10. Organohalides

Based on McMurry's *Organic Chemistry*, 7th edition

What Is an Alkyl Halide

- An organic compound containing at least one carbon-halogen bond (C-X)
  - X (F, Cl, Br, I) replaces H
- Can contain many C-X bonds
- Properties and some uses
  - Fire-resistant solvents
  - Refrigerants
  - Pharmaceuticals and precursors

Trichloroethylene (a solvent)

Halothane (an inhaled anesthetic)

Dichlorodifluoromethane (a refrigerant)

Bromomethane (a fumigant)

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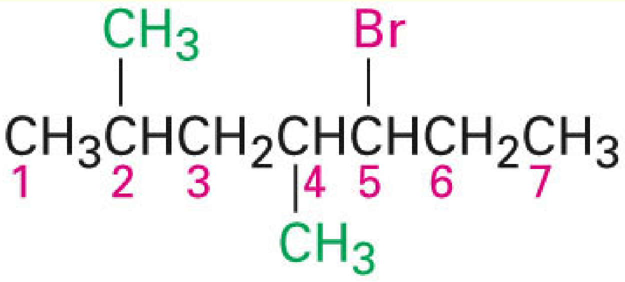
Why this Chapter?

- Reactions involving organohalides are less frequently encountered than other organic compounds, but reactions such as nucleophilic substitutions/eliminations that they undergo will be encountered frequently

- Alkyl halide chemistry is model for mechanistically similar but more complex reactions

10.1 Naming Alkyl Halides

- Find longest chain, name it as parent chain
  - (Contains double or triple bond if present)
  - Number from end nearest any substituent (alkyl or halogen)



$CH_3CH(CH_3)CH_2CH(CH_3)CH(Br)CH_2CH_3$

5-Bromo-2,4-dimethylheptane

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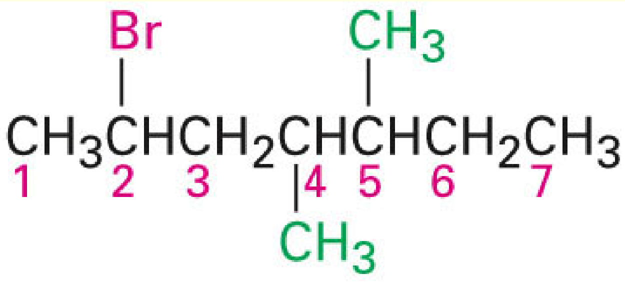
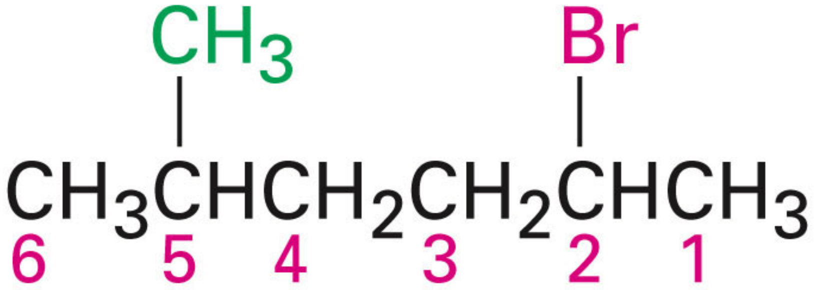


$CH_3CH(Br)CH_2CH(CH_3)CH(CH_3)CH_2CH_3$

2-Bromo-4,5-dimethylheptane

Naming if Two Halides or Alkyl Are Equally Distant from Ends of Chain

- Begin at the end nearer the substituent whose name comes first in the alphabet



$$\underset{6}{CH_3}\underset{5}{\overset{\overset{\displaystyle CH_3}{|}}{CH}}\underset{4}{CH_2}\underset{3}{CH_2}\underset{2}{\overset{\overset{\displaystyle Br}{|}}{CH}}\underset{1}{CH_3}$$

2-Bromo-5-methylhexane

(*NOT* 5-bromo-2-methylhexane)

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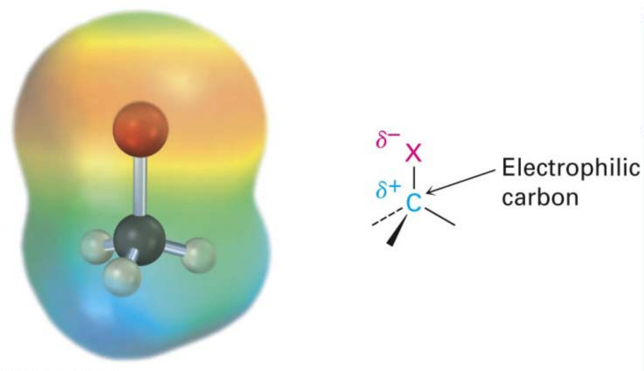
10.2 Structure of Alkyl Halides

- C-X bond is longer as you go down periodic table
- C-X bond is weaker as you go down periodic table
- C-X bond is polarized with partial positive charge on carbon and partial negative charge on halogen



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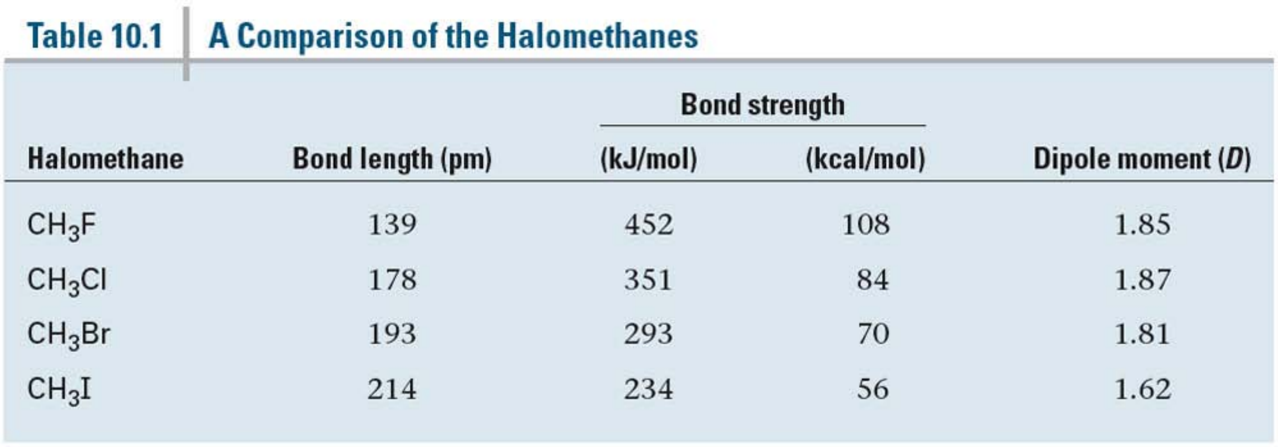

Table 10.1 A Comparison of the Halomethanes

Halomethane	Bond length (pm)	Bond strength (kJ/mol)	Bond strength (kcal/mol)	Dipole moment (*D*)
CH_3F	139	452	108	1.85
CH_3Cl	178	351	84	1.87
CH_3Br	193	293	70	1.81
CH_3I	214	234	56	1.62

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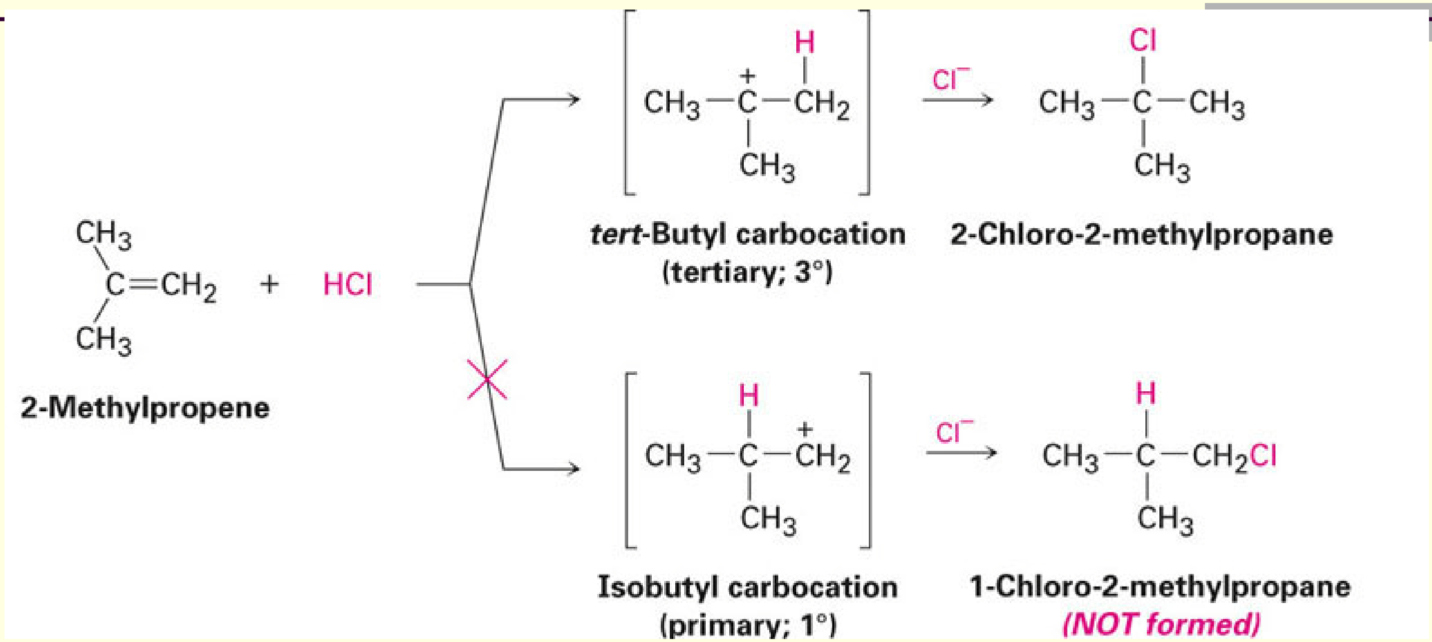
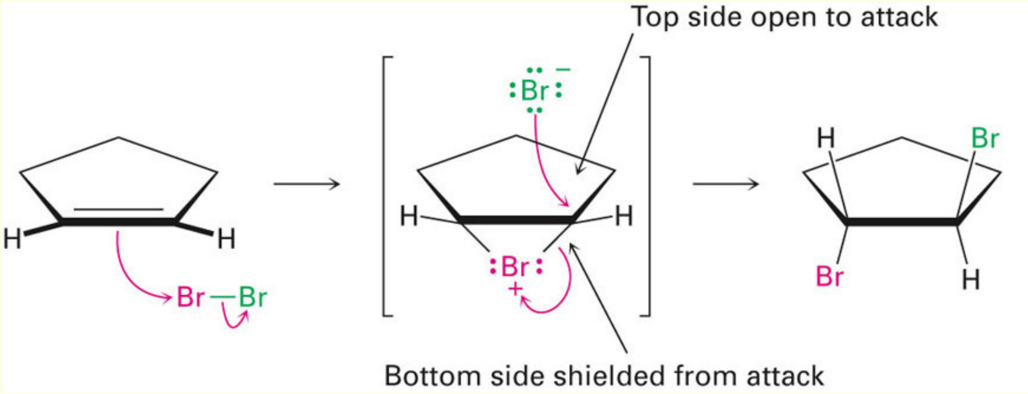
Preparing Alkyl Halides from Alkenes

- Alkyl halide from addition of HCl, HBr, HI to alkenes to give Markovnikov product (see Alkenes chapter)

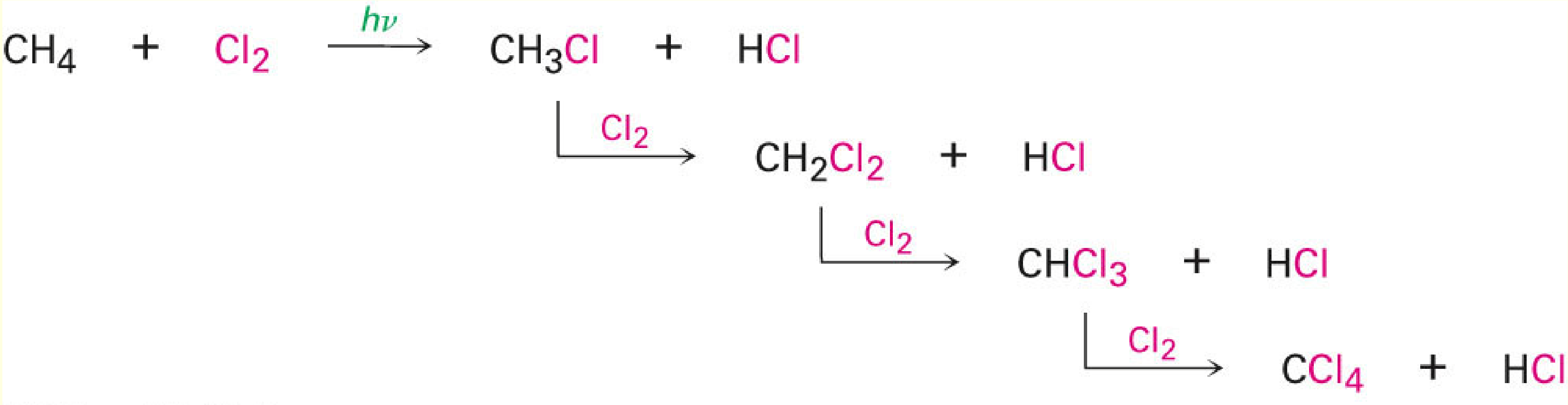


- Alkyl dihalide from *anti* addition of bromine or chlorine



Preparing Alkyl Halides from Alkanes: Radical Halogenation

- Alkane + Cl_2 or Br_2, heat or light replaces C-H with C-X but gives mixtures
  - Hard to control
  - Via free radical mechanism
- It is usually not a good idea to plan a synthesis that uses this method—multiple products



