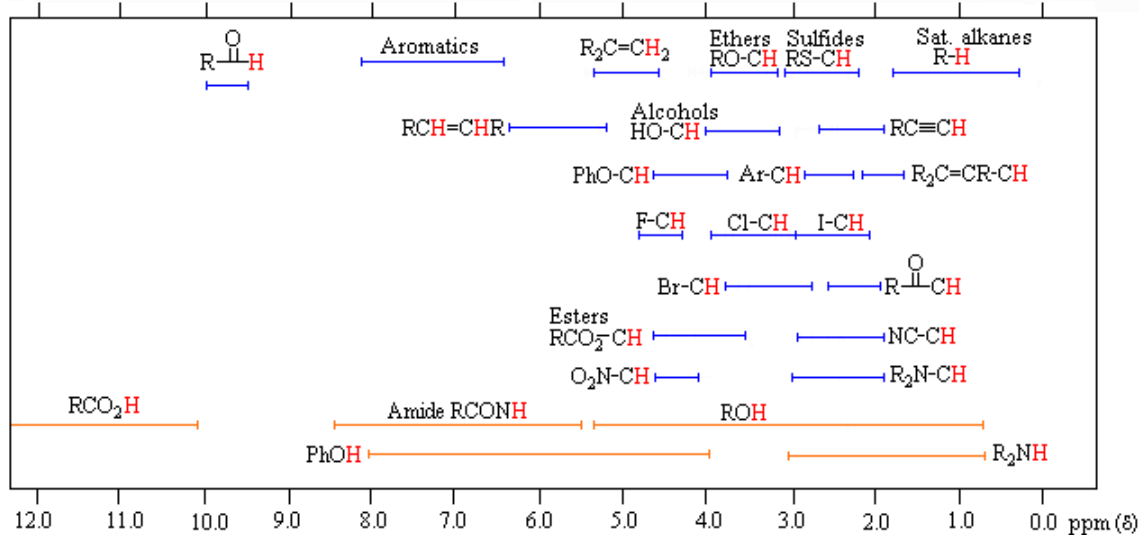
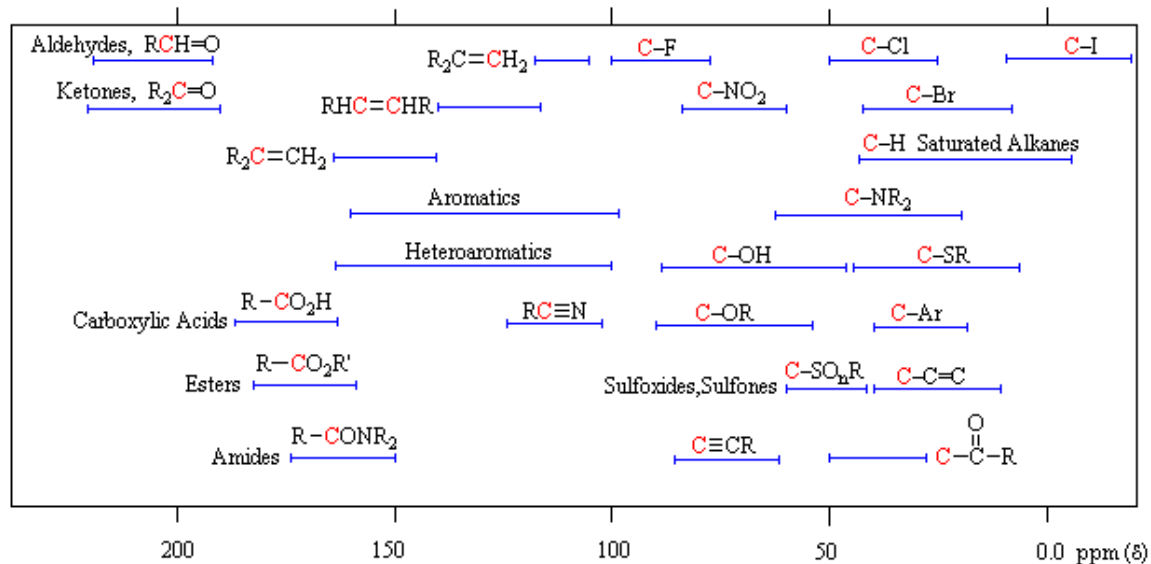


