

Lecture 12

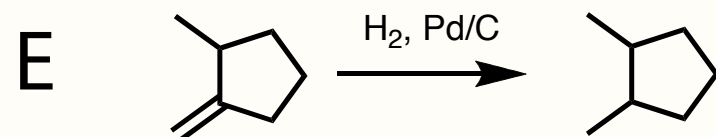
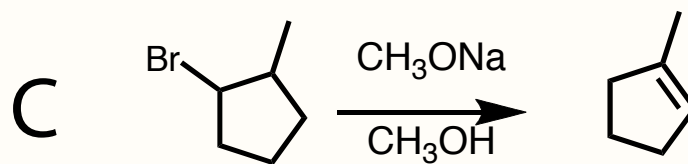
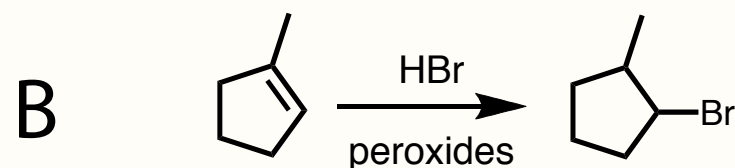
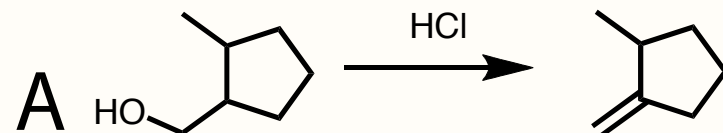
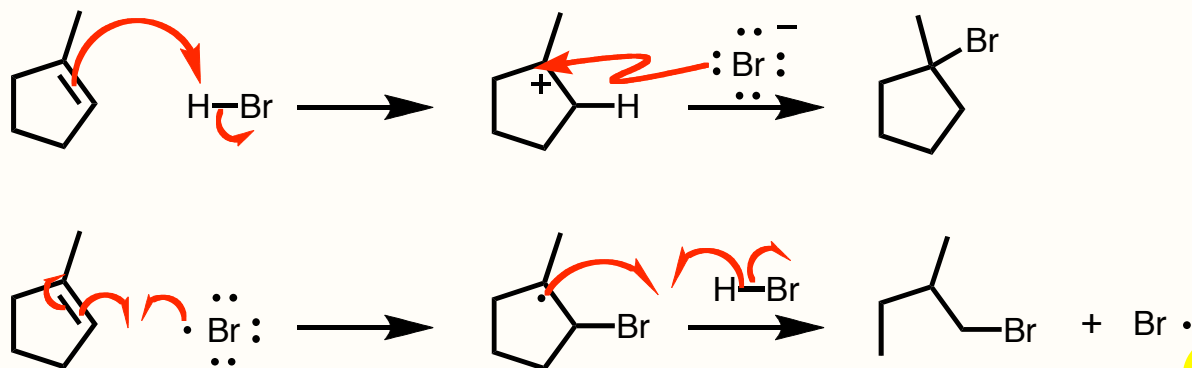
Organic Chemistry 1

Professor Duncan Wardrop

February 18, 2010

Self Test Question

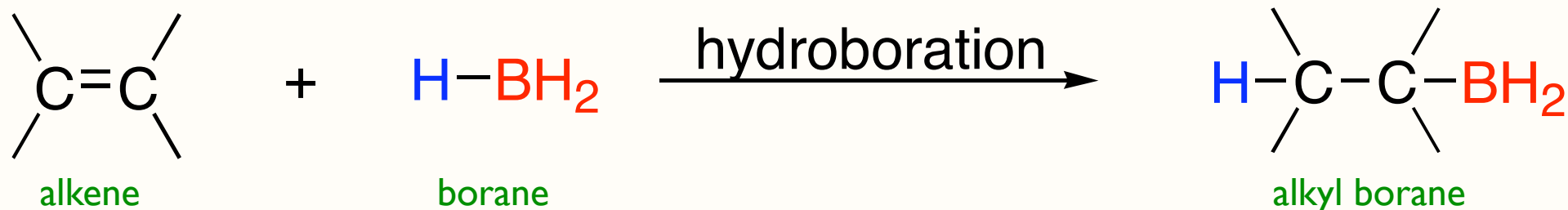
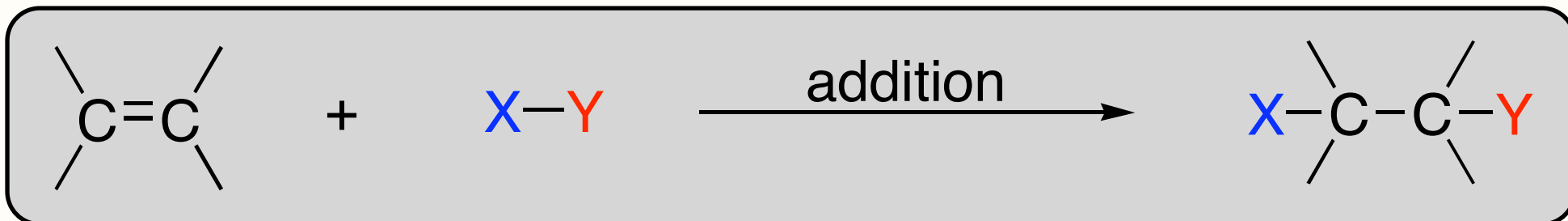
Which of the following reactions proceeds through a carbocation intermediate?



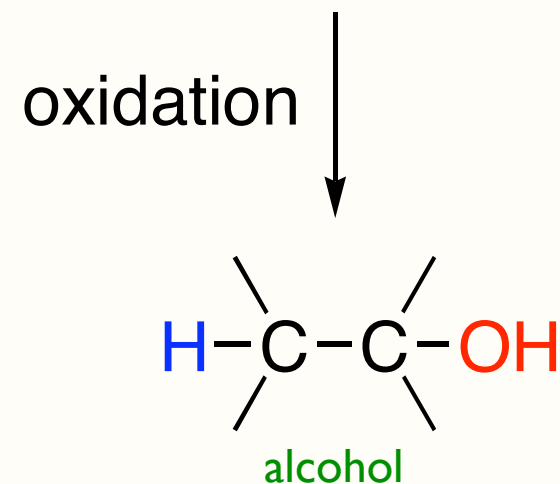
Hydroboration–Oxidation

Section 6.12-6.14

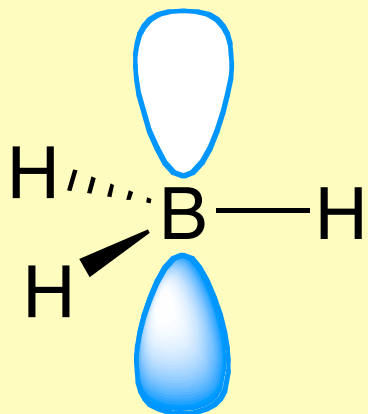
Addition of B-H Bonds to Alkenes



oxidation is a separate step and requires a separate set of conditions and reagents

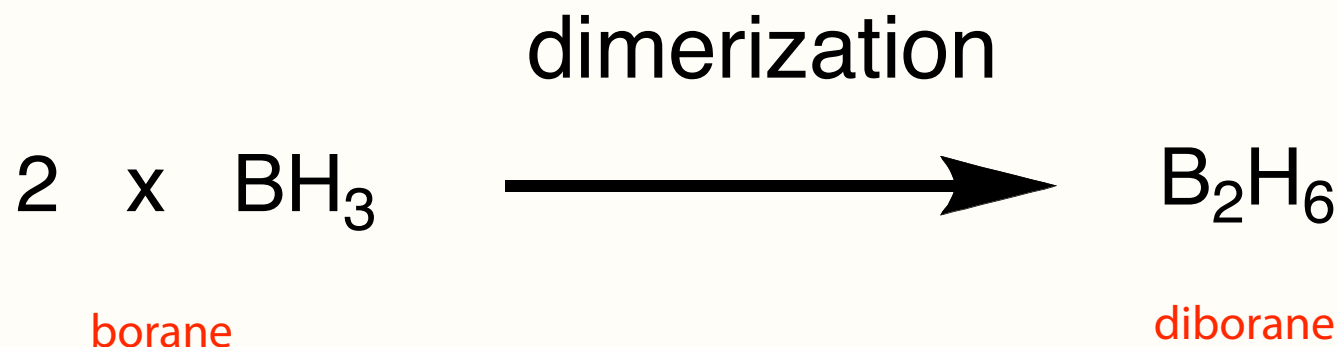


Boranes - Structure & Electronics

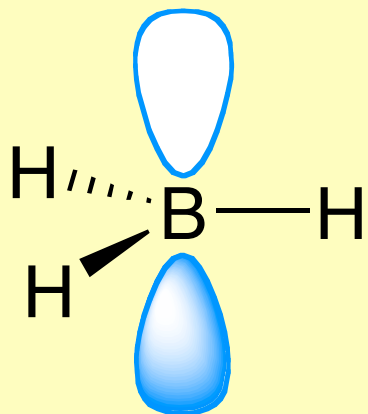


- boron is exception to octet rule
- sp^2 -hybridized (only 3 valence e⁻s)
- contains an empty p -orbital
- strong Lewis acid (electron pair acceptor)
- forms 3-bonds (neutral) & 4-bonds (-/ve)

“Free” borane (BH_3) only exists in gas phase, otherwise undergoes dimerization to diborane (B_2H_6)

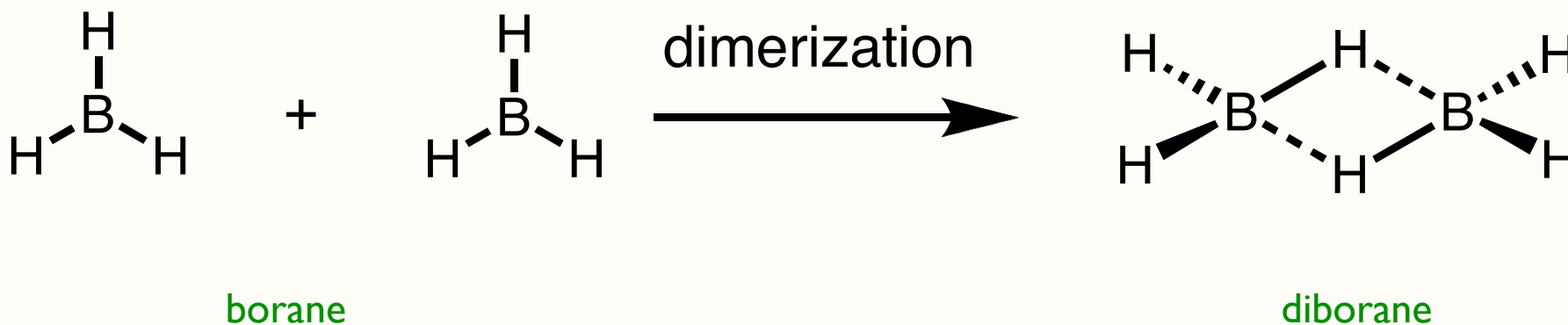


Conditions: Hydroboration



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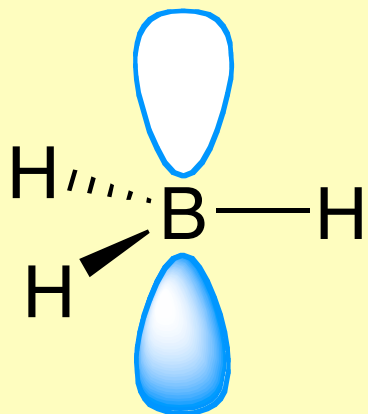
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borane