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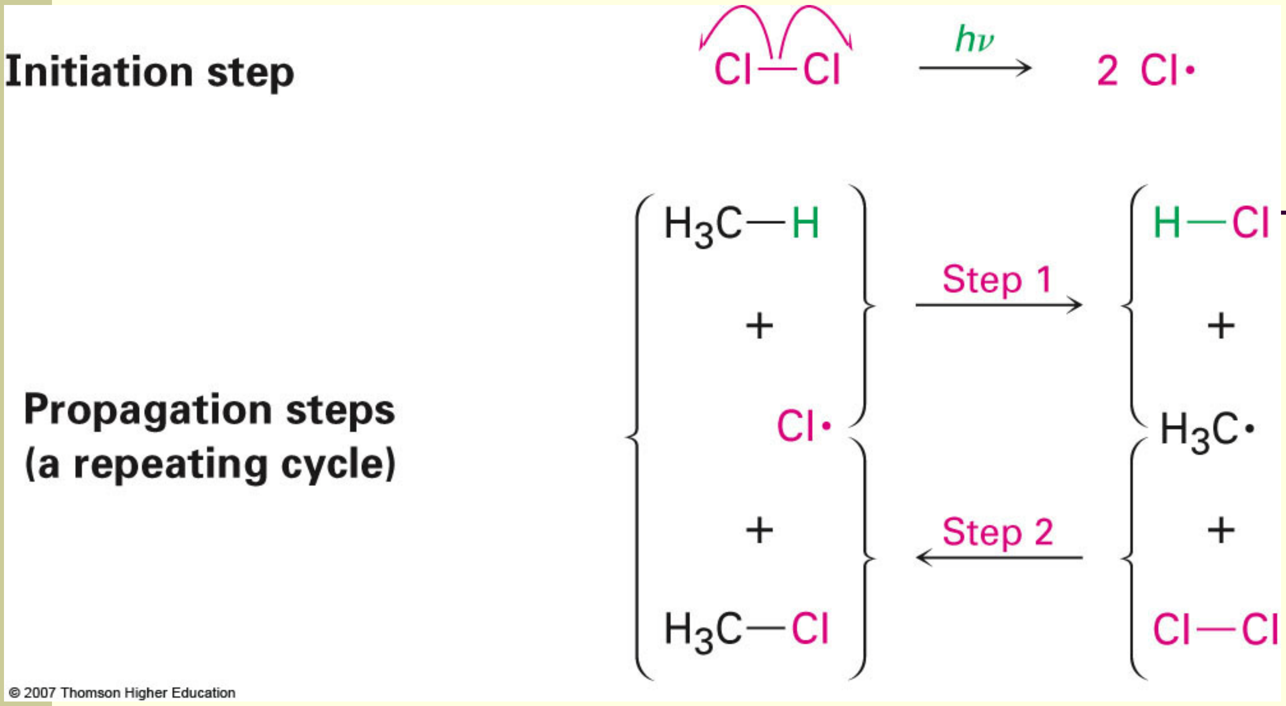
Radical Chain Mechanism



Initiation step

$$Cl{-}Cl \xrightarrow{h\nu} 2\ Cl\cdot$$

Propagation steps (a repeating cycle)

$$H_3C{-}H + Cl\cdot \xrightarrow{\text{Step 1}} H{-}Cl + H_3C\cdot$$

$$H_3C\cdot + Cl{-}Cl \xrightarrow{\text{Step 2}} H_3C{-}Cl + Cl\cdot$$

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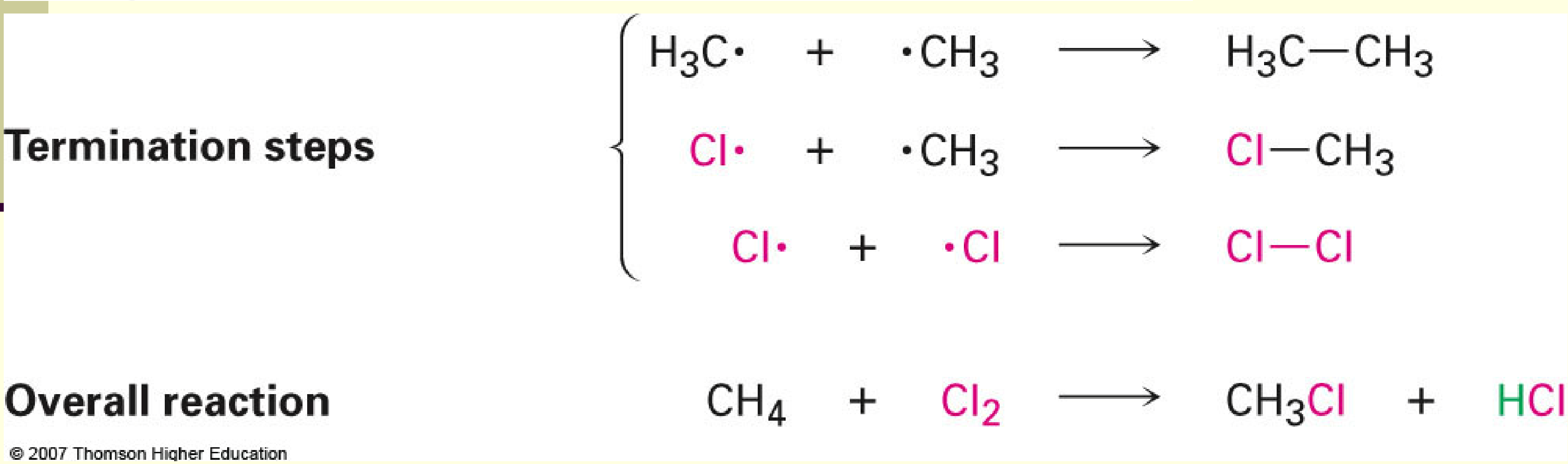

Termination steps

$$H_3C\cdot + \cdot CH_3 \longrightarrow H_3C{-}CH_3$$

$$Cl\cdot + \cdot CH_3 \longrightarrow Cl{-}CH_3$$

$$Cl\cdot + \cdot Cl \longrightarrow Cl{-}Cl$$

Overall reaction

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$

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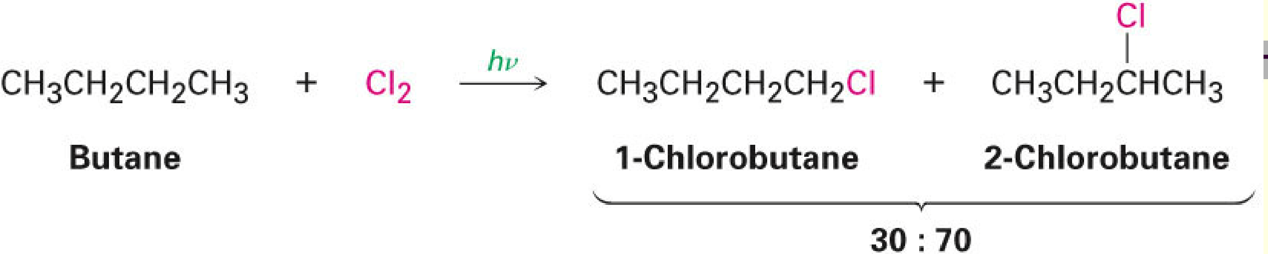
Radical Halogenation: Selectivity

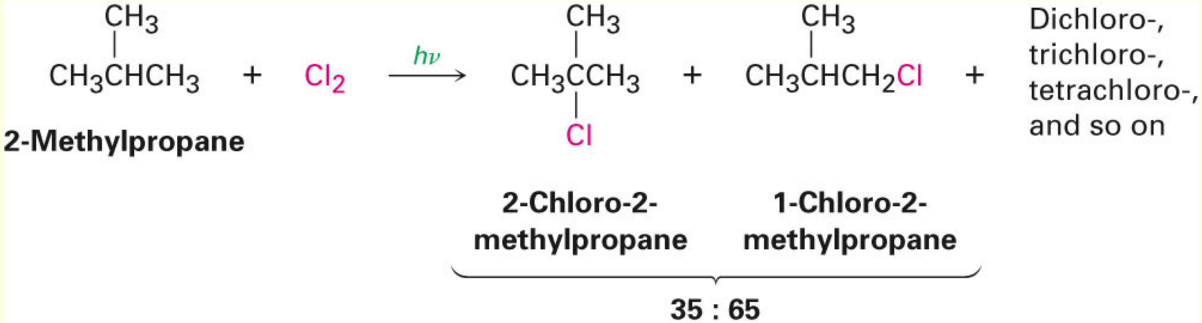
- If there is more than one type of hydrogen in an alkane, reactions favor replacing the hydrogen at the most highly substituted carbons



$$\frac{30\%\,(1^{o})\text{ Product)}}{6\,(1^{o})\text{ H's}} = 5\% \text{ per } (1^{o})\text{ H}$$

$$\frac{70\%\,(2^{o})\text{ Product)}}{4\,(2^{o})\text{ H's}} = 17.5\% \text{ per } (2^{o})\text{ H}$$

$$\frac{17.5\% \text{ per } (2^{o})\text{ H}}{5\% \text{ per } (1^{o})\text{ H}} = \mathbf{3.5 : 1 \text{ relative reactivity}}$$



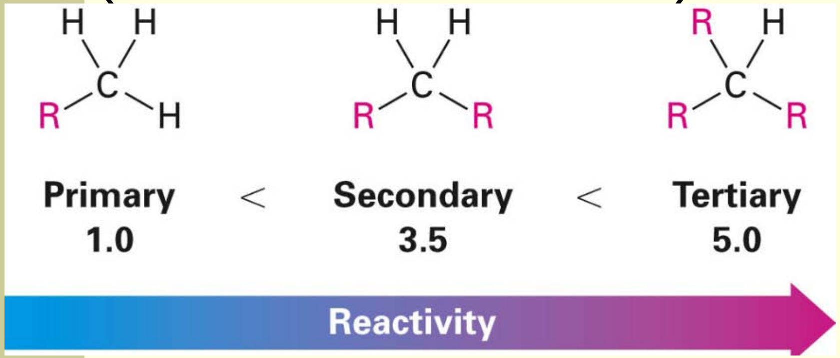
$$\frac{65\%\,(1^{o})\text{ Product)}}{9\,(1^{o})\text{ H's}} = 7.2\% \text{ per } (1^{o})\text{ H}$$

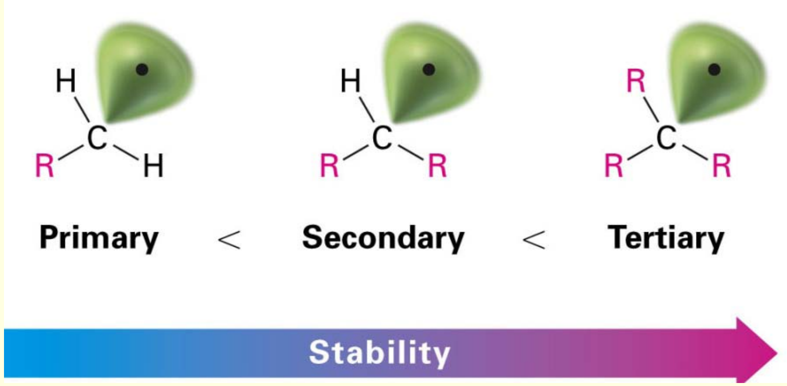
$$\frac{35\%\,(3^{o})\text{ Product)}}{1\,(1^{o})\text{ H's}} = 35\% \text{ per } (3^{o})\text{ H}$$

