

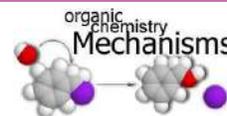
CHEM 344

ORGANIC REACTION MECHANISM

FOR CHEMISTRY' STUDENTS, COLLEGE OF SCIENCE

PRE-REQUISITES COURSE; CHEM 241

CREDIT HOURS; 2 (2+0+0)



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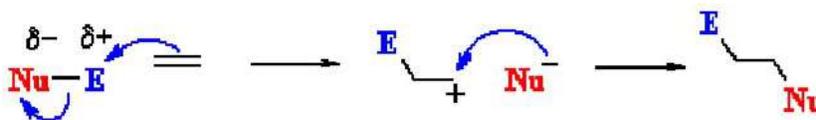
Addition to Carbon–Carbon Double bond
Electrophilic Addition Reactions

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ELECTROPHILIC ADDITION REACTION

- **Electrophilic addition reactions** are an important class of reactions that allow the interconversion of C=C and C≡C into a range of important functional groups. .
- Conceptually, addition is the reverse of elimination
- What does the term "**electrophilic addition**" imply ?

A **electrophile, E⁺**, is an electron poor species that will react with an electron rich species (C=C)
An **addition** implies that two systems combine to a single entity.



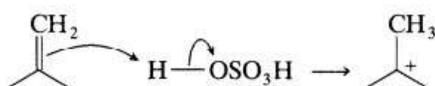
- **Electrophilic addition reaction involves two major steps:**
 - (1) Addition of the electrophile to the nucleophilic π bond to give **carbocation intermediate**,
 - (2) Reaction of the carbocation with a nucleophile.
- Simultaneous formation of the **two σ bonds**

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ELECTROPHILIC ADDITION REACTION

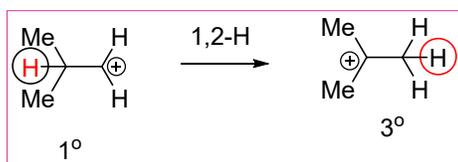
FORMATION AND STABILITY OF CARBOCATION

- **Protonation of an olefin;** Intermediate cations are often produced by addition of a proton or a Lewis acid to a π bond.

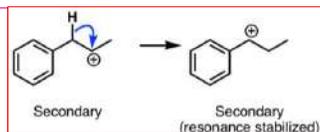
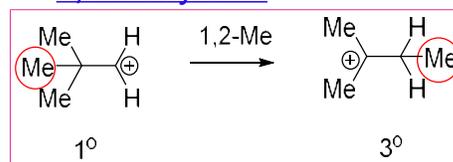


- **Carbocation rearranges to another carbocation of equal or greater stability.**

- **1,2-Hydride Shift**



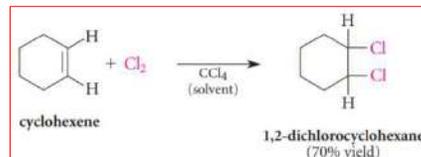
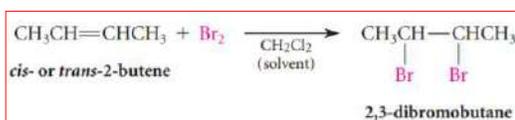
- **1,2-methyl shift**



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HALOGENATION OF ALKENES

A) ADDITION OF CHLORINE AND BROMINE



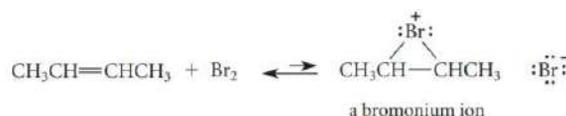
- The products of these reactions are **vicinal dihalides** "compounds with halogens on adjacent carbons".
 - **Bromine and chlorine** are the two halogens used mostly in halogen addition.
 - **Fluorine** is so reactive that it not only adds to the double bond but also rapidly replaces all the hydrogens with fluorines, often with considerable violence.
 - **Diiodides** are unstable and decompose to the corresponding alkenes and I_2 .
 - These reaction run at **low temperature**, and **Dark** (Avoid Radicals).
 - Inert solvents such as methylene chloride (CH_2Cl_2) or carbon tetrachloride (CCl_4) are used as these solvents dissolve both halogens and alkenes.
 - In fact, this discharge of color is a useful qualitative test for alkenes.

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A) ADDITION OF CHLORINE AND BROMINE

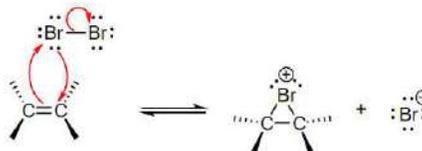
MECHANISM

- Addition of bromine to alkene involves a **reactive intermediate called a bromonium ion**.
- **Carbocations** are not actual intermediates in most halogen additions.



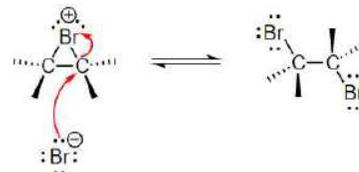
○ Step 1,

Heterolytic cleavage of polarized Br-Br bond occurs and Br with the positive charge forms a cyclic intermediate "bromonium ion" with the two carbons from the alkene.



○ Step 2,

Bromide anion attacks either carbon of the bridged bromonium ion from the back side of the ring.

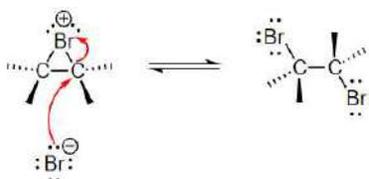


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A) ADDITION OF CHLORINE AND BROMINE

MECHANISM

- The ring opening up with the two halogens on opposite sides as each other.
- **Anti stereochemistry**;
 - The two bromine atoms come from opposite faces of the double bond.
 - The product is that the bromines add on **trans** to each other.
- The halide ion can attack any carbon from the opposite side of the ring it creates a mixture of steric products.
- Optically inactive starting material produce optically inactive achiral products; **a racemic mixture**.



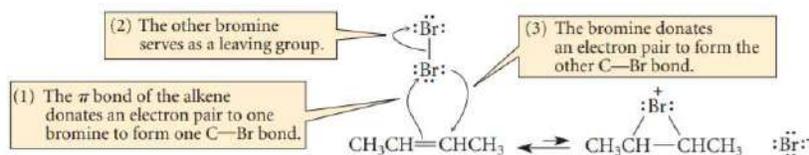
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A) ADDITION OF CHLORINE AND BROMINE

EXAMPLE 1

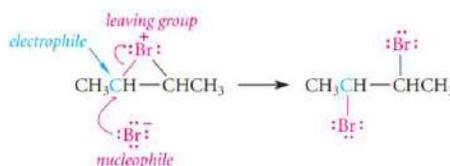
○ Step 1,

The electrons of the π -bond are donated to one of the bromines, the other bromine acts as a leaving group, and a carbocation is formed.



○ Step 2,

The carbocation undergoes a Lewis acid-base association reaction with the neighboring bromine. (*intramolecular (internal) Lewis acid-base association reaction*)

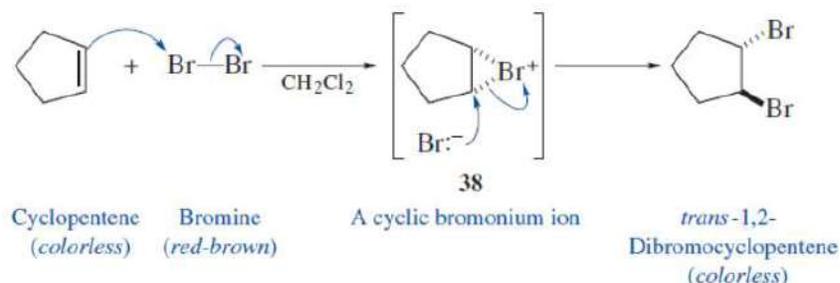


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A) ADDITION OF CHLORINE AND BROMINE

EXAMPLE 2

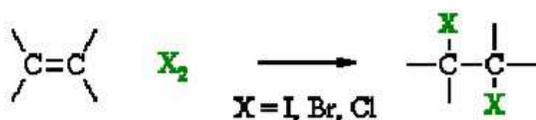
- The reaction of bromine with cyclopentene is stereospecific and proceeds by *anti* addition.



