

E.J. Corey (Nobel Prize, 1990)
“for his development of the theory and methodology of organic synthesis”



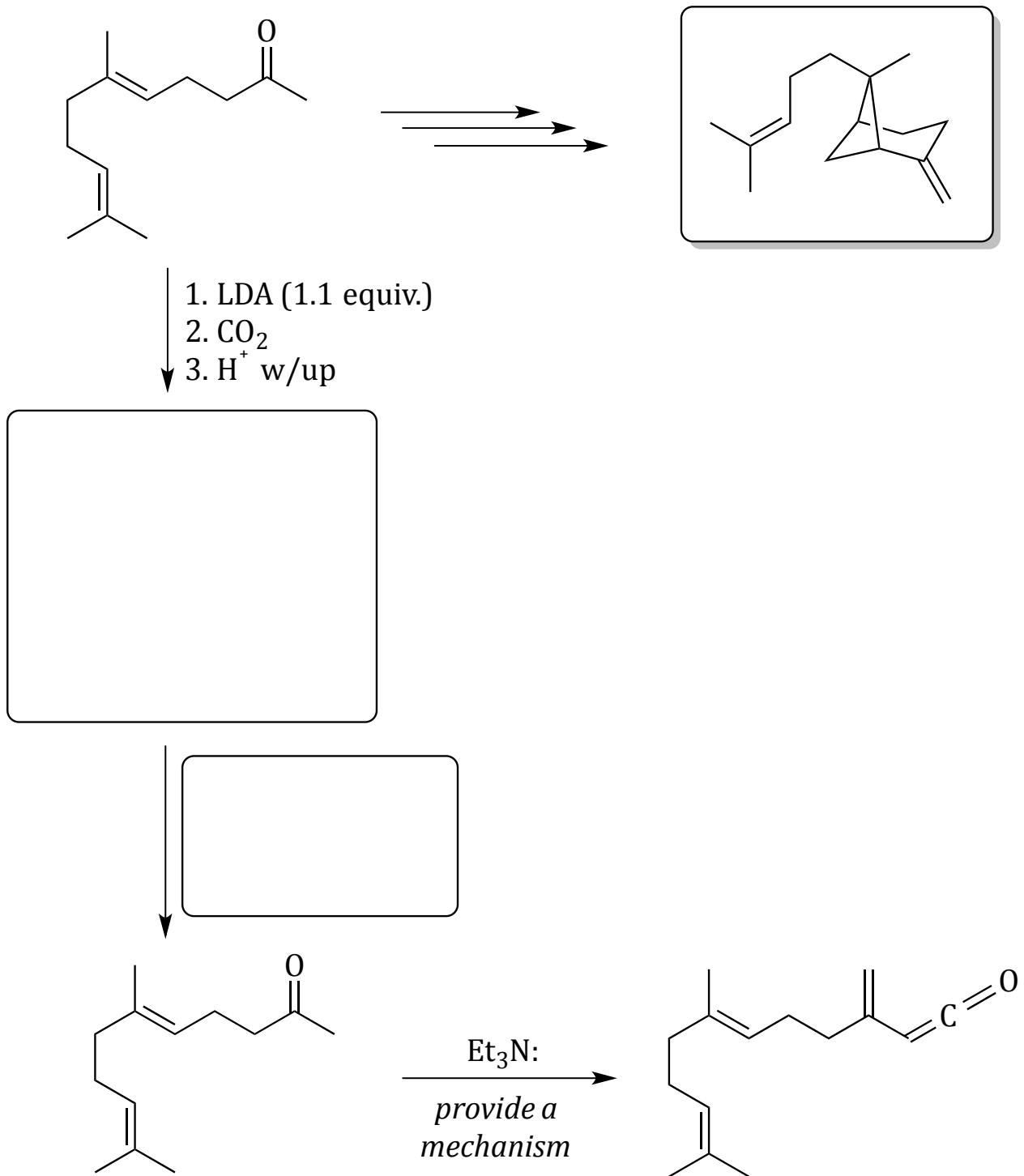
From the Nobel Committee, 1990:

This year's Nobel Prize in Chemistry has been awarded to Professor Elias J. Corey, USA, for his important contributions to synthetic organic chemistry. He has developed theories and methods that have made it possible to produce a large variety of biologically highly active, complicated natural products, thereby making, among other things, certain pharmaceuticals commercially available. Corey's work has also led to new general methods of producing, synthesizing, compounds in simpler ways.