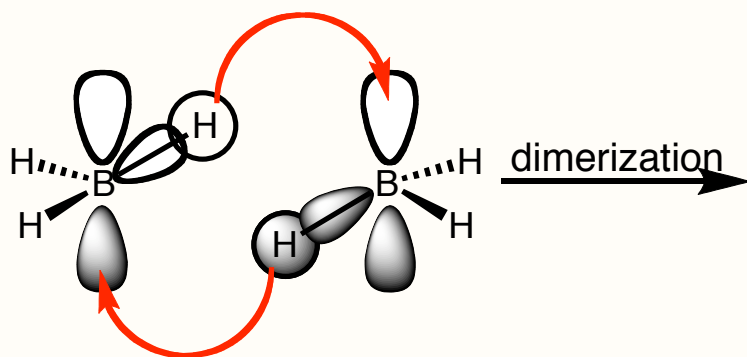
diborane

Conditions: Hydroboration

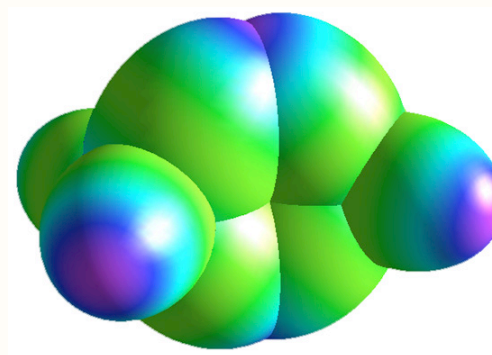


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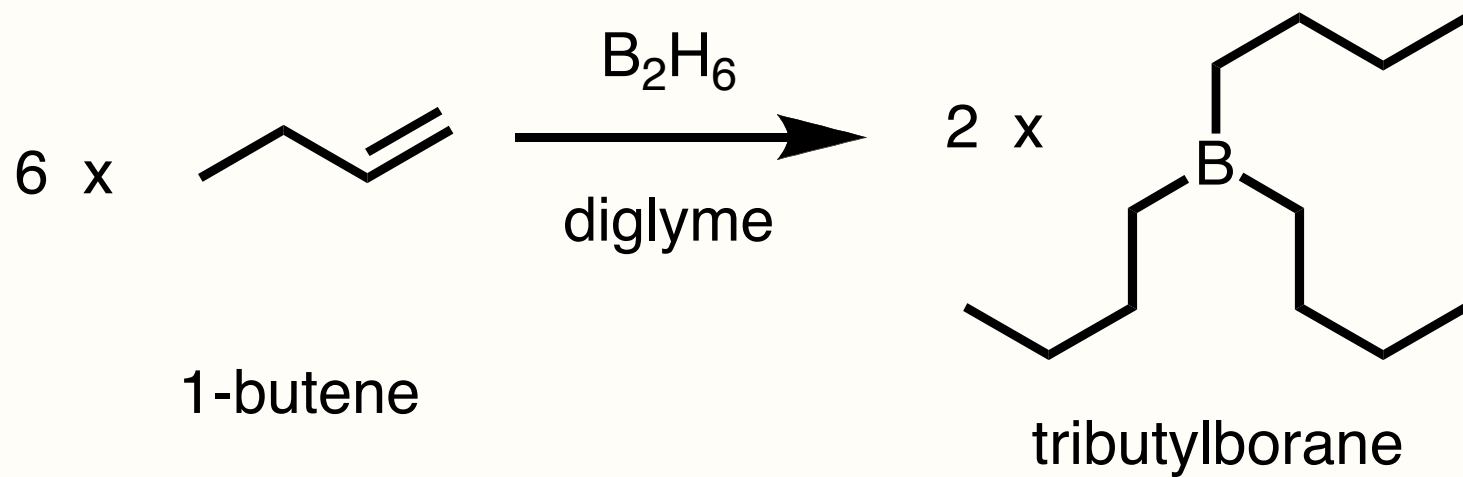


borane

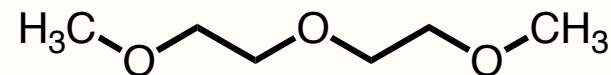


diborane

Stoichiometry of Hydroboration



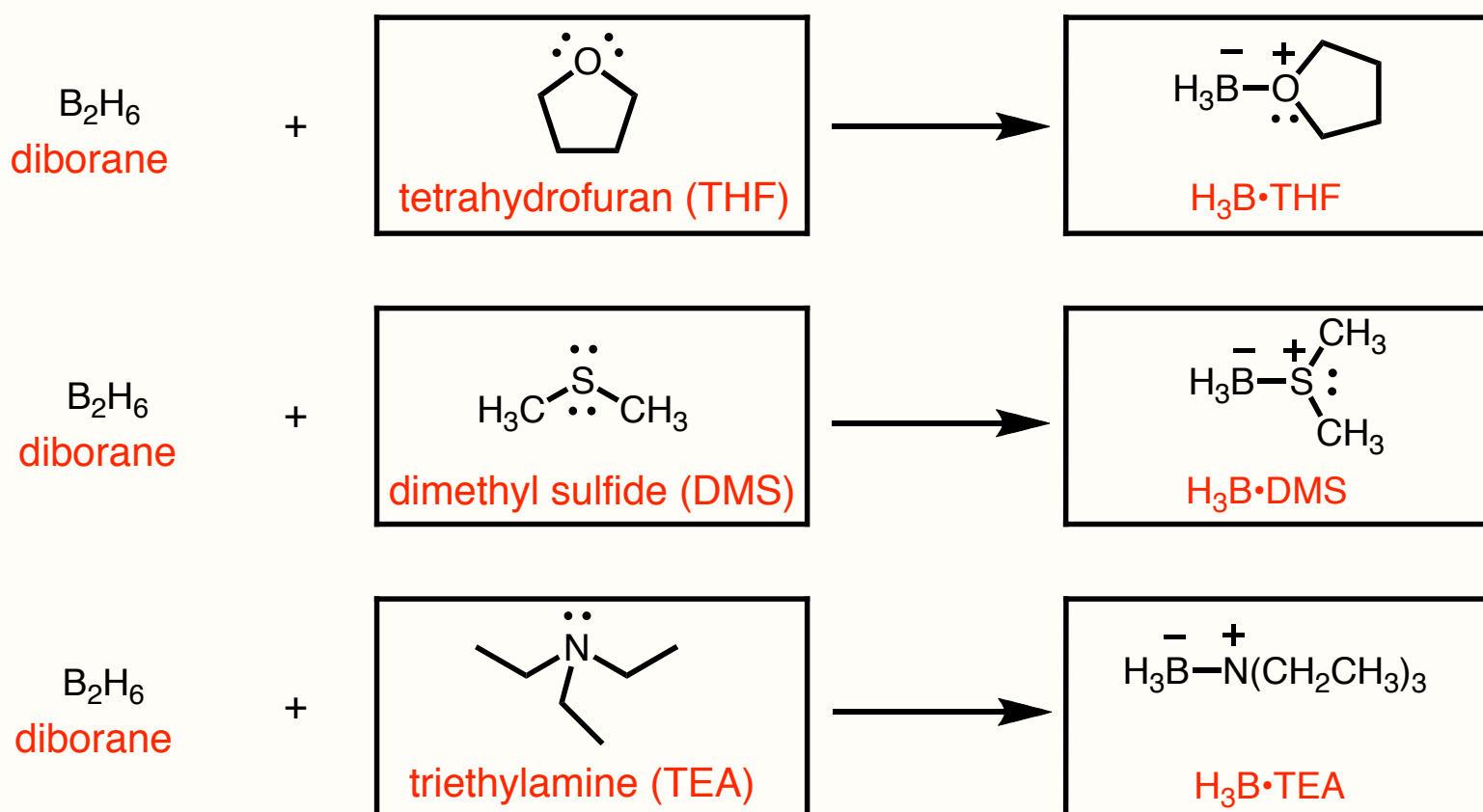
- diglyme is a common solvent
- hydroborations typically at room temp.
- generally very fast reactions



diglyme: **di**ethylene **gly**col **dim**ethyl **e**ther

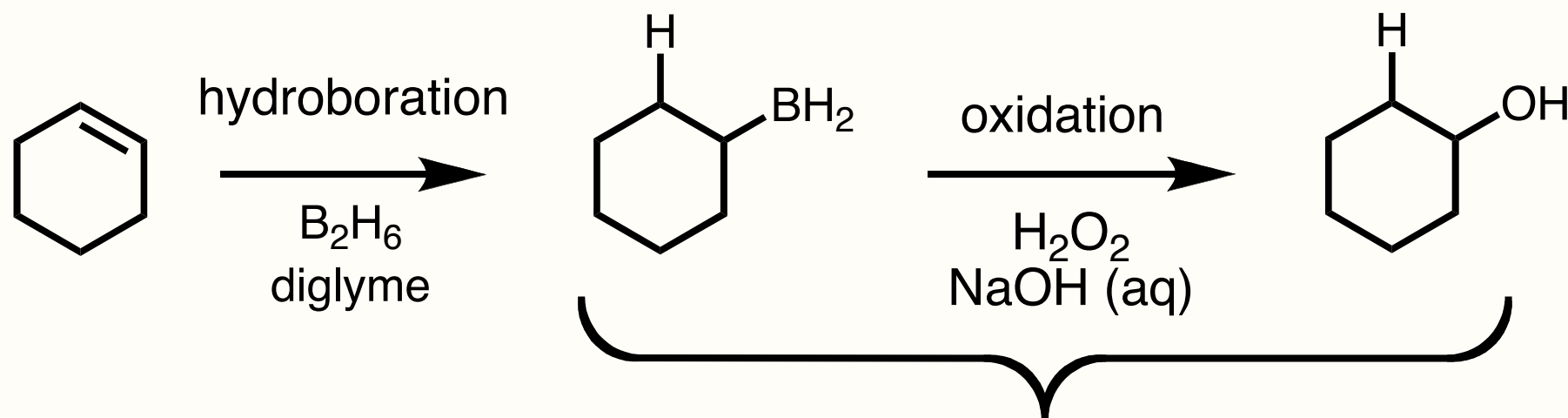
Borane is a Lewis Acid & Reducing Agent!

Other hydroborating reagents with different reactivities may be prepared by adding Lewis bases to diborane (B_2H_6)



Lewis Acid-Base Complexes

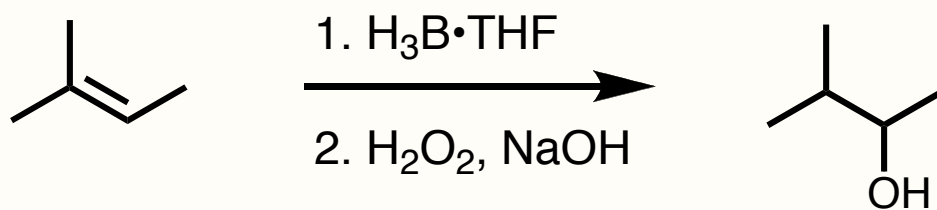
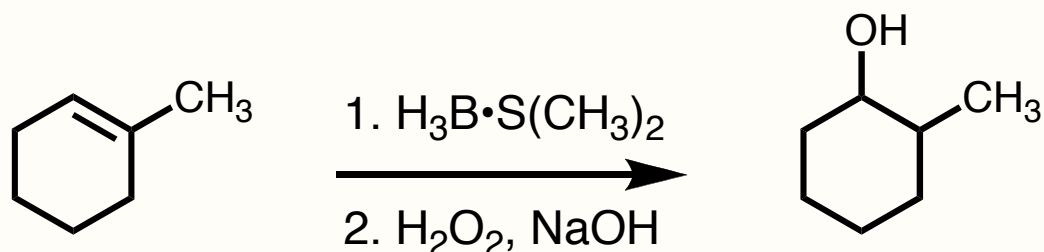
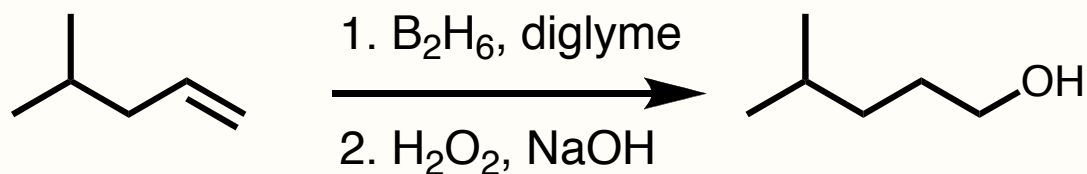
Oxidation Step



carried out in the same reaction vessel
(boranes are reactive)

- boron is replaced by more electronegative atom (O); therefore: oxidation
- oxidation using peroxide (H₂O₂) & hydroxide (OH⁻); added immediately after hydroboration
- I will not ask you to learn the mechanism for this step; for the curious, see textbook page 250