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A) ADDITION OF CHLORINE AND BROMINE

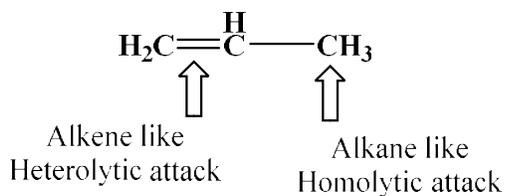
SUMMARY



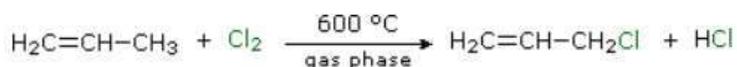
- Overall transformation : C=C to X-C-C-X.
- Reagent: normally the halogen (e.g. Br₂) in an inert solvent like methylene chloride, CH₂Cl₂.
- Regioselectivity:** not relevant since both new bonds are the same, C-X.
- Reaction proceeds *via* cyclic halonium ion.
- Stereoselectivity:** anti since the two C-X bonds form in separate steps one from X₂ the other X.

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ELECTROPHILIC ADDITION vs. FREE- RADICAL SUBSTITUTION



- The propylene molecule has two sites where the halogen can attack, the double bond and the methyl group.
 - **Alkanes** undergo **substitution** by halogen at *high temperatures* and generally in the *gas phase conditions* favor to form free radicals.
 - **Alkenes** undergo **addition** of halogen at *low temperatures* and generally in *liquid phase conditions* favor to form heterolytic reactions.

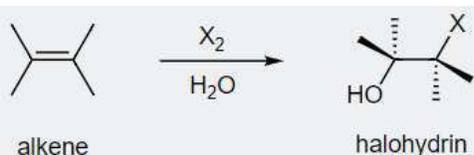


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HALOGENATION OF ALKENES

B) HALOHYDRIN FORMATION

- The addition of hypohalous acid (HO-X) such as *hypobromous acid, HO-Br*, or *hypochlorous acid, HO-Cl* to an alkene to give a 1,2-halo alcohol, called a *halohydrin*.
- Bromohydrin and chlorohydrin are examples of halohydrins (where X = Br or Cl).

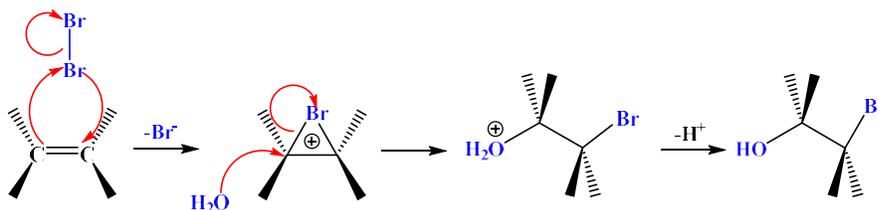


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B) HALOHYDRIN FORMATION

MECHANISM

- 1) Reaction of the alkene with Br_2 yields a **bromonium ion intermediate**.
- 2) **Water acts as a nucleophile**, using a lone pair of electrons to open the bromonium ion ring and form a bond to carbon.
Since oxygen donates its electrons in this step, it now has the positive charge.
- 3) Loss of a proton from oxygen then gives H_3O^+ and the neutral bromohydrin addition product.



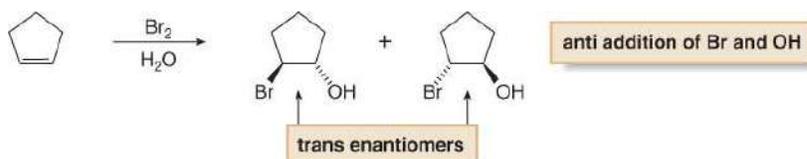
Nucleophilic Solvents (H_2O) can open Bromonium ion

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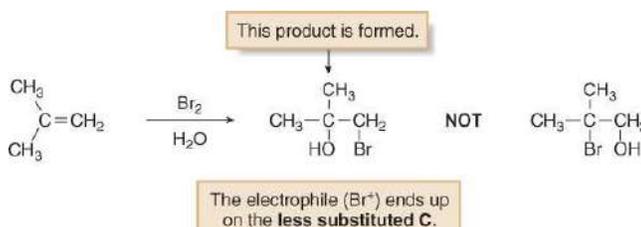
B) HALOHYDRIN FORMATION

EXAMPLES

- **Symmetric alkene**; anti addition of Br and OH



- **Unsymmetric alkene**; The **reaction is highly Regioselective**.
- The reaction of water with the bromonium ion can give two possible products.

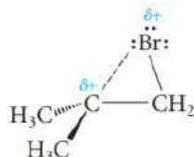


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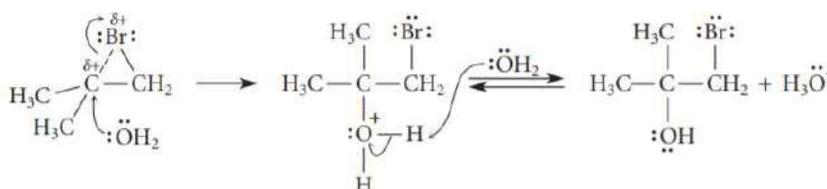
B) HALOHYDRIN FORMATION

EXAMPLES

- The bond between this carbon and the bromine is *so long and weak* that this species is essentially a carbocation containing a weak carbon–bromine interaction.



- Water reacts with the bromonium ion at the *tertiary carbon*, and the weaker bond to the leaving group is broken, to give the observed regioselectivity.

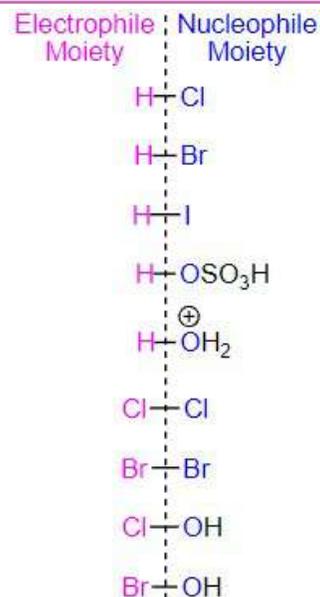
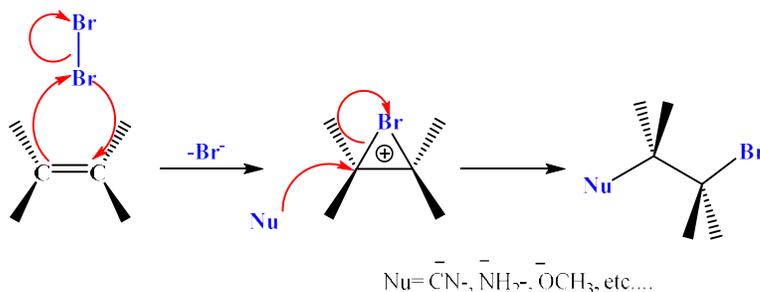


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B) HALOHYDRIN FORMATION

MECHANISM

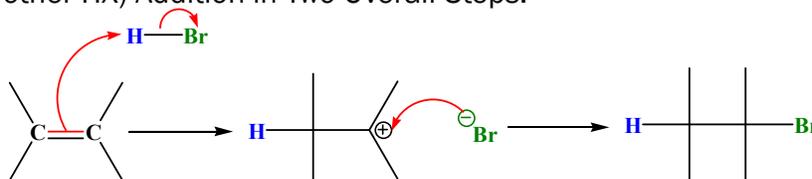
- Water is available at a higher concentration than the bromine ion,
- Water is also a better nucleophile than the bromine ion.
- The better a nucleophile, the more likely it is to attack.



