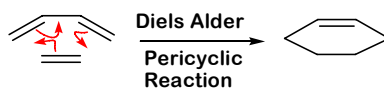
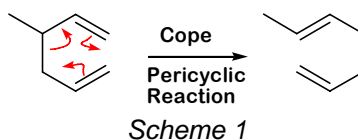


The Cope and Claisen rearrangements are pericyclic reactions. Pericyclic reactions are reactions that have a cyclic transition state. The reactions proceed in a concerted method and one can have multiple bond making and/or breaking components all in one step. The first pericyclic reaction we studied was the Diels Alder reaction between a diene and an alkene acting as a dienophile. It involved a 6 electron cyclic rearrangement of electrons. See the Diels Alder study guide for more information and a molecular orbital analysis.

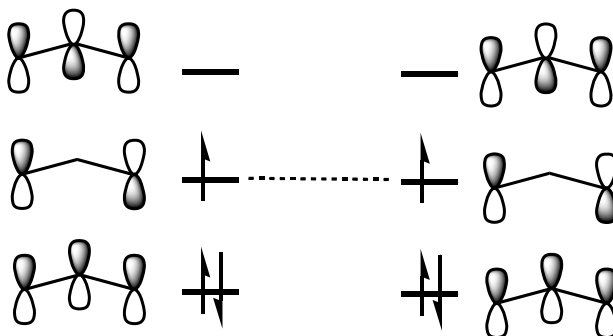


Cope Rearrangement

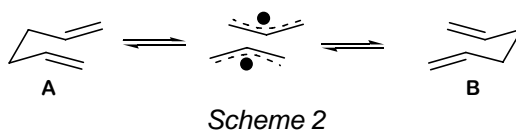
The Cope reaction also involves a cyclic rearrangement of electrons, but there is no ring.



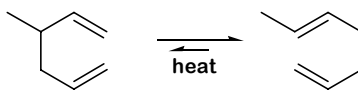
What is going on here? Imagine a fictitious reaction with two allyl radicals coming together in space. The HOMO of an allyl radical on one has the same symmetry as the HOMO of the other. The two unpaired electrons can interact.



These radicals could approach each other and form a new bond. But the new bond could form at either end of the pair of radicals.

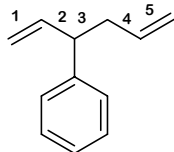


Molecules **A** and **B** are the same molecule so in this simplest case it would not matter which way you went, but if the molecules were not symmetric then one side could be favored. So does this reaction occur? Well actually no, not as described. The reaction of two radicals coming together in space is not a well known process. However molecules like **A** certainly exist and if you heat them up their bonds can rearrange to give structure **B**. This is known as the Cope rearrangement. A real example is shown in Scheme 1. In the real transition state the geometry must look like the intermediate drawn in Scheme 2, but there is no evidence that the electrons ever become unpaired.

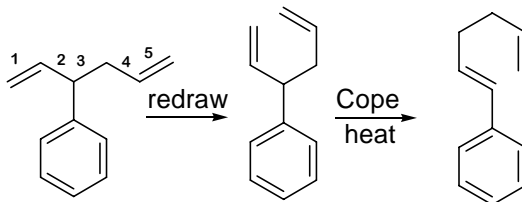


The Cope Rearrangement is an equilibrium process. The direction of the equilibrium will depend upon the relative stability of the two compounds. In the case shown above the equilibrium lies to the right because one double bond has more substituents. These reactions are not low energy reactions. You have to heat them up to make them go.

It is not always easy to recognize a potential Cope Rearrangement. The key thing is that the reactant has to be a 1-5-diene like the molecule shown below.

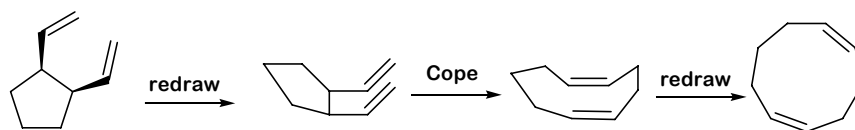


Once you recognize the molecule as a 1-5-diene you should redraw it to bring the ends together, then do the bond rearrangement.



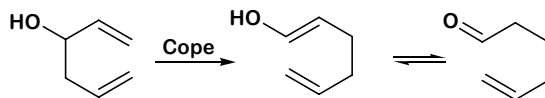
In this case the driving force behind the reaction is the formation of a higher substituted double bond and conjugation between the double bond and the phenyl ring.

Sometimes the Cope gives rather unexpected products. Here is a synthesis of a nine membered ring.



