

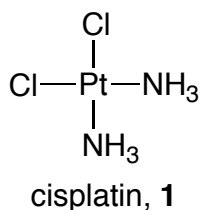
Recommended reading: 23, 29

Ch 102 Problem Set 7

Due: Tuesday, May 24, before class

Problem 1 (20 points)

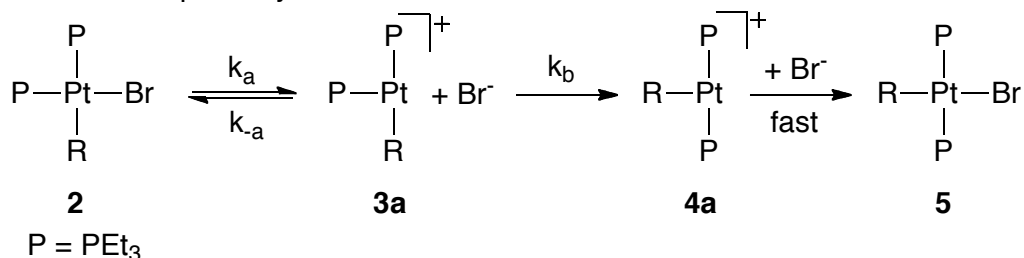
Square planar,  $d^8$  platinum complexes have been the focus of much research for several decades due to their involvement in many industrial and pharmaceutical processes. One of the chief players in platinum chemistry is cisplatin (**1**), a simple platinum coordination complex which causes DNA crosslinking and, ultimately, cell death in cancer cells.



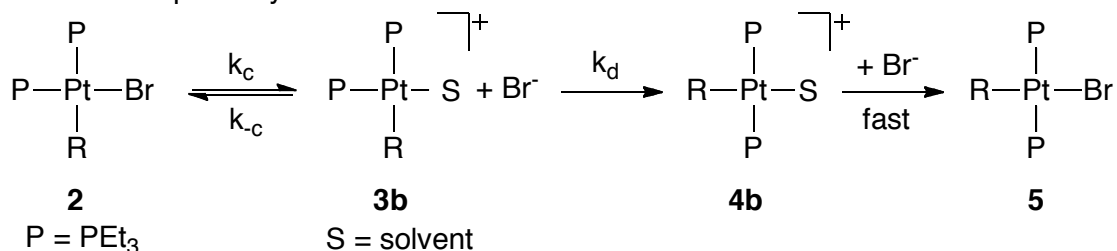
The use specifically of the *cis*-isomer of diamminedichloroplatinum(II) is crucial as the *trans*-isomer does not display the same kind of biological activity. Therefore, *cis*-/*trans*- isomerism in  $d^8$ , square-planar platinum complexes has been extensively investigated.

Platinum(II) species **2** has received some attention with regards to its isomerization. Two mechanisms have been suggested for this process. One proposal invokes dissociation of bromide to yield a  $14e^-$ , three-coordinate intermediate (**3a**) followed by isomerization and trapping by bromide. A second postulated mechanism proceeds by an associative mechanism involving a solvent molecule to give solvent-coordinated species **3b** which then undergoes isomerization.

Dissociative pathway:



Associative pathway:



a) For each proposed reaction pathway, derive a rate law describing formation of the isomerized product **5**. Give expressions for  $k_{obs}$  for the two mechanisms. Note that since bromide coordination to generate **5** from **4** is a very fast process you do not need to include this last step in your analysis. For each reaction use the steady-state approximation on the product of the first, reversible step (intermediates **3a** and **3b**, respectively). Based on the derived expressions for  $k_{obs}$ , do you expect to be able to distinguish these two mechanisms using concentration-dependence kinetics experiments?

b) The observed isomerization rates were recorded upon variation of bromide concentration in the reaction solution. The recorded data is shown in the table below.

	$10^4[\text{Br}^-], \text{M}$	$10^4 k_{obs}, \text{s}^{-1}$
R = <i>p</i> -MeC <sub>6</sub> H <sub>4</sub>	0.0	38.40
	1.0	12.60
	2.0	7.25
	4.0	3.71
	6.0	2.42
	8.0	2.03
	10.0	1.45
	20.0	0.76
	30.0	0.58
R = <i>o</i> -MeC <sub>6</sub> H <sub>4</sub>	0.0	6.95
	0.6	3.91
	0.8	3.34
	2.0	1.74
	4.0	0.96
	8.0	0.58
	10.0	0.38
R = 2,4,6-Me <sub>3</sub> C <sub>6</sub> H <sub>2</sub>	0.0	2.13
	2.0	1.05
	4.0	0.69
	6.0	0.53
	8.0	0.43

Analyze the above data by utilizing a double-reciprocal plot, and determine relevant rate constants as applicable (note: your plot will only have one concentration dependence, while the one presented in class had two).

c) The dependence of the observed rate on temperature was also investigated, and the data below was recorded (R = 2,4,6-Me<sub>3</sub>C<sub>6</sub>H<sub>2</sub>).

