

Organic Synthesis Course



Krishna P Kaliappan

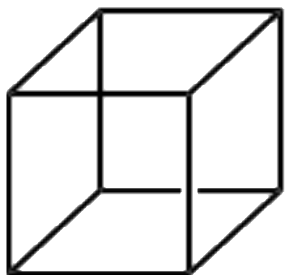
Department of Chemistry

Indian Institute of Technology Bombay



Lecture on Total Synthesis of Cubane

Total Synthesis of Cubane

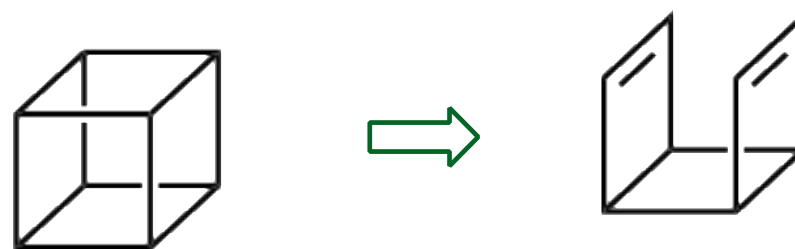


Challenges

1. **Six** - 4 membered rings fused together
2. **No** functional groups
3. Highly **strained**
4. Low molecular weight **$C_8H_8=104$**

4-membered rings could be formed by photochemical reaction

How many 4-membered rings could be formed by photochemical reaction?



Is it feasible?

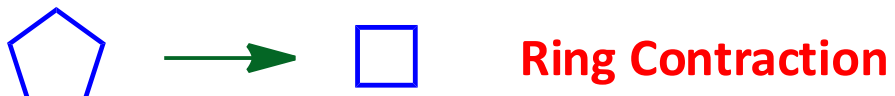
Many Problems:

1. Reversibility
2. Stability of the starting material
3. Intermolecular reaction

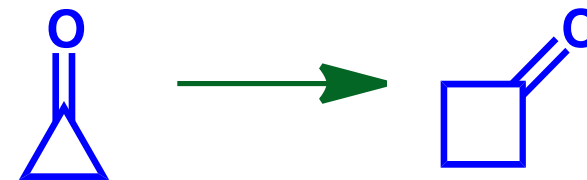
Solutions

1. **Introduce** a functional group
2. **Which** functional group?
 - a. The functional group should be **removed** easily
 - b. It also should be formed **easily** from another **precursor**
 - c. This should be introduced along with either **ring contraction** or **ring expansion**

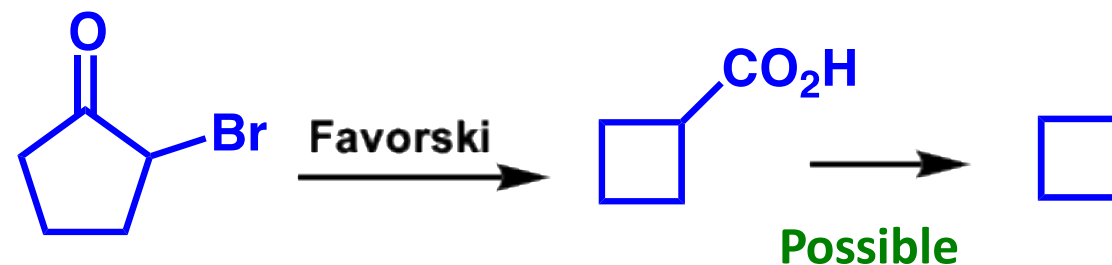
Ring Expansion or Ring Contraction?



Which functional group could be formed along with this reaction?



