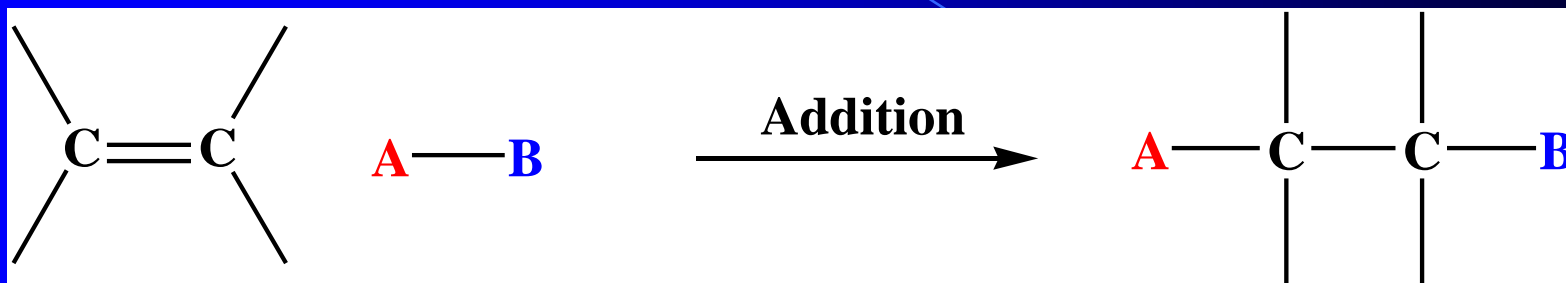


Addition Reactions to $C=C$ and $C\equiv C$

- Addition Reactions to Alkenes
- Markovnikov's Rule
- Stereochemistry of Ionic Addition to Alkenes
- H_2SO_4 Additions to Alkenes
- H_2O Additions to Alkenes
- Oxymercuration/Demercuration
- Hydroboration/Oxidation
- Addition of Br_2 and Cl_2 to Alkenes
- Stereochemistry of Dihalide Additions
- Halohydrin Formation
- Divalent Carbon Compounds: Carbenes
- Oxidations of Alkenes
- Additions to Alkynes
- Oxidative Cleavage of Alkynes
- Applications in Synthesis

Addition Reactions: Addition to Alkenes

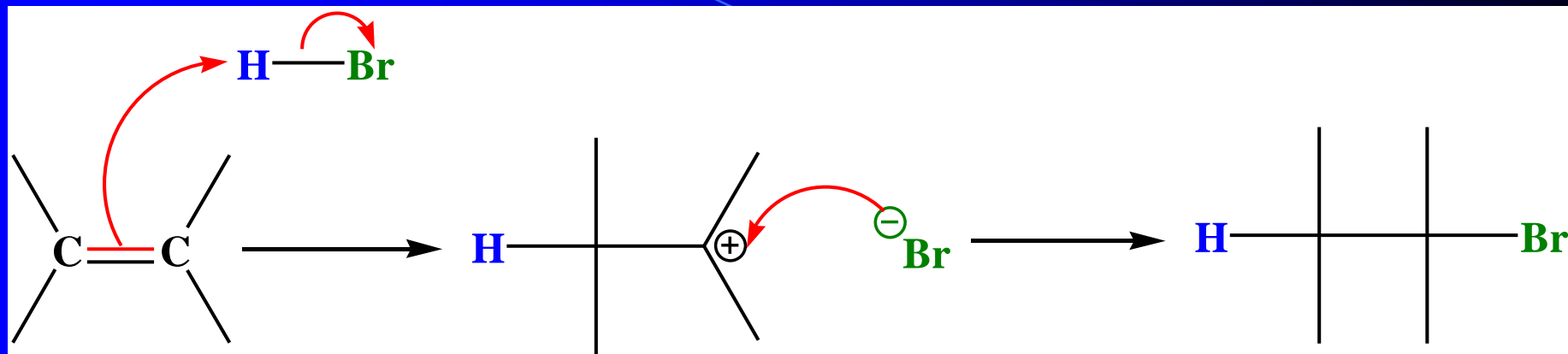


- Have Already Looked at Addition of H₂ (Hydrogenation)
- Will Now Add Additional Reagents
 - HX (I, Br, Cl)
 - Br₂
 - H₂SO₄
 - Cl₂
 - H₂O
 - I₂

Why Do Additions to Alkenes Work?

- Conversion of π Bond to 2 σ Bonds Typically Energy Favored
- Two σ Bonds Higher Energy than One π + One σ
- Overall Process is thus Typically Exothermic
- π Electrons are Exposed (ABOVE and BELOW sp^2 Plane)
- π Bonds Good at Capturing Electrophiles (H^+ , Lewis Acids, X_2)
- Metal Ions With Vacant Orbitals Also Good Electrophiles
- Let's Look at the Addition Reaction of a Hydrogen Halide

Addition Reactions: HX to Alkenes

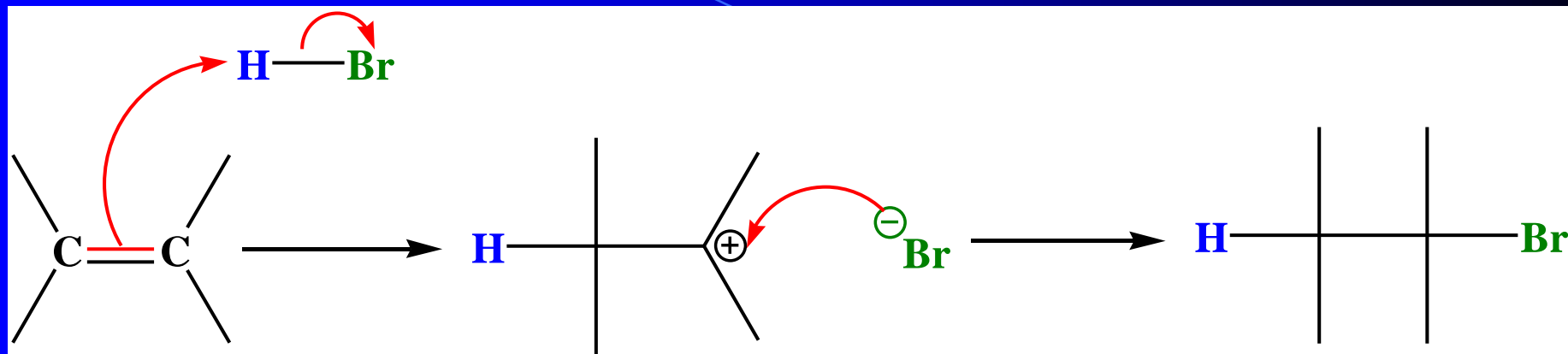


- General Order of HX Reactivity:



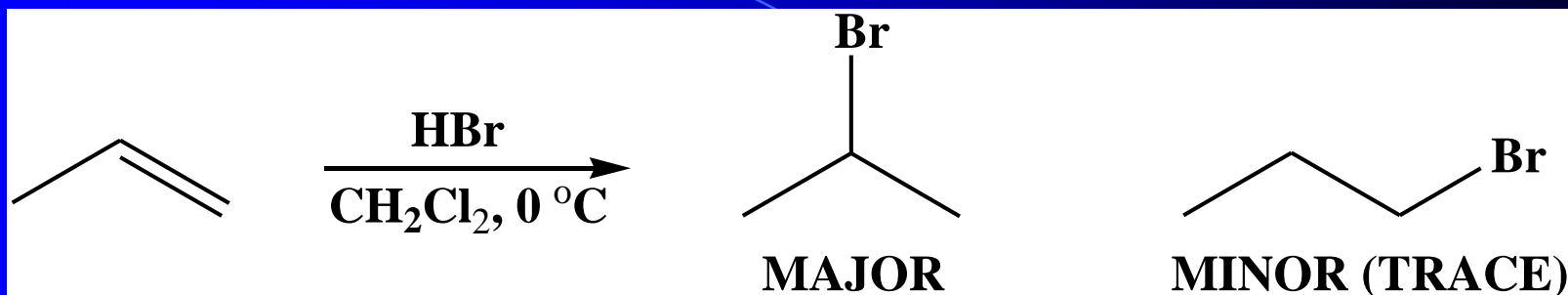
- Usually Dissolved in Solvent ($\text{CH}_3\text{CO}_2\text{H}$, CH_2Cl_2)
- Can be Bubbled Through Solution as a Gas

Addition Reactions: HBr to Alkenes

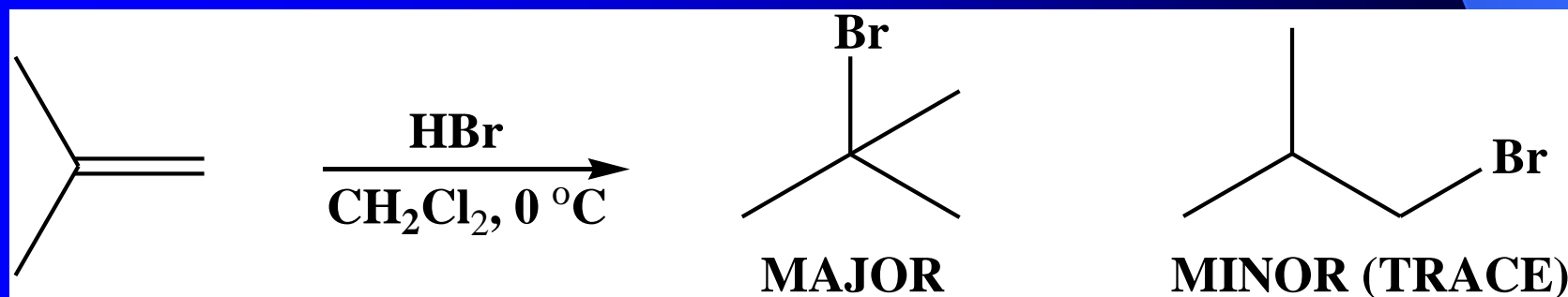


- π Bond (Nucleophile) Protonate \rightarrow Carbocation Intermediate
- Carbocation Captured by Br^- (Nucleophile) \rightarrow HBr Added
- HBr (or other HX) Addition in Two Overall Steps
- H^+ and Carbocation are the Respective Electrophiles
- This is a **SYMMETRIC** Alkene \rightarrow **ASYMMETRIC ALKENES?**

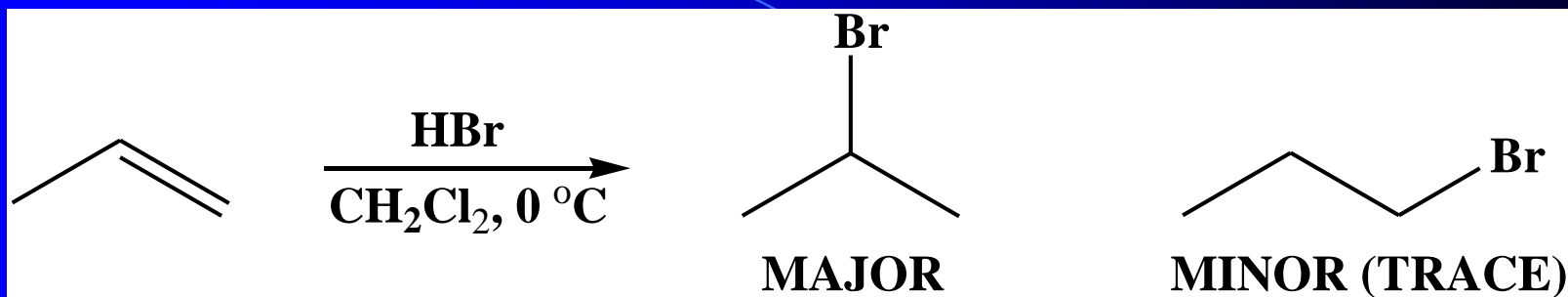
Markovnikov's Rule: HBr to Alkenes



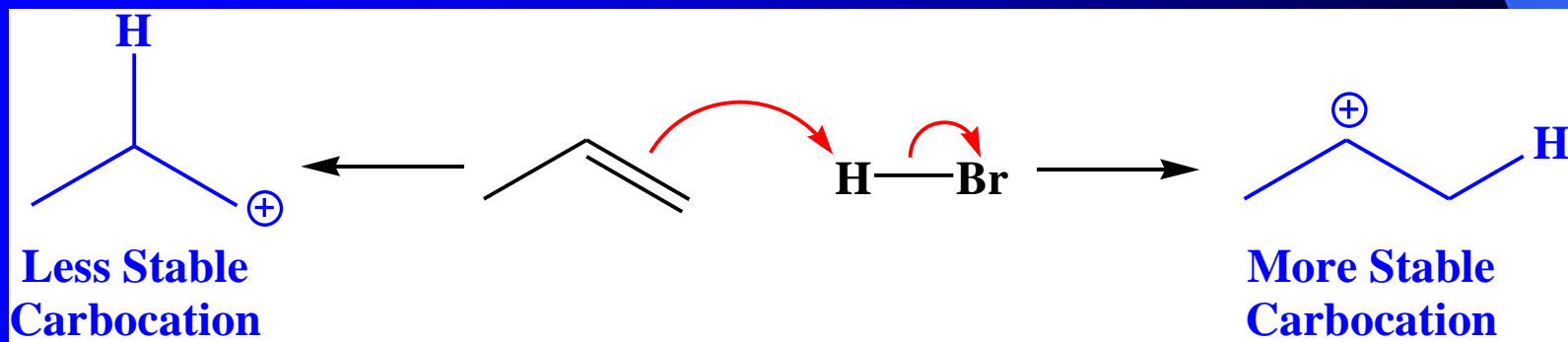
- 2-Bromopropane is Major Product
- Only Very Small Amount of 1-Bromopropane Observed
- True With Other Alkenes



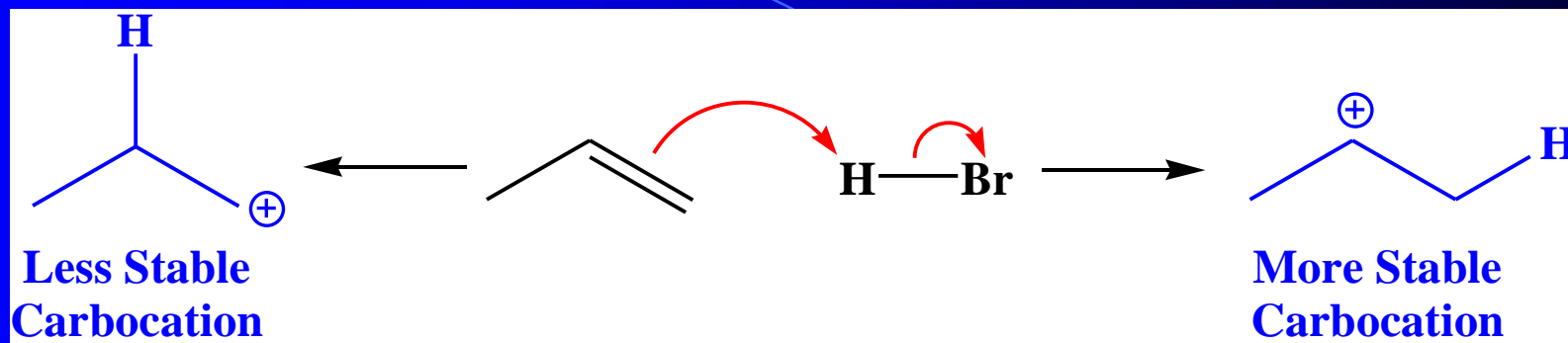
Markovnikov's Rule: Why?



