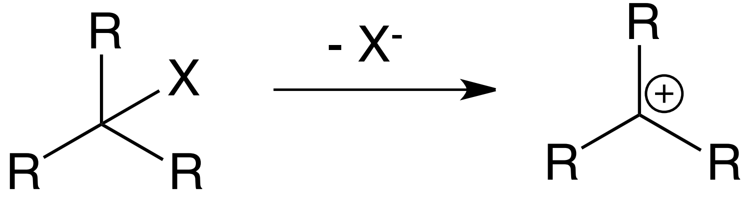
Chemistry of Alkenes

Outline of Topics and Reactions

- Carbocation Structure and Stability
  - Markovnikov's Rule
  - Hammond postulate
  - Carbocation rearrangements
  - Redox Definitions for Organic Chemistry
- Preparation of Alkenes via Elimination
  - Dehydrohalogenation
  - Dehydration
- Reactions of Alkenes
  - Halogenation of alkenes with X_2
  - Halohydrins from HOX (hypohalous acids)
  - Hydration (oxymercuration, hydroboration)
  - Reductive hydrogenation
  - Oxidation to epoxides and alcohols
  - Addition of carbenes (cyclopropane synthesis)
- Stereochemical Considerations

Carbocation stability

- Thermodynamic measurements (i.e. dissociation enthalpies of alkyl chlorides) have been used to confirm carbocation stabilities

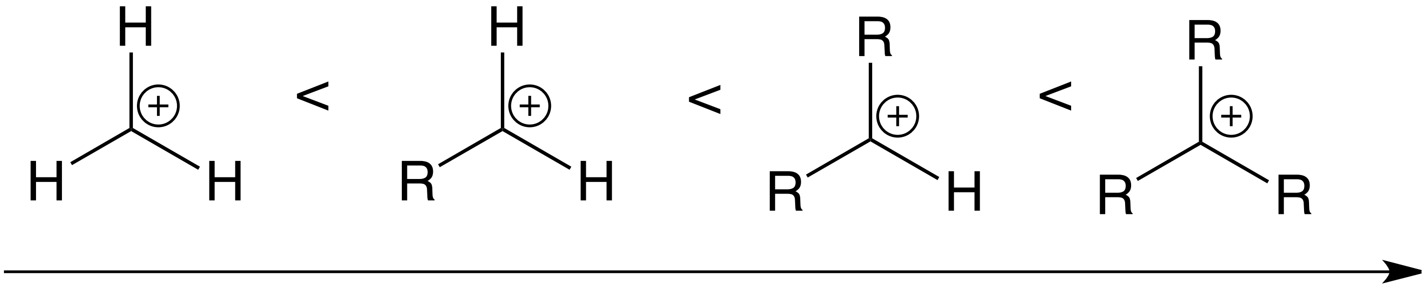


R = H or alkyl

X = Cl
methyl ~ 950 kJ/mol
1^{o} ~ 800 kJ/mol
2^{o} ~ 725 kJ/mol
3^{o} ~ 650 kJ/mol

Carbocation stability

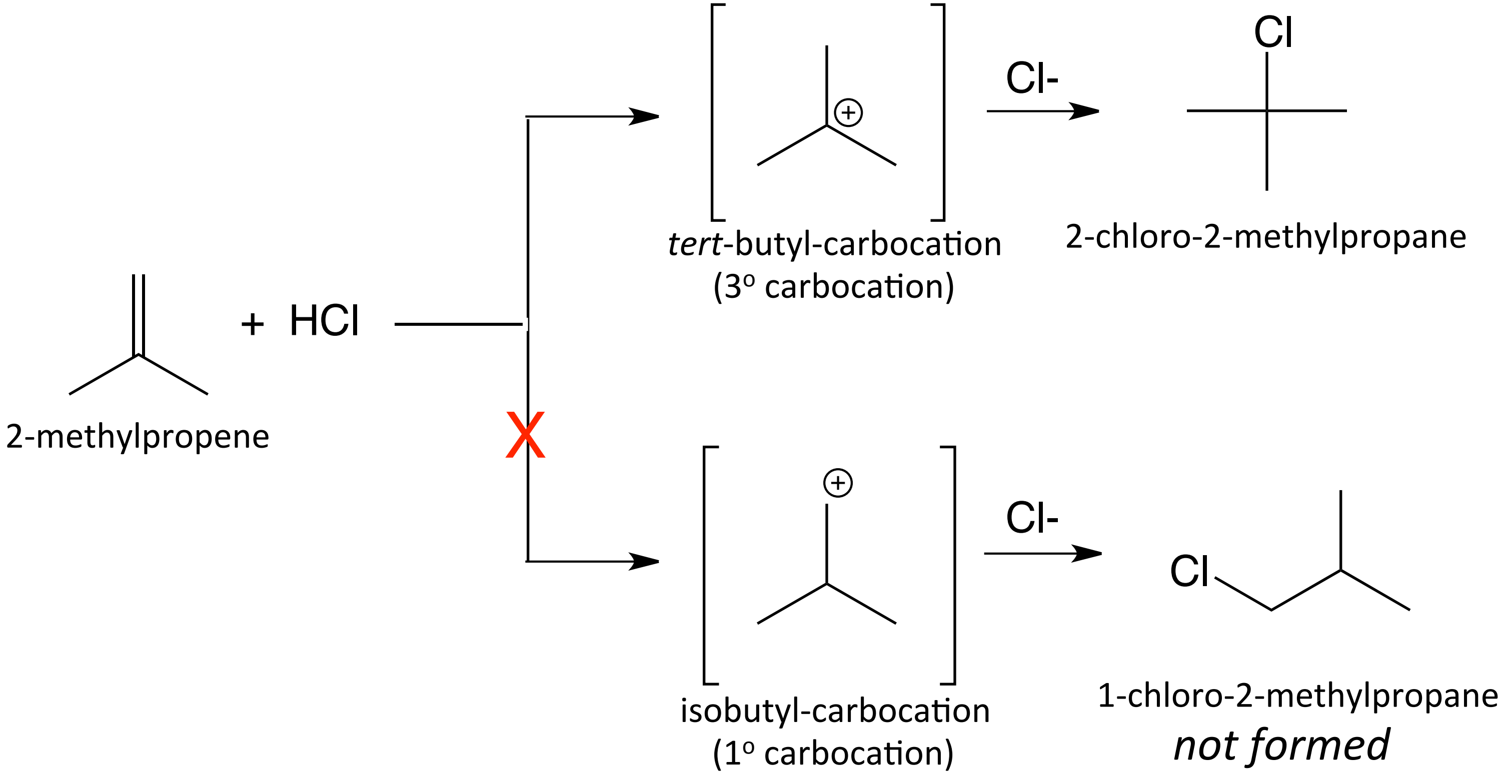
- ***Increased substitution leads to greater carbocation stability***
  - *Inductive effects*: groups larger than H can more easily shift electron density to stabilize +ve charge
  - *Hyperconjugation*: Stability arises from interaction of *p* atomic (or π molecular) orbitals with C-H σ bonds on neighboring atoms. The more alkyl groups, the more possibilities for hyperconjugation to occur



Increasing carbocation stability

Markovnikov's Rule:
"Them that has 'em gets 'em"

- In the addition of HX to an alkene, the H attaches to the carbon atom with fewer alkyl substituents and the X attaches to the carbon with more alkyl substituents
- The most highly substituted carbocation is formed as the intermediate



2-methylpropene

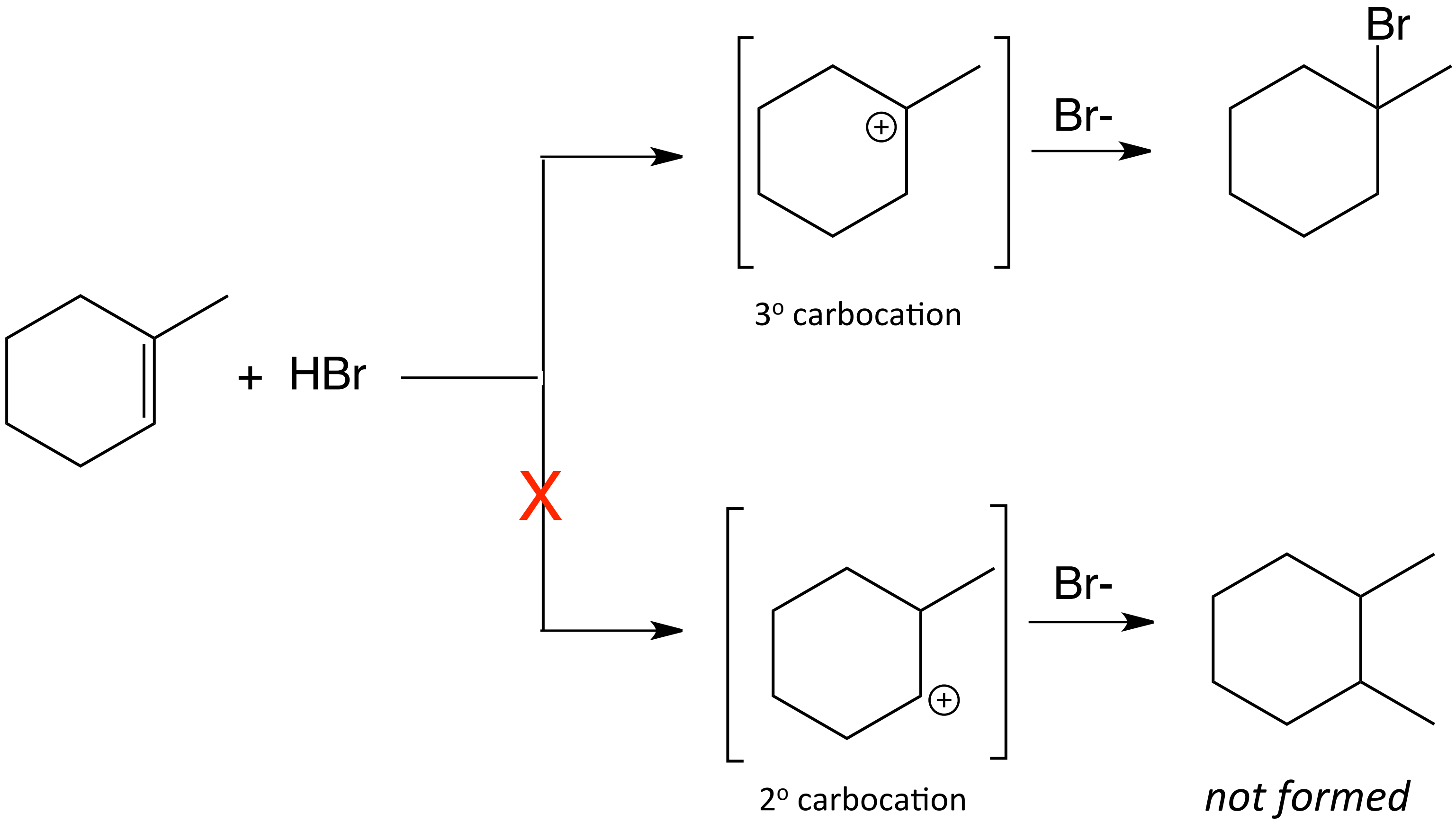
tert-butyl-carbocation
(3° carbocation)

2-chloro-2-methylpropane

isobutyl-carbocation
(1° carbocation)

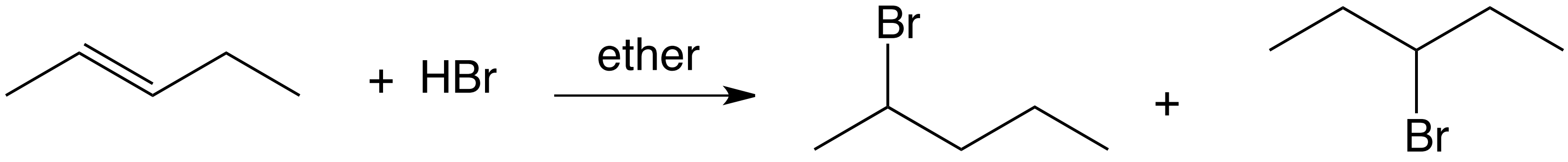
1-chloro-2-methylpropane
not formed

Markovnikov addition of HBr



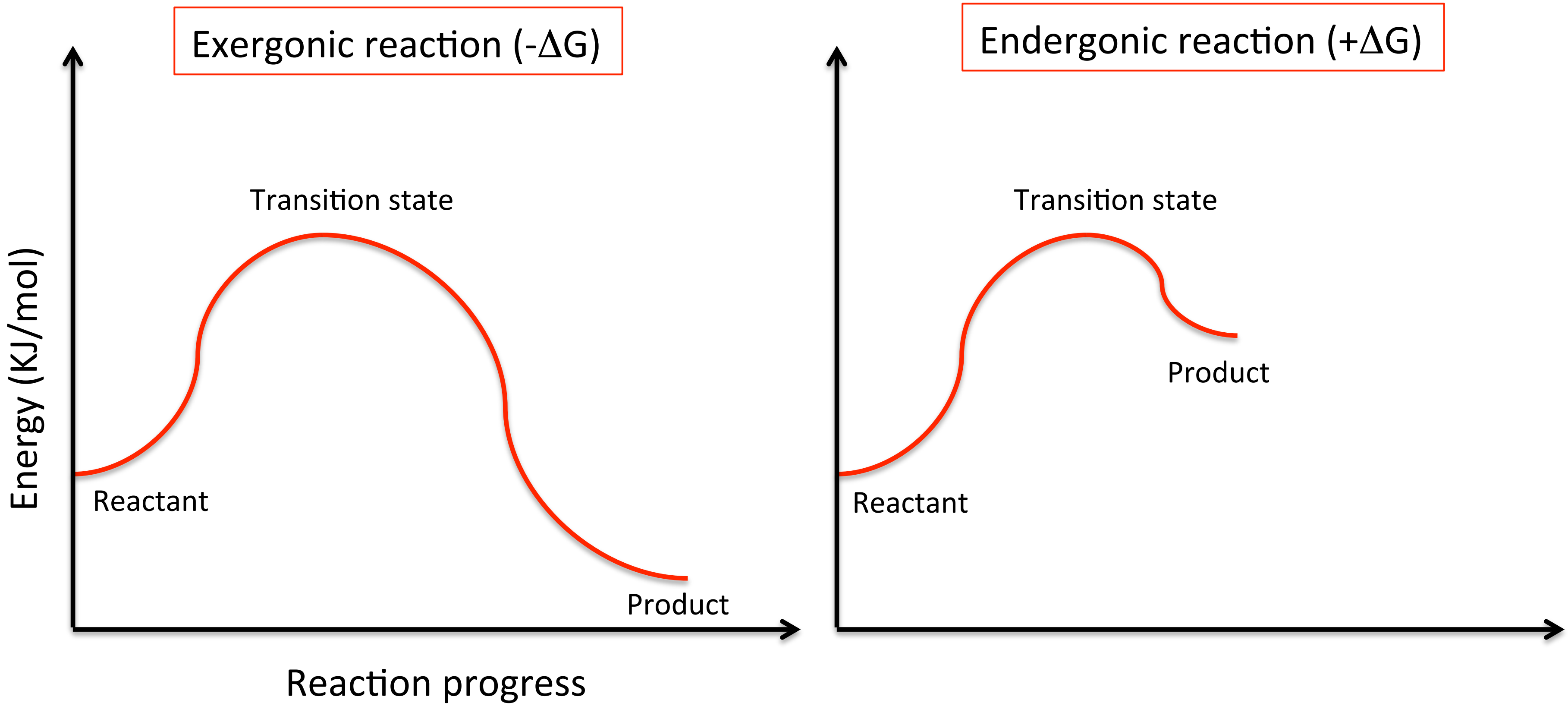
Product mixtures

- When both double bonded carbon atoms have the same degree of substitution, a mixture of addition products results



The Hammond Postulate

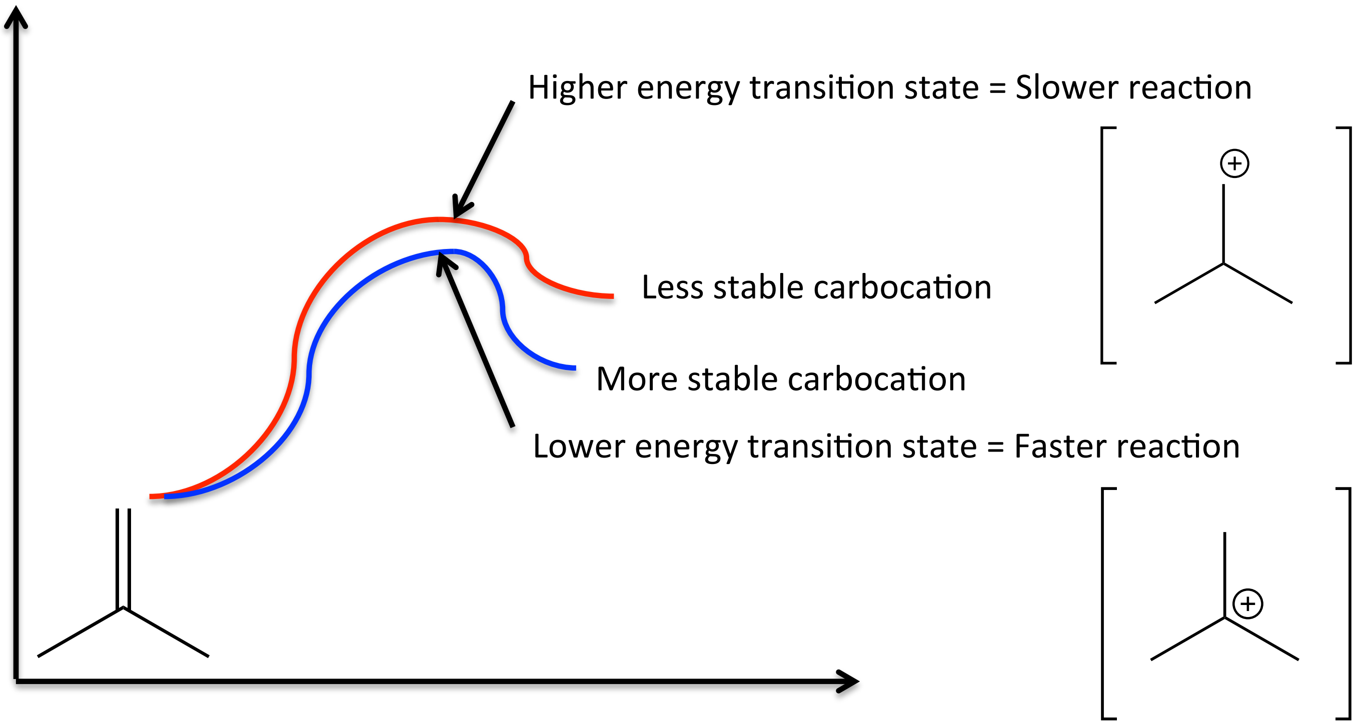
- The ***structure*** of the transition state resembles the structure of the nearest stable species.
  - Transition states for *endergonic steps structurally resemble the products*
  - Transition states for *exergonic steps structurally resemble the reactants*



Exergonic reaction (-ΔG)

Endergonic reaction (+ΔG)

Implications of the Hammond Postulate for electrophilic substitution reactions



Higher energy transition state = Slower reaction

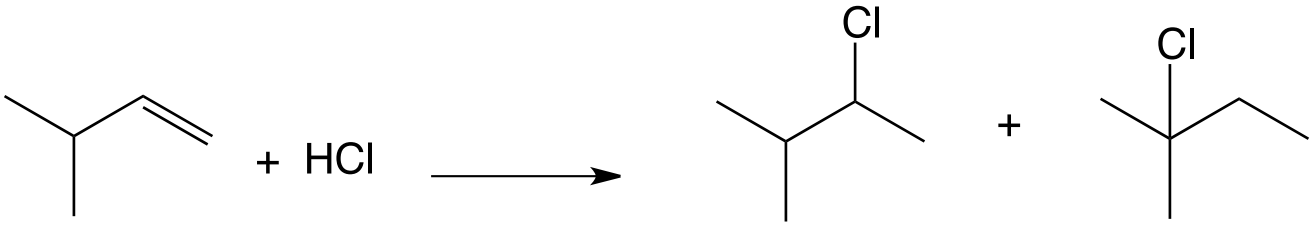
Less stable carbocation

More stable carbocation

Lower energy transition state = Faster reaction

Mechanistic evidence for electrophilic addition reactions: Carbocation rearrangements