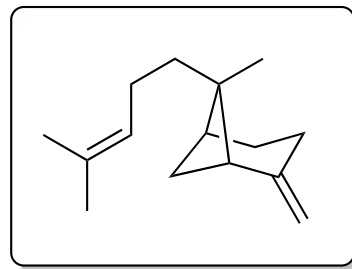
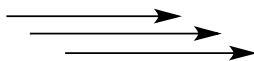
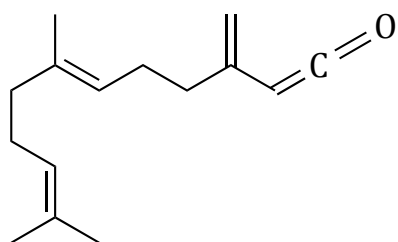
The background to Elias J. Corey's successes lies in the fact that **he has in a strictly logical way developed the principles of what is termed retrosynthetic analysis**. This involves starting from the planned structure of the molecule one wishes to produce, the target molecule, and analyzing what bonds must be broken, thus simplifying the structure step by step. One then finds that certain fragments are already known and their structure and synthesis already described. After working backwards in this way from the complex to the already known, it is possible to start building, synthesizing, the molecule. This method has proved very amenable to data processing, which has entailed rapid developments in synthesis planning. Combining this synthesis planning with singular creativity, Corey has developed new methods of synthesis. He has produced some hundred important natural products, for example the active substance in an extract from the ginkgo tree, used in folk medicine in China.

To review for our final exam, let's take a close look at some of Corey's syntheses...

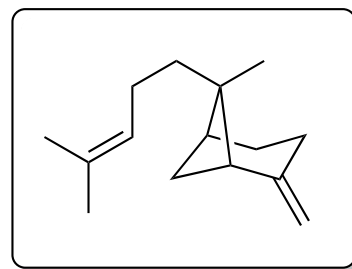
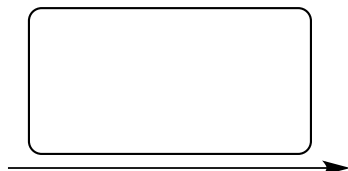
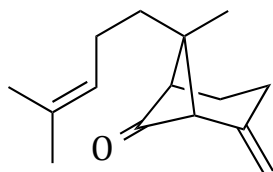
Synthesis of β -*trans*-bergamotene (1)