- Product Distribution Explained When Looking at Intermediates
- Recall Discussion of Carbocation Stability ($2^\circ > 1^\circ$)
- Major Product Formed From More Stable C^+ Intermediate



Markovnikov's Rule: C⁺ Stability

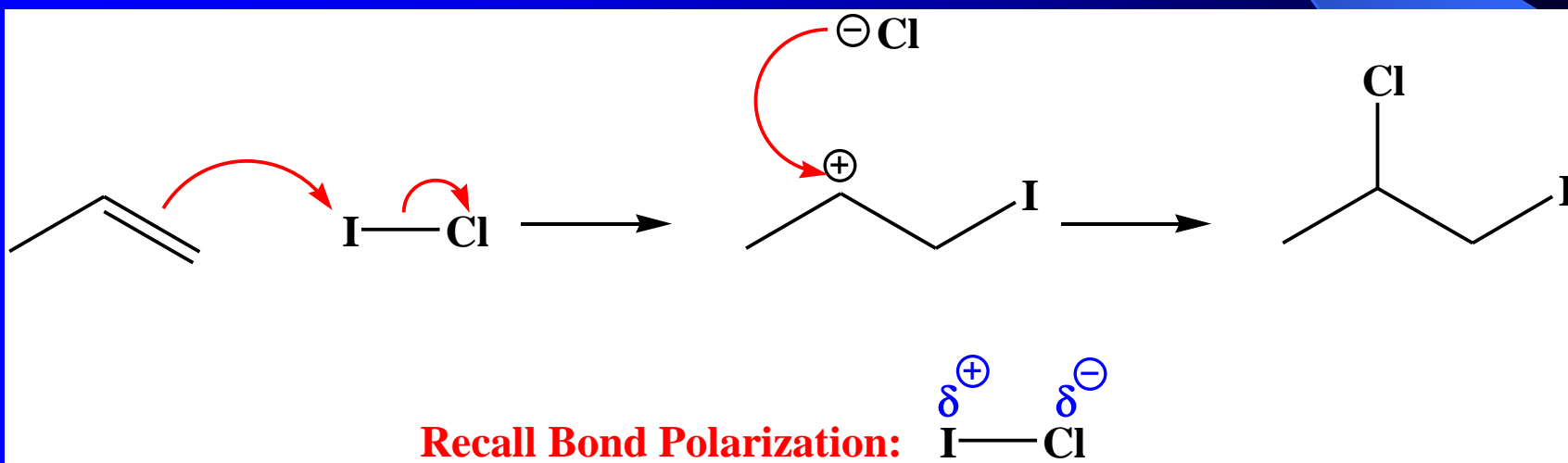


- We Know 2° Carbocations More Stable Than 1°
- Major Product Formed From More Stable C⁺ Intermediate
- Means TS in 2° Carbocation Pathway Lower in Energy
- Lower Energy of Activation
- Activation Energies in 1° Carbocation Pathways Much Larger

Markovnikov's Rule: Summary

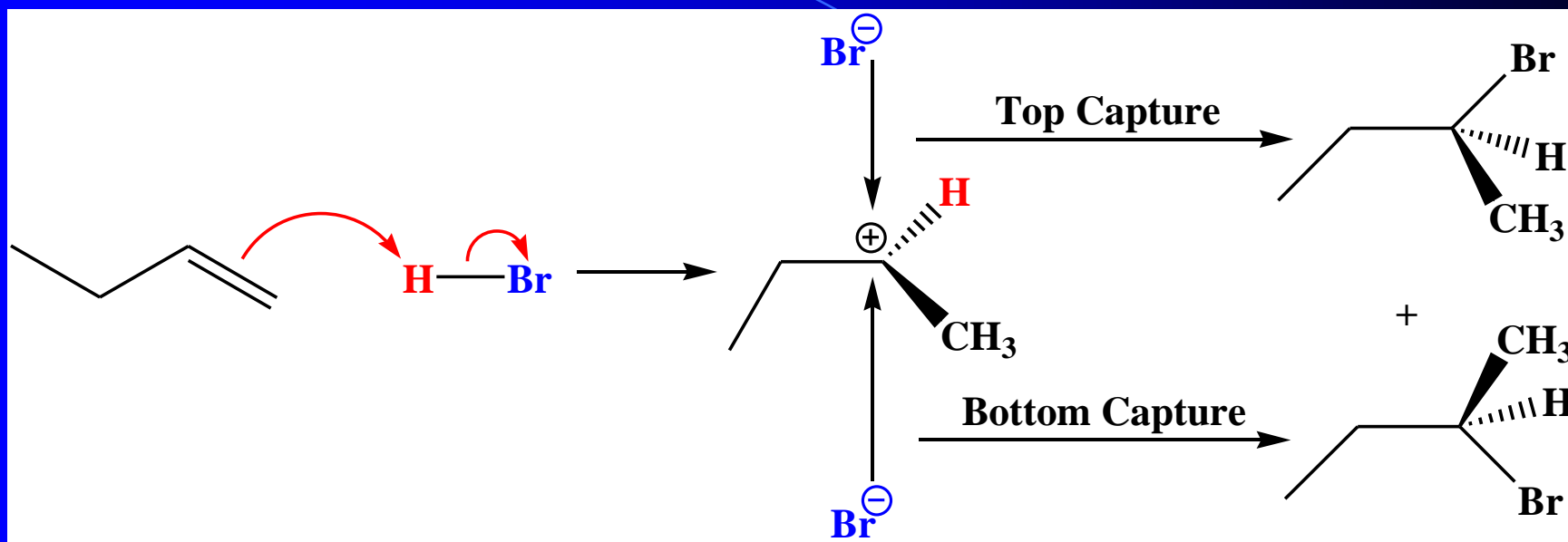
MARKOVNIKOV'S RULE:

*In the ionic additions of an unsymmetrical reagent to a double bond, the positive portion of the adding reagent attaches itself to a carbon atom of the double bond so as to yield the **MORE STABLE CARBOCATION** as an **INTERMEDIATE***



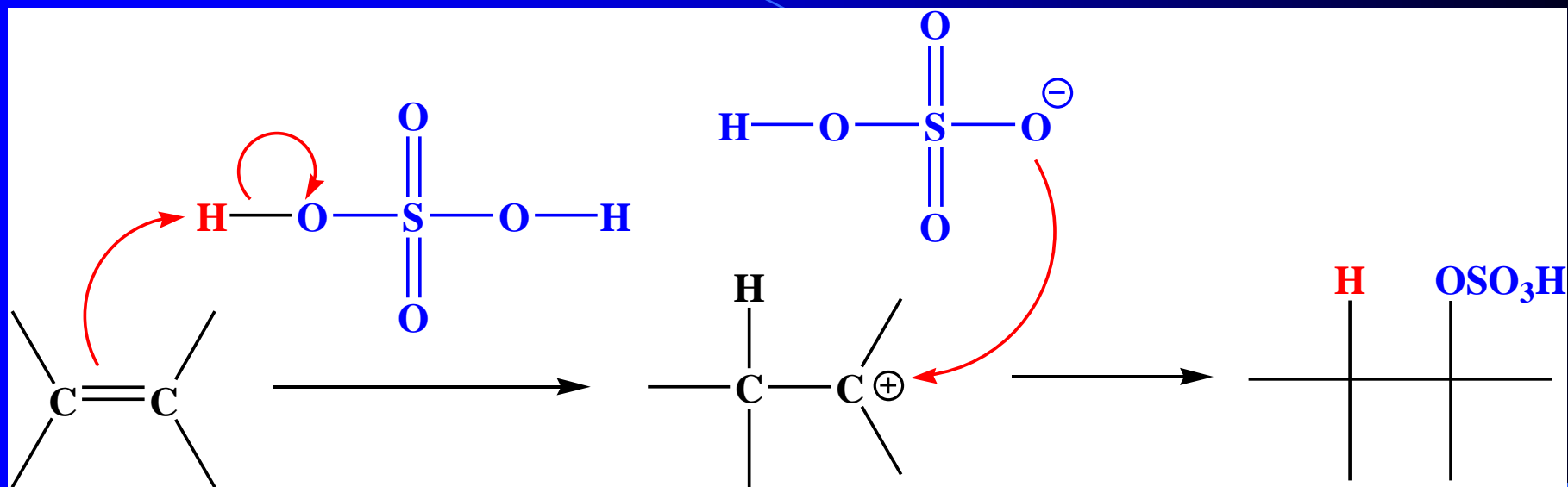
*This Addition "Preference" is Called **REGIOSELECTIVITY***

Stereochemistry in Ionic Additions



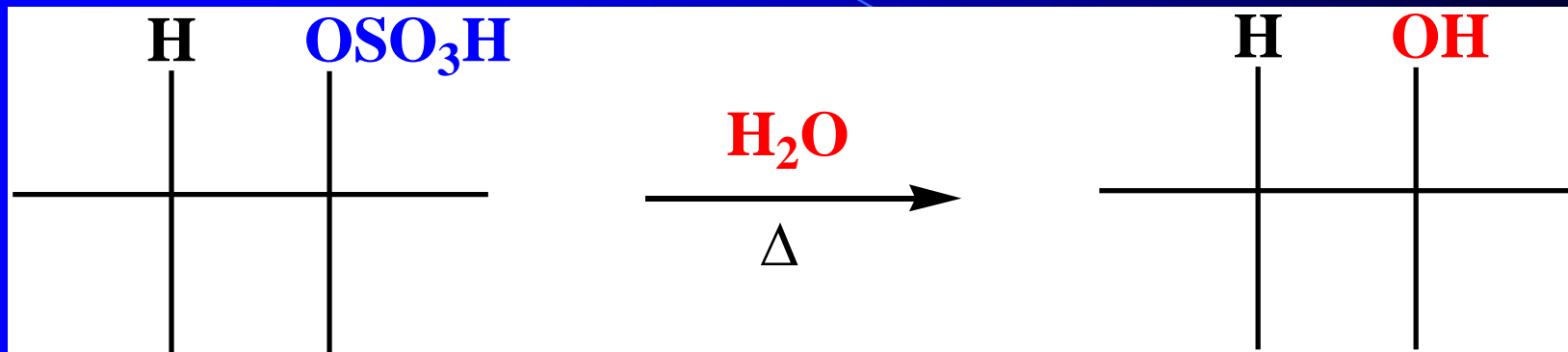
- Just as we saw in S_N1: C⁺ Has TWO FACES
- Top and Bottom Attack Give Two Stereochemical Products
- *R* and *S* Enantiomers Formed as a Racemic Mixture (50:50)

H₂SO₄ Addition to Alkenes



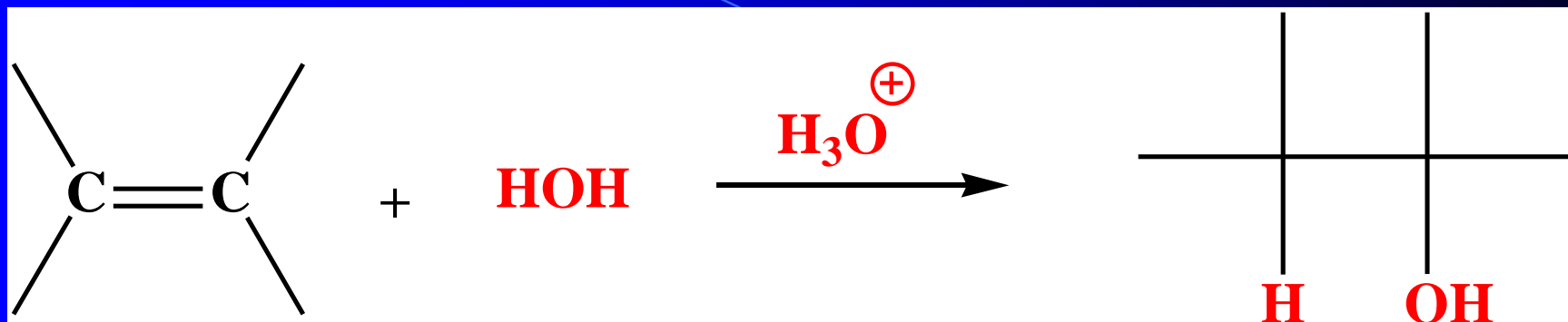
- Must Add **COLD** Sulfuric Acid; Form Alkyl Hydrogen Sulfates
- Regioselective Reaction: Obeys **Markovnikov's Rule**
- Note Mechanistic Similarities w/ HX Addition to Alkenes

Alcohols From Alkyl Hydrogen Sulfates



- **HYDROLYSIS** Reaction of Alkyl Hydrogen Sulfate
- Simply Heat the Sulfate in Water
- Net Reaction is **Markovnikov Addition of H₂O to Alkene**
- Used in One Industrial Ethanol Making Process

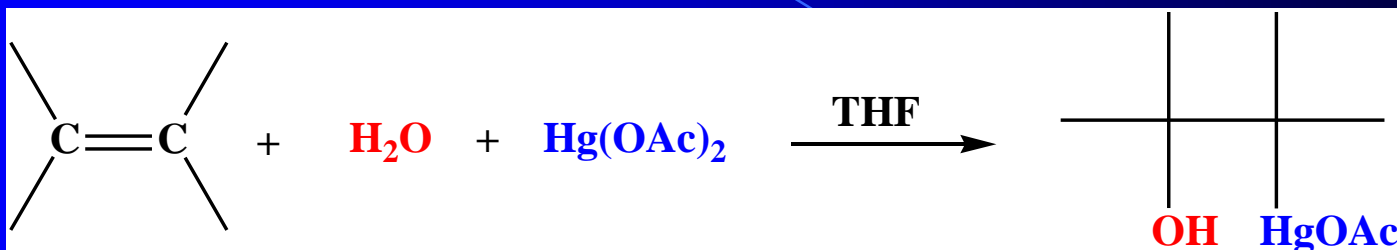
Addition of H₂O to Alkenes: Hydration



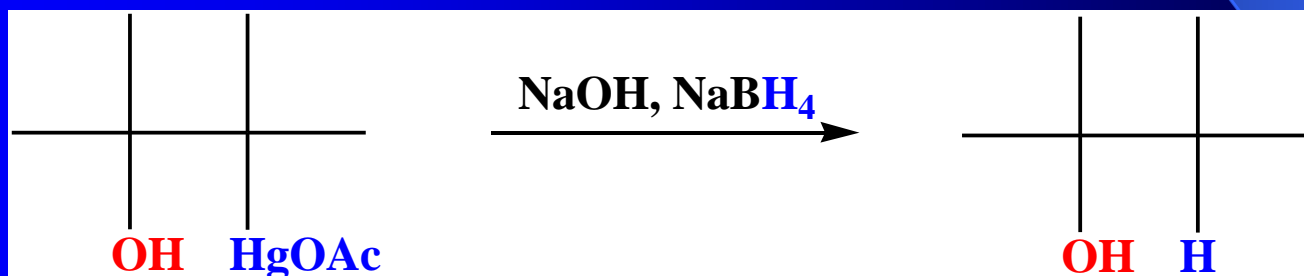
- **HYDRATION** Reaction of an Alkene
- Acid Catalyzed Addition of H₂O Across Double Bond
- Net Reaction is **Markovnikov Addition of H₂O to Alkene**
- We've Seen a Similar Reaction: Acid Catalyzed Dehydration
- Carbocation Rearrangements Possible w/ Dehydration Reactions

Oxymercuration-Demercuration

OXYMERCURATION:

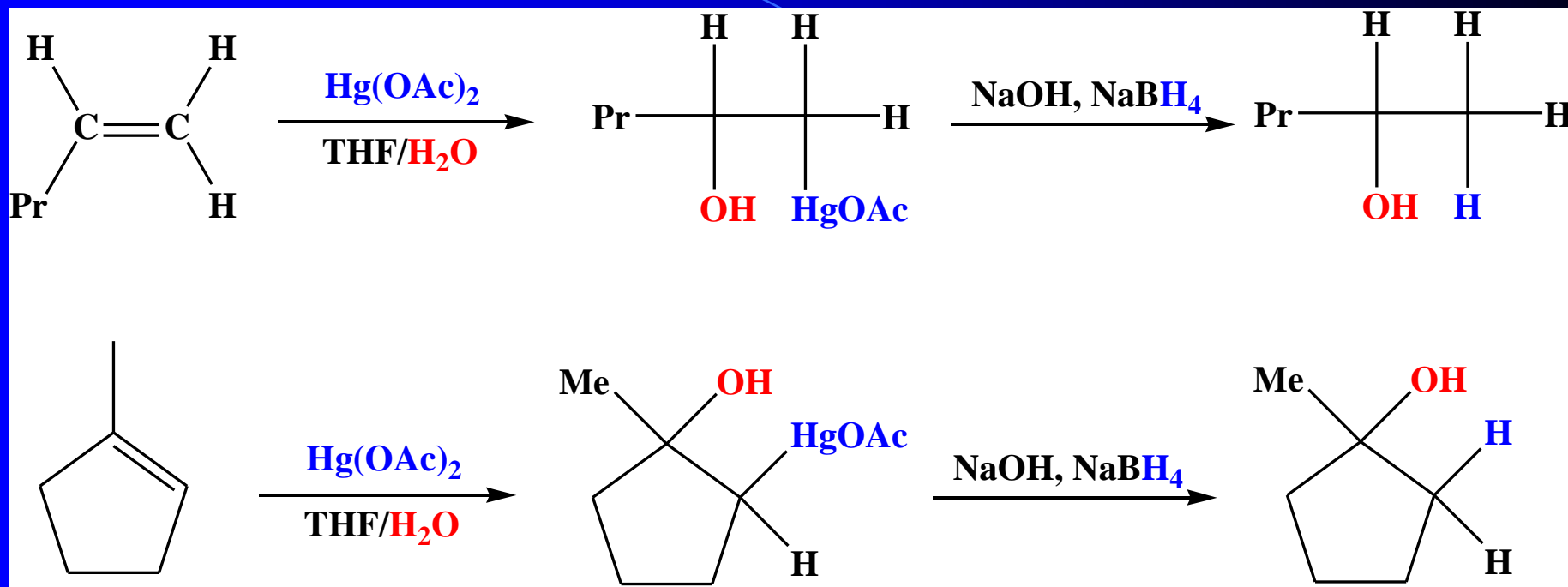


DEMERCURATION:



- Net Reaction: Markovnikov Addition of H_2O to Alkene
- Both Reactions Quite Rapid; Alcohol Yields Usually $> 90\%$
- NaBH_4 : Sodium Borohydride \rightarrow “ H^- ” Delivering Agent

Oxymercuration-Demercuration (2)