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ADDITION OF HX TO ALKENE

- All of the halides (HI > HBr > HCl > HF) can participate in this reaction with different rates due to *the H-X bond getting weaker as X gets larger (poor overlap of orbitals)*.
- This reaction works well with HBr and HCl.
- HI can also be used by reacting potassium iodide (KI) with phosphoric acid (H₃PO₄).
- Overall reaction;
 - The π-bond of the alkene is broken to form two single, σ-bonds.
 - π Bond (Nucleophile) Protonate → Carbocation Intermediate.
 - Carbocation Captured by Br⁻ (Nucleophile) → HBr Added.
 - HBr (or other HX) Addition in Two Overall Steps.



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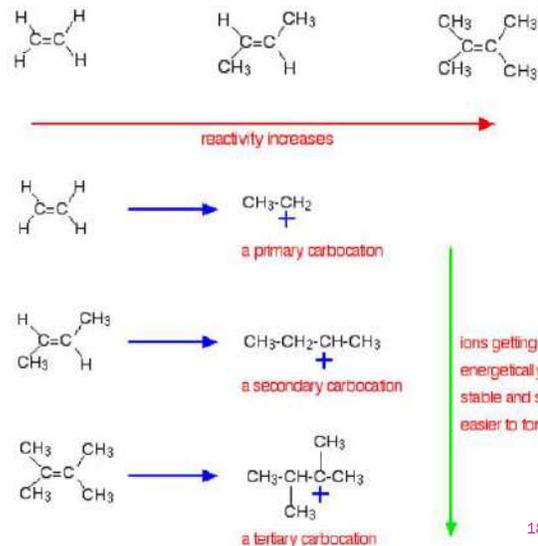
ADDITION OF HX TO ALKENE

REACTION RATES

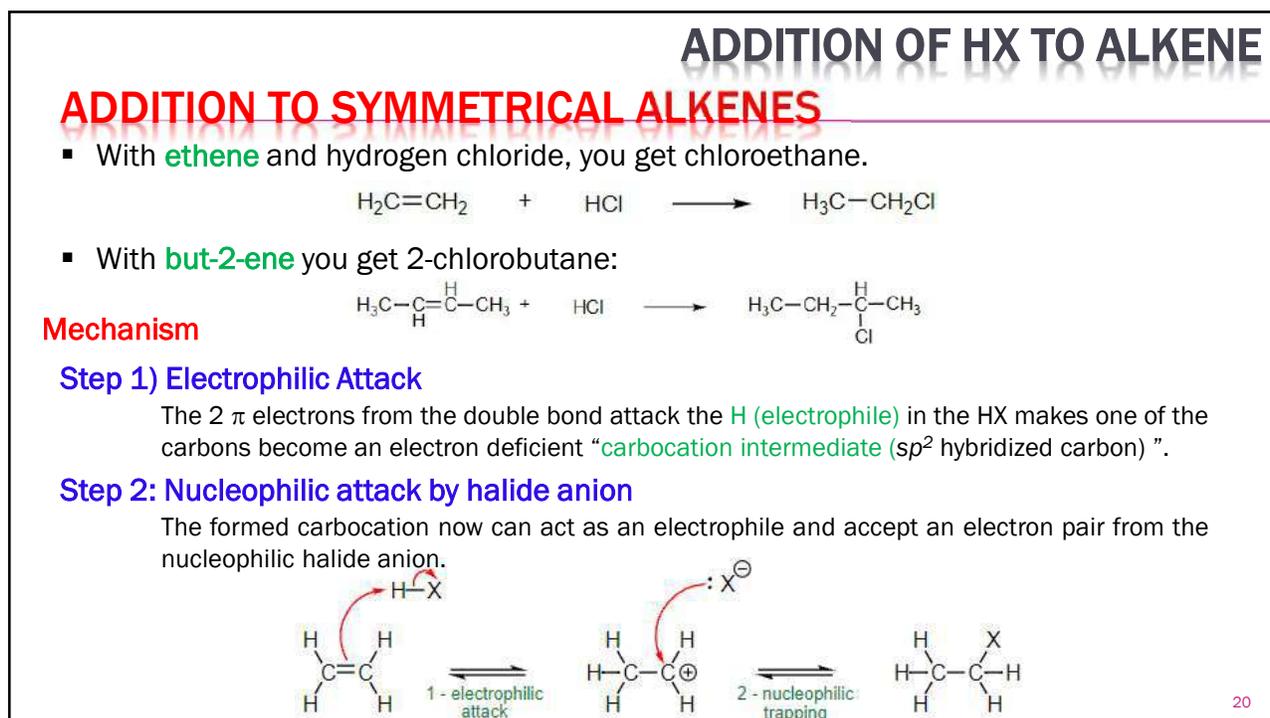
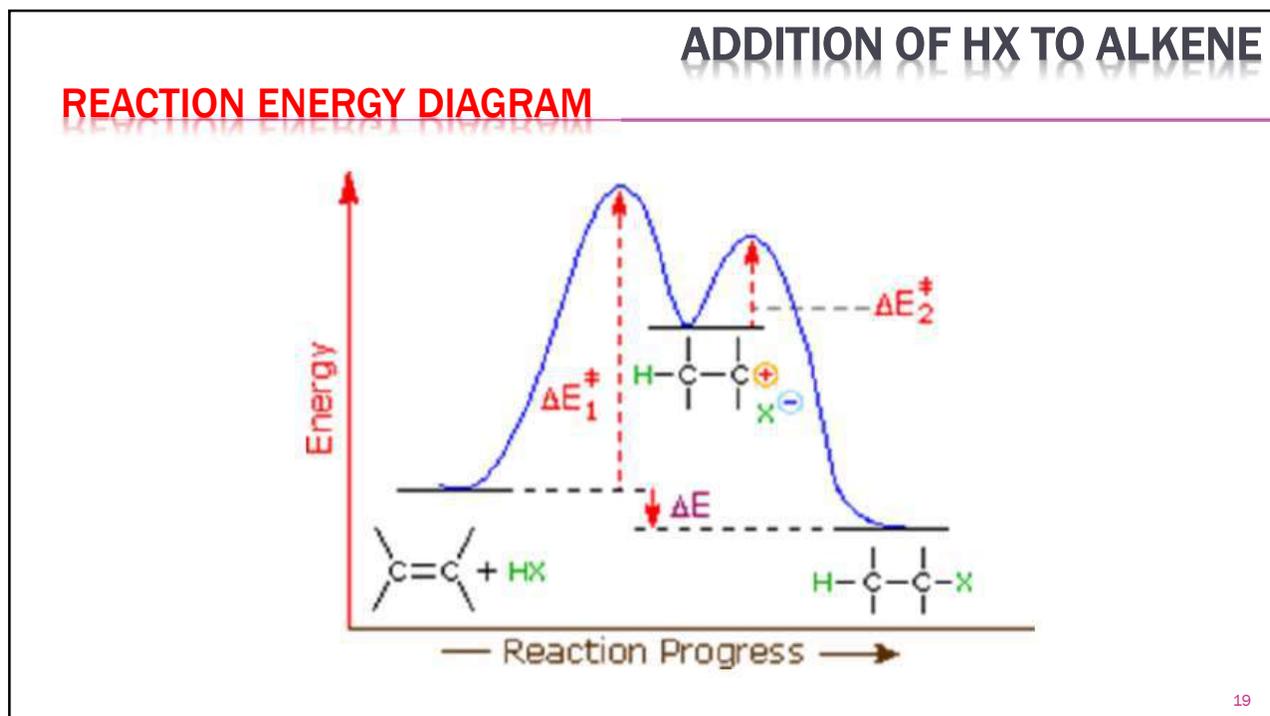
Variation of rates when you change the alkene