- F.C. Whitmore (Penn State) 1930s
- Product mixtures also resulting when not expected
- Carbocation intermediate undergoes rearrangement to form a more stable species



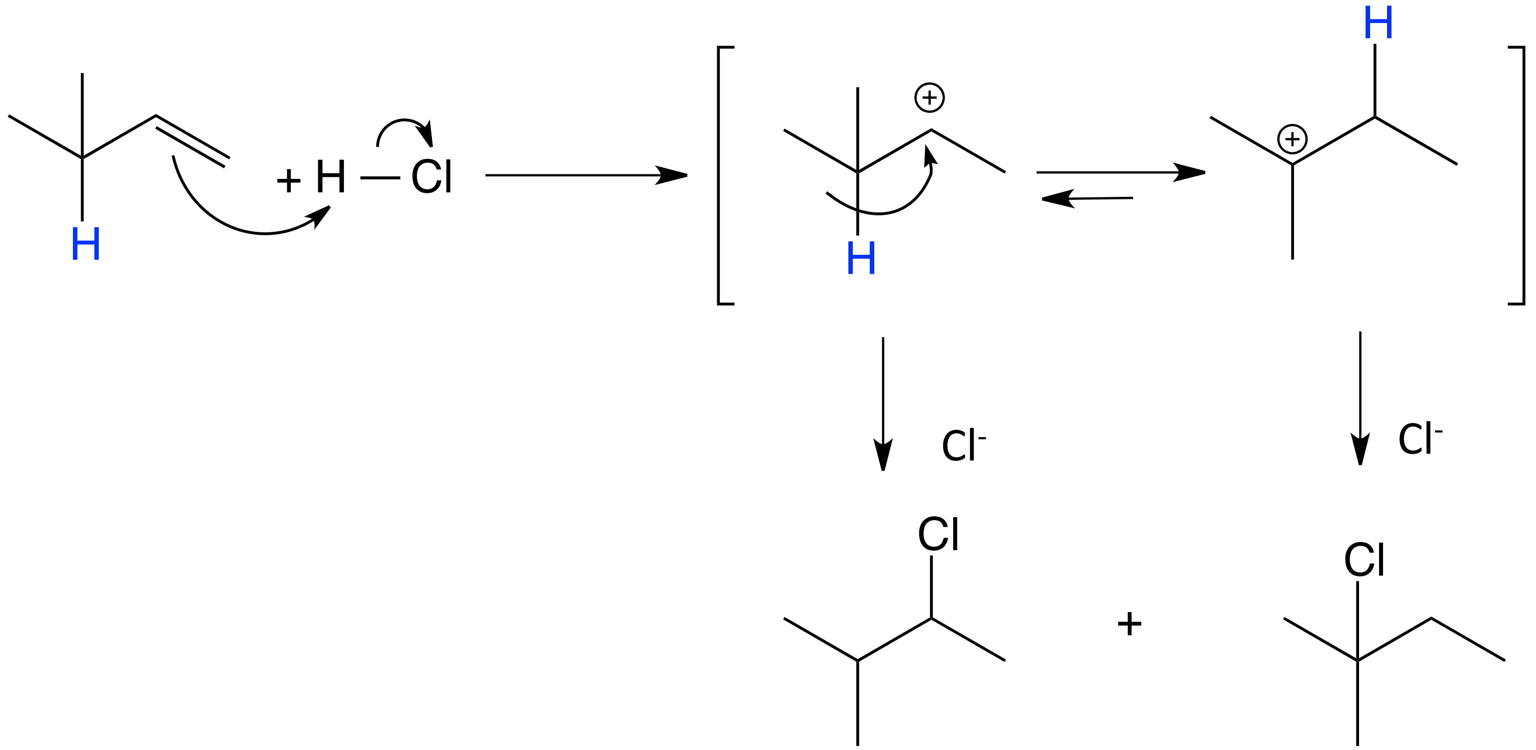
3-methyl-1-butene

2-chloro-3-methylbutane 2-chloro-2-methylbutane

~ 50% each

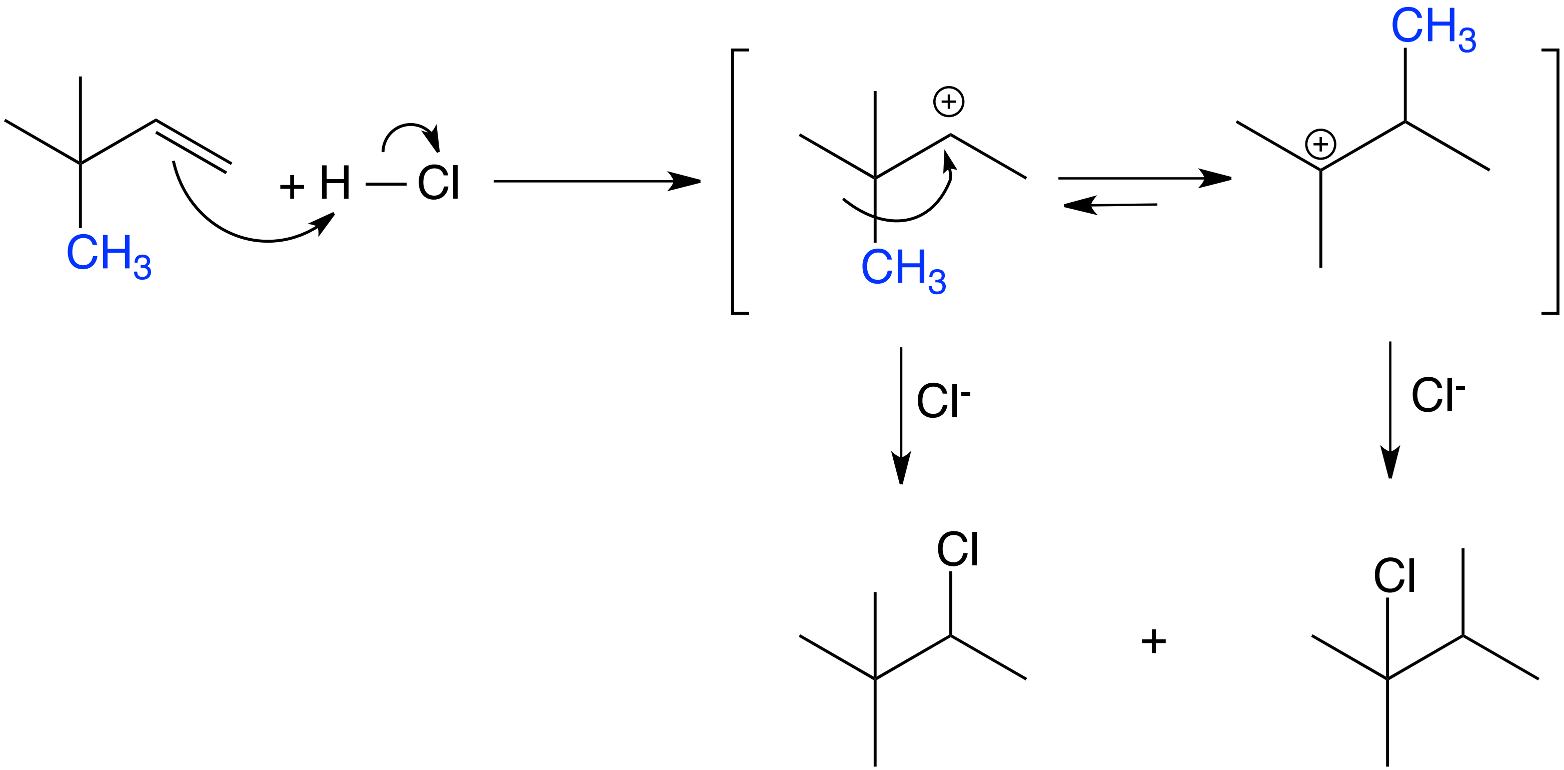
Hydride Shift

- Rearrangement reaction
- Hydride ion (H:$^-$) moves over 1 carbon atom
- Formation of a more stable (3^o) carbocation



Alkyl Shift

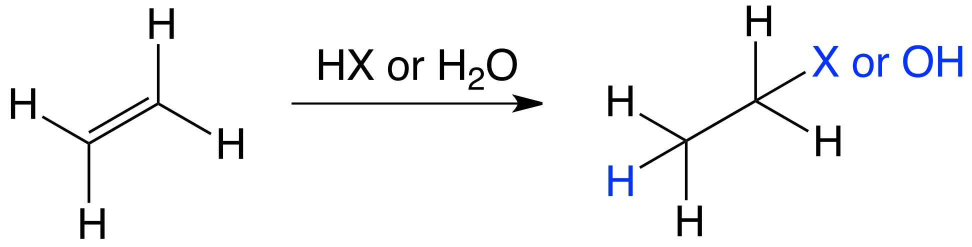
- Rearrangement reaction
- Methide ion ($CH_3:^-$) moves over 1 carbon atom
- Formation of a more stable (3^o) carbocation



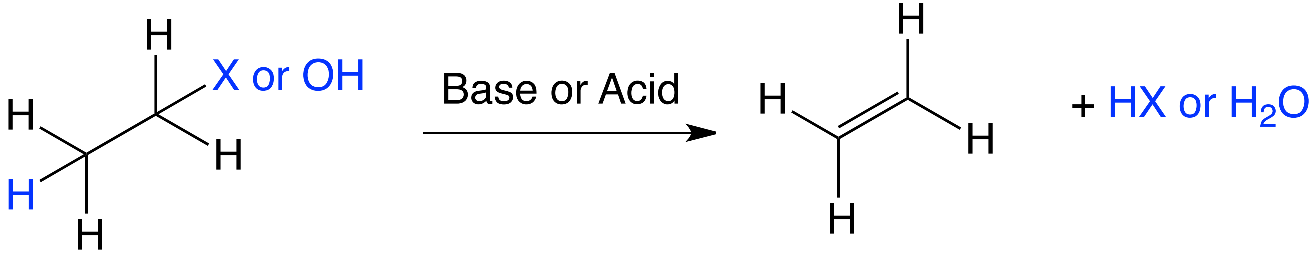
Alkene preparation *via* elimination

- Elimination is opposite of addition reaction
- Dehydrohalogenation (laboratory synthesis)
- Dehydration (lab or biological systems)

Addition

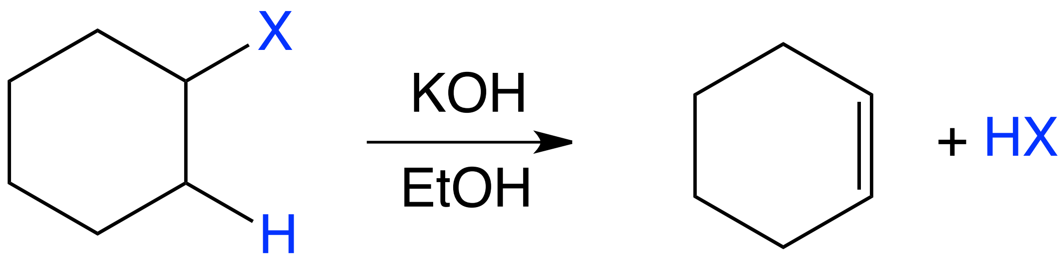


Elimination



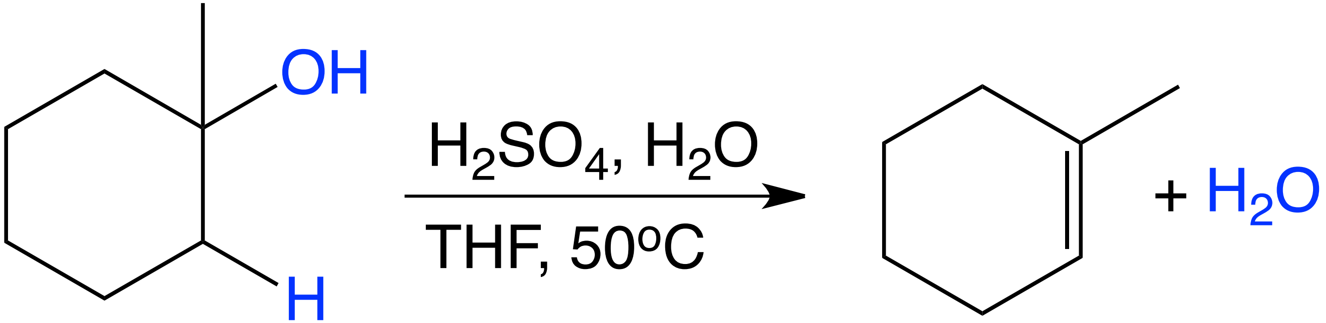
Dehydrohalogenation

- Loss of HX from an alkyl halide
- Base catalyzed
- Three mechanisms (E1, E2, E1cB) differ in the rates of C-H and C-X bond breaking
- Zaitsev's Rule: Base-induced eliminations give most substituted alkene product

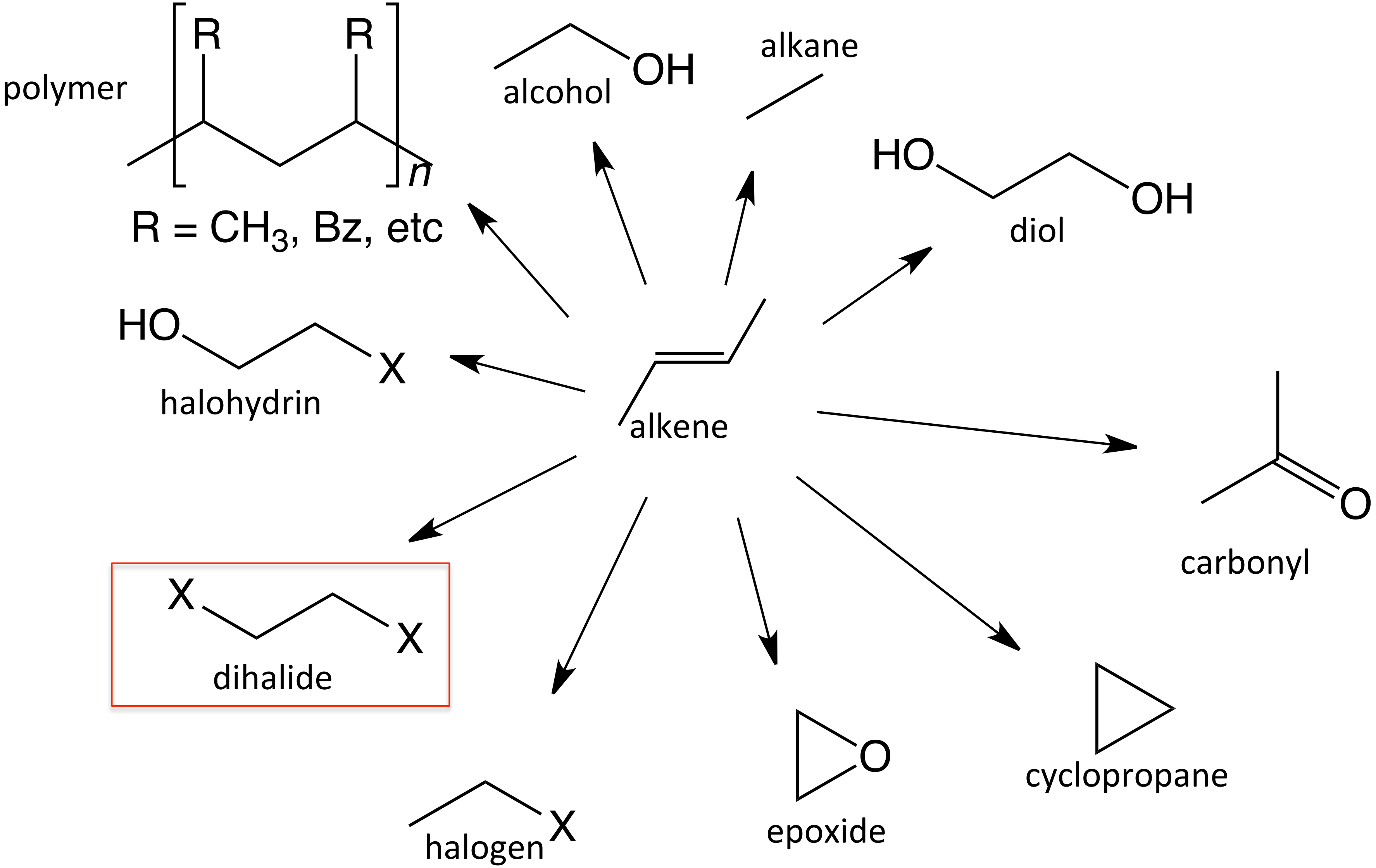


Dehydration

- Loss of H_2O from an alcohol
- Often acid catalyzed, with H_2O participating as a base
- THF = moderately polar, aprotic solvent
- In biological systems these occur to form α, β unsaturated carbonyl compounds



Halogenation



polymer

R = CH_3, Bz, etc

alcohol

alkane

diol

halohydrin

alkene

carbonyl

dihalide

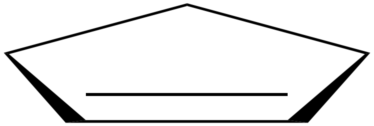
halogen

epoxide

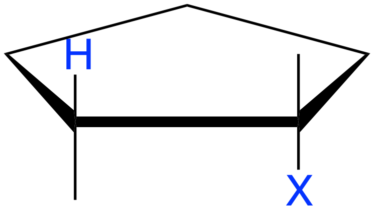
cyclopropane

Syn vs *Anti* Addition Stereochemistry

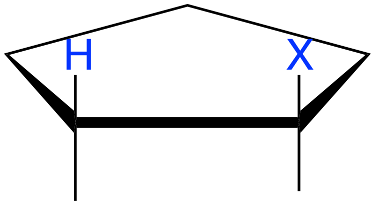
- Like *cis* and *trans* for single bonds
- Used to describe additions of X_2, HX, H_2O, etc.



