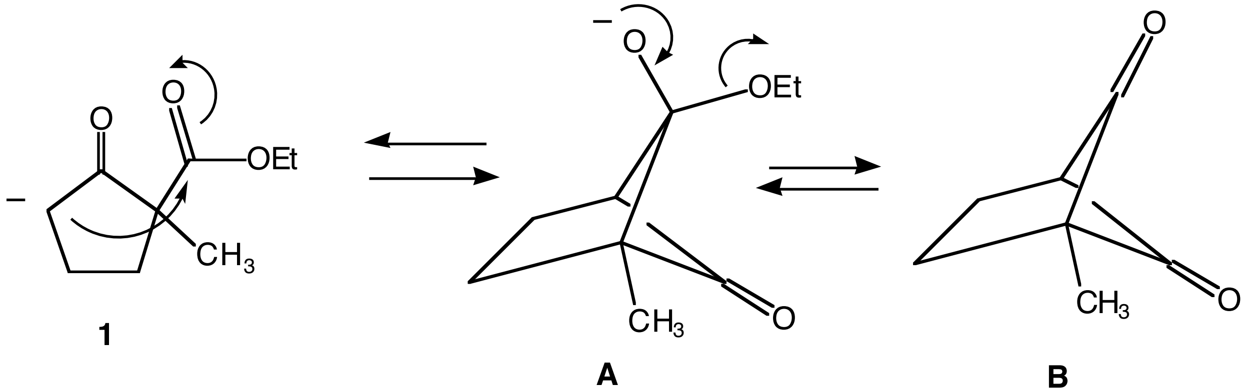
Answers to Hour Examination #3, Chemistry 302X, 2006

1.

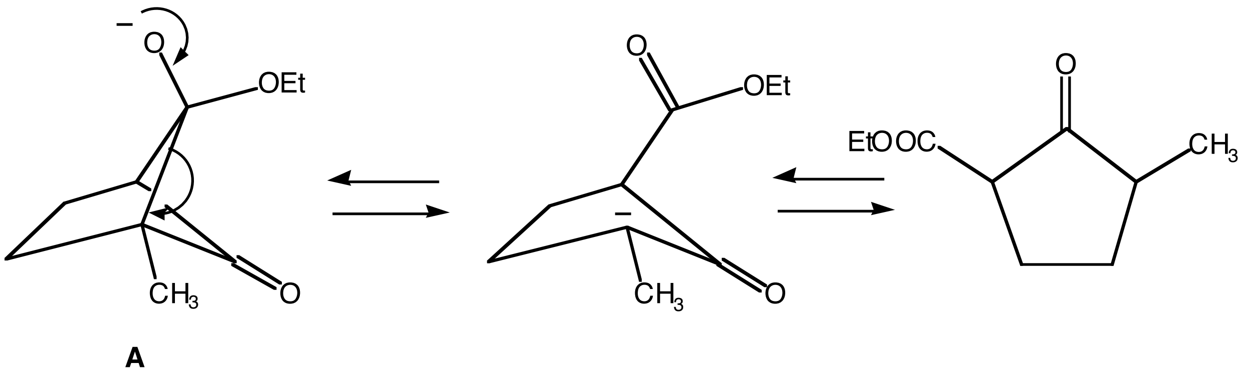
(a). That S$_N$2 shown just can't happen with the required inversion. The "back" of that methyl group is not reachable by the putative nucleophile, the pi system of the enolate.

(b). Although displacement of the methyl can't happen, addition to the ester carbonyl can. So, one mechanism begins with the addition of the ketone enolate to the ester carbonyl to give **A**, then, perhaps, the symmetrical intermediate **B**.