**<sup>1</sup>H NMR chemical shifts**

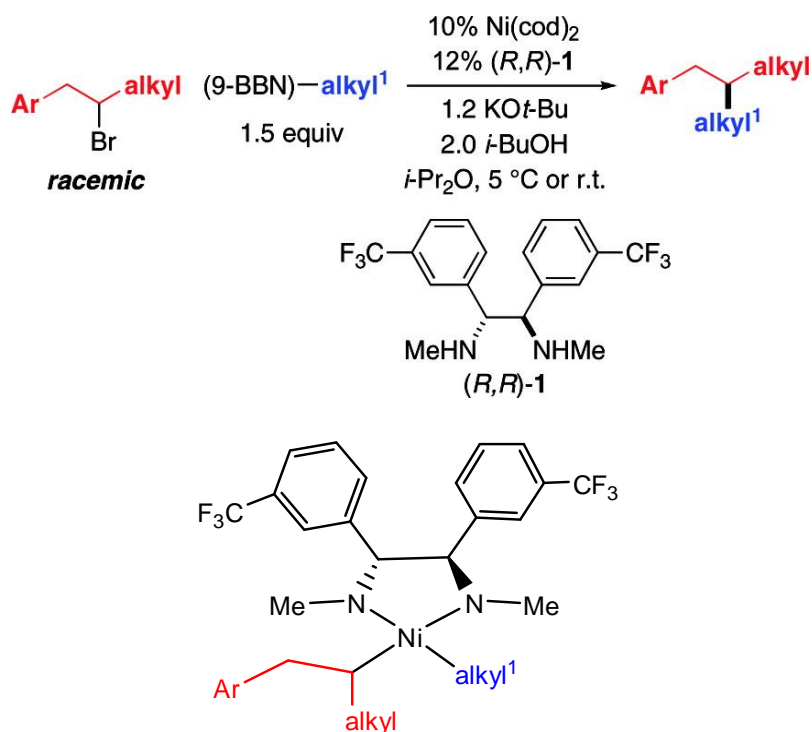


**<sup>13</sup>C NMR chemical shifts**



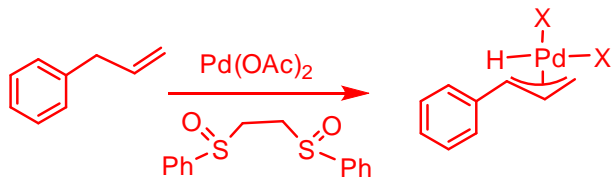
1. In the following reaction, draw the metal complex which would be the intermediate in the catalytic cycle immediately before the reductive elimination to form the product shown. (8 pts.)

Bunnai Saito and Gregory C. Fu. *J. Am. Chem. Soc.*, **2008**, *130* (21), pp 6694–6695.

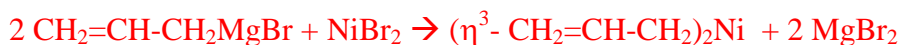


2. White et al. (*J. Am. Chem. Soc.* **2008**, *130*(43), pp. 14090-14091) recently reported alkylation reactions with Pd-allyl complexes. Key to the process was the formation of a Pd-allyl complex. During the course we discussed several different ways to make metal-allyl complexes. Provide two examples of reactions that form metal-allyl complexes. Be as explicit as possible with your answers. (10 pts.)

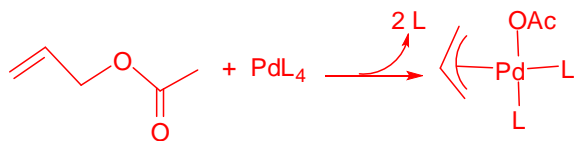
1. Oxidative addition to C-H bond used by White et al.



2. Ligand substitution on a metal by an allyl nucleophile.

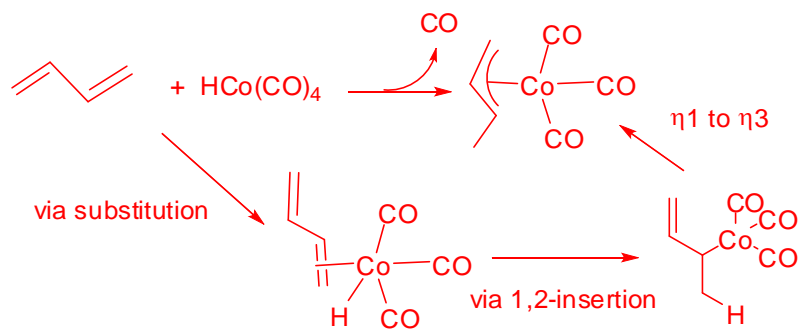


3. Ligand substitution on a metal by an allyl electrophile. (most common method)

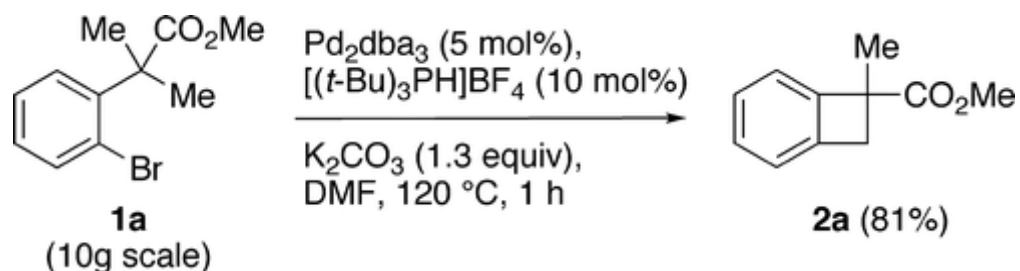


4. From diene protonation or insertion:

\_\_\_\_\_/18 pts.