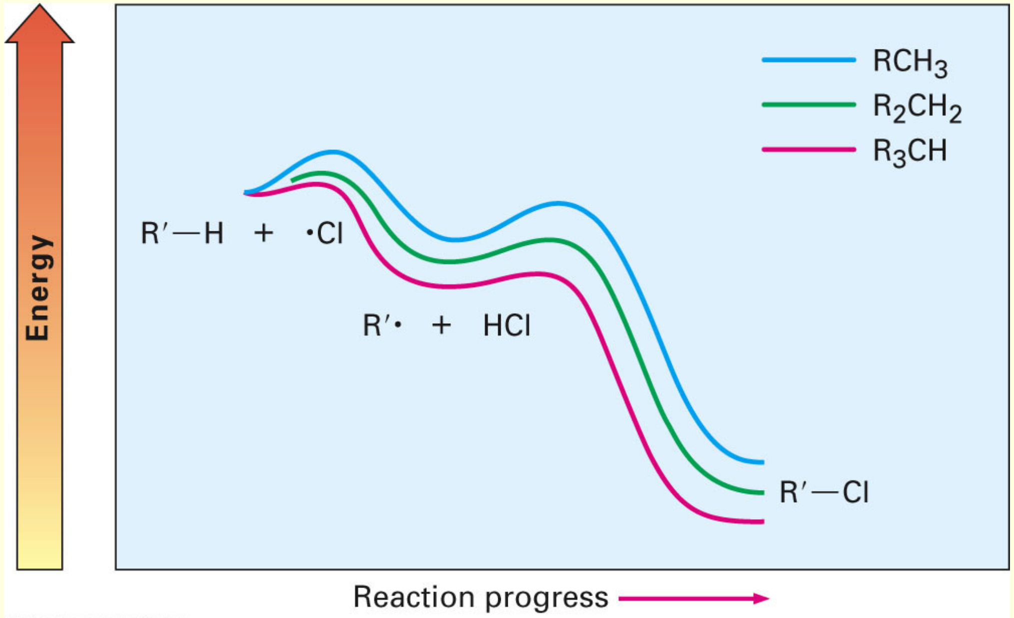
$$\frac{35\% \text{ per } (3^{o})\text{ H}}{7.2\% \text{ per } (1^{o})\text{ H}} = \mathbf{5 : 1 \text{ relative reactivity}}$$

Relative Reactivity

- Based on quantitative analysis of reaction products, relative reactivity is estimated for Cl_2: (5:3.5:1 for 3°:2°:1°)
- Order parallels stability of radicals
- Reaction distinction is more selective with bromine than chlorine (1700:80:1 for 3°:2°:1°)







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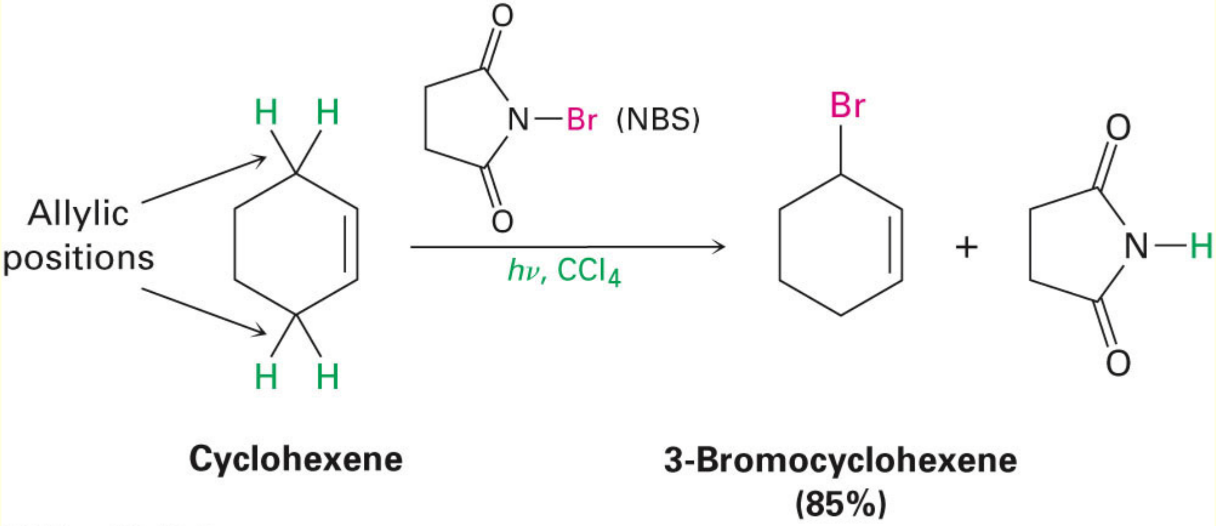
Allylic Bromination

- N-bromosuccinimide (NBS) selectively brominates allylic positions (**Allylic** = next to a double bond)
- Requires light for activation—just like radical halogenation
- NBS is just a source of dilute bromine radicals (Br▪)



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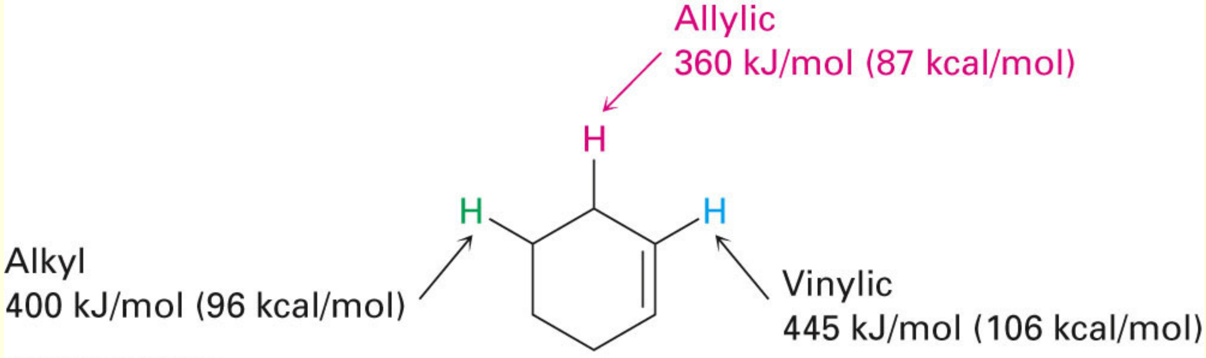

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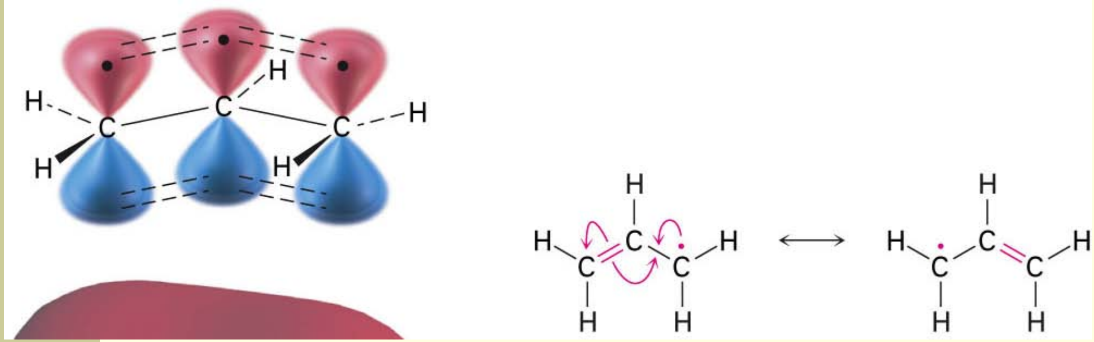
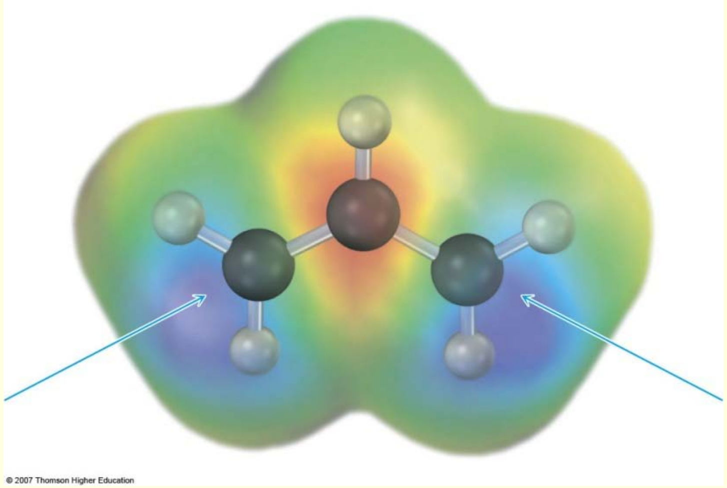
Allylic Stabilization

- Allyl radical is delocalized—radical is shared over 2 carbons
- More stable than typical alkyl radical by 40 kJ/mol (9 kcal/mol)
- Allylic radical is more stable than tertiary alkyl radical

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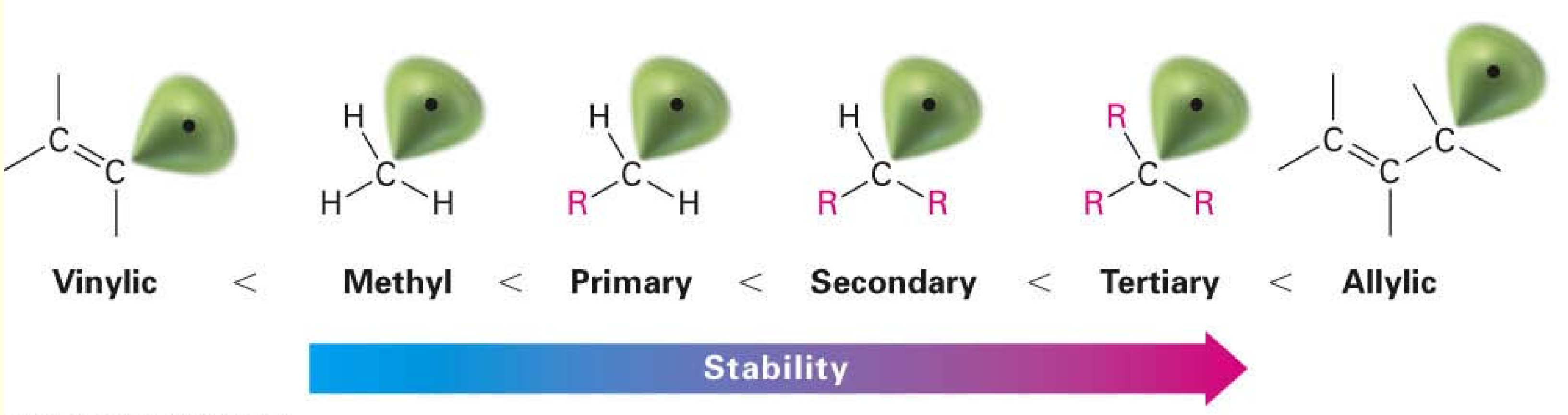

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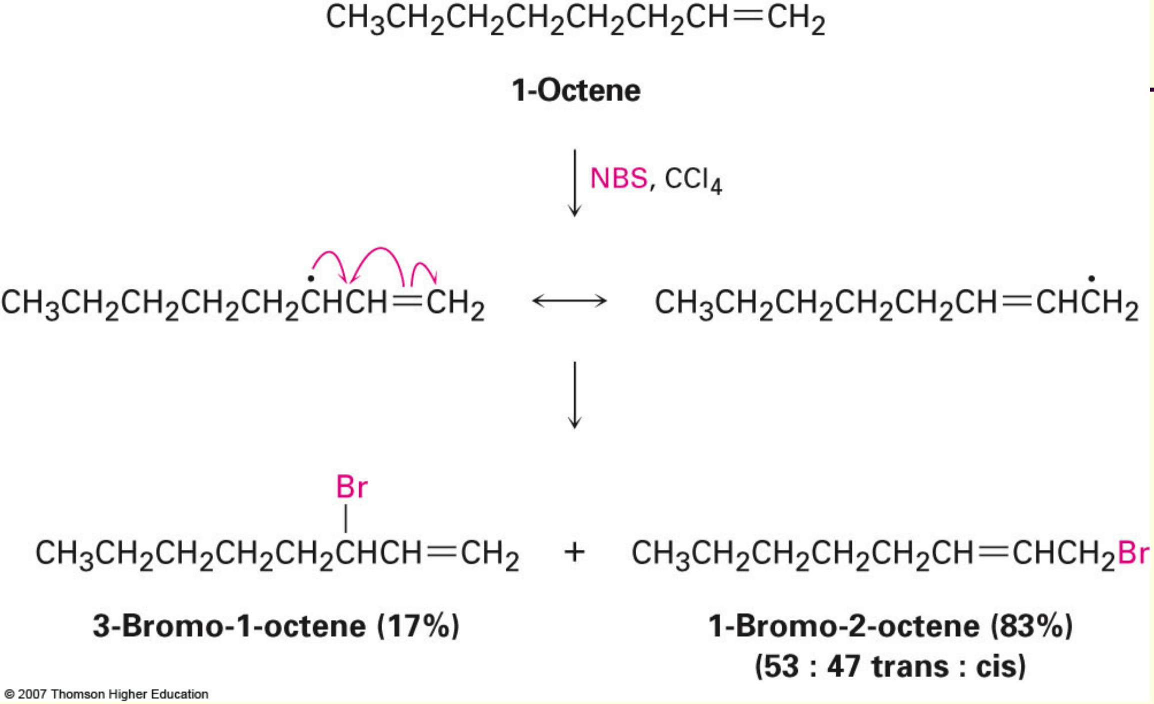
Use of Allylic Bromination