Cyclopentene (planar)



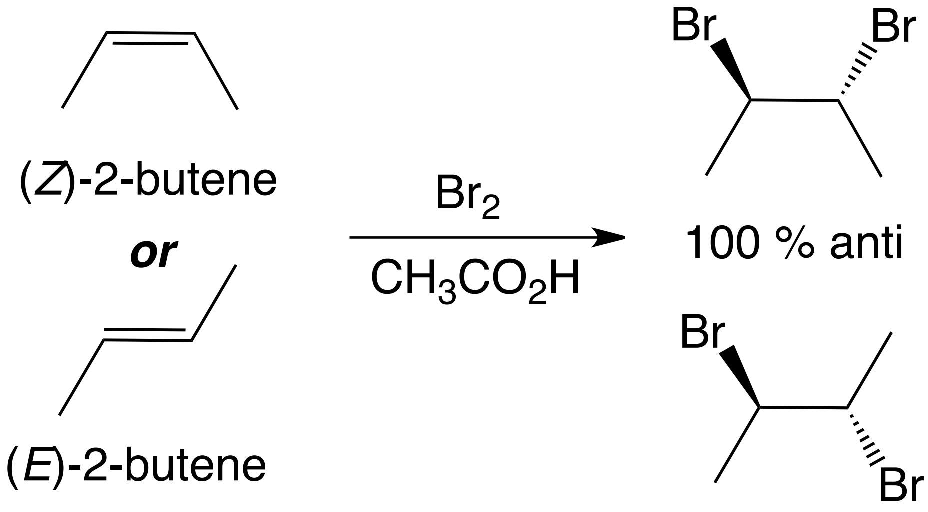
anti (*trans*)



syn (*cis*)

Halogenation of Alkenes to form 1,2-dihalides

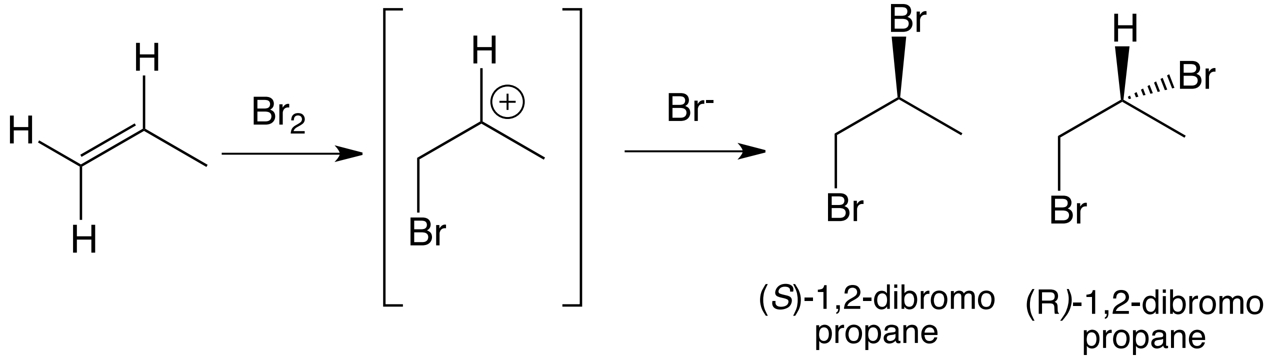
- Halogens Cl_2 and Br_2 rapidly add to alkenes
- Heterolytic (non-radical) process
- Used to make PVC
- Electrophilic reaction mechanism does not explain 100% *trans* stereochemical outcome
- *Anti*-stereochemistry = Halogen atoms add from opposite faces of the double bond (top and bottom)
- Halonium (X^+) intermediate



Carbocation vs. Bromonium ion: Effects on stereoselectivity

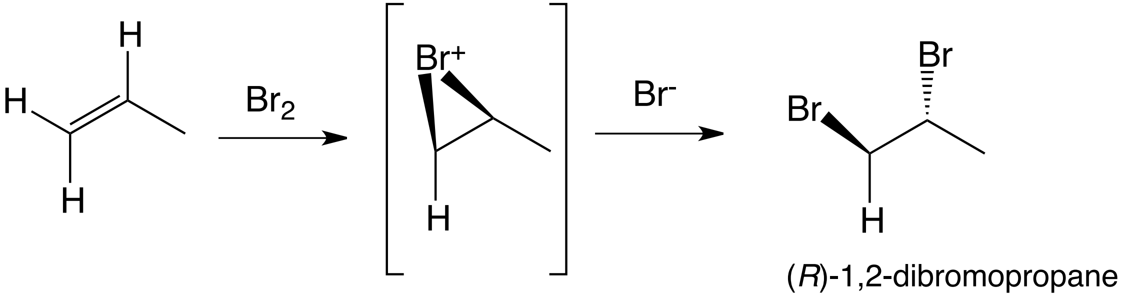
Planar carbocation

- Attack by Br- possible from either face of sp^2 carbon
- Results in a mixture of *syn* and *anti* products

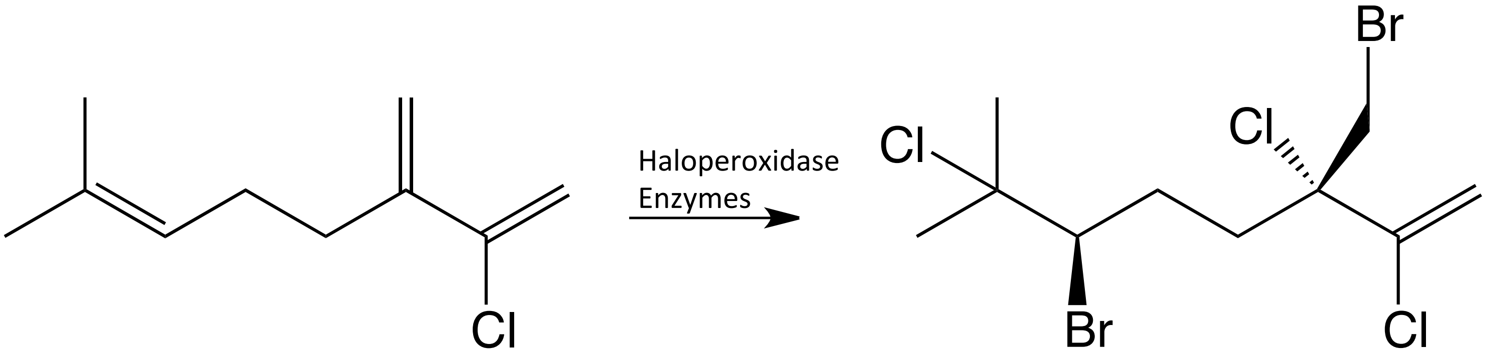


Tetrahedral bromonium ion

- Attack by Br- only possible from opposite face of sp^3 carbon
- Results in 100% *anti* product



Halogenation in nature



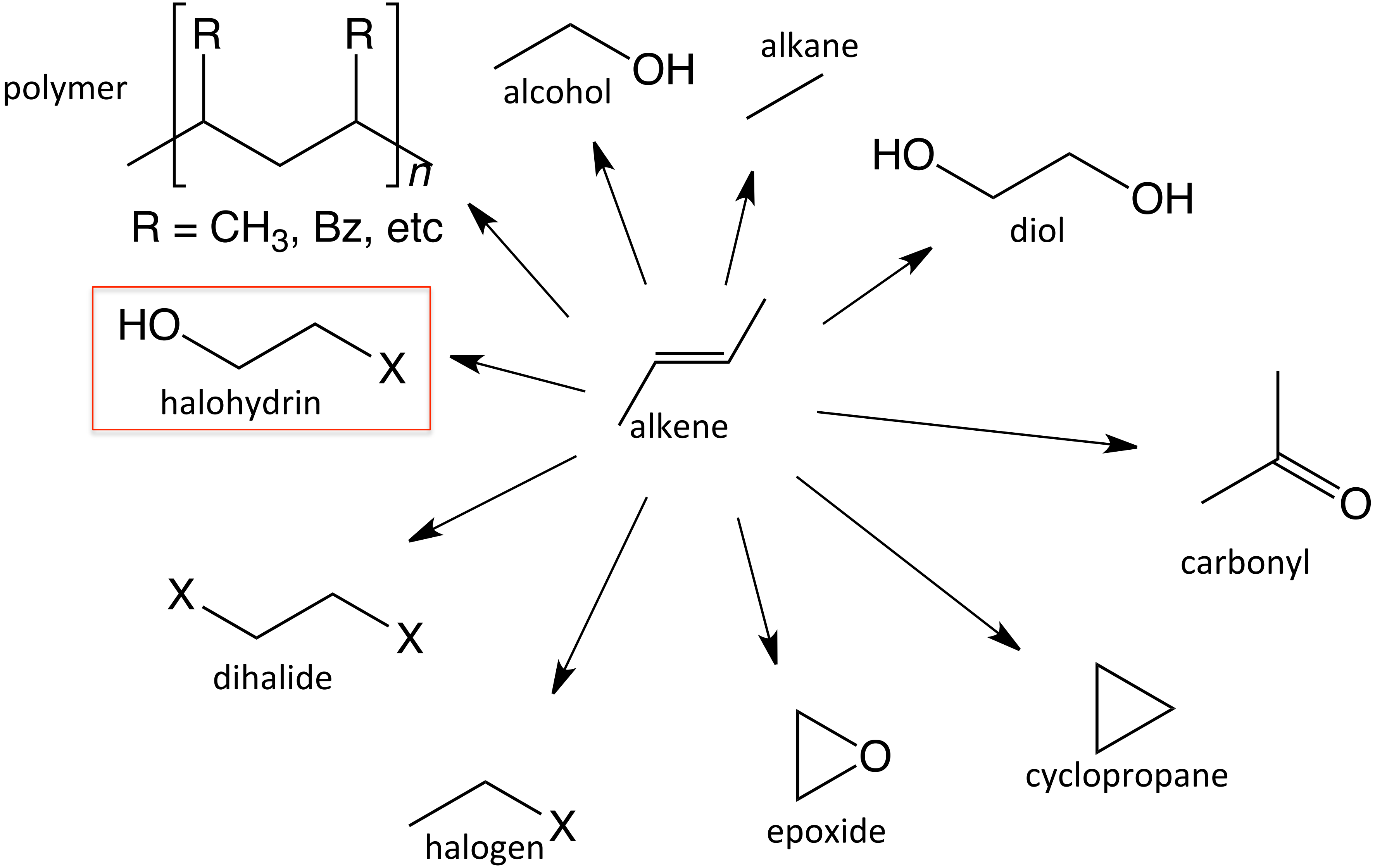
Chlorinated monoterpene isolated from red alga

Halomon - an anticancer polyhalogenated monoterpene (J. Faulkner, 1974)

Portieria honemannii

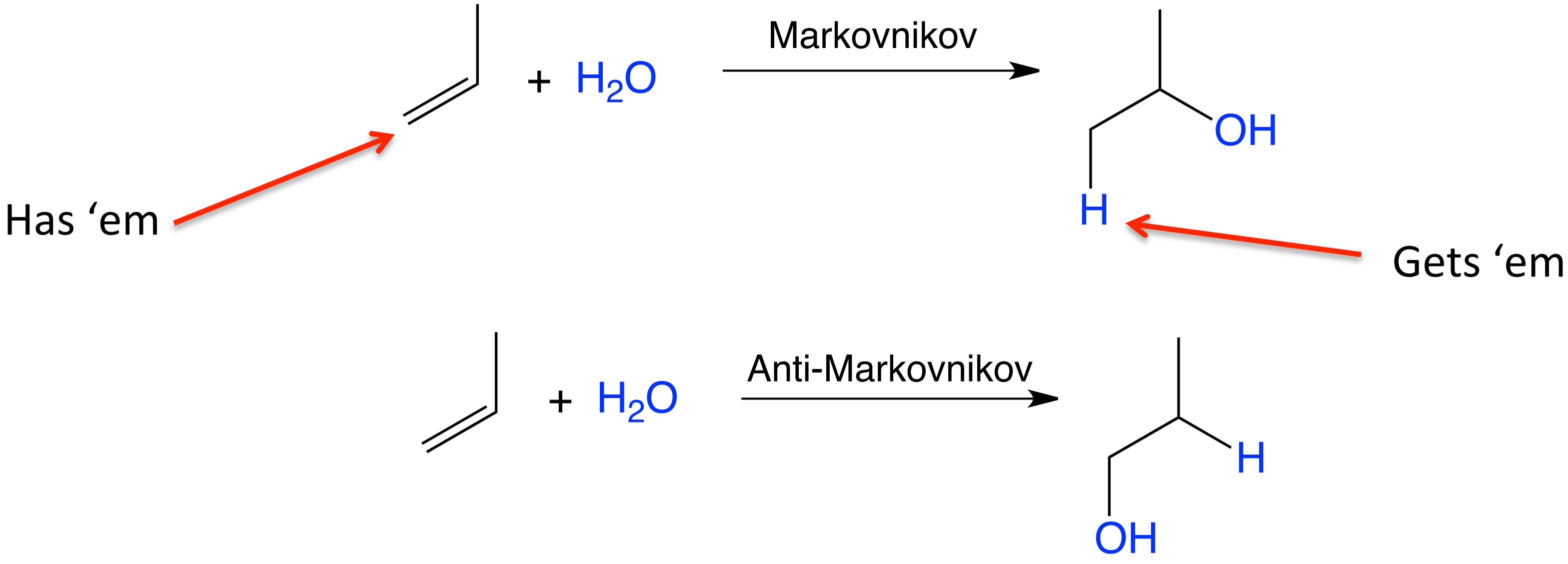
- Exclusively marine derived
- Enzymes use H_2O_2 to oxidize Br- and Cl- to Br+ and Cl+ ions
- 1 electrophilic addition of Br^+ and 1 of Cl^+
- 1 nucleophilic additions of Br^- and 1 of Cl^-

Halohydrin formation



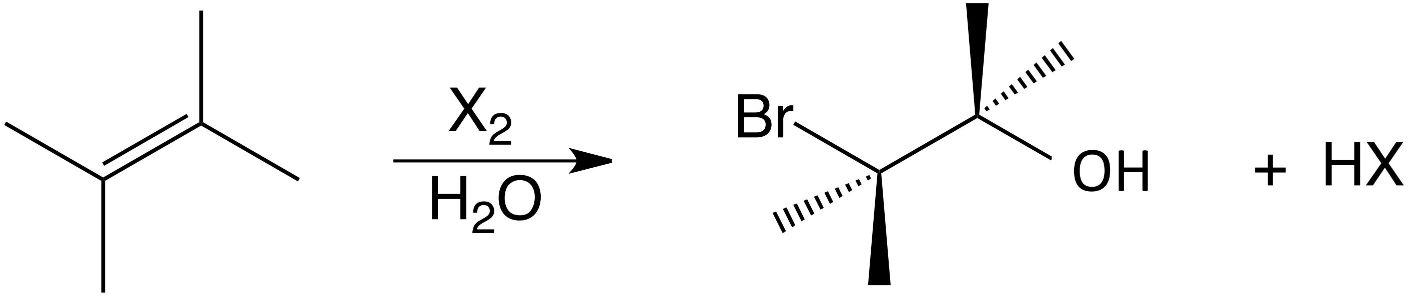
Markovnikov addition of H_2O

- OH to most substituted carbon
- H to least substituted C
- “Them that has ‘em gets ‘em” still applies
- Regiochemistry



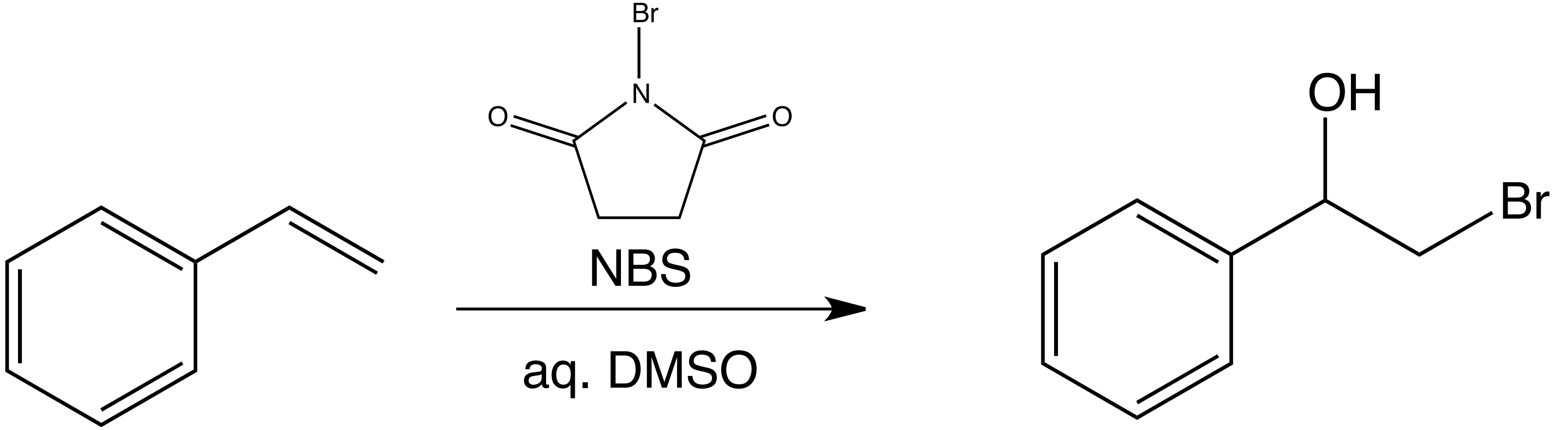
Halohydrins from alkenes: Addition of H-OX

- Electrophilic addition reaction
- Hypohalous acids (HO-Cl and HO-Br)
- 1, 2-haloalcohol (aka halohydrin) products
- Alkene reacts with X_2 in H_2O
- H_2O outcompetes X^- as nucleophile
- Halonium ion intermediate gives *anti* product



Bromohydrin Formation in Practice

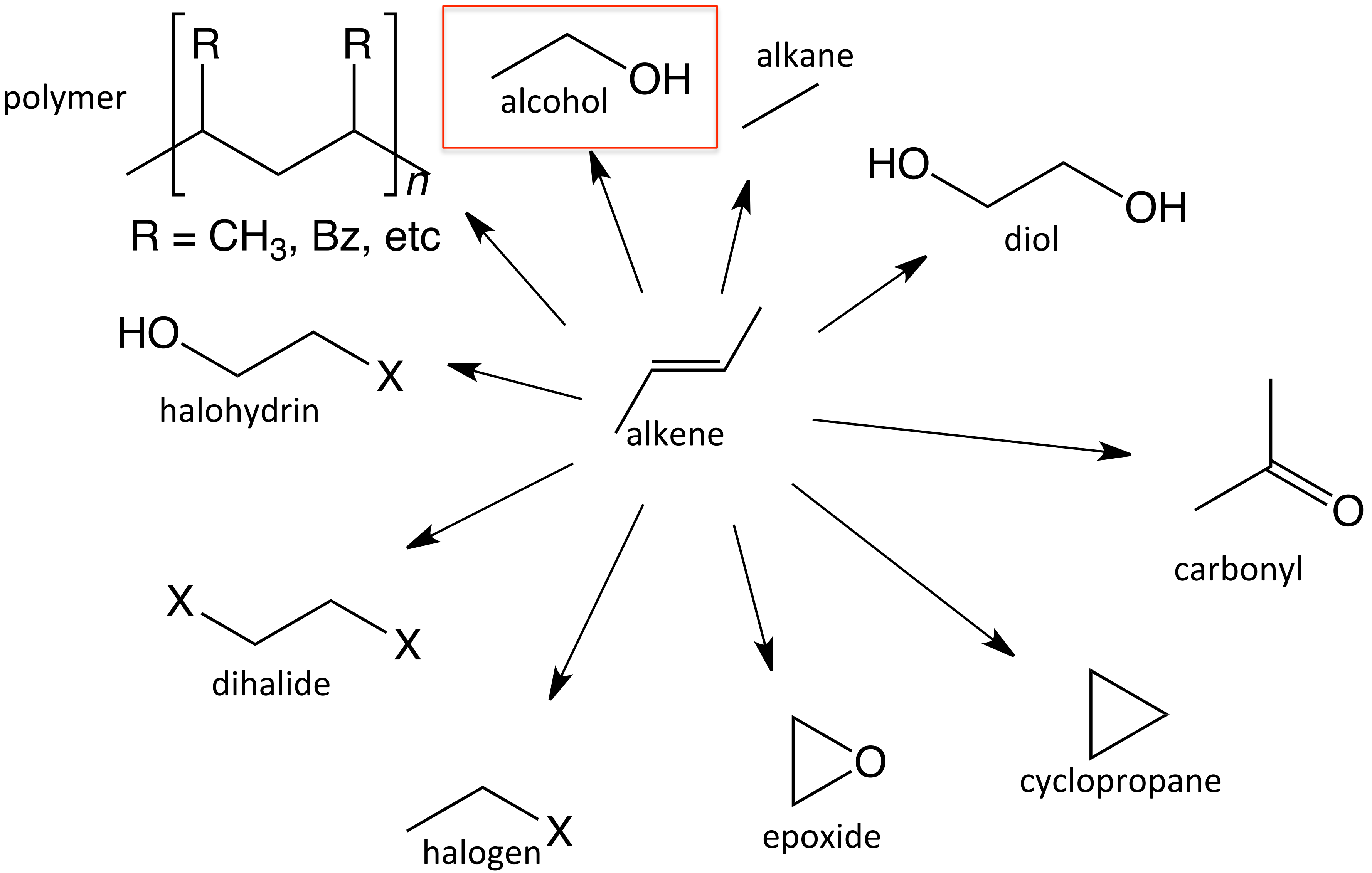
- In practice, few alkenes are water soluble
- Unsymmetrical alkenes give Markovnikov products
- *Anti* arrangement of Br and OH
- Bromoperoxidase enzymes also used
- Common solvents used = aqueous DMSO or acetone
- *N*-bromosuccinimide (NBS)
    - stable, easily handled, slowly decomposes in water to give Br_2 at a controlled rate
    - NBS reactions also give trans products due to bromonium intermediate



styrene

2-bromo-1-phenylethanol
(70%)