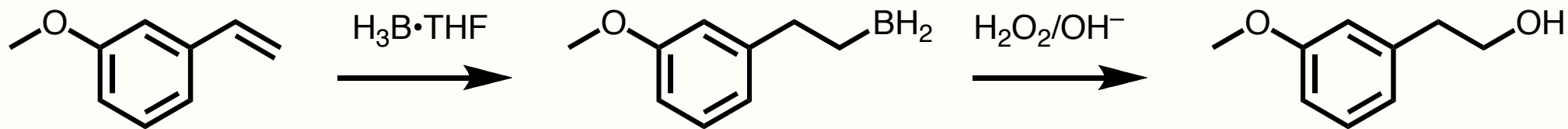
Hydroboration-Oxidation is Regioselective



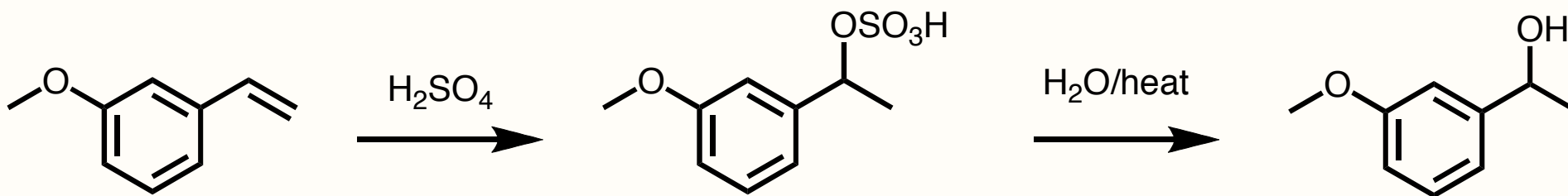
- usually written as a two-step process
- works with diborane (B_2H_6) or a borane complex with another Lewis base
- diglyme is a common solvent
- affords alcohol products; similar to hydration (H_2O/H_3O^+)

Which carbon of the alkene becomes bonded to the $-OH$ group? Do you see a pattern here?

Regioselectivity Determined During Hydroboration

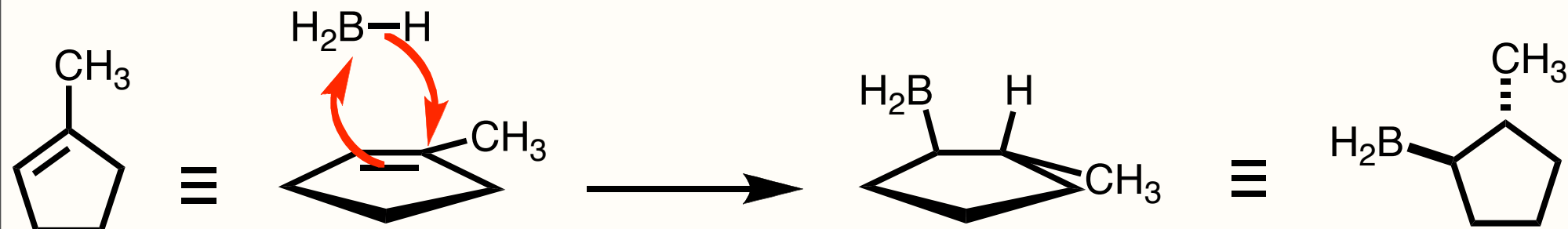


compare to ...



- *boron atom is added to least substituted carbon atom, hydrogen atom is added to most substituted*
- *after oxidation, gives the least substituted product*
- *opposite regioselectivity of Markovnikov addition*

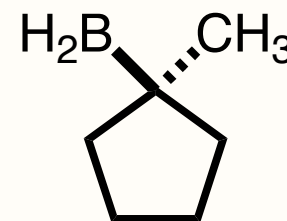
Mechanism of Hydroboration



Why this regioselectivity?

- **Syn Addition:** B and H atoms add to same side (face) of C-C double bond at same time
- hydride (H:) adds to most substituted carbon
- boron adds to least substituted carbon
- this is NOT a PROTONATION

not

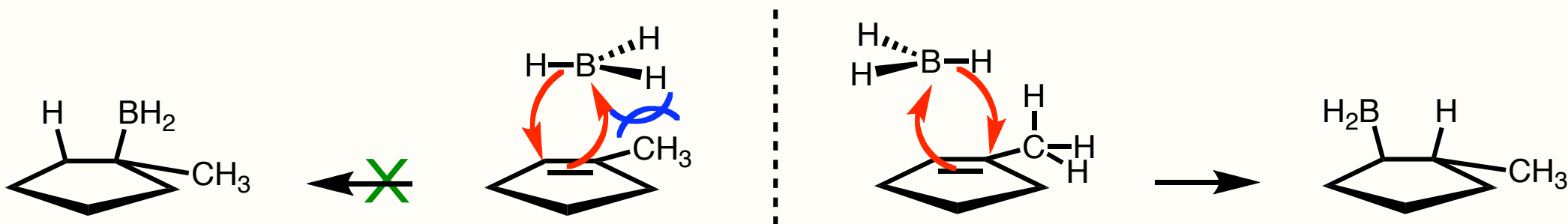


Note that although the borane generated upon monohydroboration of methylcyclopentene is itself trans-substituted, the hydroboration remains a syn-addition. In other words, it is the BH_2 group and beta-hydrogen on the carbon bearing the methyl group which are in a syn relationship.

Regioselectivity - 1st Rationale

Steric Effects Control Regioselectivity...

boron is larger than hydrogen; it prefers to add to the less sterically hindered side of the double bond, which is the least substituted side.

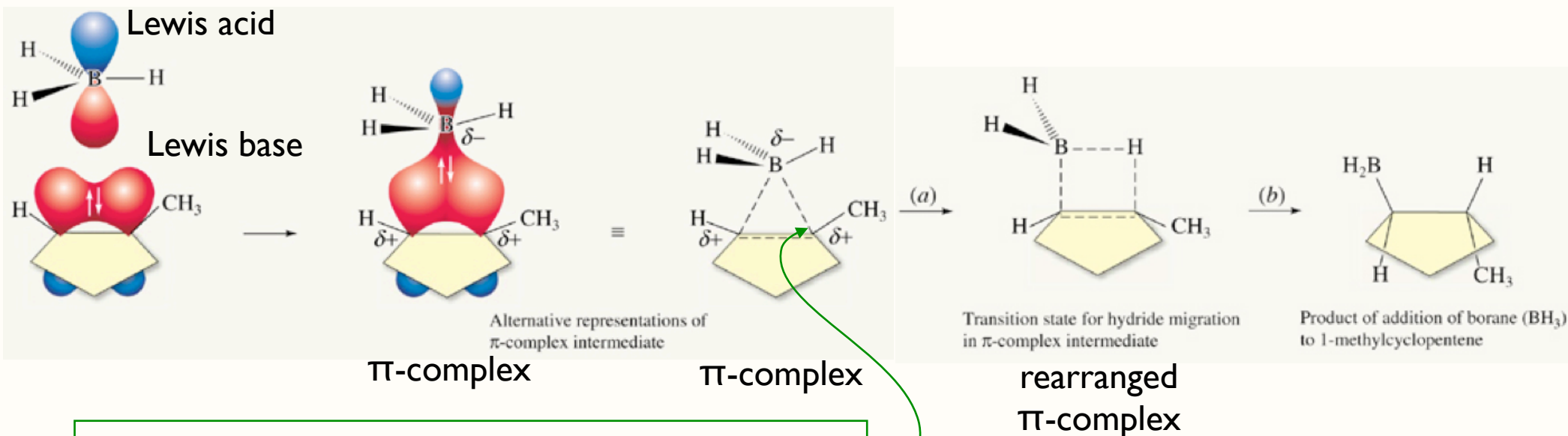


Steric strain in transition state raises E_{act} for this pathway - slower reaction

Regioselectivity - 2nd Rationale

Electronic Effects Control Regioselectivity...

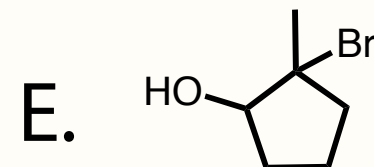
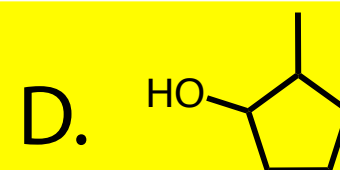
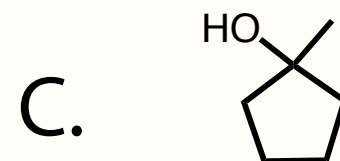
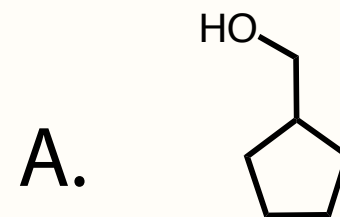
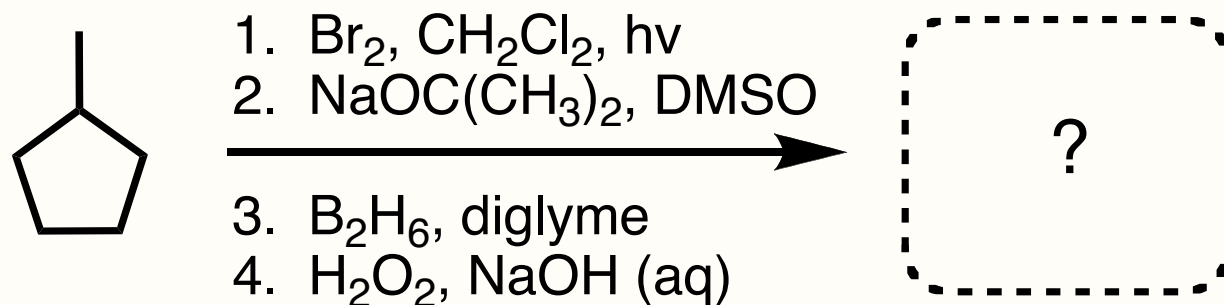
both carbons in alkene develop partial positive charge in transition state; more substituted = more partially positively charged = hydride (H:) transfer preferred (faster) to that carbon atom.



most substituted =
most partially positively charged =
most electrophilic carbon atom =
want electrons from a nucleophile most

Self Test Question

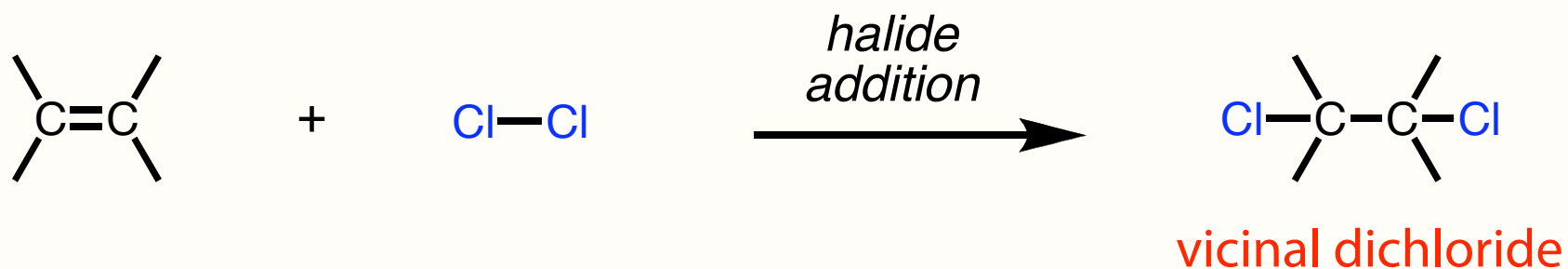
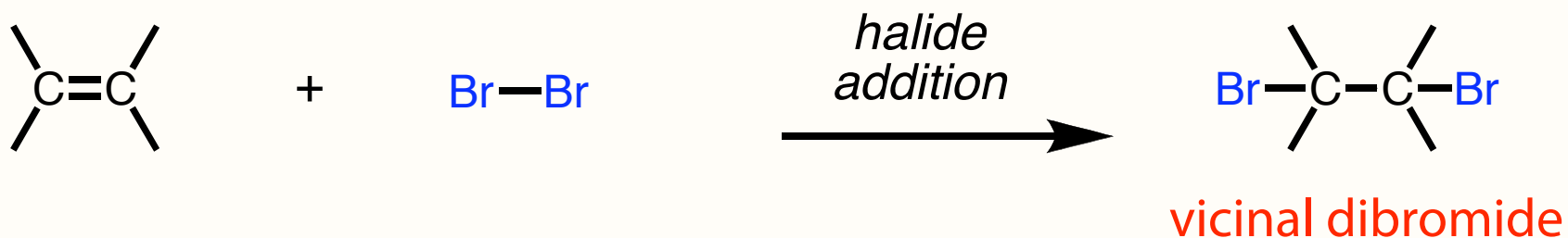
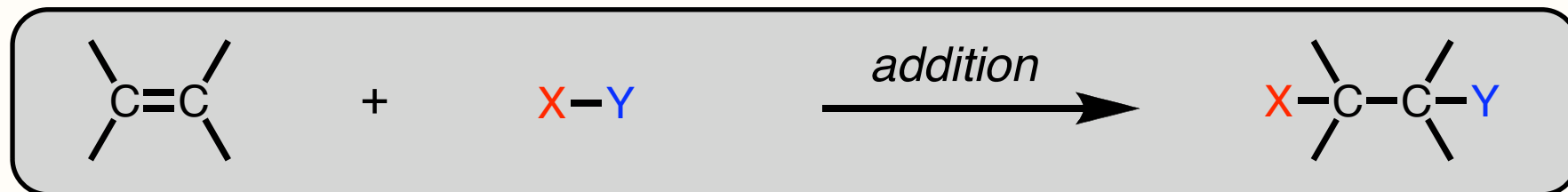
What is the product of the following reaction sequence?