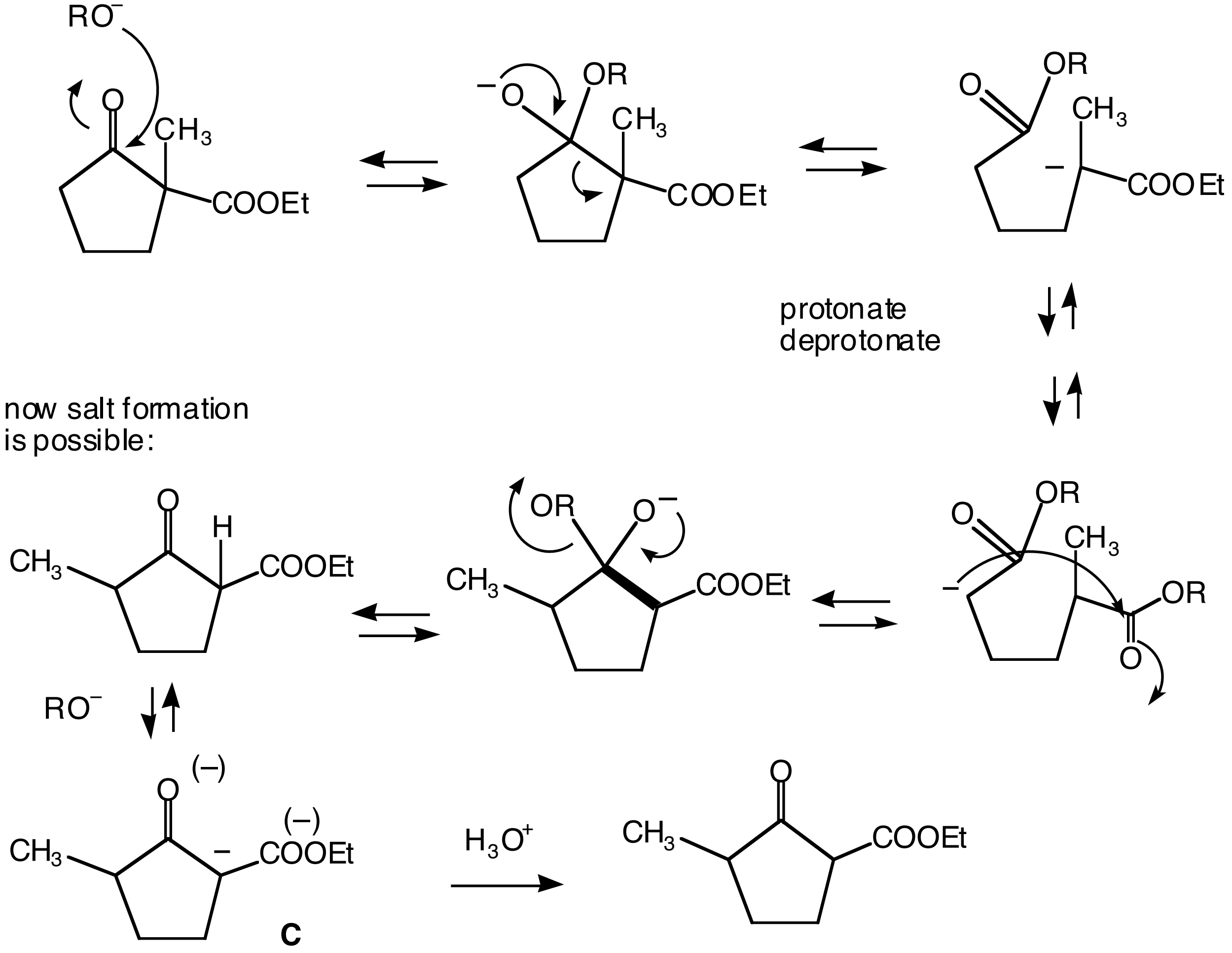


Intermediate **B** can undergo addition of ethoxide to either carbonyl (right-hand reverse arrow above) to regenerate **A** and go on to products shown below.

Even better (probably) would be the direct opening of the initial adduct **A** to give an enolate that protonates to product.

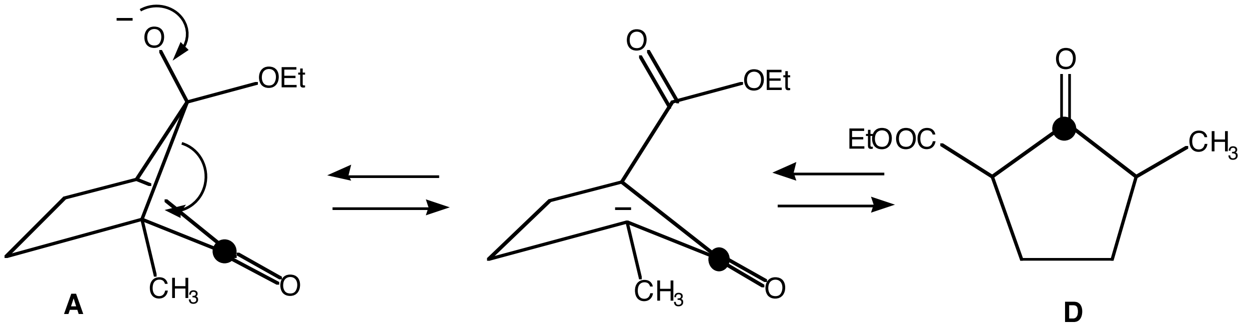


Alternatively (and better) we could do the other archetypal reaction of carbonyl groups and add alkoxide to the ketone C=O. A reverse Claisen, followed by a forward Claisen, leads to enolate **C**. A final protonation gives the product.