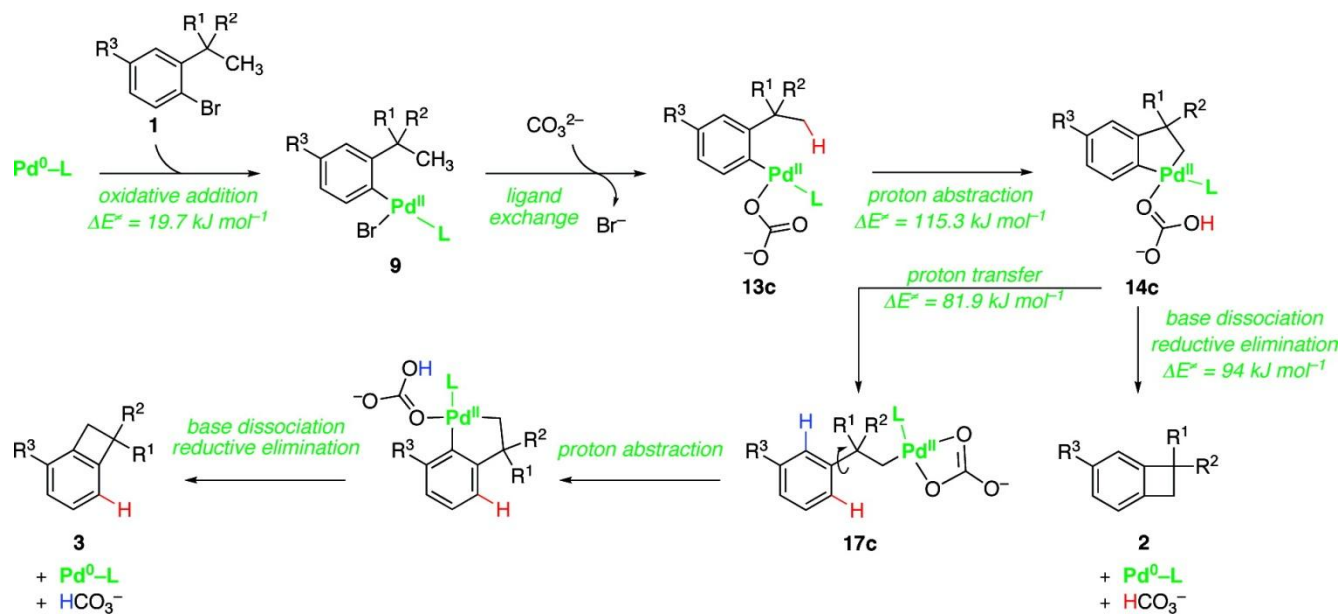


3. Propose a mechanism or catalytic cycle for the following reaction. Label each step with the reaction type shown. (12 pts.)



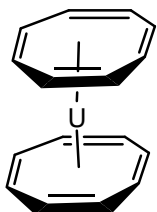
Manon Chaumontet, Riccardo Piccardi, Nicolas Audic, Julien Hitce, Jean-Louis Peglion, Eric Clot and Olivier Baudoin. *J. Am. Chem. Soc.*, **2008**, *130* (45), pp. 15157–15166

The path from **1** to **2** as shown below from the article.



\_\_\_\_\_/12 pts.

4. Answer the following questions about the uranium complex,  $U(\text{cot})_2$ , shown below.



a) What is the oxidation state of the uranium? (2 pts.) **zero**

b) What is the coordination number of the uranium? (2 pts.) **CN=8**

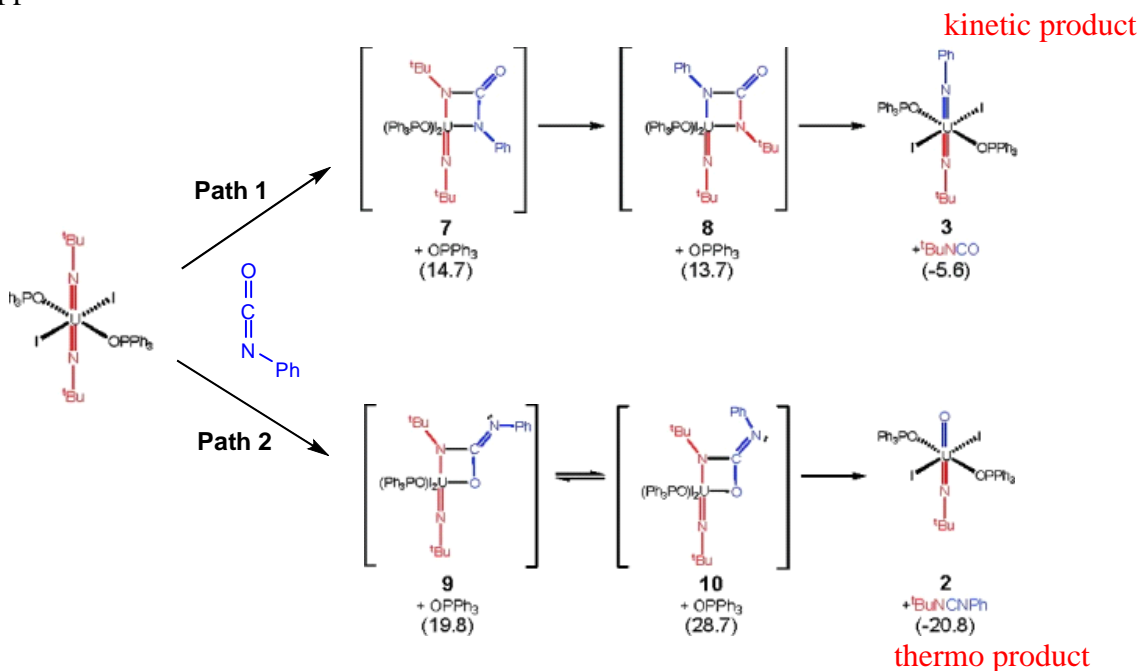
c) What is the electron count of the uranium? (2 pts.)  **$d^6 + (2 \times 8 \text{ for each cot}) = 22 e^-$ s**

d) Why doesn't the uranium complex obey the 18 electron rule? (3 pts.)