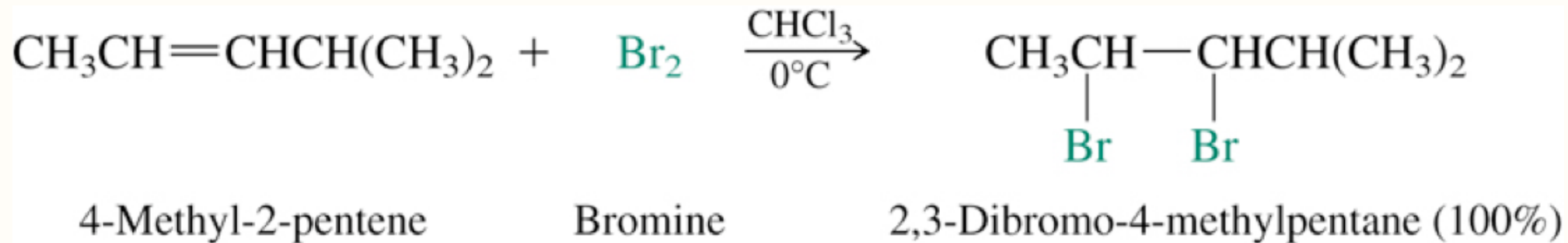
Halide Addition to Alkenes

Section 6.15-6.18

Alkene-Halogen Addition

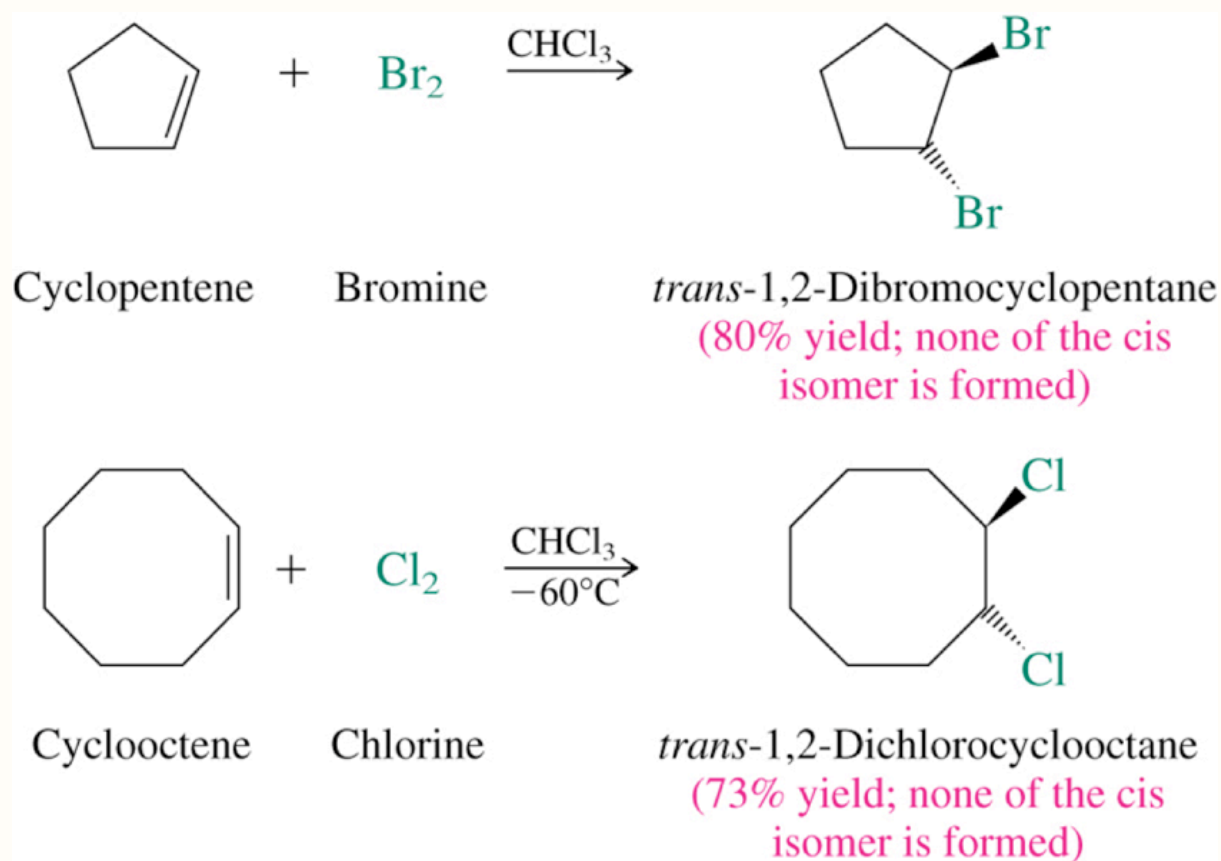


Typical Reaction Conditions for Halogen Addition



- only bromine (Br₂) and chlorine (Cl₂) undergo this reaction
- typically use a halogenated solvent like chloroform (CHCl₃)
- low temperature (0 °C)
- no light (avoid radical halogenation at saturated carbons)

Halogenation is *Stereospecific*



- *anti* addition of Br₂ or Cl₂ across double bonds
- two halogen atoms are *trans* to each other in rings

Stereospecific Reactions?

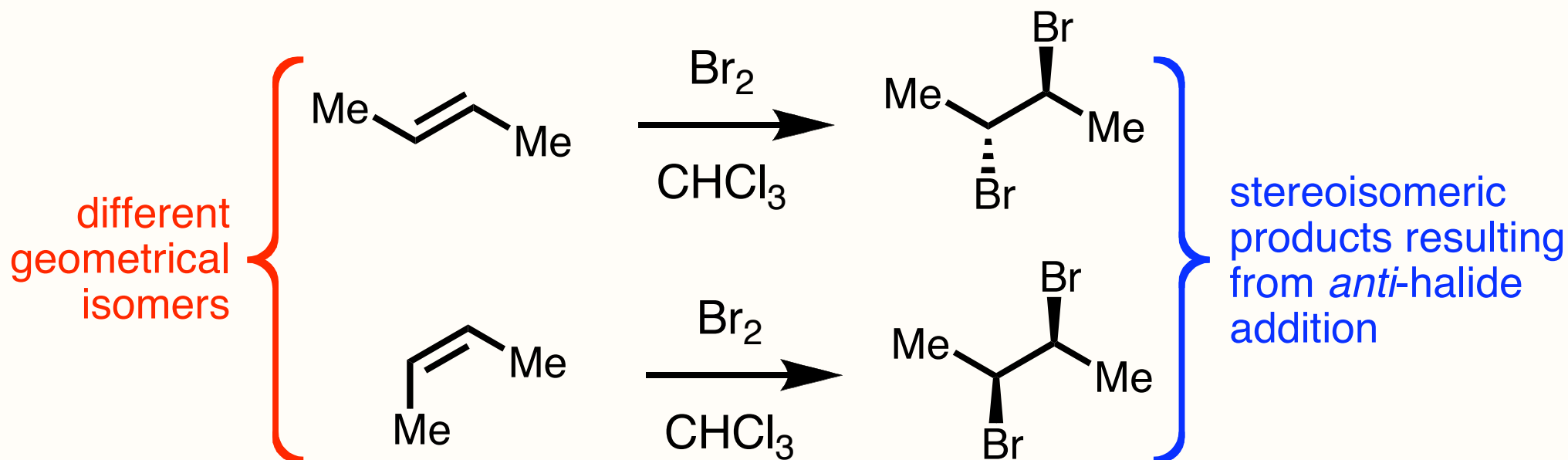
stereospecificity is the property of a [reaction](#) mechanism that leads to different [stereoisomeric](#) reaction products from different [stereoisomeric reactants](#), or which operates on only one (or a subset) of the stereoisomers

Stereospecific Reactions

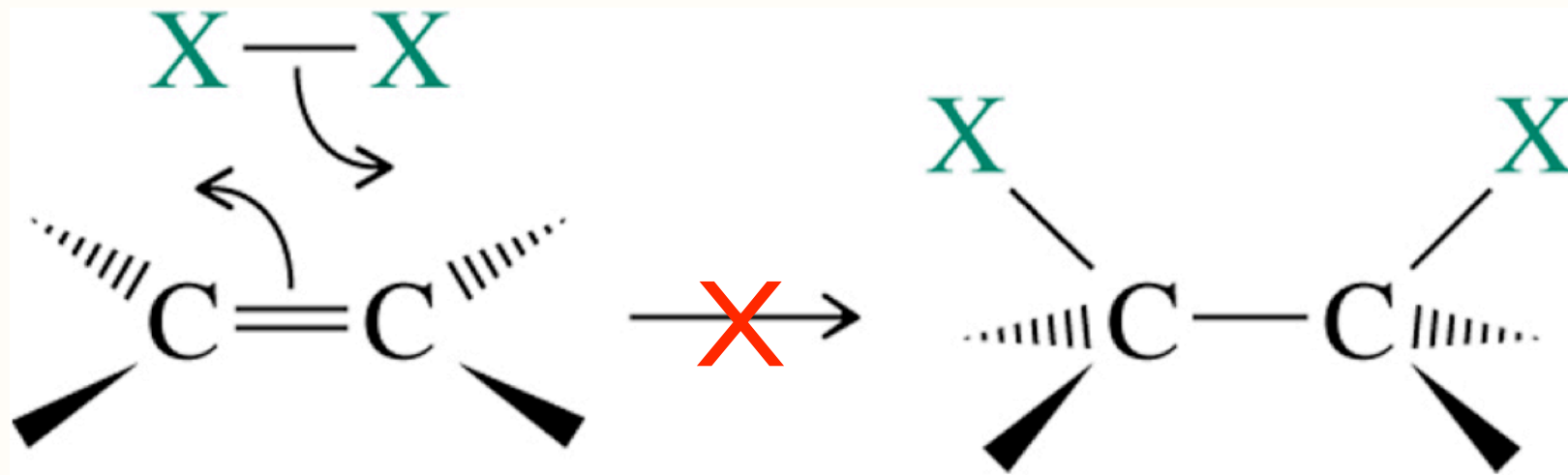
Stereospecific

In stereospecific reactions, the configuration of the product is *directly* related to the configuration of the reactant and is determined by the reaction mechanism. Stereoisomeric reactants will give different, stereoisomeric products.