- The more important reason, is the stability of the intermediate ion formed during the reaction.
- **Two-step** electrophilic addition mechanism
- The *first step* of the mechanism is the *rate-determining step*.
- This electrophilic addition is a *second order reaction*.

$$\text{Rate} = k[\text{Alkene}][\text{HX}]$$



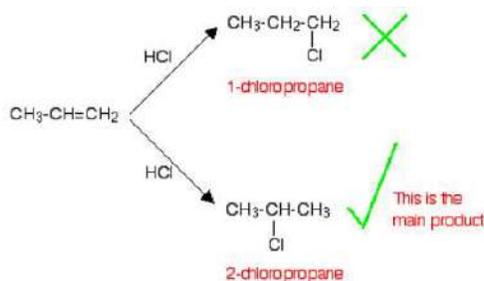
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ADDITION OF HX TO ALKENE

ADDITION TO UNSYMMETRICAL ALKENES

Regioselectivity of Hydrogen Halide Addition: Markovnikov's Rule



- If HCl adds to an unsymmetrical alkene like propene; there are two possible ways it could add.
- However, in practice, there is only one major product according to **Markovnikov's Rule**;
"When a compound HX is added to an unsymmetrical alkene, the hydrogen becomes attached to the carbon with the most hydrogens attached to it already."

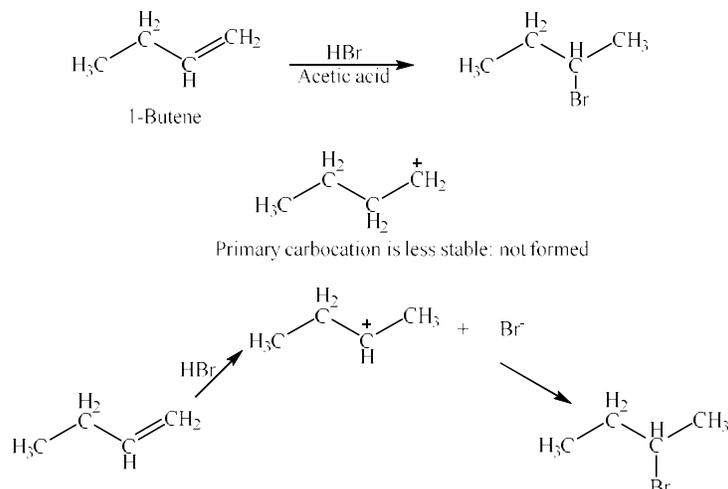
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REGIOSELECTIVITY OF HX ADDITION: ADDITION OF HX TO ALKENE

Markovnikov's Rule

Mechanism for Markovnikov's Rule; Stability of Carbocation

Protonation of double bond occurs in direction that gives the more stable of two possible carbocations.



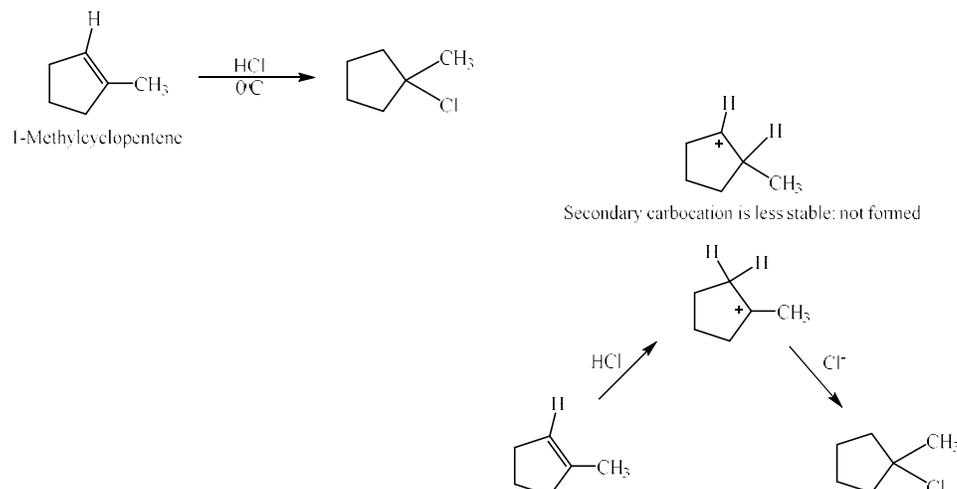
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REGIOSELECTIVITY OF HX ADDITION: ADDITION OF HX TO ALKENE

Markovnikov's Rule

Mechanism for Markovnikov's Rule; Stability of Carbocation

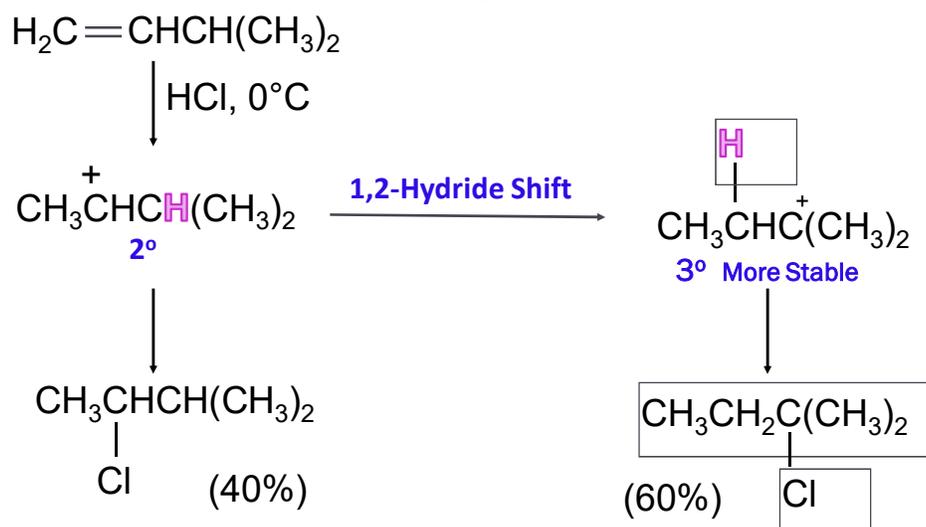
Protonation of double bond occurs in direction that gives the more stable of two possible carbocations.