Uranium is an actinide element and therefore it has seven f orbitals in addition to one s, three p and five d orbitals in its valence shell. The seven f orbitals can accommodate 14 electrons giving the uranium atom the ability to have 32 electrons in the valence shell, much more than the 18 electron limit of the d block elements.

5. a) In the following scheme, identify the thermodynamic and kinetic product by writing 'thermo' or 'kinetic' next to each. Note: calculated energy values are written beneath each intermediate or product. (4 pts.)

Liam P. Spencer, Ping Yang, Brian L. Scott, Enrique R. Batista, and James M. Boncella. *J. Am. Chem. Soc.*, **2008**, *130* (10), pp 2930–2931

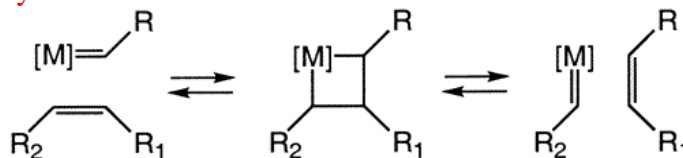


b) What is the reaction shown in the first step of path 1 and 2 to form compound **7** and **9**? (2 pts.)

In both path 1 and 2, the first step was a [2+2] cycloaddition.

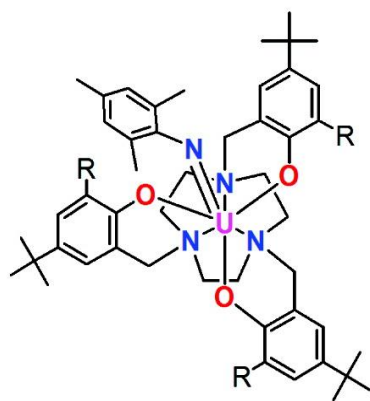
c) The reaction to form **7** and **9** was NOT a reaction that we discussed during the course, but it was very similar to a reaction that we did discuss. Name this reaction and show a brief example. (4 pts.)

The [2+2] cycloaddition is very similar to the olefin metathesis reaction shown schematically below.



\_\_\_\_\_/19 pts.

6. Answer the following questions about the structure shown below which comes from Karsten Meyer. et al: *J. Am. Chem. Soc.*, **2008**, *130* (37), pp 12536–12546.



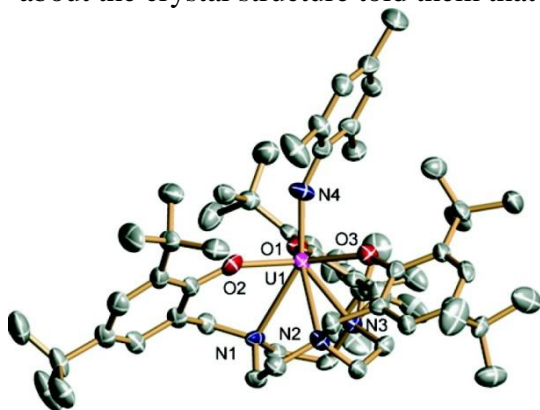
R = <sup>t</sup>Bu **2-tBu**  
= Ad **2-Ad**

a) Identify all the X-type and L-type ligands on the uranium atom. (5 pts.)

X-type: the three -OR ligands and the U=N imido ligand.  
L-type: the three U-NR<sub>3</sub> ligands.

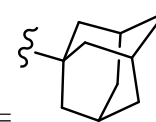
b) What is the oxidation state of the uranium? (3 pts.) **U(V), +5**

c) The authors of the research on uranium compounds **2** reported a crystal structure of **2-tBu** (below). What about the crystal structure told them that there was an imido bond or U=N in the structure? (3 pts.)



The bond length of the U=N imido bond was shorter (2.047 Å) than the other U-N bonds (2.72 Å) and it correlated with previously reported U=N imido bonds.

7. Three different phosphines, P(<sup>t</sup>Bu)<sub>3</sub>, P(<sup>t</sup>Bu)<sub>2</sub><sup>n</sup>Bu and P(1-Ad)<sub>2</sub><sup>n</sup>Bu, were analyzed in the aryl bromide hydroformylation study reported by Beller et al. (*J. Am. Chem. Soc.* **2008**, *130*(46), pp. 15549-15563).



1-Ad=

a) Briefly discuss the steric and electronic properties of these phosphines relative to the full range of phosphines that we discussed in the course. (5 pts.)

These phosphines are sterically demanding with a relatively wide cone angle due to the large alkyl substituents. Electronically they are strong sigma donors and weak pi acceptors.