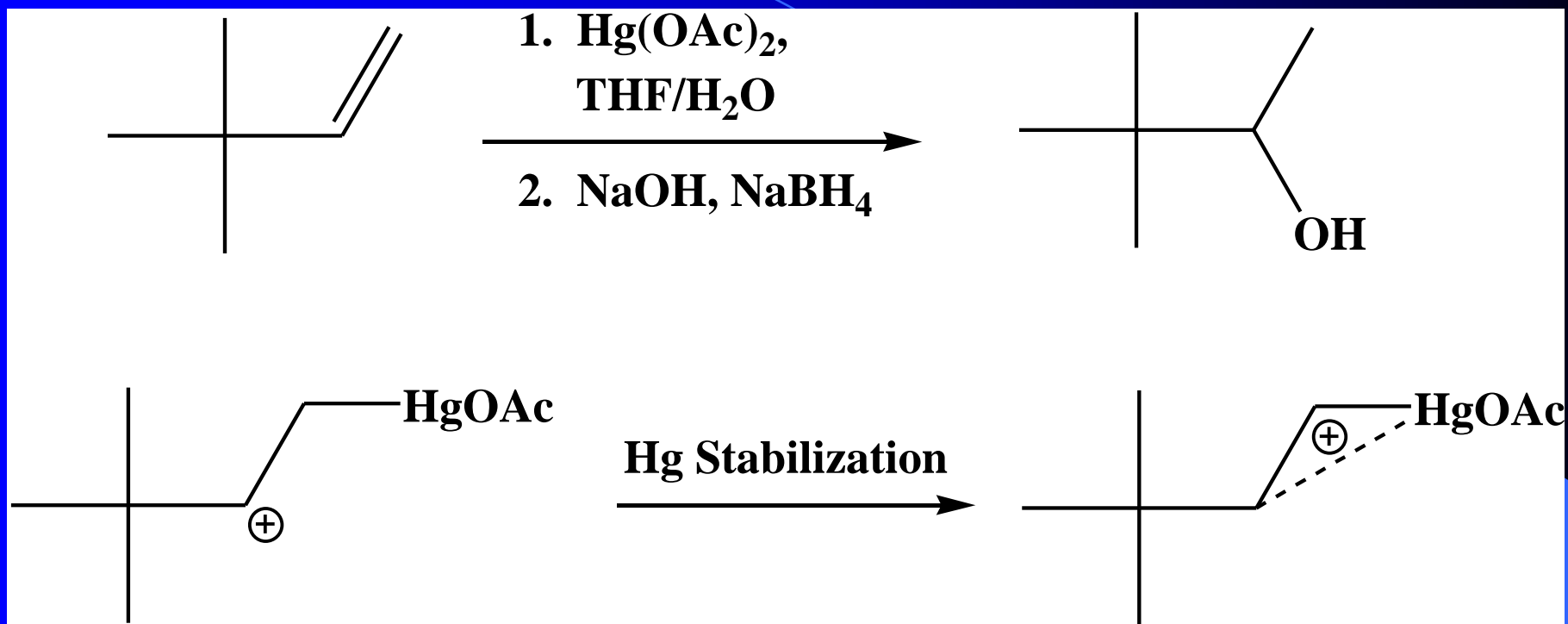


- Added Benefit of Oxymercuration/Demercuration:

- **C⁺ REARRANGEMENTS Seldom Observed**

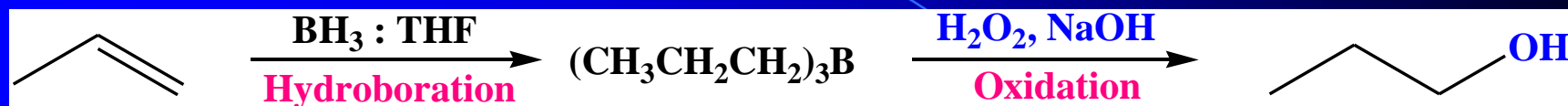
- Consider Example Seen on Next Slide

Oxymercuration-Demercuration (3)



- Would Expect 2° Carbocation to Rearrange to 3°
- Added C^+ Stabilization from Hg Atom Prevents Rearrangement
- Useful Hydration Process for Avoiding Skeletal Migrations

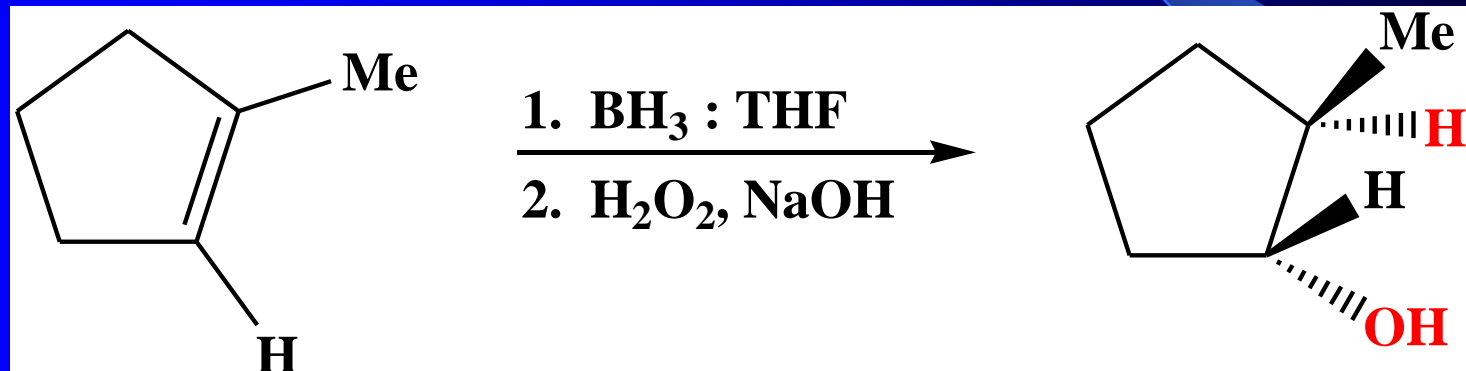
Hydroboration—Oxidation Reactions



- Hydroboration: Addition of H and B to Alkene
- Neutral Boron has 3 Coordination Sites
 - Get Trialkyl Boranes as an Intermediate (Tripropylborane)
- Oxidation: $\text{H}_2\text{O}_2, \text{NaOH}$ Oxidize to Trialkylborate Ester
- Oxidation Followed by a Hydrolysis, Cleaves Borate Ester
- ANTI-MARKOVNIKOV Product (Good for 1° Alcohols!)

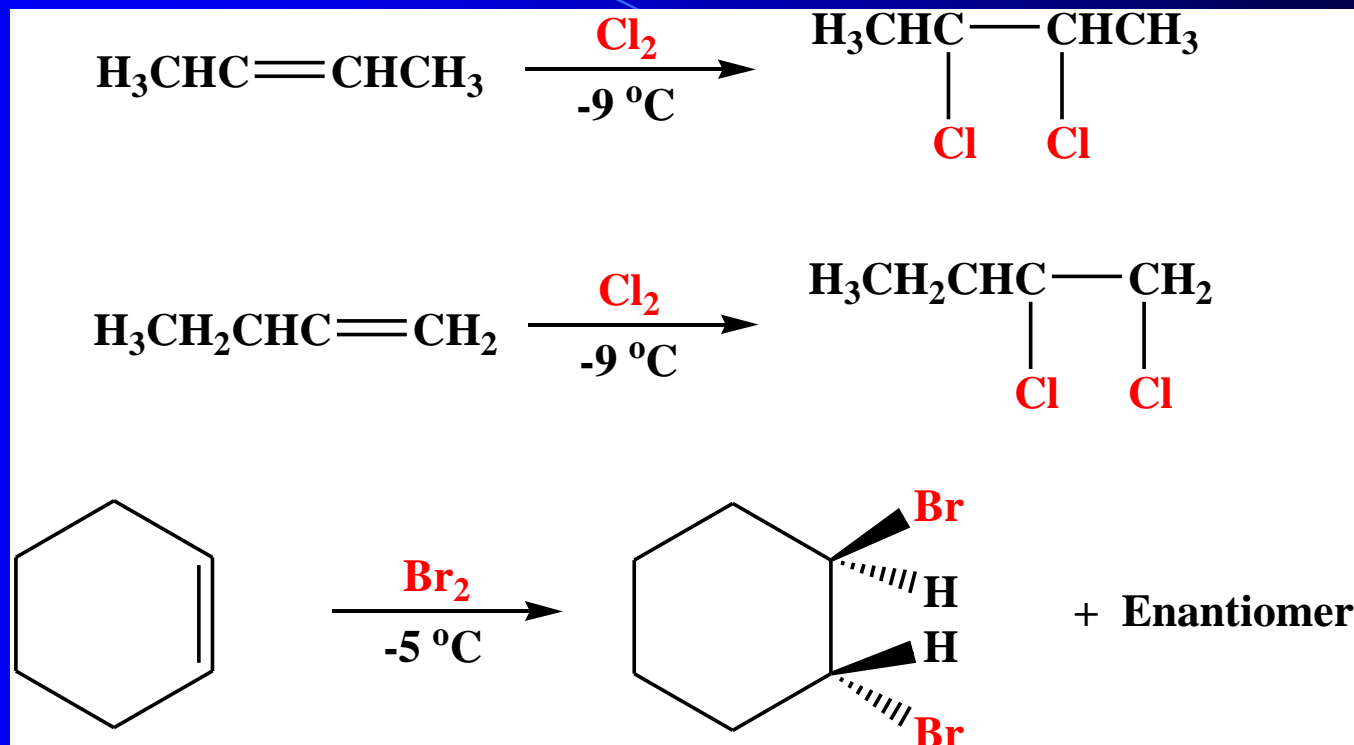
Hydroboration—Oxidation Reactions

- We Mentioned **anti-Markovnikov Regiochemistry**
- Reaction also Proceeds with **SYN Stereochemistry**



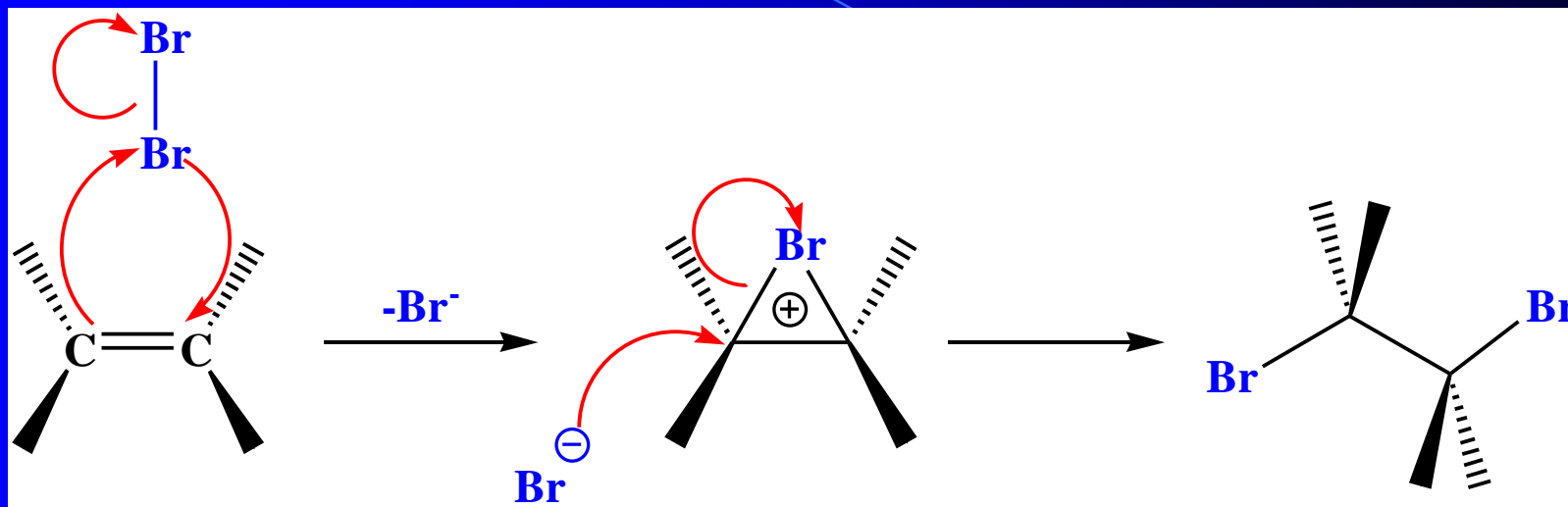
***H** and **OH** Delivered anti-Markovnikov to the
SAME FACE of the π Bond*

Addition of Cl₂ and Br₂ to Alkenes



- Obtain Vicinal Dihalides as Reaction Products
- Want to use a Non-Nucleophilic Solvent (Due to Intermediate)
 - Important to Run Reactions in Dark (Avoid Radicals)

General Mechanism of Dihalide Addition

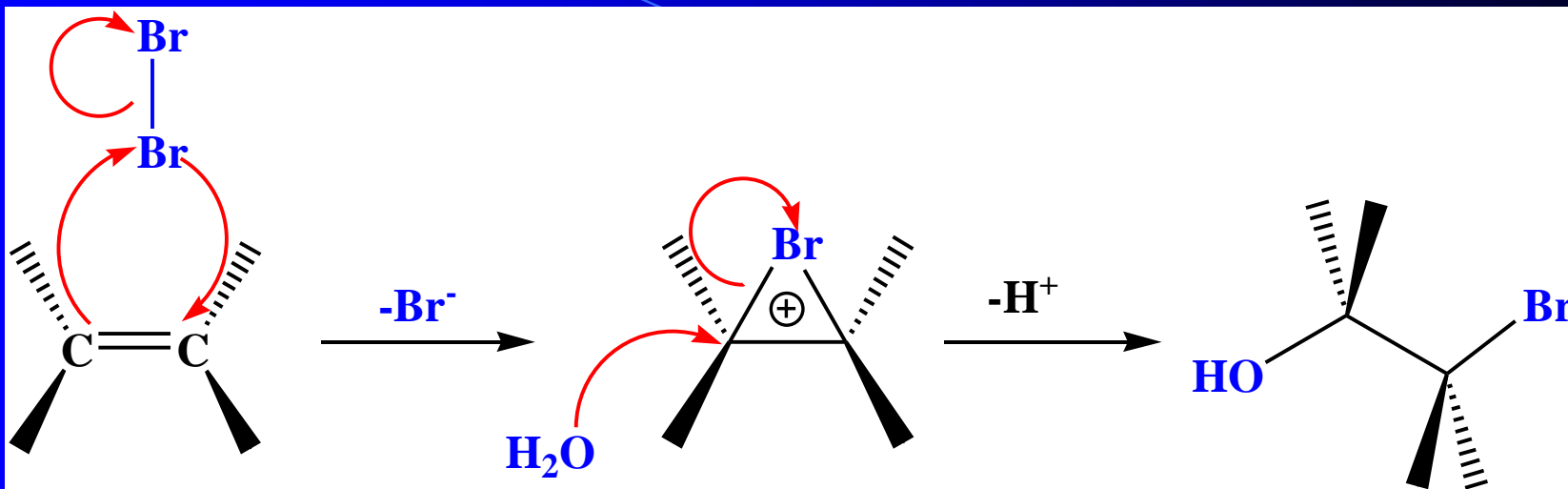


- Intermediate is a **BROMONIUM ION** (in Br_2 Case)
- **Nucleophilic Solvents Can Capture (Open) Bromonium Ion**
 - Bromonium Ion Opening is $\text{S}_{\text{N}}2 \rightarrow$ Anti Addition of Br_2

Stereochemistry of Dihalide Additions

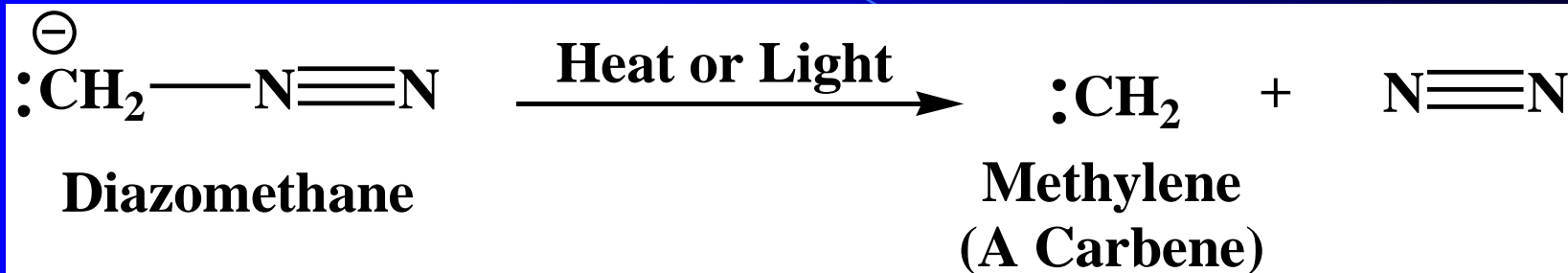
- Can Open Symmetric Bromonium Ions at Either Carbon
- Always (for now) Anti (Trans) Addition of X_2
- Reaction Products Are Enantiomers
- Racemic Mixtures (50:50) in Symmetric Bromonium Ions
- Will Get Excess of One Enantiomer in Asymmetric Cases
- Stereospecific Reactions: One Stereoisomeric Form of the Starting Material Reacts in Such a Way to Form a Specific Stereoisomeric Form of the Product

