

Problem Set PS12

ISSUED: 11/29/01 Due: 12/13/01

Prof. Darin J. Ulness

Name _____

Instructions. Complete all questions before class on the due date. You are encouraged to work together. Be sure to struggle with the problem before seeking help. Many of the exercises are very similar to problems in the book. Understanding the solution to these problems will be helpful in completing the assigned exercises.

Exercises

- Our very own Drew Rutherford is very interested in partition coefficients because of his post-doc experience at the University of Utah. There Drew worked with a reaction scheme as illustrated in the figure below. The scheme exploits the fact that many fluorinated solvents (molecules with most or all of the hydrogens replaced with fluorines) are immiscible with organic solvents at low temperatures but then become miscible at higher temperatures. This allows one to keep the reactants in the organic phase and a catalyst in the fluorinated phase. Warming the mixture allows for mixing of the reactants and catalyst allowing the reaction to proceed. Cooling the solution results in phase separation and partitioning of the products from the catalyst. Obviously it is important to know how molecules distribute themselves in the fluorinated and organic phases. Table 1 gives data that allows the partition function to be calculated for a number of molecules. The fluorinated phase is perfluoro-methyl-cyclohexane ($\text{CF}_3\text{C}_6\text{F}_{11}$) and toluene ($\text{CH}_3\text{C}_6\text{H}_5$). The data is given as a mass ratio for the particular compound in the fluorinated versus organic phase.

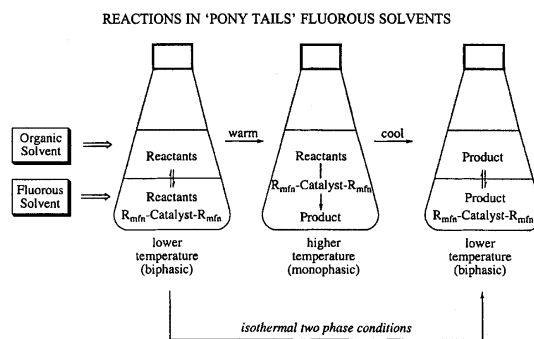


Figure 1. One possibility for catalysis with fluorinated solvents [$\text{R}_{\text{mfn}} = (\text{CH}_2)_m(\text{CF}_2)_{n-1}\text{CF}_3$]

Table 1. Partition coefficients (24°C)

No.	Compound	$\text{CF}_3\text{C}_6\text{F}_{11}/\text{CH}_3\text{C}_6\text{H}_5$						
14		49.5:50.5	21		73.7:26.3	29	$\text{CH}_3(\text{CH}_2)_6\text{CH}_3$	1.1:98.9
15		91.2:8.8	22		97.4:2.6	30		1.2:98.8
16		90.7:9.3	23	$\text{ICH}_2\text{C}_6\text{H}_4\text{R}_n$	50.7:49.3	31		0.9:99.1
17		91.1:8.9	24	$\text{CH}_3(\text{CH}_2)_6\text{CH}_3$	5.4:94.6	32		22.4:77.6
18		>99.7: <0.3	25	$\text{CH}_3(\text{CH}_2)_7\text{CH}_3$	4.2:95.8	33		28.0:72.0
			26	$\text{CH}_3(\text{CH}_2)_8\text{CH}_3$	3.4:96.6			
			27	$\text{CH}_3(\text{CH}_2)_9\text{CH}_3$	2.4:97.6			
			28	$\text{CH}_3(\text{CH}_2)_{10}\text{CH}_3$	1.9:98.1			

