -(\alpha - \alpha_s)(\beta - \beta_s) + 6 \text{ kJ mol}^{-1}$

 $\Delta\Delta G = -2(2.9-2.2)(8.3-0.8) - (2.9-2.2)(7.0-0.8) + 6$ $\Delta\Delta G = -10.5 - 4.3 + 6$ $\Delta\Delta G = -8.8 \text{ kJ mol}^{-1}$

now $\ln K = -(\Delta \Delta G_{\rm HB})/RT$

hence $K = \ln^{-1} - (-8.8)/0.008314 \times 298$

 $K = \ln^{-1} 3.55$ $K = 35 \text{ M}^{-1}$

In DMSO at 298 K

 $\Delta\Delta G_{\rm HB} = -(\alpha - \alpha_{\rm s})(\beta - \beta_{\rm s}) + 6$ $\Delta\Delta G_{\rm HB} = -2(2.9 - 0.8)(8.3 - 8.9) - (2.9 - 0.8)(7.0 - 8.9) + 6$ $\Delta\Delta G_{\rm HB} = -(-2.52 - 3.99) + 6$ $\Delta\Delta G_{\rm HB} = + 12.51 \text{ kJ mol}^{-1}$

and again in $\ln K = -(\Delta \Delta G_{\text{HB}})/\text{RT}$ $K = \ln^{-1} - (12.51)/0.008314*298$ $K = 0.006 \text{ M}^{-1}$ Which is to be expected since DMSO is a highly competitive solvent!