REGIOSELECTIVITY OF HX ADDITION: ADDITION OF HX TO ALKENE

Markovnikov's Rule

Carbocation Rearrangements in Hydrogen Halide Addition to Alkenes

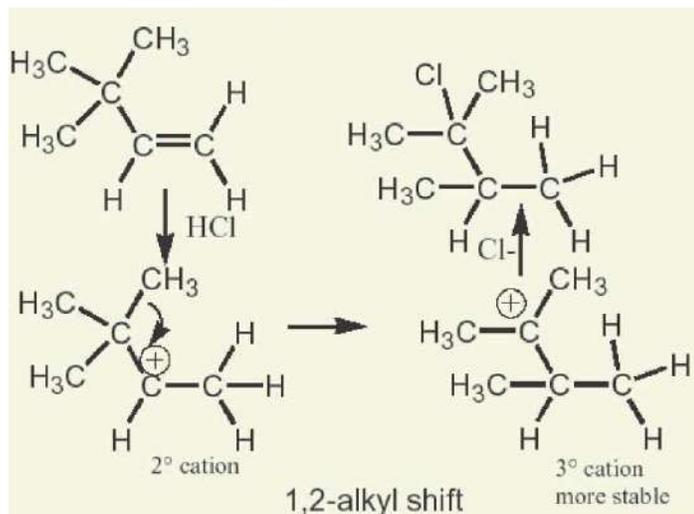


REGIOSELECTIVITY OF HX ADDITION: ADDITION OF HX TO ALKENE

Markovnikov's Rule

Carbocation Rearrangements in Hydrogen Halide Addition to Alkenes

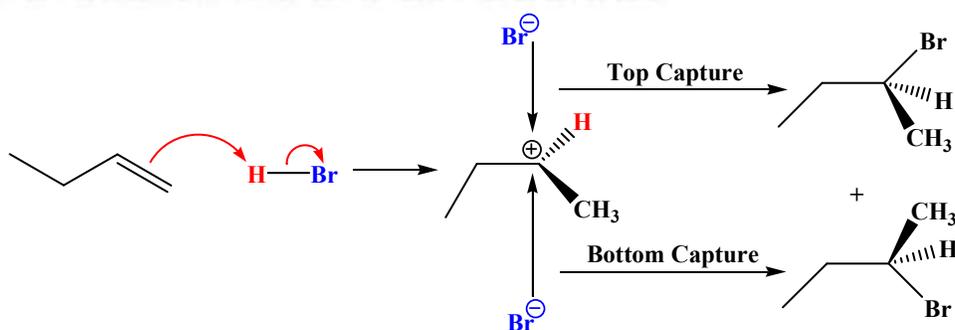
1,2- Methyl Shift



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ADDITION OF HX TO ALKENE

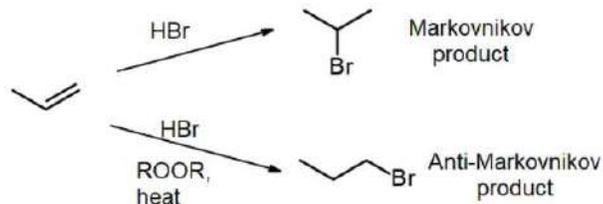
STEREOCHEMISTRY IN IONIC ADDITIONS



- Just as We Saw in $\text{S}_{\text{N}}1$: C^+ Has TWO FACES
- Top and Bottom Attack Give Two Stereochemical Products
- R and S Enantiomers Formed as a **Racemic Mixture** (50:50)

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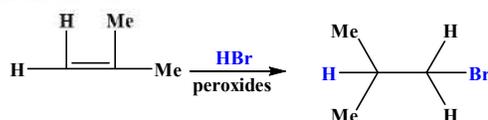
ANTI-MARKOVNIKOV HBR ADDITION: ADDITION OF HX TO ALKENE "Free Radical Addition"



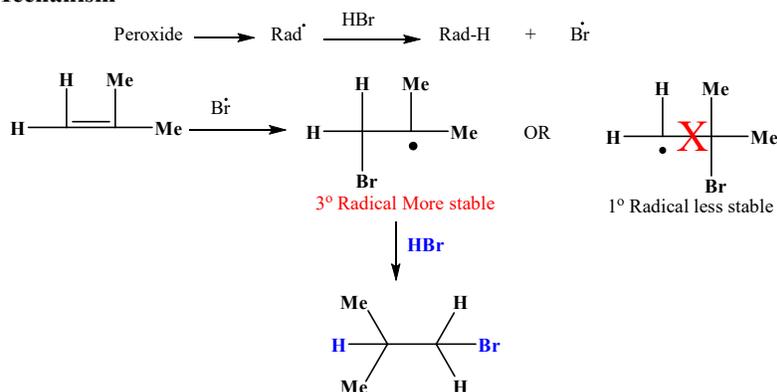
- HBr adds to an unsymmetrical alkene to form an alkyl halide forming "Markovnikov product"
- When HBr heated in the presence of a dialkyl peroxide (often written as ROOR), a radical mechanism takes over forming "anti-Markovnikov product"- due to the so-called "peroxide effect".

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ANTI-MARKOVNIKOV HBR ADDITION: ADDITION OF HX TO ALKENE "Free Radical Addition"



Mechanism

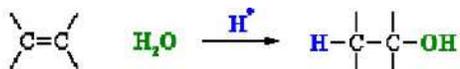


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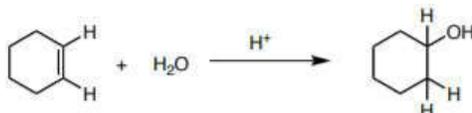
ADDITION OF H₂O TO ALKENE

HYDRATION OF ALKENES

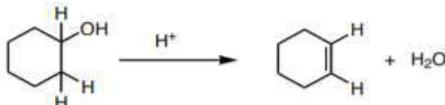
- o Addition of water (H-OH) across a double bond to give an alcohol



1) Acid catalyzed hydration- Markovnikov addition of H-OH



- Acid catalysts are used in high temperature industrial processes: ethylene is converted to ethanol
- **Carbocation Rearrangements.**
- Similar Reaction: Acid Catalyzed Dehydration

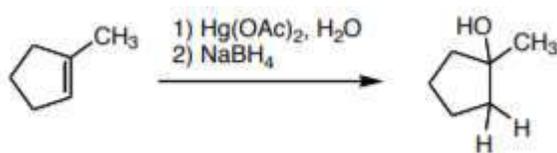


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ADDITION OF H₂O TO ALKENE

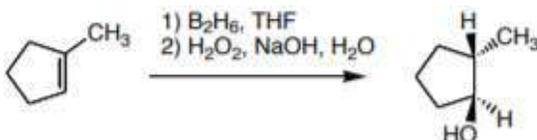
HYDRATION OF ALKENES

2) Oxymercuration- Markovnikov addition H-OH



- **No Carbocation Rearrangements.**

3) Hydroboration- Anti-Markovnikov addition of H-OH, Syn addition of H-OH



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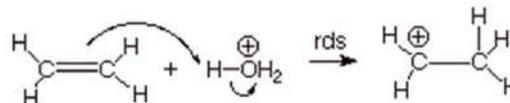
HYDRATION OF ALKENES

ACID CATALYZED HYDRATION; Mechanism

○ Step 1:

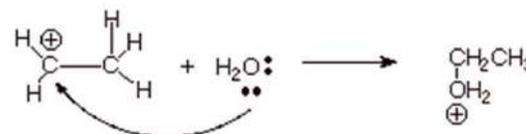
An acid/base reaction; Protonation of the alkene to generate the more stable carbocation.

The π electrons act pairs as a Lewis base.



○ Step 2:

Attack of the nucleophilic (H_2O) on the electrophilic carbocation creates an oxonium ion.



○ Step 3:

An acid/base reaction; Deprotonation by a base generates the alcohol and regenerates the acid catalyst.

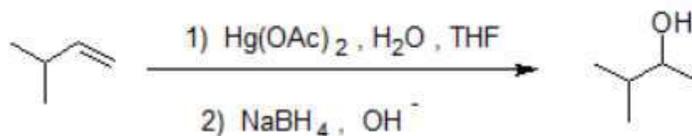


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HYDRATION OF ALKENES

OXYMERCURATION-DEMERCURATION

- Addition of water follows *Markovnikov's rule* with *no rearrangement* for the carbon carbocation due to the formation of cyclic intermediate



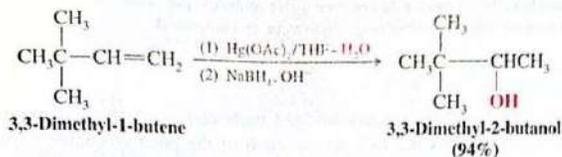
- Net Reaction: *Markovnikov Addition* of H_2O to Alkene.
- Both Reactions Quite Rapid; Alcohol Yields Usually $> 90\%$
- *Strong acids are not required*
- Carbocation rearrangements are avoided because no discrete carbocation intermediate forms.

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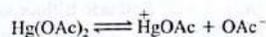
HYDRATION OF ALKENES

OXYMERCURATION-DEMERCURATION; Mechanism

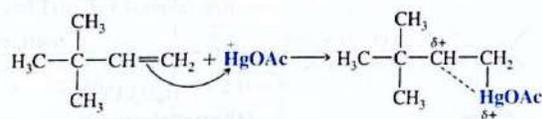
OXYMERCURATION



Step 1

Mercuric acetate dissociates to form a $\overset{+}{\text{Hg}}\text{OAc}$ cation and an acetate anion.