CHEM 232 Definition, 2009

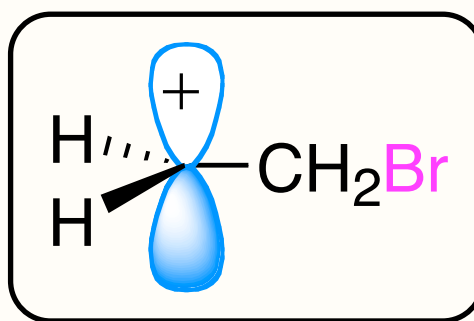
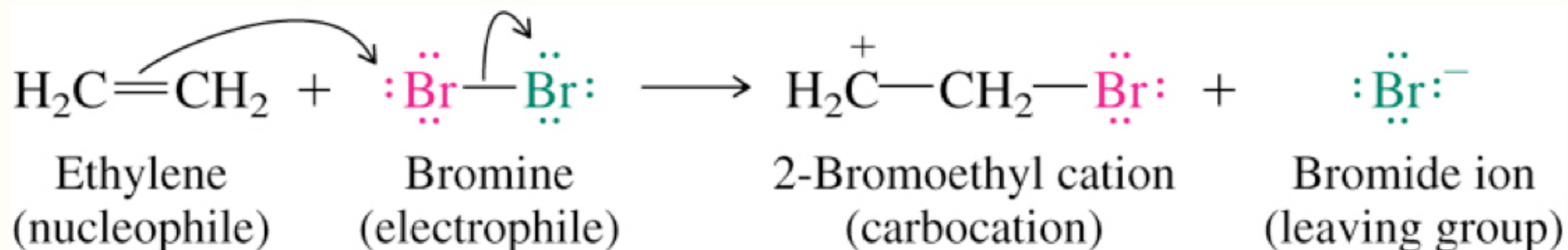


Halogen Addition Does Not Involve Syn Addition



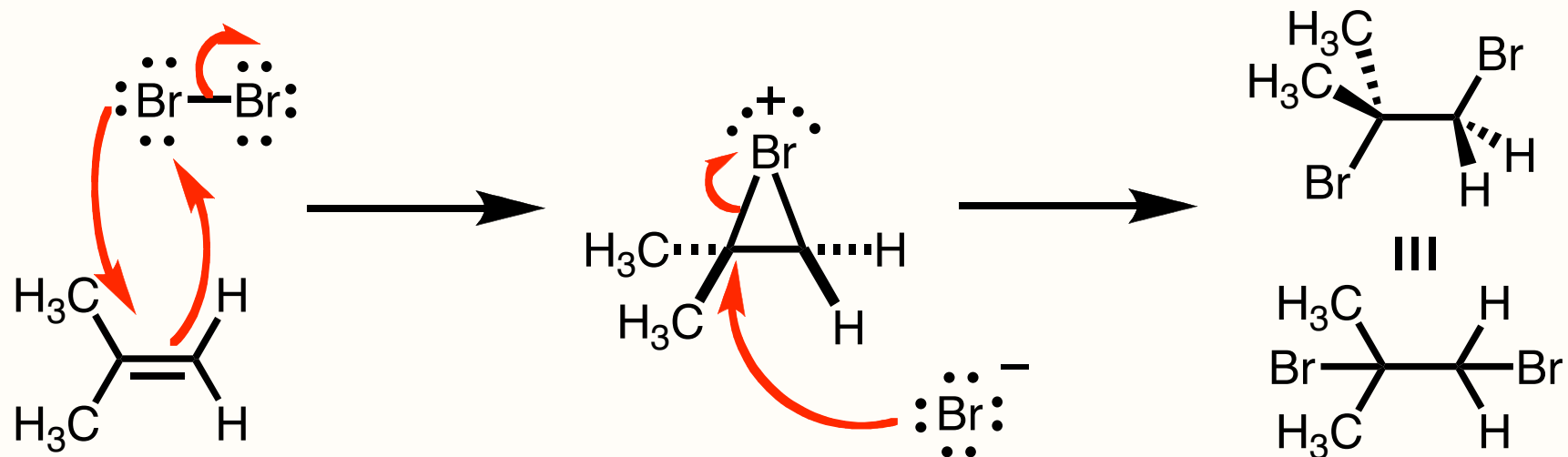
- concerted process would require *syn* addition of two halogen atoms
- therefore mechanism is not concerted.

Halogen Addition Does Not Involve Free Carbocations



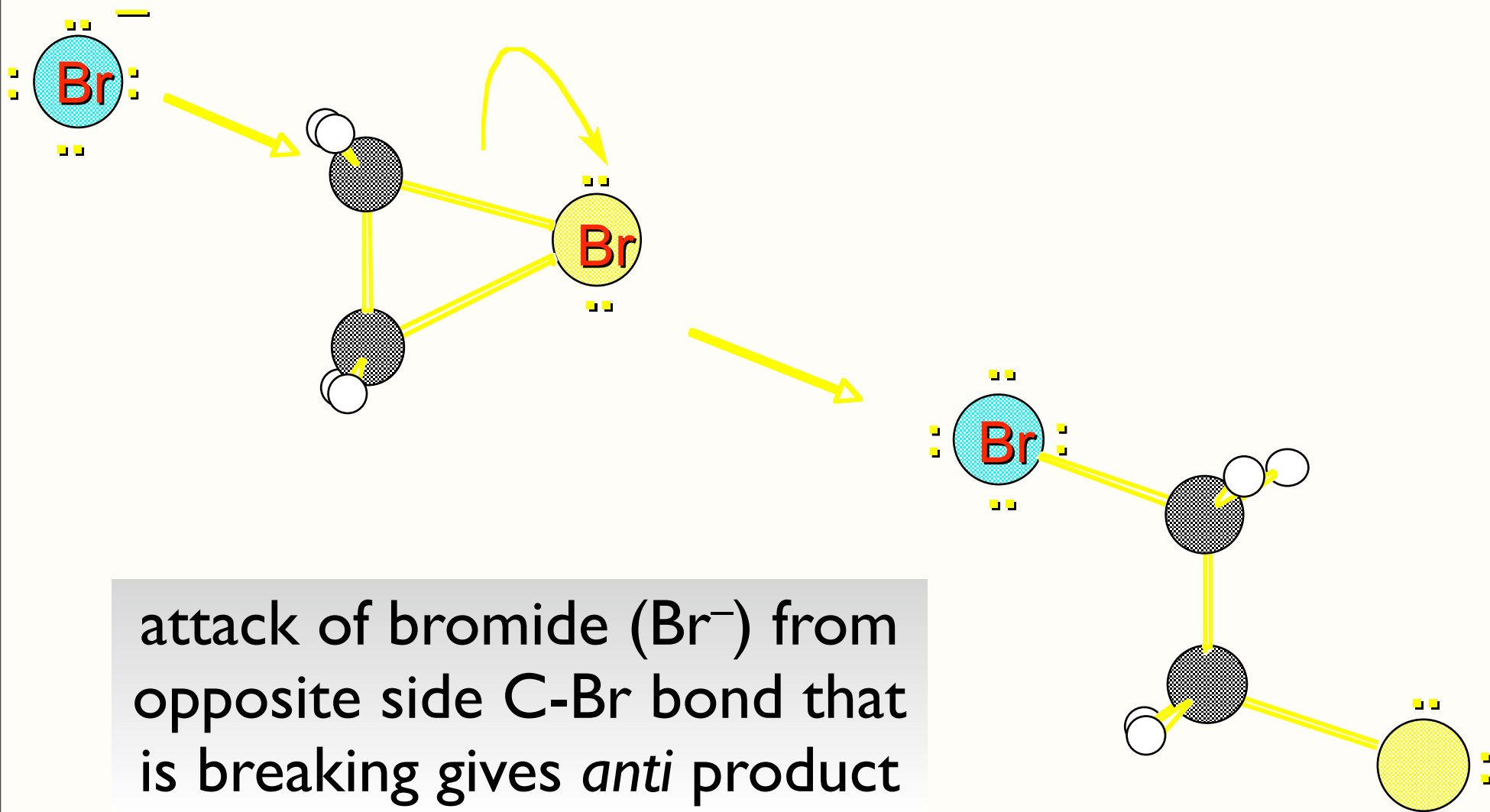
- carbocation intermediates are planar (flat)
- addition of second halide could approach either lobe of empty *p*-orbital on carbocation
- therefore this mechanism is not possible because it would not be stereoselective

Halogen Addition *Does* Involve Halonium Ions

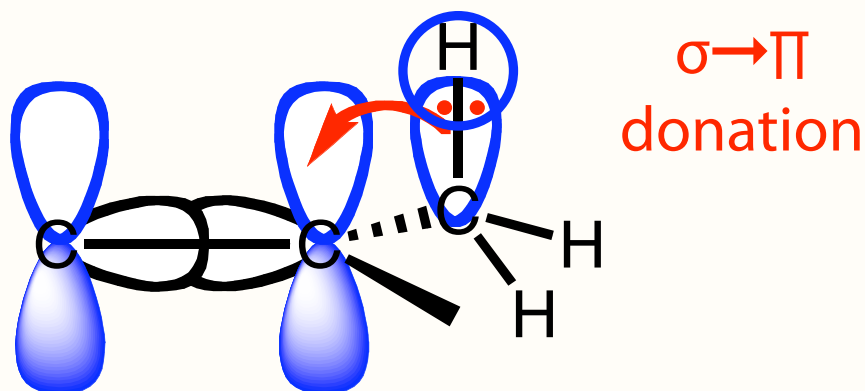


- electron pair in π -bond form new bond to bromine atom as Br-Br bond breaks
- lone pair of electrons on bromine form new bond to alkene carbon losing a bond at the same time (concerted)
- halonium ions (three-membered rings with one halogen) are intermediates; no carbocation intermediates

Anti Addition



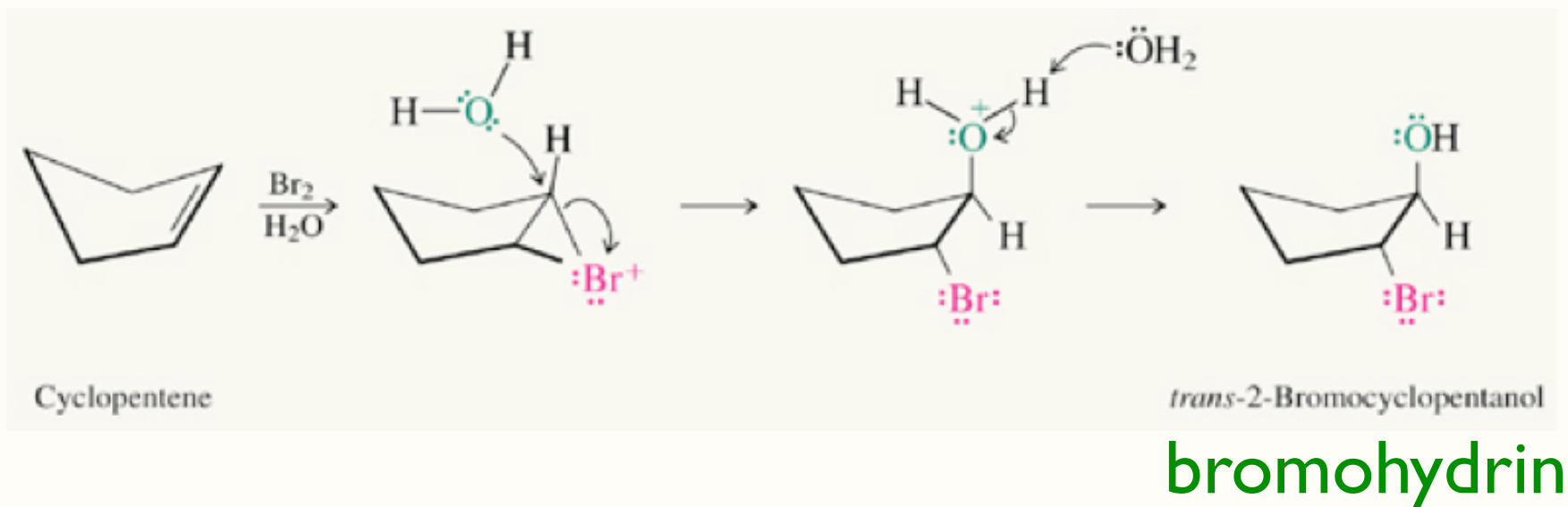
Hyperconjugation ($\sigma_{C-H} \rightarrow \pi_{C=C}$) Increases Rate of Halogenation



