Supplementary Lecture

Halogenation Reactions

Mechanism: Free Radical Substitution Reactions

$$R\text{-}H + X_2 \xrightarrow{\text{hv or heat}} R\text{-}X + H\text{-}X$$

Chain Reaction Mechanism

$$CH_4 + Cl_2 \xrightarrow{\text{hv or heat}} CH_3Cl + H\text{-}Cl$$

Initiation Step

$$\left\{ (1) \quad Cl_2 \longrightarrow 2Cl^{\cdot} \right.$$

Propogation Step

$$\left\{ \begin{array}{ll} (2) & Cl^{\cdot} + CH_3\text{-}H \longrightarrow CH_3^{\cdot} + H\text{-}Cl \\ (3) & CH_3^{\cdot} + Cl\text{-}Cl \longrightarrow CH_3\text{-}Cl + Cl^{\cdot} \end{array} \right.$$

Termination Step

$$\left\{ \begin{array}{ll} (4) & CH_3^{\cdot} + CH_3^{\cdot} \longrightarrow CH_3\text{-}CH_3 \\ (5) & CH_3^{\cdot} + Cl^{\cdot}_{\cdot} \longrightarrow CH_3\text{-}Cl \\ (6) & Cl^{\cdot} + Cl^{\cdot} \longrightarrow Cl\text{-}Cl \end{array} \right.$$

- *1. The chlorination does not occur at room temperature in the absence of light.* The reaction begins when light falls on the mixture or when it is heated. Thus, we know this reaction requires some form of energy to *initiate* it.

- *2. The most effective wavelength of light is a blue color that is strongly absorbed by chlorine gas.* This finding implies that light is absorbed by the chlorine molecule, activating chlorine so that it initiates the reaction with methane.

- *3. The light-initiated reaction has a high quantum yield.* This means that many molecules of the product are formed for every photon of light absorbed. Our mechanism must explain how hundreds of individual reactions of methane with chlorine result from the absorption of a single photon by a single molecule of chlorine.

- 4. $R^{\bullet} + O{=}O \longrightarrow R{-}O{-}O^{\bullet}$

Inhibitor

- 1. The **mechanism** is the complete, step-by-step description of exactly which bonds break, and which bonds form, and in what order to give the observed products.

- **2. Thermodynamics** is the study of the energy changes that accompany chemical and physical transformations. It allows us to compare the stability of reactants and products and predict which compounds are favored by the equilibrium.

- **3. Kinetics** is the study of reaction rates, determining which products are formed fastest. Kinetics also helps to predict how the rate will change if we change the reaction conditions.

$$R\text{-}H + X_2 \xrightarrow{\text{hv or heat}} R\text{-}X + H\text{-}X$$

Reactivity of alkanes in halogenation reactions:

R-H: $3^o > 2^o > 1^o$

Reactivity of halogens in halogenation reactions:

$F_2 > Cl_2 > Br_2 > I_2$

Heat of Reaction

$$CH_3\text{-}H + Cl\text{-}Cl \longrightarrow CH_3Cl + H\text{-}Cl$$

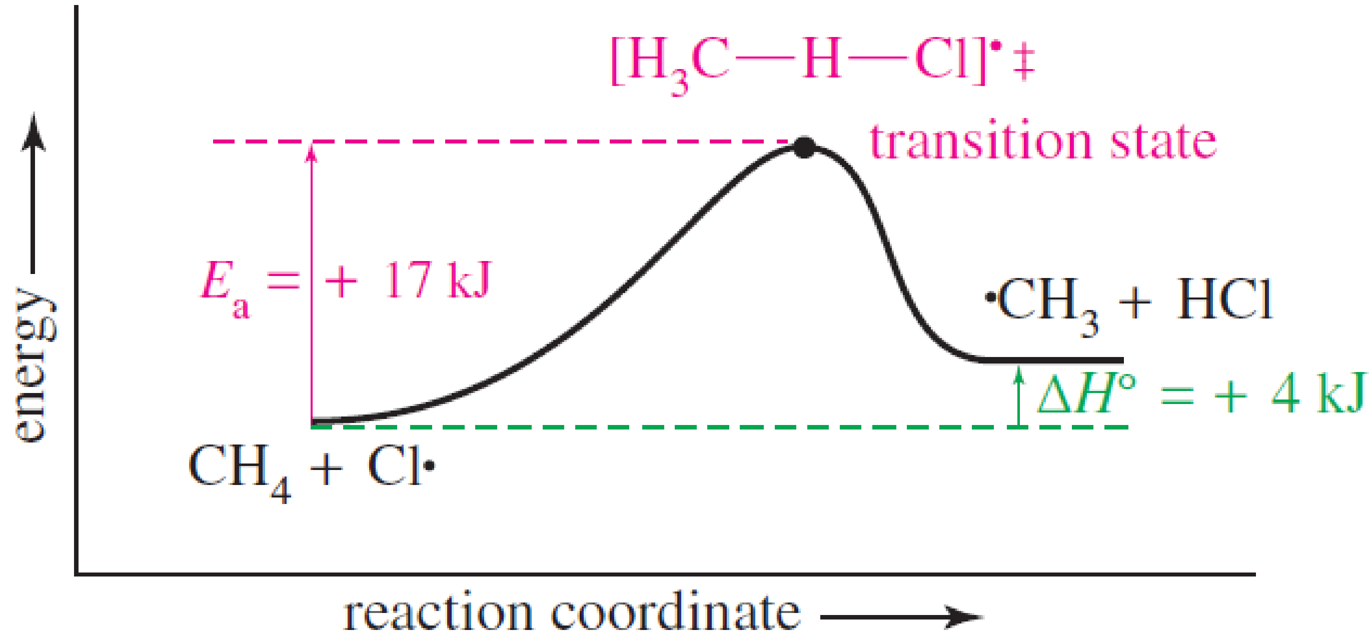
$$\underline{104 \qquad 54} \qquad\qquad \underline{84 \qquad 103}$$

Consuming: 162 Kcal/mol

Liberated: 187 Kcal/mol

$\Delta H = 162 - 187 = -25$ Kcal/mol

Exothermic Reaction



E_a = 17 KJ/Mol

ΔH^o = +4 KJ/Mol

Endothermic Reaction: E_a at least as large as the ΔH^o

Rate of reaction = Collision frequency X Probability factor X Energy factor

Size and weight do not change collision frequency

Temperature and energy factor affect significantly on rate

Organometallic Compounds

$$RX + Mg \xrightarrow{\text{Ether}} RMgX$$

$$R^{-}\ {}^{+}MgX \xrightarrow{H_2O} R\text{-}H + HOMgX$$

$$R^{-}\ {}^{+}MgX \xrightarrow{NH_3} R\text{-}H + H_2NMgX$$

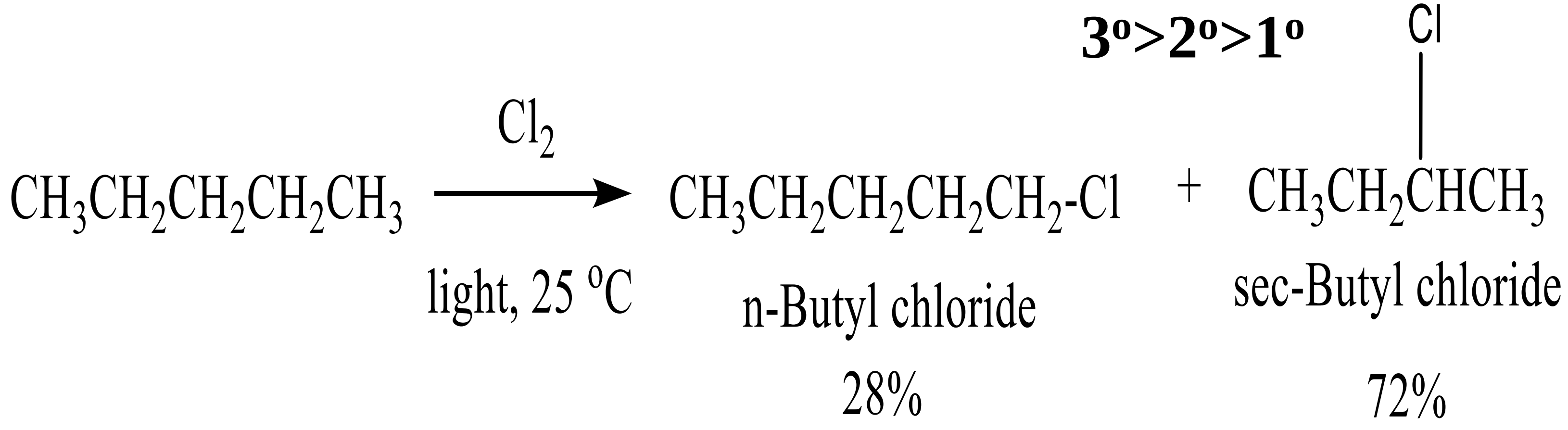
Reactivity and Selectivity

$$CH_3\text{-}CH_2\text{-}CH_3 \xrightarrow[\text{light, 25 }^{o}\text{C}]{Cl_2} \underset{45\%}{CH_3\text{-}CH_2\text{-}CH_2\text{-}Cl} + \underset{55\%}{CH_3\text{-}CHCl\text{-}CH_3}$$

$$CH_3\text{-}CH_2\text{-}CH_3 \xrightarrow[\text{light, 127 }^{o}\text{C}]{Br_2} \underset{3\%}{CH_3\text{-}CH_2\text{-}CH_2\text{-}Br} + \underset{97\%}{CH_3\text{-}CHBr\text{-}CH_3}$$

