

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, $\alpha = 0.8$, $\beta = 8.9$

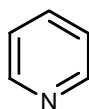
You will need the following data:

Pyridine $\alpha = 1.4$, $\beta = 7.0$

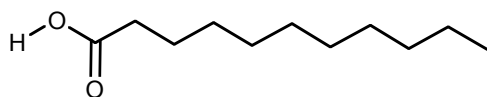
(Carboxylic acid) $\alpha = 3.6$, $\beta = 5.3$

$R = 0.008314 \text{ kJ K}^{-1} \text{ mol}^{-1}$

Note units!

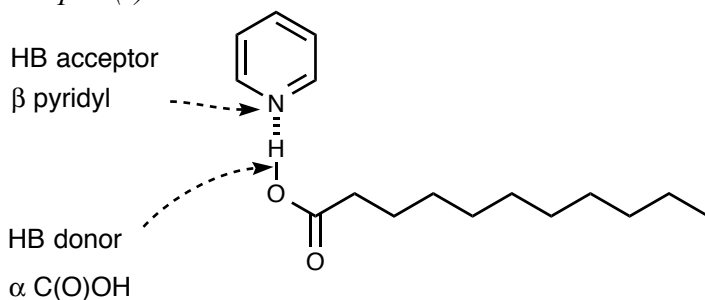


1



2

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



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

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

$$\Delta\Delta G = -(3.6 - 2.2)(7.0 - 0.8) + 6$$

$$\Delta\Delta G = -8.68 + 6 \text{ kJ mol}^{-1} = -2.68 \text{ kJ mol}^{-1}$$

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

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

$$K = \ln^{-1} 1.08$$

$$K_a = 3.0 \text{ M}^{-1}$$

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

(b) DMSO

$$\Delta\Delta G = -(\alpha - \alpha_s)(\beta - \beta_s) + 6$$

$$\Delta\Delta G = -(3.6 - 0.8)(7.0 - 8.9) + 6$$

$$\Delta\Delta G = 5.32 + 6 \text{ kJ mol}^{-1} = +11.32 \text{ kJ mol}^{-1}$$

$$\text{hence } K = \ln^{-1} -((11.32))/0.008314 \times 298$$

$$K = 0.01 \text{ M}^{-1}$$

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

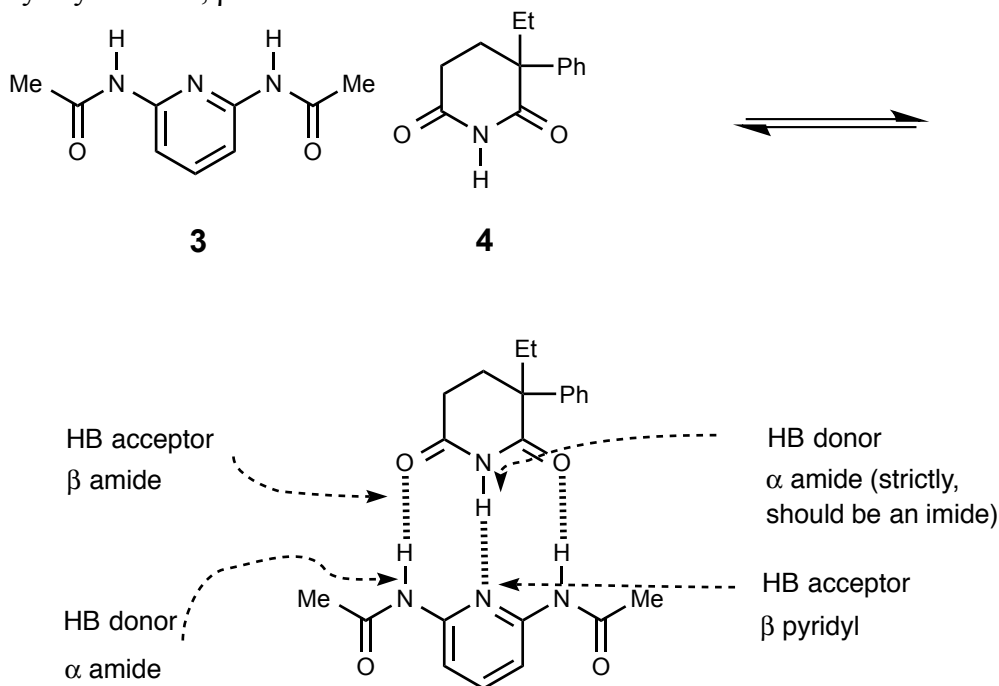
(a) chloroform $\alpha = 2.2$, $\beta = 0.8$

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

You will need the following data:

Amide $\alpha = 2.9$, $\beta = 8.3$

Pyridyl $\alpha = 1.4$, $\beta = 7.0$



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:

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

$$\Delta\Delta G = -2(2.9 - 2.2)(8.3 - 0.8) - (2.9 - 2.2)(7.0 - 0.8) + 6$$

$$\Delta\Delta G = -10.5 - 4.3 + 6$$

$$\Delta\Delta G = -8.8 \text{ kJ mol}^{-1}$$

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

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

$$K = \ln^{-1} 3.55$$

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

In DMSO at 298 K

$$\Delta\Delta G_{\text{HB}} = -(\alpha - \alpha_s)(\beta - \beta_s) + 6$$

$$\Delta\Delta G_{\text{HB}} = -2(2.9 - 0.8)(8.3 - 8.9) - (2.9 - 0.8)(7.0 - 8.9) + 6$$

$$\Delta\Delta G_{\text{HB}} = -(-2.52 - 3.99) + 6$$

$$\Delta\Delta G_{\text{HB}} = +12.51 \text{ kJ mol}^{-1}$$

and again in $\ln K = -(\Delta\Delta G_{\text{HB}})/RT$

$$K = \ln^{-1} -(12.51)/0.008314 \cdot 298$$

$$K = 0.006 \text{ M}^{-1}$$

Which is to be expected since DMSO is a highly competitive solvent!