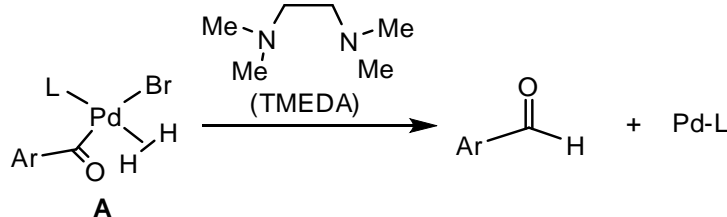
b) As we heard on several occasions over the last two weeks of the course, the slow step in Pd catalytic cycles is often the oxidative addition. How would these type of ligands facilitate the oxidation step? (4 pts.)

As bulky phosphines, they would limit the number of ligands on the Pd and promote the presence of monoligated Pd, a particularly active form of Pd. The absence of other ligands makes the addition of two ligands, as occurs in the oxidative addition, easier.

Electronically, these phosphine ligands increase electron density on Pd, thereby facilitating electron donation from Pd to the σ\* of the cleaving bond in the oxidative addition reaction.

\_\_\_\_\_/20 pts.

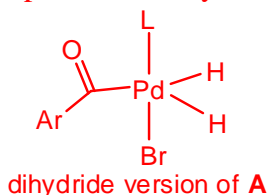
8. The following reaction was reported by Beller et al. (*J. Am. Chem. Soc.* **2008**, *130*(46), pp. 15549-15563) as the hydrogenolysis step in the formylation of aryl bromides.



a) This semester we discussed two basic types of transition metal complexes with hydrogen. List both types of complexes, identify which type complex **A** is and, using complex **A** as an example compound, draw the second type of metal complex with hydrogen. (6 pts.)

(1) Complex **A** is a sigma bond  $\eta^2$  dihydrogen complex.

(2) The second type of complex is called a classic dihydride complex. The structure below shows complex **A** as a palladium dihydride complex.



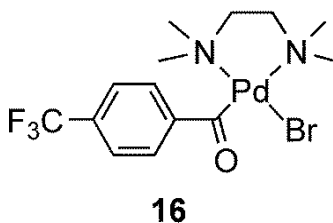
b) Beller et al. state that the dihydride version is very unstable and prone to reductive elimination. Explain why this would be. (2 pts.)

The dihydride version of **A** is a Pd(IV) complex and this is a rather high oxidation state of Pd that would be prone to reductive elimination to return to a Pd(II) oxidation state.

c) In the case of  $L=P(t-Bu)_2n-Bu$  or  $P(1-Ad)_2n-Bu$  the reaction of complex **A** succeeded in forming the benzaldehyde product as shown. What role did TMEDA play in this case? Be as explicit as possible. (2 pts.)

TMEDA acted as a base and removed a proton from the  $Pd-\eta^2-H_2$  complex thereby facilitating the formylation reaction.

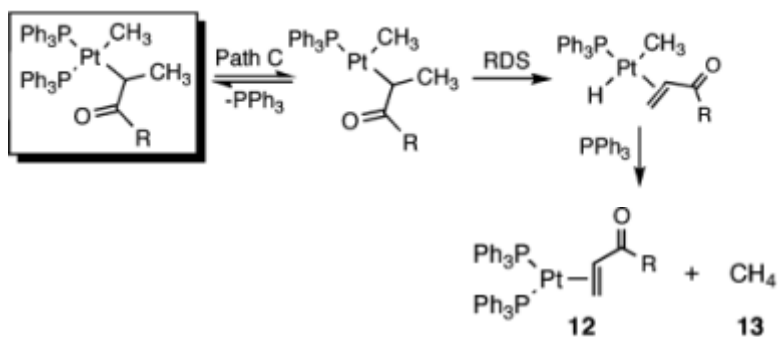
d) In the case of  $L=P(t-Bu)_3$ , complex **A** failed and it formed another Pd complex. Draw the structure of that Pd complex below. (2 pts.)