T (°C)	$10^4 k_{obs}, \text{s}^{-1}$
7.6	0.19
12.0	0.50

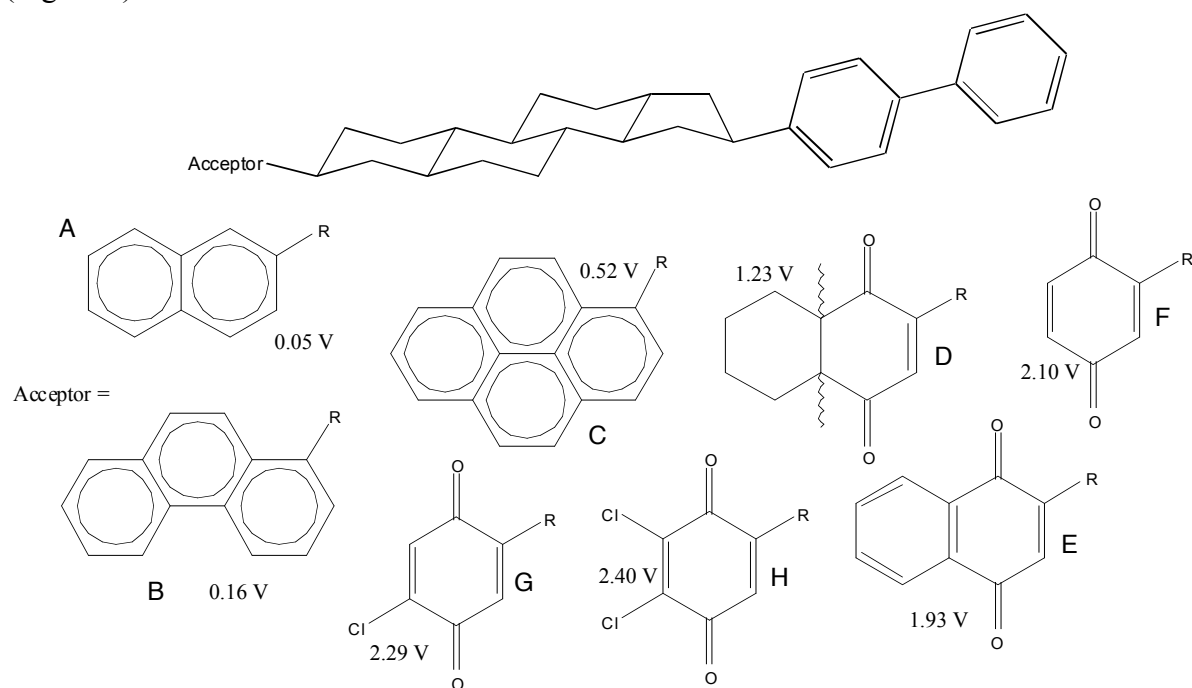
T (°C)	$10^4 k_{\text{obs}}, \text{s}^{-1}$
17.3	0.79
15	0.39
22.9	1.13
30.0	2.25

Derive the enthalpy ( $\Delta H^\ddagger$ ) and entropy ( $\Delta S^\ddagger$ ) of activation for the reaction. Are these values consistent with the associative or the dissociative mechanism?

d) Consider the rates of reaction you calculated in part (b). Explain any differences in the observed rates for different R ligands (hint: think of sterics).

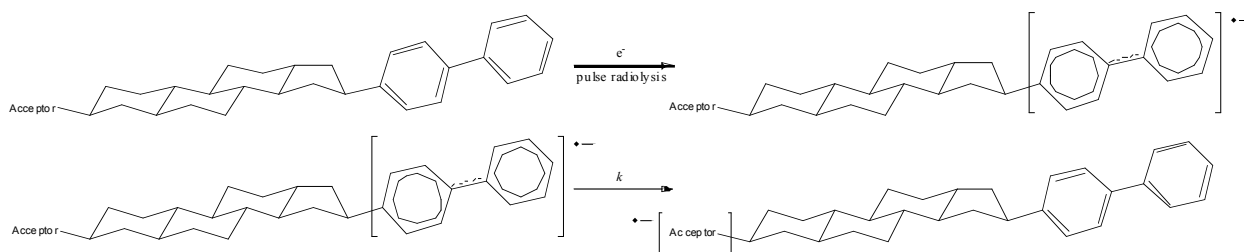
### Problem 2 (15 points)

A key result of Marcus theory is that the reaction barrier can increase when the reaction becomes too highly exergonic. One of the first experimental studies to test this was carried out in the 80s by Miller, Calcaterra, and Closs. They synthesized a class of organic compounds consisting of a biphenyl electron donor and variable acceptor tethered by a rigid aliphatic steroid scaffold (Figure 1).



