

Problem Set 3

Condensations

3.1 Problems 1, 4, and 8

- 9/16:
- David works with Rick Danheiser.
 - We now begin discussing Problem 1.

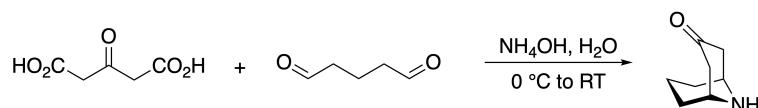


Figure 3.1: Wendlandt PSet 1, Q1.

- The reagents: NH_4OH in water is approximately $\text{pH} = 11$.
- Keto-enol tautomerization and amine condensation gets the carbons bonded in the right way.
 - Dialdehyde forms an imine.
 - The enol is not unreasonable because hydrogen bonding stabilizes a 6-membered ring.
 - Then the enol can be a H-bond acceptor from the other carboxylate.
- Watch out for reversible steps!!
- Loss of CO_2 helps drive some of the steps.
- There are multiple right answers; David's sequence of events works, but others could be valid, too.
- Aldehyde is more electrophilic than the monoprotonated imine, so if we're gonna react with an imine, we need to change both aldehydes into imines first. Alternatively, we need to diprotonate the imine.
- It's not clear whether decarboxylation happens earlier or later in the mechanism.
- Altogether, the full solution to PSet 1, Q1 is on the next page.

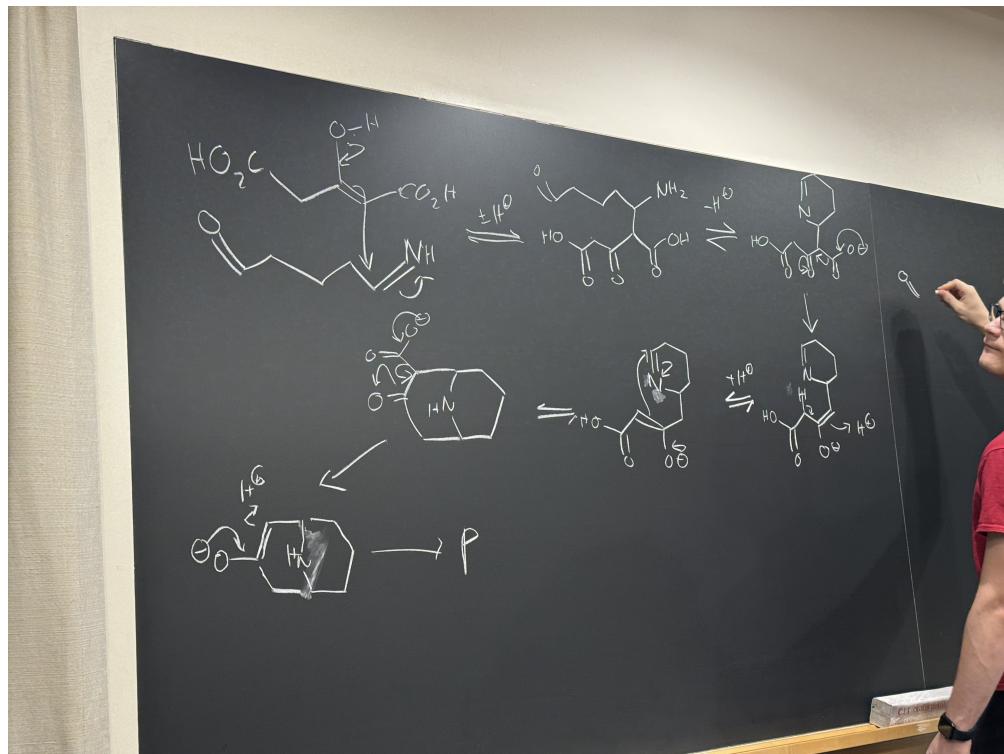


Figure 3.2: Wendlandt PSet 1, Q1 solution.