Reactivity of Cl: Energy Factor: 5.1>3.8>1

$3^o > 2^o > 1^o$

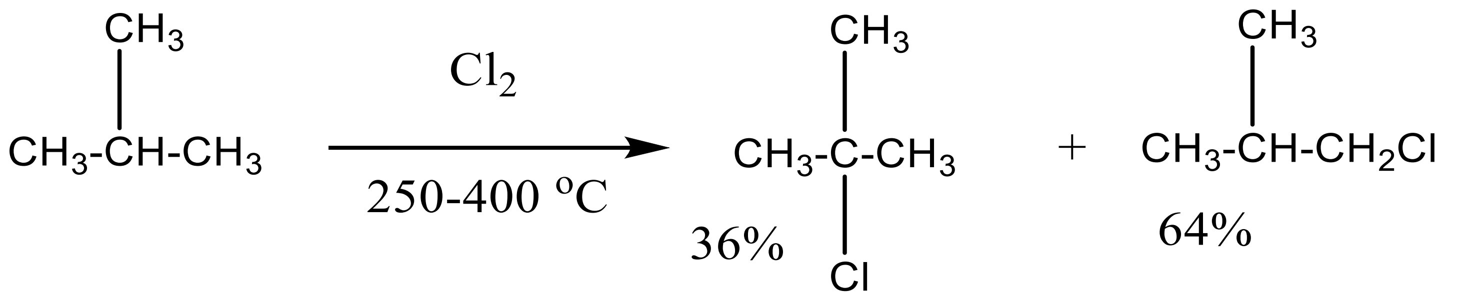


$$CH_3CH_2CH_2CH_2CH_3 \xrightarrow[\text{light, 25 }^oC]{Cl_2} CH_3CH_2CH_2CH_2CH_2\text{-}Cl + CH_3CH_2\overset{Cl}{C}HCH_3$$

n-Butyl chloride 28%

sec-Butyl chloride 72%

$$\frac{\text{n-Butyl chloride}}{\text{sec-Butyl chloride}} = \frac{\text{no of }1^0\text{H}}{\text{no of }2^0\text{H}} \text{ X } \frac{\text{Reactivity of }1^0\text{H}}{\text{Reactivity of }2^0\text{H}} = \frac{6}{4} \text{ X } \frac{1.0}{3.8} = \frac{6.0}{15.2}$$



$$CH_3\text{-}\overset{CH_3}{C}H\text{-}CH_3 \xrightarrow[250\text{-}400\ ^oC]{Cl_2} CH_3\text{-}\underset{Cl}{\overset{CH_3}{C}}\text{-}CH_3 + CH_3\text{-}\overset{CH_3}{C}H\text{-}CH_2Cl$$

36%

64%

Ease of Abstraction of Hydrogen:

$3^{o}H > 2^{o}H > 1^{o}H$

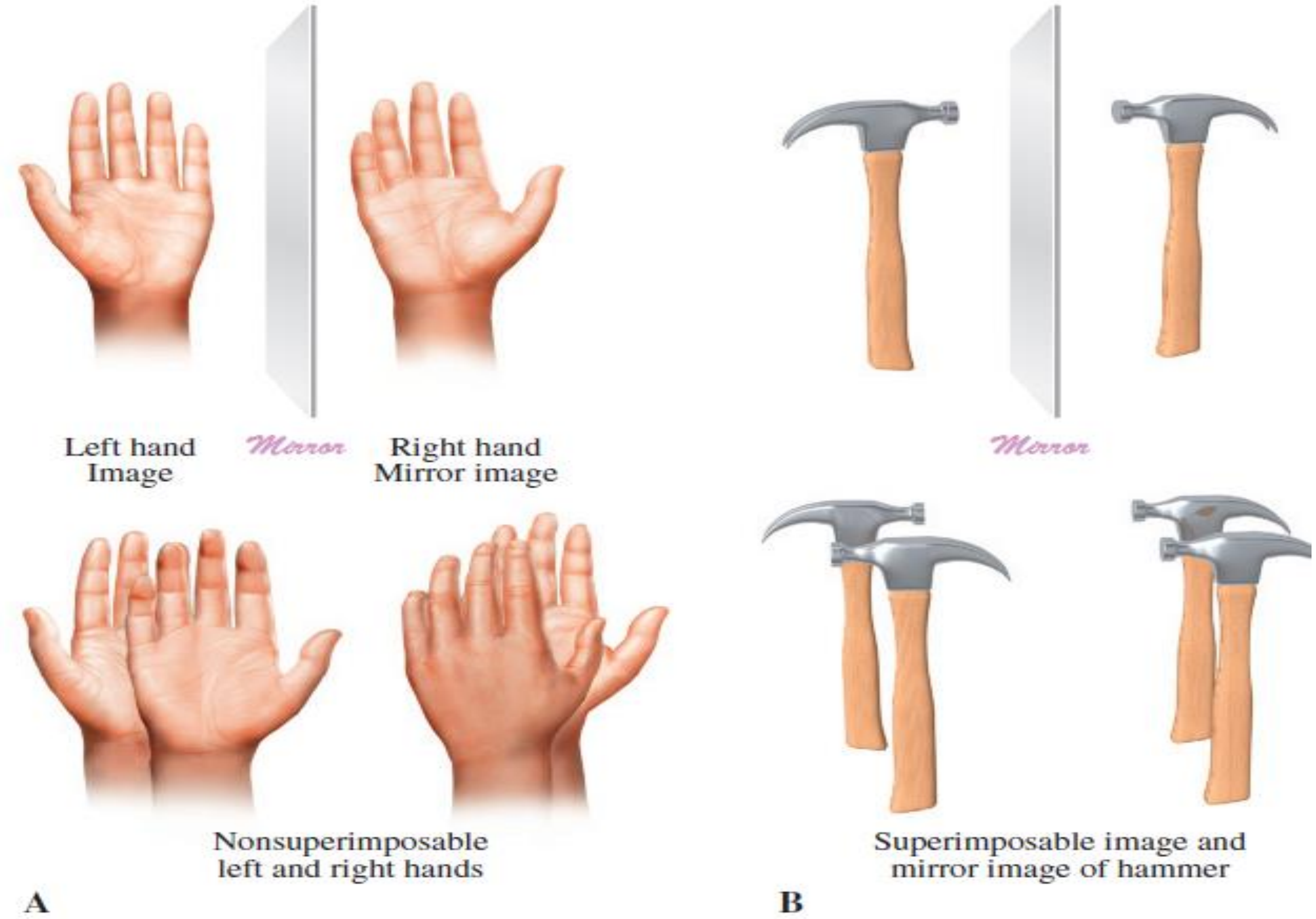
Stability of Free Radicals:

$3^{o}H > 2^{o}H > 1^{o}H$

Ease of Formation of Free Radicals:

$3^{o}H > 2^{o}H > 1^{o}H$

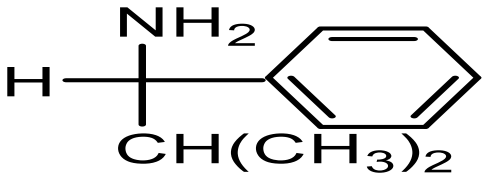
Chiral and Achiral Compounds



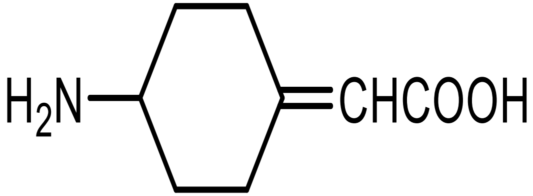
Chiral and Achiral Compounds

A shoe, A glove, A screw (Chiral)

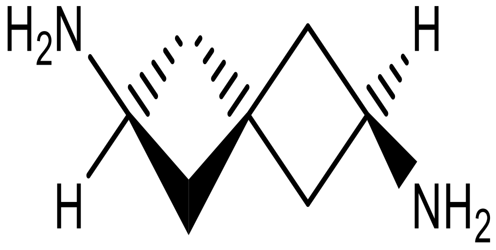
A ball, A scissoes, A spon, A chair (Achiral)



S Configuration

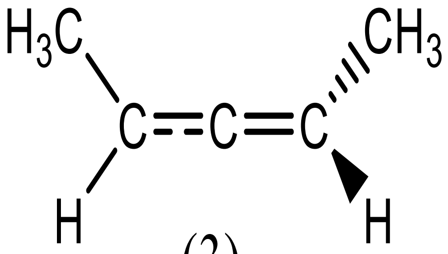


(1)



