

Problem Set 2

Cycloadditions and Photochemistry

2.1 Problems 2 and 5

9/6: • We begin with Problem 5.

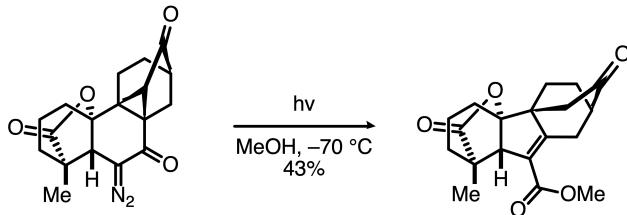


Figure 2.1: PSet 2, Q5.

- The first step — and the light-activated step — is a photolytic **Wolff rearrangement**.
 - Specifically, the light will photoexcite the diazo functional group. We don't really need to show this, though.
- After that, we have methanol addition to the ketene.
 - By using two methanol molecules, we can access a six-membered transition state.
 - On ketenes.
 - The $\text{C}=\text{O}$ and $\text{C}=\text{C}$ π -bonding orbitals are orthogonal.
 - More specifically, this means that the $\text{C}=\text{O}$ π -bond orbital lies in the plane of the page, and the $\text{C}=\text{C}$ π -bond orbital lies out of the plane of the page.
 - Implication: We must be careful about choosing the side of the ketene to which the methanol adds.
- Hydrogen bonding from methanol stabilizes many of the steps, as drawn in the third intermediate.
- There may be a **retro-Michael addition** somewhere in here. However, this was said to form an enolate, and thus be a step we'd like to avoid???
- Jasmin: Where can we learn about photoexcitation problems?
 - There are two types of photoexcitation regimes: Broad spectrum and specific wavelength.
 - The majority of productive photochemical processes use lower energy photons.
 - As a consequence, photochemistry is rare among unsaturated systems because anything powerful enough to drive something there will rupture bonds everywhere.

- By contrast, conjugated systems are more easily photoexcited.
- Example: The most reliable way to generate 4-membered rings is with photoexcitation! We can form 4-membered rings in such a system because we're pumping more than enough energy to overcome the ring strain. Here's how it works.

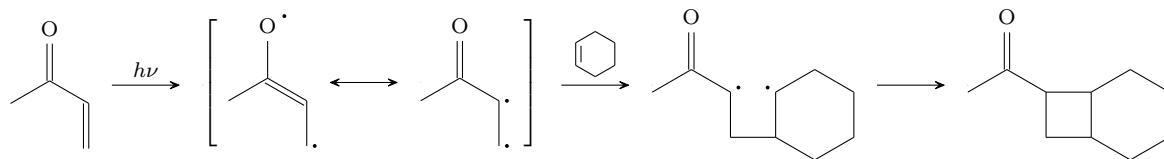
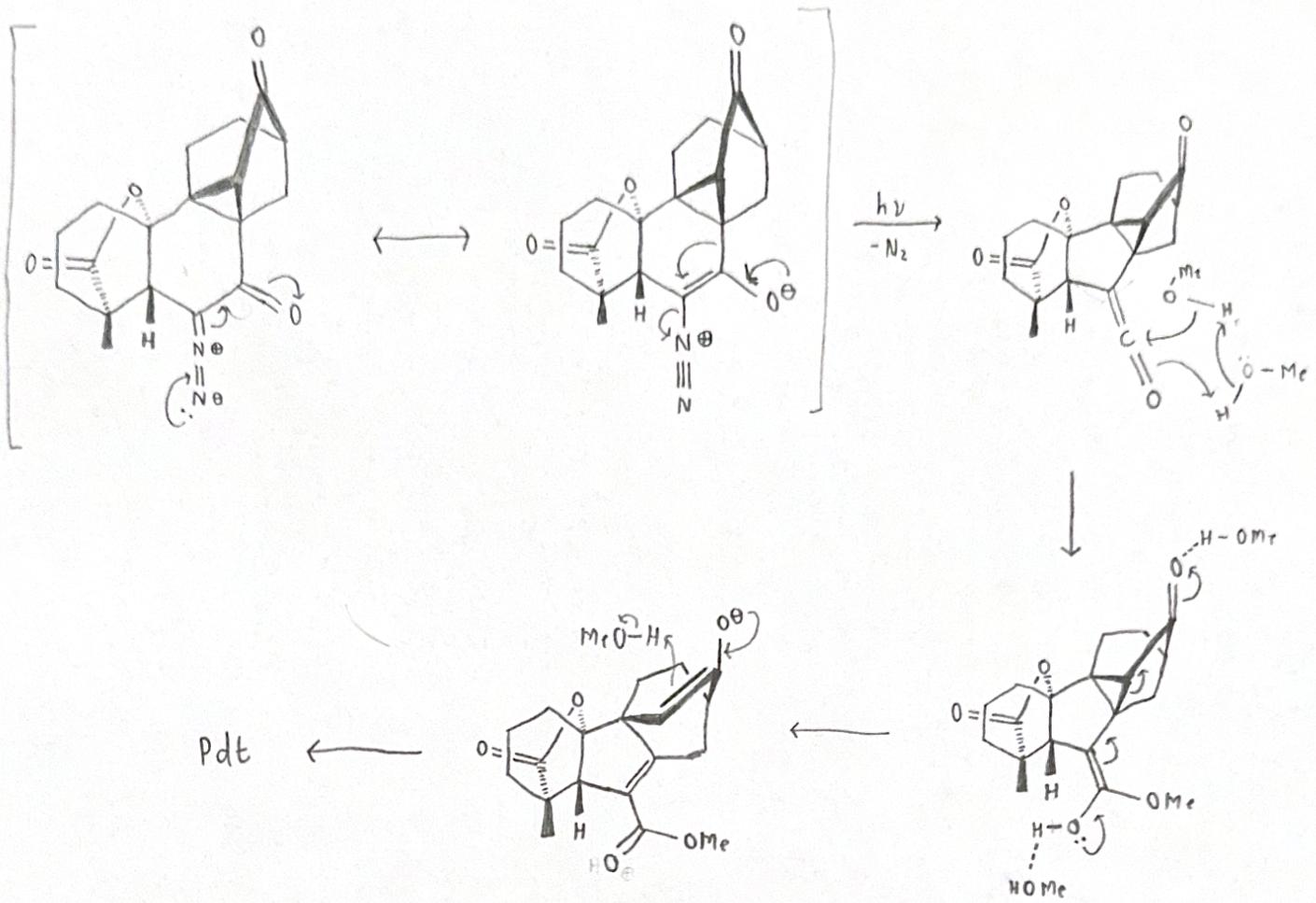


