

Problem Set 1

Carbonyls

1.1 Problems 18 and 19

- 9/11:
- We should still continue reviewing the list of topics (at least before second year orals)!!
 - I should also continue reading the textbook!!
 - Come in with good solutions on Friday!!
 - Problem 22 is the **Dakin-West reaction**, if we want to look it up after class.
 - We now begin discussing Problem 19.

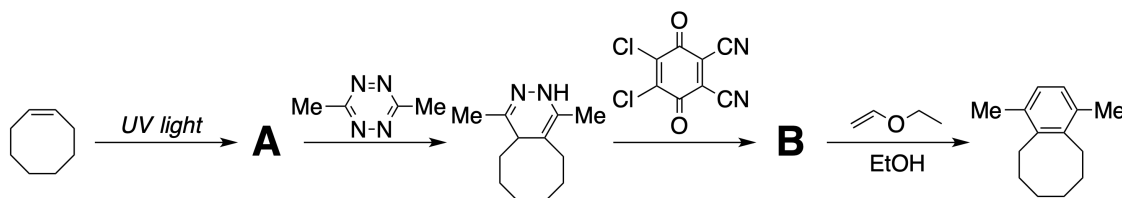


Figure 1.1: Johnson PSet 1, Q19.

- With UV light, we'll get isomerization to *trans*-cyclooctene. *picture*; *Frank's HOMO/LUMO diagram*.
 - *trans*-cyclooctene is a pretty strained molecule.
 - Jeremiah has us draw out the HOMO and LUMO of the alkene, i.e., matching phases and un-matching phases.
 - Jeremiah thinks the Woodward-Hoffmann rules are hard to understand without HOMO/LUMO diagrams.
 - Light excites an electron to a higher energy state, in a process in which a spin is conserved.
 - Learn **Jablonski diagrams**!!
 - Absorption of a photon happens on a femtosecond timescale, way faster than any other process can happen.
 - The flip of an electron spin is called **intersystem crossing**. This gets you from a singlet to a triplet state. ISC (flipping a spin) is technically a **forbidden** process, because a change in spin angular momentum must be matched by a change in orbital angular momentum or some such thing.
 - The electrons are still paired, even after excitation.
 - **Fluorescence** and **internal conversion** are by far the fastest and most favorable processes (photorelaxation and vibrational relaxation, respectively).

- The double bond does break into a biradical, and now the molecule is much more conformationally flexible.
- Jeremiah likes to show a biradical as the unpaired electrons with their spins.
- What is the driving force for this thermodynamically uphill reaction?
 - The *trans* and *cis* molecules absorb different wavelengths, so we need to shine exactly the wavelength that *cis* can absorb so that the reaction doesn't go backwards.
 - Once the *trans* species forms, it will form in a 75:25 ratio or something like that because "the energy difference is matching the extinction coefficient" or something like that.
 - Trans alkenes coordinate strongly to silver, and then we can flush it off of a silica column.
 - The trans coordinates more to silver because...
- An isolated double bond will need high intensity, low wavelength UV light be activated.
 - If you wanted to get this to work with lower energy light, you'd need a photocatalyst.
 - The reaction might start to have a bright color because the absorption peaks shift.
- The *trans*-cyclooctene does a cycloaddition to form an intermediate.
 - How do we do the proton shuffle? Perhaps using one of the nitrogens as a base.
 - **Inverse electron demand Diels-Alder.** Here, the dieneophile is electron rich and the diene (a tetrazine) is electron poor.
 - For this kind of reaction, we care about the LUMO of our diene and the HOMO of our dienophile (inverse of the regular Diels-Alder!).
 - And we do see that the symmetry matches.
- Kicking out N₂ and forming the double-bonded intermediate happens concerted; the zwitterion Frank drew probably doesn't exist.
- Then this intermediate tautomerizes to the intermediate in the question.
 - Use an external molecule (or the solvent) to do the tautomerization. The second tautomer is more stable!
- The third step is a **DDQ reaction**.
 - There is no established mechanism for this reaction!
- Net driving force: Taking two quinones and aromatizing both of them.
- It's also a dehydrogenation reaction.
- We believe the mechanism is radical-enabled.
- A π -bond (relatively nucleophilic) on the intermediate can do a single-electron transfer and become a radical cation.
 - Single-electron transfer from a π -bond can and will happen if it's thermodynamically favorable because DDQ is such a good electron acceptor.
 - You might also use light to accelerate this reaction.
- There's a nice resonance structure that's aromatic, even though oxygen-centered radicals are unstable. But then this leads to rapid proton transfer of the resonance-stabilized positive proton.
- **Semiquinone** intermediate.
- Then the O radical steals an electron, becoming a negatively charged O that can steal a proton for aromaticity.

- There is also a proposed two-electron mechanism.
 - Start with a hydride transfer of the most electron-rich hydride to DDQ.
 - Using resonance structures to predict nucleophilic sites! Draw an aromatic resonance structure, which puts a positive charge on oxygen.
- Why couldn't we use TEMPO to disprove the radical mechanism?
 - It's a matter of relative rates; these radicals could only be formed transiently, far faster than TEMPO could interfere.
- There are computational papers in the last few years on DDQ mechanisms, but they are heavily substrate dependent.
- Some calculations suggest an **asynchronous** process.
- There are some reactions that would almost definitely suggest asynchronous mechanisms.
 - SRN1 reaction fills the gaps where SN1 and SN2 don't work.
 - Trigonal pyramidal carbocation is very unstable.
 - Tertiary radical is much more simple.
 - Dougherty and Anslyn has a whole chapter on SRN1 reactions!
 - Prior to photoredox catalysis, these reactions were more just a curiosity; now we're trying to make them useful.
 - Corey Stephenson's work on the early photoredox reactions.
- Lastly, we get another Diels-Alder reaction followed by a retro-Diels-Alder to kick out N₂.
- Then six-membered transition state proton transfer.
 - Heat or acid would help the end.
 - Jeremiah ran this reaction when he first got to MIT, and thought that the spontaneous aromatization was quite interesting.
- Altogether, the full solution to PSet 1, Q19 is on the next page.

- We now begin discussing Problem 18.

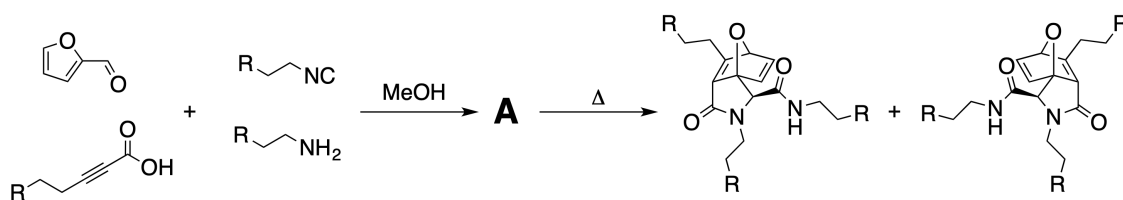


Figure 1.2: Johnson PSet 1, Q18.

- Altogether, the full solution to PSet 1, Q18 is on the next page.



Figure 1.3: Johnson PSet 1, Q18 solution.

- We now begin discussing Problem 21.
- The first step is a **Fischer indole synthesis**.
- That's all we got to today.
- Jeremiah's list of named reactions.
 - 15: Benzoin condensation reaction.
 - 18: Ugi reaction followed by Diels-Alder.
 - 19: Inverse electron-demand Diels-Alder and another Diels-Alder.
 - 20: A Michael addition and Mannich reaction.
 - 22: A Dakin-West.
 - 21: Fischer indole synthesis.