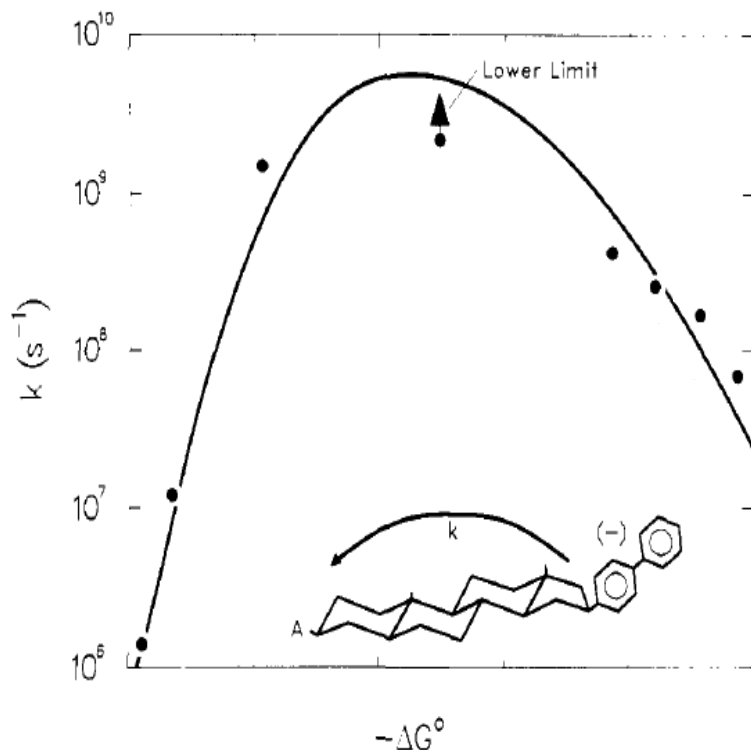
**Figure 1.** Donor-acceptor molecule, acceptor groups and standard reduction potentials ( $E^\circ$ ; A is hardest to reduce, H is easiest).

Pulse radiolysis generates a biphenyl radical anion in the donor region. The rate of electron transfer to the acceptor was measured (Figure 2).



**Figure 2.** Electron transfer measurements.

A graph showing electron transfer rate versus thermodynamic favorability for each of the donor-acceptor pairs is given below. A trendline is also given, confirming the presence of an inverted region, as predicted by the Marcus theory.

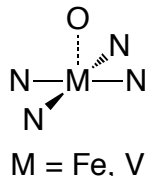


**Figure 3.** Marcus plot.

- Assign each point on figure 3 to the corresponding acceptor.
- Indicate clearly the location of the Marcus inverted region in figure 3.
- Which acceptor gives an activation energy closest to zero?
- Which acceptor gives the most thermodynamically favorable electron transfer? Does it lie in the Marcus Inverted Region?
- Draw a qualitative plot of the activation energy versus  $-\Delta G^\circ$ .

### Problem 3 (15 points)

Vanadium(IV)-oxo porphyrin species, such as VO-DPEP, (DPEP = deoxyphyloerythroetioporphyrin), have not been shown to be effective oxidizing agents, while Fe(IV)-oxo porphyrin species can effectively transfer oxygen atoms to organic substrates. An MO diagram may help elucidate the different reactivities of these oxo-metalloporphyrin species. For simplicity, we will treat the porphyrin ring as a symmetric  $X_2L_2$  type ligand as shown below:



- Generate a d-orbital splitting diagram taking into account only  $\sigma$ -interactions. Label the five d-parentage orbitals ( $xy$ ,  $x^2-y^2$ ,  $xz$ ,  $yz$ ,  $z^2$ ; z-axis is along the M-O bond and x and y along M-N bonds). You do not need to draw a full MO diagram, just the d-orbital splitting diagram. Label each orbital as  $\sigma$ ,  $\sigma^*$ , or nb. Sketch these orbitals (including contributions from the ligands as applicable).
- To consider the  $\pi$ -bonding in these oxo-species, consider the two  $\pi$ -symmetry p-orbitals on oxygen. Generate a partial MO diagram between the five d-parentage orbitals you described in part (b) and the two p-orbitals on oxygen. Remember to place all orbitals at the appropriate relative energies. Label each resulting MO as  $\sigma$ ,  $\sigma^*$ ,  $\pi$ ,  $\pi^*$ , or nb. Sketch these orbitals (including contributions from the ligands as applicable).
- Fill in the diagram from part (c) with the appropriate number of electrons for  $M=Fe(IV)$  and  $M=V(IV)$ . Remember to include the appropriate number of electrons contributed by the oxygen ligand (since only two oxygen p-orbitals are considered in this analysis you should count 4 electrons from oxygen).
- Using your MO diagrams, explain why the Fe(IV)-oxo porphyrin species is more reactive with respect to oxygen transfer than the V(IV) analogue. What is the M-O bond order in each case? (Remember that there is one occupied M-O  $\sigma$ -bonding orbital of lower energy that is not described in the above analysis).