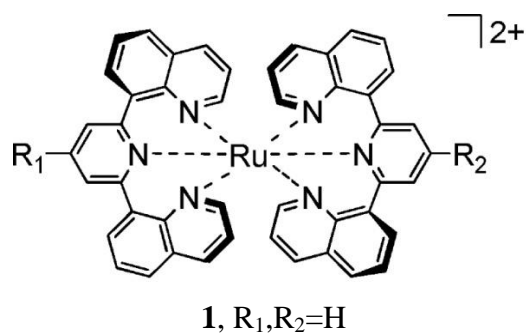
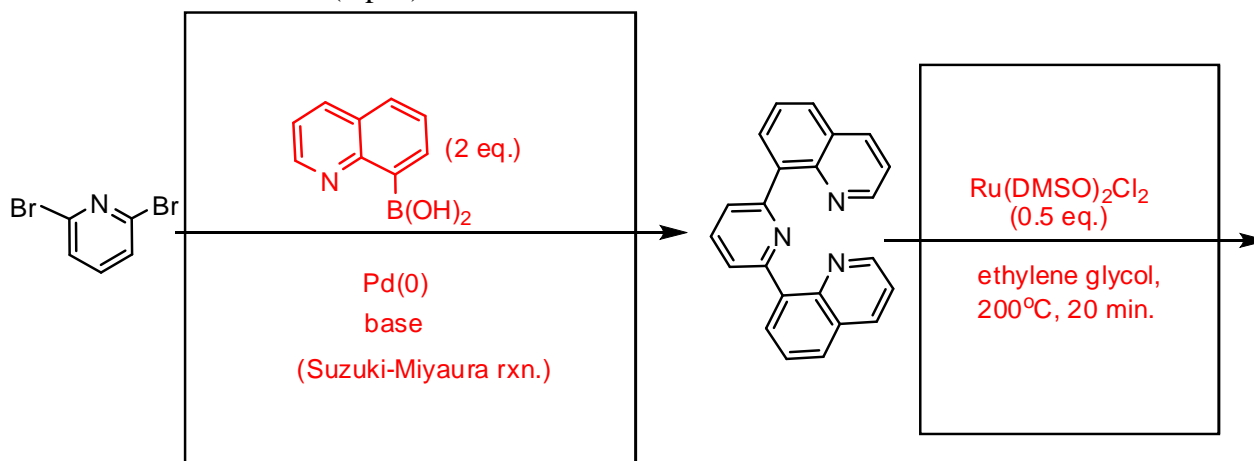
\_\_\_\_\_/12 pts.

9. After some experimentation, path C, shown below, was selected by Hartwig et al. (*J. Am. Chem. Soc.*, **2008**, *130* (46), pp 15627–15635) as the most likely path for the beta-hydride elimination of Pt enolates. The authors highlighted two classic mechanistic experiments as evidence that supported path C. Briefly describe the experiments that supported path C shown below. (Note: these experiments did not rule out another path (E); a second set of considerations lead them to favor path C.) (9 pts.)

The authors saw a suppression of the reaction with added  $\text{Ph}_3\text{P}$  and a kinetic isotope effect with a ketone enolate substrate that had deuterium ( $\text{d}_3$ ) substitution in the beta position. Additional  $\text{PPh}_3$  would suppress the ligand dissociation equilibrium seen in step 1 of path C based on Le Chatelier's principle. Since the second step, beta-hydride elimination, is the rate-determining step (RDS), the substitution of D for H in the beta position would be expected to slow the reaction.

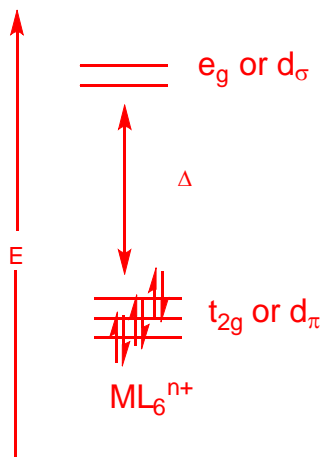


10. Complete the synthesis of complex **1** from the pyridine starting material by filling in the necessary reagents or reactants in the boxes. (8 pts.)



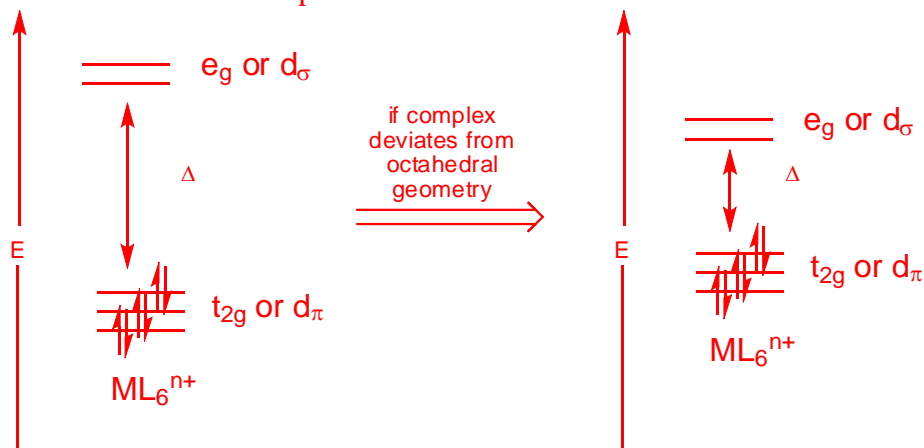
11. a) What type of geometry would be expected for complex **1** in the previous problem? (3 pts.) \_\_\_\_\_/17 pts.  
**octahedral**

b) Show the d orbital arrangement for Ru based on this geometry and the metal's oxidation state. Label the  $d_\pi$  and  $d_\sigma$  orbital groups. (4 pts.)



c) One key to the success of complex **1** in the photosensitization studies of Hammarstrom et al. (*J. Am. Chem. Soc.* **2008**, *130*(46), pp. 15533-15542.) was the angle of the N-Ru-N bonds and the close adherence of the structure to the geometry as noted in part a of this question. Based on crystal field theory, what happens to the relative energies of the d orbitals in your diagram of part b if the N-Ru-N angle becomes smaller and the geometry departs from the standard structure? (4 pts.)