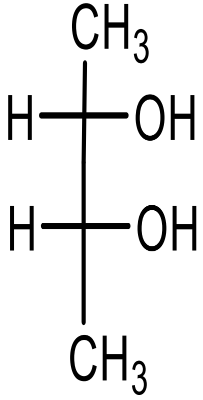
(2)

3,3'-Diaminospiro[3,3]heptane

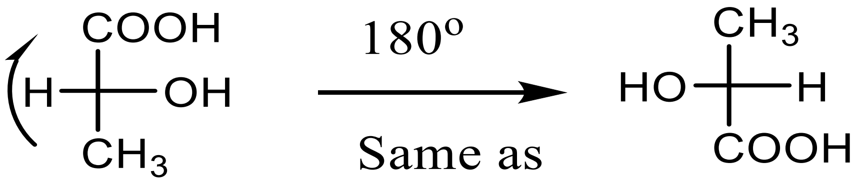


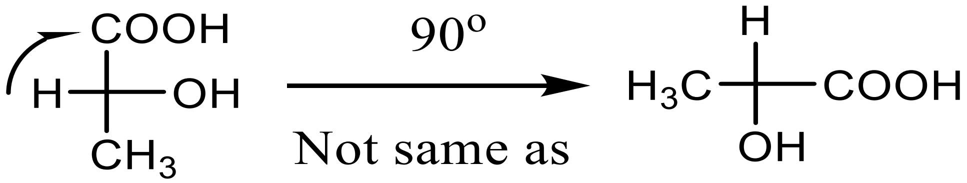
(3)

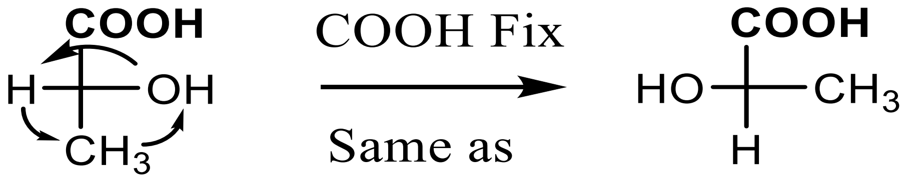
Allene system



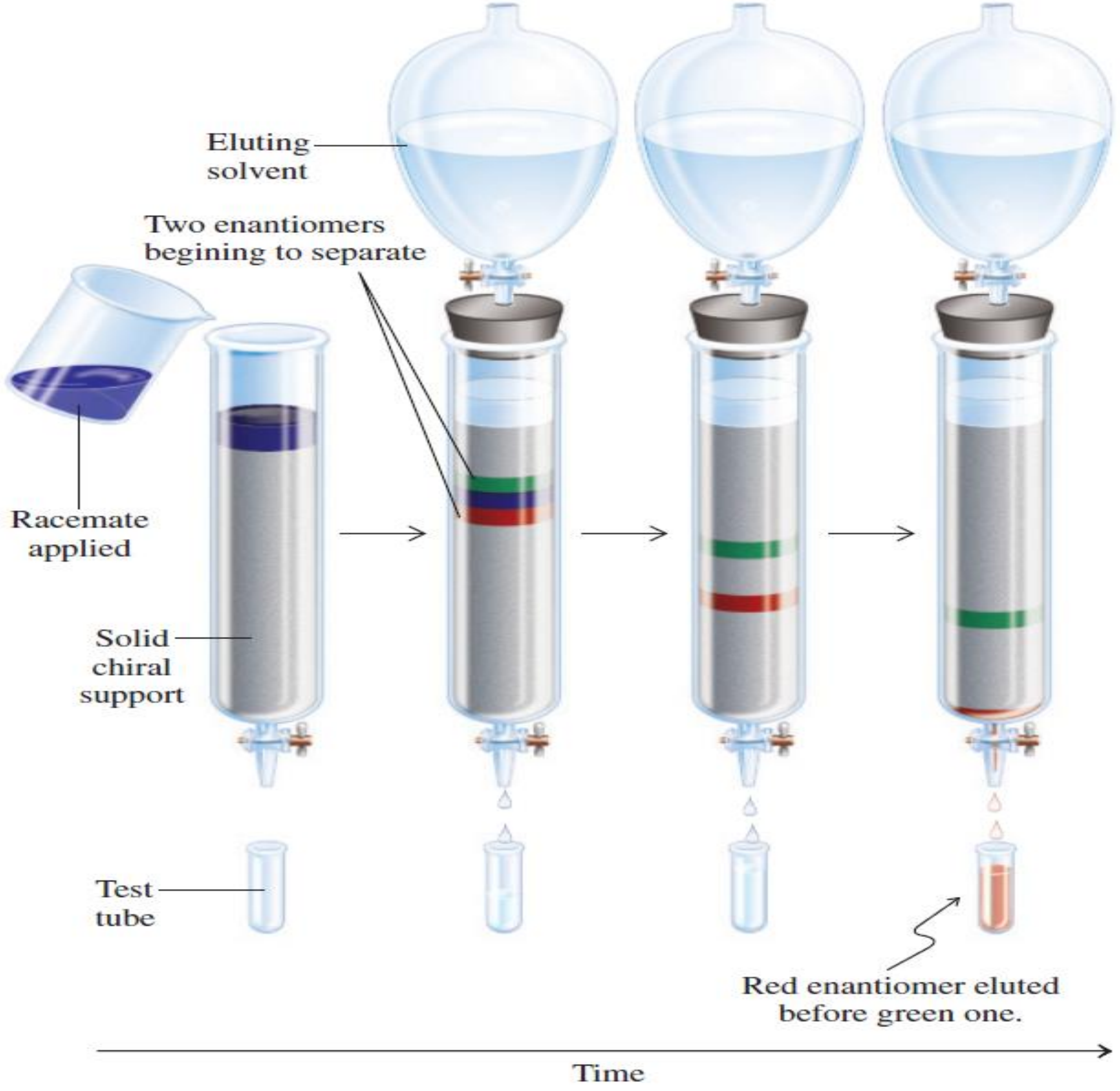
(4)

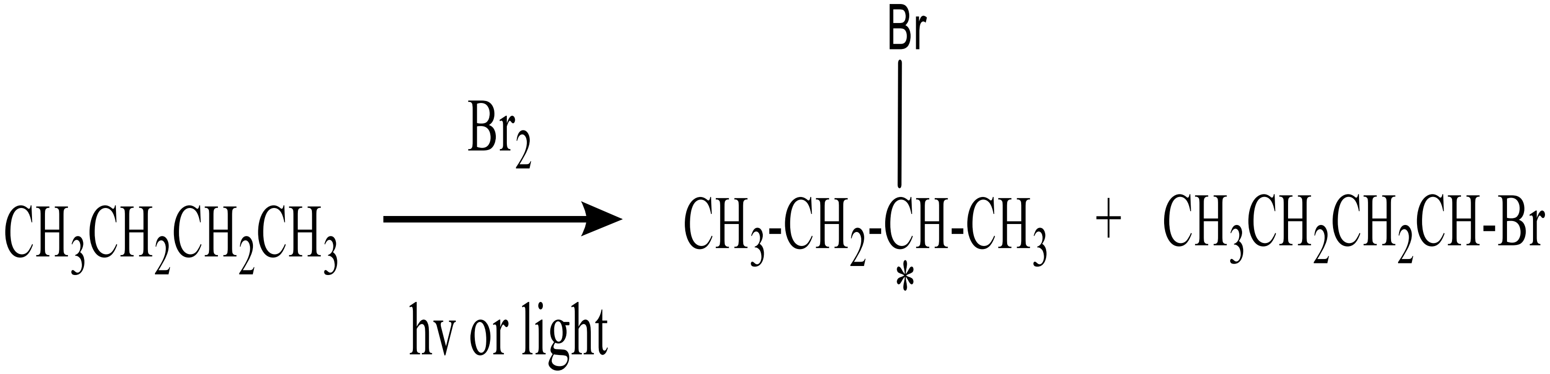

COOH
H
OH
CH3
180°
Same as
CH3
HO
H
COOH


COOH
H
OH
CH3
90°
Not same as
H
H3C
COOH
OH

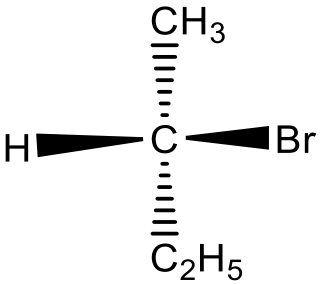

COOH
H
OH
CH3
COOH Fix
Same as
COOH
HO
CH3
H

Separation of enantiomers



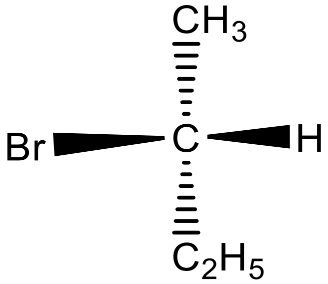


$$CH_3CH_2CH_2CH_3 \xrightarrow[\text{hv or light}]{Br_2} CH_3\text{-}CH_2\text{-}\overset{Br}{\underset{*}{C}}H\text{-}CH_3 + CH_3CH_2CH_2CH\text{-}Br$$