Hydration



polymer

R = CH_3, Bz, etc

alcohol

alkane

diol

halohydrin

alkene

carbonyl

dihalide

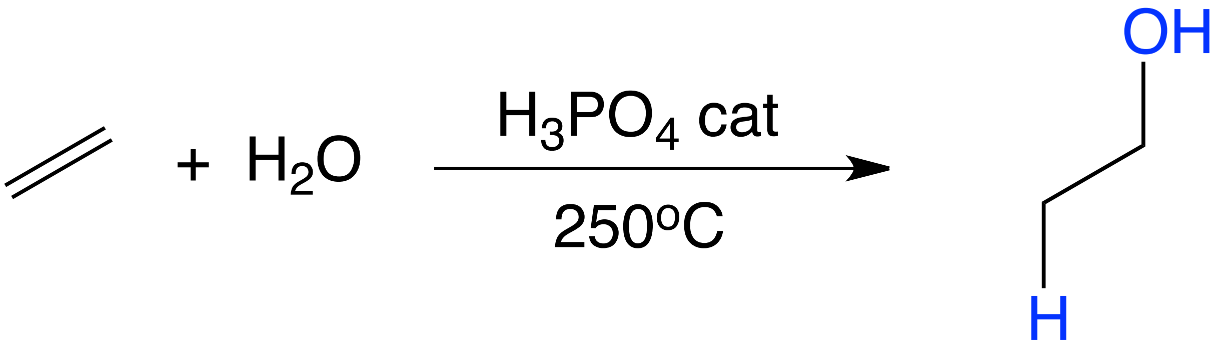
halogen

epoxide

cyclopropane

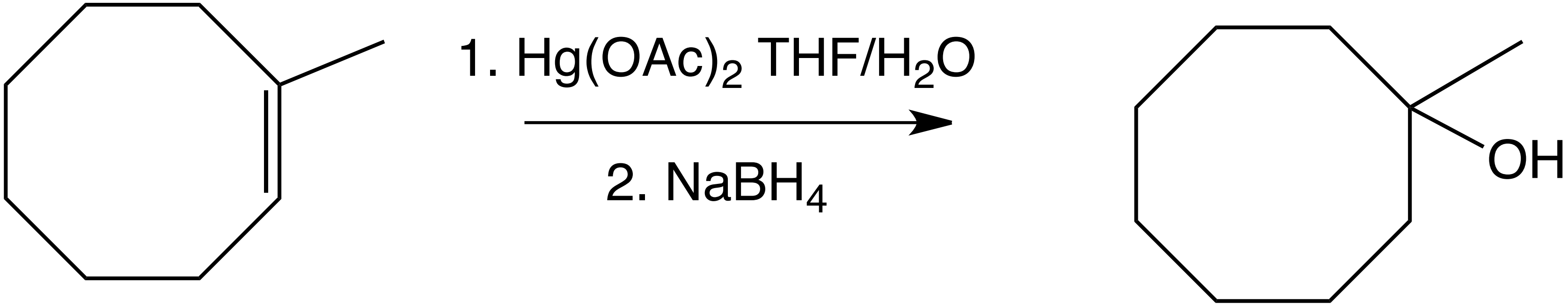
Acid-catalyzed alkene hydration

- Simplest, least expensive way to produce alcohols
- Best performed in large-scale industry setting
- Little use in lab setting due to high temps/strong acid conditions (H_2SO_4 also works)
- 300,000 tons of ethanol produced yearly from ethylene this way



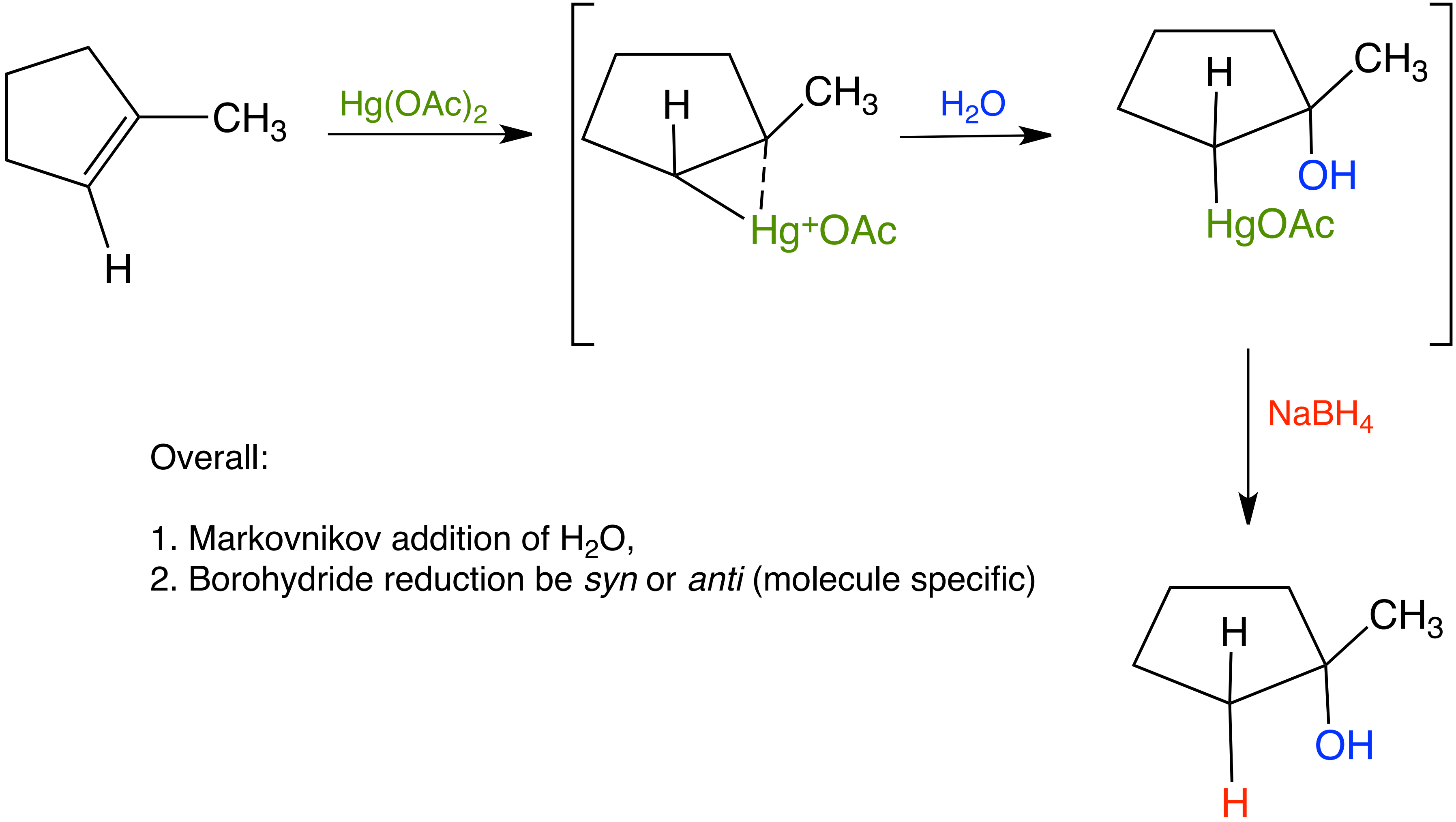
Oxymercuration/Demercuration

- Suitable for lab-scale syntheses of alcohols
- Electrophilic addition of alkene to Hg^{2+}
- Organomercury intermediate (oxidation)
- Sodium borohydride ($NaBH_4$) is a reducing agent
- No carbocation rearrangements
- Can be *syn* or *anti* addition depending on borohydride complex
- Follows Markovnikov's rule for addition of water:
  (OH to most substituted carbon, H to least substituted C)



1-methylcyclooctene

Mechanism of Oxymercuration/Demercuration

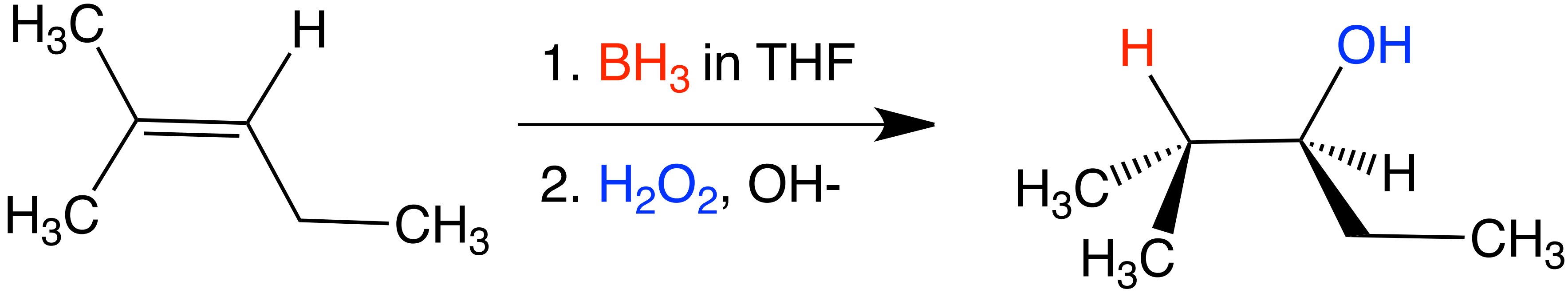


Overall:

1. Markovnikov addition of H_2O,
2. Borohydride reduction be *syn* or *anti* (molecule specific)

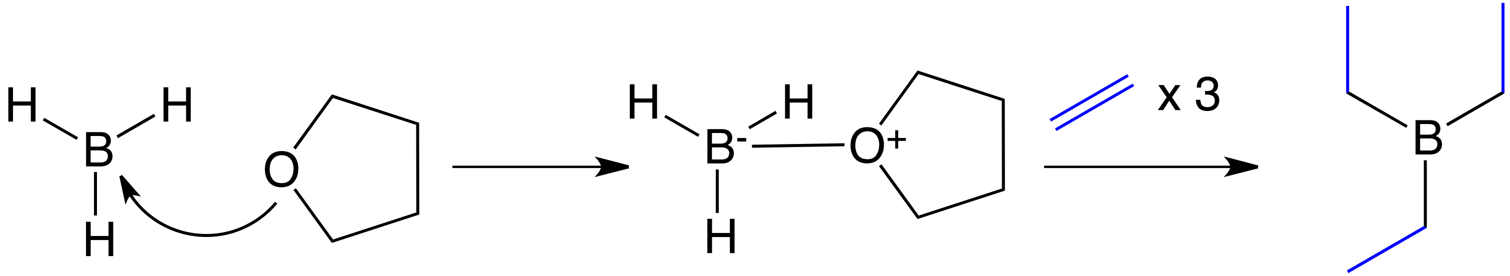
Hydroboration/Oxidation

- 1957 discovered by H.C. Brown (1979 Nobel Laureate)
- Organoborane intermediate
- Anti-Markovnikov (regiochemistry)
  - OH adds to *least* substituted carbon of alkene
- *Syn* hydration (stereochemistry)
  - H and OH addition are *cis* to one another

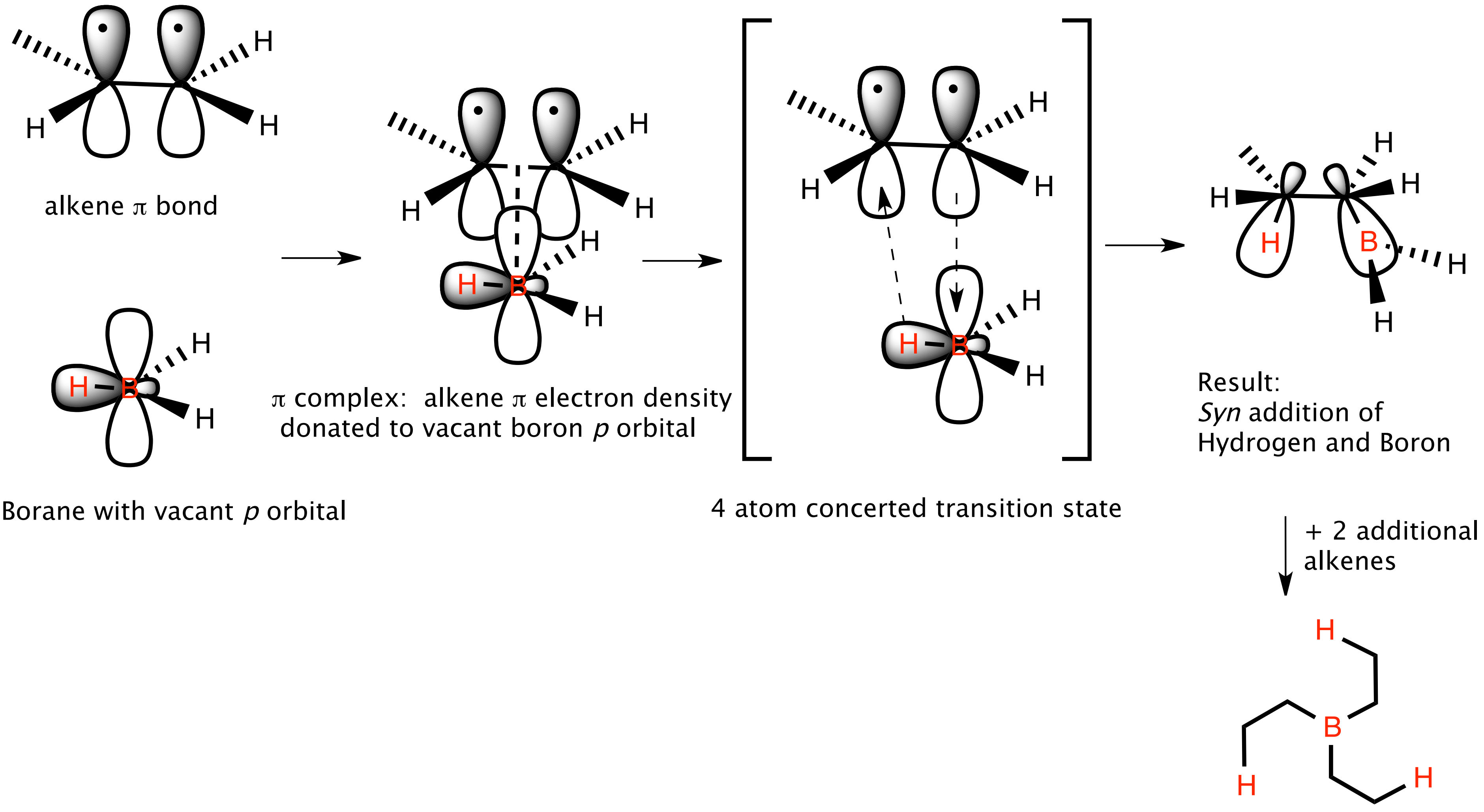


Step 1: Hydroboration

- Borane is a reactive Lewis acid with only 6 electrons in valence shell
- Forms stable complex with Lewis basic solvents (ethers, THF, for example) to complete octet
- Three equivalents of alkene readily replaces the solvent complex to form trialkylborane



Hydroboration mechanism



alkene π bond

Borane with vacant *p* orbital

π complex: alkene π electron density donated to vacant boron *p* orbital

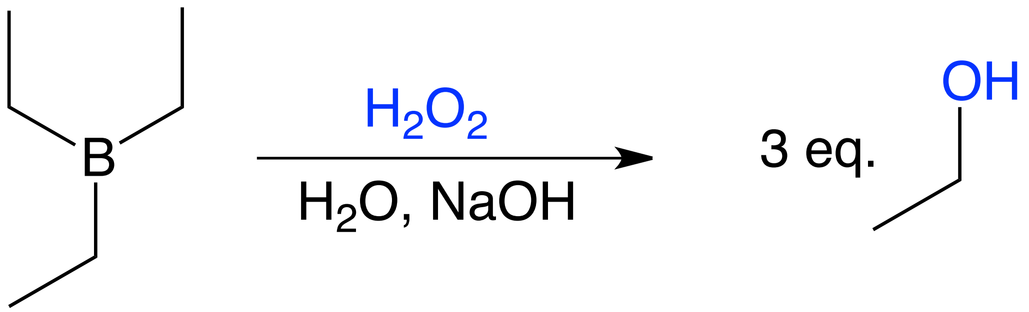
4 atom concerted transition state

Result:
Syn addition of
Hydrogen and Boron

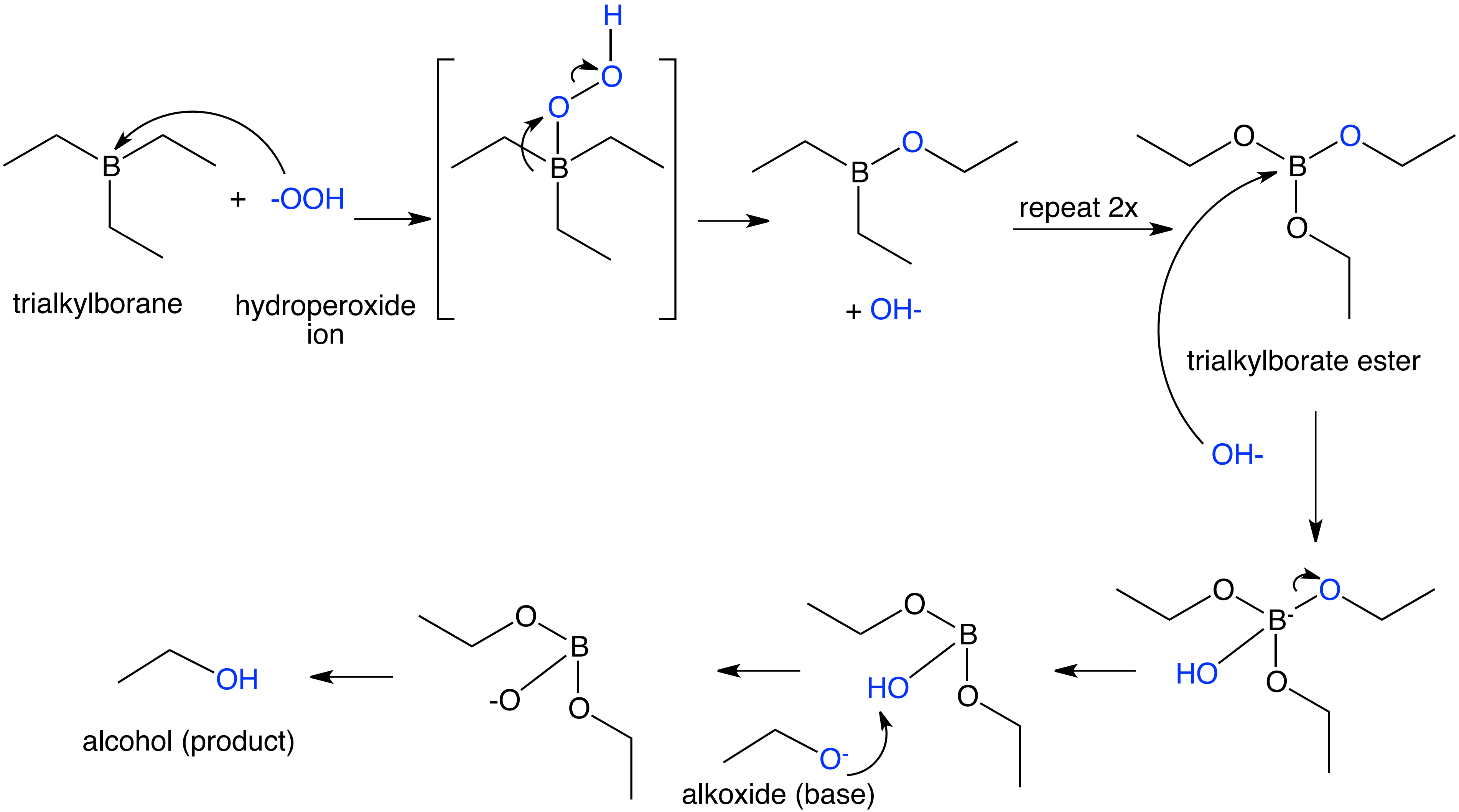
+ 2 additional alkenes

Step 2: Oxidation

- Oxidation occurs with hydrogen peroxide (H_2O_2) in aqueous base
- Three equivalents of alcohol produced from one equivalent of borane