alkene	relative rate (k_{rel})
	1
	61
	5400
	920,000

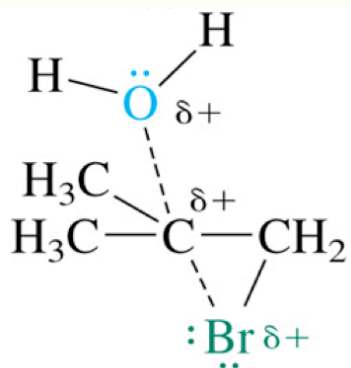
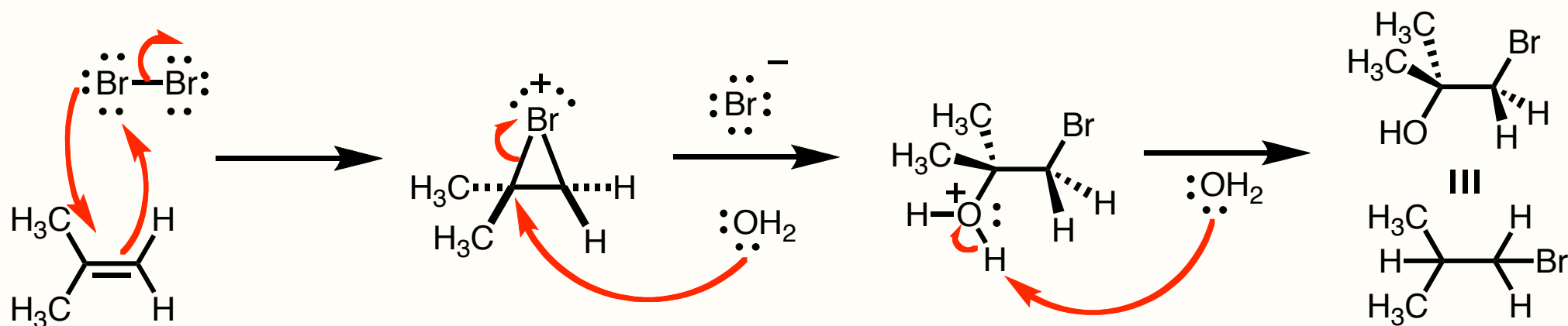
- more alkyl groups attached to double bond ➡
- more $\sigma \rightarrow \pi$ orbital donation/overlap ➡
- double bond has more electron density ➡
- double bond is a stronger nucleophile (Lewis base) ➡
- reacts faster with electrophiles like Br-Br

Halogen Addition Modification: Aqueous Solutions Give Halohydrins

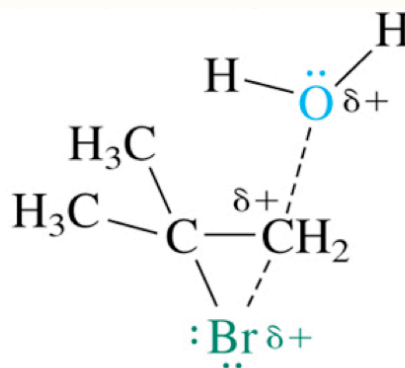


- if the solvent for the reaction is changed to water, halohydrins are formed
- since water is much more concentrated, it will add to halonium ion intermediate faster than the halide

Ring Opening of Halonium Ions is Regioselective



More stable transition state;
has some of the character
of a tertiary carbocation



Less stable transition state;
has some of the character
of a primary carbocation

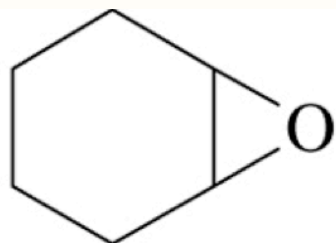
- product is most substituted alcohol;
least substituted halide
- most substituted carbon is most
partially positively charged in
transition state = strongest
electrophile = water most attracted
to that carbon

Epoxidation & Ozonolysis

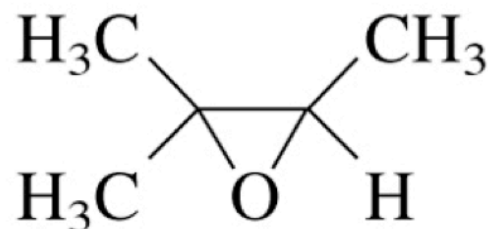
Sections 6.19

We will skip epoxide nomenclature for now.

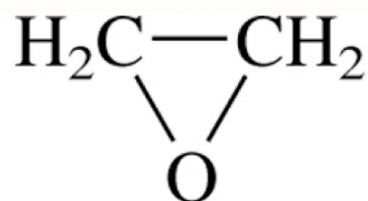
Epoxides (a.k.a Alkene oxides)



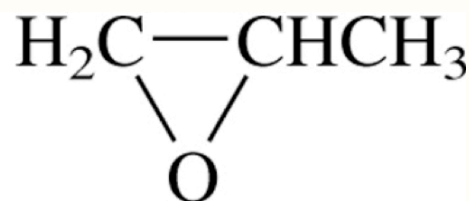
1,2-Epoxycyclohexane



2,3-Epoxy-2-methylbutane



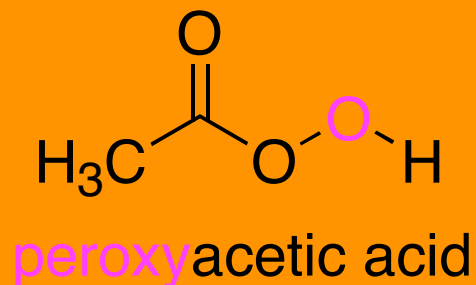
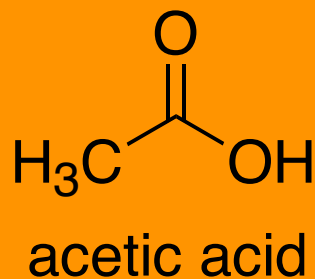
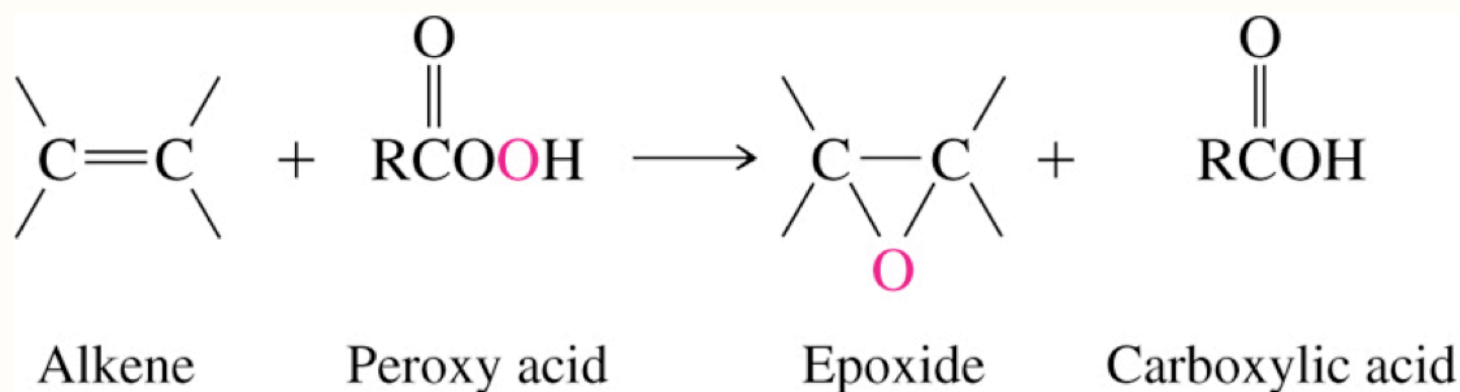
Ethylene oxide



Propylene oxide

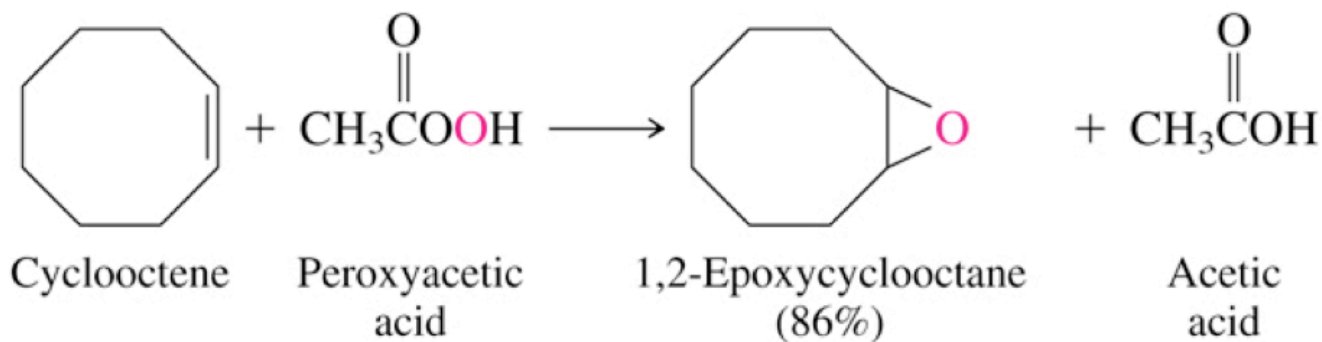
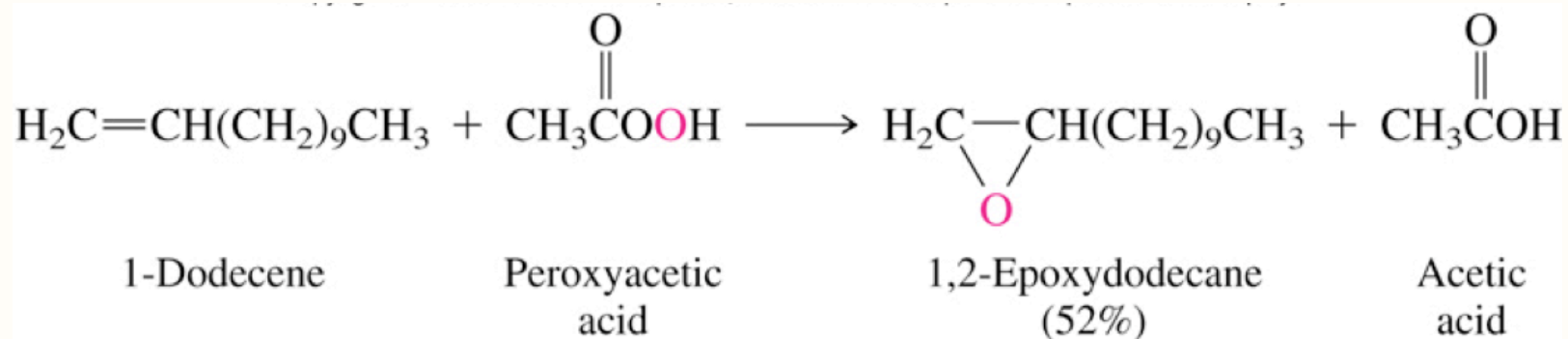
- three-membered rings containing an oxygen atom
- common intermediates in organic synthesis