- We now begin discussing Problem 4.

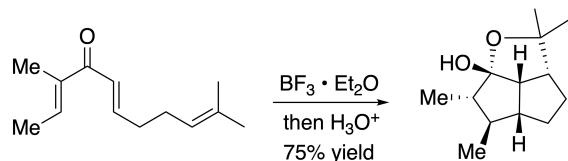


Figure 3.3: Wendlandt PSet 1, Q4.

- This is a **Nazarov reaction**, which is covered in Clayden.
- The initial electrocyclization is conrotatory; we need a continuous sequence of π -orbitals to get this.
- The Nazarov is a very powerful tool for making 5-membered rings, but the cation that it leaves oblates a ton of the stereochemical information.
- Torquoselective reaction:** ...
- Orbital analysis yields a structure with the stereochemistry that
- 5,5-trans ring fusions aren't known outside of very unique synthetic constructs. The difference in energy is a huge 5 kcal/mol to 7 kcal/mol.
- Scott Denmark has developed strong Lewis acid activation of strong Lewis bases.
 - Thus, from the perspective of both the activated Lewis base heteroatom and the perspective of the carbocation, this C–O bond-forming reaction should proceed before the acid workup.
- Whenever you see a cycloaddition, start thinking about the orbital structure of the HOMO and LUMO.
- Altogether, the full solution to PSet 1, Q4 is on the next page.

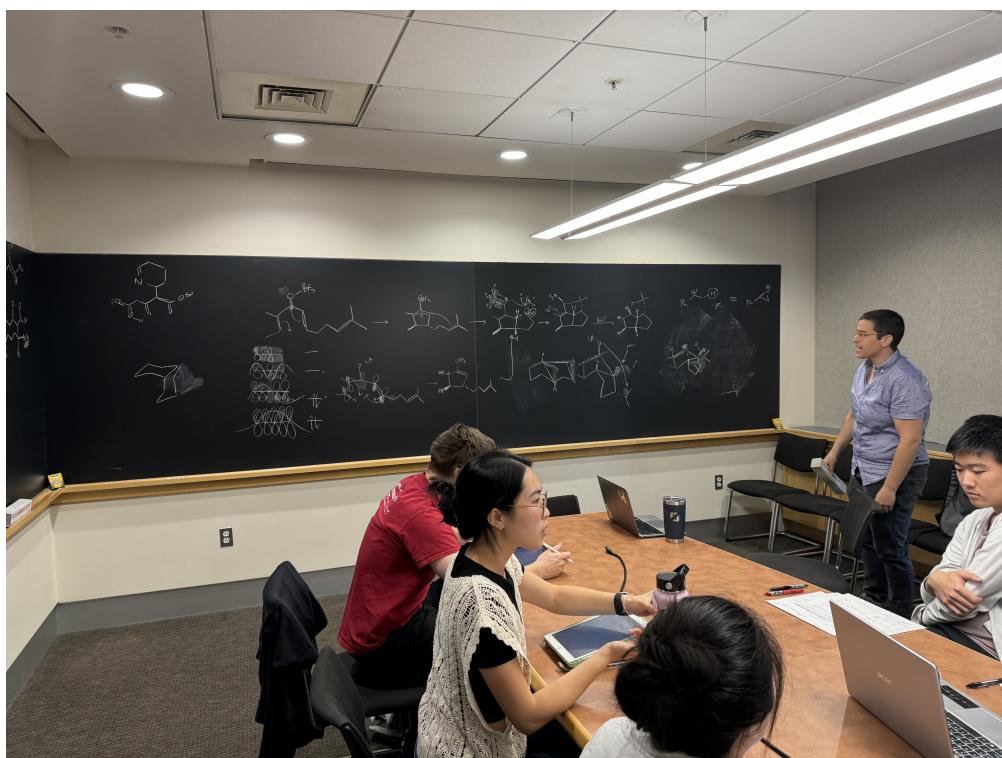


Figure 3.4: Wendlandt PSet 1, Q4 solution.