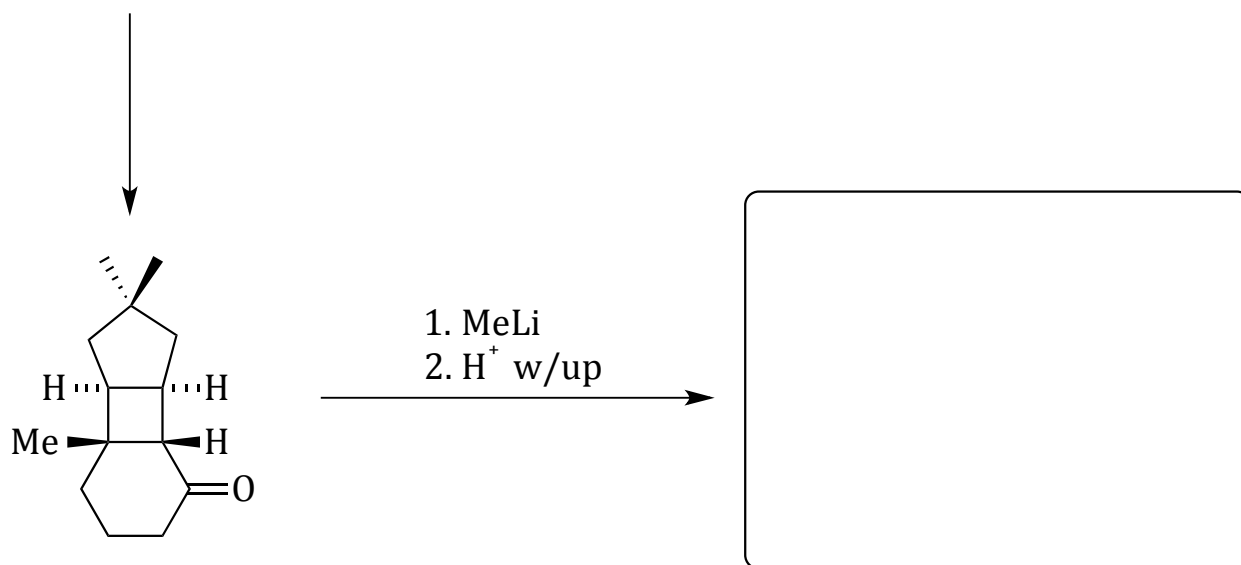
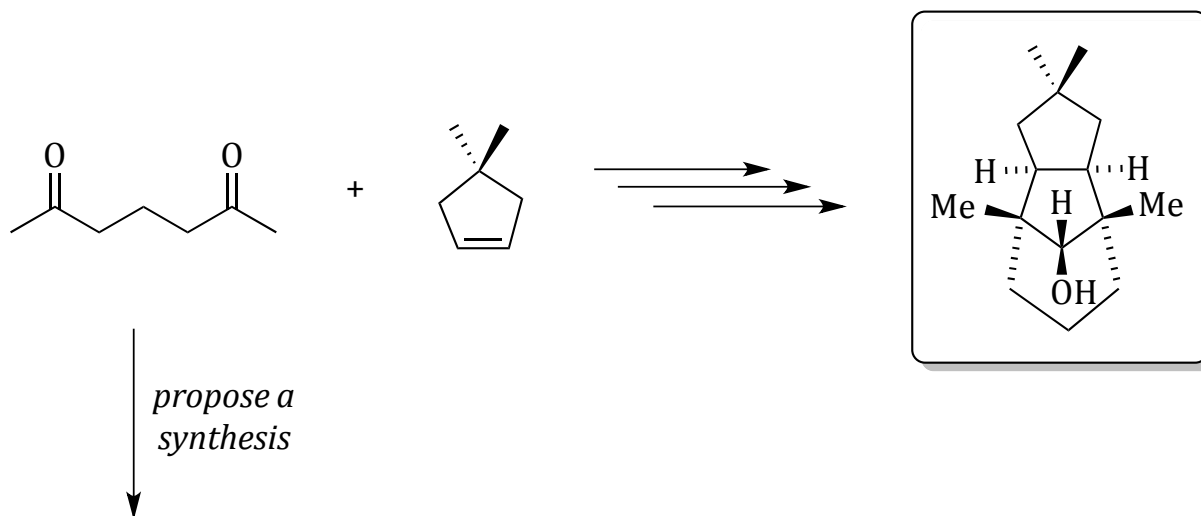
Synthesis of β -*trans*-bergamotene (2)



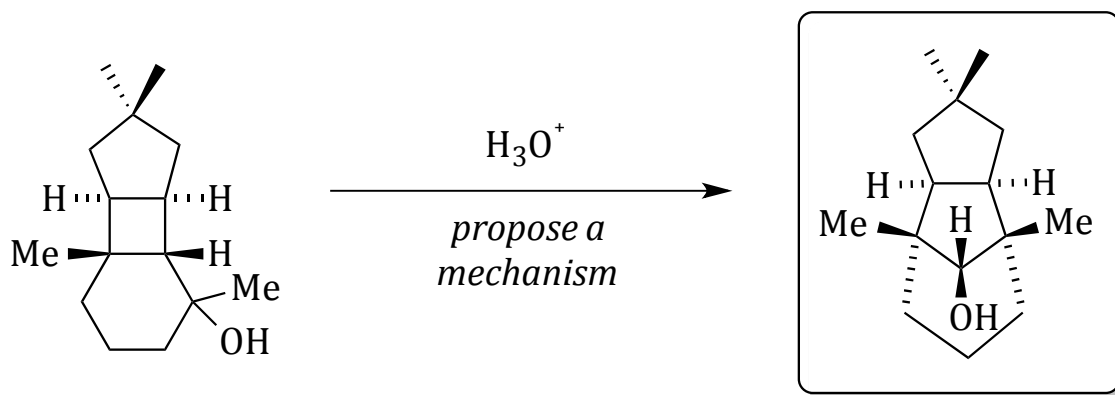
*provide a
mechanism*



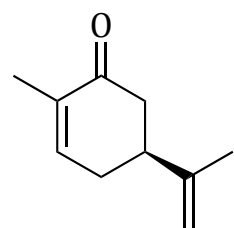
Synthesis of α -Caryophyllene Alcohol (1)