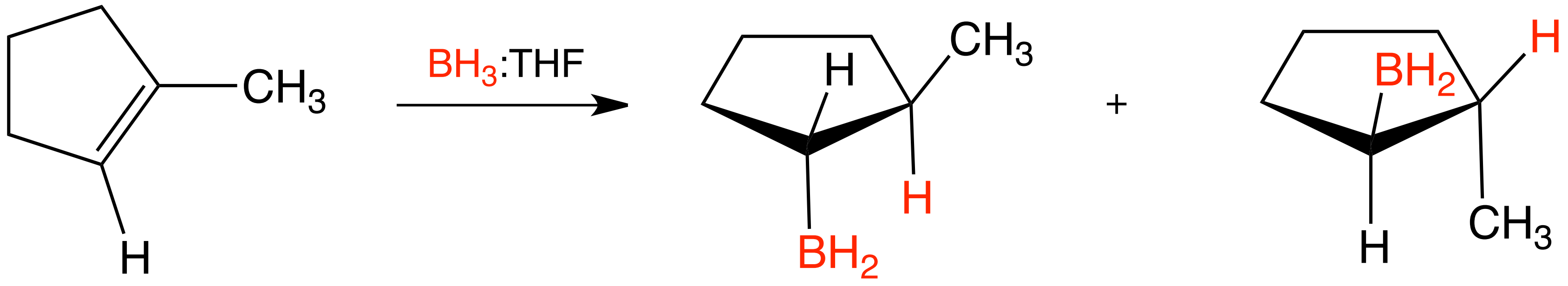


Oxidation mechanism



Overall Hydroboration/Oxidation reaction is anti-Markovnikov with syn addition of water

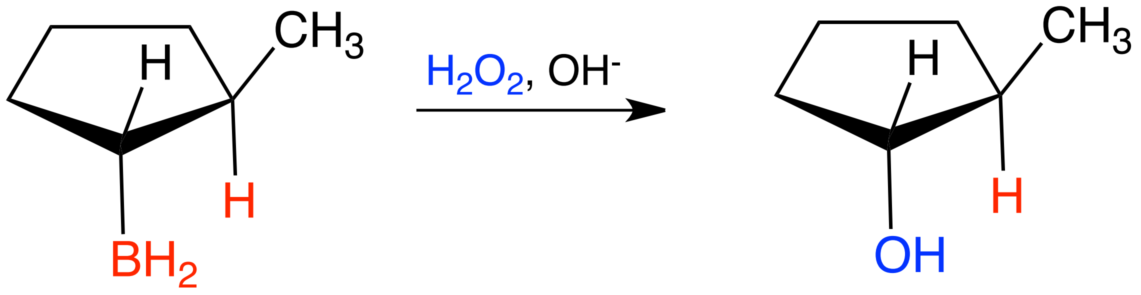
Hydroboration: Anti-Markovnikov and *syn* addition of Hydrogen and Boron



((1*R*,2*R*)-2-methylcyclopentyl)borane

((1*S*,2*S*)-2-methylcyclopentyl)borane (enantiomer)

Oxidation: Boron group is replaced by OH, configuration is retained

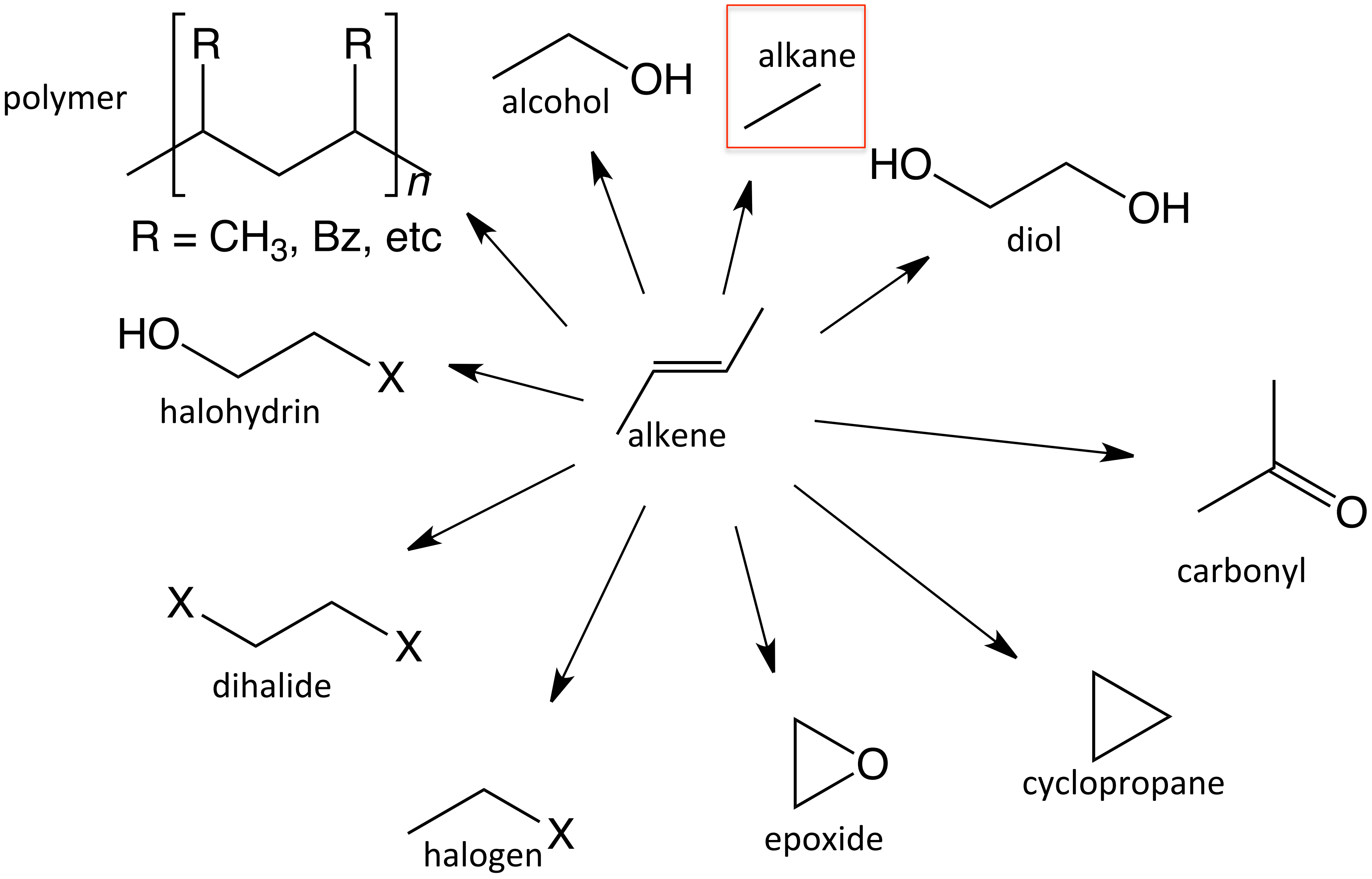


(+ enantiomer)

Comparison of Alkene Hydration Procedures

- **Acid-catalyzed hydrolysis**: Markovnikov addition, reversible, rearrangements possible
- **Oxymercuration/Demercuration**: Markovnikov addition, *syn* or *anti* addition depending on $NaBH_4$ complex exact circumstances, no rearrangements possible
- **Hydroboration/Oxidation**: Anti-Markovnikov, *syn* addition OF H_2O no rearrangements possible

Hydrogenation (aka alkene reduction)



Review of Organic ***Reduction***

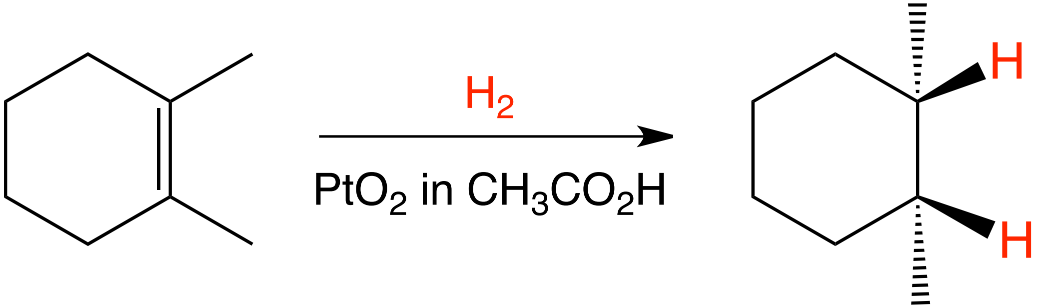
- General chemistry definition of reduction = ***gain of electrons***
- Organic chemistry definition of reduction = gain of ***electron density*** by carbon

- bond ***formation*** with ***less*** electronegative atom (usually H)

- or by bond ***breaking*** with a ***more*** electronegative atom (usually N, O or halogen)

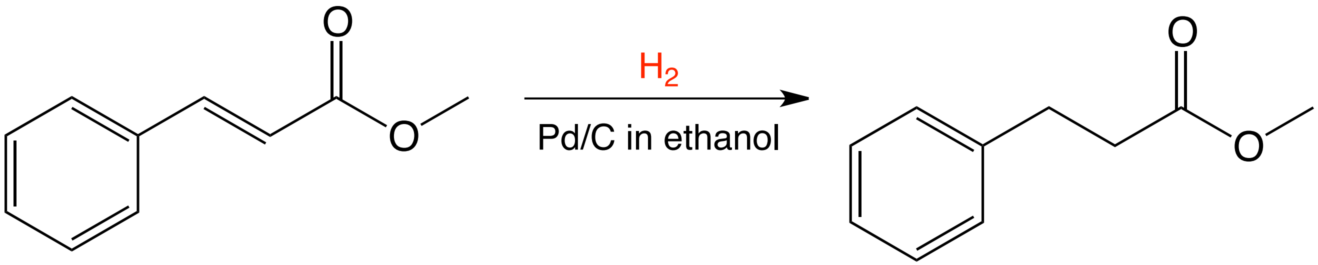
Reduction *via* Hydrogenation

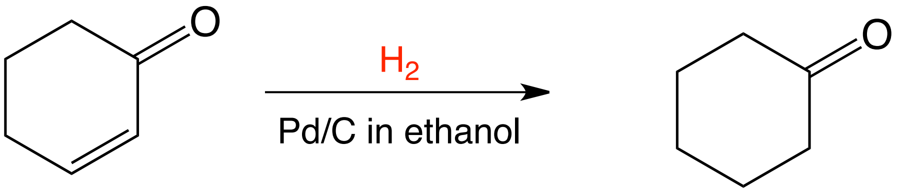
- Reduction = gain of electron density by a carbon atom
- H_2, formic acid, borohydride and aluminum hydride reagents, NADPH are common reducing agents
- Metal catalysts are often required (e.g. Pd, Pt, Ni, Cu, with H_2 and formic acid)
- Heterogeneous catalysis: Occurs a a particle (e.g. a carbon support like Pd/C)
- *Syn* stereochemistry

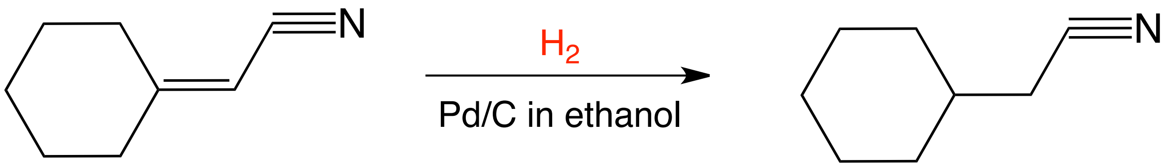


Catalytic Hydrogenation

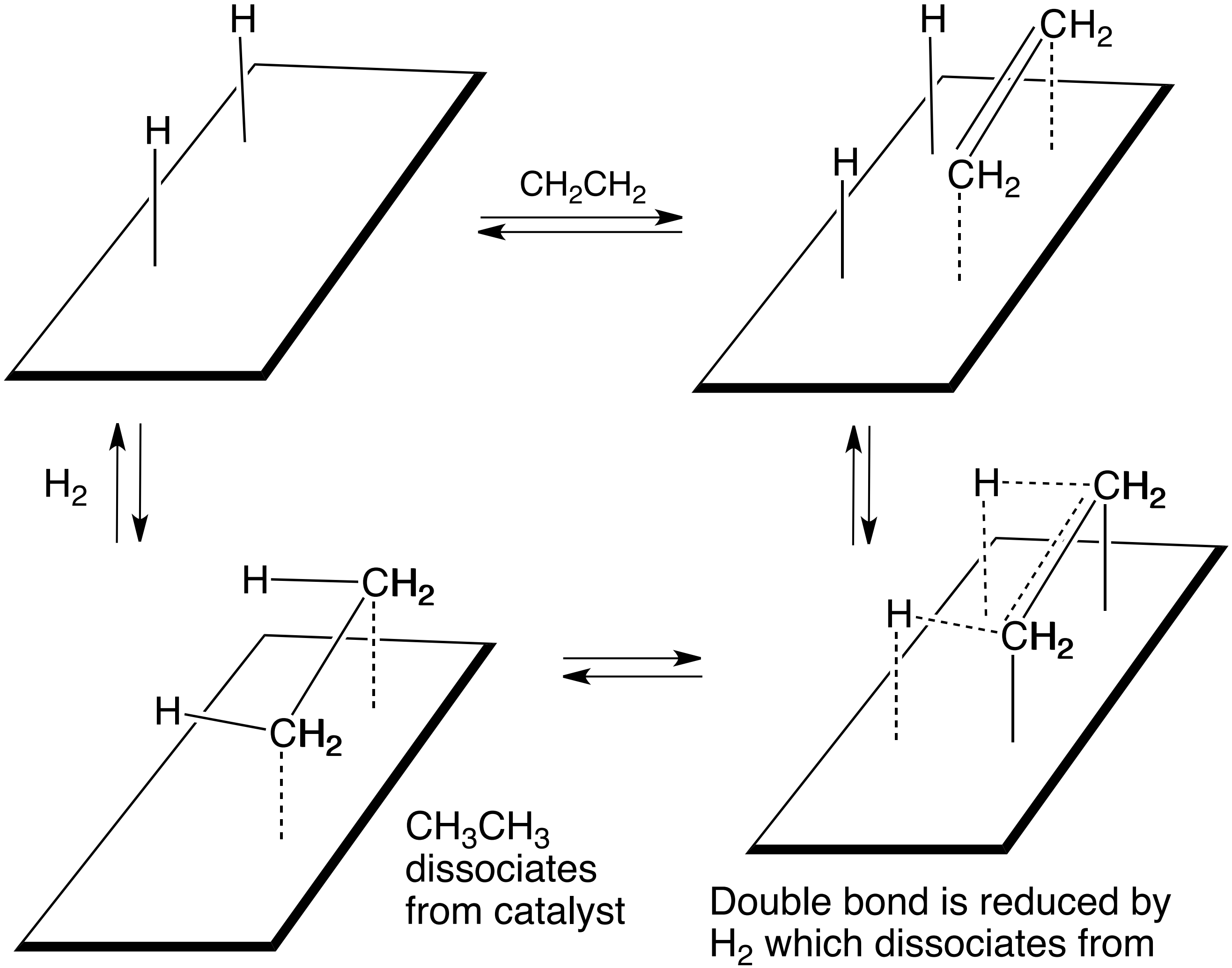
- Alkenes more reactive than other functional groups
- Aldehydes, esters, ketones and nitriles survive, but can be reduced at harsher conditions (temp, pressure)







Catalytic hydrogenation mechanism



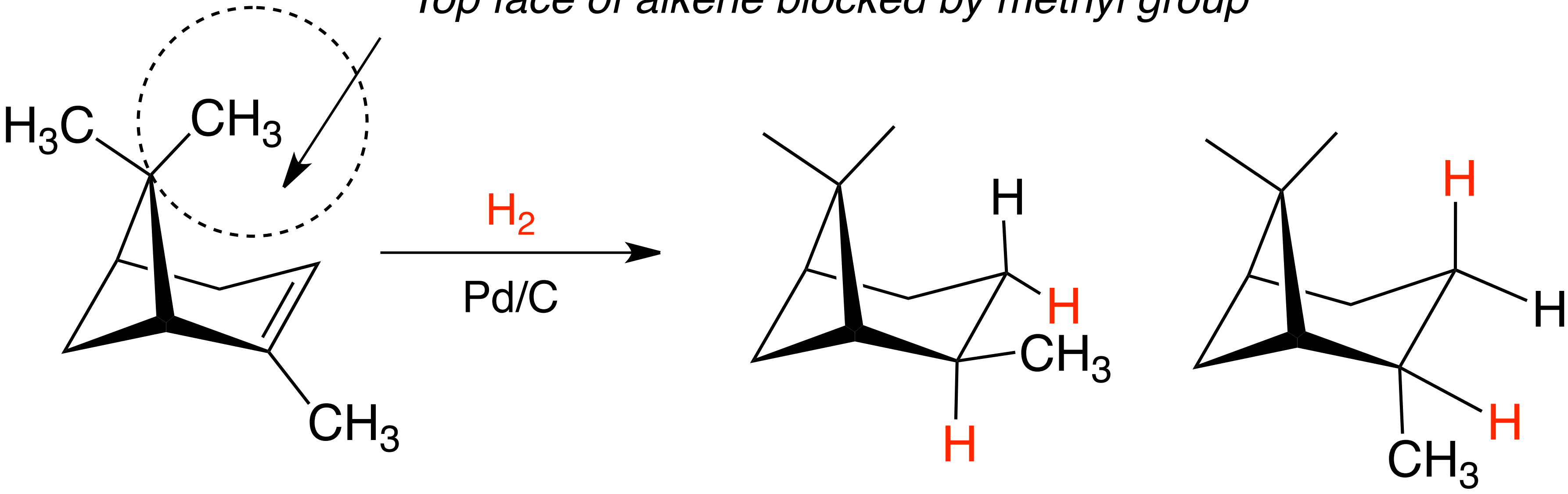
Adsorption of H_2 to
solid supported catalyst
(e.g. Pd/C)

Adsorption of alkene to
solid supported catalyst

Double bond is reduced by
H_2 which dissociates from
catalyst

CH_3CH_3
dissociates
from catalyst

Sensitivity to steric environment



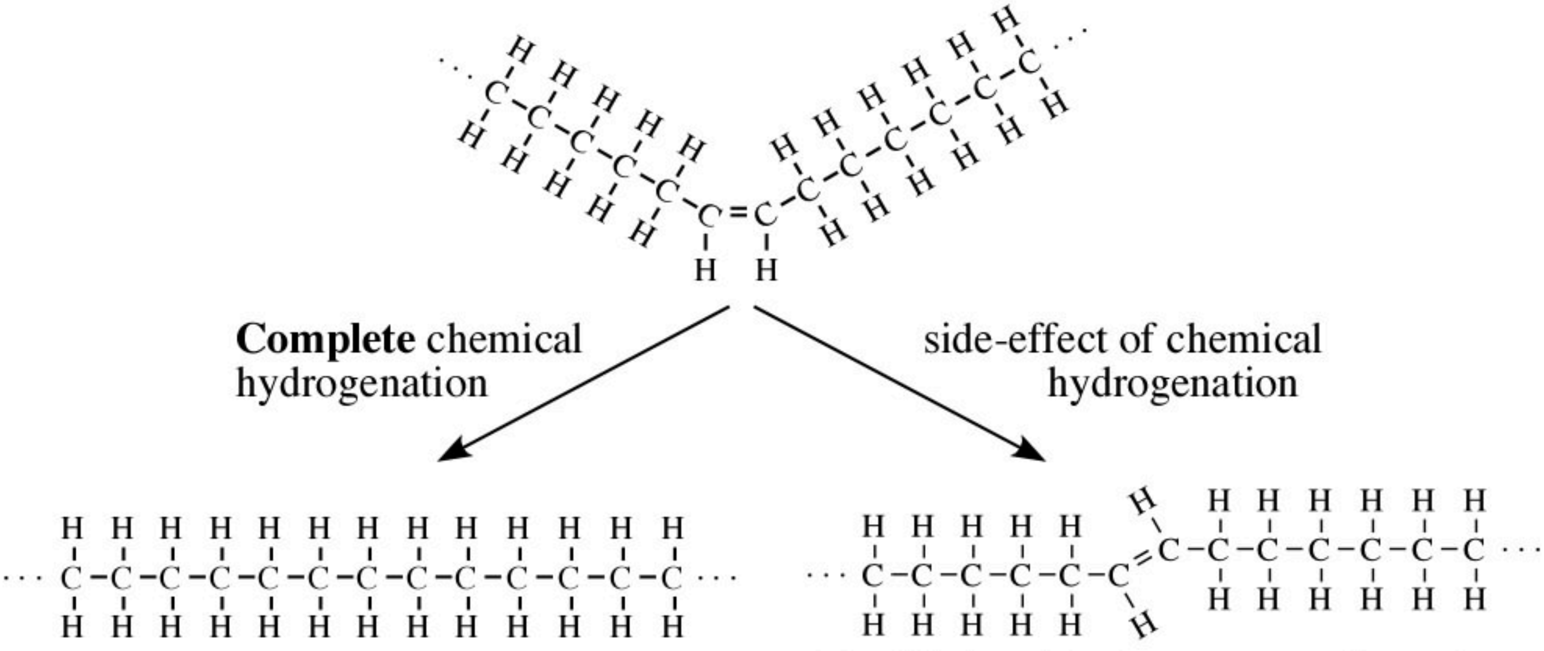
Top face of alkene blocked by methyl group

syn (formed)