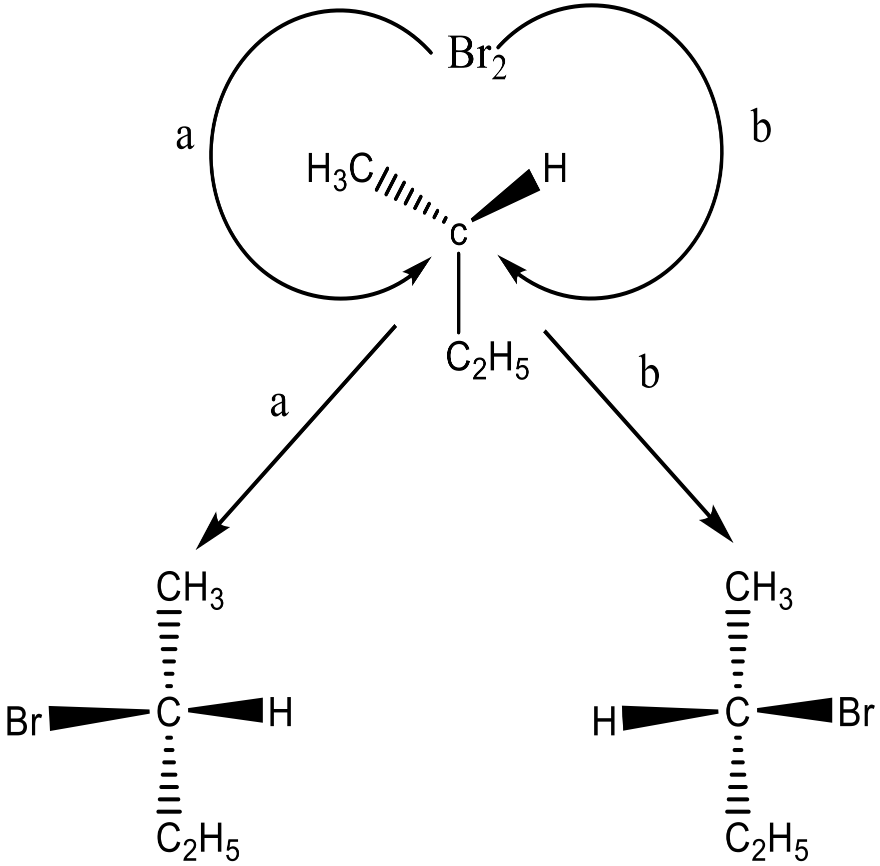


S-sec-Butyl bromide

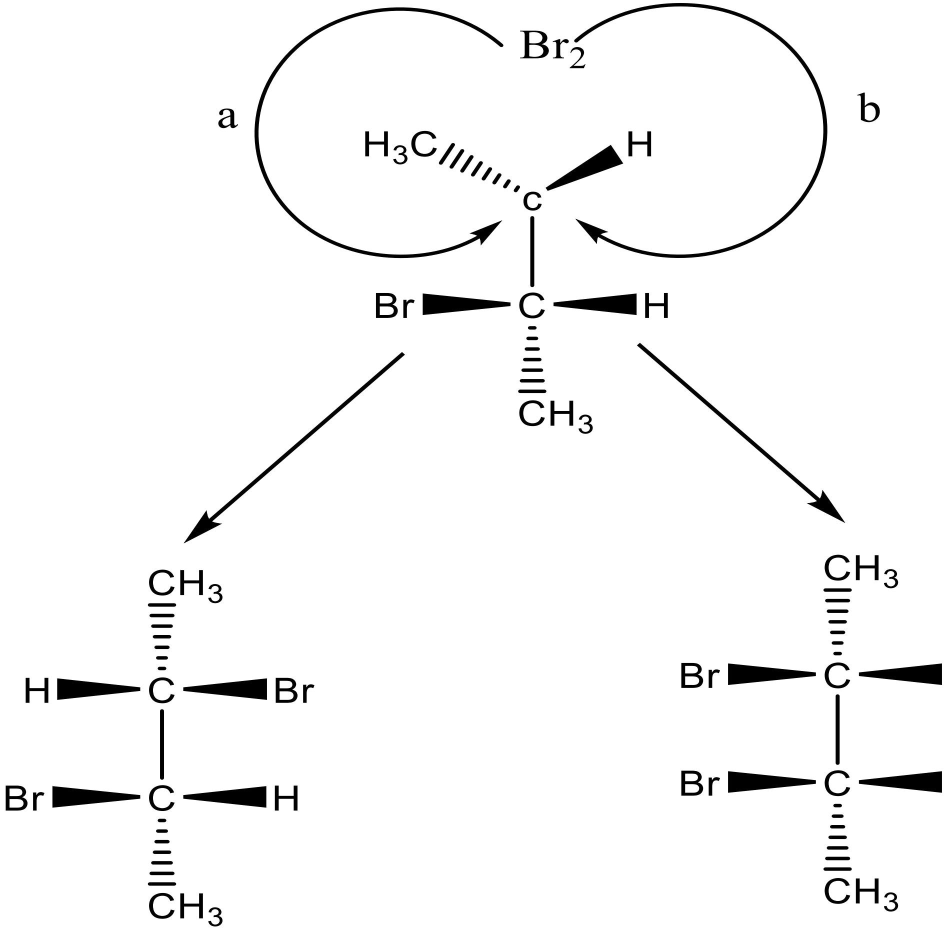
mirror



R-sec-Butyl bromide



Enantiomers form in equal amounts



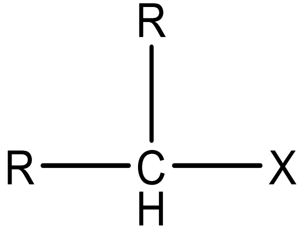
(S,S)

(R,S or meso)

Diastereomers formed in unequal amounts

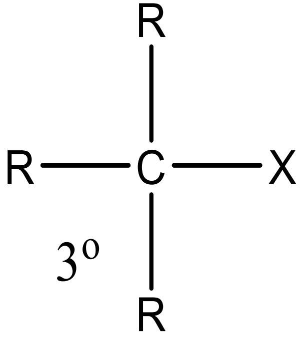
$R\text{-}CH_2\text{-}X$

1°



$R\text{-}CH(R)(H)\text{-}X$

2°



$R\text{-}C(R)(R)\text{-}X$

3°

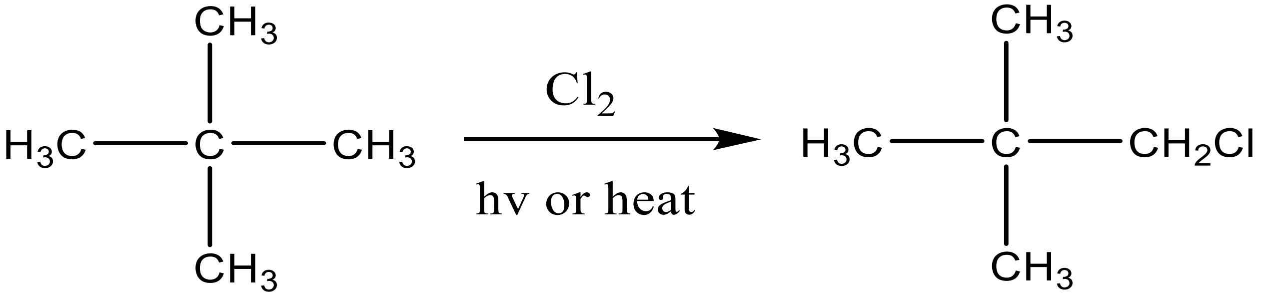
Preparation

1) $R\text{-}H + X_2 \xrightarrow{\text{hv or heat}} R\text{-}X + H\text{-}X$

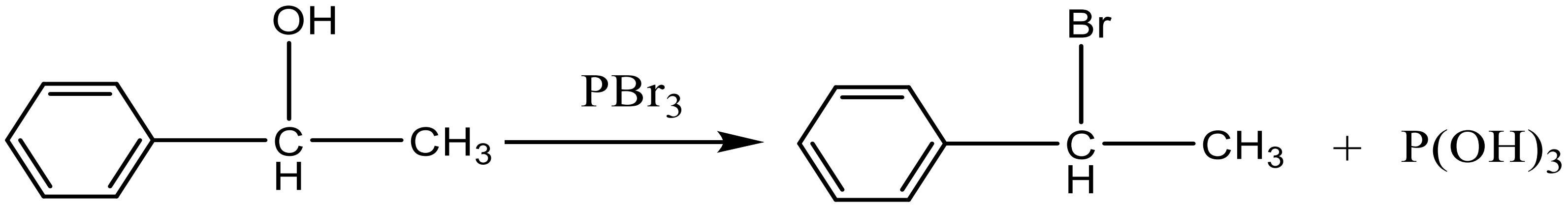
2) $R\text{-}OH + HX \longrightarrow R\text{-}X + H_2O$