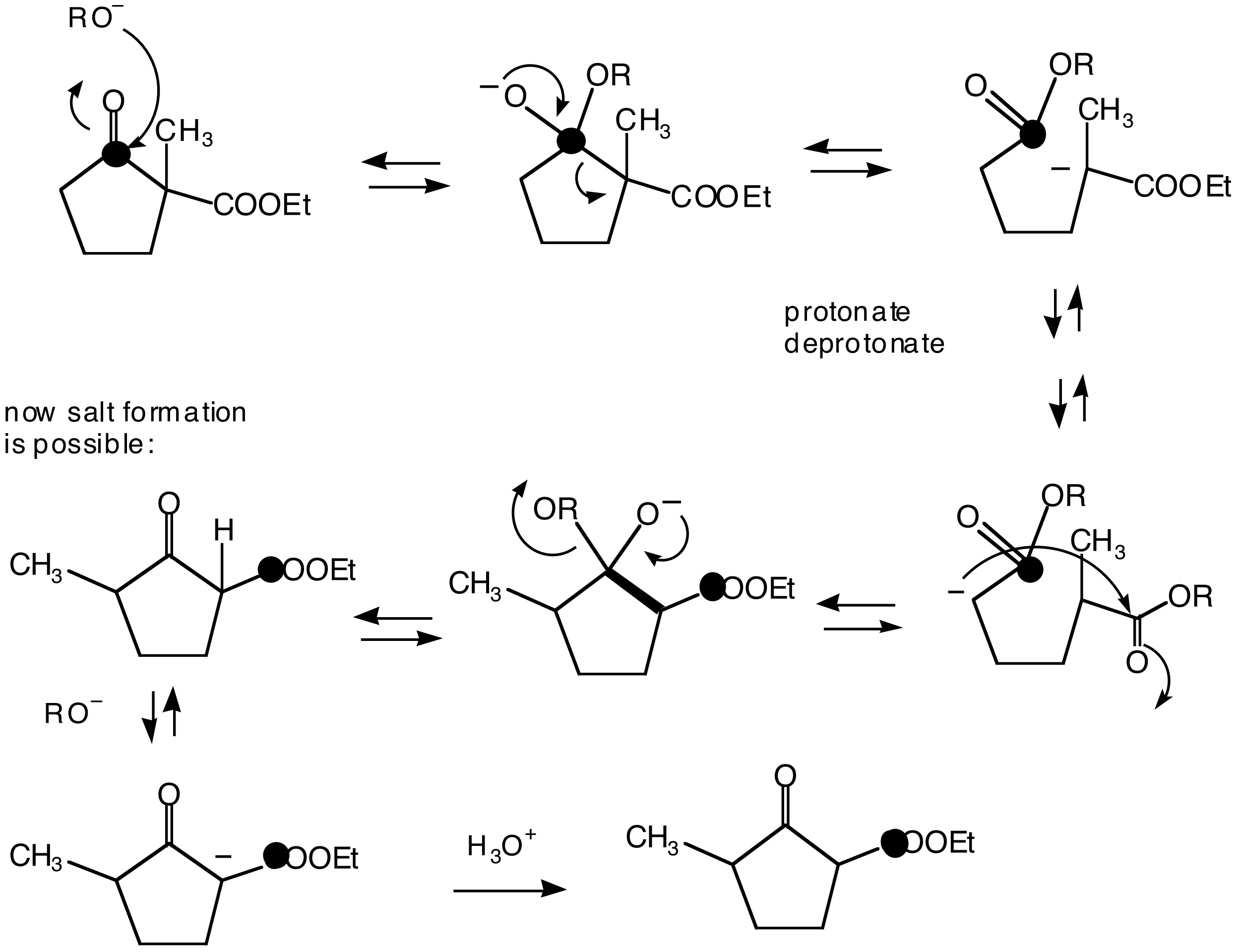
(c). Now, how to tell them apart? Label one (either) carbonyl group. Here are the three possibilities, starting with labelled ketone:

Direct opening of **A** gives product labelled as in **D**:



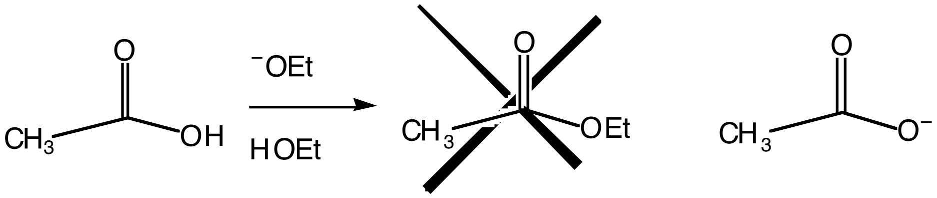
If the symmetrical intermediate is formed, there must be 50% of **4** produced with the other 50% in the ester carbonyl.