- Allylic bromination with NBS creates an allylic bromide



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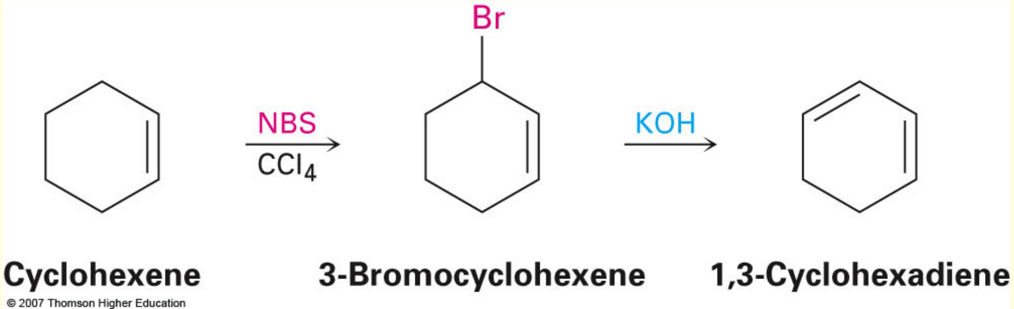
Why this Major Product?

1. Less Hindered Radical Gives Major Product

2. More substituted alkene is more stable

- Reaction of an allylic bromide with base produces a conjugated diene (by elimination), useful in synthesis of complex molecules



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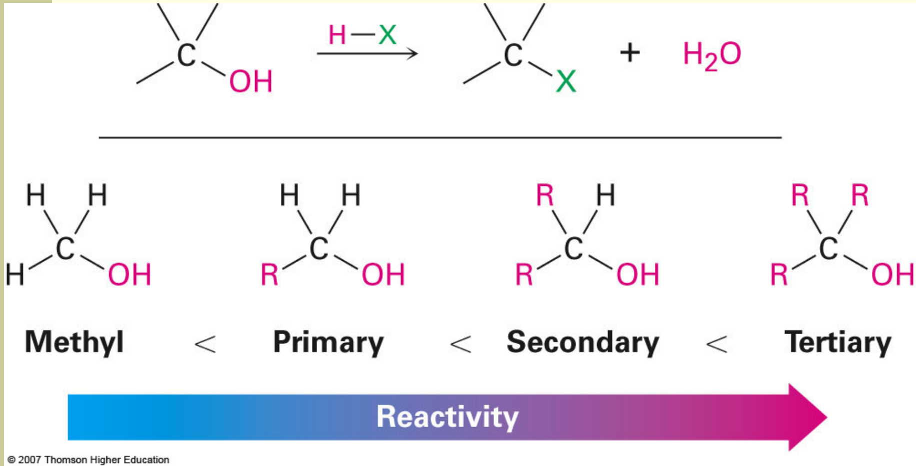
Preparing Alkyl Halides from Alcohols

- Reaction of tertiary C-OH with HX is fast and effective
  - Add HCl or HBr gas into ether solution of tertiary alcohol



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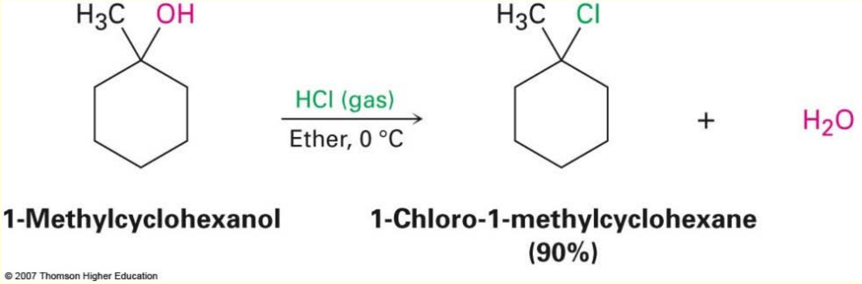

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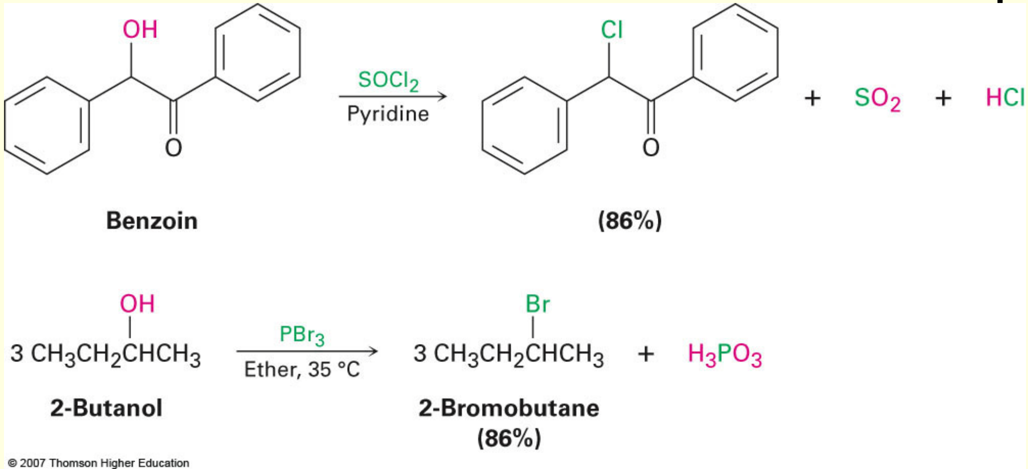
- Primary and secondary alcohols react very slowly and often rearrange, so alternative methods are used: $SOCl_2$ or PBr_3
- Mechanisms of all of these reactions in next chapter



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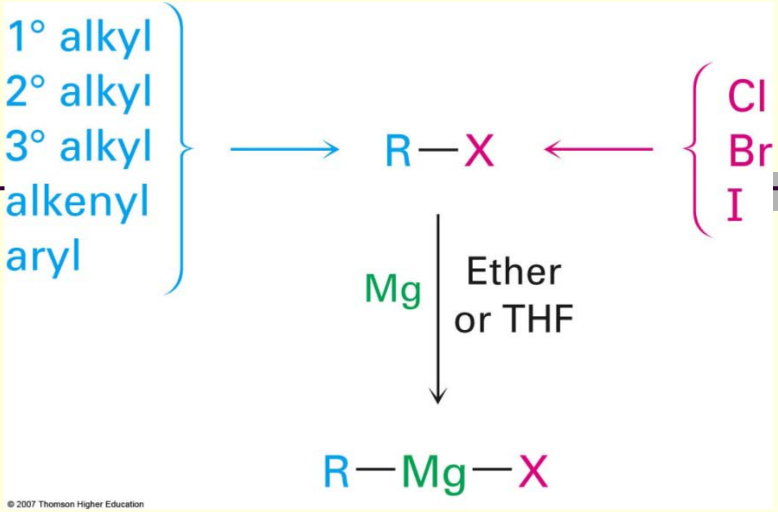
Reactions of Alkyl Halides: Grignard Reagents

- Reaction of RX with Mg in ether or THF
- Product is RMgX – an organometallic compound (alkyl-metal bond)



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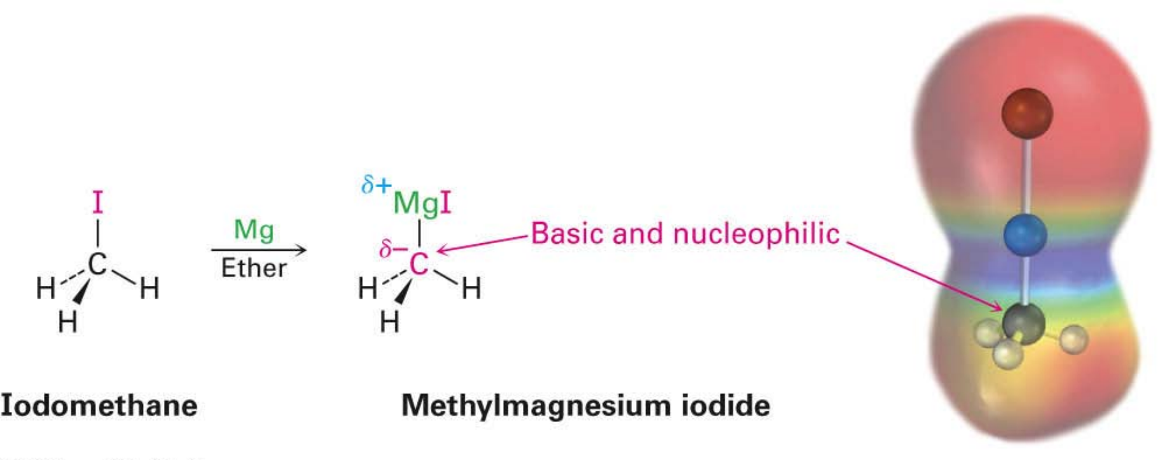

Iodomethane Methylmagnesium iodide

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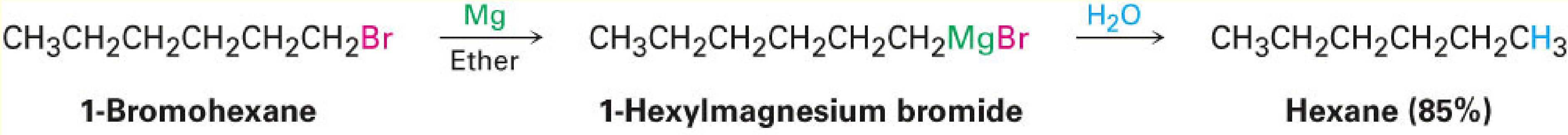
Carbanions (CH_3^- MgX^+) are very strong bases

Deprotonate water, alcohols Carboxylic acids, etc…



$$CH_3CH_2CH_2CH_2CH_2CH_2Br \xrightarrow[\text{Ether}]{\text{Mg}} CH_3CH_2CH_2CH_2CH_2CH_2MgBr \xrightarrow{H_2O} CH_3CH_2CH_2CH_2CH_2CH_3$$

1-Bromohexane 1-Hexylmagnesium bromide Hexane (85%)

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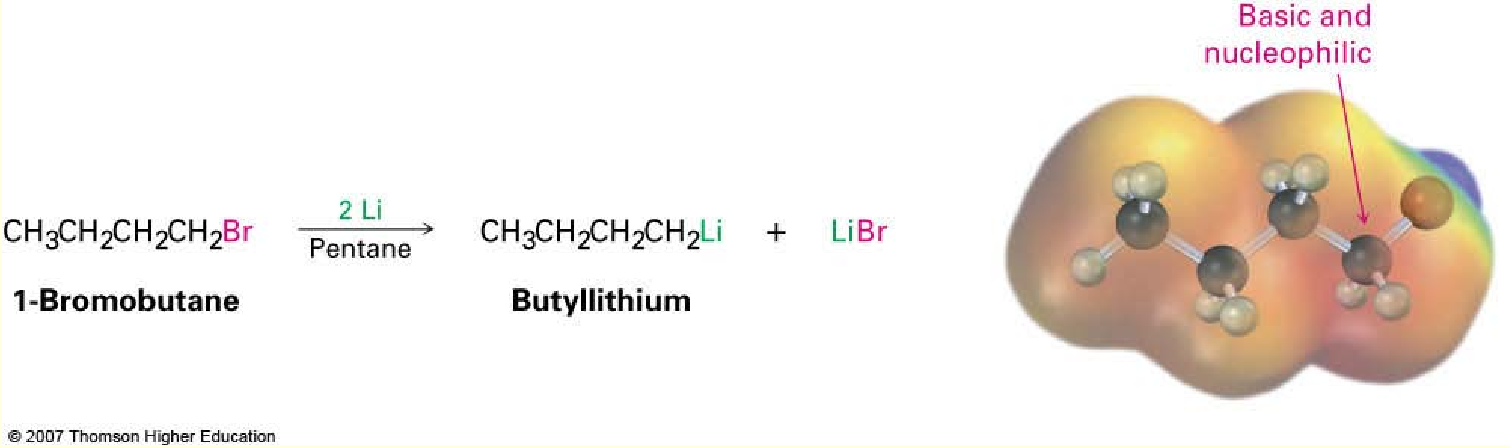
Organometallic Coupling Reactions