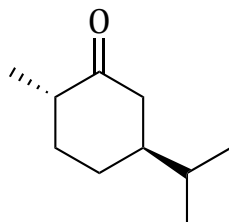
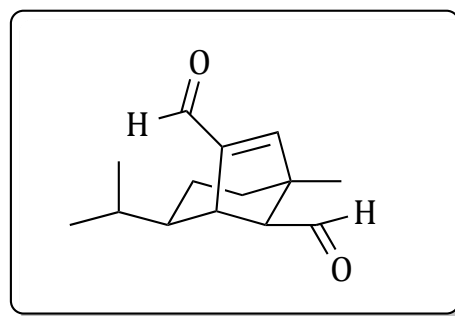
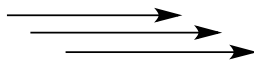
Synthesis of α -Caryophyllene Alcohol (2)



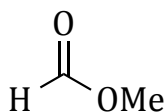
Synthesis of Helminthosporal (1)



(*S*)-(+)-carvone

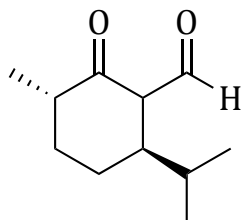


1. NaOMe,

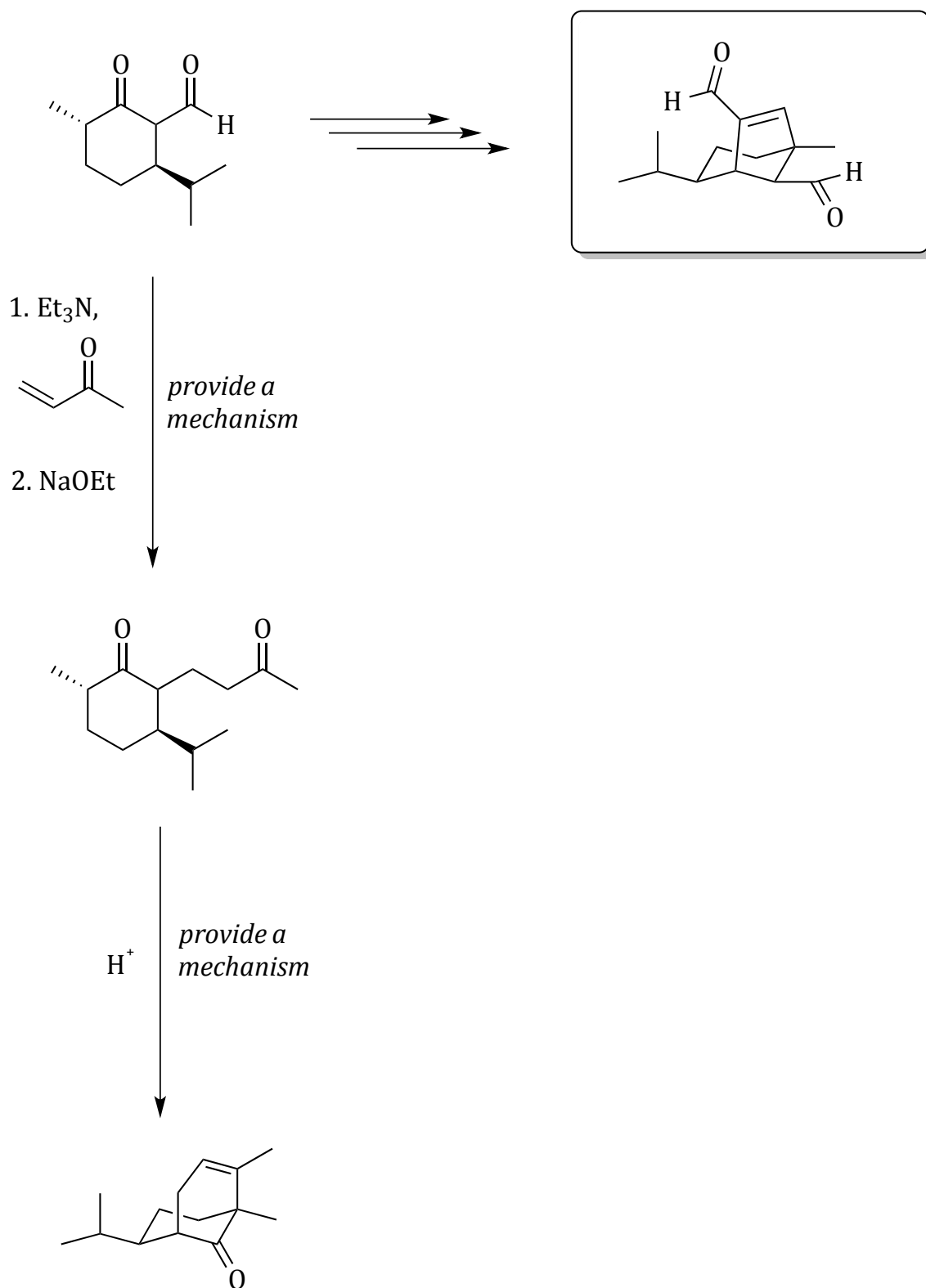


2. H^+ w/up

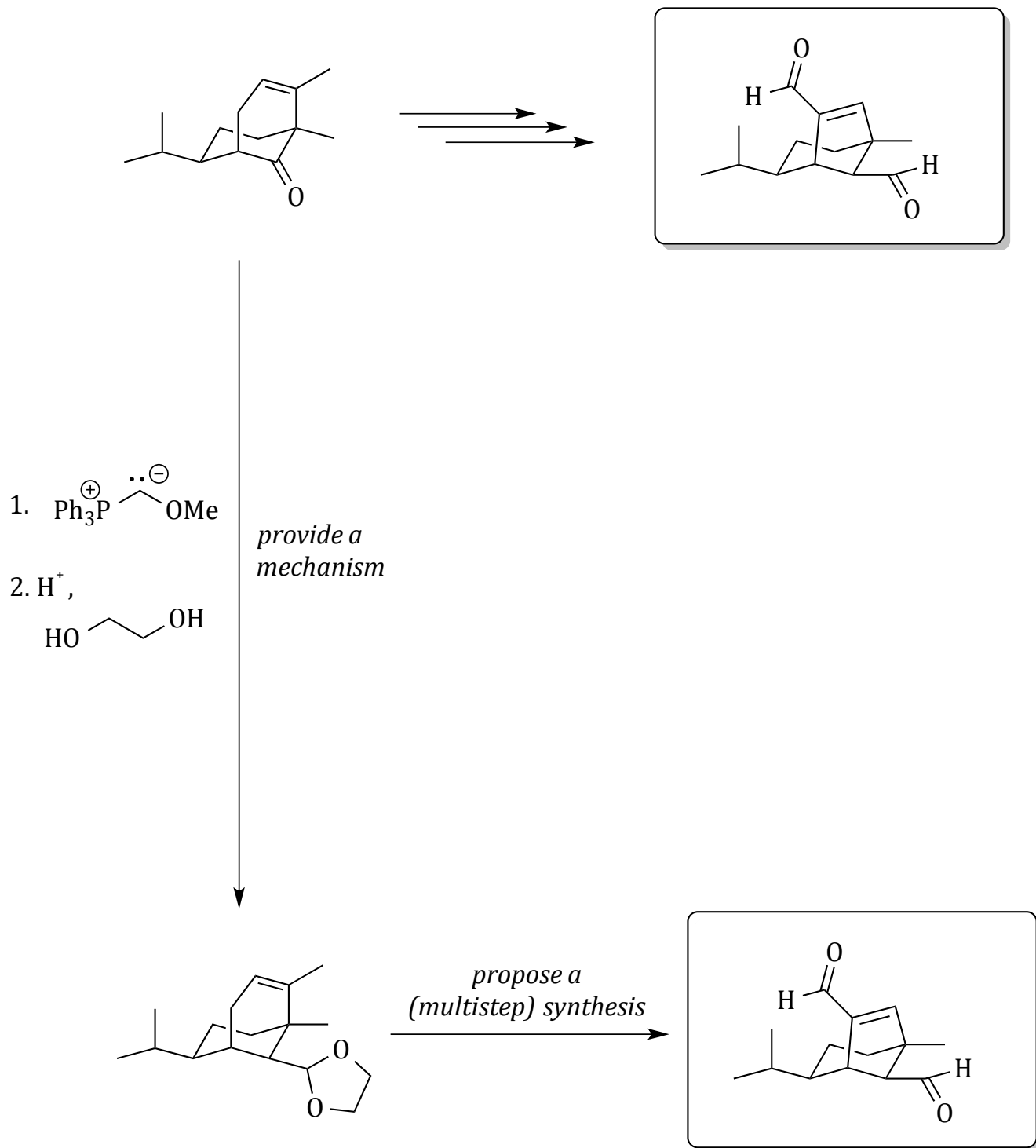
**provide a
mechanism;**
explain why the product
appears to have undergone
reaction at the *less*
substituted side