The reverse Claisen puts the label completely in the final ester product.:

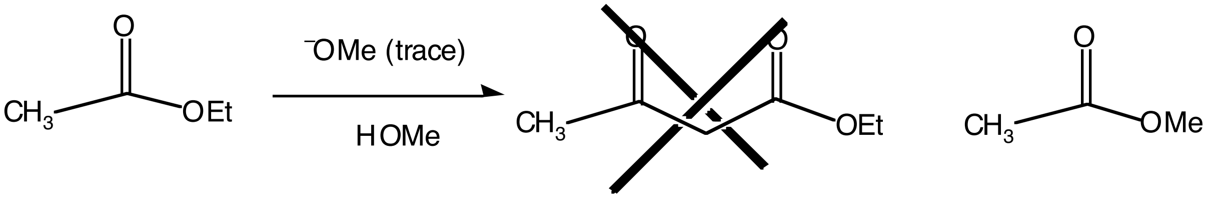


now salt formation is possible:

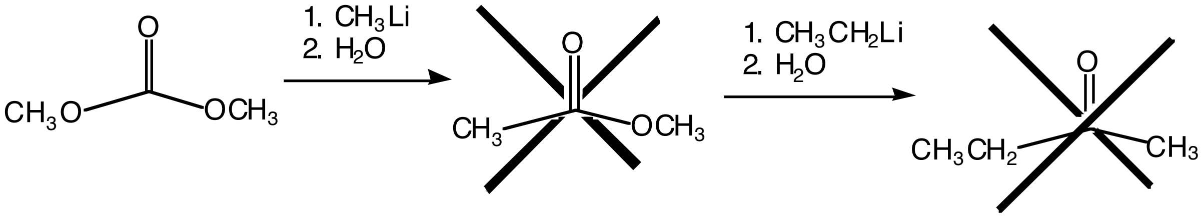
2.



proper reagent: HOEt/$H_2\overset{+}{O}Et$

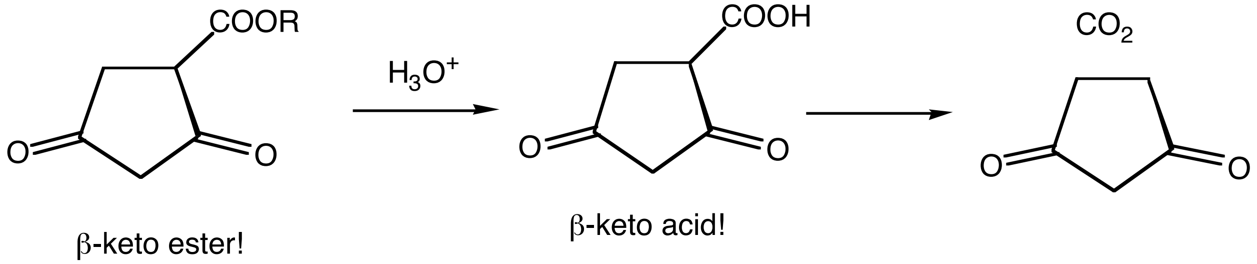


Won't work with only a catalytic amount of base; a full equivalent is needed. And, I. B., the dope, used methoxide, not ethoxide - a transesterification reaction will lead to the methyl ester not the desired ethyl ester.

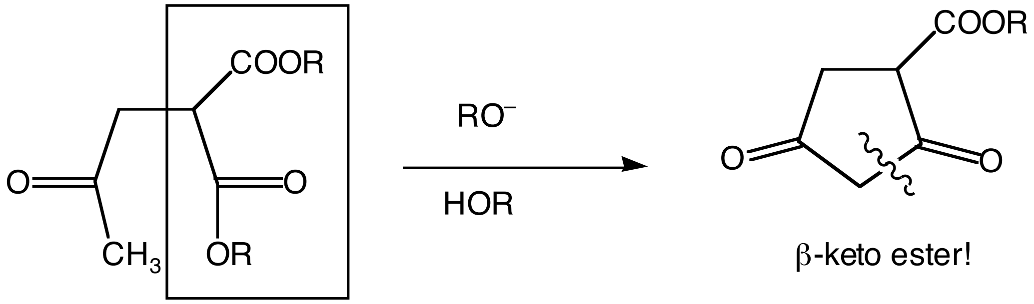


Neither of these reactions can succeed. The reaction will go further, ultimately leading to the tertiary alcohol, R_3COH. The second transformation requires formation of the acid, then reaction with two equivalents of ethyllithium, followed by hydrolysis. Although there is no easy way to convert dimethyl carbonate into the desired methyl acetate, you could convert it into *tert*-butyl alcohol, eliminate to isobutene, ozonize to acetone, do a haloform reaction to get to the acid stage, and then a Fischer esterification.

3. We think this one is hard. The CO_2 is there as a clue - the last step must be a decarboxylation. What could the molecule that decarboxylates be? A β-keto acid is surely implicated. In turn, that β-keto acid must come from a β-keto ester.