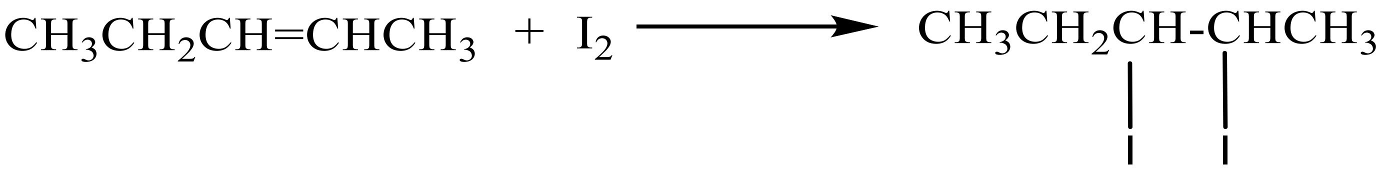
3) $R\text{-}OH + PX_3 \longrightarrow R\text{-}X + P(OH)_3$

4) $RCH{=}CHR + X_2 \longrightarrow RCHX\text{-}CHXR$

1)


2) $$CH_3CH_2CH_2\text{-}OH \xrightarrow{\text{Conc.HBr}} CH_3CH_2CH_2\text{-}Br + H_2O$$

3)


4)


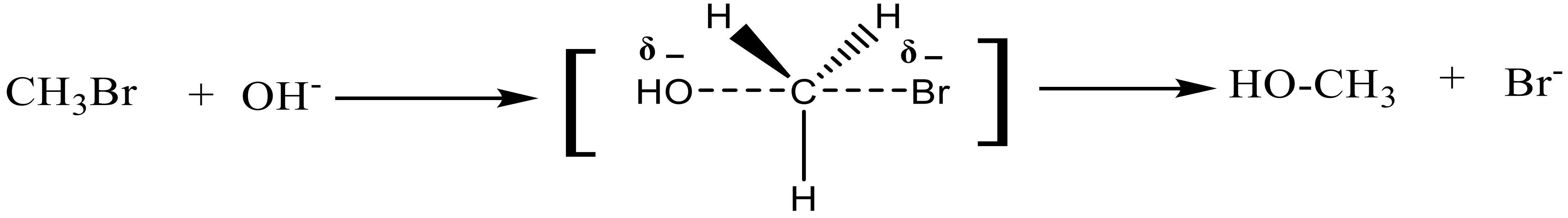
$$CH_3CH_2CH{=}CHCH_3 + I_2 \longrightarrow CH_3CH_2\underset{I}{CH}\text{-}\underset{I}{C}HCH_3$$

Reactions

Nucleophilic Substitution Reactions

$$\underset{\text{Substrate}}{CH_3Br} + \underset{\text{Nucleophile}}{OH^-} \xrightarrow{\text{Solvent}} \underset{\text{Product}}{HO\text{-}CH_3} + Br^-$$

Alkyl + Leaving group



S_N2 Mechanism

$$\mathrm{R\text{-}Br} + \mathrm{Nu^-} \longrightarrow \mathrm{Nu\text{-}R} + \mathrm{Br^-}$$

$$\mathrm{CH_3CH_2\text{-}Br} + \mathrm{OH^-} \longrightarrow \mathrm{CH_3CH_2\text{-}OH}$$

$$\mathrm{H_2O} \longrightarrow \mathrm{CH_3CH_2\text{-}OH}$$

$$\mathrm{R'OH} \longrightarrow \mathrm{CH_3CH_2\text{-}O\text{-}R'}$$

$$\mathrm{R'C{\equiv}C^-} \longrightarrow \mathrm{CH_3CH_2\text{-}C{\equiv}CR'}$$

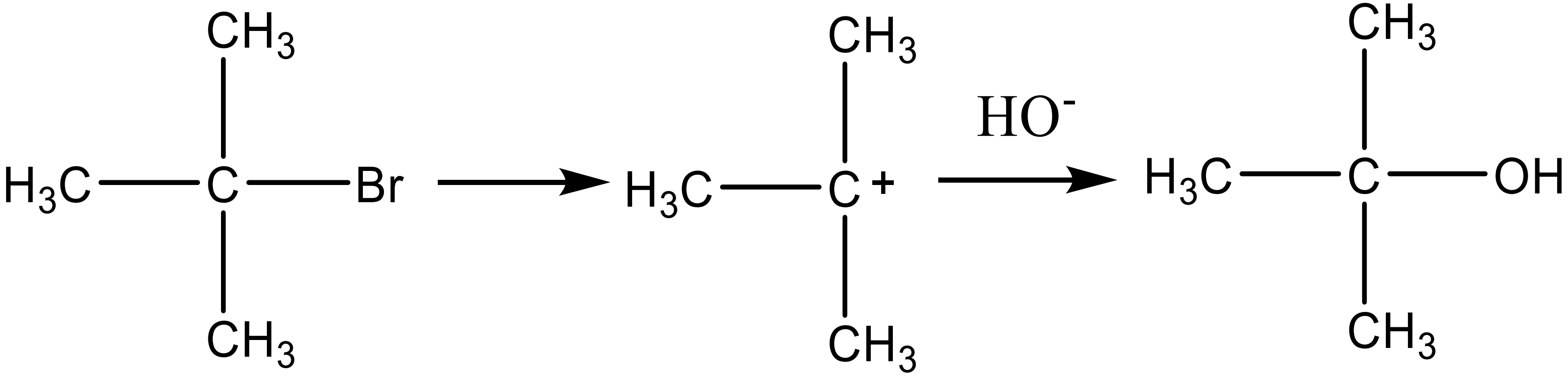
$$\mathrm{R'COO^-} \longrightarrow \mathrm{CH_3CH_2\text{-}OCOR'}$$

$$\mathrm{RNH_2} \longrightarrow \mathrm{CH_3CH_2\text{-}NHR}$$

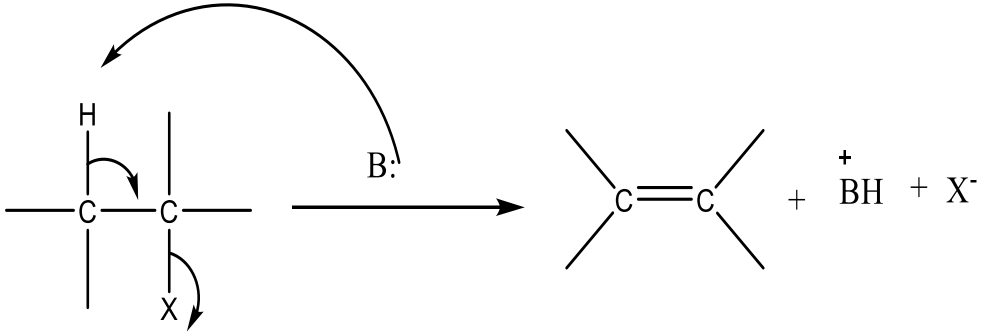
$$\mathrm{R'S^-} \longrightarrow \mathrm{CH_3CH_2\text{-}SR'}$$

