

## Partition Coefficients

1. 100 moles of a compound is dissolved in an octane/water mixture (1 L each). When equilibrium is reached, 91 moles are found to be dissolved in octane.

a. How many moles are dissolved in water?

$$\text{Total} = \text{octane} + \text{water}$$

$$100 = 91 + x$$

b. What is the concentration of the compound in each phase?

$$x = 9 \text{ moles}$$

$$[X]_{\text{H}_2\text{O}} = \frac{9 \text{ mol}}{1 \text{ L}} = 9 \text{ M} \quad [X]_{\text{octane}} = \frac{91 \text{ mol}}{1 \text{ L}} = 91 \text{ M}$$

c. What is the partition coefficient?

$$P = \frac{91}{9} = 10.11$$

d. What is the value of logP?

$$\log 10.11 = 1.005$$

2. A compound has a logP = -2.

a. Calculate the partition coefficient.

$$10^{-2} = 0.01$$

b. Would this compound preferably dissolve in your blood or fat tissue?

Since  $P < 1$ , this compound would preferably dissolve in aqueous solvents

c. If 10 moles of this compound were added to a mixture containing 1 L octane and 0.5 L water, how many moles would be dissolved in octane once equilibrium is reached?

lets call the compound A

$$V_{\text{octane}} = 1 \text{ L}$$

$$10 = x + y$$

(x = moles in octane)

$$V_{\text{H}_2\text{O}} = 0.5 \text{ L}$$

$$x = 10 - y$$

(y = moles in H<sub>2</sub>O)

$$[A]_{\text{H}_2\text{O}} = \frac{y}{0.5} \quad [A]_{\text{octane}} = \frac{x}{0.5}$$

$$0.01 = \frac{\left(\frac{y}{0.5}\right)}{\left(\frac{x}{0.5}\right)} = \frac{\left(\frac{10-y}{1}\right)}{\frac{y}{0.5}} = \frac{20-2y}{y}$$

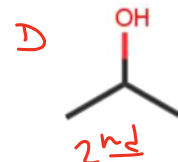
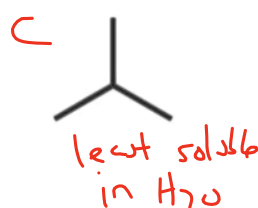
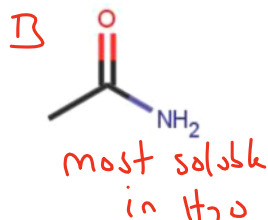
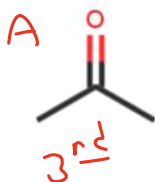
$$0.01y = 20 - 2y$$

$$y = 9.95 \text{ moles}$$

$$x = 10 - 9.95$$

$$x = 0.05 \text{ mol}$$

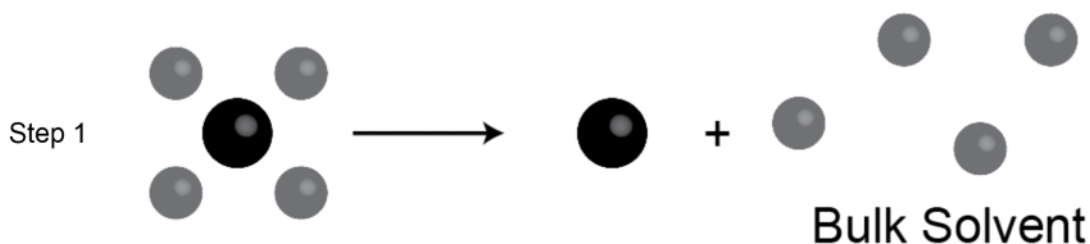
3. Rank the following by increasing log P



The hydrophobic effect is a phenomenon that causes nonpolar substances to aggregate in water – this forms the energetic foundation of lipid bilayers forming (also proteins folding...but more on that later). This exercise aims to help you think about the role of enthalpy and entropy in the aggregation of hydrophobic molecules.

Consider the dimerization of methane in water:  $2 \text{CH}_4 \rightarrow (\text{CH}_4)_2$ . This process can be thought of as two separate steps:

- The dehydration of each methane (several water molecules start by weakly interacting with methane and are released to the bulk solvent).
- The newly dehydrated methane molecules interact to form a dimer.