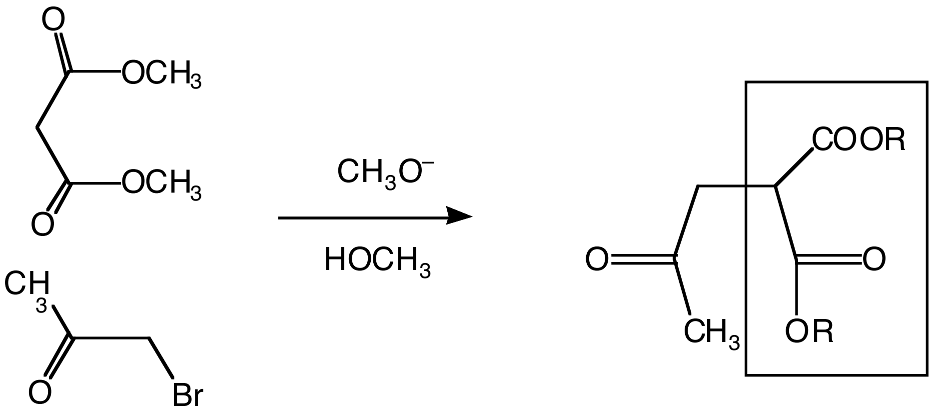


How does one make this cyclic β-keto ester? Dissect the desired product to see the condensation leading to it (retrosynthetic analysis). So:



X

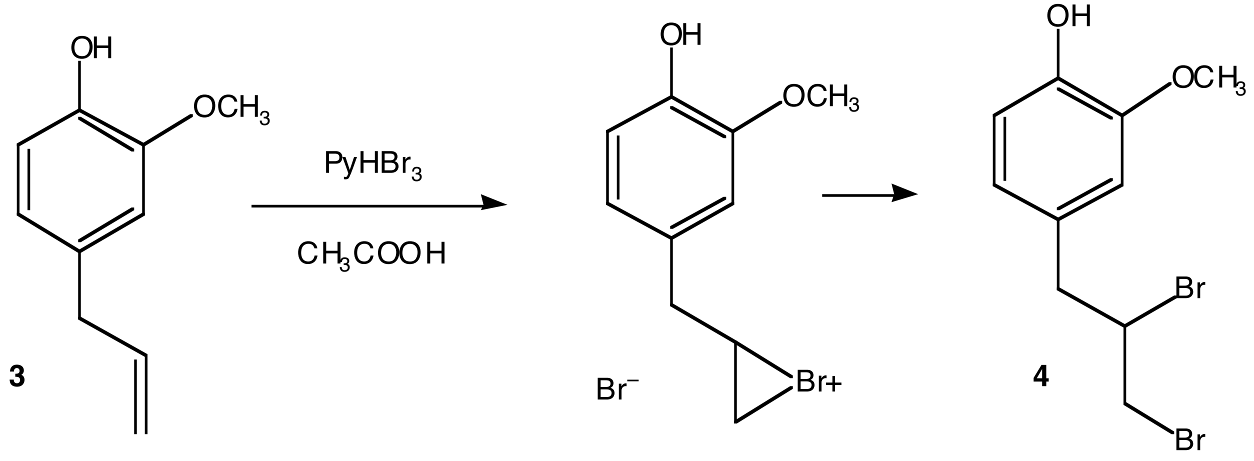
Now you can see the old malonic ester in the box, and a straightforward alkylation reaction leads to the desired compound **X**.