$$\mathrm{^-C{\equiv}N} \longrightarrow \mathrm{CH_3CH_2\text{-}C{\equiv}N}$$

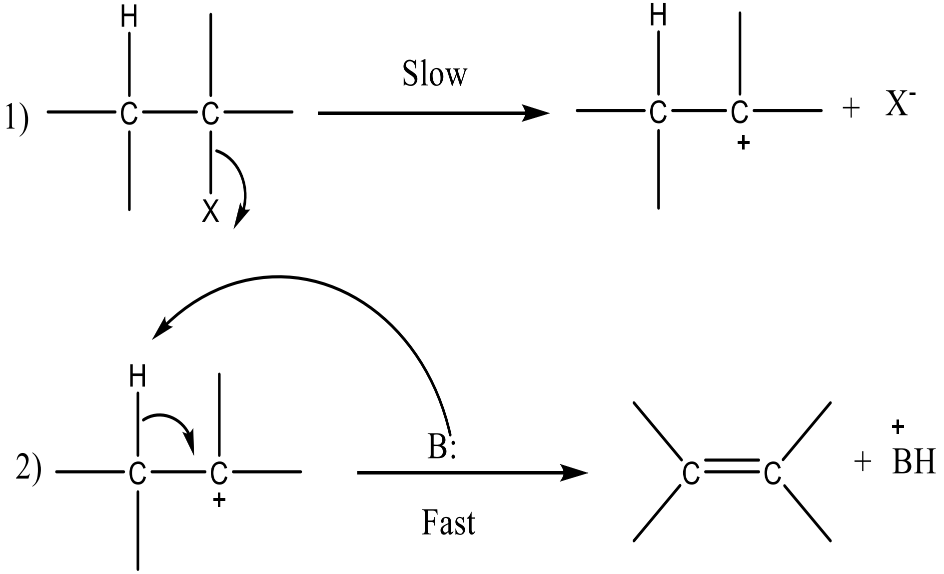
S_N1 Mechanism



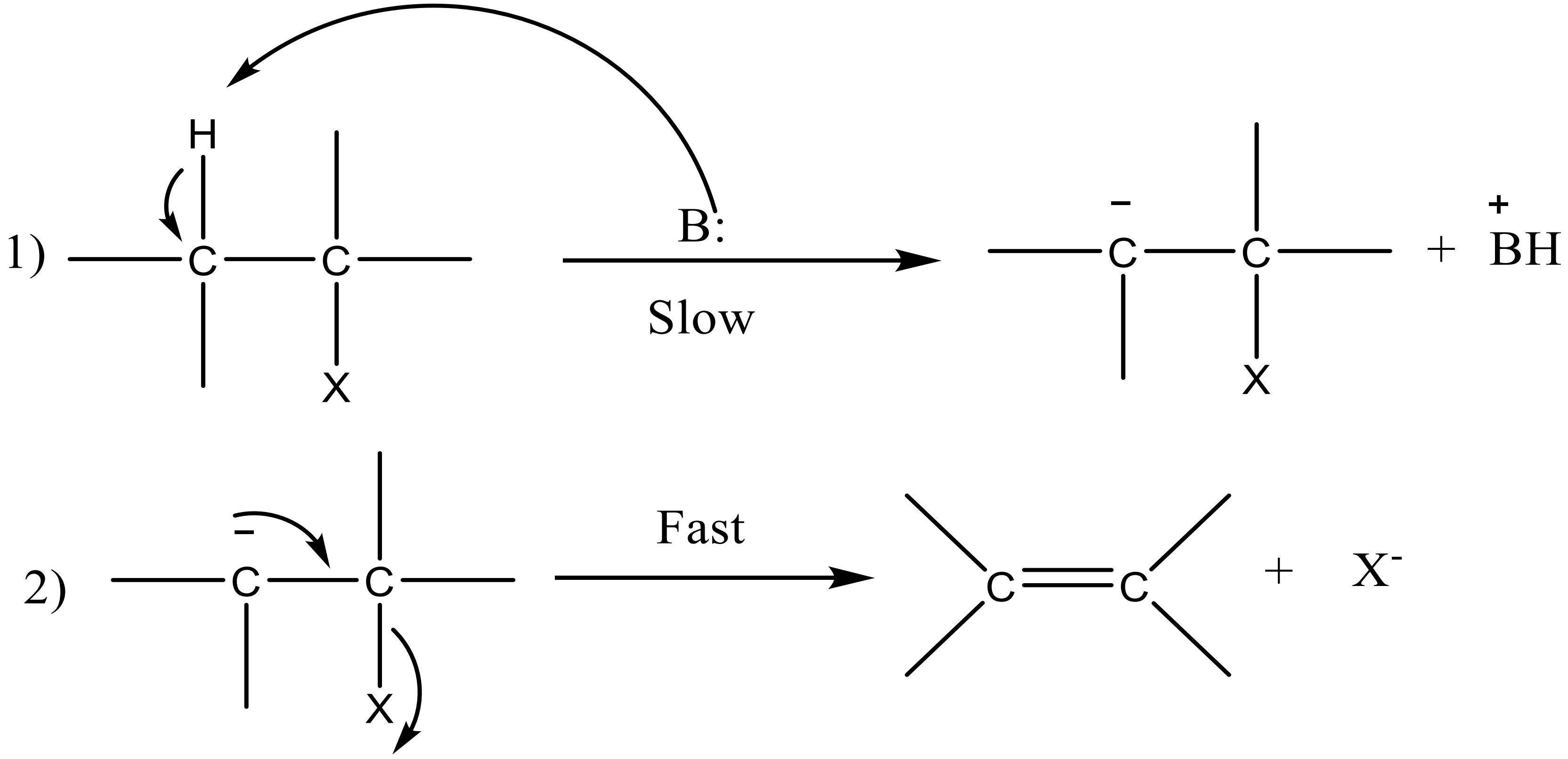
Elimination Reactions (E2)



Elimination Reactions (E1)



Elimination Reactions (E1cb)

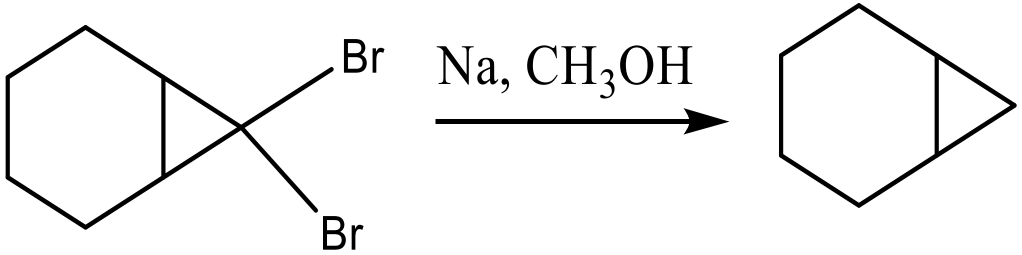


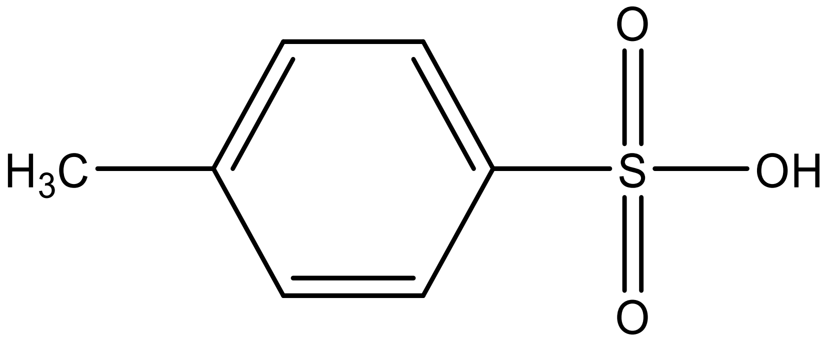
Preparation of Grignard Reagent

$$R\text{-}X + Mg \xrightarrow{\text{Ether}} RMgX$$

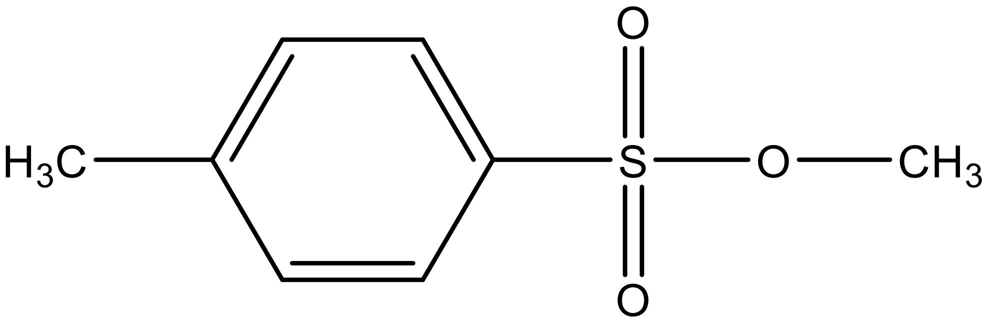
Reduction Reactions

$$R\text{-}X + Mg \xrightarrow{\text{Ether}} RMgX \xrightarrow{H_2O} R\text{-}H + XMgOH$$

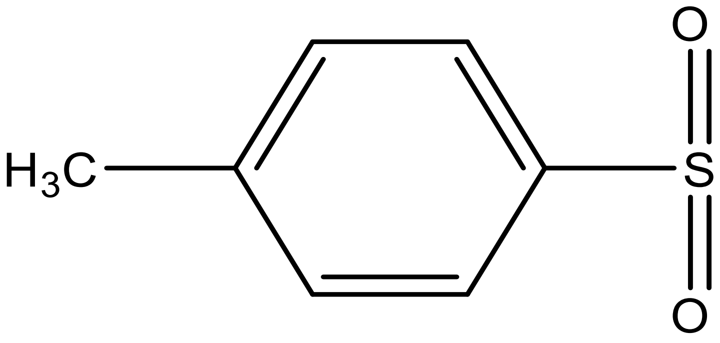




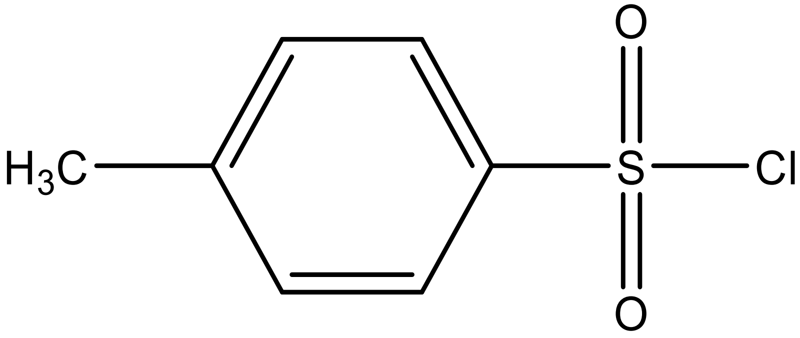
p-Toluene sulphonic acd (TsOH)



Methyl-*p*-toluenesulphonate (TsOMe)