Step 2



3,3-Dimethyl-1-butene

Mercury-bridged carbocation

The alkene donates a pair of electrons to the electrophilic $\overset{+}{\text{Hg}}\text{OAc}$ cation to form a mercury-bridged carbocation. In this carbocation, the positive charge is shared between the 2° (more substituted) carbon atom and the mercury atom. The charge on the carbon atom is

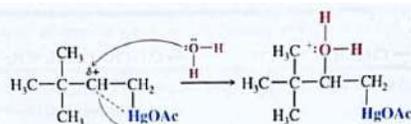
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HYDRATION OF ALKENES

OXYMERCURATION-DEMERCURATION; Mechanism

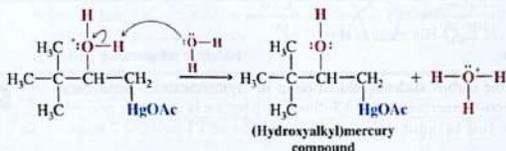
OXYMERCURATION

Step 3



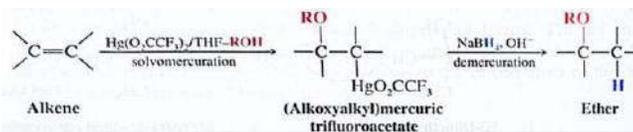
A water molecule attacks the carbon of the bridged mercurinium ion that is better able to bear the partial positive charge.

Step 4



An acid-base reaction transfers a proton to another water molecule (or to an acetate ion). This step produces the (hydroxyalkyl)mercury compound.

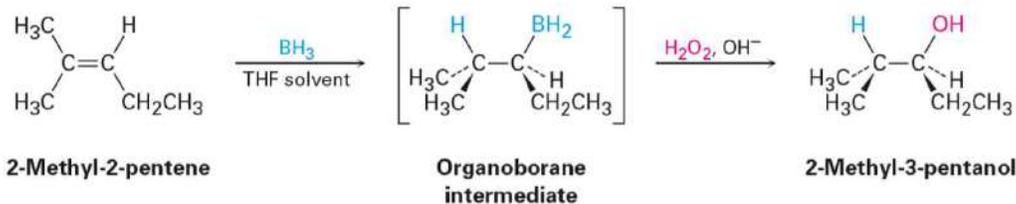
DEMERCURATION



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HYDRATION OF ALKENES

HYDROBORATION-OXIDATION



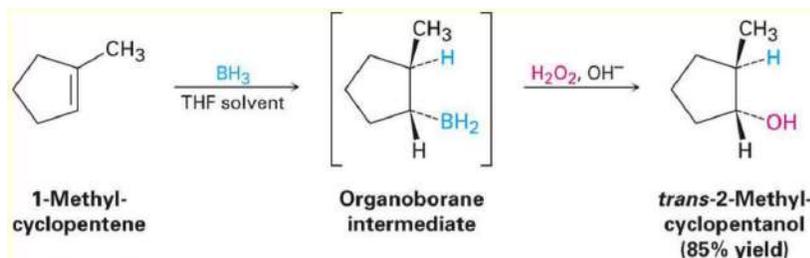
- The reaction proceeds in an **Anti-Markovnikov manner**; (Good for 1° Alcohols)
- In the alkene double bond;
 - **Hydrogen** (from BH_3 or BHR_2) attaches to the **more substituted carbon**.
 - **Boron** attaches to the **least substituted carbon**.
- This process does not require any activation by a catalyst.
- **Oxidation:** H_2O_2 , NaOH Oxidize to Trialkylborate Ester.

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HYDRATION OF ALKENES

HYDROBORATION-OXIDATION

- **Regiochemistry** is opposite to Markovnikov orientation
OH is added to carbon with most H's
- H and OH add with **syn stereochemistry**, to the same face of the alkene (opposite of anti addition),
- **STEREOSPECIFIC**

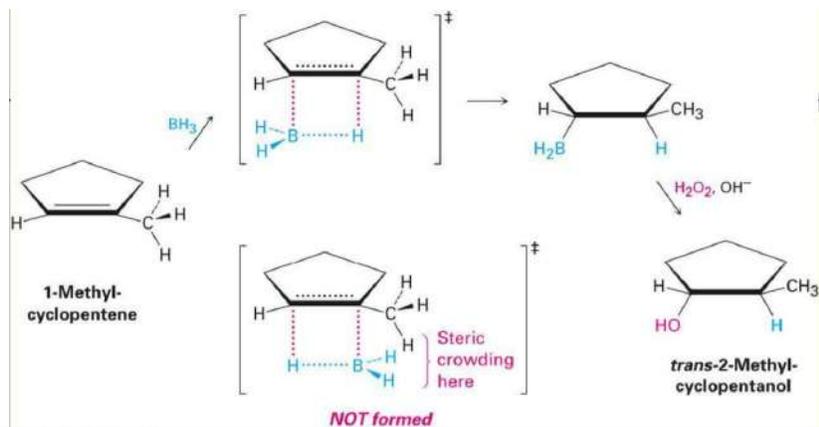


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HYDRATION OF ALKENES

HYDROBORATION-OXIDATION

- Borane (BH_3) is electron deficient and is a *Lewis acid* and Alkene is *Lewis base*
- Transition state involves anionic development on B
- The components of BH_3 are added across $\text{C}=\text{C}$
- More stable carbocation is also consistent with steric preferences



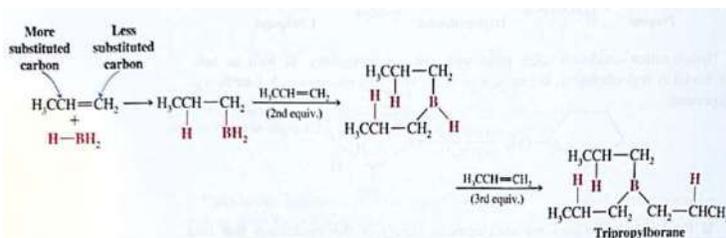
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HYDRATION OF ALKENES

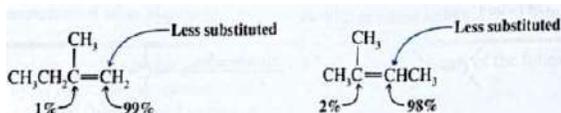
HYDROBORATION-OXIDATION; Mechanism

Step 1: Hydroboration of alkene

In this first step the addition of the borane to the alkene is initiated and proceeds as a concerted reaction because bond breaking and bond formation occurs at the same time.



- The boron atom becomes attached to the less substituted carbon atom of the double bond.

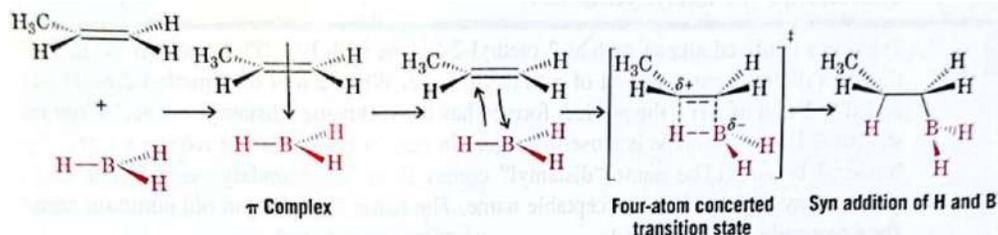


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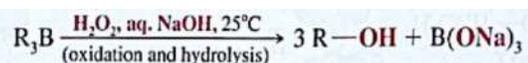
HYDRATION OF ALKENES

HYDROBORATION-OXIDATION; Mechanism

- Both electronic and steric factors account for the anti-markovnikov orientation of the addition.