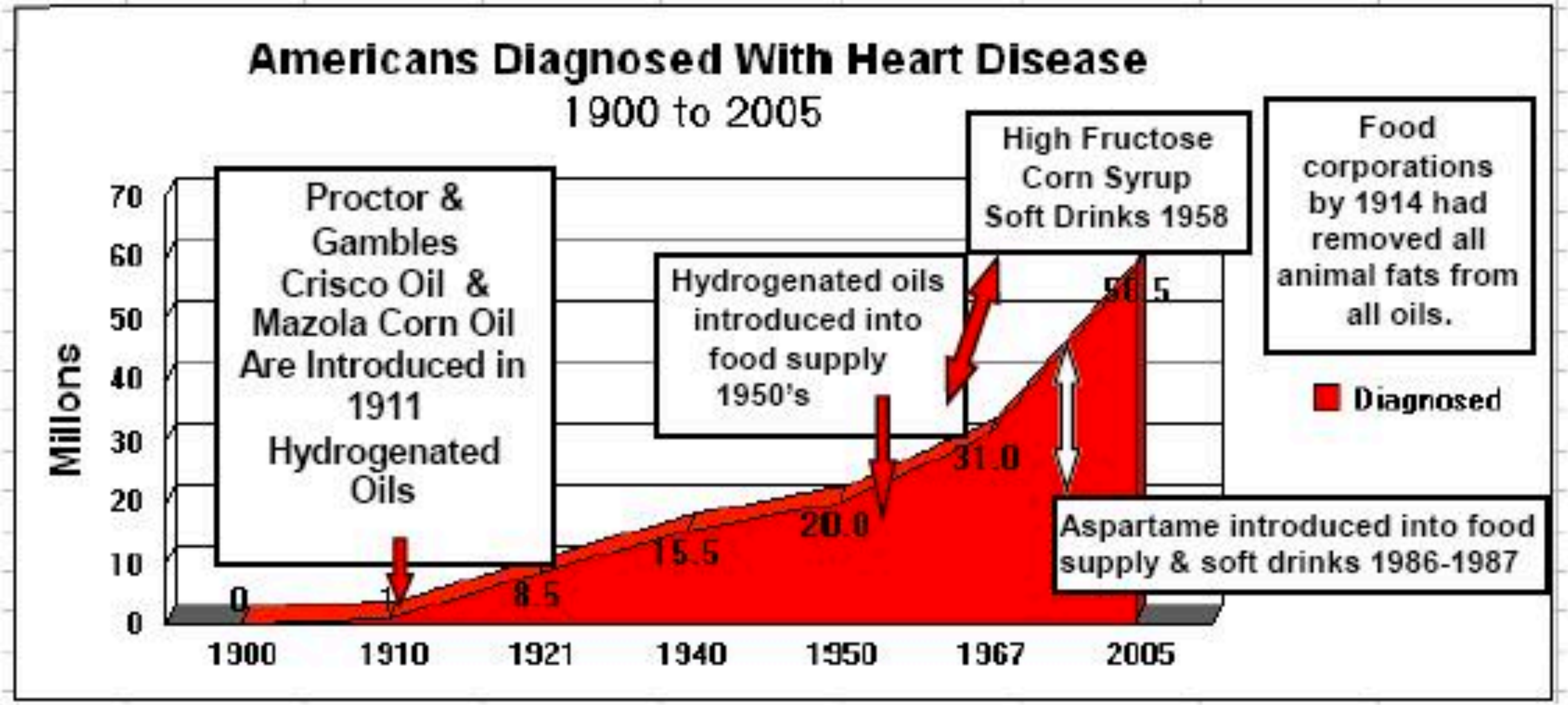
syn (not formed)

“Incomplete” hydrogenation gives rise to trans-fats

- Hydrogenation performed with 2-step Ni catalyst + heat
- Heat or incomplete interaction with catalyst will allow partially broken double bond to reform
- Reformation thermodynamically and geometrically favors the *trans*, rather than *cis*, geometry. (e.g. *trans* butene is 2.8 kJ/mol more stable than *cis*-)



Double bond in the ***trans*** configuration



Americans Diagnosed With Heart Disease
1900 to 2005

Proctor & Gambles Crisco Oil & Mazola Corn Oil Are Introduced in 1911 Hydrogenated Oils

Hydrogenated oils introduced into food supply 1950's

High Fructose Corn Syrup Soft Drinks 1958

Food corporations by 1914 had removed all animal fats from all oils.

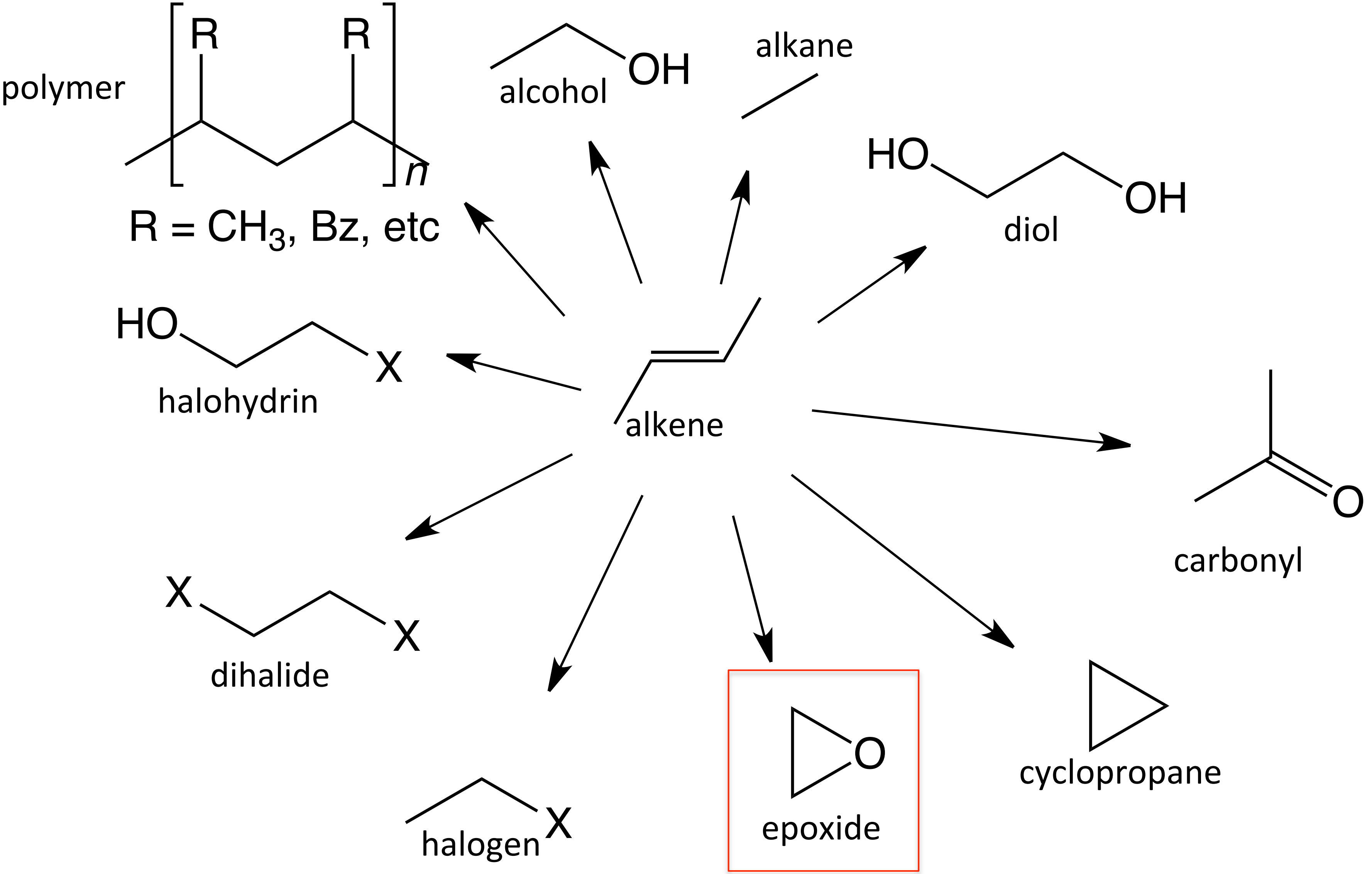
Aspartame introduced into food supply & soft drinks 1986-1987

Hydrogenation Process
Patented 1903
Heart Disease was basically
an old person's disease in 1900
basically unknown of in 1900

Heart Disease First Written Up As A
Medical Condition By Medical Doctor in 1921

Diagnosed heart disease has increased
5,850% from 1910 to 2005
1,000 in 1910 to 58.5 million in 2005

Oxidation of Alkenes



polymer

R = CH_3, Bz, etc

alcohol

alkane

diol

halohydrin

alkene

carbonyl

dihalide

halogen

epoxide

cyclopropane

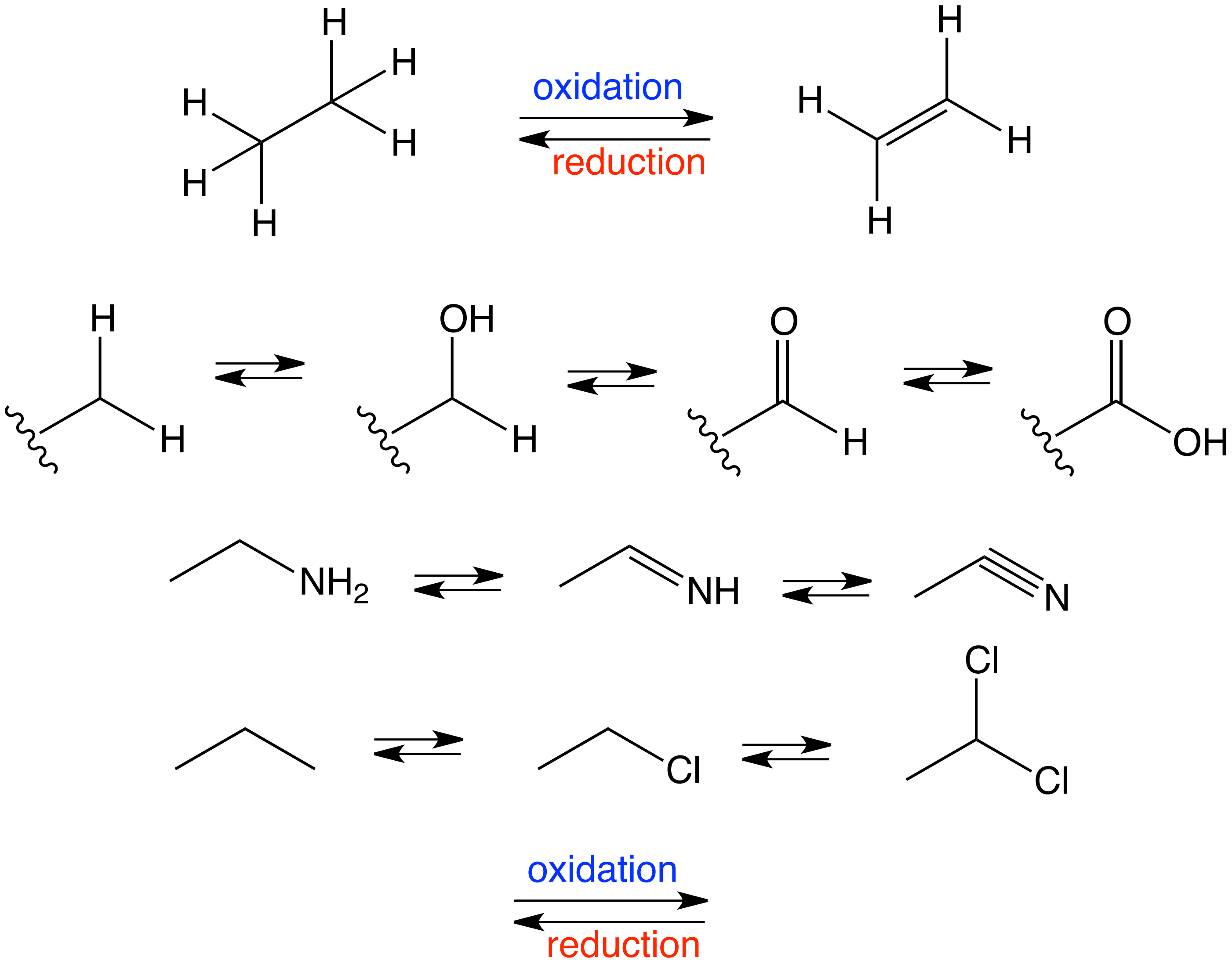
Organic ***Oxidation***

- General Chemistry definition of oxidation = loss of one or more electrons by an atom
- Organic Chemistry definition = loss of electron *density* by carbon

- bond ***formation*** between C and ***more*** electronegative atom (O, N, Halogen)

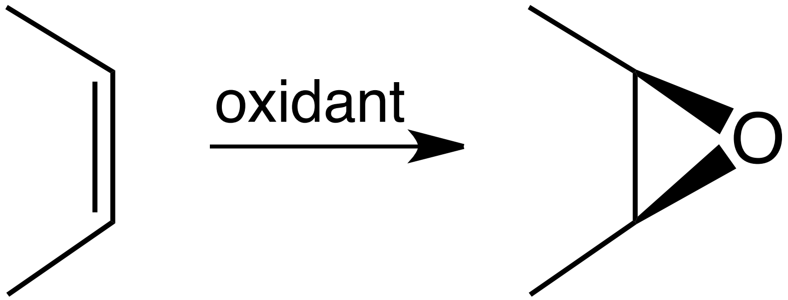
- bond ***breaking*** between between C and a ***less*** electronegative atom (usually H)

Examples of Organic Redox Reactions



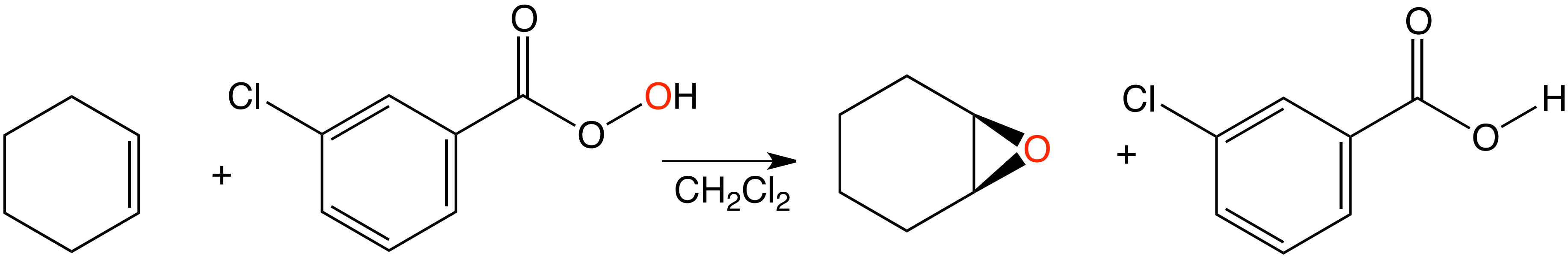
Preparation of Epoxides

- Laboratory synthesis: Alkenes are oxidized to give epoxides (a.k.a *oxiranes,*)
- Epoxides cyclic ethers (3 membered ring)
- Mild oxidants (NaOCl, peroxides or peroxyacids) used



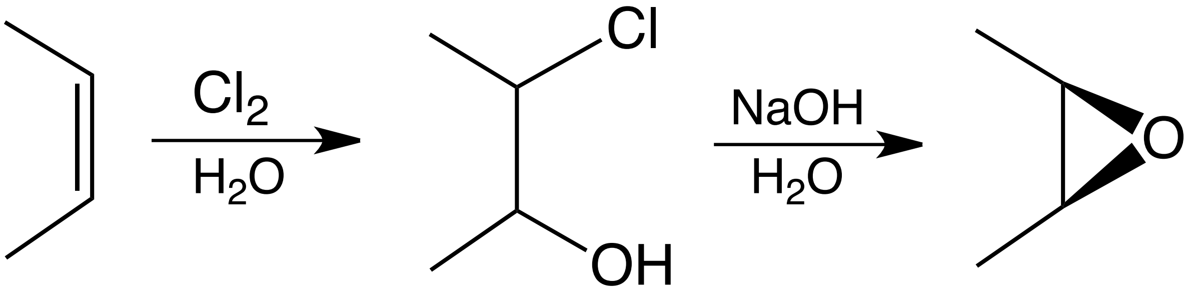
Epoxide Preparation with *m*CPBA

- *m*-chloroperoxy-benzoic acid (*m*CPBA) is a "per-acid"
- O-O bond is weak (138 kJ/mol)
- *m*CPBA always transfers oxygen atom with *syn* stereochemistry
- One step mechanism with no intermediates

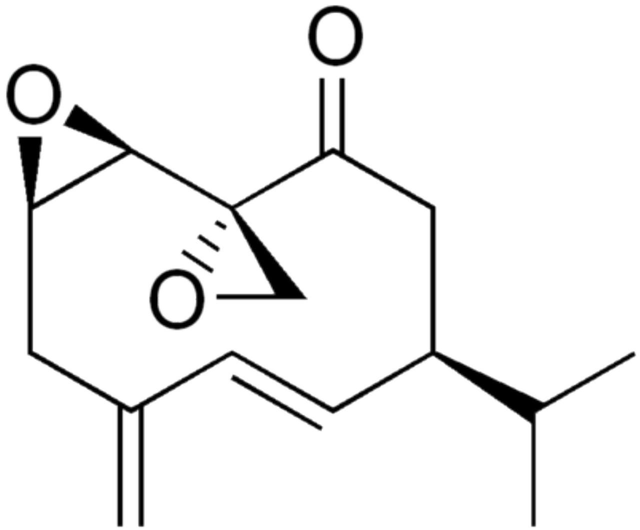


Preparation of Epoxides *via* Halohydrins

- Electrophilic addition of H-OX to alkenes
- Two-step mechanism, halohydrin intermediate
- Halohydrin is treated with base, H-X is eliminated, epoxide is formed