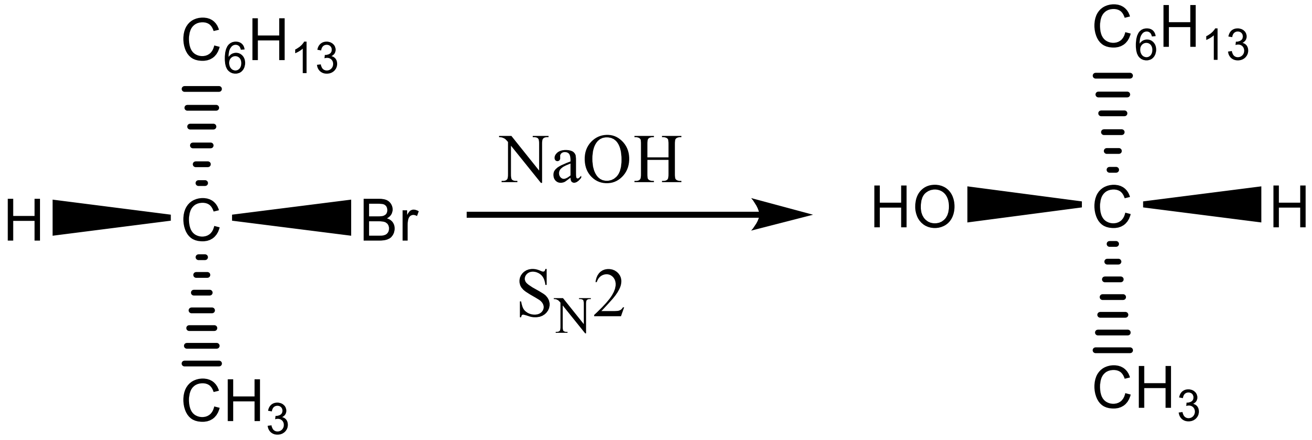
p-Toluenesuphonyl (Tosyl = Ts)



p-Toluene sulphonyl chloride (TsCl)

S_N2 Mechanism

Inversion of Configuration



(-)-2-Bromooctane

[a] = 39.6^{o}

(+)-2-Butanol

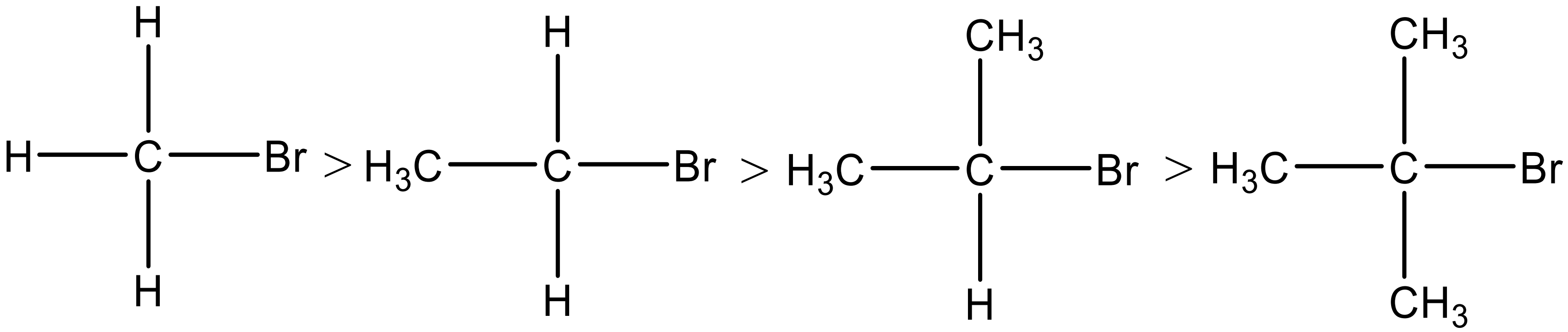
[a] = +10.3^{o}

Kinetic of Reaction

$$\text{rate} = k_2[\text{2-Bromooctane}]\,[\text{NaOH}]$$

Steric Effect

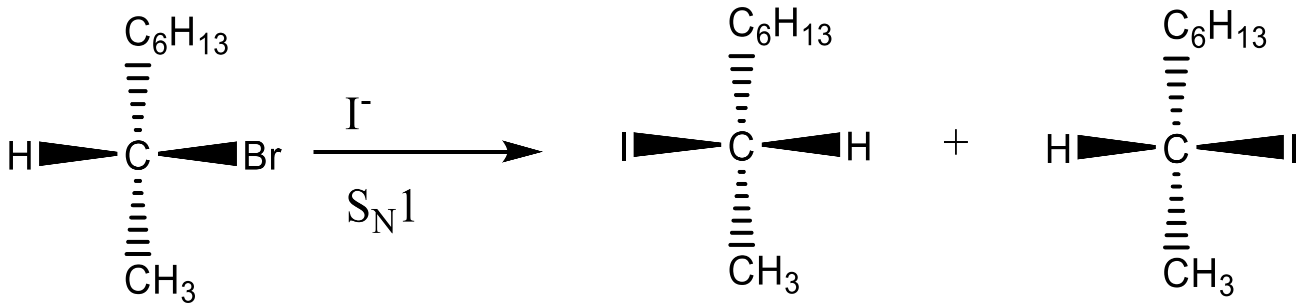
$$\text{R-Br} + \text{Cl}^- \xrightarrow{\text{DMF}} \text{R-Cl} + \text{Br}^-$$



relative rate: 37 1 0.02 0.0008

S_N1 Mechanism

Racemization (Inversion + Racemization)



(-)-2-Bromooctane

[a] = 39.6°

(S)-2-Iodooctane

Inversion

(R)-2-Iodooctane

Retention

$$R{:}X \rightleftharpoons R^+ X^- \rightleftharpoons R^+ \| X^- \longrightarrow R^+ + X^-$$

Intimate ion pair

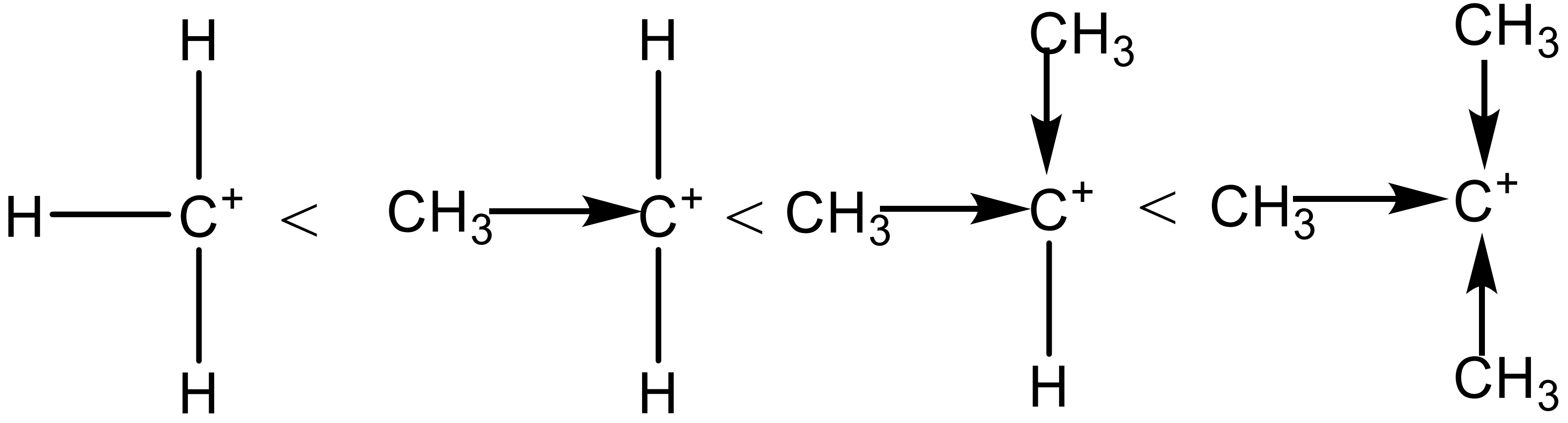
Free ions

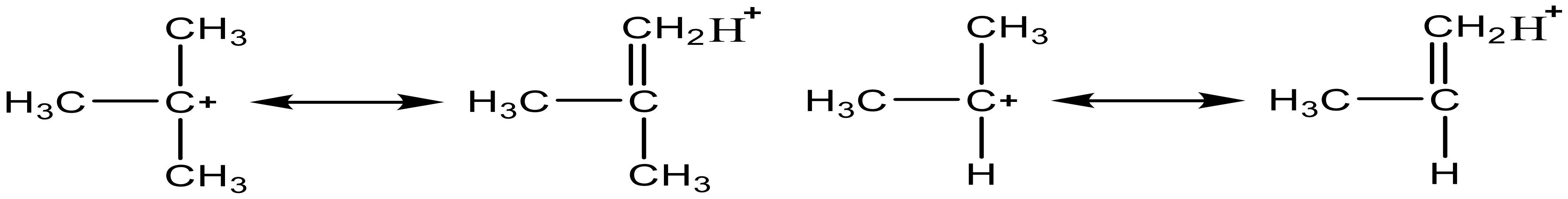
Solvent separated ion pair

Kinetic of Reaction

rate = k_1[2-Bromooctane]