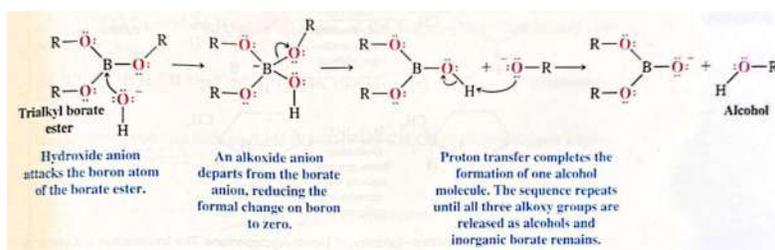
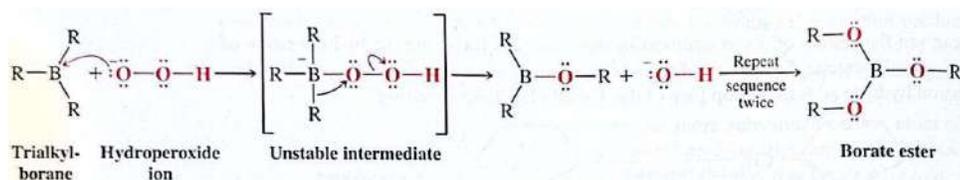
- Step 2: Oxidation and hydrolysis of trialkylborane



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HYDRATION OF ALKENES

HYDROBORATION-OXIDATION; Mechanism

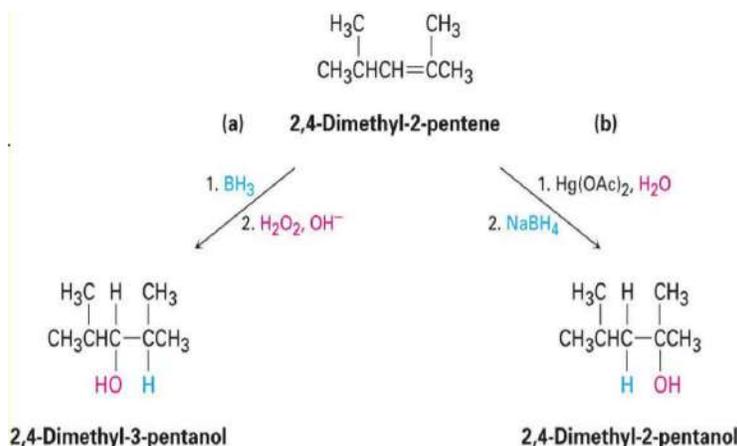


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HYDRATION OF ALKENES

HYDROBORATION-OXIDATION & OXYMERCURATION

- Hydroboration/oxidation occurs with *syn stereochemistry* and gives the *anti Markovnikov addition* product
- Oxymercuration gives the *Markovnikov* product .

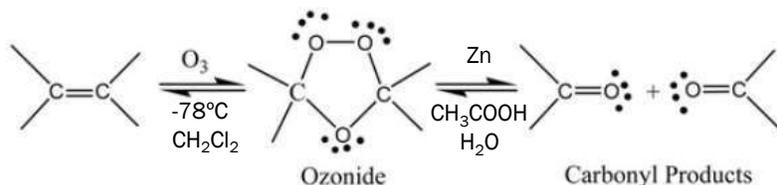


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OZONOLYSIS

OZONOLYSIS: ALKENE CLEAVAGE

- **Ozonolysis** is a method of oxidative cleaving alkenes using ozone (O_3).
- The process allows for *carbon-carbon double bonds* to be replaced by *double bonds with oxygen*.
- This reaction is often used to identify the structure of unknown alkenes by breaking them down into smaller, more easily identifiable pieces.



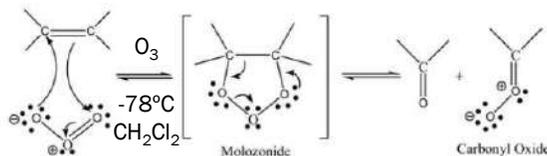
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OZONOLYSIS

MECHANISM

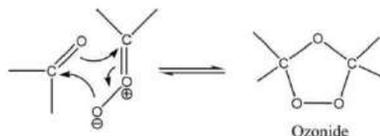
○ **Step 1:**

Initial **electrophilic addition of ozone** to the Carbon-Carbon double bond forming the unstable **molozone intermediate**, which breaks apart to form a **carbonyl and a carbonyl oxide molecule**.



○ **Step 2:**

The **carbonyl and the carbonyl oxide rearranges** and reforms to create the **stable ozonide intermediate**.

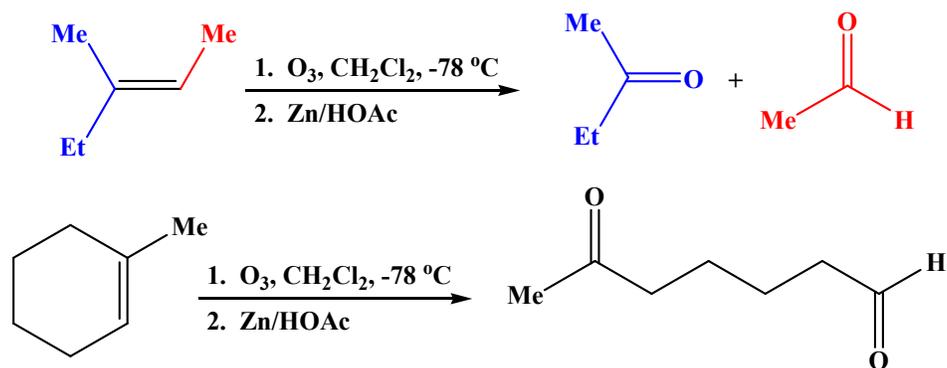


A reductive workup could be performed to convert the ozonide molecule into the desired carbonyl products.

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OZONOLYSIS

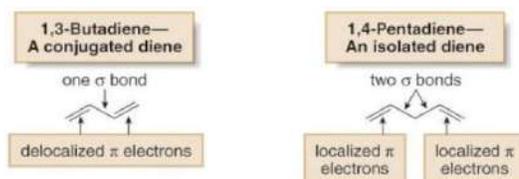
EXAMPLES



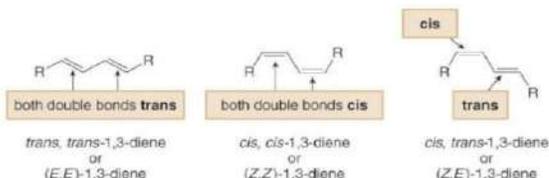
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CONJUGATED DIENES

- Compounds have more than one double bond.
- If they are separated by only one single bond they are **conjugated**.
- The **conjugated diene 1,3-butadiene** has properties that are very different from those of the **nonconjugated diene, 1,5-pentadiene**



- Three **stereoisomers** are possible for 1,3-dienes with alkyl groups bonded to each end carbon of the diene.

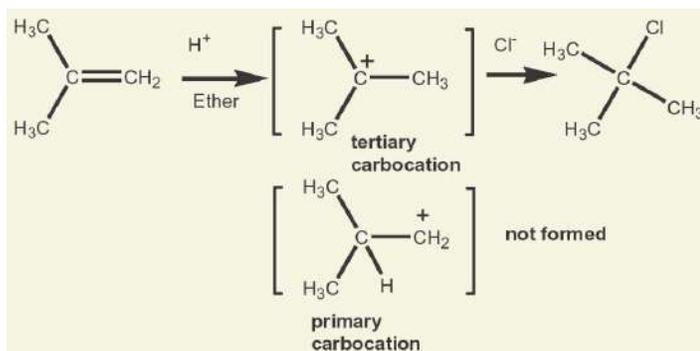


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CONJUGATED DIENES

ALLYLIC CARBOCATIONS

- The **allyl carbocation** is another example of conjugated system.
- Conjugation stabilizes the allyl carbocation** and making it more stable than a normal primary carbocation.
- With conjugated dienes the allylic carbocation intermediately generated has different resonance forms.