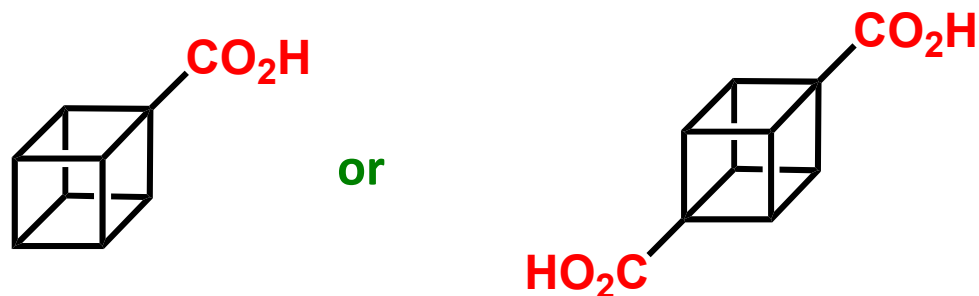
Difficult
 sp^2 carbon in cubane?



It is better to move forward with ring contraction strategy

- Favorskii reaction will be better

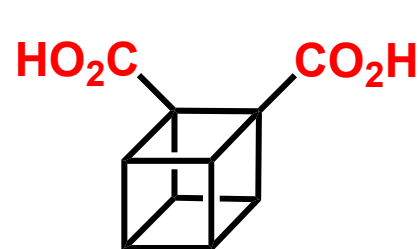
One Carboxylic Acid or Two Carboxylic Acids?



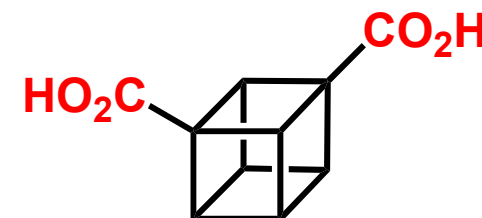
1. One carboxylic acid- precursor will have only two 5-membered rings and remaining will be 4-membered

2. Two carboxylic acids- precursor will have four 5-membered rings and remaining will be 4-membered

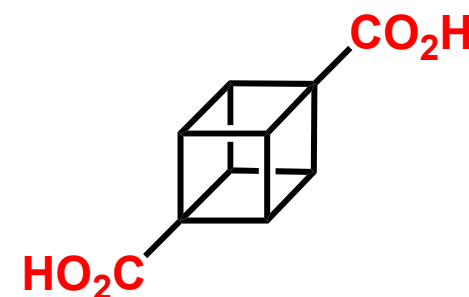
Where and what is the relationship?