Epoxides are Prepared via Alkene Epoxidation



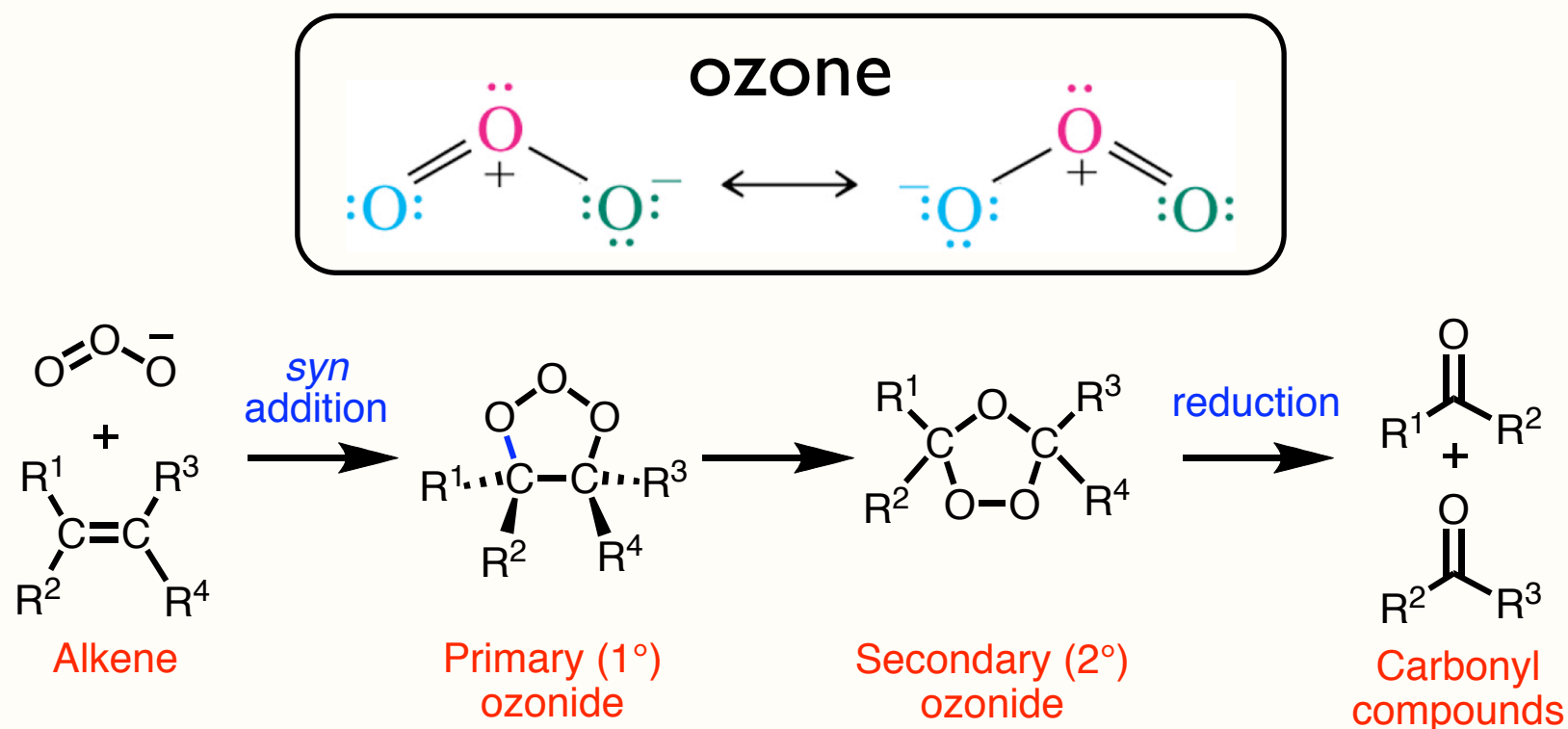
- peroxyacids are source of electrophilic oxygen atoms
- addition of a single oxygen atom across double bond
- similar to formation of bromonium ion intermediate
- don't worry about mechanism; for curious see textbook page 257

Examples



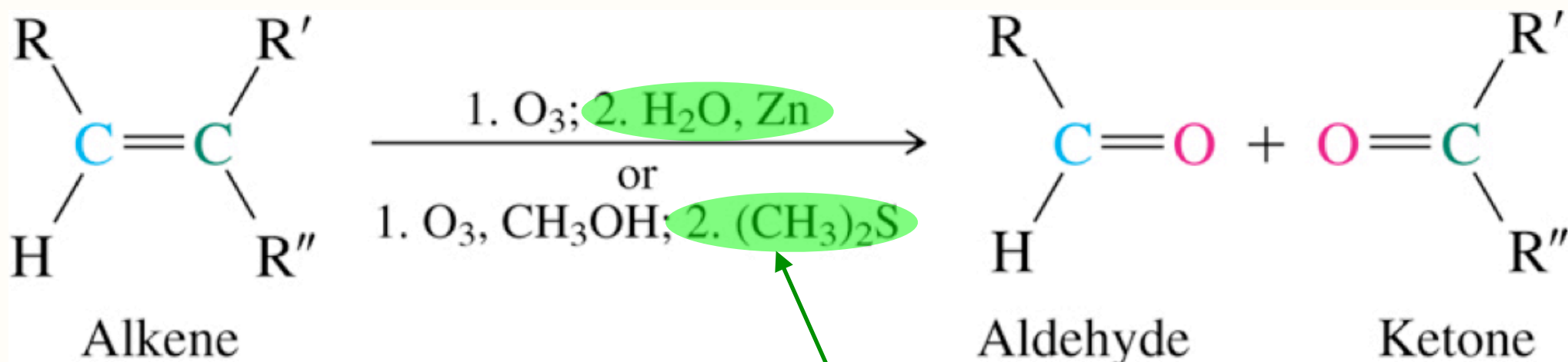
- any peroxyacid will work
- more substituted double bonds react faster
- because only adding one atom across double bond, must be *syn* addition

Alkenes are Cleaved via Ozonolysis



- ozone adds across double bonds to give ozonides
- ozonides react further with reducing agents to provide carbonyl compounds
- we will not discuss mechanism for this reaction

Ozonolysis is a Two Step Process



reducing agents;
reduce ozonide intermediate

pattern = alkene is cut in half and replaced by an oxygen atom at each end
carbonyl product depends on substitution of alkene

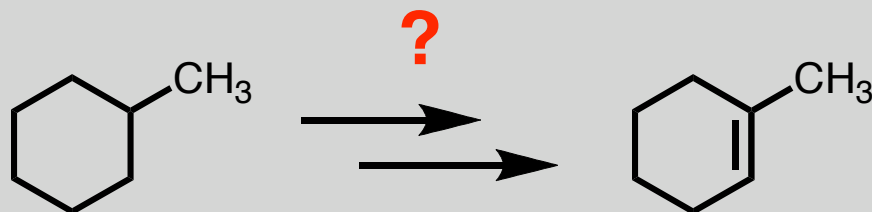
Organic Synthesis

Section 6.21

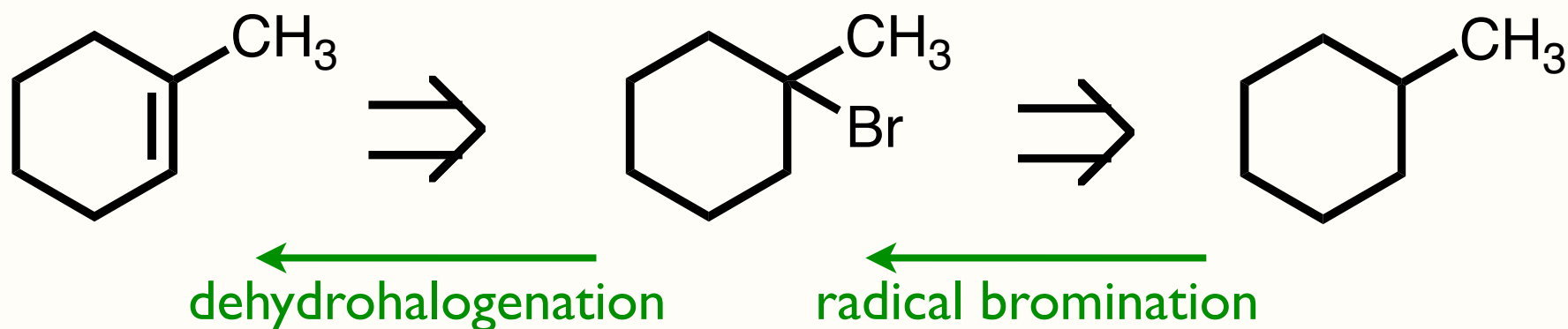
We will not cover section 6.22.

Retrosynthetic Analysis

How could you prepare 1-methylcyclohexene from methylcyclohexane?

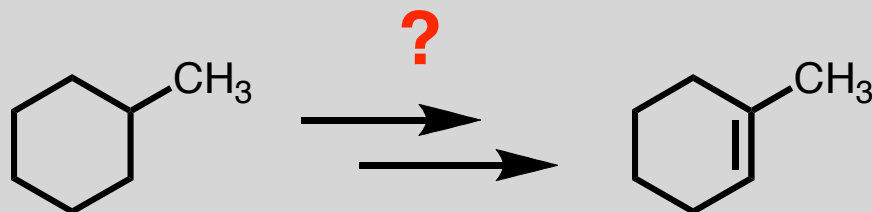


Step One: Devise a retrosynthesis. Work backwards from the target molecule. Each step backward you should ask, How can I prepare the target functional group.

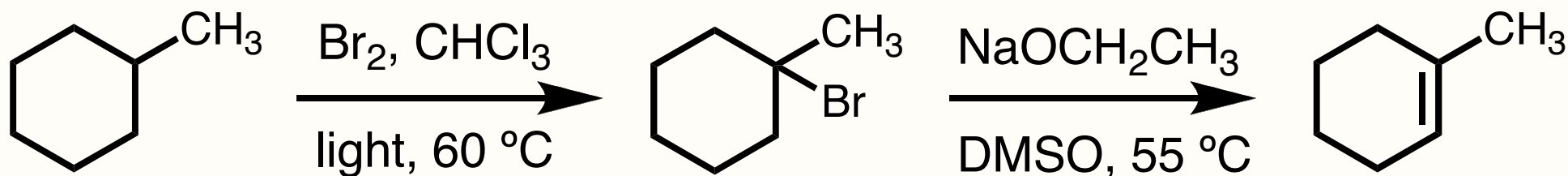


Synthetic Route

How could you prepare 1-methylcyclohexene from methylcyclohexane?

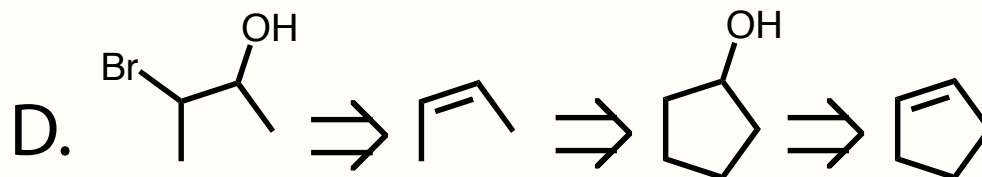
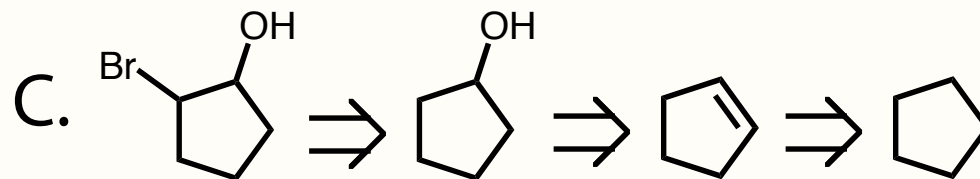
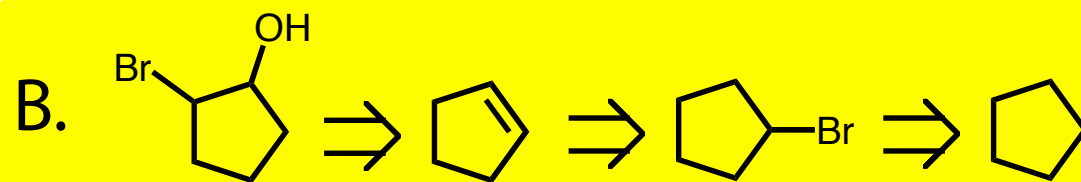
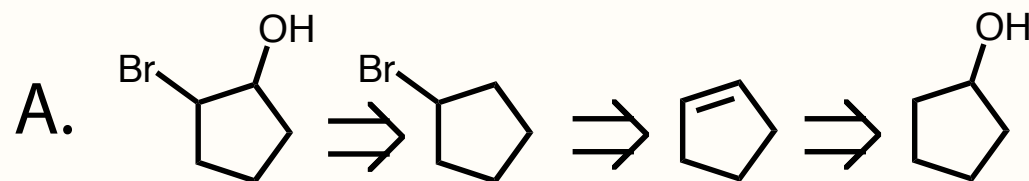
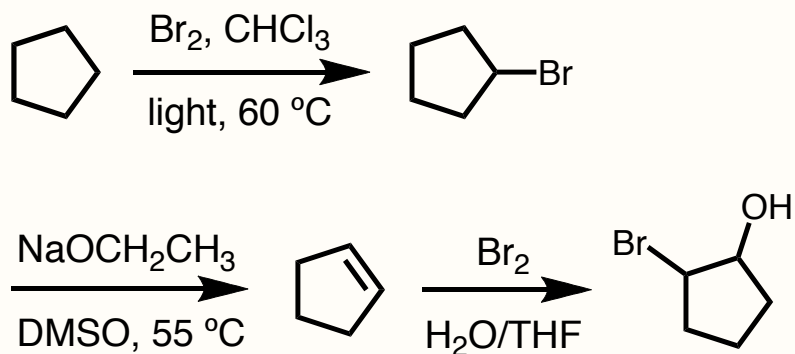


Step One: Write the synthesis out in the forward direction including all necessary reagents and conditions.



