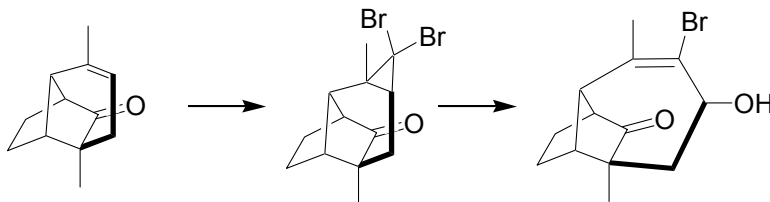


## Chem 535-Synthetic Organic Chemistry

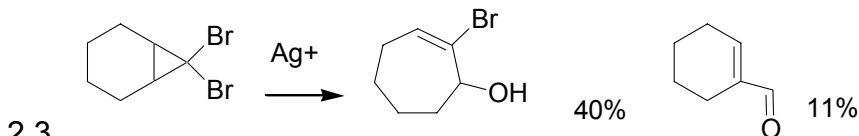
### Ring Expansion

Ideas for this lecture were taken from: Kantorowski, E. J.; Kurth, M. J. "Expansion to seven-membered rings." *Tetrahedron* **2000**, *56*, 4317-4353 and Stach, H.; Hesse, M. "Synthesis of Macrocyclic Compounds by Ring Enlargement" *Tetrahedron* **1988**, *44*, 1573-1590.

1. In the synthesis of longifolene that we considered last, there was a ring expansion from a six to a seven-membered ring.
  - 1.1. The stereochemistry of the products of six-membered rings is in general better defined than in other rings.
  - 1.2. If this is so, mother nature is encouraging us set the stereochemistry then ring expand if we are seeking a specific product containing more than six atoms.
    - 1.2.1. Likewise—ring contraction would be necessary if the desired ring is smaller than six.

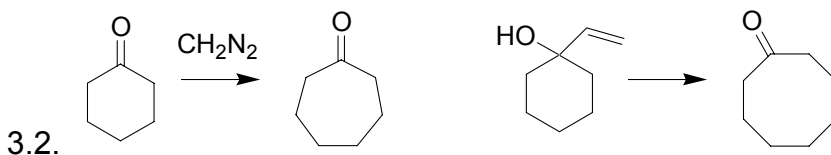


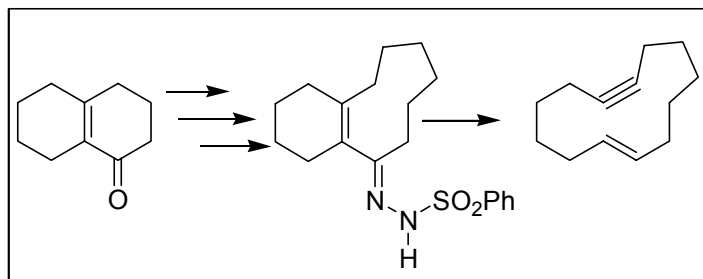
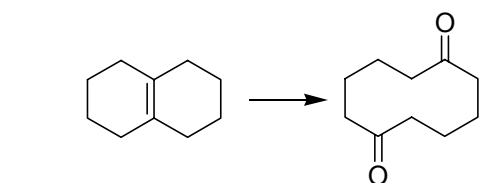
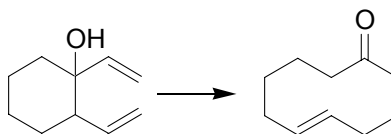
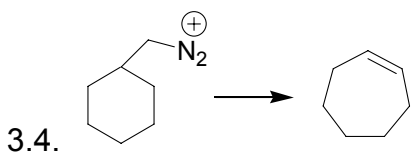
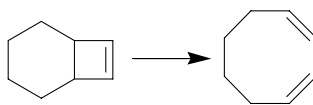
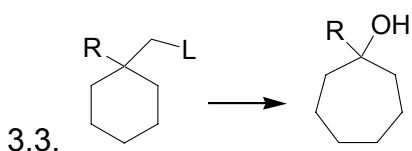
2.
  - 2.1. Critical ring expansion in Longifolene synthesis
  - 2.2. McMurry, J.E. *JACS* **1972**, *94* 7132.



### 3. Methods of ring expansion

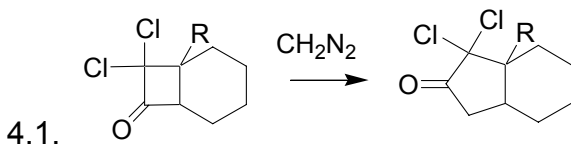
- 3.1. Don't just commit these to memory, understand how they work. In most (all) cases you can work out alignment of molecular orbitals that lead to facile fragmentation.
  - 3.1.1. Because the MO concept is so important we are going to spend some time talking about the mechanisms of many of the examples.



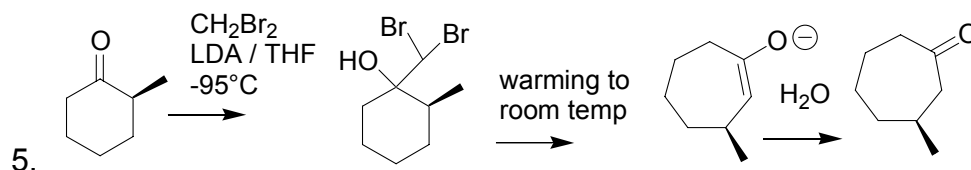
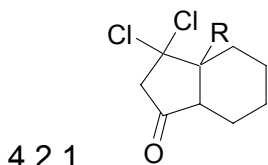


3.5.1. careful, diketone easily closes by aldol condensation.

#### 4. Diazomethane ring expansion of ketones



4.2. The less substituted bond migrates. The other possible structure is



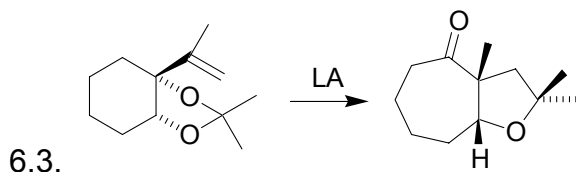
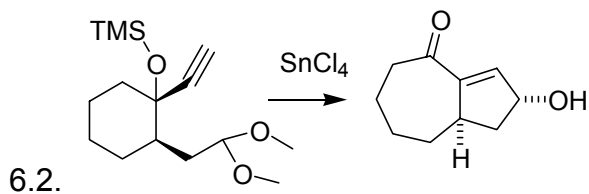
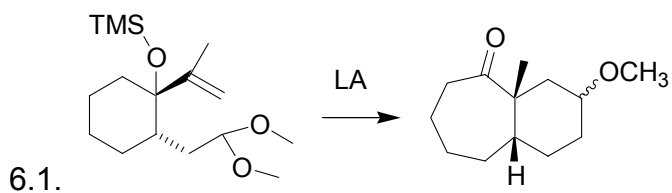
5.1. can quench cold and get dibromocarbiniol.

5.2.  $\text{CH}_2\text{Br}_2$  is a little more acidic than acetone  $\sim 20$ .

5.3. Can you think of something else to do with this enolate?

5.3.1. What do you think the structure of the product of alkylation would be?

#### 6. Expansion by carbocations



6.4. Why are the seven-membered rings in the structures above more complex?

6.4.1. Remember we are seeking complexity in synthesis and simplicity in retrosynthesis.