1,2



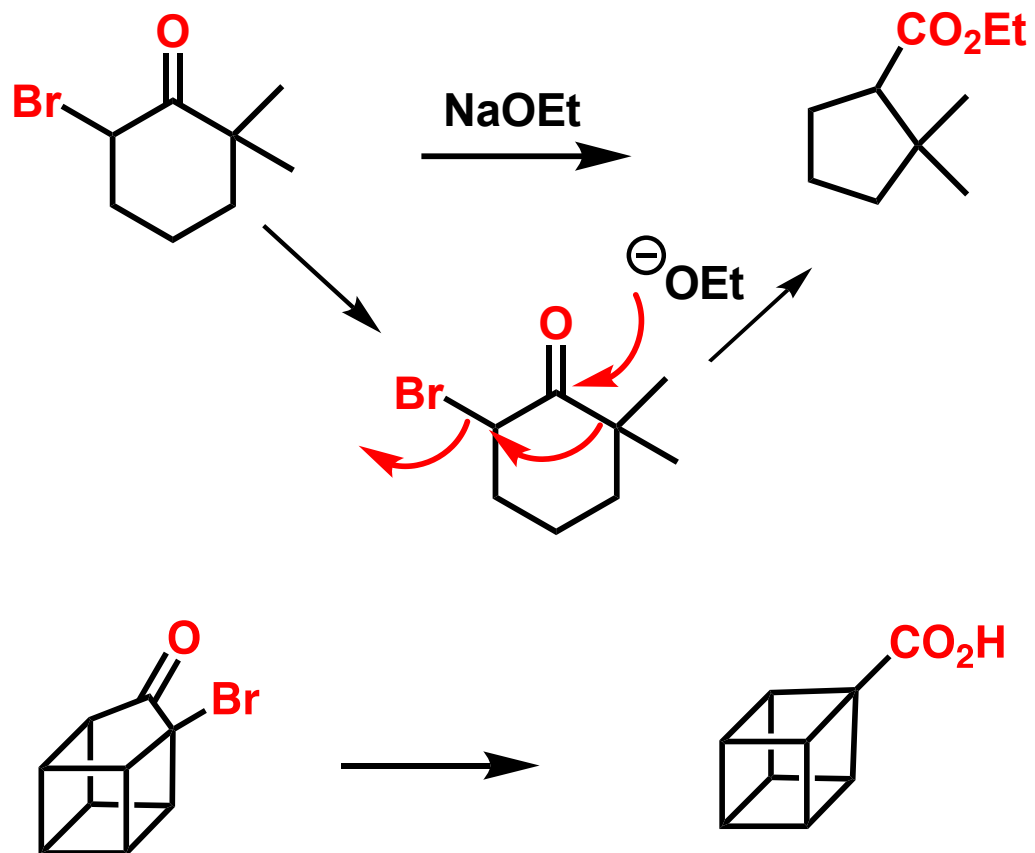
1,3



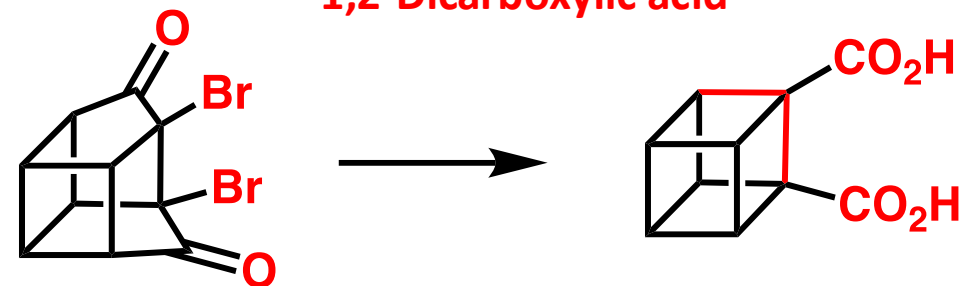
1,4

Which will be easier from synthetic point of view?