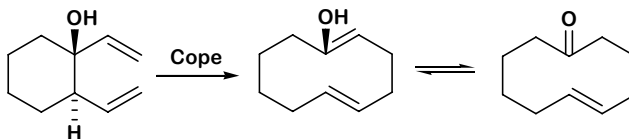
Oxy-Cope Rearrangement

If hydroxyl is involved there can be an extra driving force to the Cope reaction. The following reaction is an example of an oxy-Cope reaction. A hydroxyl group at the 3 or 4 position of the 1,5-diene means that the product of the oxy-Cope will be a ketone.



The formation of the carbonyl group gives the reaction an added driving force.

Here is another example.

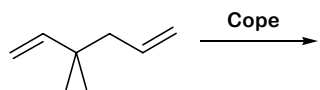


The cyclic ketone has an *E* double bond, something a bit unusual for a small ring.

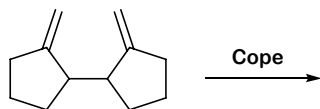
Problem 1.

Predict the products of the following Cope reactions.

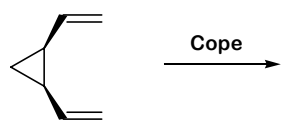
a.



b.

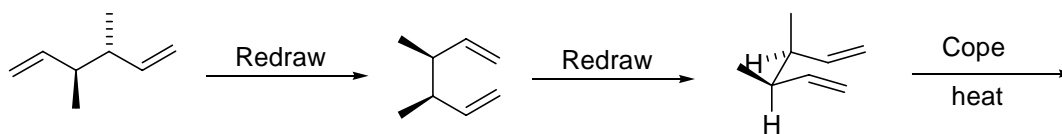


c.



d. Here is a good thinking question. (Hard)

The following 1,5-diene is an achiral *meso* molecule.

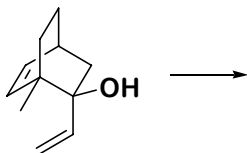


(3*R*,4*S*)-3,4-dimethylhexa-1,5-diene

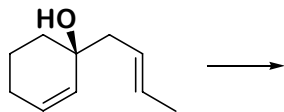
It can undergo a Cope rearrangement to give a more stable diene. The picture on the right shows it in the pseudo chair form that will lead to the reaction. Rearrange the bonds and draw the final product. Are the double bonds *E* or *Z*?

Problem 2. Predict the product of the following oxy-Cope reactions.

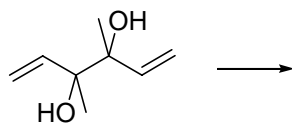
a.



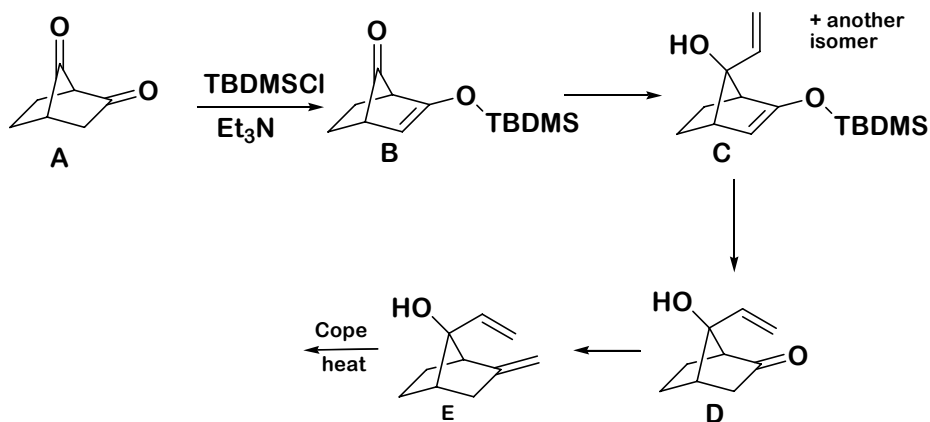
b.



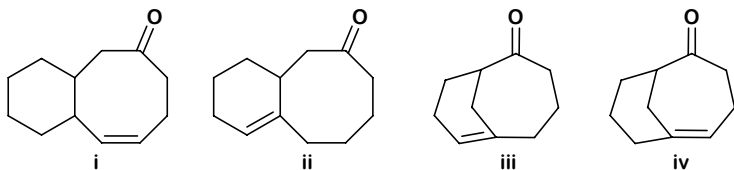
c.



Problem 3. Here is a reaction scheme that uses the oxy-Cope reaction.