- We now begin discussing Problem 8.

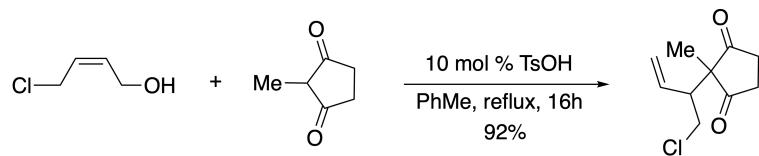


Figure 3.5: Wendlandt PSet 1, Q8.

- The thing I proposed is called an $\text{S}_{\text{N}}2'$ reaction, i.e., the attack of one species not on the leaving group but on the conjugated position a couple of carbons away.
 - My mechanism is *plausible* but not *defensible*.
 - The OH is not the most Lewis basic species in solution.
- Protonating a hemiacetal will be easier than Frank's proposition of protonating the alcohol.
 - Alison proposed 1,2-addition and 1,4-addition.
- We end with a **Claisen rearrangement**.
- You get a *stabilized* enol structure. Enol is better than enolate for acidic solution.
- You use the nucleophilic part to rearrange the electrophilic part.
- Altogether, the full solution to PSet 1, Q8 is on the next page.

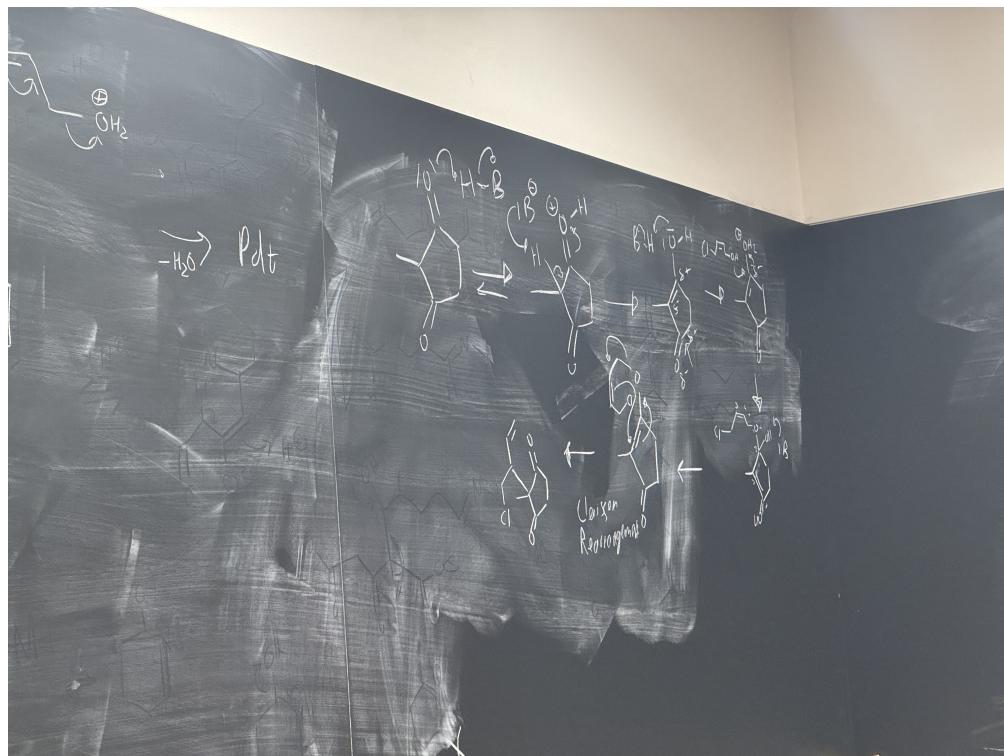


Figure 3.6: Wendlandt PSet 1, Q8 solution.