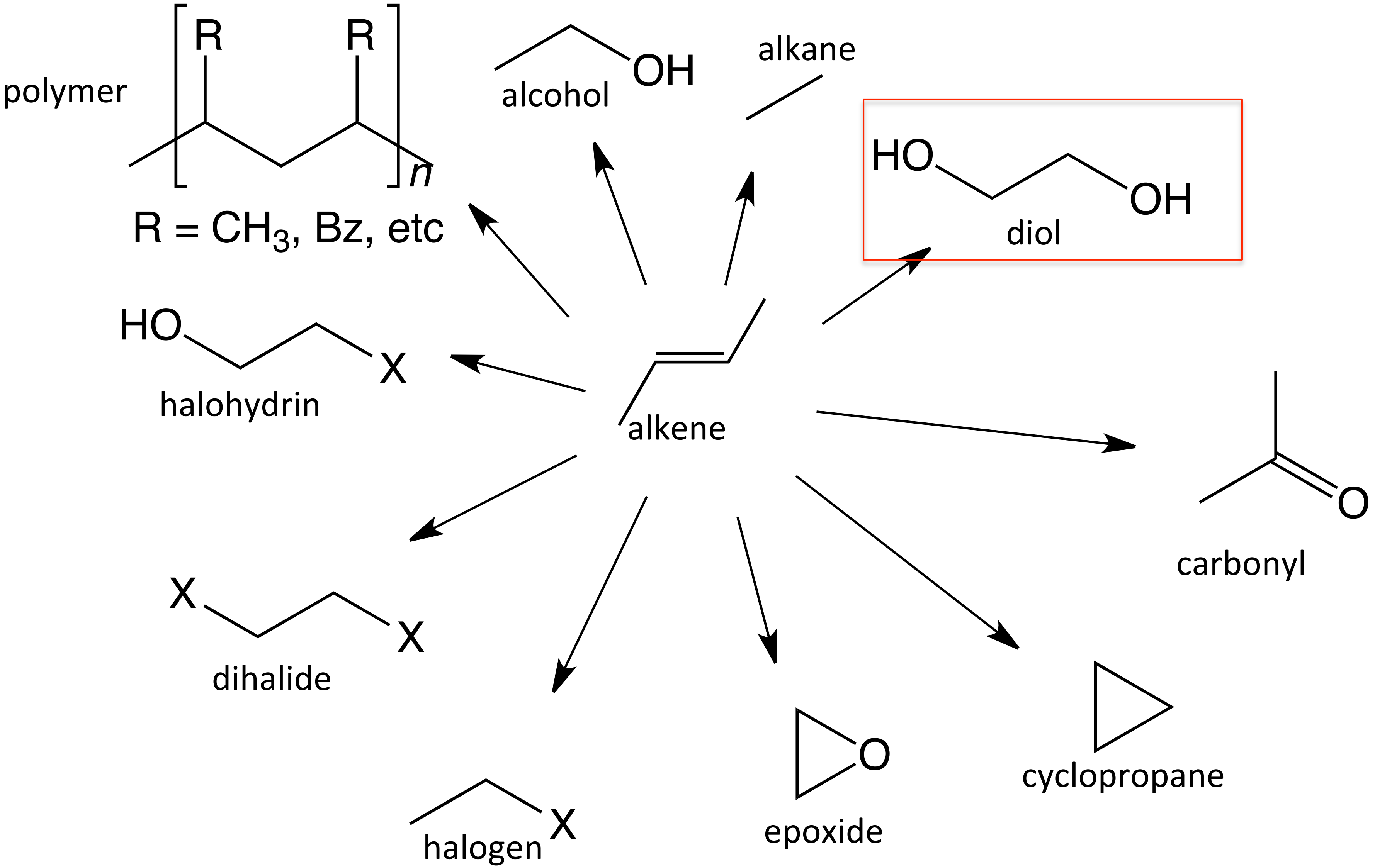


Epoxides in Nature



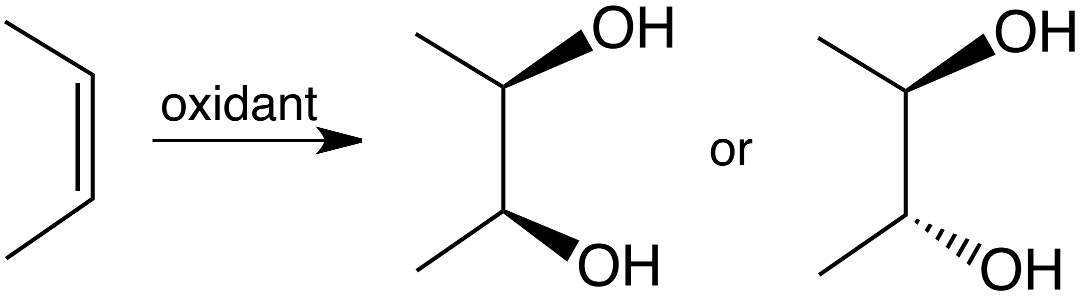
Periplanone B – female cockroach hormone (<< 1μg in nature)
Okada et al. *Journal of Chemical Ecology* 1990, Nicolauo K.C. “Classics in Total Synthesis” 1996; W Clark Still (1979)

Preparation of Diols



Preparation of Diols

- Diols (a.k.a. 1,2-dialcohols or glycols)
- Acid-catalyzed ring opening of epoxides produces *trans* diols
- Osmium tetroxide produces *cis* diols from alkenes

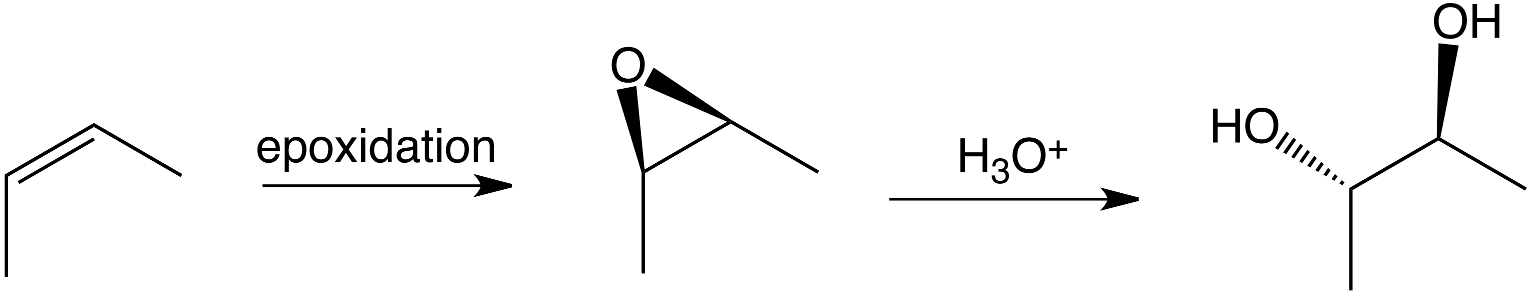


cis diol

trans diol

Acid catalyzed epoxide ring opening

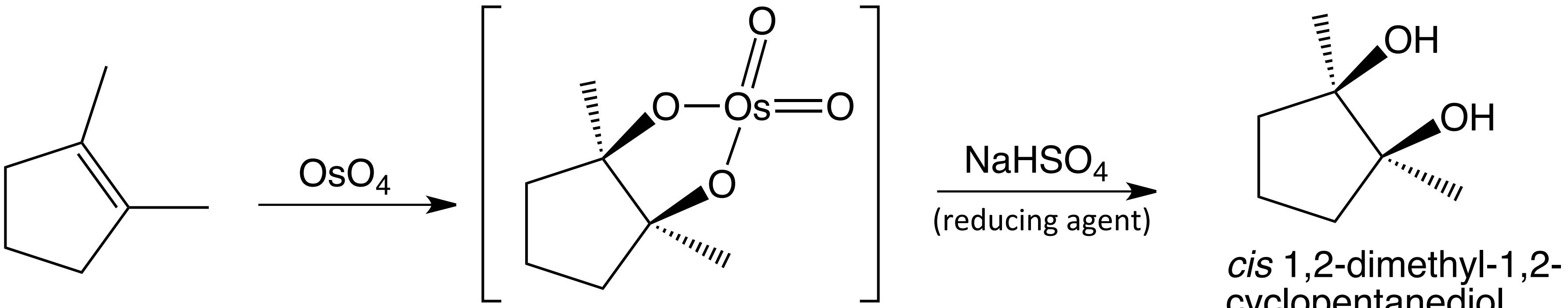
- Acid catalyzed
- Water is nucleophile
- Analogous to alkene halogenation (oxiranium intermediate similar to halonium intermediate)
- Produces *trans*-diols



trans 2,3-butanediol

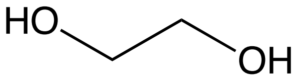
Synthesis of Diols Directly from Alkenes

- Osmium tetroxide (OsO_4) = rare, expensive, toxic
- Intermediate is cyclic osmate ester, not epoxide
- Diols produced are *cis*
- Cleave with aqueous sodium bisulfite ($NaHSO_3$)
- Stoichiometric use of *N*-methylmorpholine *N*-oxide (NMO) as co-oxidant makes OsO_4 catalytic (save $)



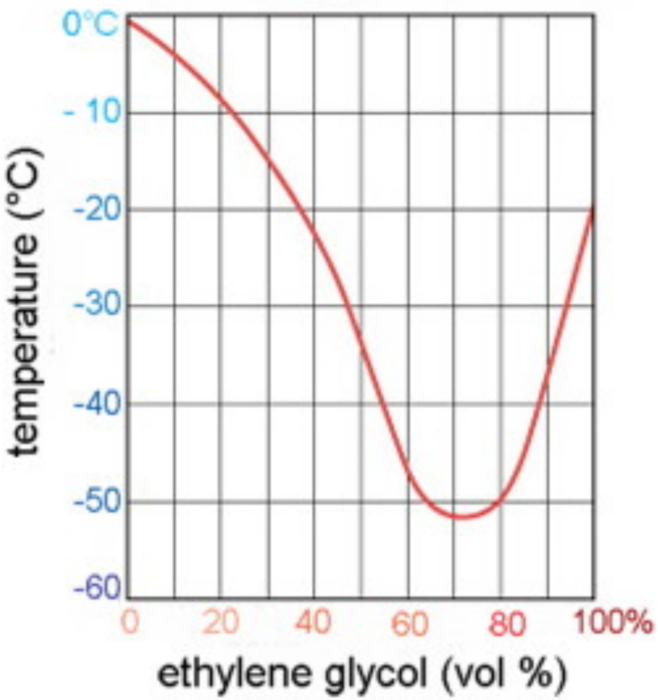
cis 1,2-dimethyl-1,2-cyclopentanediol

Ethylene Glycol: Anti-Freeze, Anti-Boil

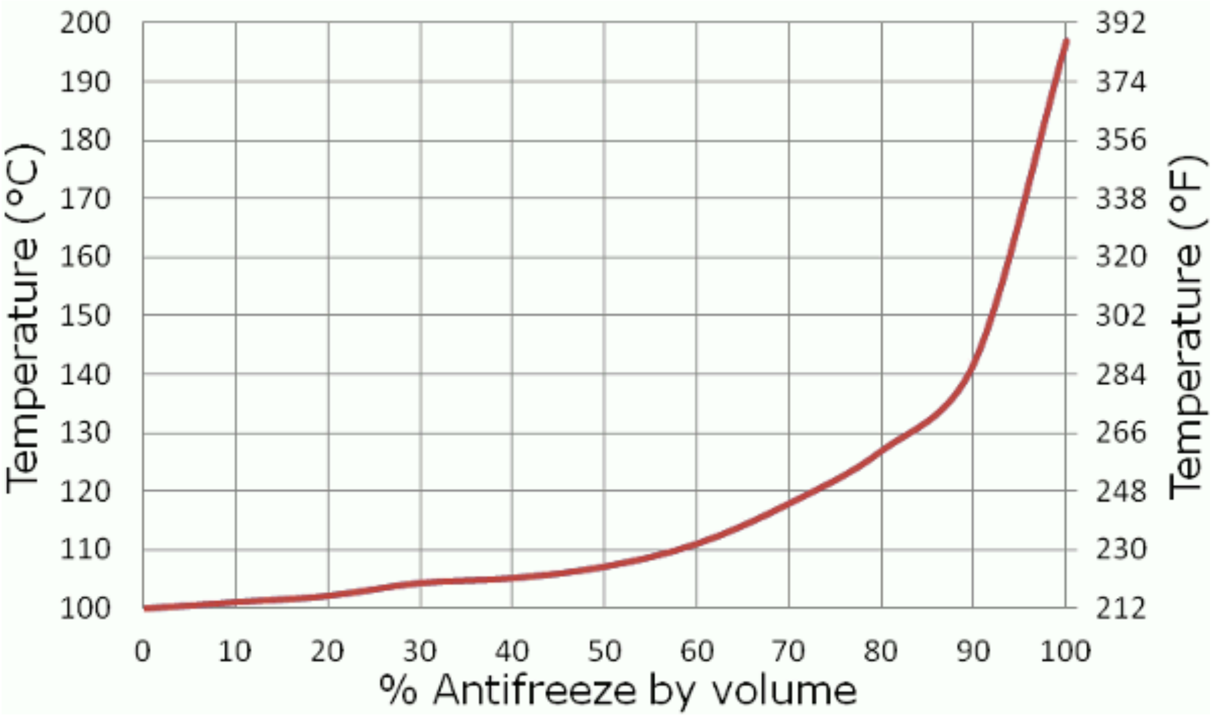


Industrial production = 10M tons/yr/worldwide

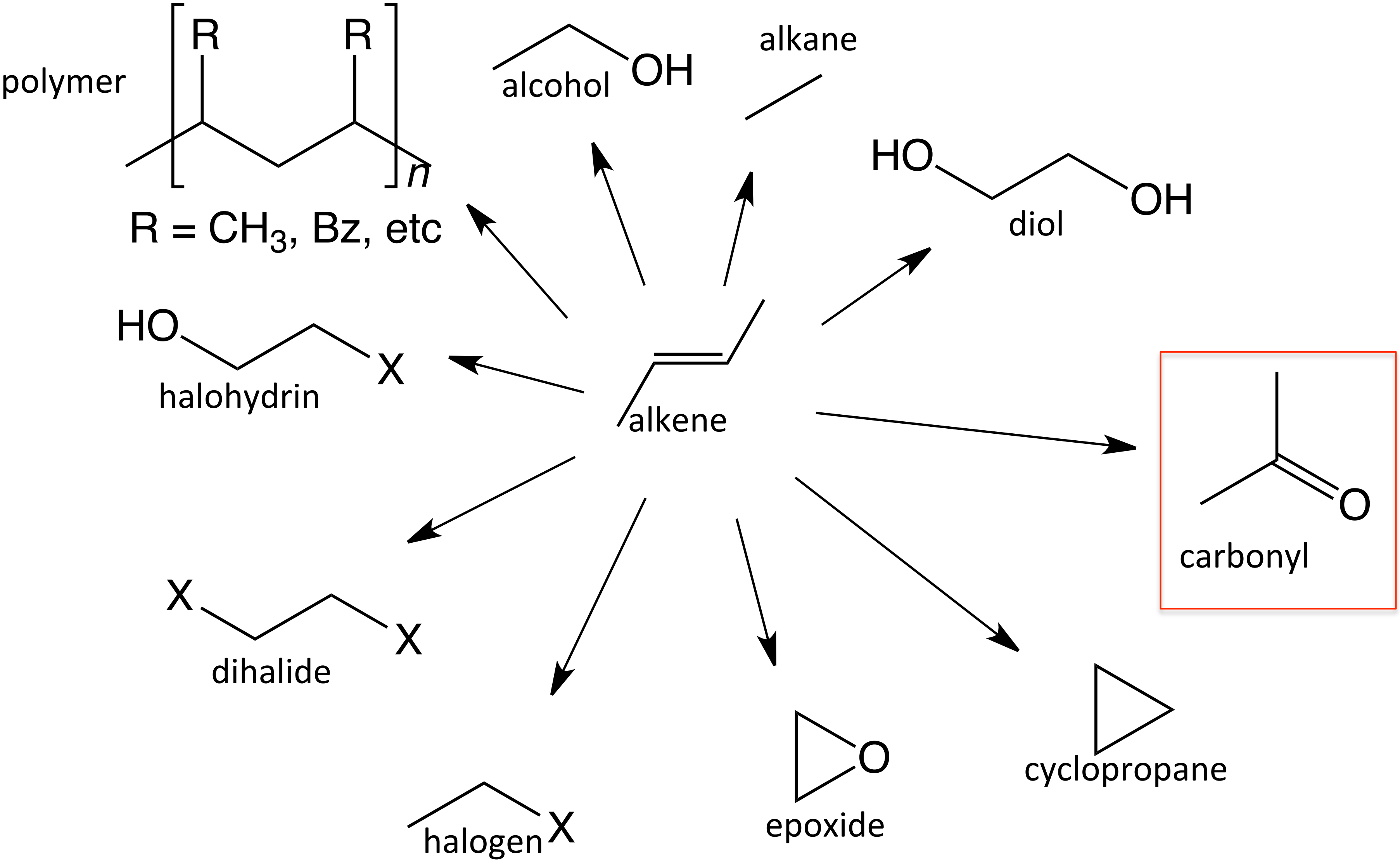
Freezing Point Depression



Boiling Point Elevation

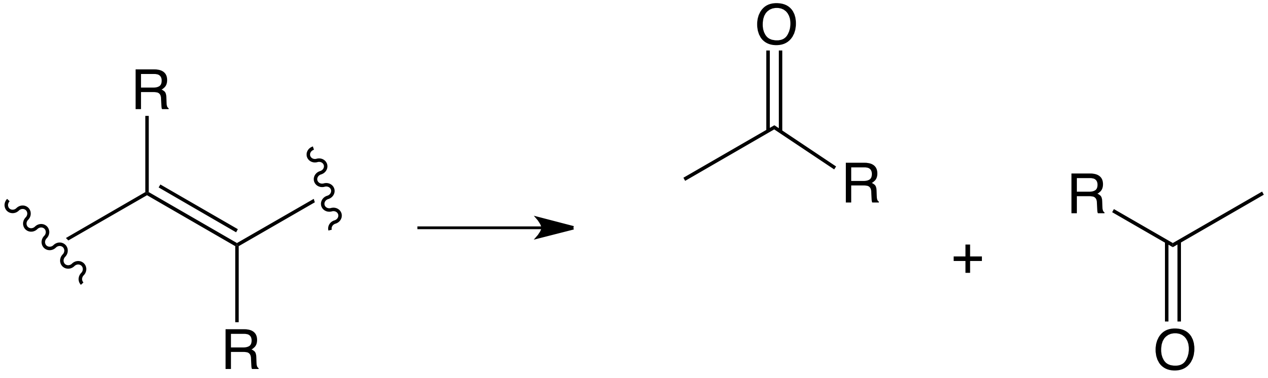


Oxidative Cleavage of Alkenes



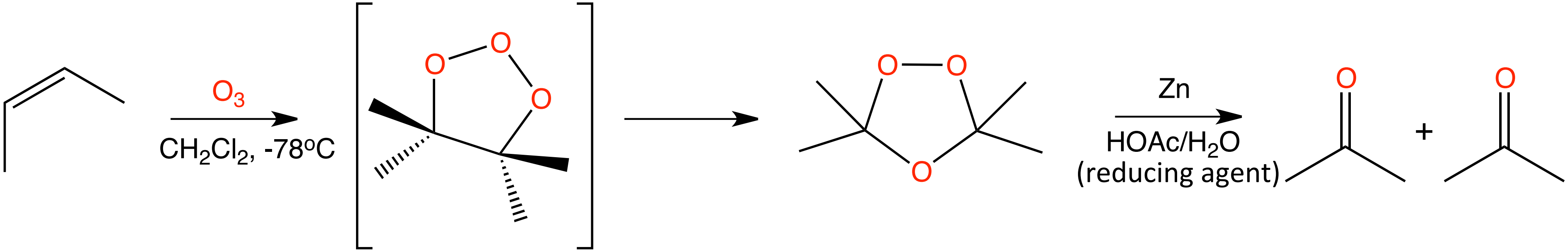
Oxidative Cleavage of Alkenes to Carbonyl Compounds

- Powerful oxidizing agents required to break C=C bond
- Ozonolysis (O_3)
- Potassium Permanganate ($KMnO_4$)
- Periodic Acid (HIO_4)
- Lead tetraacetate ($Pb(OAc)_4$)