- (a) Convert the mass ratio to partition coefficients for molecules 18, 24, 30 and 33. (Note R_{fn} means n carbons saturated with fluorine atoms.) Assume equal volumes of fluorous and organic phases, also assume the mixture is perfectly immiscible.
- (b) Which molecules listed in the table would work well for this type of scheme? Which wouldn't work well? Why?
- (c) Consider a catalyzed hydrogenation reaction involving decene and decane (molecule #24). Say one begins 1.00g of decene in the organic phase of a 10ml organic/10ml fluorous immiscible mixture. Assume the hydrogenation reaction goes via the above scheme to completion. How many grams of decane are immediately recoverable from the organic phase. Now lets say 4 extractions are done. That is, the organic layer is replaced with a fresh layer three additional times. How many grams of Decane are gained for each extraction. What is the percent yield ($\frac{\text{actual}}{\text{theoretical}} \times 100\%$) of the process?
- (d) The catalyst for the process described in (c) has a partition coefficient of $P_{or}^f = 700$. What percent of the catalyst is lost in each extraction?
2. Derive expressions for the entropy and enthalpy of ion transfer from the α phase to β phase using the Born model.
3. Consider a two phase system consisting of water and dichloromethane. Use your intuition to guess whether a iodide ion would exist more stably in water phase or the dichloromethane phase. Use the following data to calculate $\Delta G_{w \rightarrow o}$ to support your guess: $\epsilon_w = 78.54$ and $\epsilon_{H_2C_2Cl_2} = 9.08$.
4. For the previous problem does the entropy increase or decrease when a iodide ion moves from the water phase to the dichloromethane phase?
5. When an ion is distributed between two immiscible phases a Galvani potential is developed between the phases. The standard state Galvani potential is related to the partition coefficient via

$$\Delta_o^w \phi^\ominus = \frac{RT}{zF} \ln P^{w/o},$$

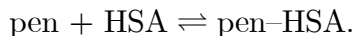
where z is the charge of the ion and F is Faraday's constant.

- (a) Derive the relation between the Galvani potential and $\Delta_o^w G^\ominus$.
- (b) $\Delta_o^w \phi^\ominus = -168\text{mV}$ for Ph_4As^+ in a water/acetophenone system. What is $P^{w/o}$ for Ph_4As^+ ?
- (c) $\Delta_o^w \phi^\ominus = 168\text{mV}$ for Ph_4B^- in a water/acetophenone system. What is $P^{w/o}$ for Ph_4B^- ?

Conceptual Problems

6. In a recent paper by P. Tobaoda *et.al.*, (*Langmuir*, **16**, 937, (2000)) the thermodynamics of penicillins and human serum albumin (HSA) is explored. The penicillins discusses

are nafcillin, cloxacillin and dicloxacillin. The small penicillin molecules bind to the large HSA protein according to the reaction



The free energy for this binding reaction depends on the number of penicillin molecules that are currently bound to the protein (called the extent of binding $\bar{\nu}$). Read the excerpt below that describes Figs. 9 and 10 from the above reference (nb., I think the ΔG , ΔH , and ΔS should be ΔG^\ominus , ΔH^\ominus , and ΔS^\ominus).

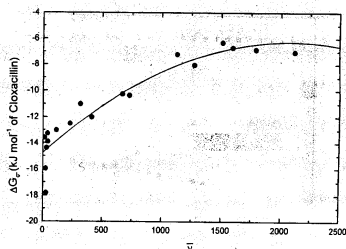


Figure 9. Gibbs energy of interaction per mole of cloxacillin (ΔG_v) as a function of extent of binding ($\bar{\nu}$) to human serum albumin, pH 7.4, 25 °C.

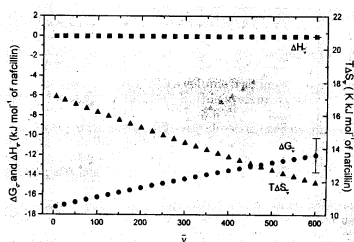


Figure 10. Thermodynamic parameters for the binding of nafcillin to human serum albumin, pH 7.4, 25 °C, as a function of extent of binding ($\bar{\nu}$).

complexes formed when large numbers of ligands are bound.