Halohydrin Formation



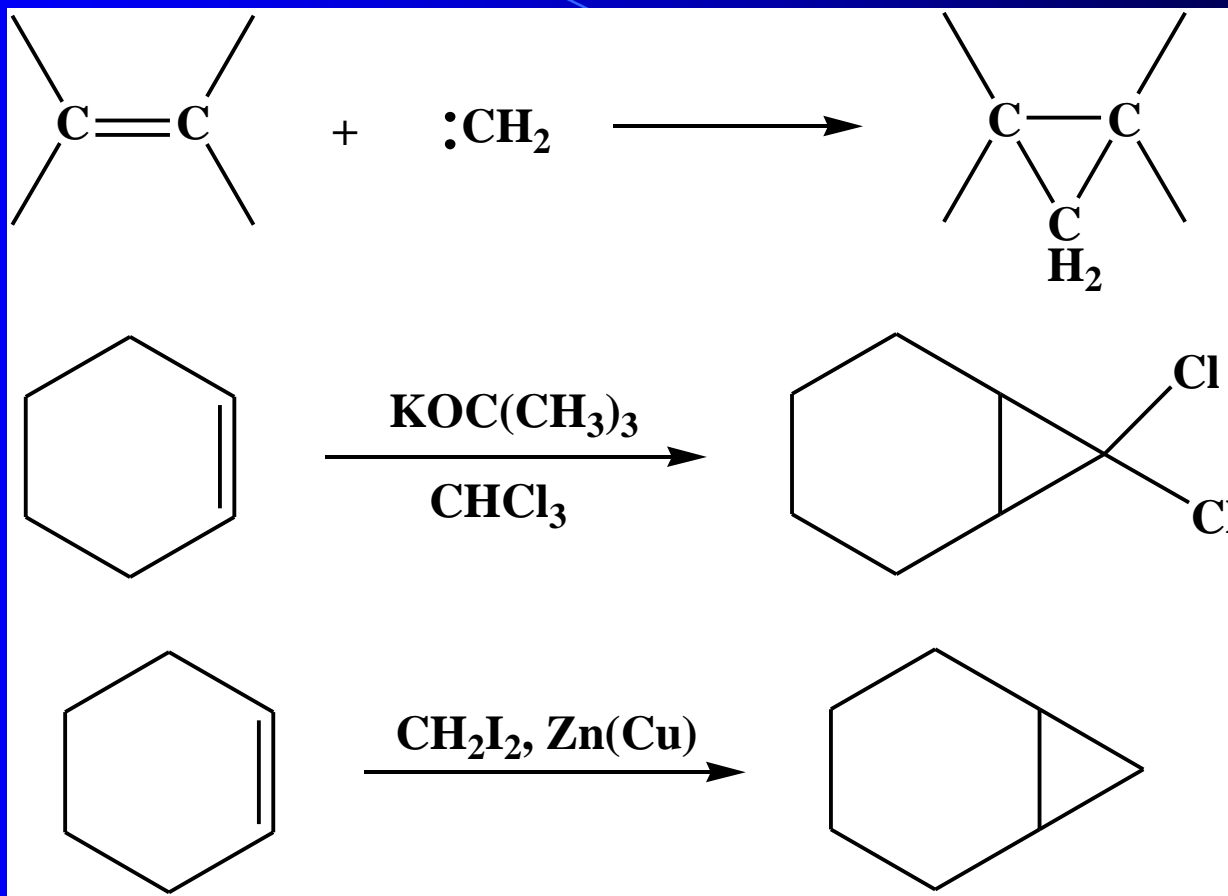
- Intermediate is Still a BROMONIUM ION (in Br₂ Case)
- Nucleophilic Solvents Can Capture (Open) Bromonium Ion
 - H₂O Opens the Bromonium Ion; Another H₂O Deprotonates
 - Product is Halohydrin → Net X-OH Addition to Alkene
 - Still Can Get Stereoisomeric Products (Open Either End)

Divalent Carbon Compounds: Carbenes



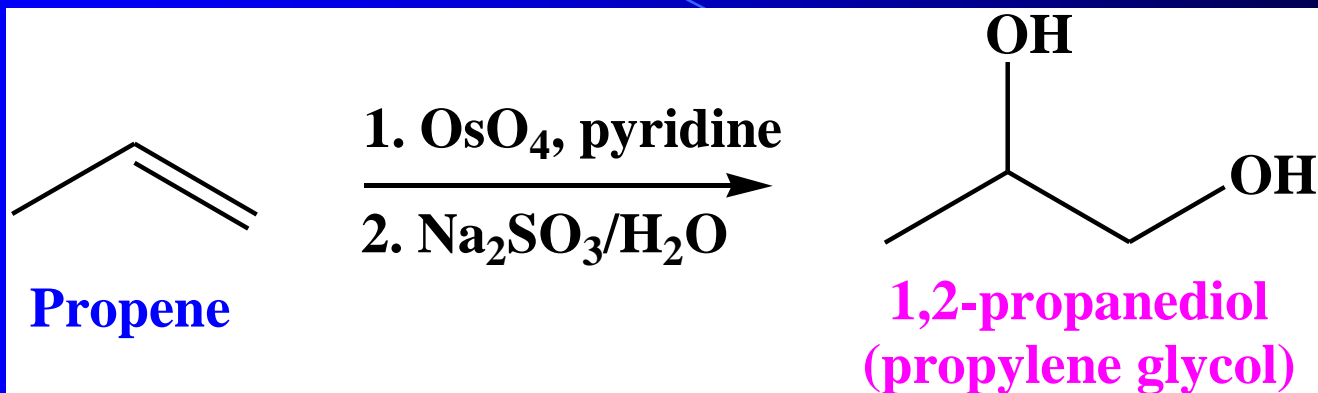
- Common Way of Generating Carbenes (Divalent Carbon)
- **Diazomethane: 3 Resonance Structures (Draw Others??)**
- Carbenes are **Highly Reactive Species**; Short-Lived
- Excellent Utility is in the **Synthesis of Cyclopropanes**

Divalent Carbon Compounds: Carbenes



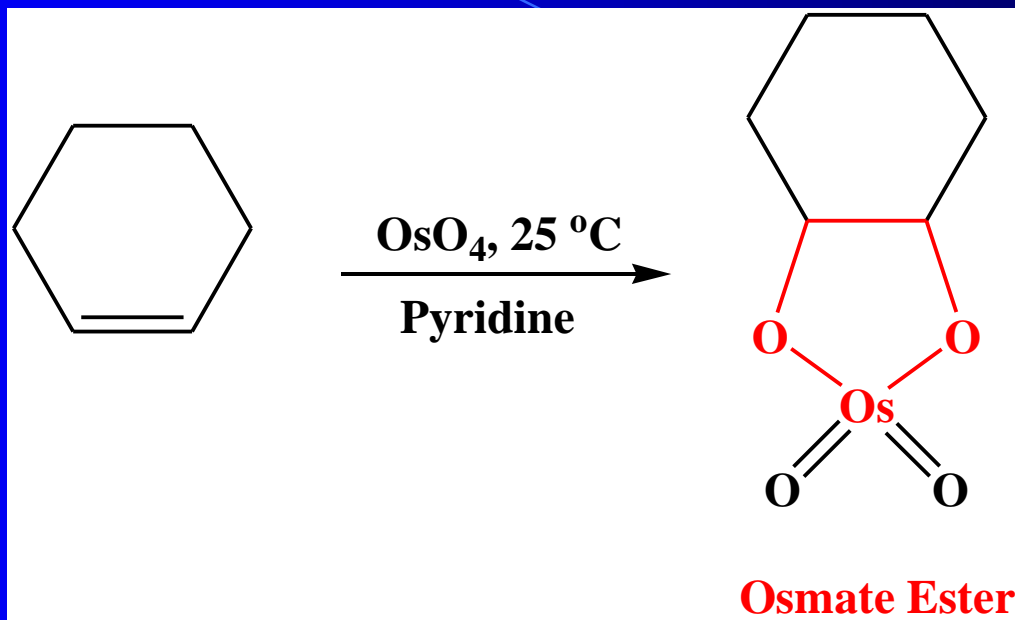
- Halogen Substituted Carbenes from Haloforms (CHCl_3 , etc.)
- Last Reaction is Called the “Simmons-Smith” Reaction

Oxidation: Syn Dihydroxylation



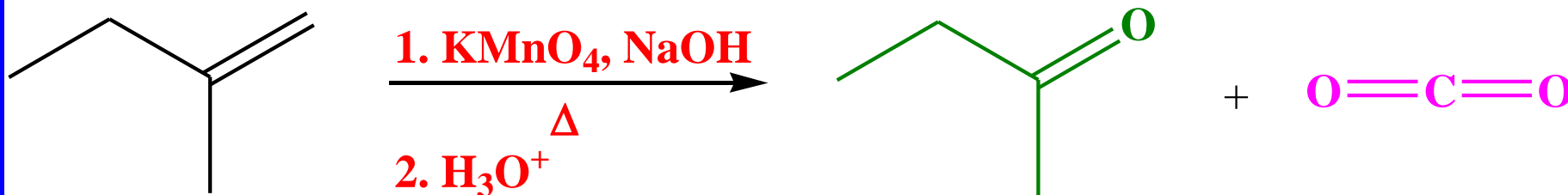
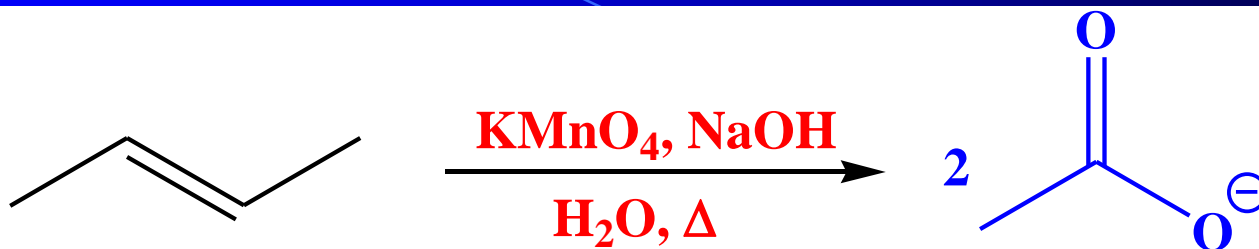
- C=C is Oxidized by OsO₄
- Addition of Hydroxyl Groups Proceeds w/ SYN Stereochemistry
- Can Also use KMNO₄ (More Powerful, May Cleave Diol)
- If Using KMNO₄, need **COLD** Reaction Temperatures

Oxidation: Syn Dihydroxylation



- Syn Addition Due to 5-membered Transition State
- Transition State Same for KMnO_4 Oxidations
- Cleavage of Osmate Ester Does Not Change C-O Stereochemistry

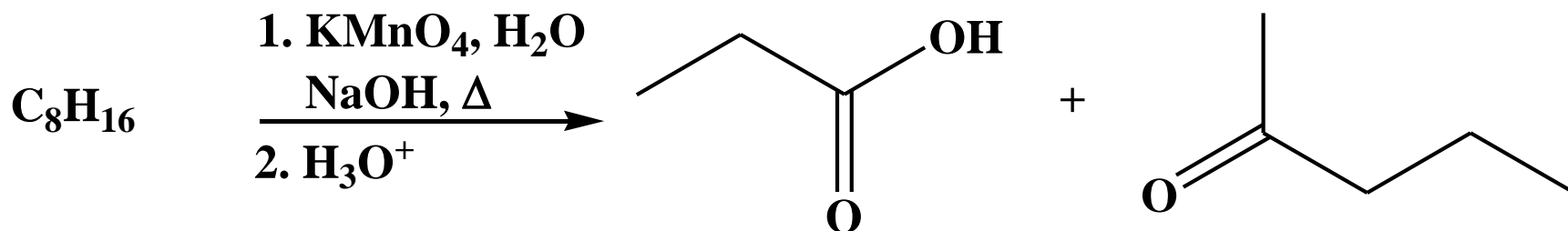
Oxidative Cleavage of Alkenes



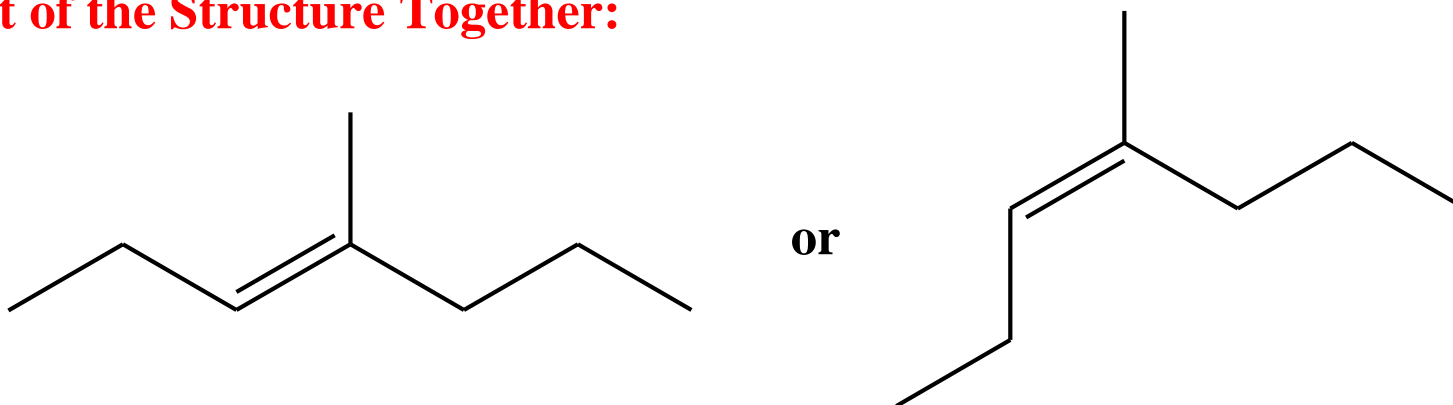
- Diol is Believed to be Intermediate in Cleavage Reaction
- Unsubstituted Alkene Carbons Oxidized to Carbon Dioxide
- Monosubstituted Alkene Carbons Oxidized to Carboxylates
- Disubstituted Alkene Carbons Oxidized to Ketones

How You May See Oxidative Cleavage

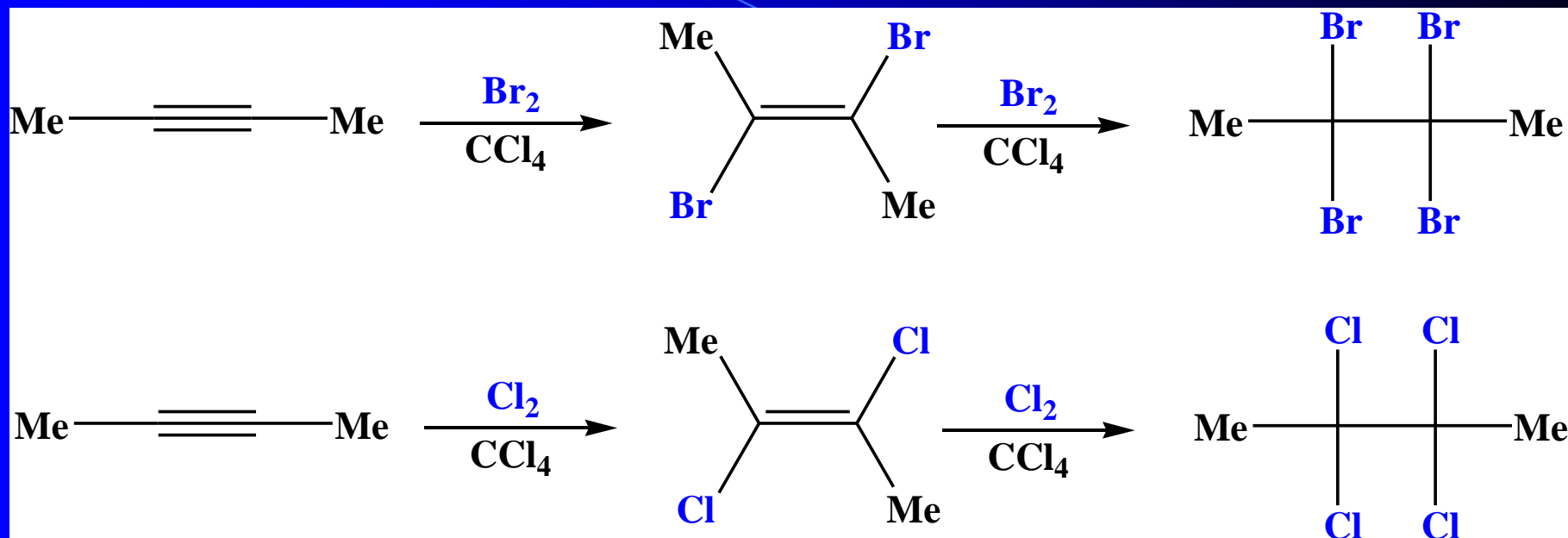
An Unknown Alkene (C_8H_{16}) Gives Two Products When Treated w/ Hot $KMnO_4$:



The Products are a Carboxylic Acid and a Ketone, So Our Alkene Must Be Trisubstituted. We Don't Know if it is CIS or TRANS, but we Can Put the Rest of the Structure Together:

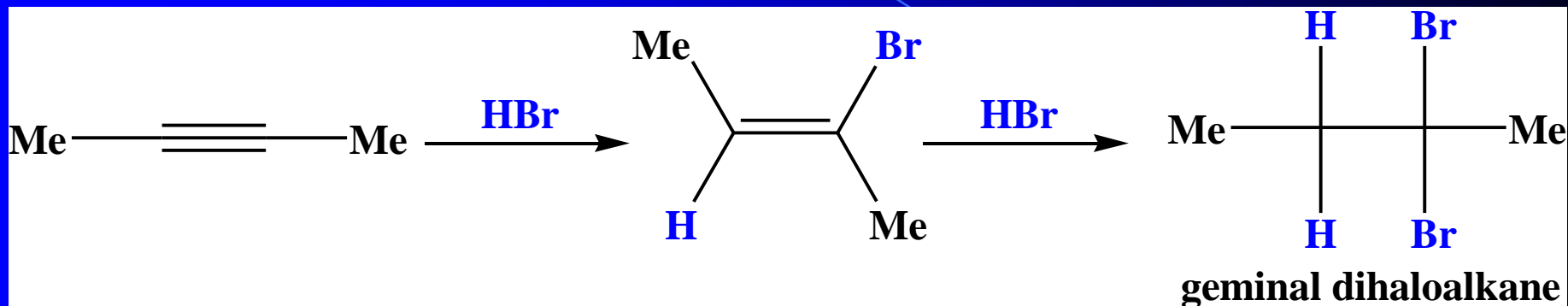


Dihalide Addition To Alkynes



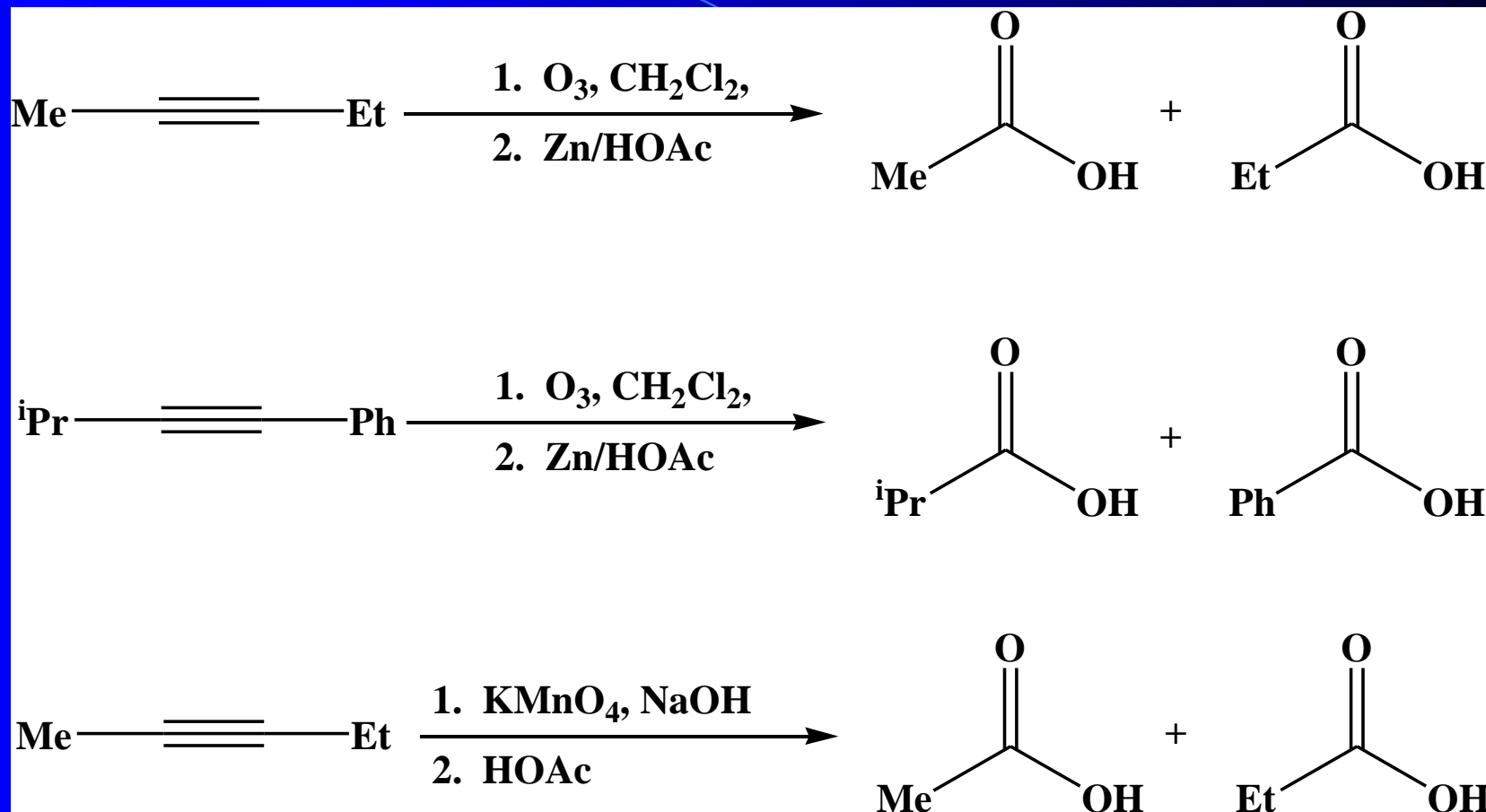
- Addition Reactions, Just as in Alkenes (adds Once or Twice)
- Anti Additions, First Product Usually a Trans Dihaloalkene
- Can Get Relatively Good Trans Dihaloalkene Yields (1 eq X_2)

Addition of HX to Alkynes



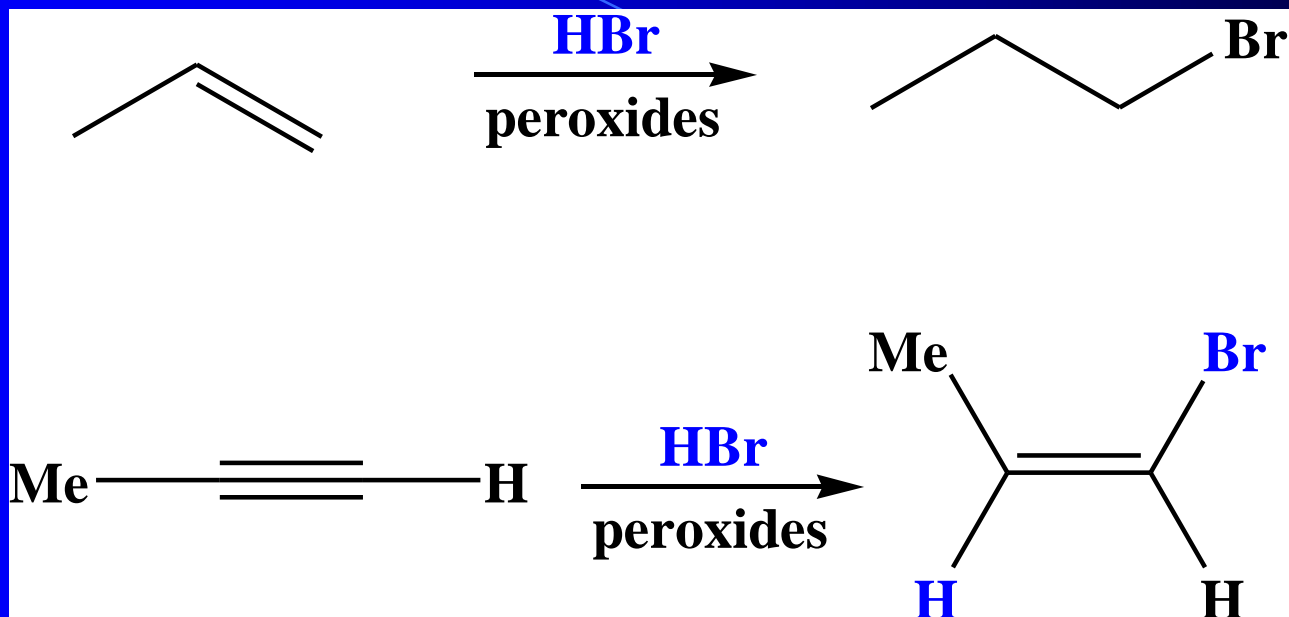
- Addition Reactions, Just as in Alkenes (adds Once or Twice)
- Final Product Typically Geminal Dihaloalkene
- Both Additions Follow Markovnikov's Rule (explains gem.)
- Alumina Accelerates Reaction Rate (as seen w/ Alkenes)

Oxidative Cleavage of Alkynes



- Can Use Either Ozonolysis or KMnO_4 as with Alkenes
- Products of the Oxidative Cleavage are Carboxylic Acids

Anti-Markovnikov HBr Addition

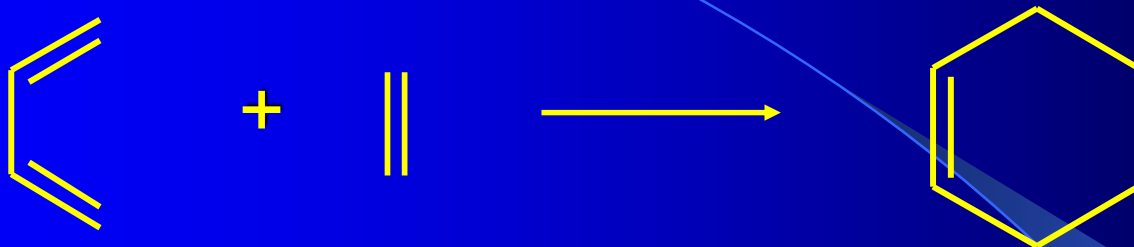


- Addition of Peroxides (ROOR) → ANTI-MARKOVNIKOV
- Goes Through a Radical Mechanism
- Right Now Focus on Regiochemistry (Know the Reaction)

The Diels-Alder Reaction

*Synthetic method for preparing
compounds containing a cyclohexene ring*

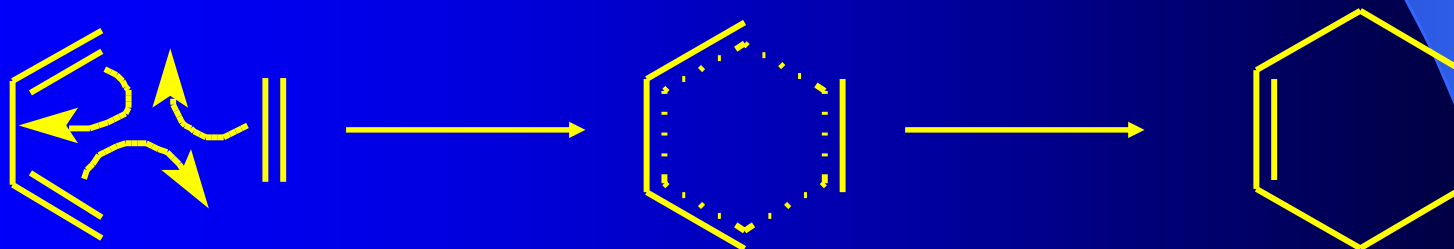
The Reaction



conjugated
diene

alkene
dienophile

cyclohexene

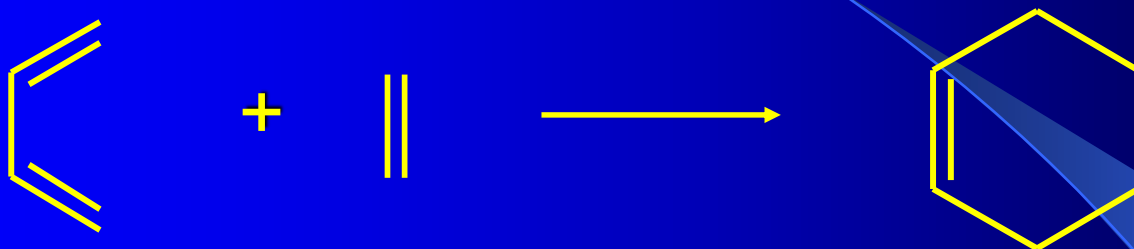


transition state

Mechanistic features

- **concerted mechanism**
- **cycloaddition**
- **pericyclic reaction**
 - **a concerted reaction that proceeds through a cyclic transition state**

Recall the general reaction...



conjugated
diene

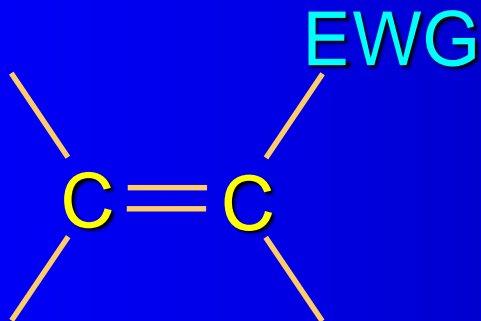
alkene
dienophile

cyclohexene

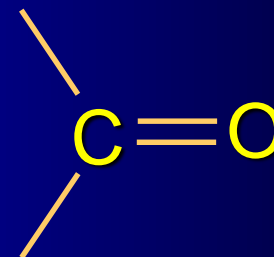
- The equation as written is somewhat misleading because ethylene is a relatively unreactive dienophile.

What makes a reactive dienophile?

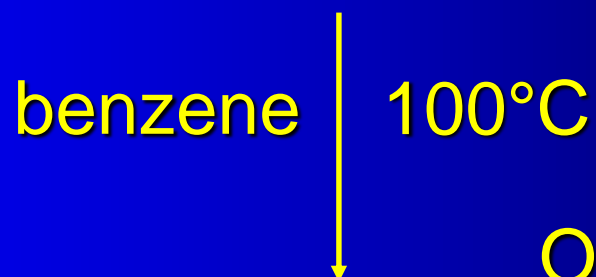
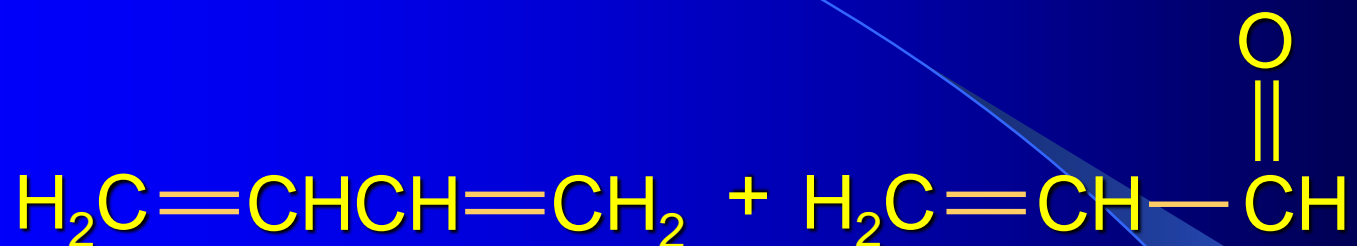
- The most reactive dienophiles have an electron-withdrawing group (EWG) directly attached to the double bond.



Typical EWGs

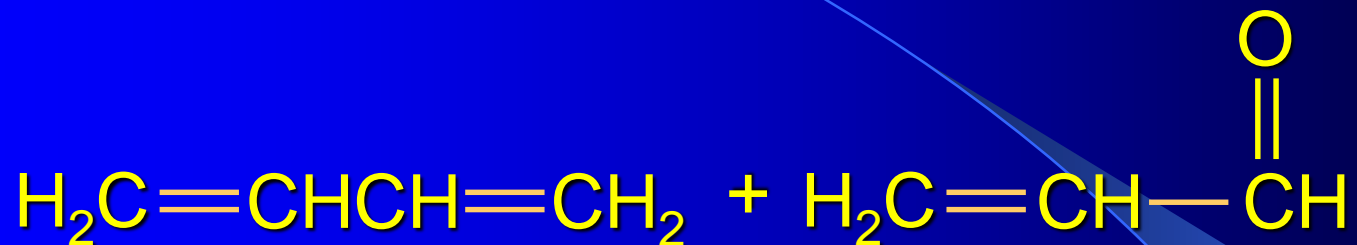


Example



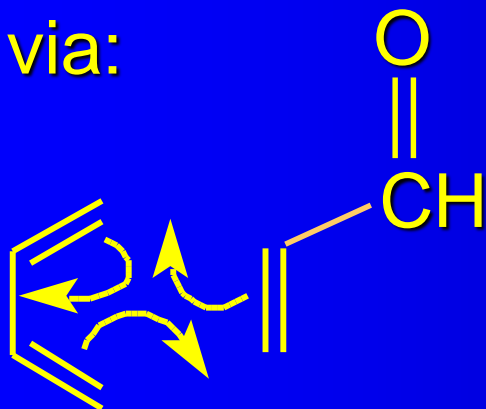
(100%)

Example



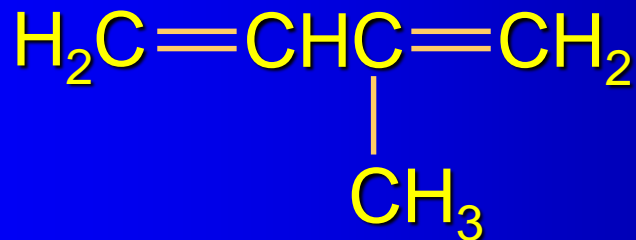
benzene \downarrow 100°C

via:

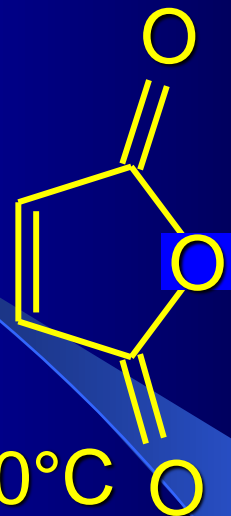


(100%)

Example



+



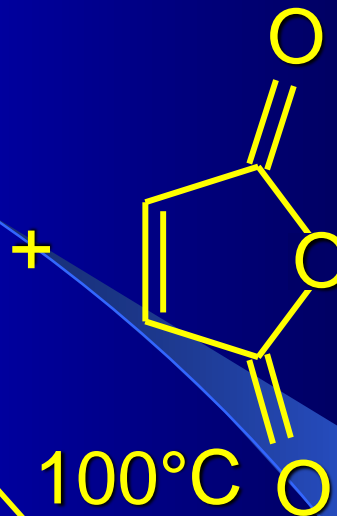
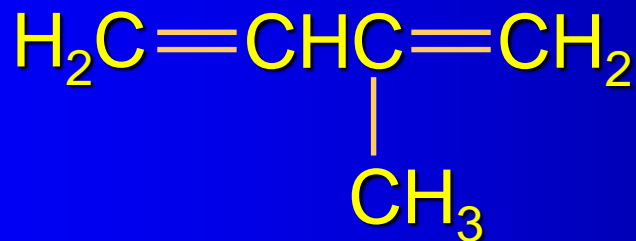
benzene