Quasi Favorski Rearrangement

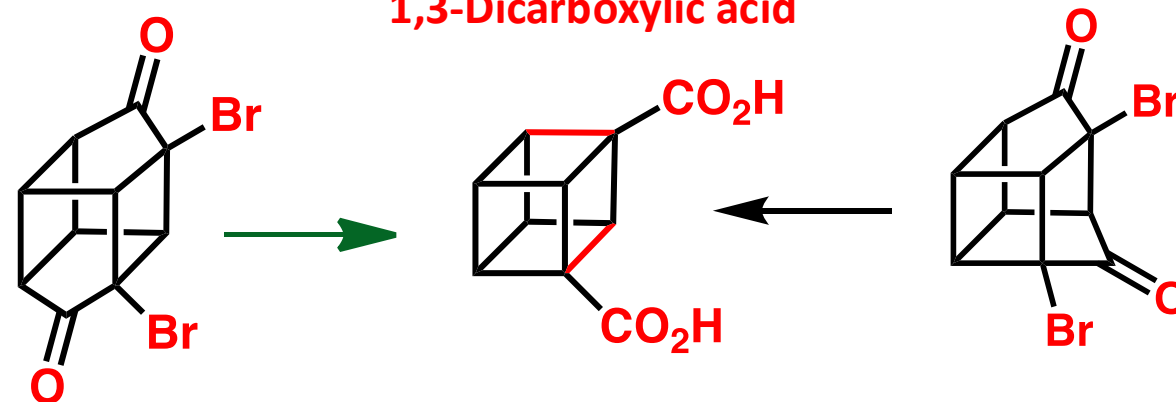


1,2-Dicarboxylic acid



Starting material has four 5-membered rings and two 4-membered rings

1,3-Dicarboxylic acid

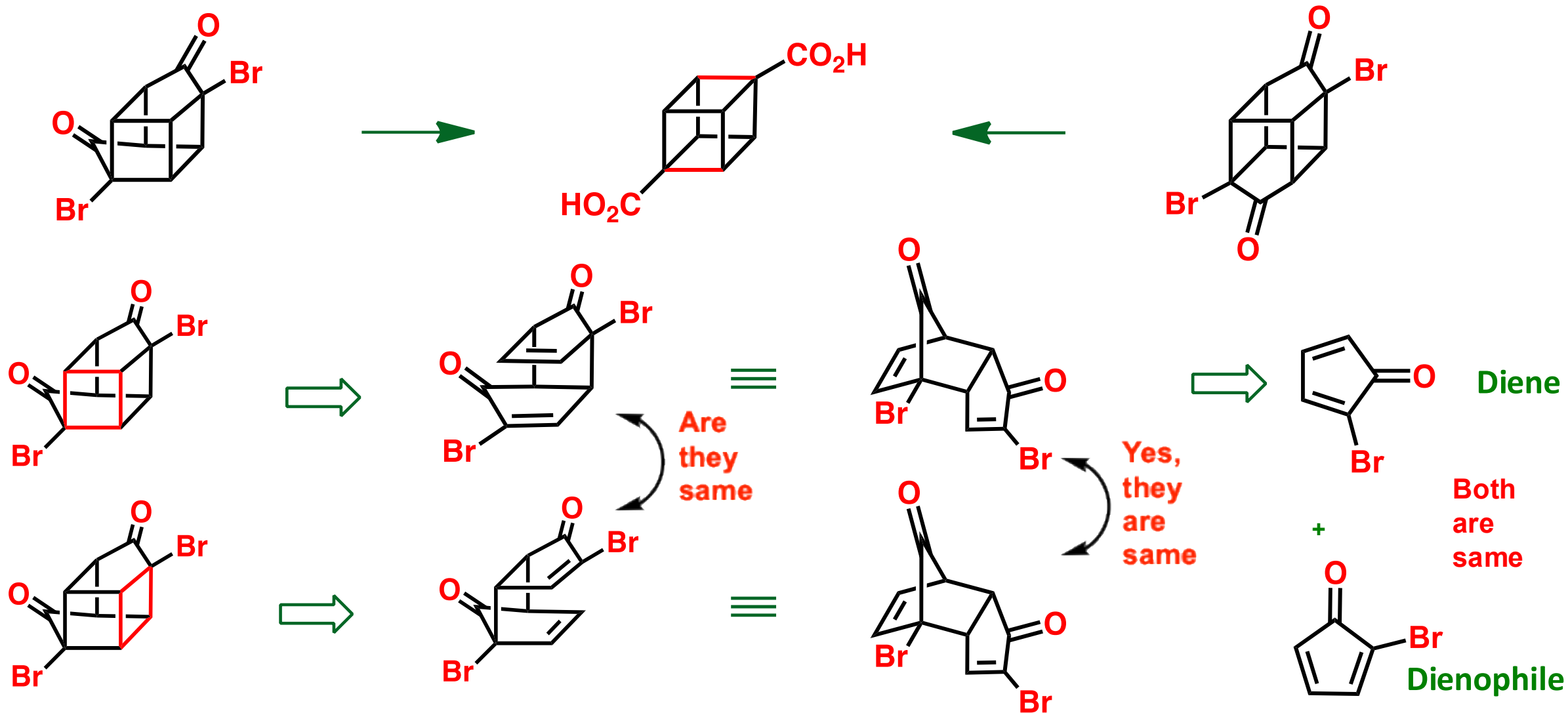