Figure 2.2: Forming 4-membered rings via photochemistry.

- A β -unsaturated carbonyl can be excited to a diradical, which can also be thought of as an excited state of the π -bond.
 - Note that the unconjugated alkene does *not* get photoexcited!
- Then we can do radical chemistry with the ketone, which is hard to excite.
- You could also have photoexcitation followed by intersystem crossing (singlet to triplet state).
- We will likely learn more about photoexcitation in 5.53.
- Takeaway: Looking at the starting material, we should identify conjugated systems, like how the ketone is conjugated to the $\beta\text{-C}=\text{N}$ bond.
- Aside: Rhodium can do very similar chemistry under thermal conditions. Instead of a carbene, we'd get a metal alkylidene, but it'd be the same end product.
 - So this can be transition-metal catalyzed.
- Reference: King et al. (1997).
- Altogether, the full solution to PSet 2, Q5 is on the next page.



- We now begin PSet 2, Q2.

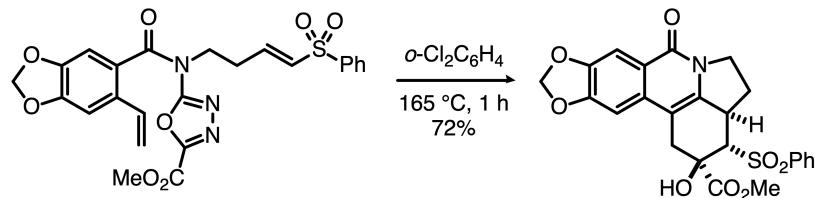
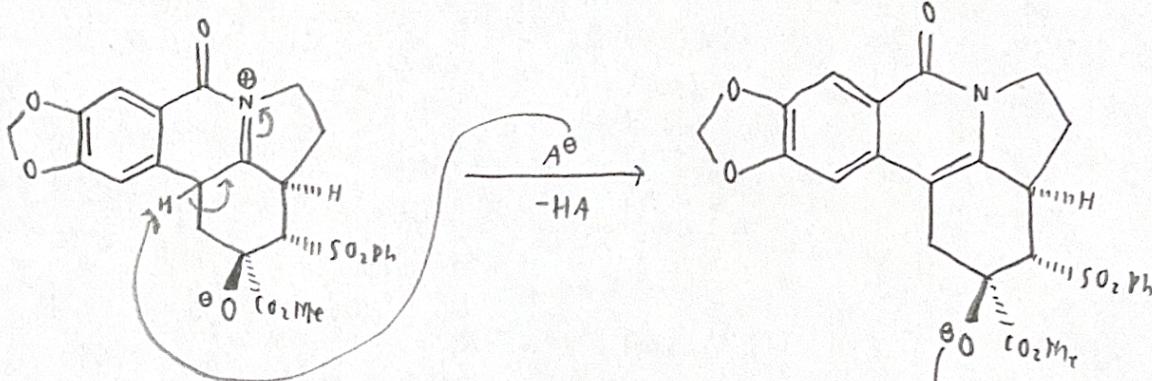
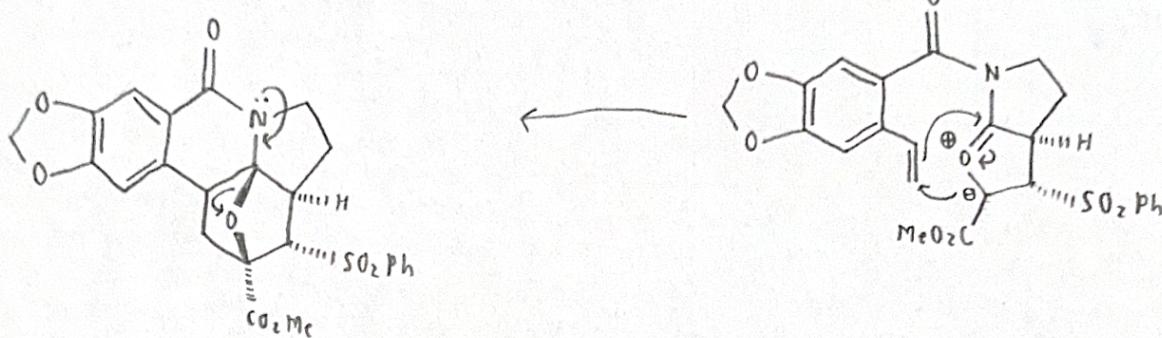
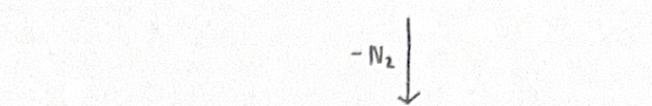
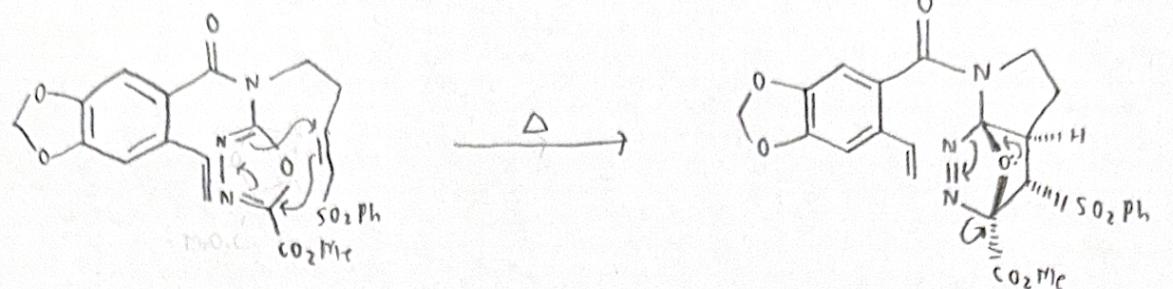


Figure 2.3: PSet 2, Q2.

- Starts off with a [4 + 2] cycloaddition, which will follow similar rules to the analogous Diels-Alder.
 - For example, this cycloaddition will also be diastereoselective, and hence will prefer to have the phenylsulfonyl EWG be *endo* in the transition state.
 - This sets the stereochemistry of the right side of the molecule.
 - This is an antarafacial/suprafacial reaction, not a suprafacial/suprafacial reaction.
 - Read up on the **Woodward-Hoffmann rules!!**
 - Forming a 5-membered ring is better than a six-membered ring??
 - Note that we choose to react with the more electron-poor alkene because it has a lower, more energetically accessible LUMO.