### Problem 4 (20 Points)

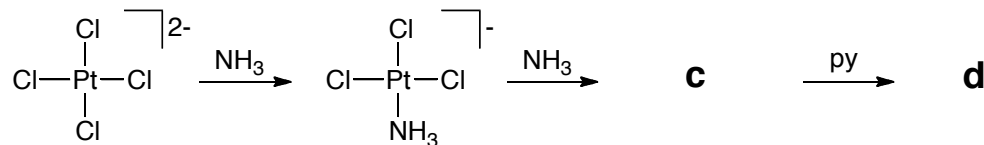
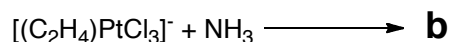
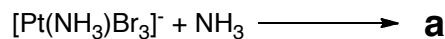
The chemical reactivity of dioxygen with organic molecules at ambient temperatures is low and oxygen does not spontaneously oxidize most organic compounds in the absence of a catalysts (if this were not the case, we would have to worry about oxygen spontaneously oxidizing us). The low kinetic reactivity of dioxygen stems from its triplet ground state; that is, dioxygen has two unpaired electrons in two degenerate  $\pi^*$  orbitals (draw the MO diagram if this is not clear). Most stable organic molecules, however, are in singlet states with all of their electrons paired, and hence display low reactivity toward dioxygen. Although singlet states of oxygen are known, the lowest energy singlet state is significantly higher in energy than the triplet state (22.5 kcal/mol) and is not easily accessible. Oxygenases are a class of enzymes that are able to bind and activate triplet oxygen leading to oxygenation of organic molecules. Cytochrome P450 is a well-studied class of oxygenases. The transition metal ion ( $Fe^{II}$ ) in this protein is bound by a porphyrin and is able to bind triplet dioxygen and activate it toward incorporation into organic substrates.

Lewis dot structures of the Fe-heme complex and O<sub>2</sub> may help clarify the movement of electrons throughout the catalytic cycle for the oxidation of an organic substrate with dioxygen.

- Draw the cytochrome P450 cycle for oxygen activation and insertion into R–H as was shown in class (NOTE: you do not need to draw rigorous Lewis dot structures for this part and the Fe complex may be abbreviated as in class)
- Draw the Lewis dot structure for O<sub>2</sub>
- Draw a Lewis dot structure for the Fe-dioxygen adduct that forms upon coordination of O<sub>2</sub> to Fe-cytochrome P450 (NOTE: The Fe–O–O bond angle is ~120°). Draw “dots” only for oxygen.
- Draw a resonance form of the Fe-O<sub>2</sub> complex that changes the oxidation state of Fe and puts a negative charge on an oxygen atom. This is an Fe-superoxide species.
- The reaction mechanism for cytochrome P450 involves a one-electron reduction of the Fe-superoxide species. If this electron transfer were slow, what would be a possible competing side reaction, leading to a reactive and potentially detrimental side-product?
- Draw a Lewis dot structure for the Fe-hydroperoxide complex resulting from the addition of a proton and an electron to the Fe-superoxide species.
- Addition of a second proton to the Fe-hydroperoxide complex generates an Fe-oxo species upon loss of H<sub>2</sub>O. If this proton delivery step were slow, what would be a possible competing side-reaction?
- Based on what you learned in class, what is the ultimate electron source for the cytochrome P450 catalytic cycle?

**Problem 5** (10 points)

Predict the products of the following ligand substitution reactions.



**Problem 6** (20 points)

Pick a topic of interest from the recommended reading (descriptive chemistry) in bold at the beginning of this problem set. Prepare two power point slides including relevant *descriptive chemistry* (background on synthesis, applications, reactivity, properties, trend, etc, as applicable), some concepts presented in class (oxidation states, electron count, symmetry, MO theory, vibrational spectroscopy, etc.) and some application of the provided software (since MO theory and vibrational spectroscopy were covered in class, you are now expected to include some molecular orbital pictures / MO diagram analysis / IR/Raman analysis).