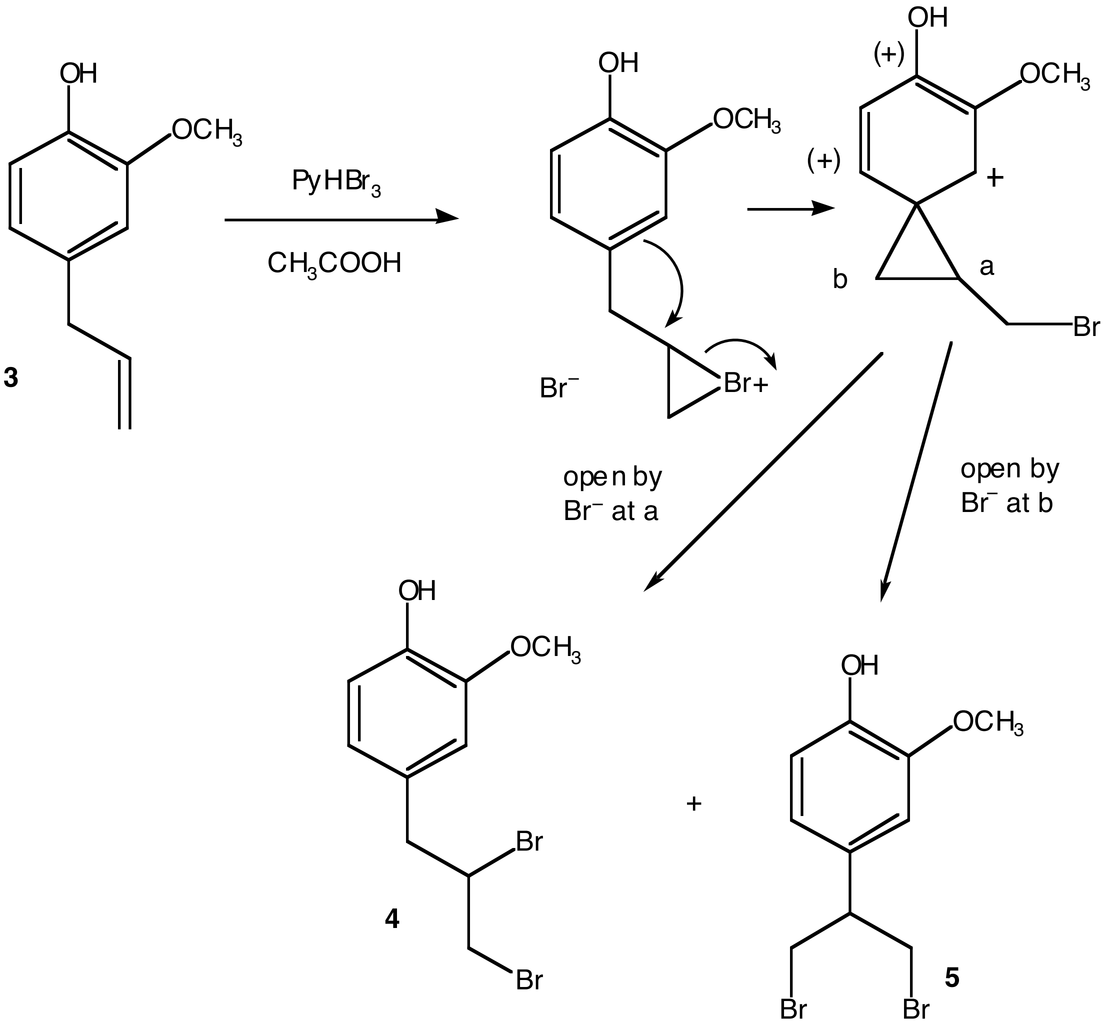
X

We'll accept that answer for most of the points, but there is a problem. If you try to do the cyclization on **X**, it is highly likely (HLG says "certain") that all you will do it to form the enolate from deprotonation of the doubly alpha position. A better synthesis for full points, hydrolyzes the ester in **X** and decarboxylates before the condensation.

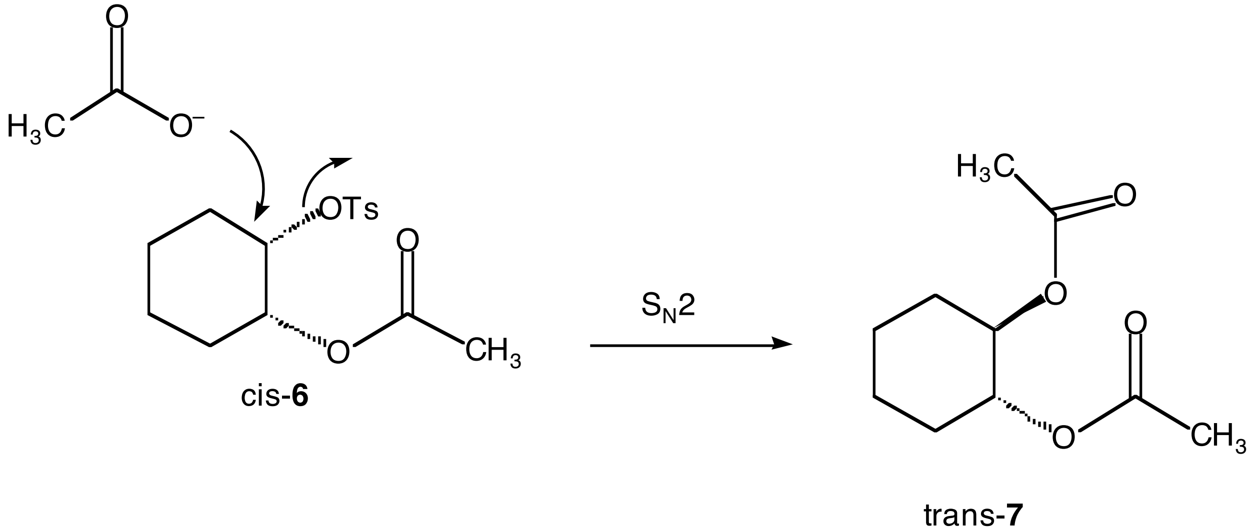
4. Addition of bromine will form the bromonium ion, which, if opened in the usual fashion would only give **4**.