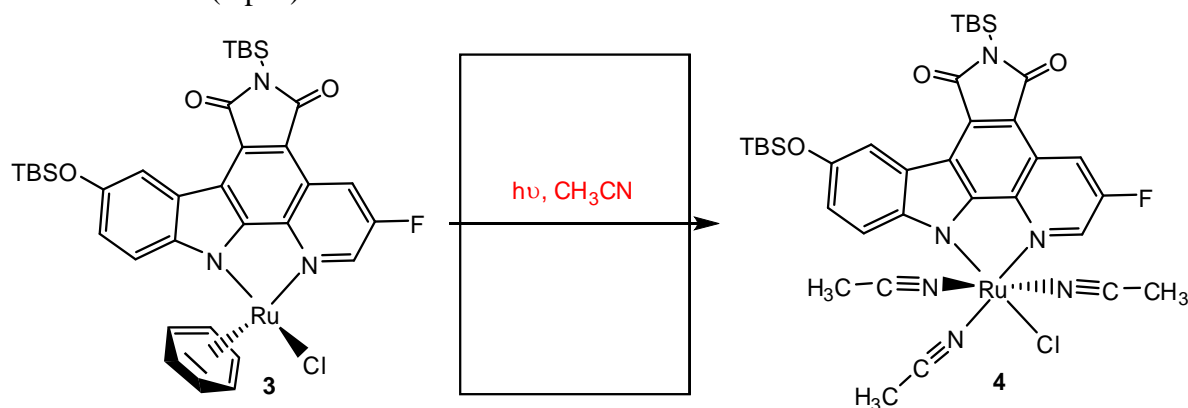
If the ligands are not centered on the x, y and z axes as in a classic octahedral complex, then the electron repulsion of the  $d_{z^2}$  and  $d_{x^2-y^2}$  orbitals will be reduced causing the  $d_\sigma$  orbitals to become more stable. Conversely, the  $d_{xy}$ ,  $d_{yz}$  and  $d_{xz}$  orbitals would start to experience greater repulsion and the  $d_\pi$  orbitals will become less stable. The  $\Delta$  would become smaller in the process.



\_\_\_\_\_/11 pts.

12. In their recent publication (*J. Am. Chem. Soc.* **2008**, *130*(47), pp. 15764-15765), Meggers et al. generated a range of Ru complexes to test as inhibitors of kinase enzymes. The authors used a variety of techniques or tricks to substitute groups on the Ru complex.

a) One such substitution is shown below for complex **3**. Provide the reagents or conditions used in the following transformation. (3 pts.)



b) Subsequent substitution reactions on complex **4** required high temperatures. Why do you think it would require such strong conditions to perform substitution reactions on complex **4** or related Ru complexes? (2 pts.)

**Complex 3 and 4 are very stable Ru complex: 18 e<sup>-</sup>, d<sup>6</sup>, Ru<sup>+2</sup>, octahedral complex.**

c) What is the most likely mechanism for ligand substitution of complex **4**, associative, dissociative or interchange dissociative/associative? (3 pts.)

**Complex 4 is more likely to undergo a dissociative or interchange dissociative ligand substitution because it is an 18e<sup>-</sup> complex and therefore not likely to add a ligand to form a 20 e<sup>-</sup> complex in the first step of a substitution event.**

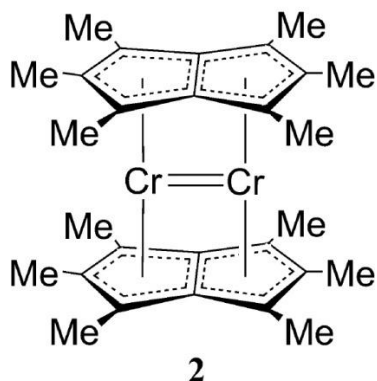
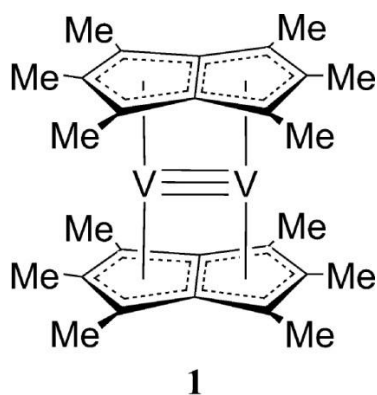
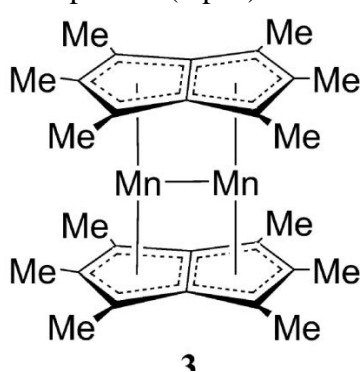
d) The challenges faced by Meggers et al. in their substitution reactions with the Ru complexes are actually an advantage in the ultimate goal: Ru metallopharmaceuticals. Why? (3 pts.)

**The stability of the Ru metallopharmaceuticals will be essential to their successful use as therapeutics. If they were to decompose easily in biological solutions before getting to their target, they would not be viable since their structure would change and their activity as an inhibitor would be unpredictable.**

\_\_\_\_\_/11 pts.