Figure 9 shows ΔG_v vs $\bar{\nu}$ for the cloxacillin–HSA system. ΔG_v is large and negative at low values of $\bar{\nu}$ where binding to the “high-energy” sites occurs and become less negative as more drug molecules bind. Similar data were obtained for the HSA with the other drugs. The data for ΔH_v vs $\bar{\nu}$ and ΔG_v vs $\bar{\nu}$ were fitted to appropriate equations and used to calculate the corresponding entropy per mole of drug bound (ΔS_v) shown in Figures 10–12 using the relationship

$$\Delta G_v = \Delta H_v - T\Delta S_v \quad (4)$$

These data show that for all the drugs, binding is characterized by large increases in entropy (right-hand axes). The enthalpy (ΔH_v) makes very little contribution to ΔG_v . The large entropy increases are characteristic of hydrophobic interactions between the drugs and the protein. The magnitudes of both ΔG_v and $T\Delta S_v$ are very similar to those reported for the interaction of the anionic surfactant, sodium *n*-dodecylsulfate (SDS), with globular proteins.²⁸ In particular the binding of the first approximately 100 SDS molecules to bovine serum albumin (BSA)²⁹ at pH 7 and 25 °C occurs with a ΔG_v of $-24.8 \text{ kJ mol}^{-1}$ and a $T\Delta S_v$ of $+17.9 \text{ kJ mol}^{-1}$. The interaction of

- (a) In your own words, what does Fig 9 tell us?
 - (b) From Fig. 10 is the reaction more “entropy driven” or “energy driven” for any given $\bar{\nu}$? (Take note of the different y -axis scales.)
 - (c) The paragraph states that “large entropy increases are characteristic of hydrophobic interactions between the drugs and the proteins.” Why?
7. Draw pictures representing the four corrections to the Born model listed on page 140 of the notes.
 8. Will a salt become more soluble or less soluble in water if you add methanol? Explain why in terms of the Born model.
 9. Considering the data given in the second computer problem below should a salt become more soluble or less soluble in hot water versus cold water according to the Born model? Does this jive with you intuition?
 10. Considering the previous two problems, is the Born model a complete description of what is going. If not what does it miss.

Computer Problems

11. Interestingly a simple linear function of molecular volume does a very good job of capturing the trends for the partitioning of solutes between aqueous and organic layers. Explicitly $\log P^{o/w} = mv + b$ where v is the molecular volume of the solute and m and b are empirical slope and intercept parameters. Calculate $\Delta G_{w \rightarrow o}^{\ominus}$ for the partitioning of straight chain alkanes between water and hexadecane ($m = 0.0466$, $b = 0.055$) and water and octanol ($m = -0.140$, $b = 0.0338$) from the data in the Table (data from P. Buchwald and N. Bodor, *J. Phys. Chem. B* **102**, 5715 (1998))

alkane	v (Å)	alkane	v (Å)
methane	22.34	pentane	78.52
ethane	36.36	hexane	92.48
propane	50.45	heptane	106.53
butane	64.55	octane	120.63

12. Use the following data regarding the dielectric constant of water from J.O'M. Bockris and A.K.N. Reddy *Modern Electrochemistry* v1 Plenum Press, New York 1970, to plot the molar $\Delta G_{v \rightarrow s}$ and $\Delta S_{v \rightarrow s}$ for Na^+ ($r_i = 0.95 \text{ \AA}$) from $T = 0 \text{ } ^\circ\text{C}$ to $T = 100 \text{ } ^\circ\text{C}$

Temp	ϵ_w	Temp	ϵ_w
0	87.74	50	69.91
10	83.83	60	66.81
20	80.10	70	63.85
25	78.30	80	61.02
30	76.54	90	58.31
40	73.15	100	55.72

Reflective Exercises

13. I say that taking PChem makes one a better person. What do I mean by that?
14. Considering the field of physical chemistry (not necessarily this particular course)
- (a) Can you list at least one *fact* you learned that you think you might need to know in the future?
 - (b) Can you list at least one *skill* that you have learned or developed that you think might be of use to you in the future (do not list POWERPOINT)?
15. It is quite likely that over time you will forget how to derive Maxwell relations. Was there any point in learning how to derive them in the first place?
16. List three things in all of science that you think are the coolest. Try to write a title for a research proposal that involves all three of your area.