Synthesis of Helminthosporal (2)

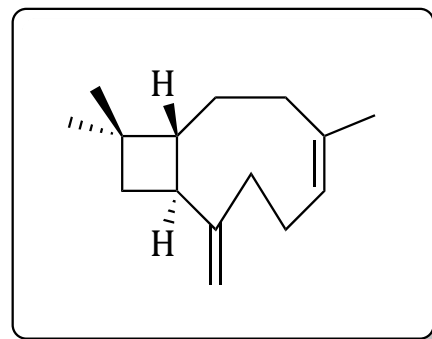
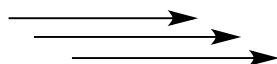


Synthesis of Helminthosporal (3)

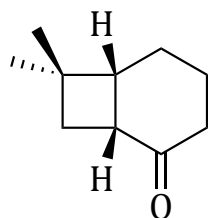


Synthesis of Isocaryophyllene (1)

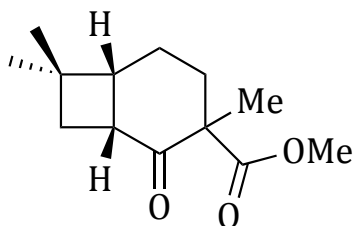
Starting materials
with **6 or fewer** carbons



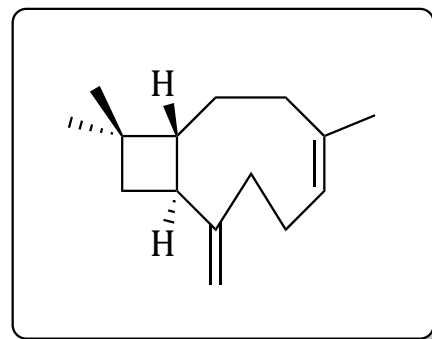
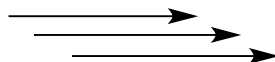
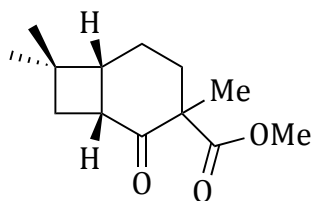
*propose a
synthesis*



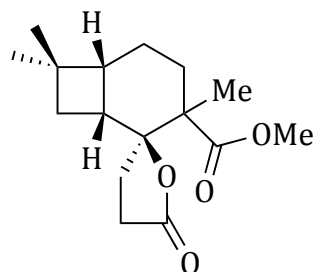
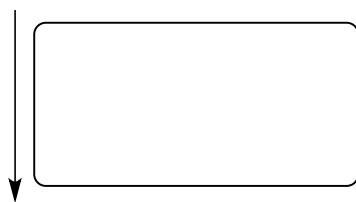
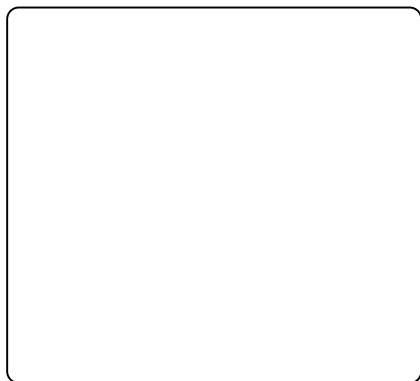
*propose a
synthesis*



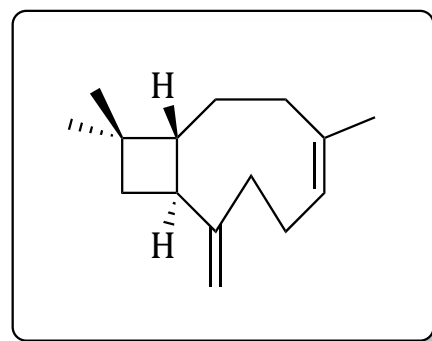
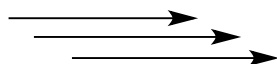
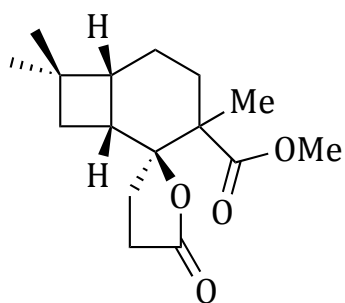
Synthesis of Isocaryophyllene (2)