13. A recent report in the *Journal of the American Chemical Society* (2008, 130(46), 15662-15667) described the synthesis of double metallocenes such as the structure shown below for Mn. Complexes for two more first row transition metals, Cr and V, were also synthesized but they had a higher M-M bond order to achieve the

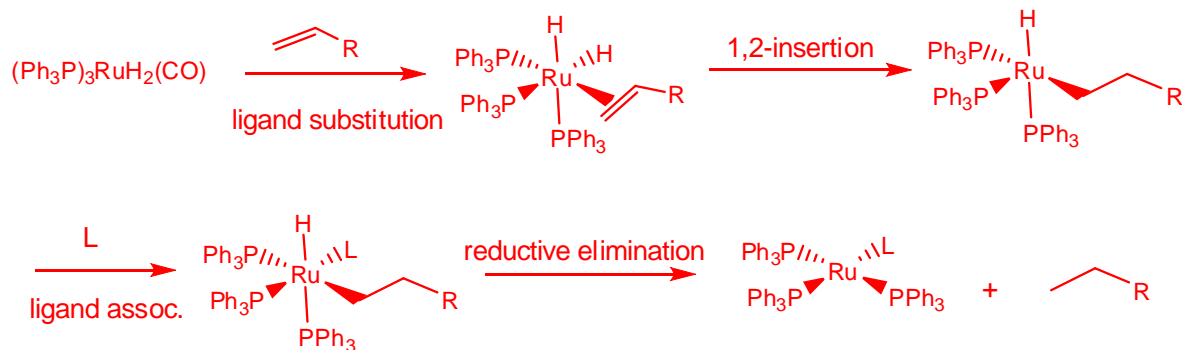
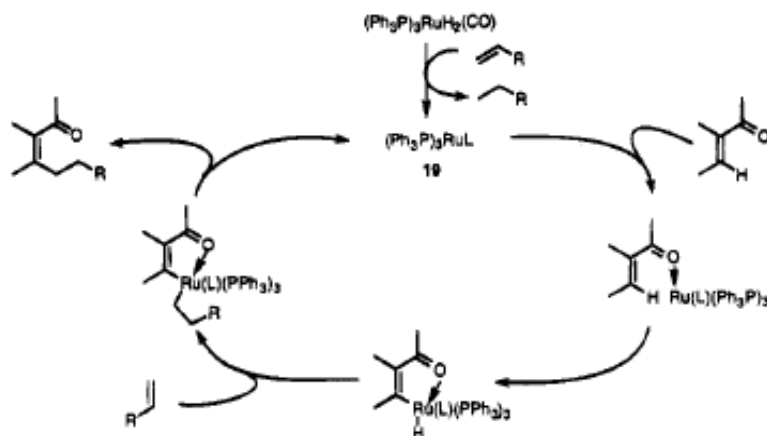
same 18 electron structure as shown for both Mn atoms below. Draw the Cr and V double metallocene complexes. (6 pts.)



The V complex has a triple bond between the two metals and the Cr complex has a double bond. The additional bonds give each metal the 18 electrons that it desires.

14. The catalytic cycle on the right was reported by Barry Trost and co-workers in 1995 (*J. Am. Chem. Soc.* **117**, 5371-5372). Several of the steps in this mechanism are shown in brief. Provide the necessary details as requested in the questions below.

a) The first step takes  $(\text{Ph}_3\text{P})_3\text{RuH}_2(\text{CO})$  to compound **19**. Draw a mechanism for this reaction. (8 pts.)



b) What is the purpose of this step in the catalytic cycle? (1 pt.)

\_\_\_\_\_/14 pts.

This serves as an activation step, making Ru(0) and making the complex coordinatively unsaturated, which is necessary for the catalytic cycle.

c) The authors provided NMR evidence for the first step. They reported the disappearance of peaks at -6.87 and -8.82 and only aromatic signals remaining in the  $^1\text{H}$  NMR. Why does this support the formation of **19** and the disappearance of  $(\text{Ph}_3\text{P})_3\text{RuH}_2(\text{CO})$ ? (3 pts.)

The -6.87 and -8.82 are the two hydride peaks of  $(\text{Ph}_3\text{P})_3\text{RuH}_2(\text{CO})$  and their disappearance indicates their transfer to the alkene ligand. Compound **19** has no hydride peaks and only the aromatic peaks of the  $\text{PPh}_3$  groups remain.

d) Identify the reaction type of each of the four steps of the catalytic cycle beginning in the top right corner and working around clockwise. *Caution:* one step in the catalytic cycle actually represents two reactions combined into one step. (4 pts.)

step 1: ligand association

step 2: oxidative addition to C-H bond

step 3: ligand substitution/association and then 1,2-insertion

step 4: reductive elimination

15. N-Heterocyclic carbenes (NHC's) are revolutionizing ligand design. Draw an N-heterocyclic carbene and briefly describe why they are similar to phosphines and how they differ from phosphines. (8 pts.)

general N-heterocyclic carbene:



N-Heterocyclic carbenes are tunable both sterically and electronically like phosphines. The R groups can be modified to influence steric hindrance. Changes to the ring or substituents on the ring can influence the electronic nature of the NHC.

The NHC's are generally better sigma donors and have little or no pi acid character.

\_\_\_\_\_/16 pts.