- Alkyllithium (RLi) forms from RBr and Li metal
- RLi reacts with copper iodide to give lithium dialkylcopper (Gilman reagents)
- Lithium dialkylcopper reagents react with alkyl halides to give alkanes



$$CH_3CH_2CH_2CH_2Br \xrightarrow[\text{Pentane}]{\text{2 Li}} CH_3CH_2CH_2CH_2Li + LiBr$$

1-Bromobutane **Butyllithium**

Basic and nucleophilic

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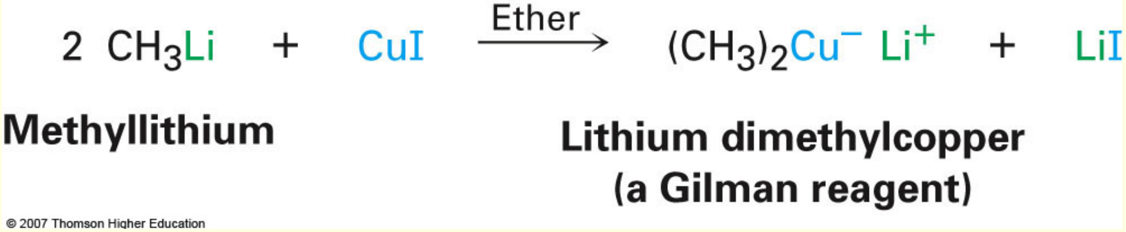

$$2\ CH_3Li + CuI \xrightarrow{\text{Ether}} (CH_3)_2Cu^- Li^+ + LiI$$

Methyllithium **Lithium dimethylcopper (a Gilman reagent)**

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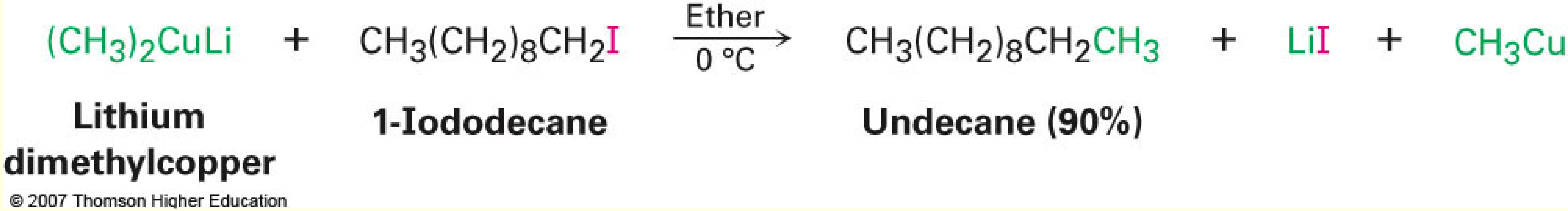

$$(CH_3)_2CuLi + CH_3(CH_2)_8CH_2I \xrightarrow[0\ ^\circ C]{\text{Ether}} CH_3(CH_2)_8CH_2CH_3 + LiI + CH_3Cu$$

Lithium dimethylcopper **1-Iododecane** **Undecane (90%)**

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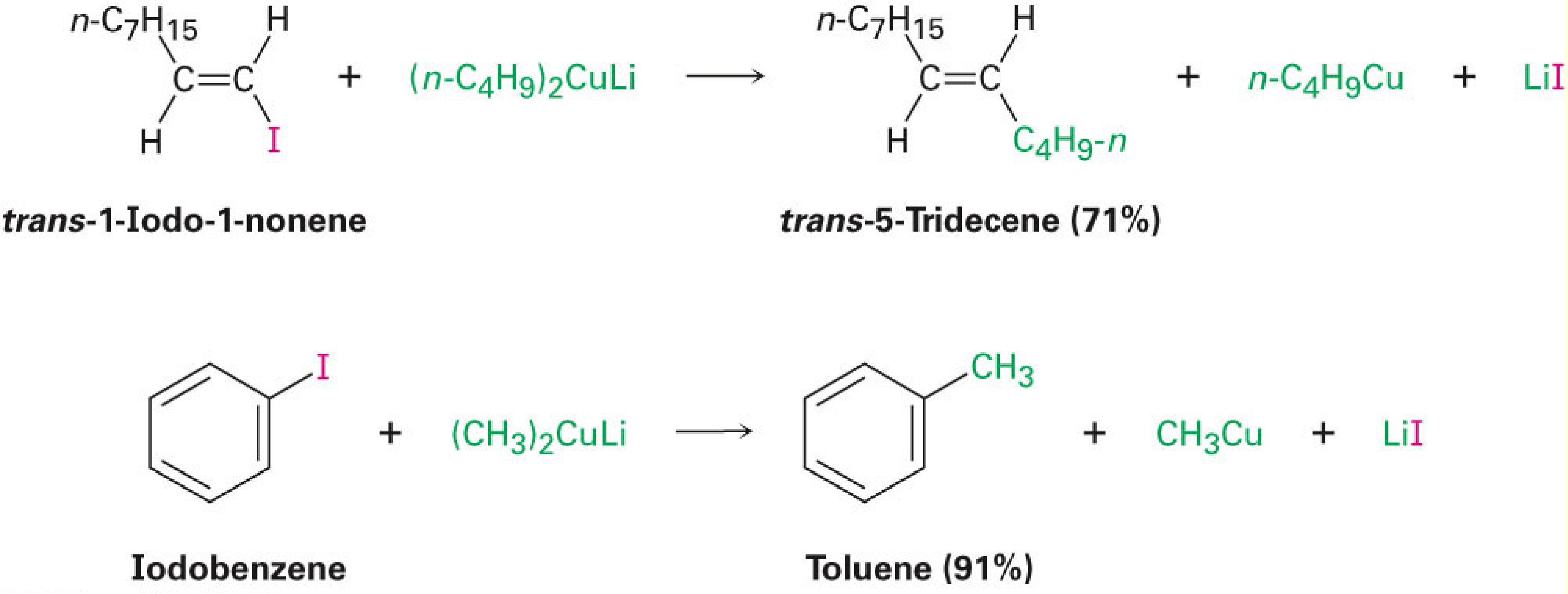
Utility of Organometallic Coupling in Synthesis

- Coupling of two organometallic molecules produces larger molecules of defined structure
- Aryl and vinyl organometallics also effective



***trans*-1-Iodo-1-nonene** **_trans_-5-Tridecene (71%)**

Iodobenzene **Toluene (91%)**

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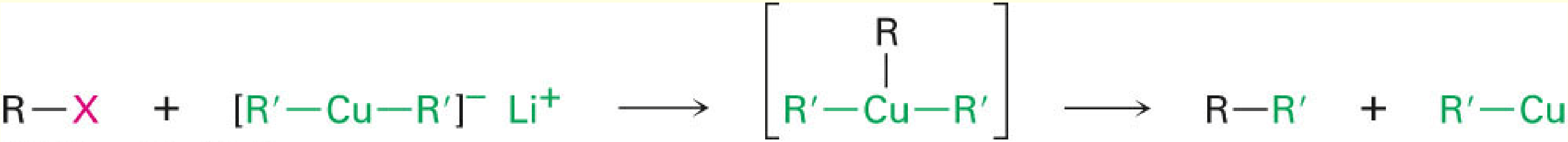
- Coupling of lithium dialkylcopper molecules proceeds through trialkylcopper intermediate



$$R{-}X + [R'{-}Cu{-}R']^{-}\ Li^{+} \longrightarrow \left[\begin{array}{c} R \\ | \\ R'{-}Cu{-}R' \end{array} \right] \longrightarrow R{-}R' + R'{-}Cu$$

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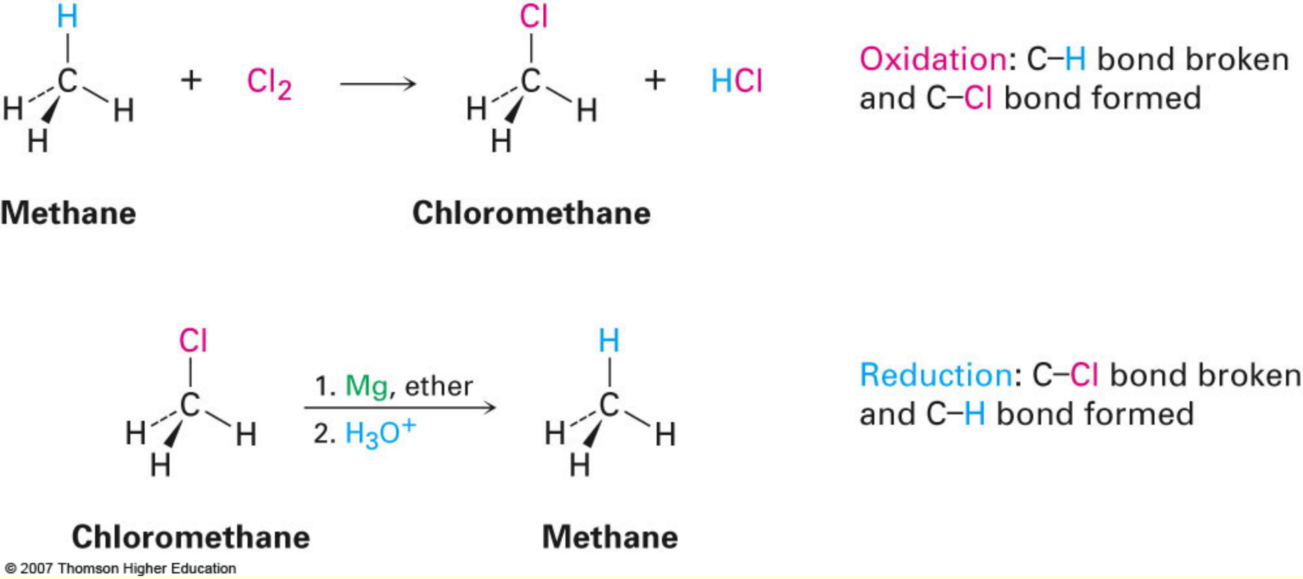
Oxidation and Reduction in Organic Chemistry

- In organic chemistry, we say that **oxidation** occurs when a carbon or hydrogen that is connected to a carbon atom in a structure is replaced by oxygen, nitrogen, or halogen
  - Not defined as loss of electrons by an atom as in inorganic chemistry
- Oxidation is a reaction that results in loss of electron density at carbon (as more electronegative atoms replace hydrogen or carbon)
- Organic reduction is the opposite of oxidation
  - Results in gain of electron density at carbon (replacement of electronegative atoms by hydrogen or carbon)

Oxidation: *break* C-H (or C-C) and *form* C-O, C-N, C-X

Reduction: *form* C-H (or C-C) and *break* C-O, C-N, C-X

Oxidation and Reduction Reactions



Oxidation: C–H bond broken and C–Cl bond formed

Reduction: C–Cl bond broken and C–H bond formed

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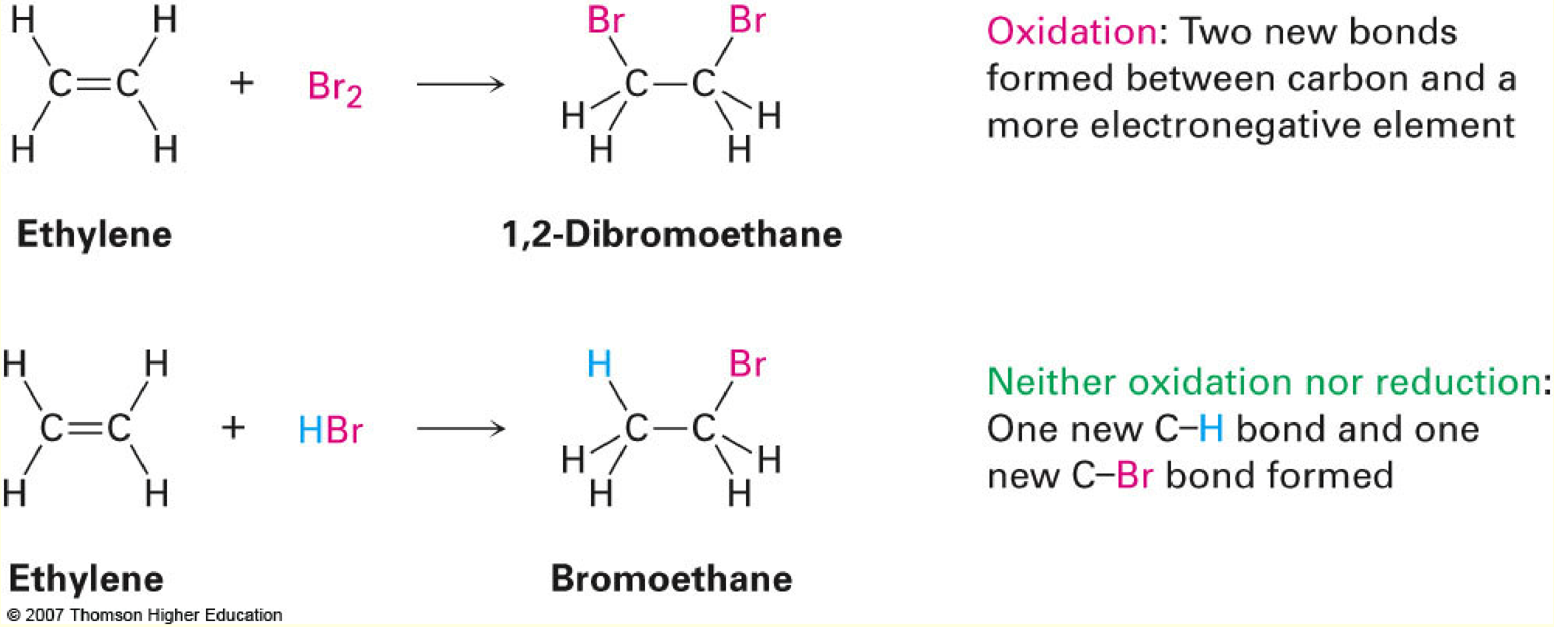