1. $\text{Li} \text{---} \text{C} \equiv \text{C} \text{---} \text{C}(\text{OMe})_2$
2. H^+ w/up
3. H_2 , Pd/C
4. H_3O^+

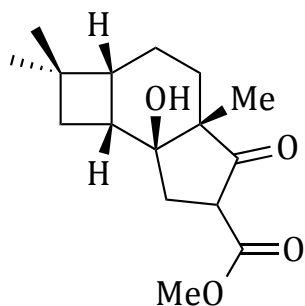


Synthesis of Isocaryophyllene (3)

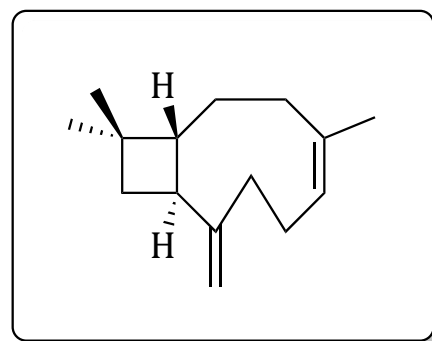
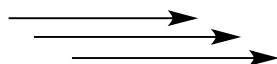
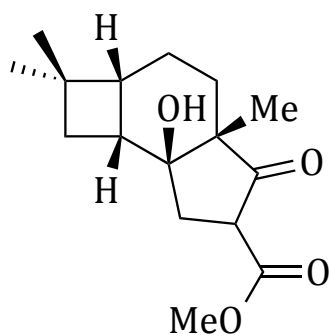


1. LDA
2. H^+ w/up

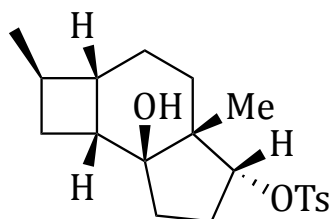
*propose a
mechanism*



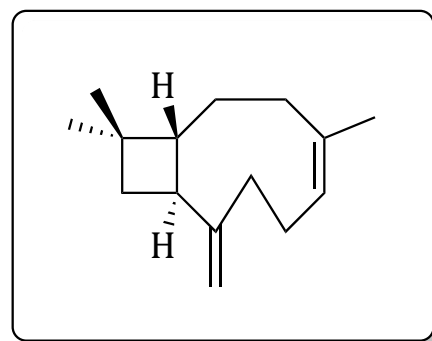
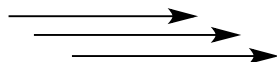
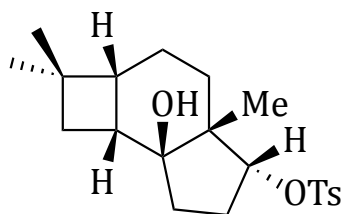
Synthesis of Isocaryophyllene (4)



*propose a
synthesis*

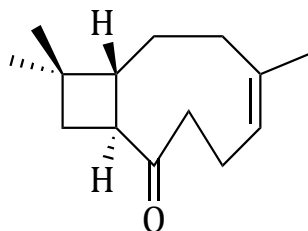


Synthesis of Isocaryophyllene (5)