Starting material has four 5-membered rings and two 4-membered rings

Carboxylic acid is found in the same place where Br was there in the reactant

Retrosynthesis of Cubane

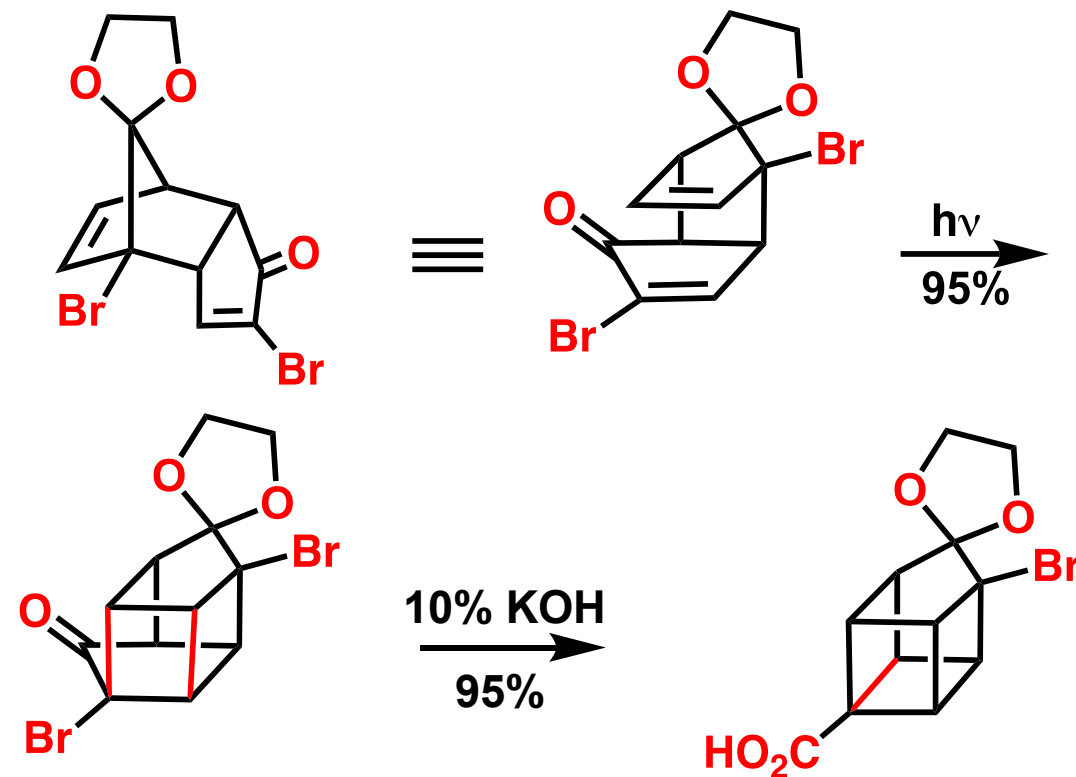
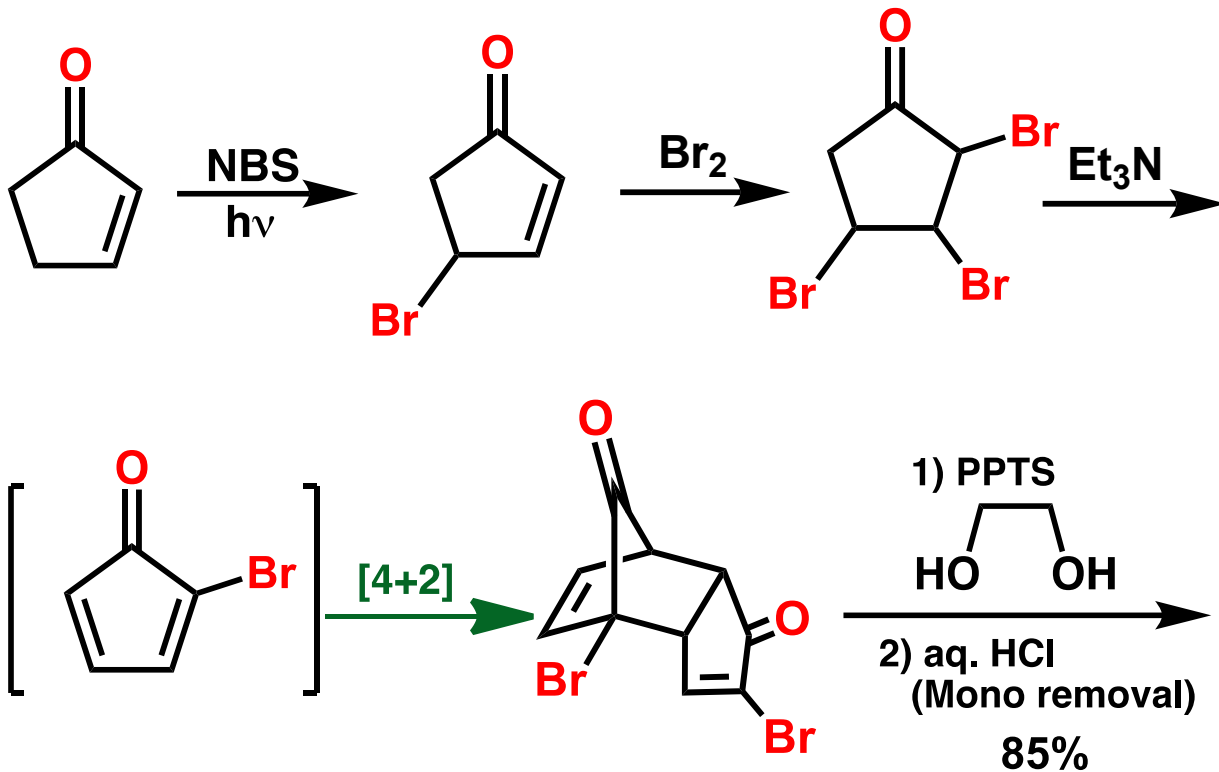
1,4-Dicarboxylic acid



