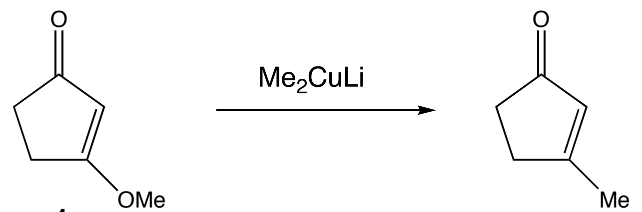
Problem Set #3 – Due March 3rd at 11am

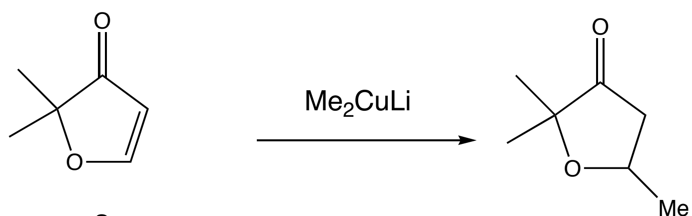
Question 1. Recall that cuprate reagents undergo conjugate addition to α,β-unsaturated carbonyl compounds. Using your understanding of reaction mechanism and stereoelectronic effects:

a) Provide a mechanism for the reactions shown below.

b) Explain why enone **1** undergoes an addition-elimination reaction, while **2** yields only the addition product. Assume the presence or absence of the geminal-dimethyl group in **2** is not important.

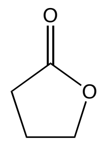


1

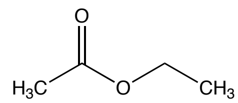


2

Question 2. Cyclic esters, commonly referred to as lactones, display quite different reactivity than acyclic esters. For example, γ-lactone **A** (common name: butyrolactone) can be reduced by $NaBH_4$ at a rate similar to a ketone, while an acylic ester such ethyl acetate (**B**) is generally inert to $NaBH_4$ reduction.



A

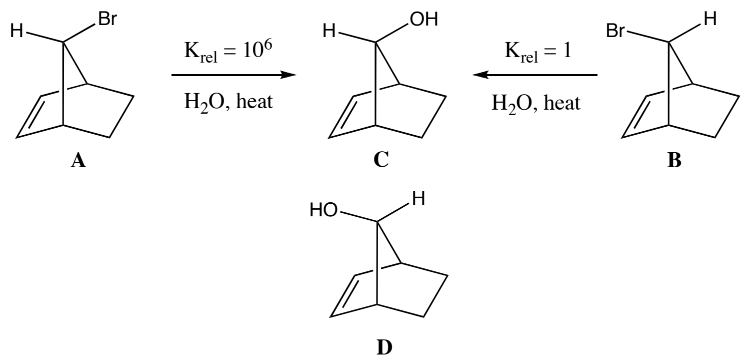


B

a) Provide a mechanism for the reduction of **A** with excess $NaBH_4$ (assume a standard, acidic aqueous workup is performed).

b) Clearly explain why lactones are far more reactive toward reduction than acyclic esters.

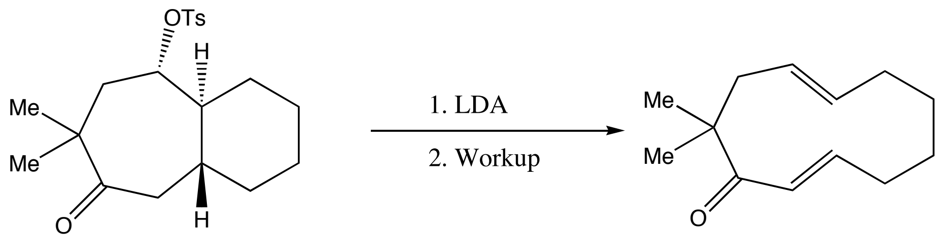
Question 3. Consider the S_N1 solvolysis of alkyl bromides **A** and **B** as shown below. Instead of furnishing the expected 50/50 mixture of secondary alcohols **C** and **D**, both bromides yield exclusively alcohol **C**. It is also rather striking that bromide **A** solvolyzes 1 million times faster than bromide **B**.



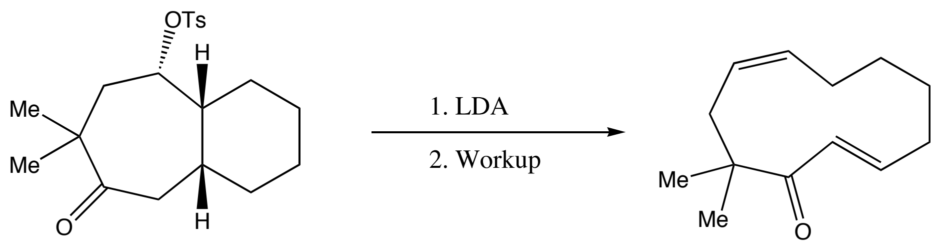
not formed

Why is bromide **A** so much more reactive than **B** to S_N1 solvolysis? Why is alcohol **C** the only product, regardless of the initial bromide stereochemistry? Use clear three-dimensional drawings in both your answers.

Question 4. Consider the following reactions:



(1)

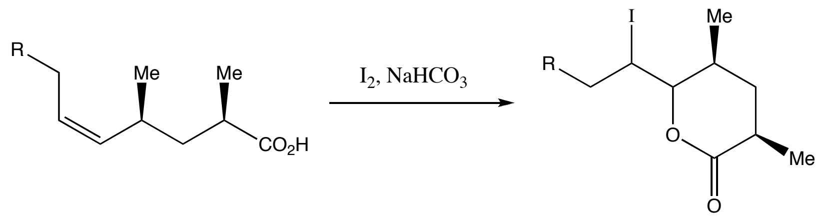


(2)

a) Draw the *cis*- and *trans*-tosylates (the starting materials) in three-dimensions ("chair" form).

b) Provide mechanisms for both reactions. In your mechanism, show how the stereochemistry of the starting materials translates into the olefin geometries observed in the products.

Question 5. Clark Still's synthesis of the natural product monensin features the diastereoselective iodo-lactonization shown below.



Provide a mechanism for this reaction, and be sure to identify all the important intermediates. In your answer, predict the stereochemistry of the major product. Make sure to draw the transition state leading to your predicted stereochemical outcome and identify the relevant control element(s) operating.