Oxidation: Two new bonds formed between carbon and a more electronegative element

Neither oxidation nor reduction: One new C–H bond and one new C–Br bond formed

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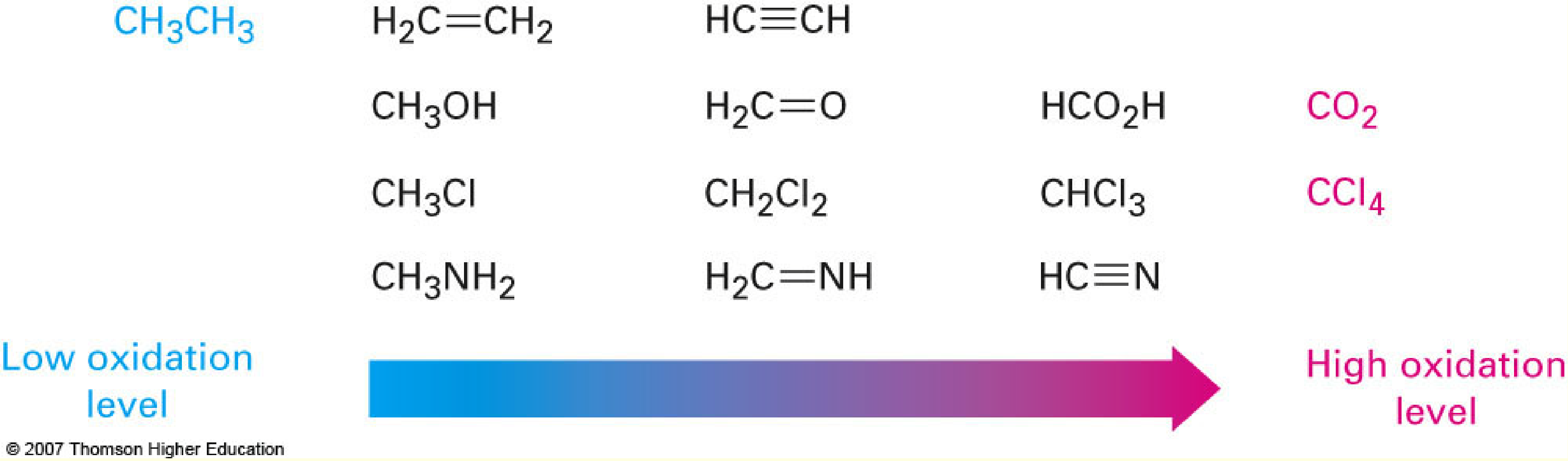
Oxidation Levels

- Functional groups are associated with specific oxidation levels



CH_3CH_3 $H_2C{=}CH_2$ $HC{\equiv}CH$

CH_3OH $H_2C{=}O$ HCO_2H CO_2

CH_3Cl CH_2Cl_2 $CHCl_3$ CCl_4

CH_3NH_2 $H_2C{=}NH$ $HC{\equiv}N$

Low oxidation level → High oxidation level

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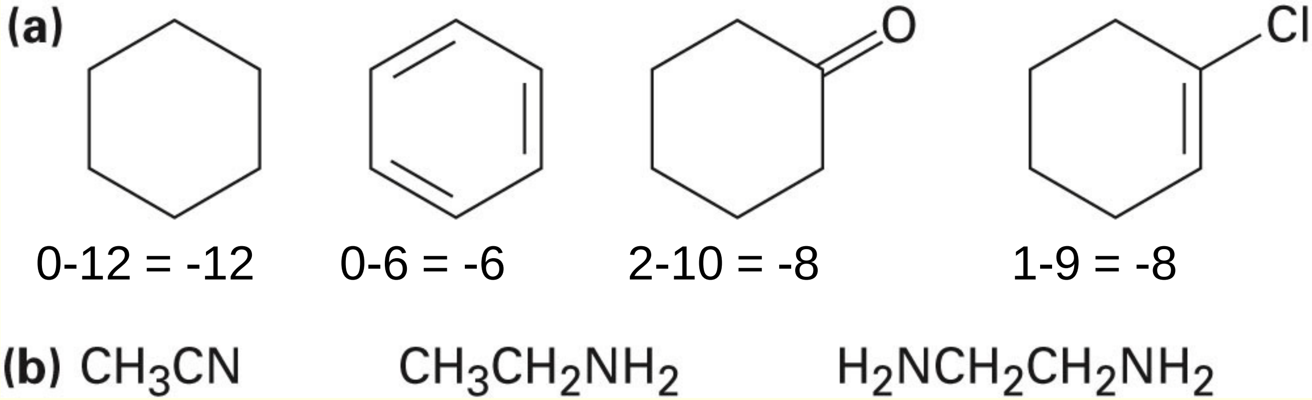
- Finding the oxidation level:

  Level = (# of C-O,C-N,C-X bonds) – (# of C-H bonds)

- Ex. 10.12



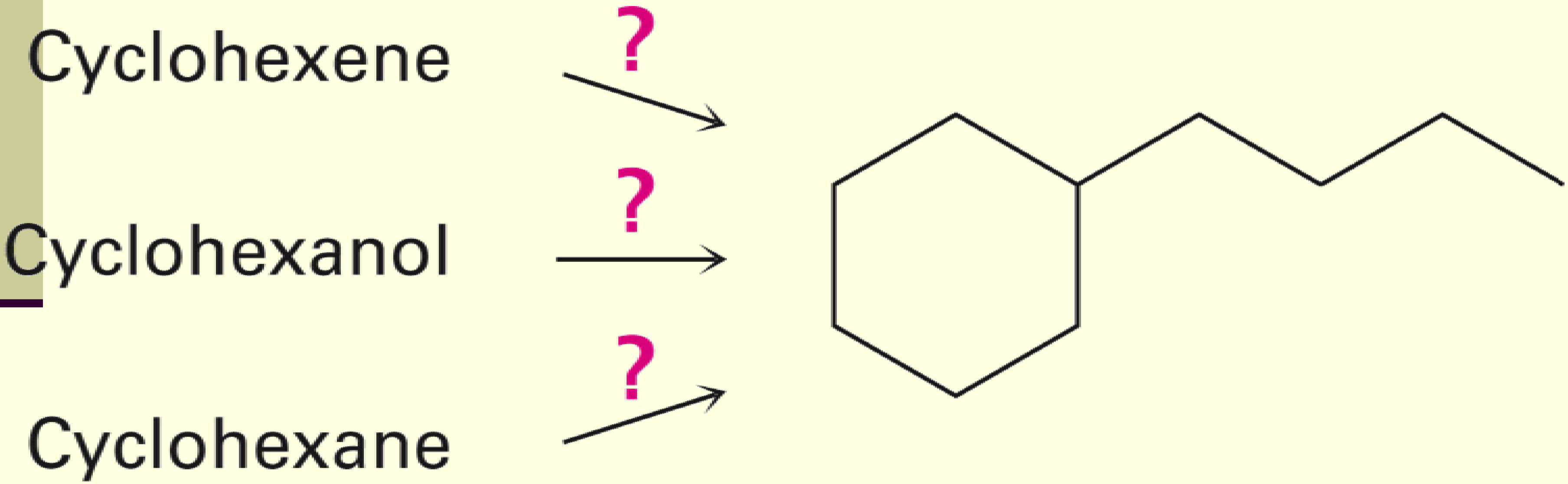
(a) 0-12 = -12 0-6 = -6 2-10 = -8 1-9 = -8

(b) CH_3CN $CH_3CH_2NH_2$ $H_2NCH_2CH_2NH_2$

3-0 = 0 1-5 = -4 2-4 = -2

Let’s Work a Problem

How would you carry out the following syntheses?



Answer

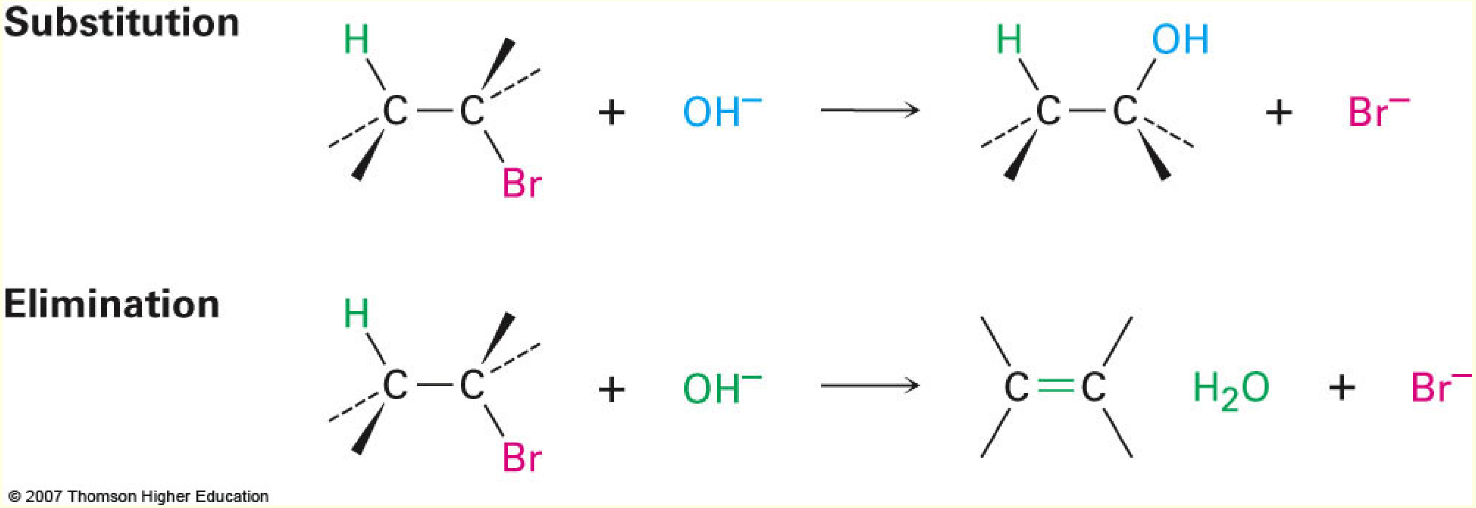
The dialkylcopper reagent should be used (di-butylCuLi) that can be added to cyclohexylBr after cyclohexene is treated with HBr.