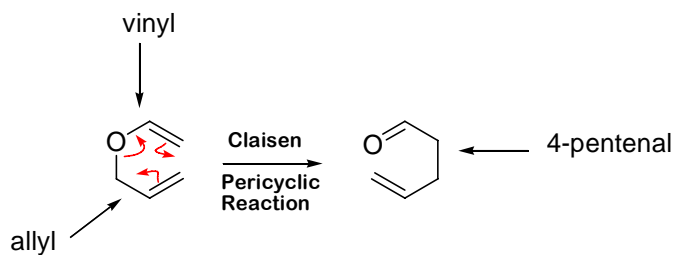


- What reagents would you use to convert B to C? What would be the most likely other product?
- How do you deprotect C to make D?
- How do you convert D to E?
- What is the final product of the Cope rearrangement of E? Four choices are shown below.
(Caution: this problem may make your head hurt.)

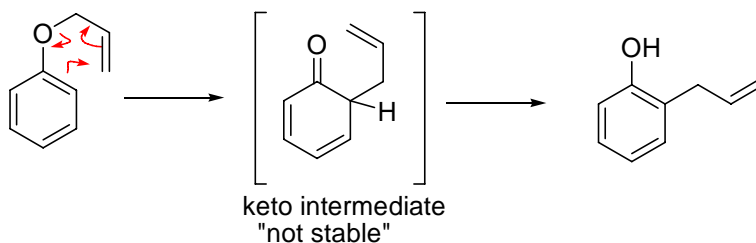


Claisen Rearrangement

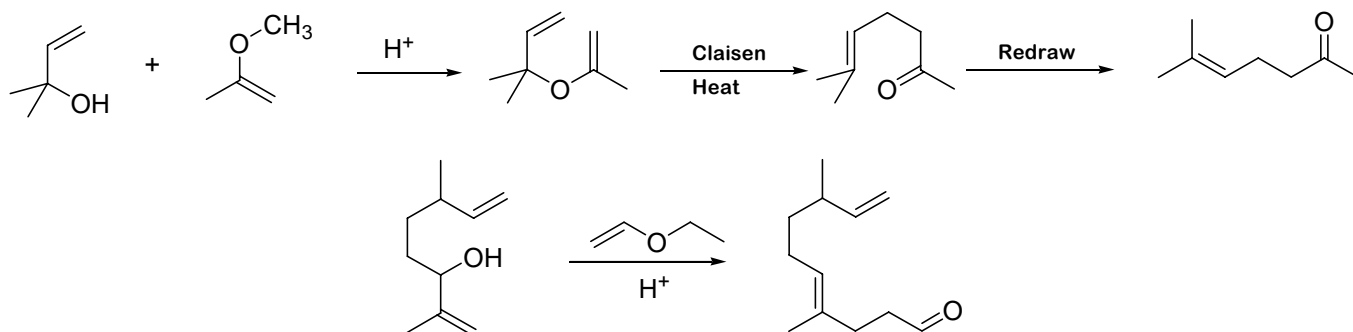
The Claisen rearrangement is a closely related reaction that involves a vinyl allyl ether



The reaction was originally discovered by heating up a sample of an allyl phenyl ether. The product has the allyl group shifted to the *ortho* position of the phenol. The intermediate is thought to be the keto form of the substituted phenol. This tautomerizes to phenol to restore the aromaticity of the ring.

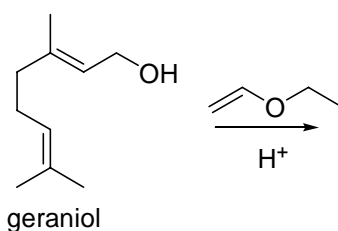


The Claisen rearrangement is actually used more often than the Cope. The two examples below show the syntheses of a ketone and an aldehyde that are an important intermediates in the fragrance industry.

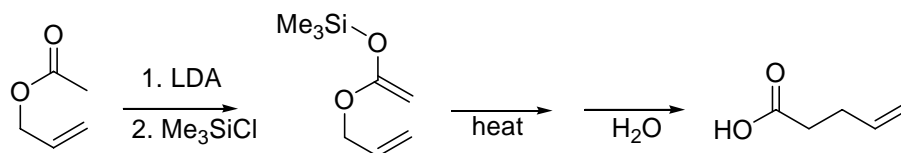


Problem 4.

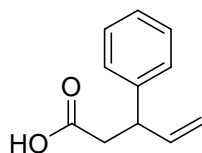
a. Geraniol can be converted to a compound with the scent of coriander. Predict its structure.



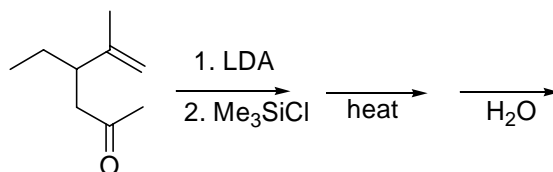
b. Sometimes the vinyl group is a trapped enolate.



How could you use this procedure to make the compound shown below?



c. Predict the product of this reaction.



d. The following reaction is called the Carroll rearrangement. Write a mechanism.