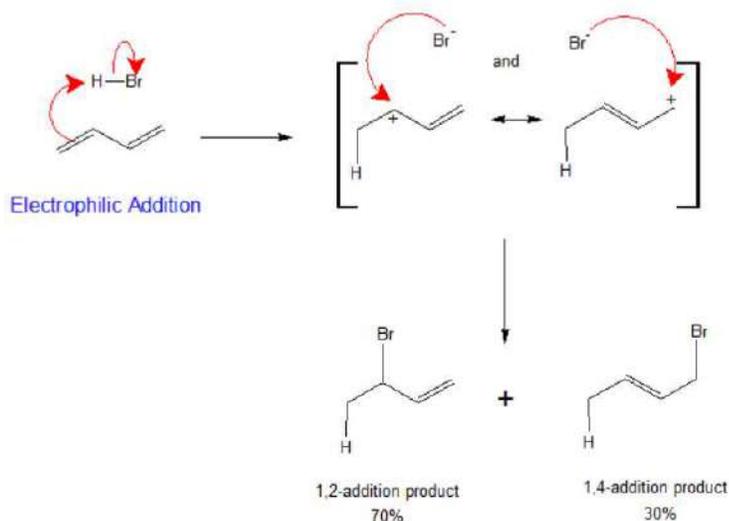


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CONJUGATED DIENES

EXAMPLE

Addition of HBr to 1,3-butadiene: 1,2-addition & 1,4-addition

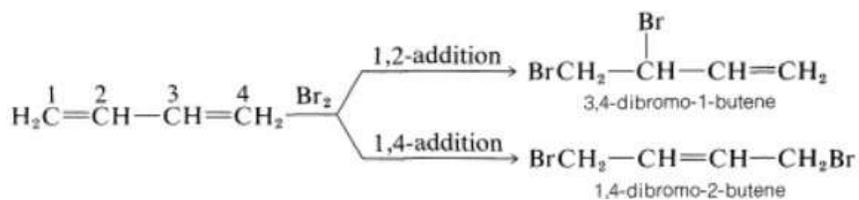


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CONJUGATED DIENES

EXAMPLE

Addition of Br₂ to 1,3-butadiene:

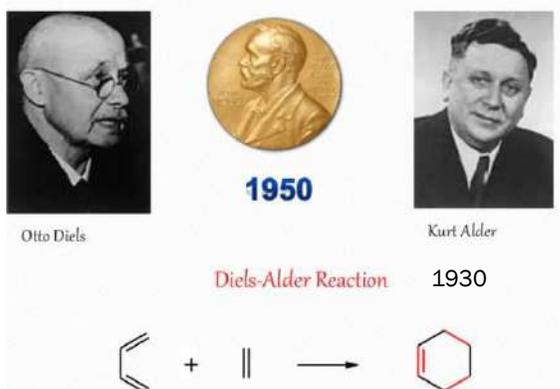


- The 1,2-addition product is favored because its secondary allylic carbocation intermediate is more stable

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CYCLOADDITION TO CONJUGATED DIENES: THE DIELS-ALDER REACTION

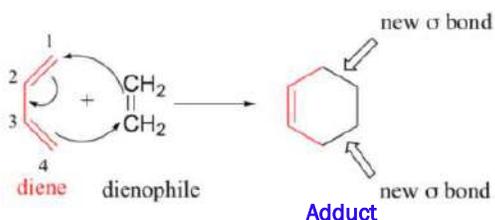
- **Polyenes** (including dienes) can undergo a variety of **pericyclic reactions** “*the π -electrons rearrange to form new bonds*”.
- In a **cycloaddition**, one π -system is “added across” another π -system (often on a different molecule), creating a ring.



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CYCLOADDITION TO CONJUGATED DIENES: THE DIELS-ALDER REACTION

- **Diels-Alder reaction** is one of the most important pericyclic reaction and is a type of cycloaddition.
 - This is a **[4+2] cycloaddition**;
meaning that one reactant contributes **4 π -electrons** while the other contributes **2 π -electrons**.
 - A Diels-Alder reaction must involve a **diene** and **dienophile** “*alkene (or alkyne)*”.
 - A Diels-Alder adduct (**addition product**) contains formation of **cyclohexene ring** by addition of the dienophile to the diene.



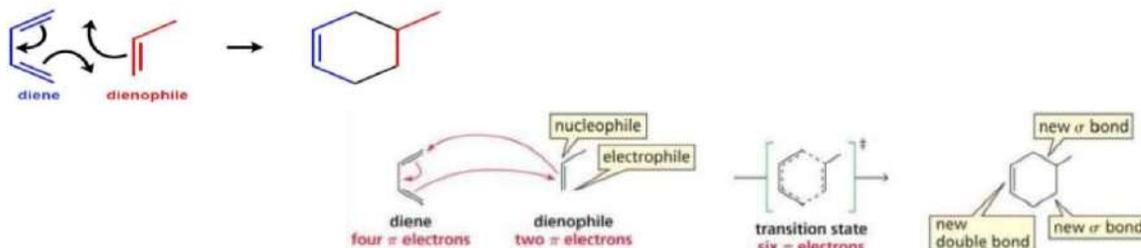
- The formation of the ring involves **no intermediate** (concerted formation of two bonds)
- Two π -bonds are converted to two sigma-bonds.
- Six-membered ring is formed

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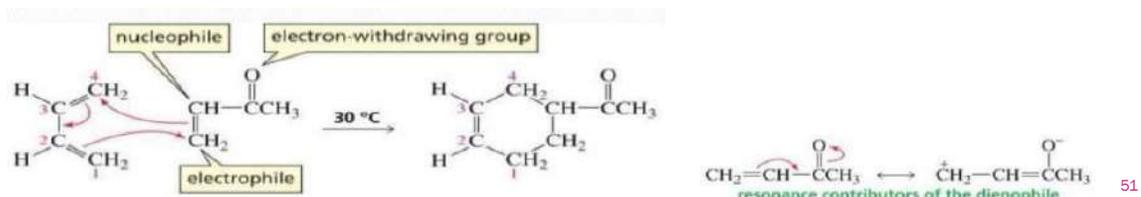
CYCLOADDITION TO CONJUGATED DIENES: THE DIELS-ALDER REACTION

MECHANISM

- A conjugated diene reacts with a double-bonded dienophile.

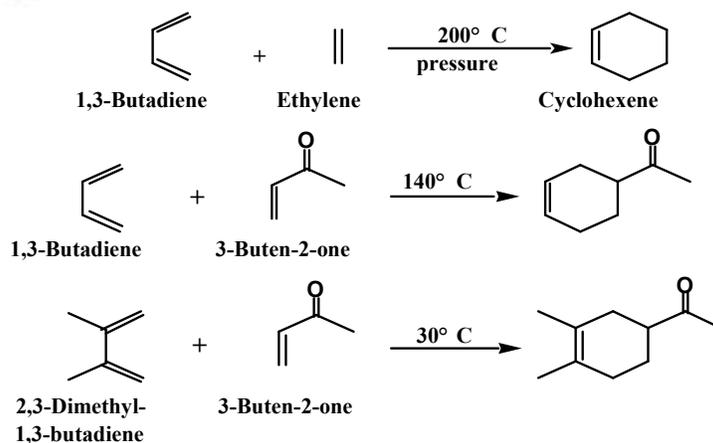


- Dienes are electron-rich; dienophiles are electron poor.



CYCLOADDITION TO CONJUGATED DIENES: THE DIELS-ALDER REACTION

MECHANISM



- Reaction is facilitated by a combination of electron-withdrawing substituents on one reactant and electron-releasing substituents on the other.

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