11. Reactions of Alkyl Halides: Nucleophilic Substitutions and Eliminations

Based on McMurry's *Organic Chemistry*, 7th edition

Alkyl Halides React with Nucleophiles and Bases

- Alkyl halides are polarized at the carbon-halide bond, making the carbon electrophilic
- Nucleophiles will replace the halide in C-X bonds of many alkyl halides(reaction as Lewis base)
- Nucleophiles that are Brønsted bases produce elimination



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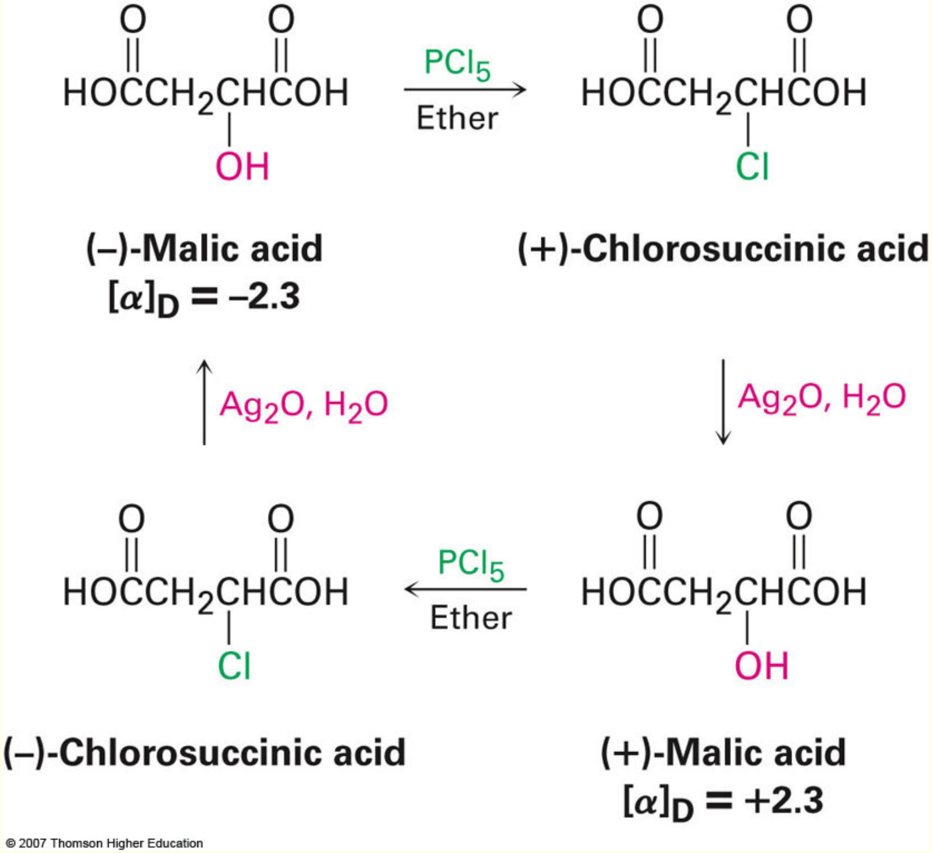
Why this Chapter?

- Nucleophilic substitution, base induced elimination are among most widely occurring and versatile reaction types in organic chemistry
- Reactions will be examined closely to see:

- How they occur
- What their characteristics are
- How they can be used

11.1 The Discovery of Nucleophilic Substitution Reactions—Walden

- The reactions alter the array at the chirality center
- The reactions involve substitution at that center
- Therefore, nucleophilic substitution can invert the configuration at a chirality center
- The presence of carboxyl groups in malic acid led to some dispute as to the nature of the reactions in Walden's cycle



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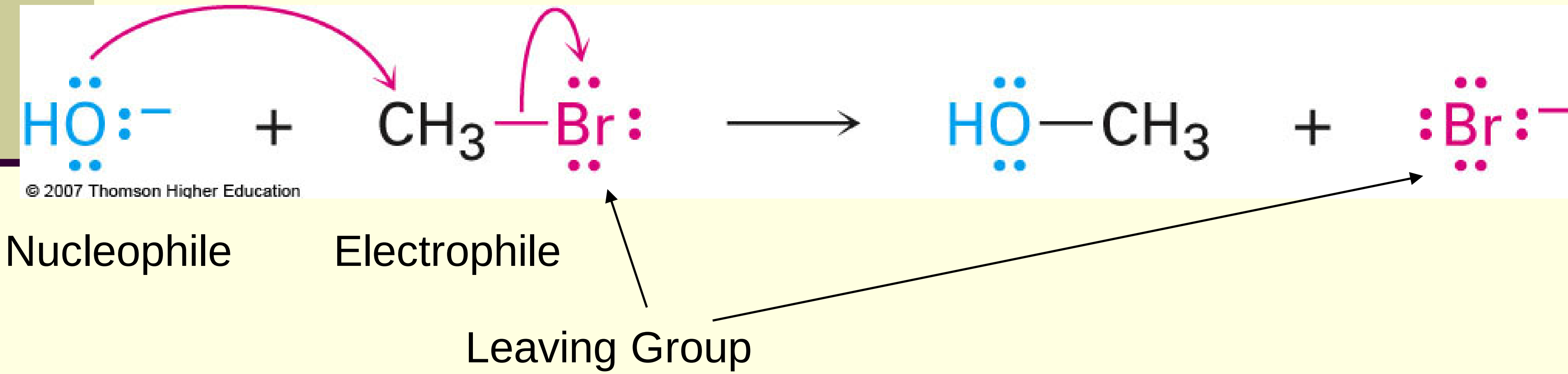
11.2 The S_N2 Reaction

- Reaction is with inversion at reacting center (substrate)
- Follows second order reaction kinetics
- Ingold nomenclature to describe characteristic step:
  - S=substitution
  - N (subscript) = nucleophilic
  - 2 = both nucleophile and substrate in characteristic step (bimolecular)



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Nucleophile

Electrophile

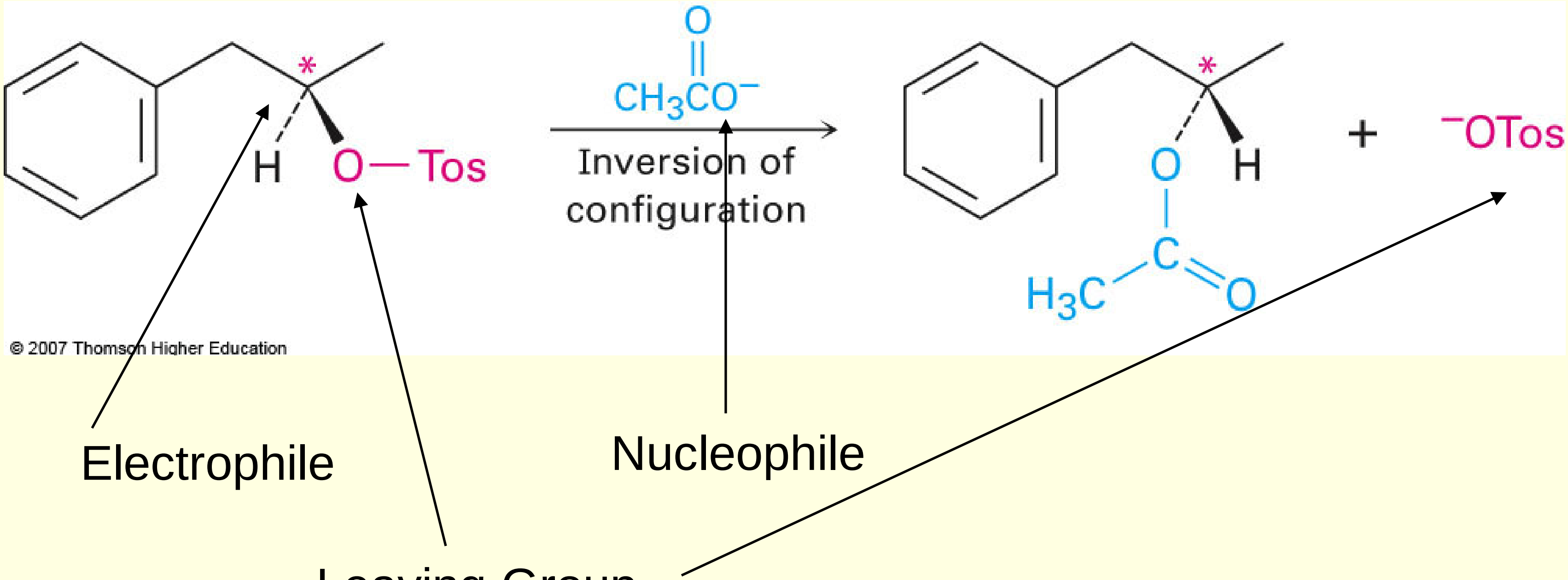
Leaving Group

Reaction Kinetics

- The study of rates of reactions is called *kinetics*
- Rates decrease as concentrations decrease but the rate constant does not
- Rate units: [concentration]/time such as L/(mol x s)
- The *rate law* is a result of the mechanism
- The *order* of a reaction is sum of the exponents of the concentrations in the rate law
- A + B -----> C + D
  - Experimentally determine the effect of increasing A/B
  - First Order: rate = k[A] (only depends on [A], not [B])
  - Second Order: rate = k[A][B] (depends on both [A],[B])
  - Third order: rate = $k[A]^2[B]$

S_N2 Process

- The reaction involves a transition state in which both reactants are together
- Rate = k[ROTs][OAc]



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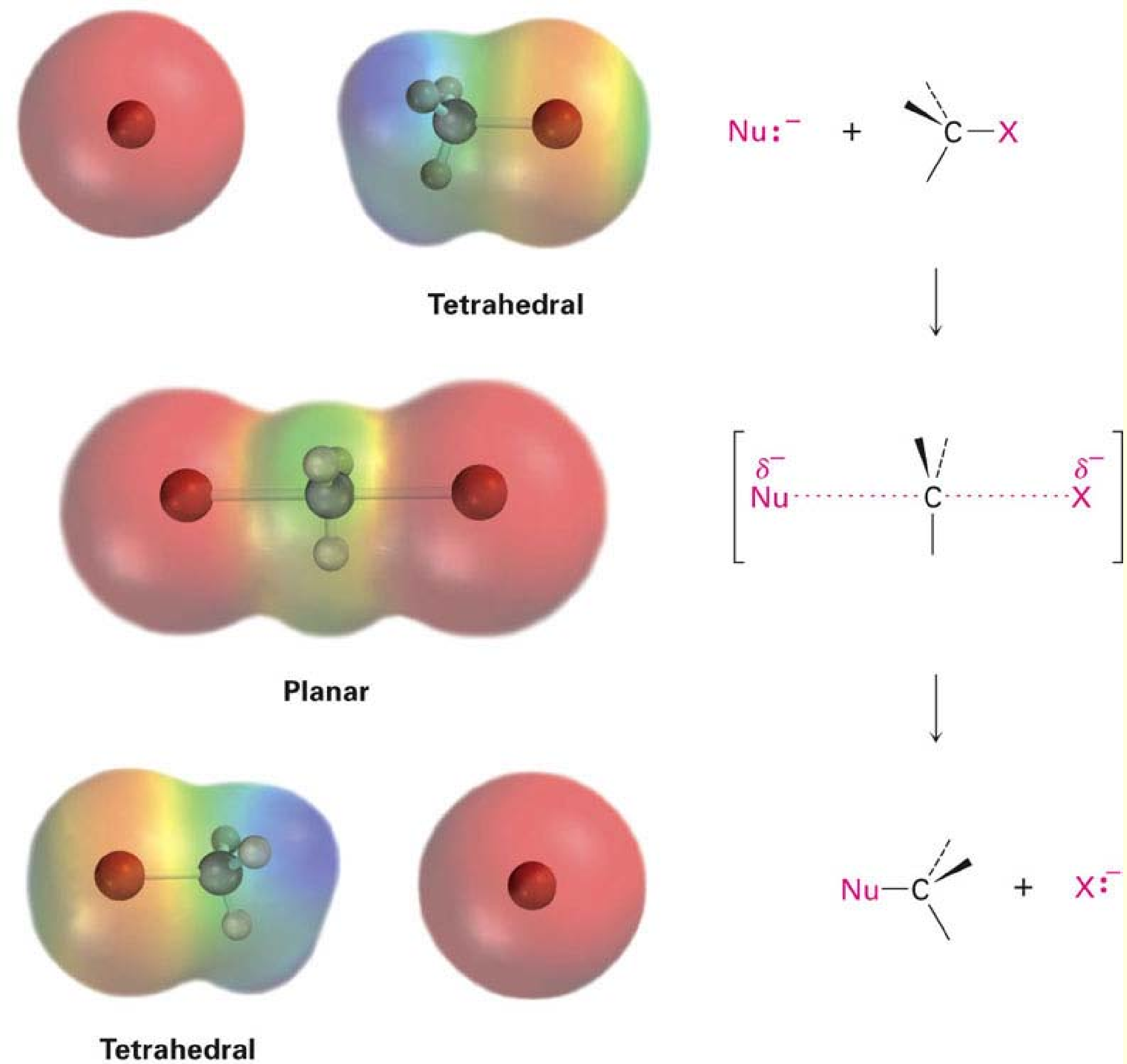
Electrophile

Nucleophile

Leaving Group

S_N2 Transition State

- The transition state of an S_N2 reaction has a planar arrangement of the carbon atom and the remaining three groups



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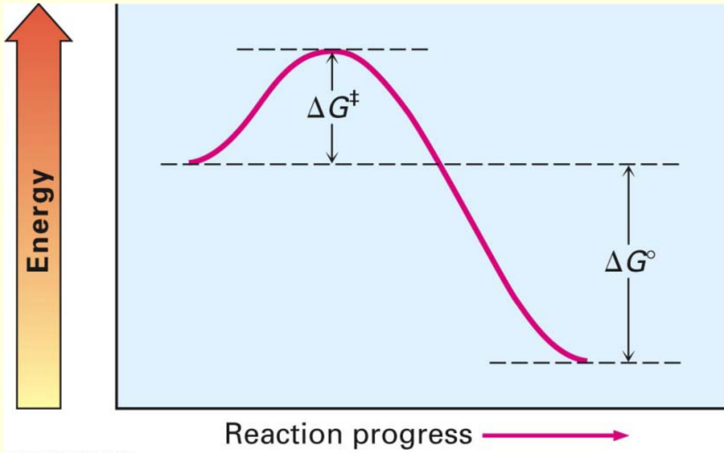