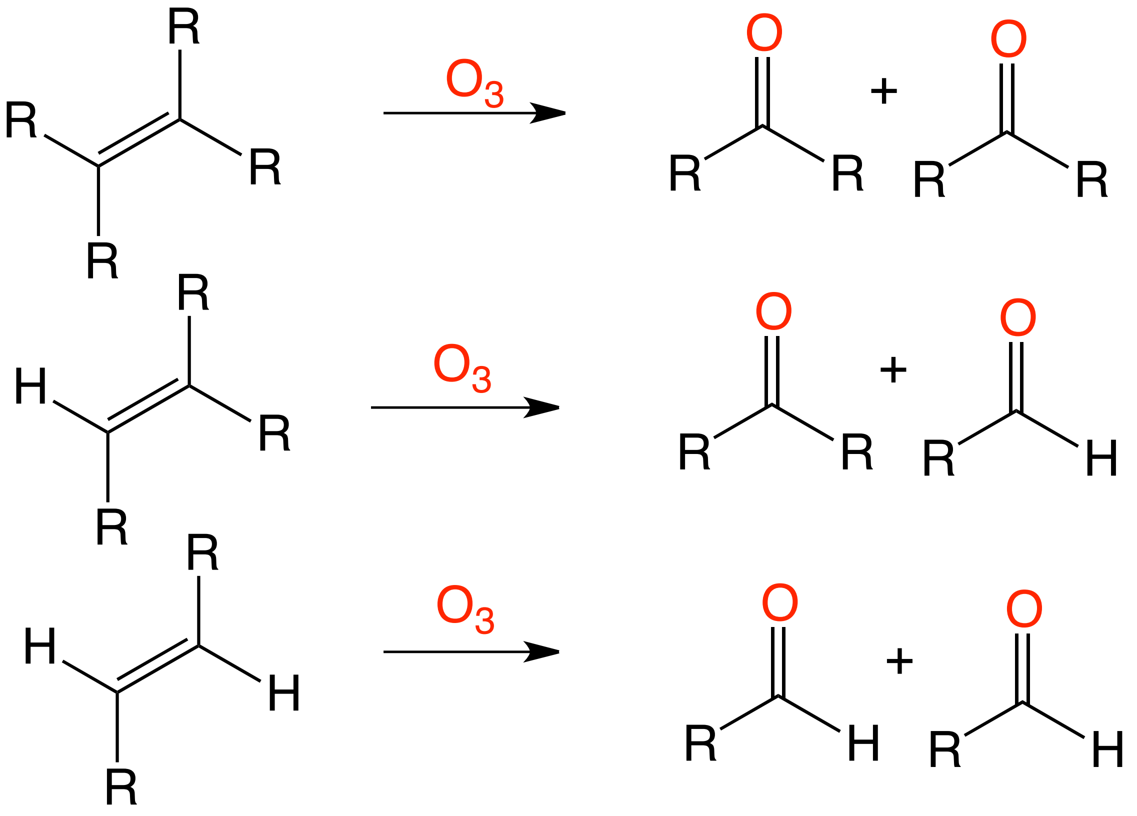


Ozonolysis

- Ozone (O_3) is generated by passing O_2 through an electrical discharge
- O_3 adds rapidly to alkene at low temp to give cyclic monolozide which spontaneously rearranges to ozonide
- Ozonide are not easily isolated and thus reduced in situ with Zn/HOAc
- Net result is two new carbonyls on two original alkene carbon atoms



Ozonolysis contd.



two ketones

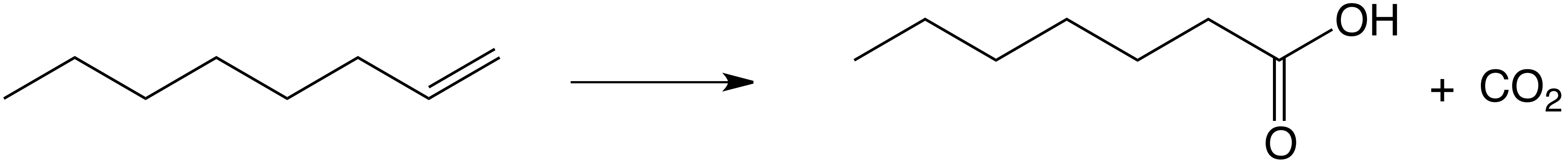
one ketones + one aldehyde

two aldehydes

etc.

$KMnO_4$ Oxidation

- Strong oxidant, seldom used outside of TLC staining
- Works in neutral or acidic solution
- Zero H on alkene = ketone produced
- One H on alkene = carboxylic acid produced
- Two H's on alkene = CO_2 produced

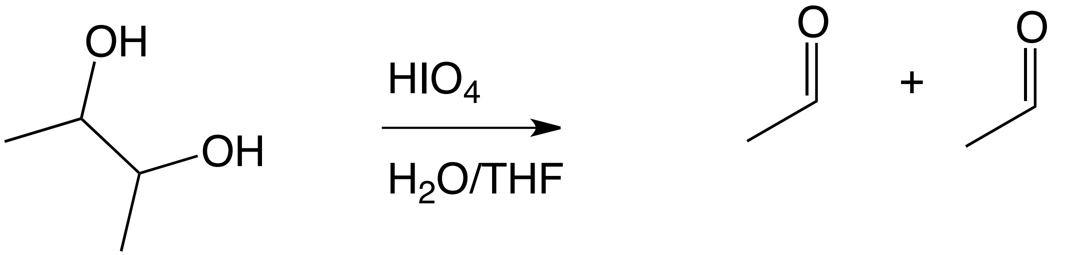


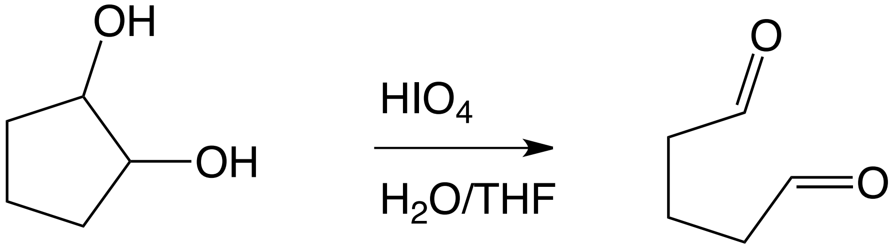
1-octene

heptenoic acid

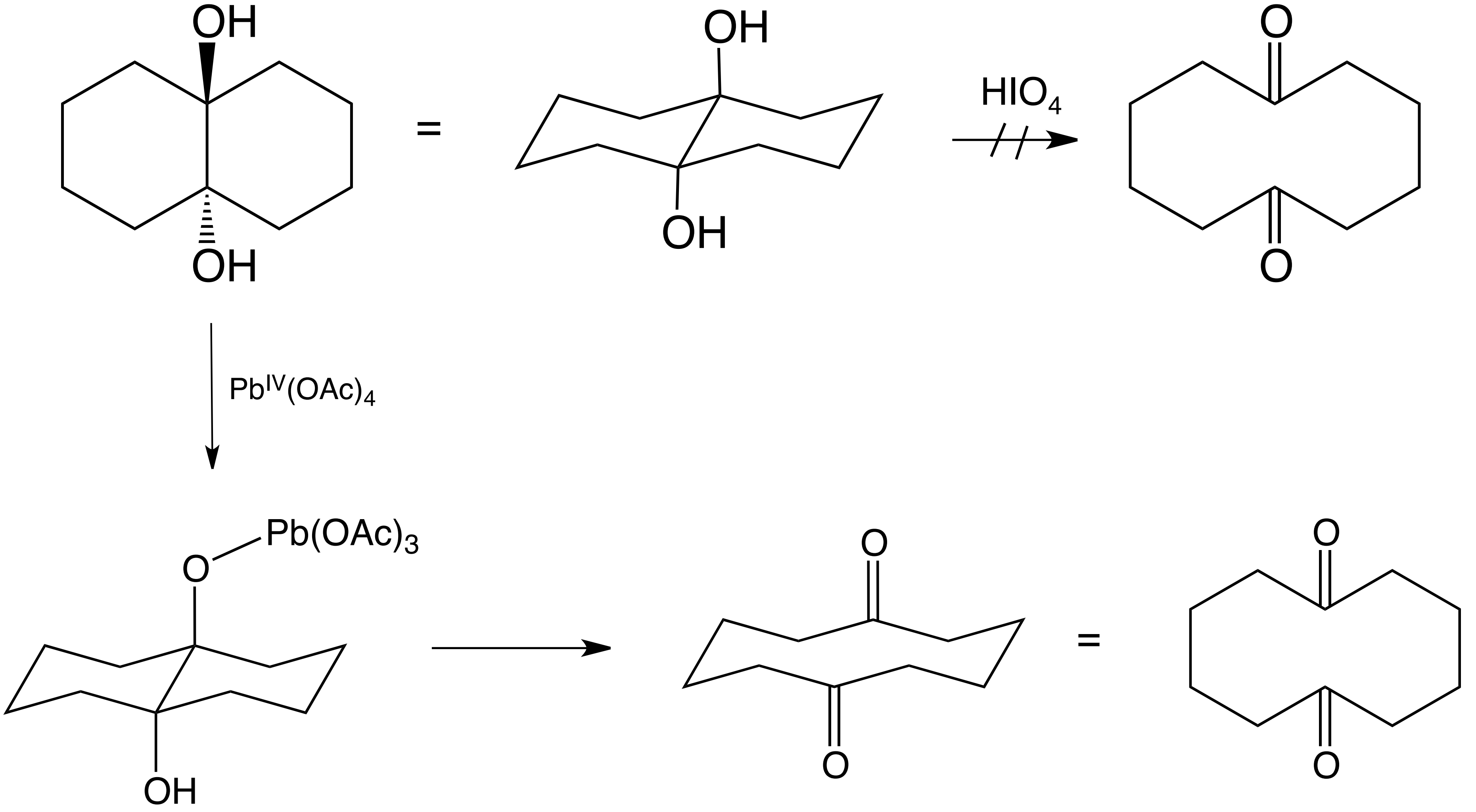
Oxidation of Diols with Periodic Acid

- Cyclic or open chain *cis* diols OK
- Mechanism involves cyclic periodate intermediate
- Diols in a ring give 1 open chain dicarbonyl product
- Diols in an open chain give 2 separate dicarbonyl products

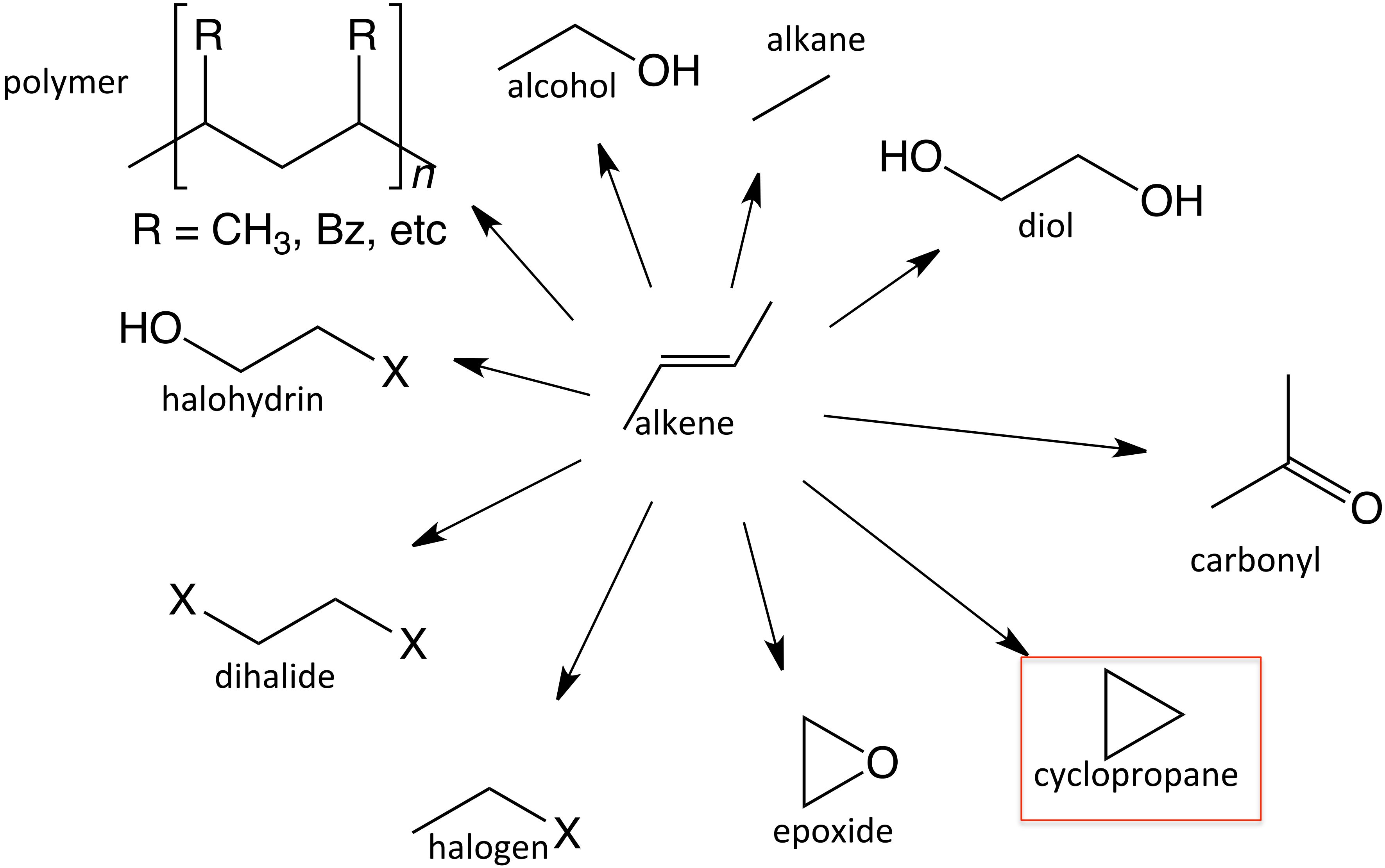




Oxidation of conformational fixed *trans* diols



Preparation of cyclopropanes



polymer

R = CH_3, Bz, etc

alcohol

alkane

diol

halohydrin

alkene

carbonyl

dihalide

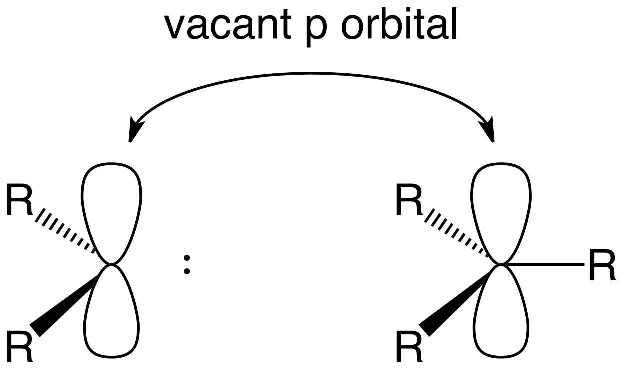
halogen

epoxide

cyclopropane

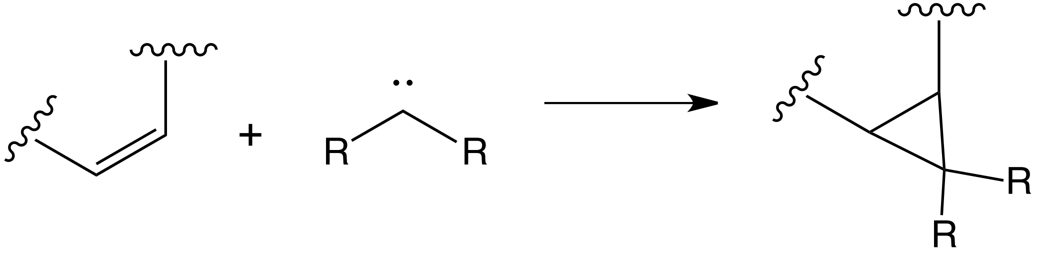
Carbene chemistry

- Carbenes are neutral molecules, with 6 e-s in valence shell
- Highly reactive, Non-isolable
- ***Electron deficient, thus act as electrophiles***
- React with nucleophilic C=C bonds



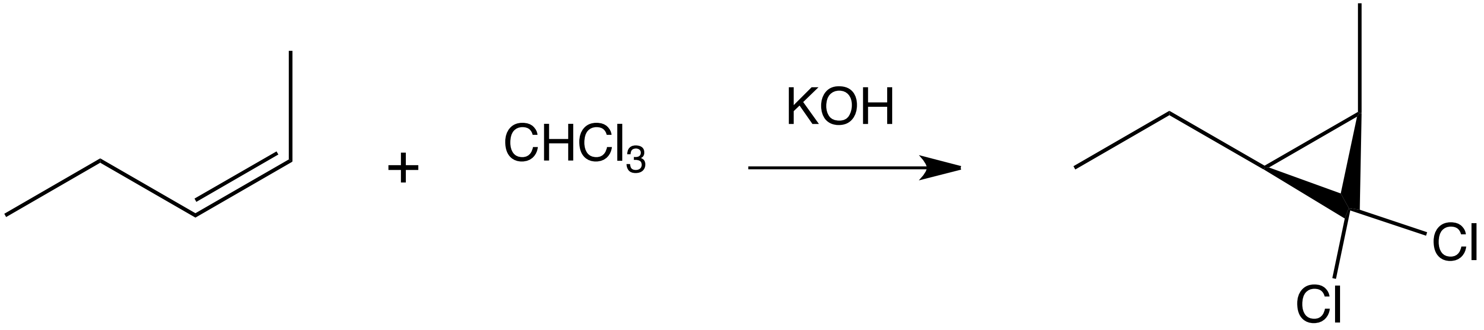
sp^2 hybridized C
"carbene"

sp^2 hybridized C
"carbocation"



Carbene Formation and Use

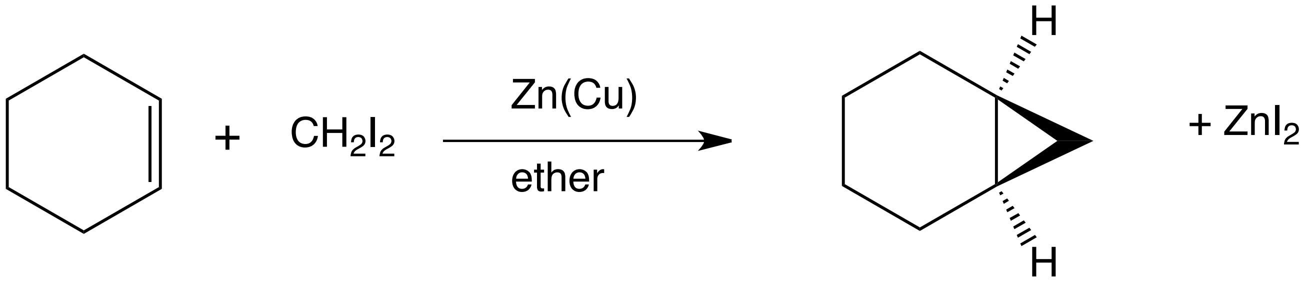
- Treat $CHCl_3$ with strong base (KOH)
- Makes trichloromethanide anion ($CCl_3:^-$)
- The anion expels Cl^- to give neutral dichlorocarbene ($CCl_2:$)
- Generate dichlorocarbene *in situ* with an alkene
- Stereospecific – adds to one face of alkene
  - *cis* alkene gives *cis* dichlorocyclopropane
  - *trans* alkene gives *trans* dichlorocyclopropane



Simmons-Smith Reaction

- "Named reaction"
- Developed by chemists at DuPont
- Carbenoid (not a free carbene, rather a metal-complexed reagent)
- Cycloaddition reaction

$$\underset{\text{diiodomethane}}{CH_2I_2} \xrightarrow[\text{ether}]{\text{Zn(Cu)}} IH_2C\text{—}ZnI \quad = \text{":}CH_2\text{"}$$



HW Problems

Chapter 8:

In Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 15, 16, 17

End of Chapter: 26, 27, 28, 35, 38