- After the cycloaddition, we rearrange the electrons and spit out nitrogen.
- We then do another [4 + 2] cycloaddition.
 - How do we retain the stereochemistry at the carbanion?? What's the alternate mechanism?
- At high temperature, the N–O ketal can drop down and (reversibly) expel the oxygen.
 - The formation of the N-acyl iminium will seriously stabilize the α -carbon's hydrogens. The stabilization effect is so extreme that any base in solution — from the starting material, to something intramolecular, to the unsilylated glass of the reaction vessel — will pick it off.
 - Then we just have to protonate the oxygen and we're done!
 - Altogether, the full solution to PSet 2, Q2 is on the next page.



Pdt

- Definitely have all of PSet 2 ready for next Monday!! And have at least looked at PSet 3.
 - PSet 2, Q3 is gonna need really good 3D transition state structures. Make sure to try this one!!
Hints:
 - You start with a Diels-Alder. Lewis acid activates the ketone.
 - This lowers the energy of the LUMO; sets the stage for an intramolecular Diels-Alder.
 - Following this, draw the intermediate, put it in a chair scenario, and then sort out the azide.
 - Azides and Lewis acids can add into the carbonyl. This will lead to loss of N₂, and how can we facilitate this?
 - Schmidt reaction.
 - Lots of antiperiplanar interactions that are responsible for product distribution.
 - This problem is something of a sequel to PSet 1, Q3.
 - We will start next time with PSet 2, Q3.
- Remember to take more pictures!!
- Use whatever time we have for this class to think about future problems, not clean copying notes.
- Jasmin and I will start next time with two PSet 2 problems; one of us will take Q3, the other Q1.
- Focus on PSet 2, but we can start PSet 3.