100°C



(100%)

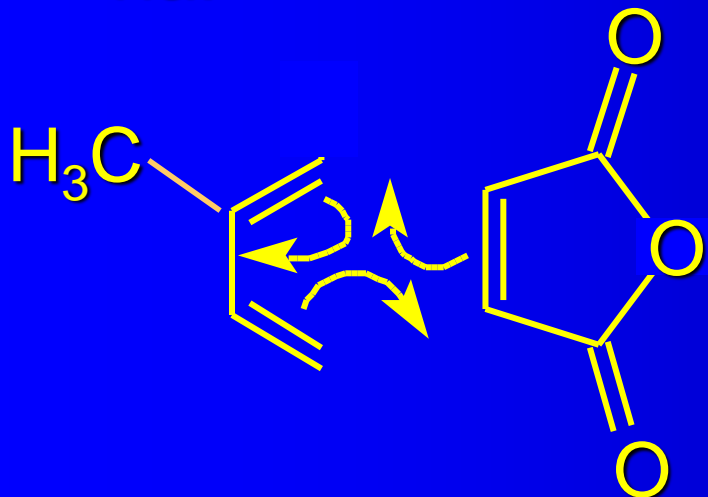
Example



benzene

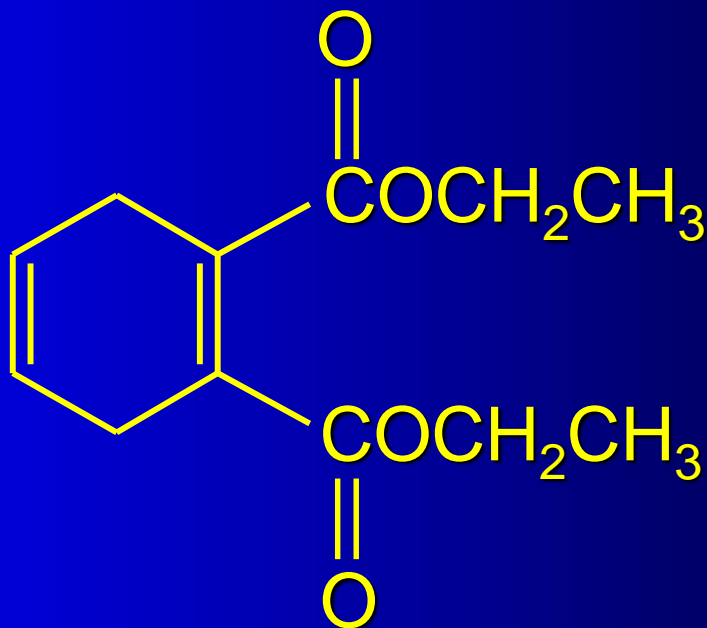
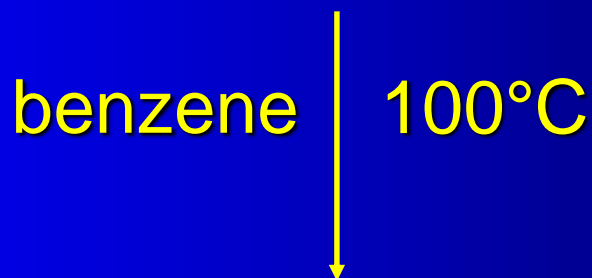
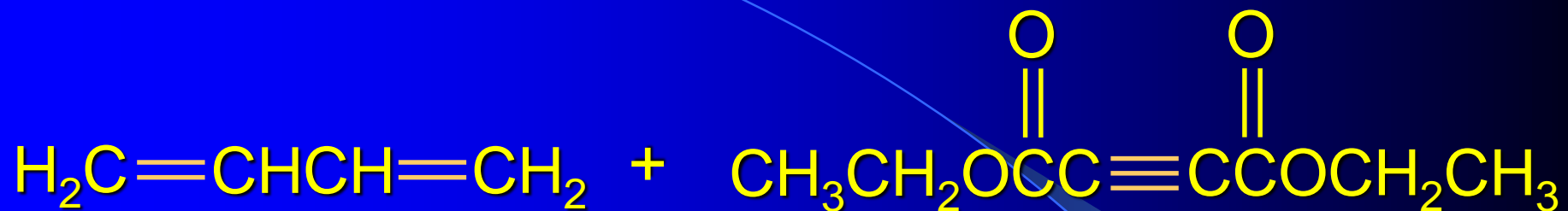
100°C

via:



(100%)

Acetylenic Dienophile

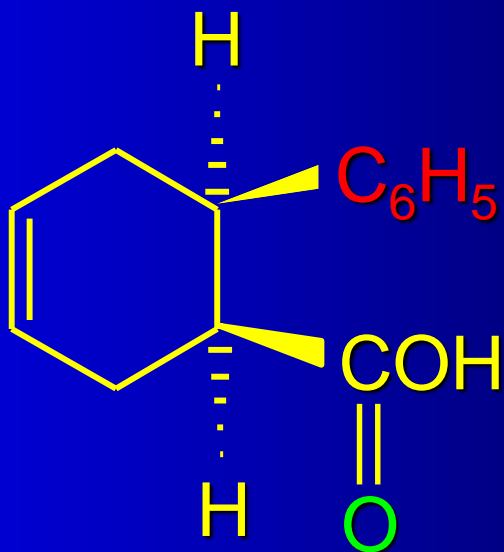
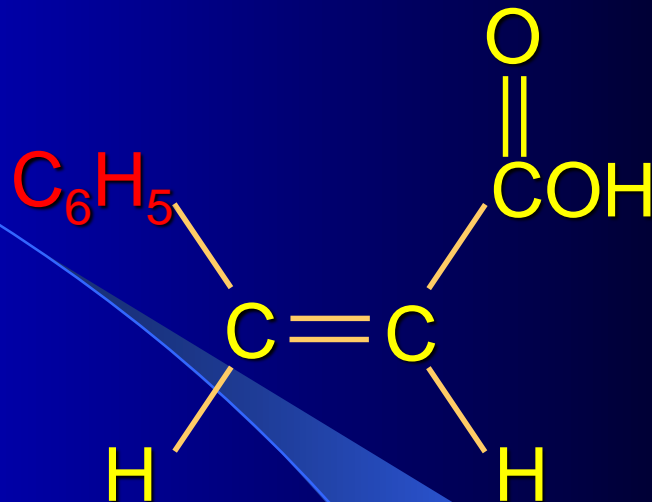


Diels-Alder Reaction is Stereospecific*

- **syn addition to alkene**
- ***cis-trans* relationship of substituents on alkene retained in cyclohexene product**

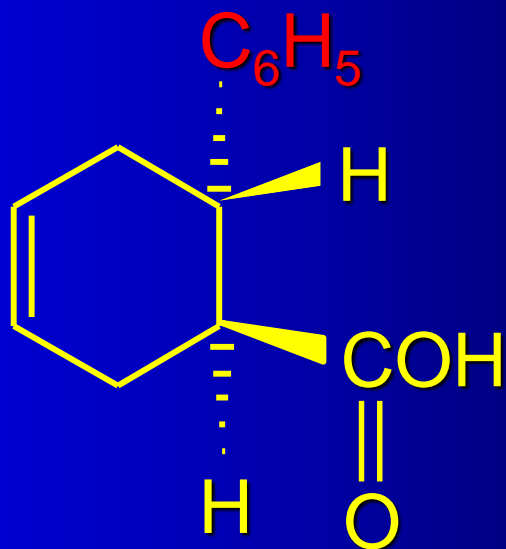
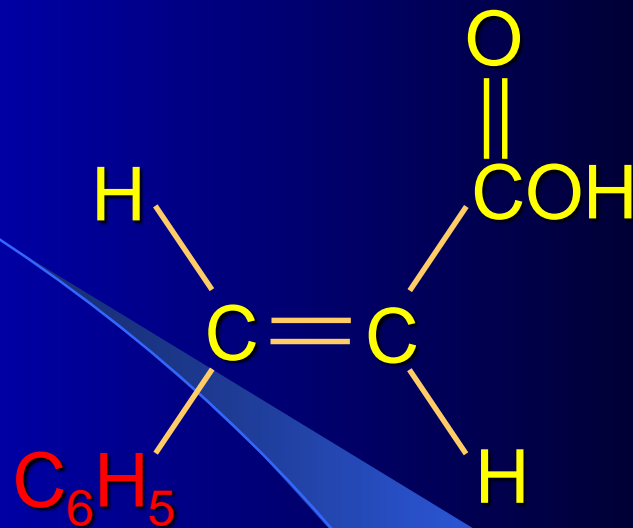
***A stereospecific reaction is one in which stereoisomeric starting materials give stereoisomeric products; characterized by terms like syn addition, anti elimination, inversion of configuration, etc.**

Example



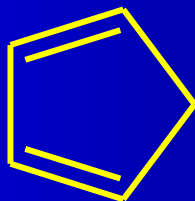
only product

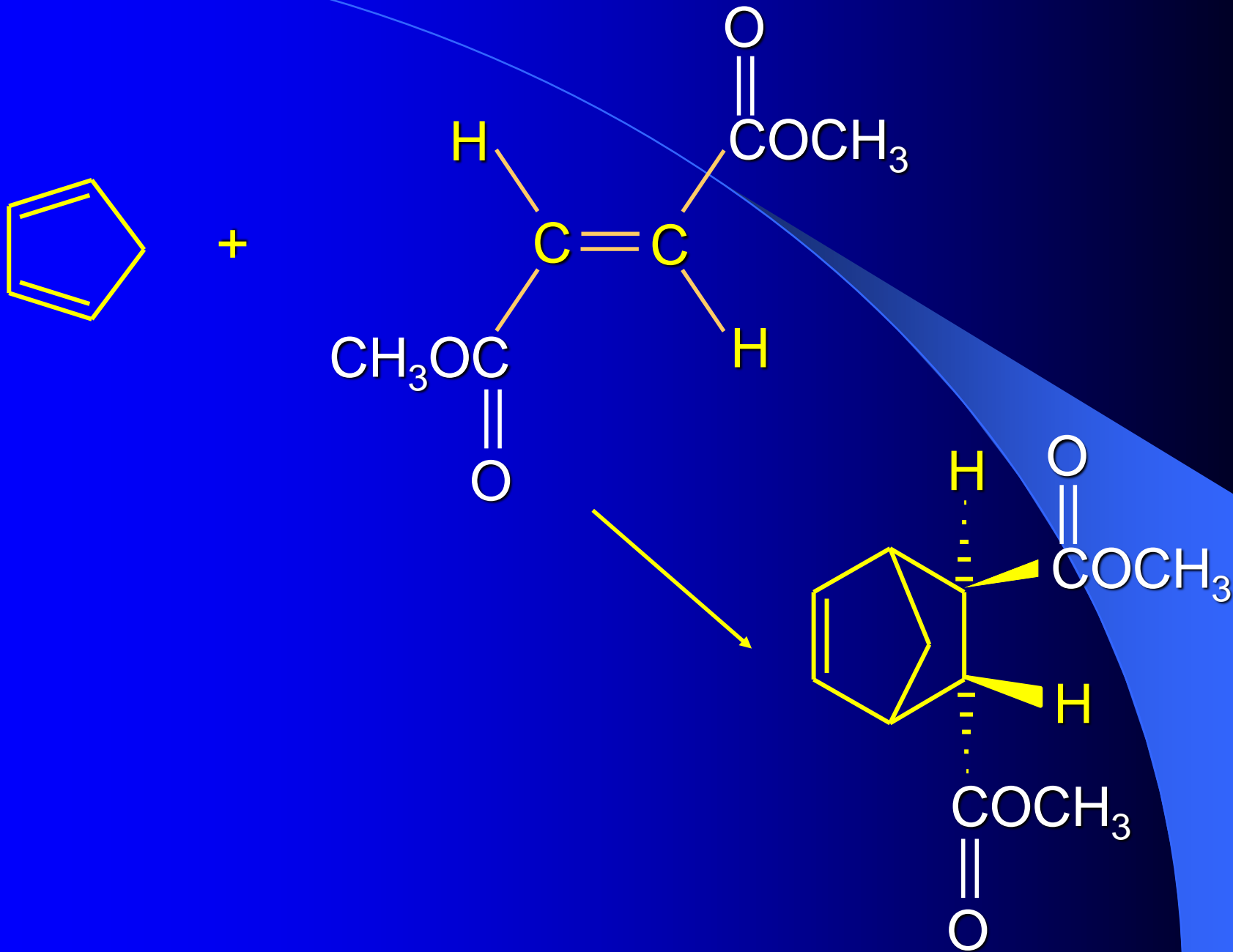
Example

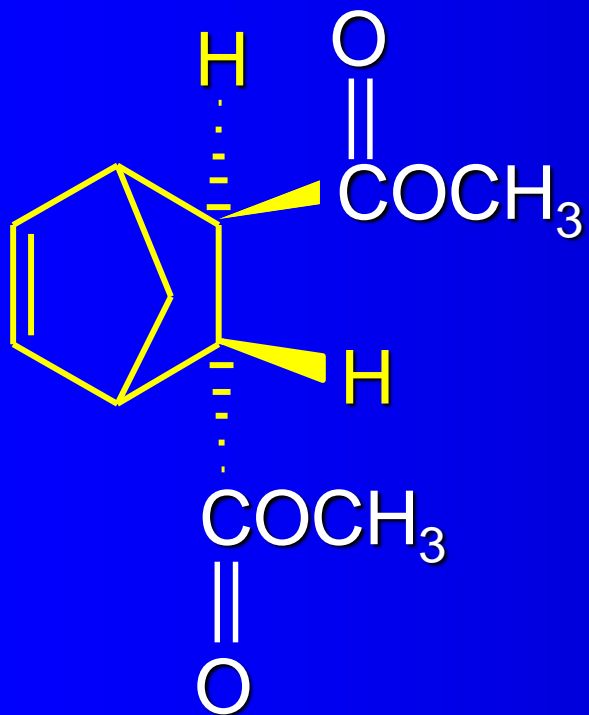


only product

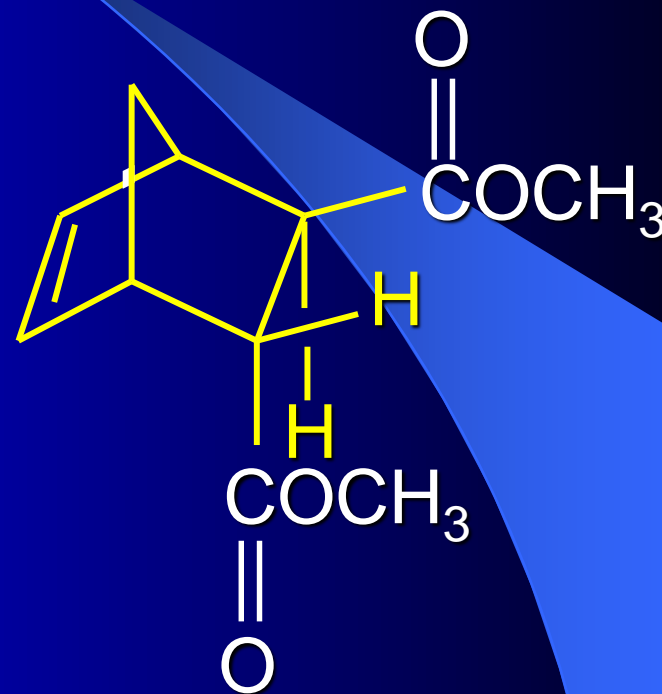
Cyclic dienes yield bridged bicyclic
Diels-Alder adducts.