10) To get the partition coefficients you should convert grams to moles. Since the volume is the same for both phases $P = \frac{\text{moles}(a)}{\text{moles}(a)}$

Short cut $P = \frac{\text{mass}(a)}{\text{mass}(a)}$

b) work well 24, 25, 26, 27
not work well 28, 29, 30, 31
 all others want most to be in the organic phase.

c) decane + H₂ → decane

1.00g decane	1 mol decane	1 mol decane	143.20g decane	= 1.014g decane
	143.3g decane/mol decane	1 mol decane		

 1st extraction: 1.014 (0.946) = 0.959g
 2nd extraction: 0.0547 (0.946) = 0.052g
 3rd extraction: 0.003 (0.946) = 0.003g
 4th extraction: 0.000g

d) $P = \frac{1.014}{1.00} \times 100\% = 0.142\%$ loss

2) $\Delta G_{D \rightarrow A} = \frac{N(\epsilon_0)^2}{8\pi\epsilon_0^2} \left(\frac{1}{\epsilon_A} - \frac{1}{\epsilon_B} \right)$
 $\Delta S_{D \rightarrow A} = - \left(\frac{\partial \Delta G_{D \rightarrow A}}{\partial T} \right)_P = - \Delta \left(\frac{1}{\epsilon_A} - \frac{1}{\epsilon_B} \right)$
 $= \Delta \left(\frac{1}{\epsilon_A} \frac{\partial \epsilon_A}{\partial T} - \frac{1}{\epsilon_B} \frac{\partial \epsilon_B}{\partial T} \right)$
 $\Delta H_{D \rightarrow A} = \Delta G_{D \rightarrow A} + \Delta S_{D \rightarrow A} T$

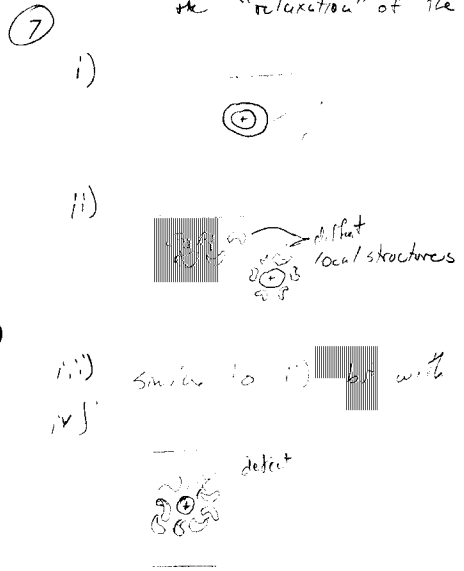
3) $\Delta G_{W \rightarrow O} \propto \left(\frac{1}{\epsilon_O} - \frac{1}{\epsilon_W} \right)$
 so more stable in water

4) $\Delta S_{W \rightarrow O} \propto \left(\frac{1}{\epsilon_O} \frac{\partial \epsilon_O}{\partial T} - \frac{1}{\epsilon_W} \frac{\partial \epsilon_W}{\partial T} \right)$
 Entropy increases.

5) a) $\Delta G^{\circ} \phi^{\circ} = \frac{RT}{zF} \ln P^{w/o}$ $P^{w/o} = e^{-\frac{\Delta G_{w \rightarrow o}^{\circ}}{RT}}$
 $\Delta G^{\circ} \phi^{\circ} = \frac{RT}{zF} \ln e^{-\frac{\Delta G_{w \rightarrow o}^{\circ}}{RT}} = \frac{RT}{zF} \left(\frac{-\Delta G_{w \rightarrow o}^{\circ}}{RT} \right)$
 $\Delta G^{\circ} \phi^{\circ} = \frac{-\Delta G_{w \rightarrow o}^{\circ}}{z}$

b) $P^{\circ} = e^{\frac{zF \Delta G^{\circ} \phi^{\circ}}{RT}} = e^{\frac{64485(-0.168V)}{(8.314)(298)}} = 1.44 \times 10^{-3}$
 c) $P^{w/o} = e^{\frac{zF \Delta G^{\circ} \phi^{\circ}}{RT}} = e^{\frac{64485(0.168V)}{(8.314)(298)}} = 694$

6) (a) your words
 (b) entropy driven
 (c) The large entropy increase comes from the "relaxation" of the water molecules



less soluble because $\epsilon \downarrow$ $\epsilon_{mixture} < \epsilon_{water}$

9) Salt should become less soluble as T ↑ does not fit with intuition

10) NO, misses lattice energies of the salt crystals.