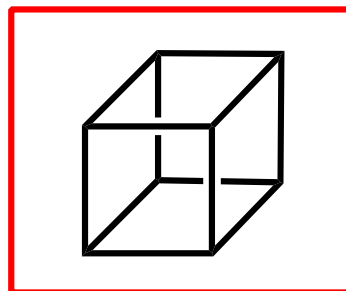
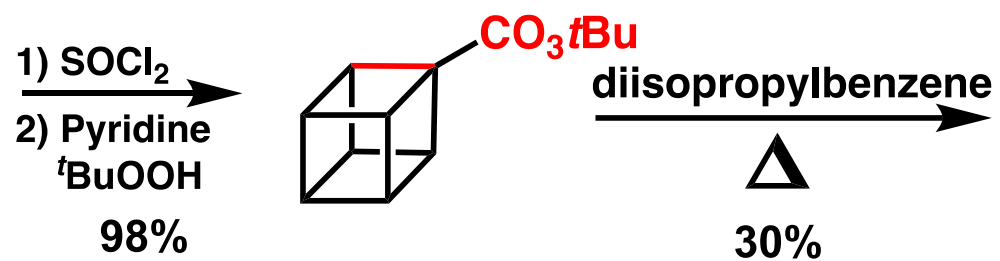
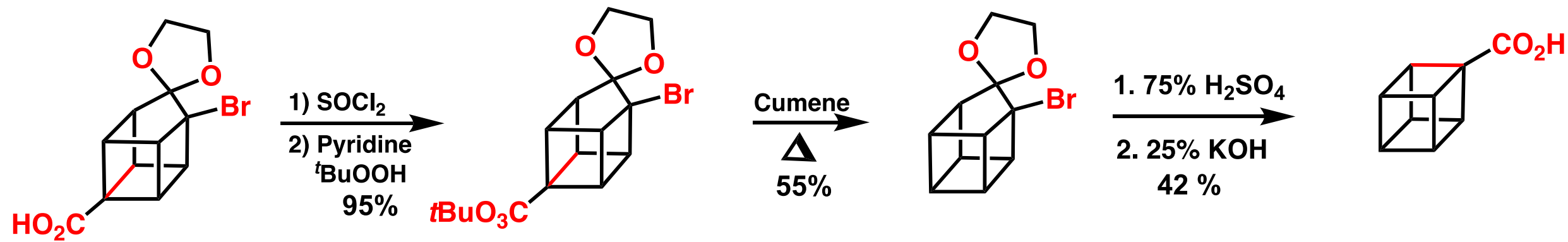
Problems in the Preparation of Starting Material

1. Cyclopentadienone is highly unstable

2. Difficult to prepare



Synthesis of Cubane



P. E. Eaton and T. W. Cole. *J. Am. Chem. Soc.*, **1964**, 86, 3157