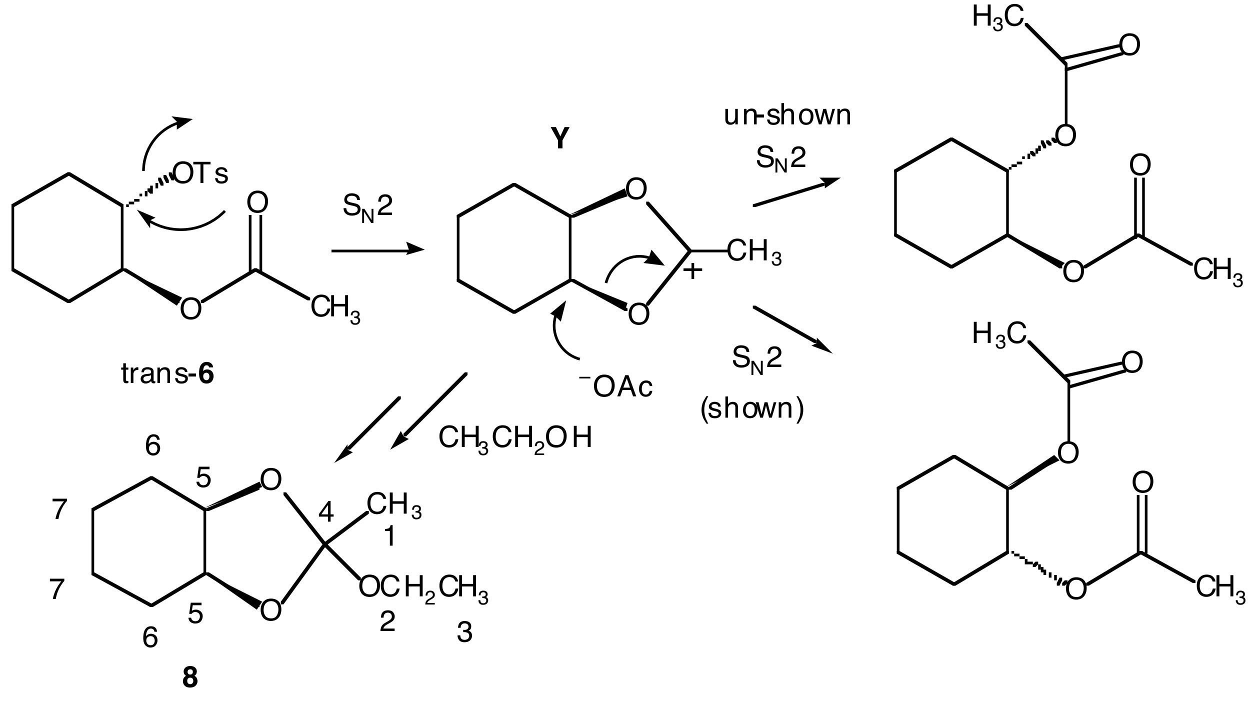
So, something else must be going on. If that bromonium ion is opened in neighboring group fashion we get an intermediate phenonium ion that can go on to **4** and **5**.



5. All the clues for a neighboring group participation are there. The cis compound cannot react through intramolecular S_N2 displacement and instead produces trans-**7** through an intermolecular S_N2 displacement. The product is optically active - there is no possibility of racemization.

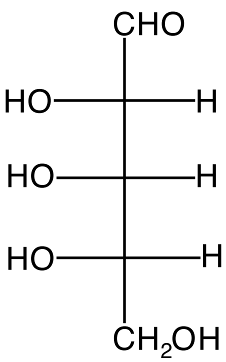


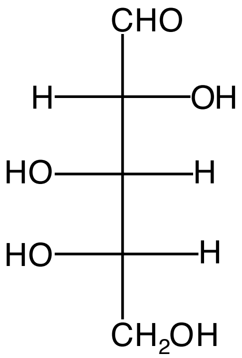
The trans-**6** has a better option, however. In this compound, intramolecular S_N2 displacement from the rear is possible and proceeds at a faster rate than the intermolecular S_N2 reaction in either cis- or trans-**6**. In this case, optical activity is lost as the achiral intermediate **Y** is formed. Capture leads to racemic trans-**7**. If ethyl alcohol is present, it can capture **Y** to give **8**, which is numbered here to show the seven different carbons.