The next several questions will guide you through thinking about the thermodynamic aspects of non-polar molecule aggregation in water. This is completely conceptual in nature, so having a firm grasp on  $\Delta H$ ,  $\Delta S$ , and  $\Delta G$  are necessary. You will regularly refer back to this image and table.

	Step 1 (dehydration and reorganization of water)	Step 2 (Methane dimerization)	Overall Process
$\Delta H$	(+) BIG	(-) small	(+)
$\Delta S$	(+) BIG	(-) smaller	(+)
$\Delta G$			(-)

- Carefully consider the intermolecular forces that exist between each compound:
  - What type of IMF exist between methane and methane? *LDF*
  - What type of IMF exist between water and water? *H-bond / dipole / LDF*
  - What type of IMF can exist between water and methane? *LDF*
  - Rank the strength of the IMF in the three previous questions. Which do you think is the most energetically costly to break? *→ B*

*c < a < b*

- The overall process (aggregation of methane in water) is spontaneous. What is the sign on  $\Delta G$ ?  
 $\Delta G = 0$        *$\Delta G < 0$*        $\Delta G > 0$

*↳ this means  $\Delta G < 0$*

Complete the  $\Delta G$  cell in the table on the next page by noting if the value is positive, negative, or zero.

- Water cannot make H-bonds with non-polar molecules. Consequently, when non-polar molecules are forced to dissolve in water, something has to give. Water ends up forming an "ice-like" structure around the non-polar molecules (these are called clathrate cages).

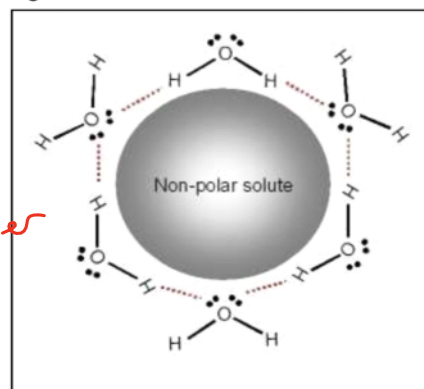
- This arrangement of water is entropically costly. What does this mean about  $\Delta S$  for the **formation** of this complex?

*$\Delta S < 0$*        $\Delta S = 0$        $\Delta S > 0$

What does it mean about the reversing this complex formation?

$\Delta S < 0$        $\Delta S = 0$        *$\Delta S > 0$*

*— creating a lot of order*



- Studies show that the H-bonds between water in these cages are much stronger than normal H-bonds with water. Based on this information, do you expect  $\Delta H$  for step 1 to be exothermic or *endothermic?* Remember that breaking bonds (or IMF) takes energy.  
*energy needed to break IMF  $\Delta H > 0$*
- Based on your predictions, complete the Step 1 column in the table on the first page by putting positive or negative in each cell in the Step 1 column.

- Now consider the  $\Delta H$  and  $\Delta S$  of the 2<sup>nd</sup> step. Complete the table by putting positive or negative in each cell in the Step 2 column.

*order created  $\Delta S < 0$*

*IMF formed  $\Delta H < 0$*

- Now think about the enthalpy and entropy for each step. Which do you think contributes to more significantly to the overall  $\Delta H$  and  $\Delta S$ ? Indicate this by putting a positive or negative in each of the remaining cells for the overall process.

*Step 1 for both  $\Delta H + \Delta S$*

6. The table that you just generated should show that the reaction is endothermic. This is because the endothermic  $\Delta H$  for step 1 is a bigger than the exothermic  $\Delta H$  for step 2. Based on this endothermic enthalpy:

a. Can a reaction be spontaneous if it is endothermic? *yes if  $\Delta S > 0$*

b. If so, what is the energetic driving force that makes the reaction spontaneous?

*entropy*

c. What equation can you use to prove support your answer to part b?

$$\Delta G = \Delta H - T\Delta S$$

d. Which step do you think provides that energy you identified in part b?

*Step 1*

e. In your own words, what is the predominant driving force for hydrophobic molecules dissolving in water?

*disordering of water as hydrophobic molecules aggregate together*

f. Now apply this idea to lipid bilayers. What do you think is the major driving force for the formation of lipids?

*lipids contain hydrophobic regions that need to aggregate together to be removed from  $H_2O$ . This spontaneous process happens because of the favorable energy provided by the reorganization of water*