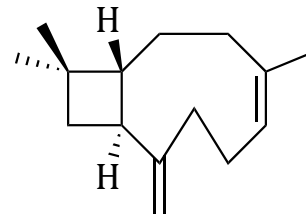


1. NaH
2. H⁺ w/up

*propose a
mechanism*

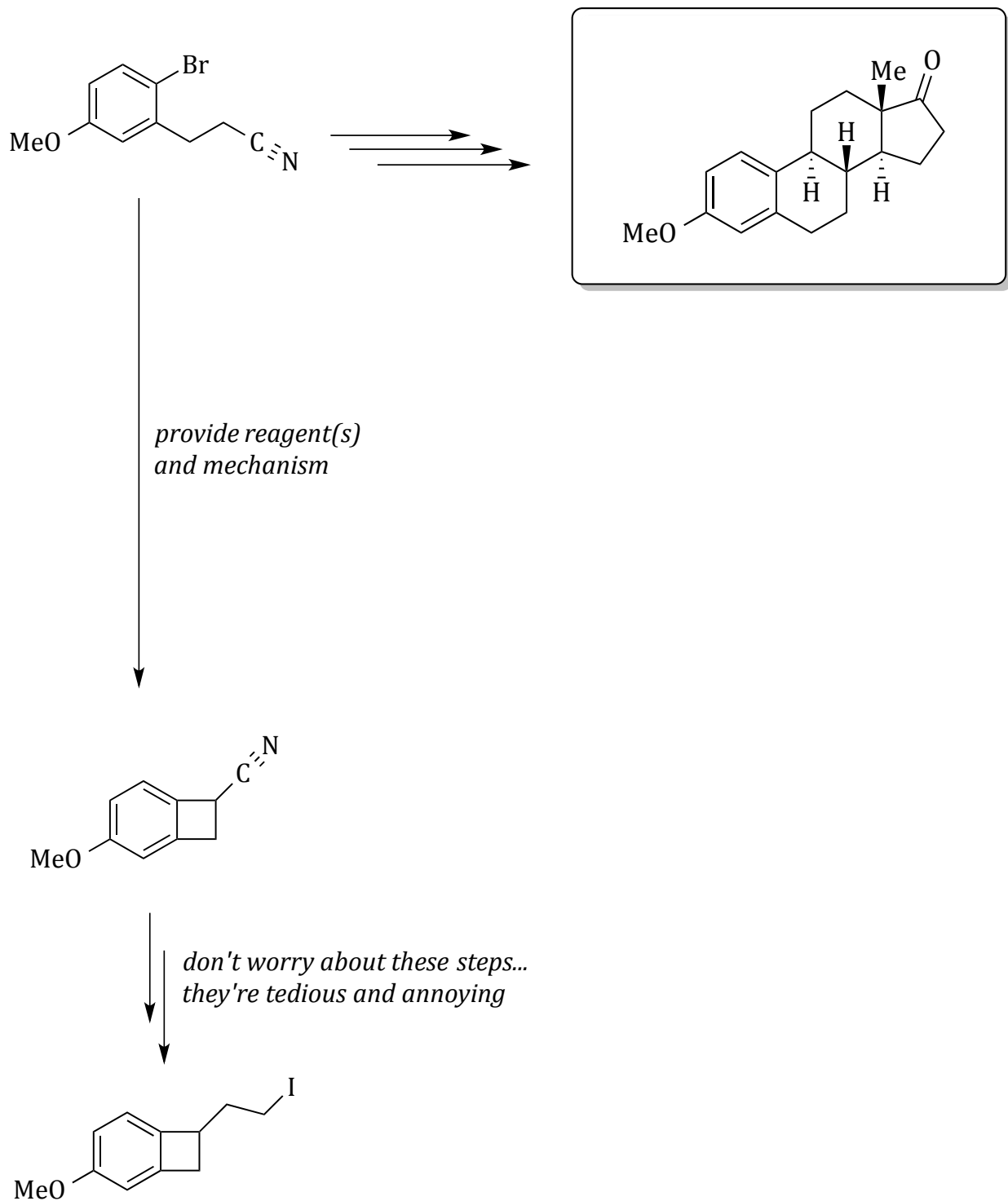


*propose a
synthesis*

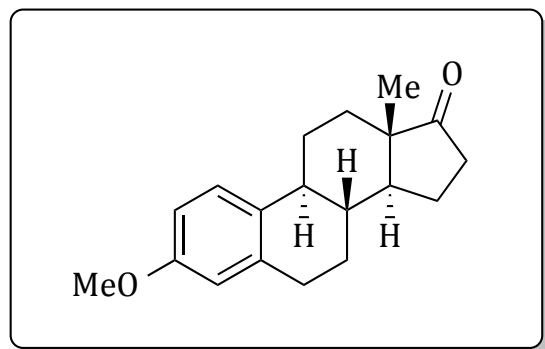
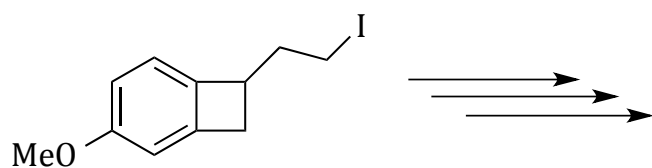


Synthesis of Estrone (1)

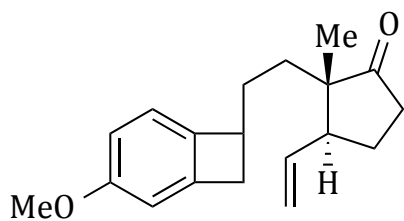
This last synthesis isn't by Corey (it was reported by Douglass Taber in 1987), but it's particularly interesting and instructive...



Synthesis of Estrone (2)



*provide reagent(s)
and mechanism*



Synthesis of Estrone (3)