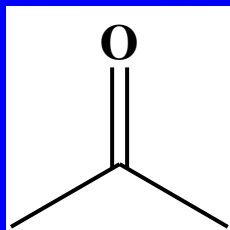
● is the same as



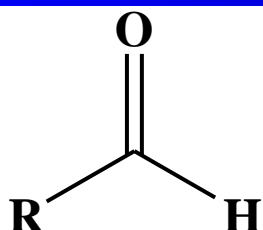
Alcohols, Carbonyls and REDOX

- The Carbonyl Group
- Oxidation/Reduction Reactions: Review
- Reduction of Carbonyls to Alcohols
- Oxidation of Alcohols
- Organometallic Compounds
- Organolithium and Magnesium Compounds
- Reactions of Organolithium/Magnesium Species
- Alcohols from Grignard Reactions
- Lithium Dialkylcuprates

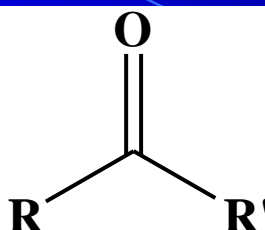
The Carbonyl Functional Group



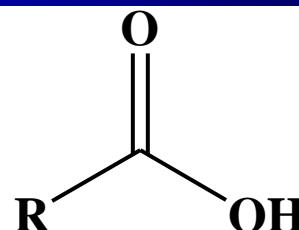
Carbonyl



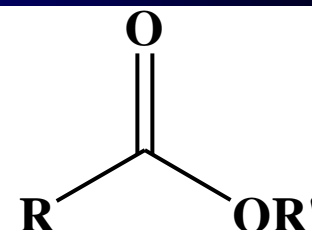
Aldehyde



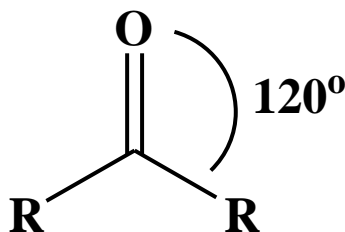
Ketone



Carboxylic
Acid



Carboxylate
Ester

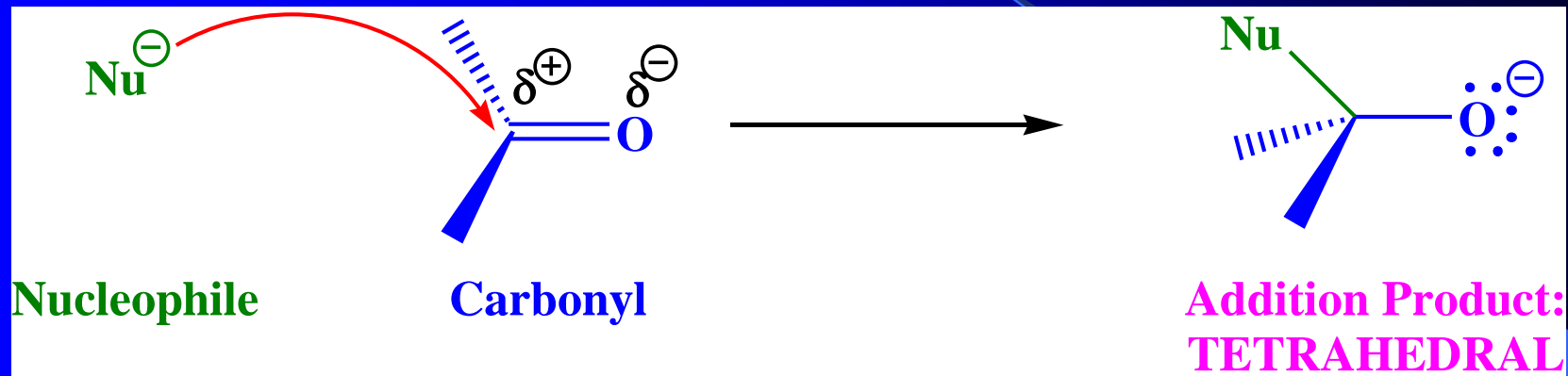


Planar, sp^2 Hybridized Carbon

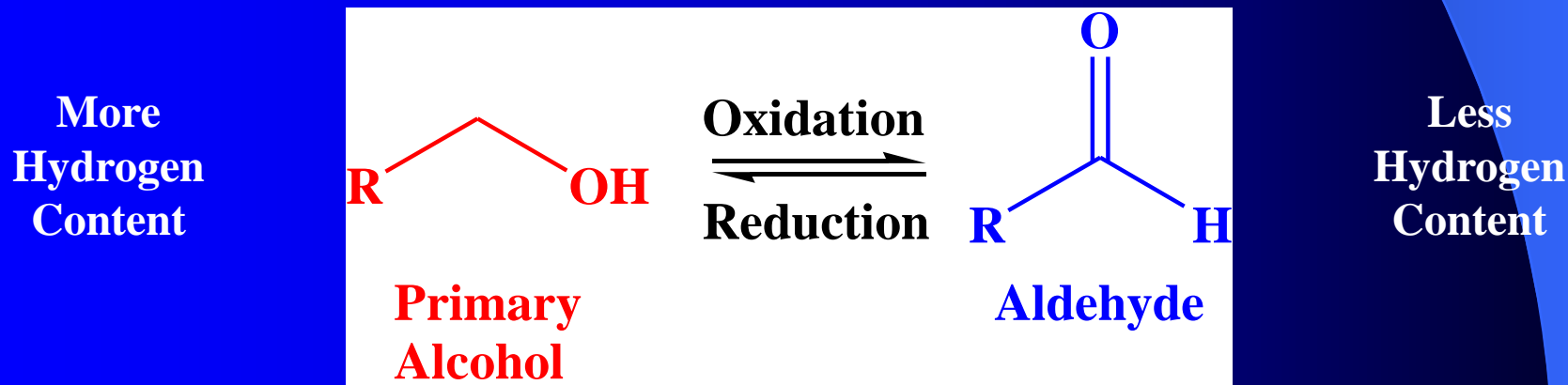
- Carbonyl Features 1 σ and 1 π Bond
- Carbonyl Group Quite Polarized ($C^{\delta+}$, $O^{\delta-}$)

General Reactions of Carbonyls

Nucleophilic Addition to Carbonyl Groups:



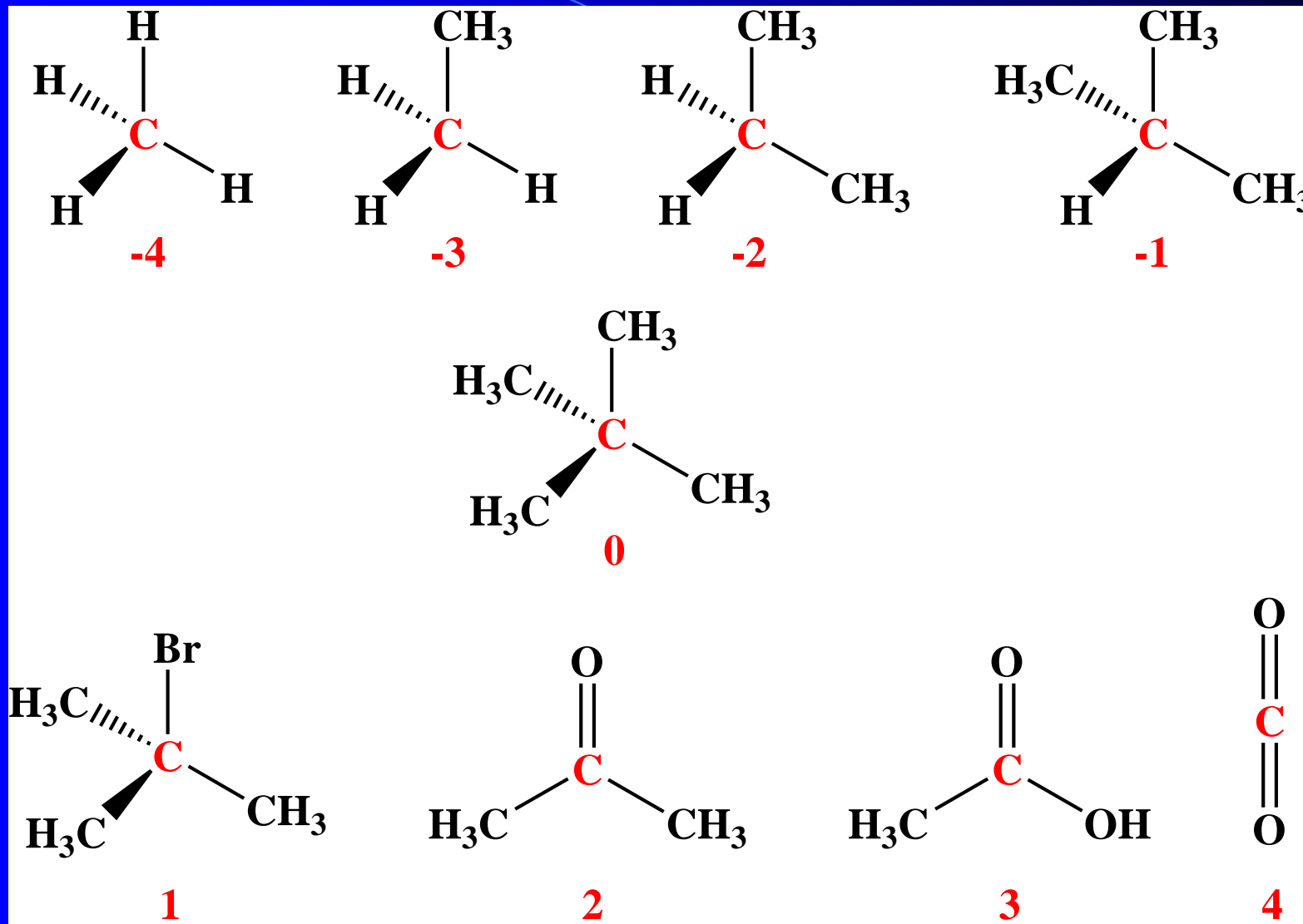
Oxidation of Alcohols/Reduction of Carbonyls:



Oxidation/Reduction Reactions

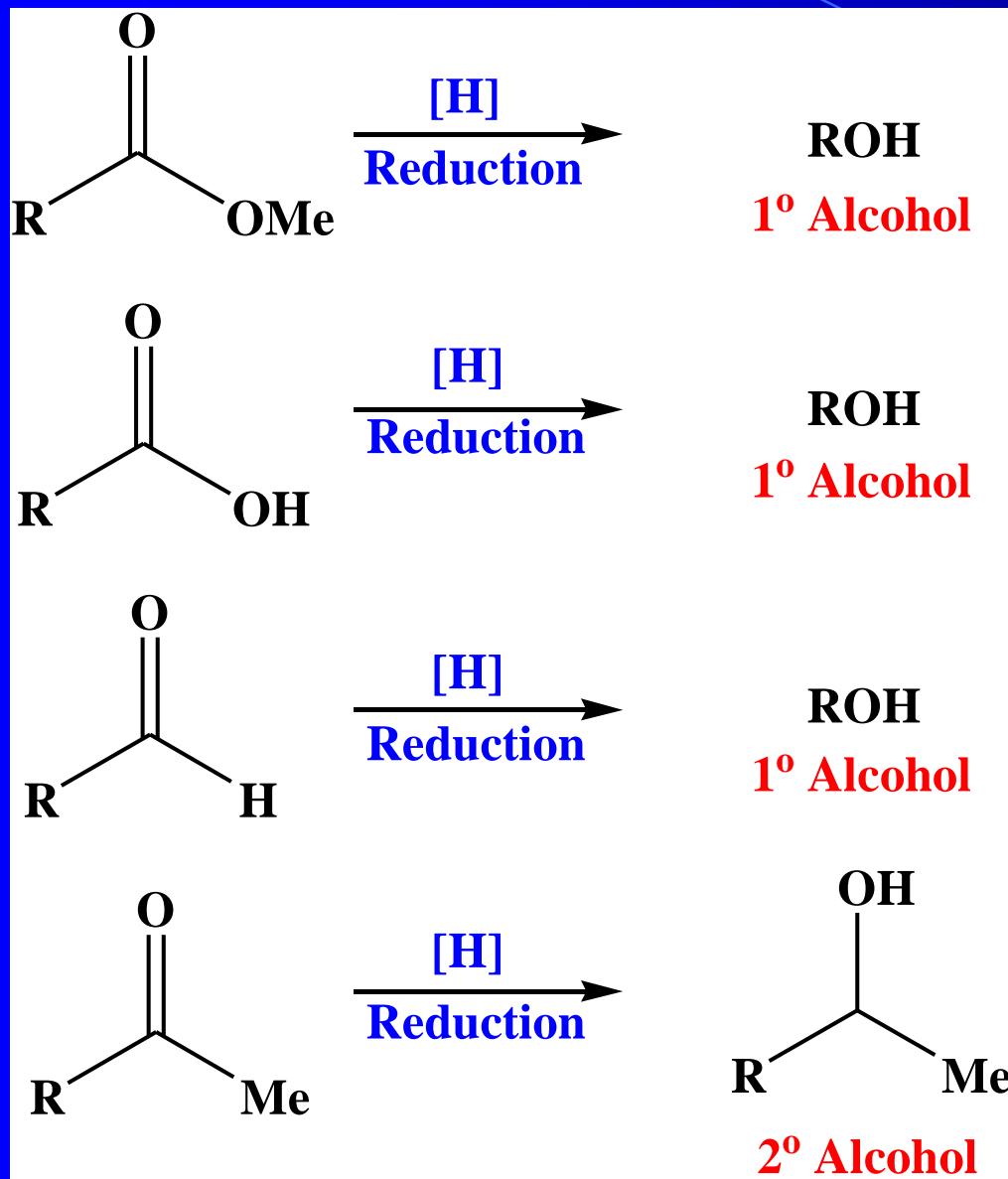
- Commonly Termed 'REDOX' Reactions
- From General Chemistry, we Will Recall
 - **Oxidation**: Loss of Electrons
 - **Reduction**: Gain of Electrons
- Organic Chemists will Typically use Different Definitions
 - **Reduction**: Increase Hydrogen Content (Decrease Oxygen)
 - **Oxidation**: Decrease Hydrogen Content (Increase Oxygen)
- **Oxidizing/Reducing** Agents: Usually Inorganic Compounds (M^+)
- We will also Recall that in REDOX Reactions:
 - **Oxidizing Agents** get **Reduced**
 - **Reducing Agents** get **Oxidized**

Oxidation States of Carbon: Organics



- +1 For More Electronegative, -1 For Less, 0 For Bonded Carbon

Alcohol Synthesis: Carbonyl Reduction



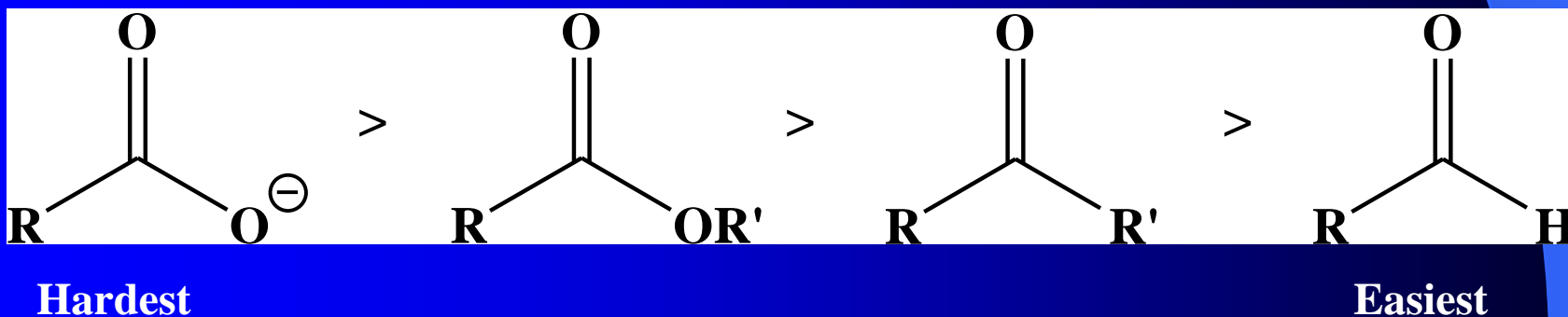
Carboxylic Acids, Esters,
Aldehydes Reduced to
1° Alcohols

Ketones Reduced to
2° Alcohols

Several Hydrogen Sources
Are Used In Organic
Reactions: We've Already
Seen NaBH_4

Reducing Agents: 1° and 2° Alcohols

- Sodium Borohydride: NaBH_4
- Lithium Aluminum Hydride: LiAlH_4 (LAH)
- H_2 /Transition Metal Catalyst
- NaBH_4 and LiAlH_4 are Hydride Transfer Agents
- Hydride (H^-) Acts as a Nucleophile
- Carbonyls Have Varying Degrees of Ease of Reduction:



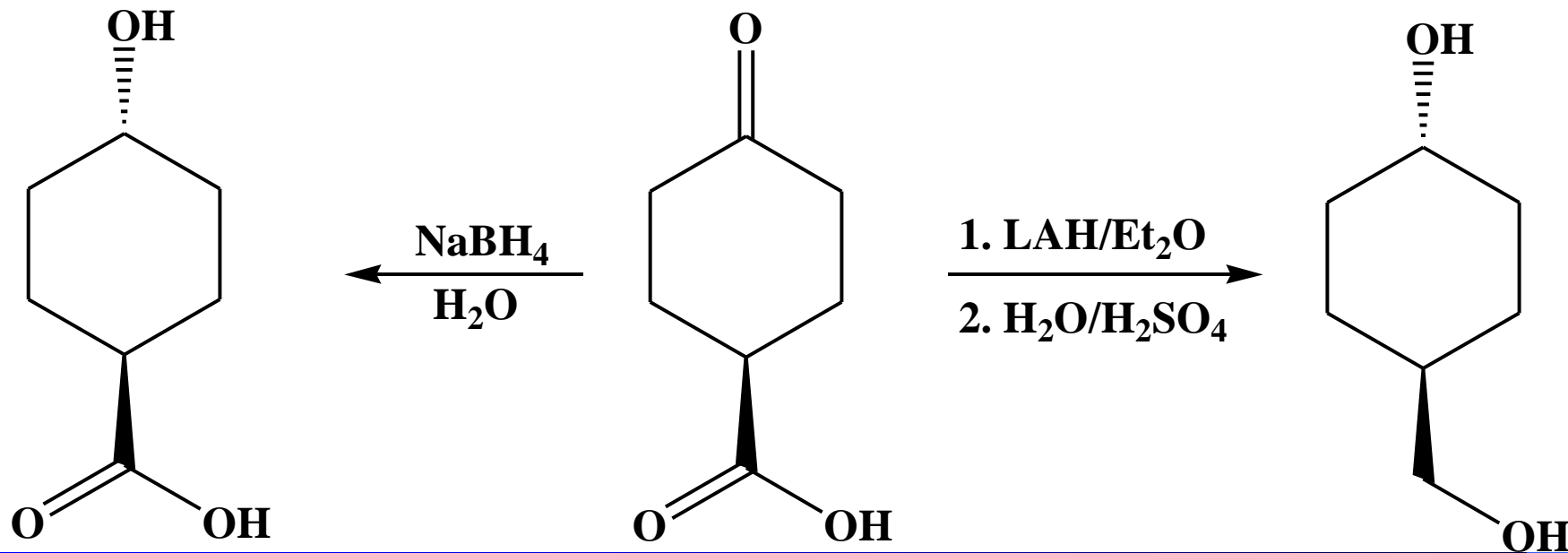
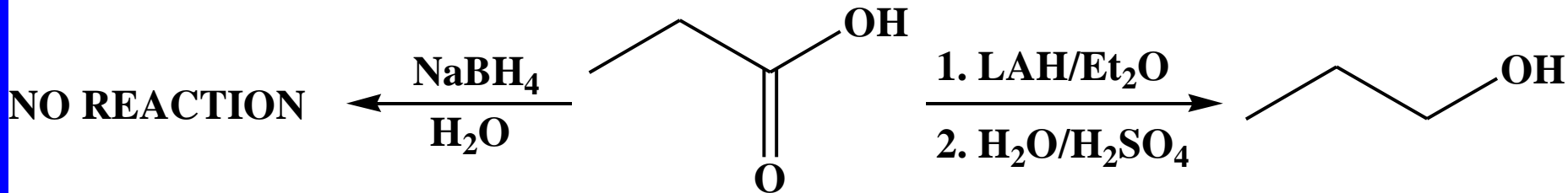
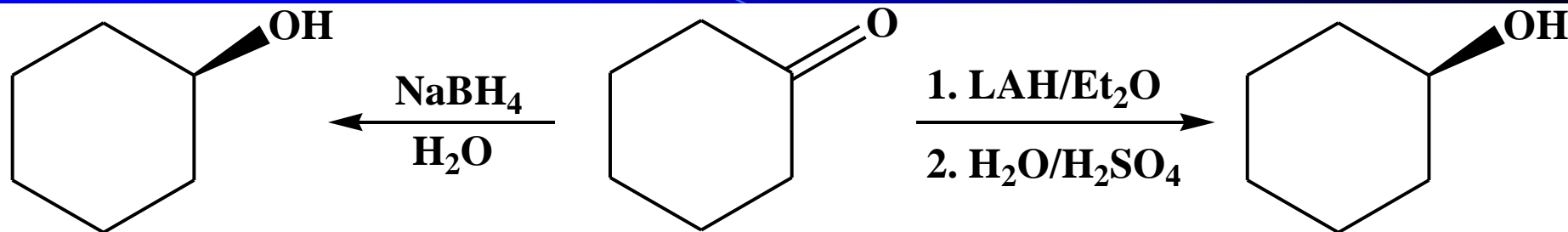
Selection of a Reducing Agent