Stability of Carbocations

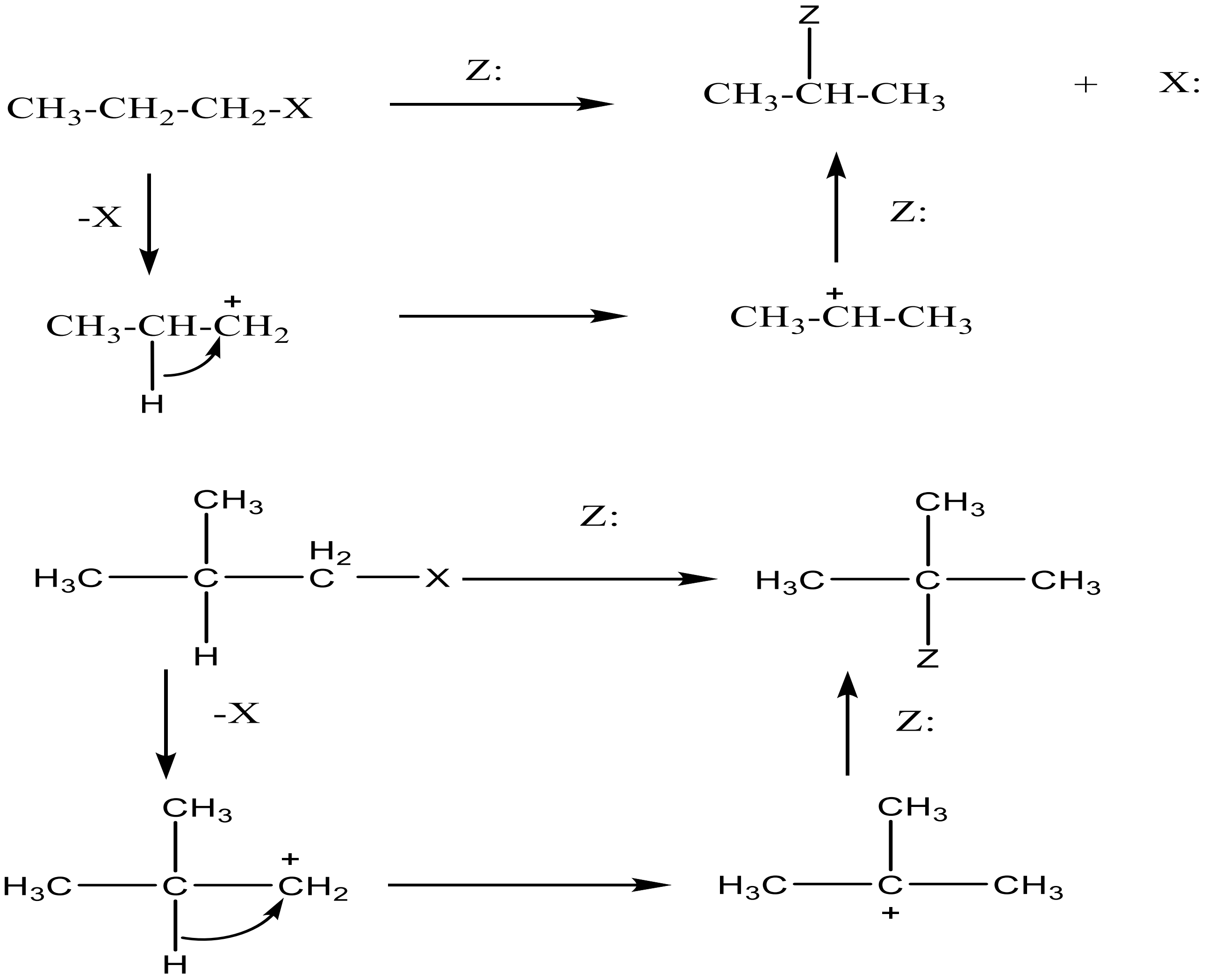




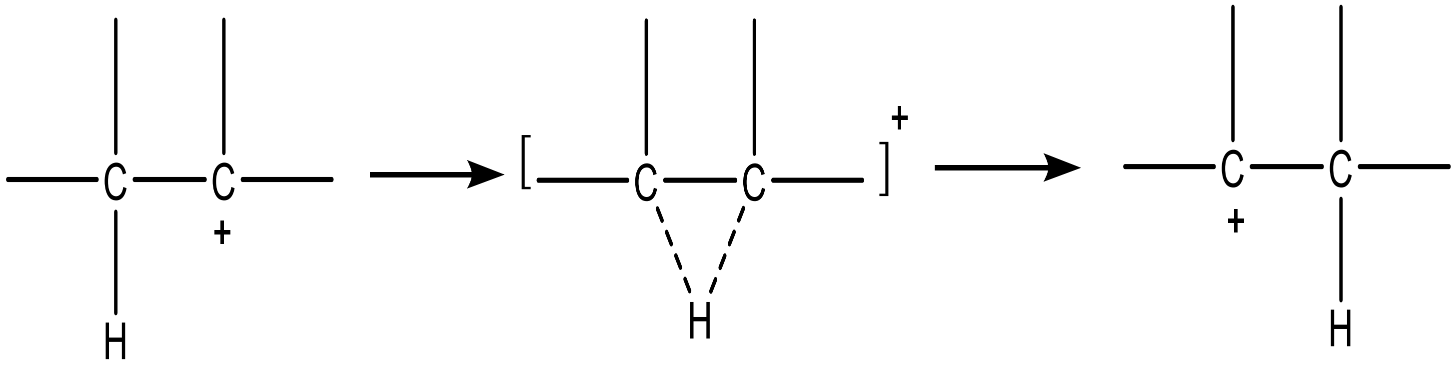
9 hyperconjugation resonance forms

6 hyperconjugation resonance forms

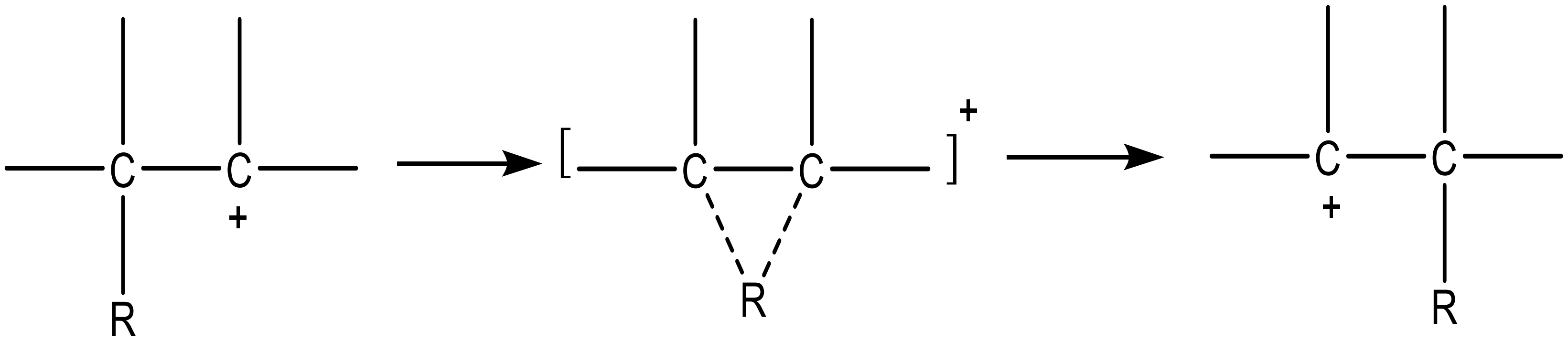
Rearrangement

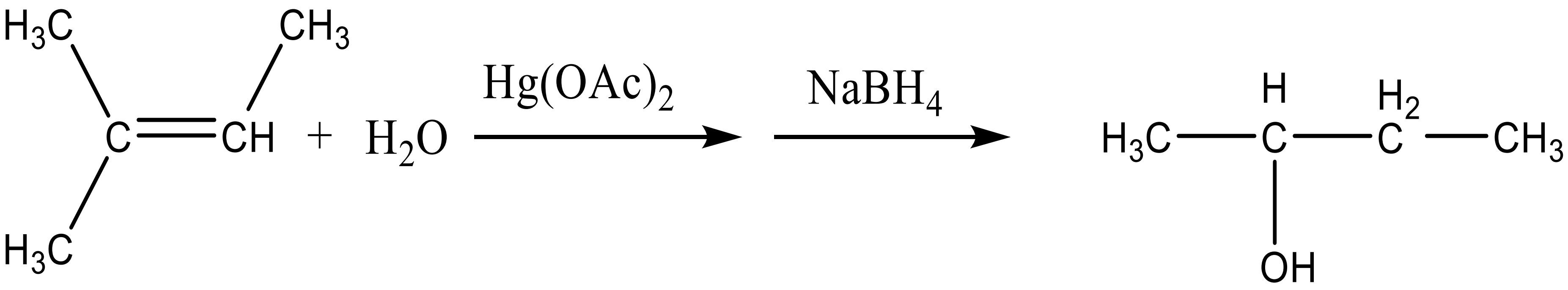


A Hydride Shift



An Alkyl Shift



H_3C
CH_3
C
CH
H_3C
+ H_2O
$Hg(OAc)_2$
$NaBH_4$
H_3C
H
C
OH
H_2
C
CH_3