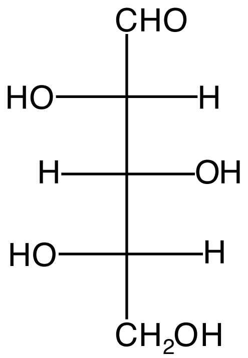


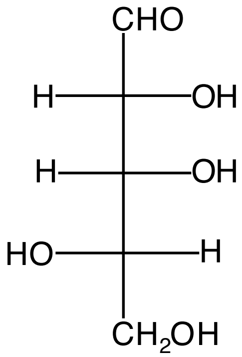
6. Years ago, in a large town in Germany, there were four bottles, each of which contained one of the four possible L-aldopentoses.

(a) What are the four possibilities?



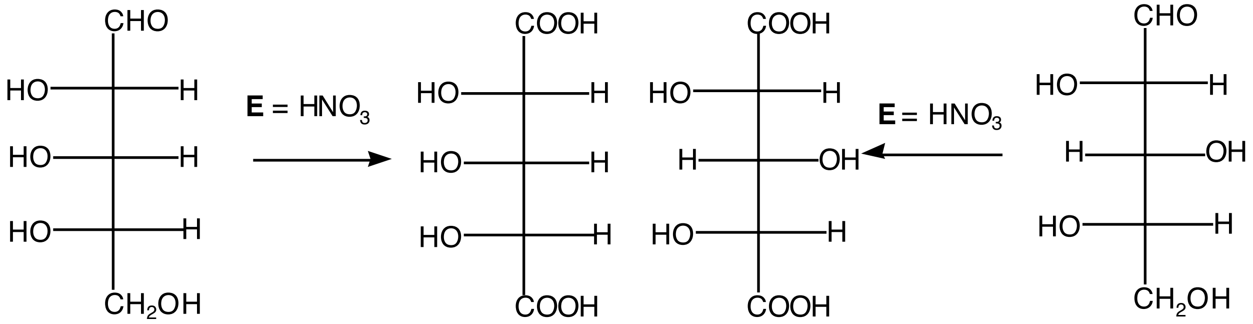






Two of these isomers, **A** and **B**, give meso diacids when treated with **E**.

(b) which isomers share **A** and **B**, and what is **E**?

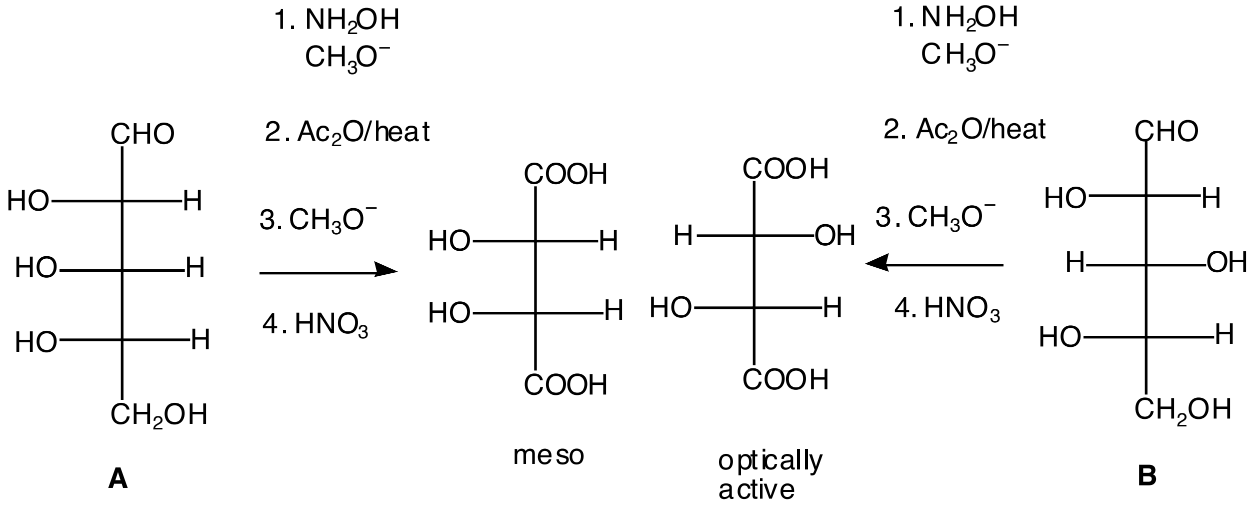


Both meso

Compound **A** gives a meso diacid when treated with 1. $NH_2OH/CH_3O^- Na^+$
2. Ac_2O, heat 3. $CH_3O^- Na^+$, followed by HNO_3.

Compound **B** gives an optically active diacid when treated with 1. $NH_2OH/CH_3O^- Na^+$
2. Ac_2O, heat 3. $CH_3O^- Na^+$, followed by HNO_3.

(c) Write Fischer projections for **A** and **B**.



Compound **C** gives L-glucose (and L-mannose) when treated under Killiani-Fischer conditions.

(d) Draw **C**.