- Choice of Reducing Agent Impacts Reaction Products
- For Ketones/Aldehydes Either Reductant Suffices

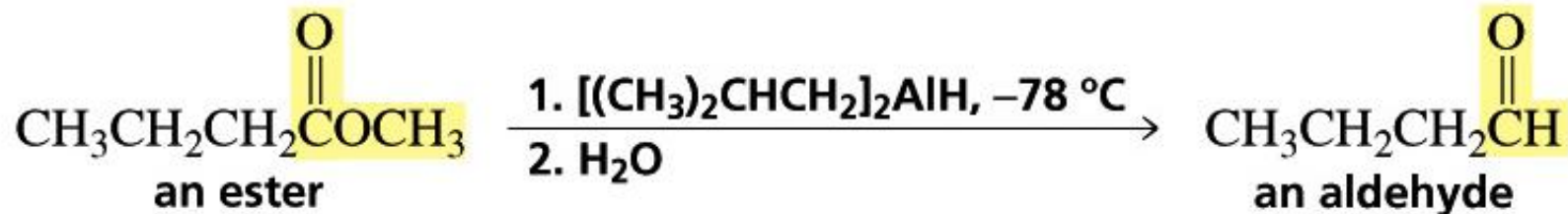
	Carboxylate	Ester	Ketone	Aldehyde
LiAlH₄	1° Alcohol	1° Alcohol	2° Alcohol	1° Alcohol
NaBH₄	No Reaction	No Reaction	2° Alcohol	1° Alcohol

- Carboxylates/Esters Only Reduced by LiAlH₄
- For Compounds w/ Multiple Carbonyl F.G.s; Select Based on Which Group(s) Need to be Reduced

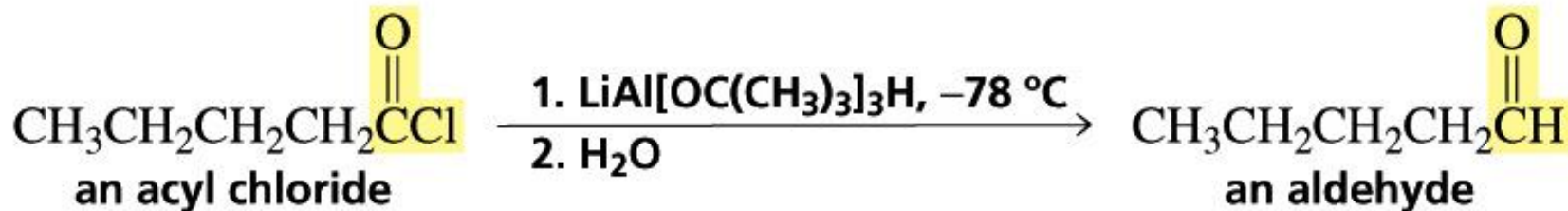
NaBH₄/LiAlH₄ Reduction Examples



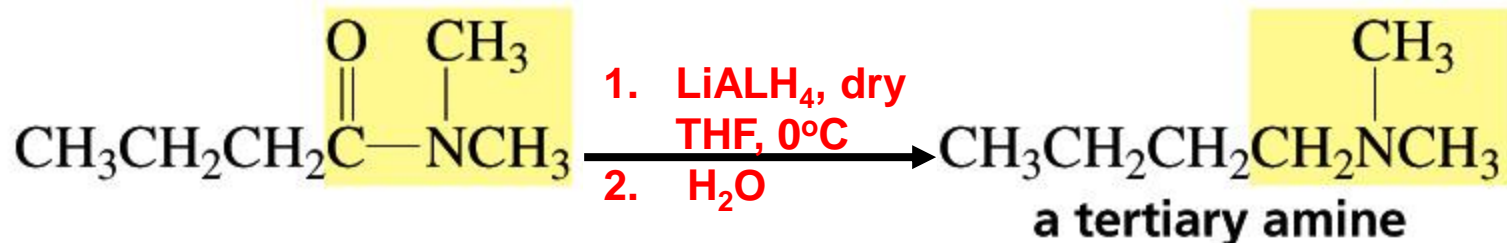
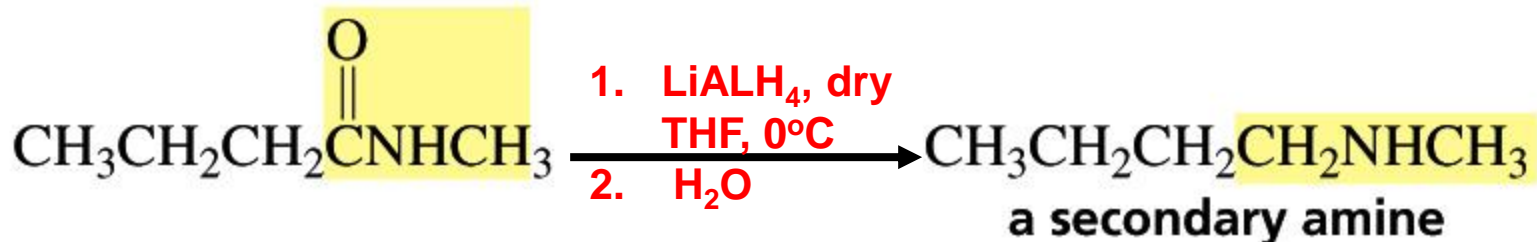
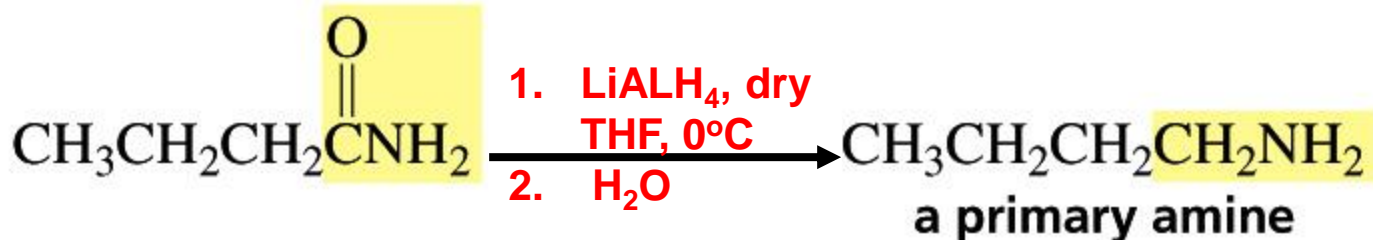
DIBAL (diisobutylaluminum hydride $[(\text{CH}_3)_2\text{CHCH}_2]_2\text{AlH}$) allows the addition of one equivalent of hydride to an ester



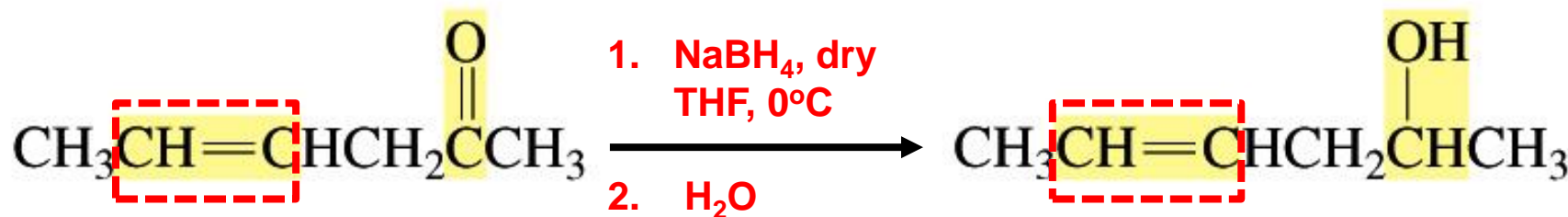
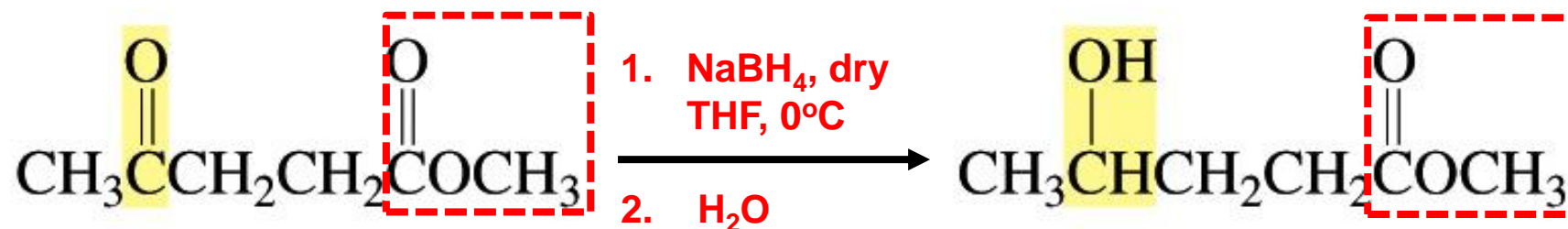
Replacing some of hydrogens of LiAlH_4 with OR groups decreases the reactivity of the metal hydride



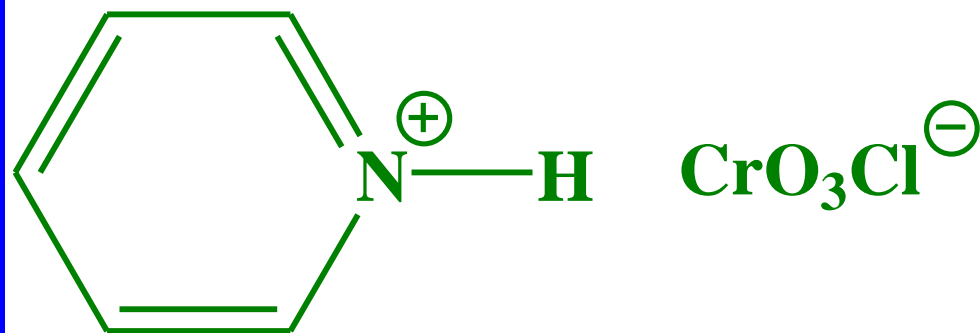
Formation of Amines by Reduction



NaBH_4 can be used to selectively reduce an aldehyde or a ketone in a compound keeping the ester or a $\text{C}=\text{C}$ unaffected



Oxidizing Agents in Organic Chemistry



**Pyridinium chlorochromate
(PCC)**



**Chromic Acid
(Jones Reagent)**

- PCC Generally a Mild Oxidant (1° Alcohol \rightarrow Aldehyde)
- Jones Reagent Harsher Oxidant (1° Alcohol \rightarrow Carboxylic Acid)
- Choose Oxidant Based on Desired Carbonyl Functional Group

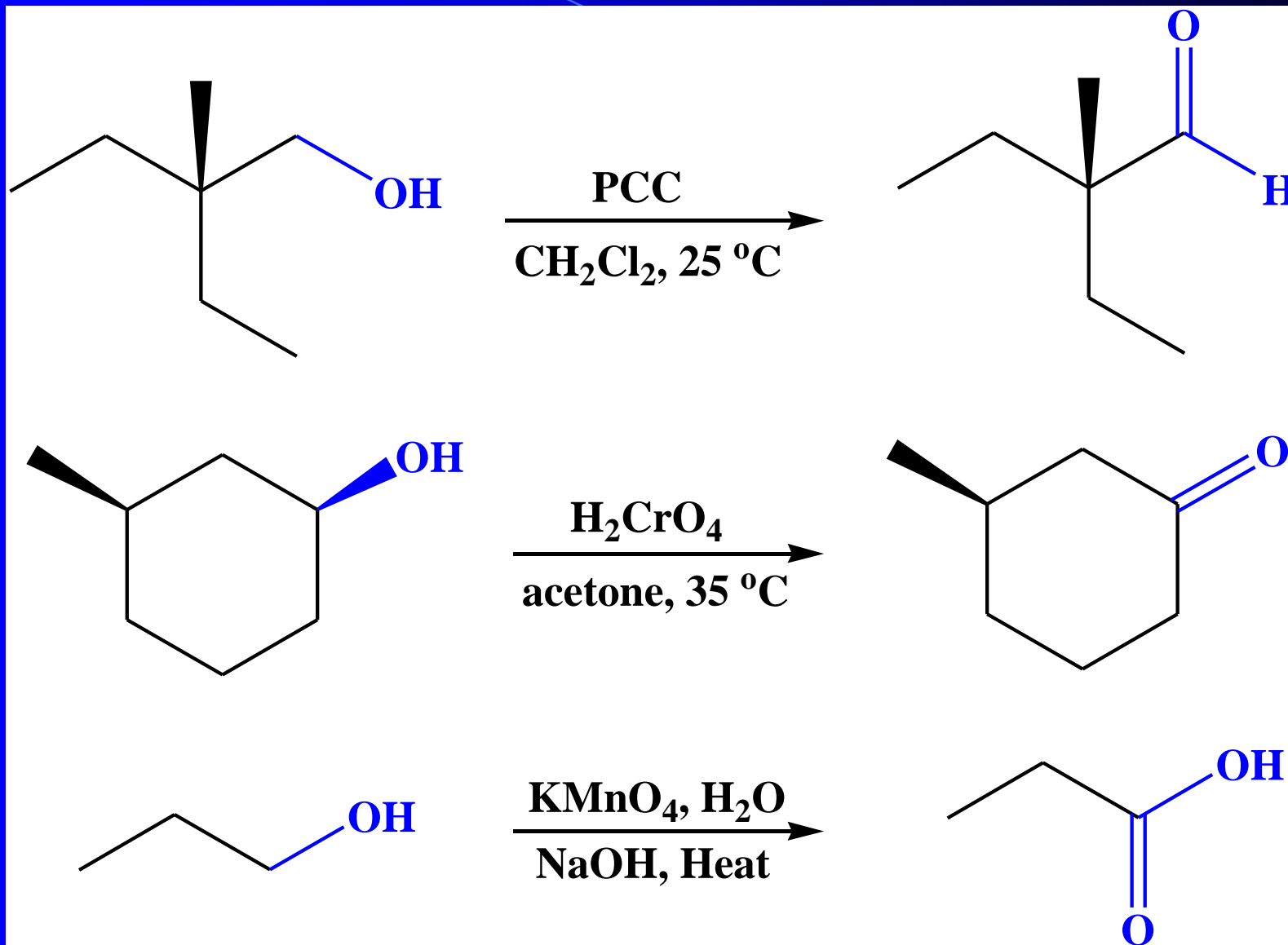
General Oxidizing Agent Selection

- Just as in Reductions, Oxidation Products Depend on Reagent
- Generally Don't Oxidize 3° Alcohols

	MeOH	1° Alcohol	2° Alcohol	3° Alcohol
PCC	$\text{H}_2\text{C}=\text{O}$	Aldehyde	Ketone	No Reaction
Cr^{6+} H_2SO_4	HCO_2H	Carboxylic Acid	Ketone	No Reaction

- PCC Good For Aldehydes From Primary Alcohols
- $\text{Cr}^{6+}/\text{H}_2\text{SO}_4$ Reagents, KMnO_4 Primary \rightarrow Carboxylic Acids
- Use What You Like For Most Ketones

Oxidation of 1°, 2° Alcohols



Oxidation Mechanisms: Chromate Esters