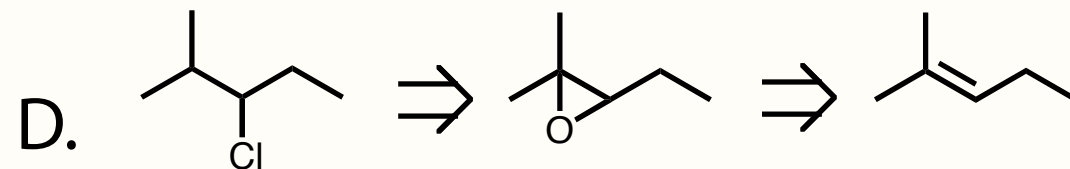
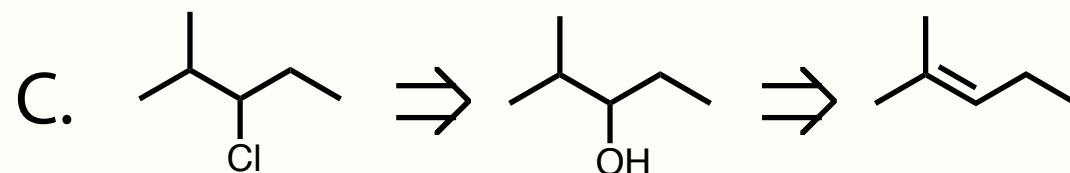
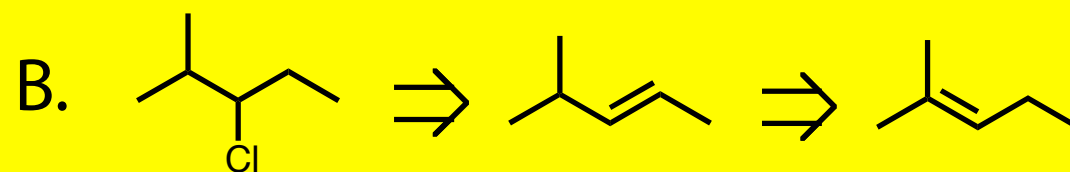
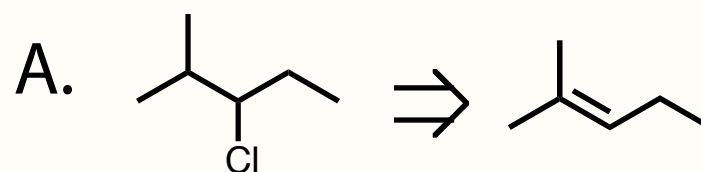
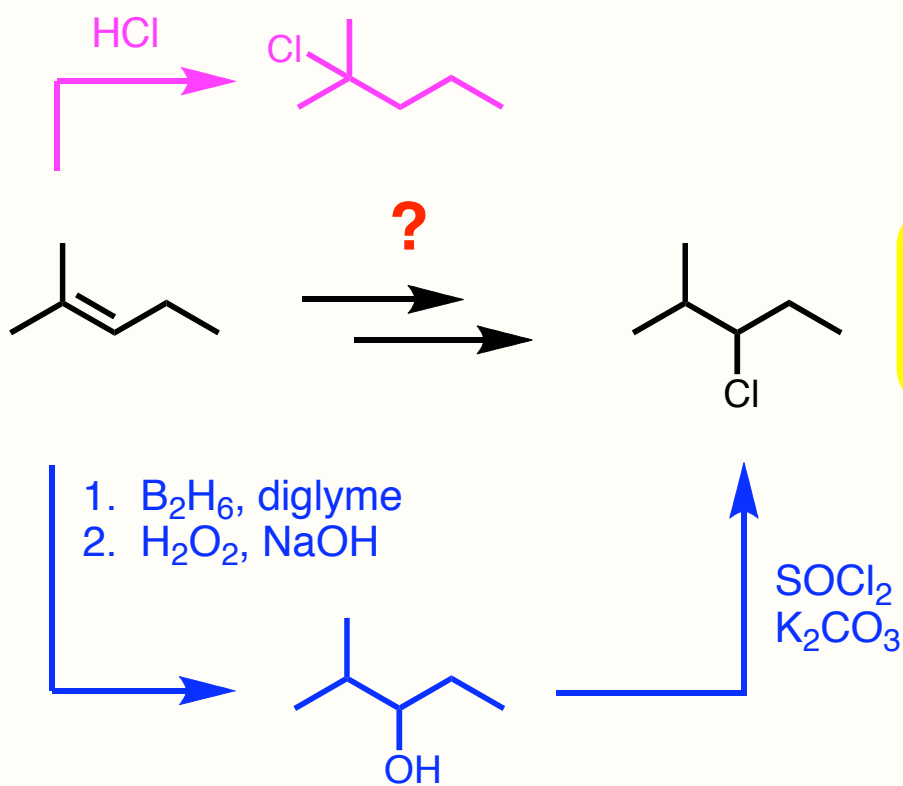
Self Test Question

Which retrosynthetic analysis is correct for the synthesis of 2-bromocyclopentanol?



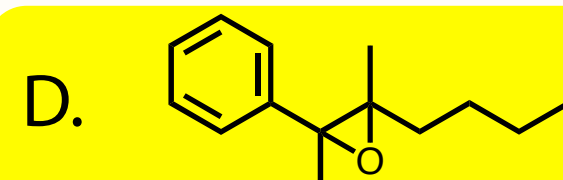
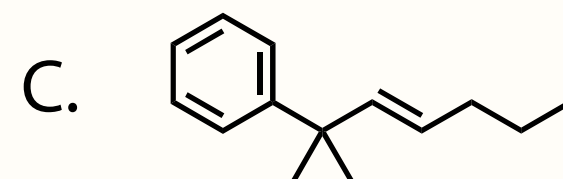
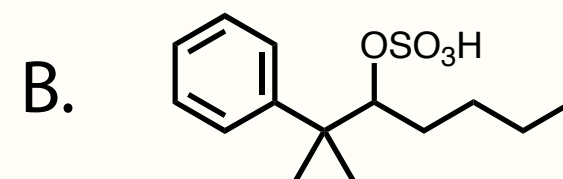
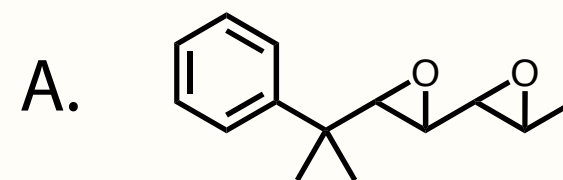
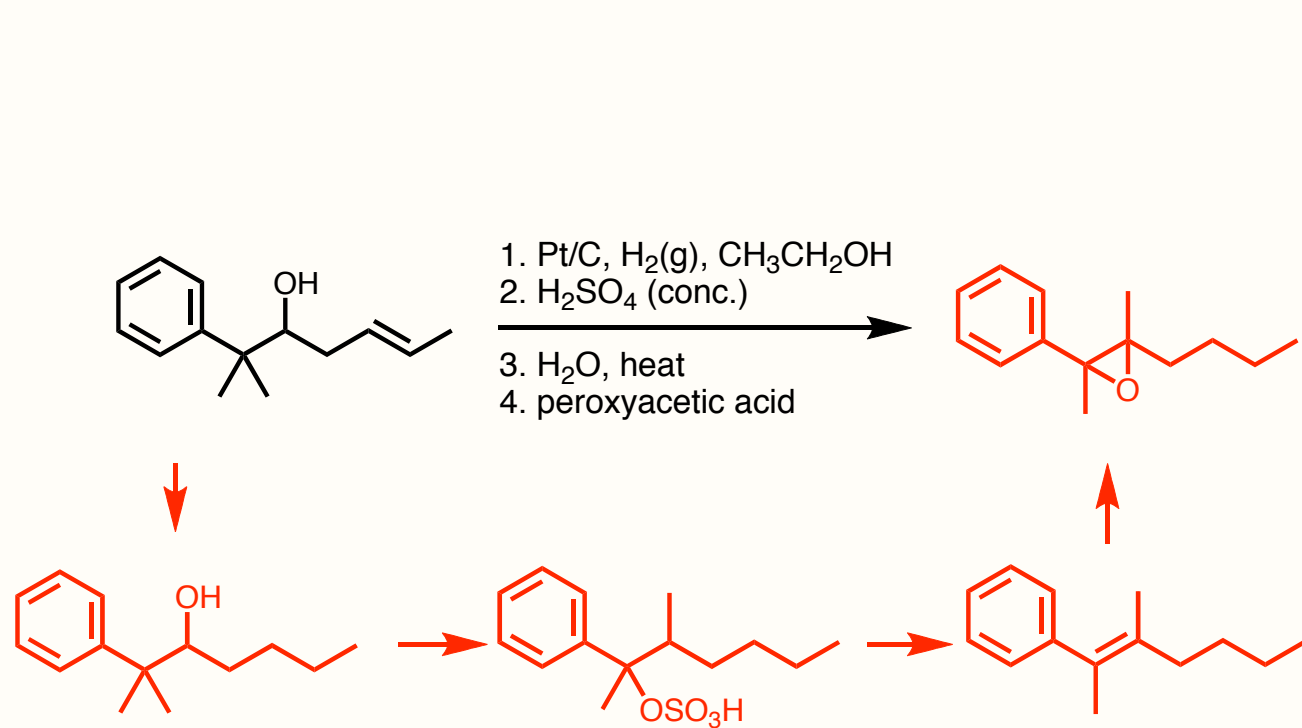
Self Test Question

Devise a retrosynthesis for the synthetic target below.



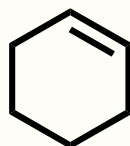
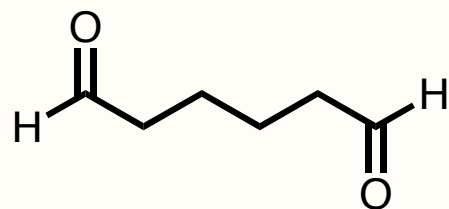
Self Test Question

What is the product of the following series of reactions?



Self Test Question

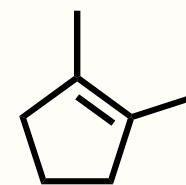
Which starting material could be used to prepare the molecule below? Write out your synthesis. Don't guess.



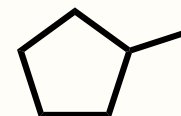
A.



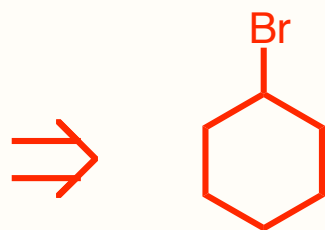
D.



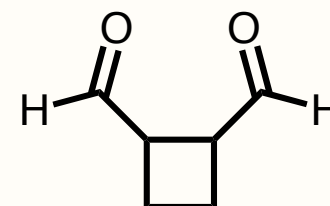
B.



E.



C.



Next Lecture...

Chapter 13: Sections 13.1-13.2 & 13.20-13.22

Quiz & Exam Averages

Quiz 1 = 61%

Quiz 2 = 61%

Quiz 3 = 50%

Quiz 4 = 50%

Midterm Exam = 51%