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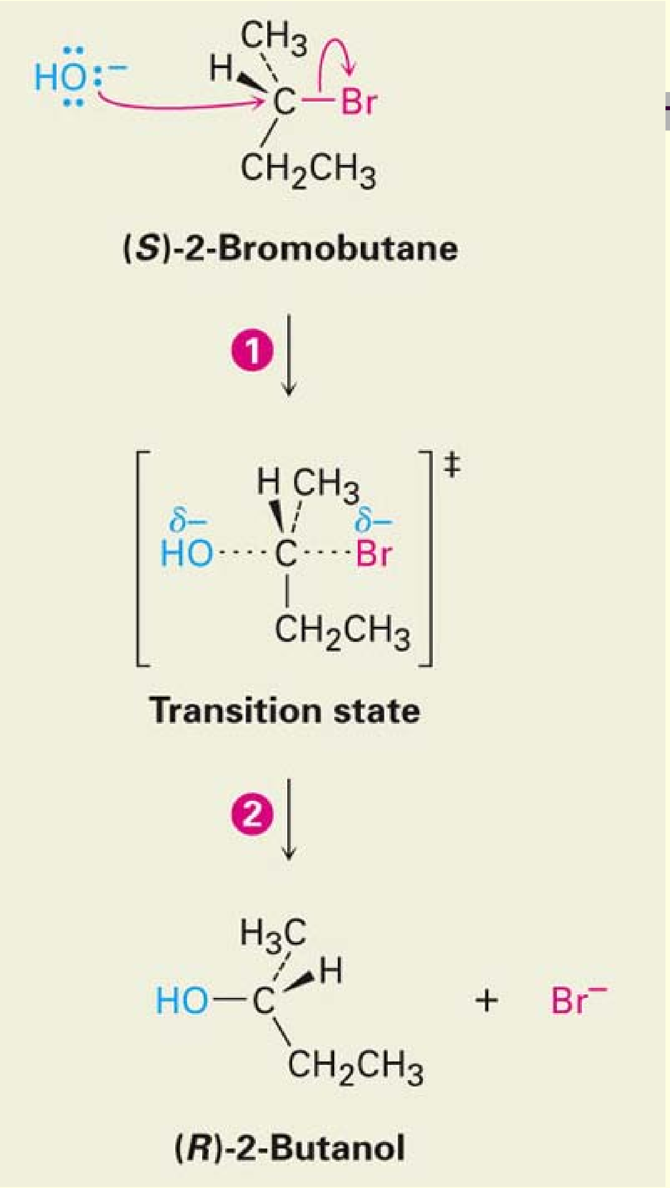
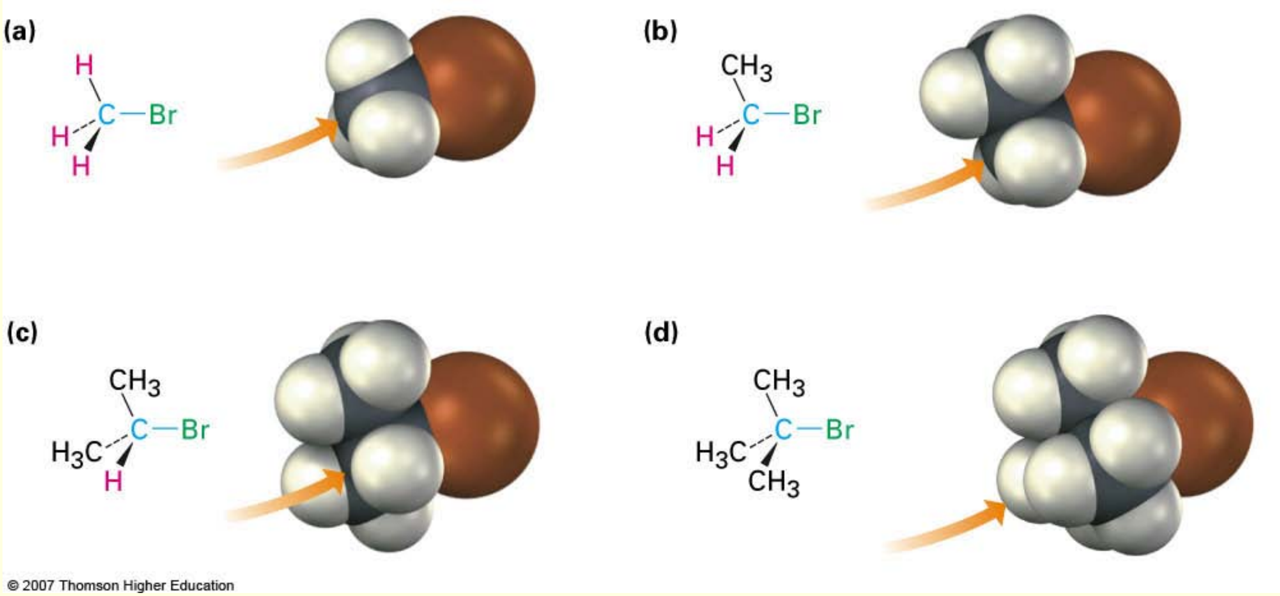
11.3 Characteristics of the S_N2 Reaction

- Occurs with inversion of chiral center
- Sensitive to steric effects
- Methyl halides are most reactive
- Primary are next most reactive
- Secondary might react
- Tertiary are unreactive by this path
- No reaction at C=C (vinyl halides)



Steric Effects on S_N2 Reactions



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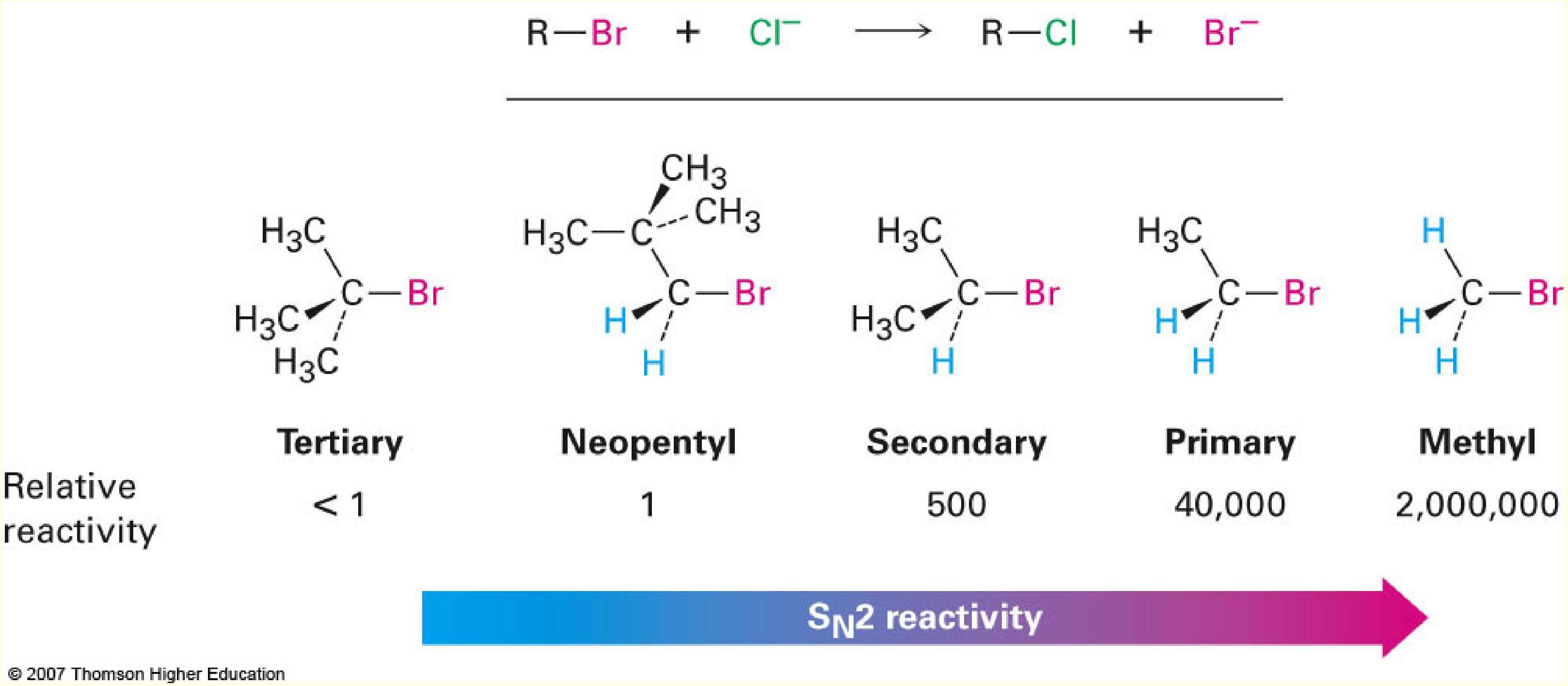
The carbon atom in (a) bromomethane is readily accessible resulting in a fast S_N2 reaction. The carbon atoms in (b) bromoethane (primary), (c) 2-bromopropane (secondary), and (d) 2-bromo-2-methylpropane (tertiary) are successively more hindered, resulting in successively slower S_N2 reactions.

Order of Reactivity in S_N2

- The more alkyl groups connected to the reacting carbon, the slower the reaction



$R{-}Br + Cl^- \longrightarrow R{-}Cl + Br^-$

	Tertiary	Neopentyl	Secondary	Primary	Methyl
Relative reactivity	< 1	1	500	40,000	2,000,000

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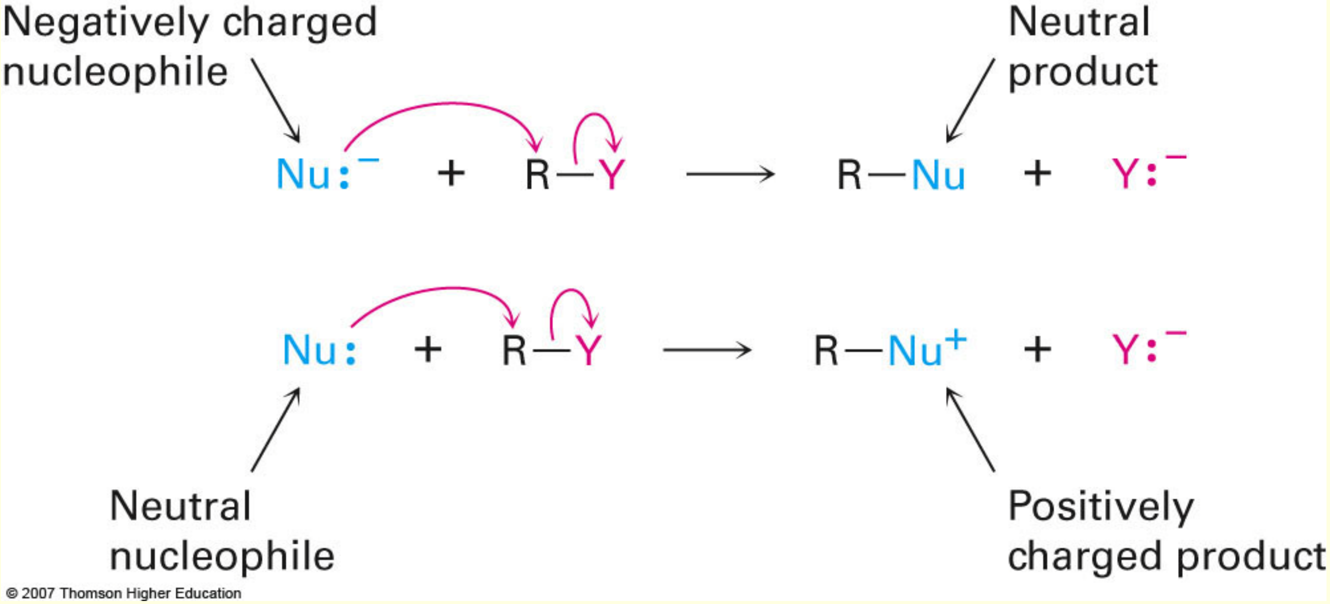
The Nucleophile

- Neutral or negatively charged Lewis base
- Reaction increases coordination at nucleophile
  - Neutral nucleophile acquires positive charge
  - Anionic nucleophile becomes neutral



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Relative Reactivity of Nucleophiles

- Depends on reaction and conditions
- More basic nucleophiles react faster
- Better nucleophiles are lower in a column of the periodic table
- Anions are usually more reactive than neutrals

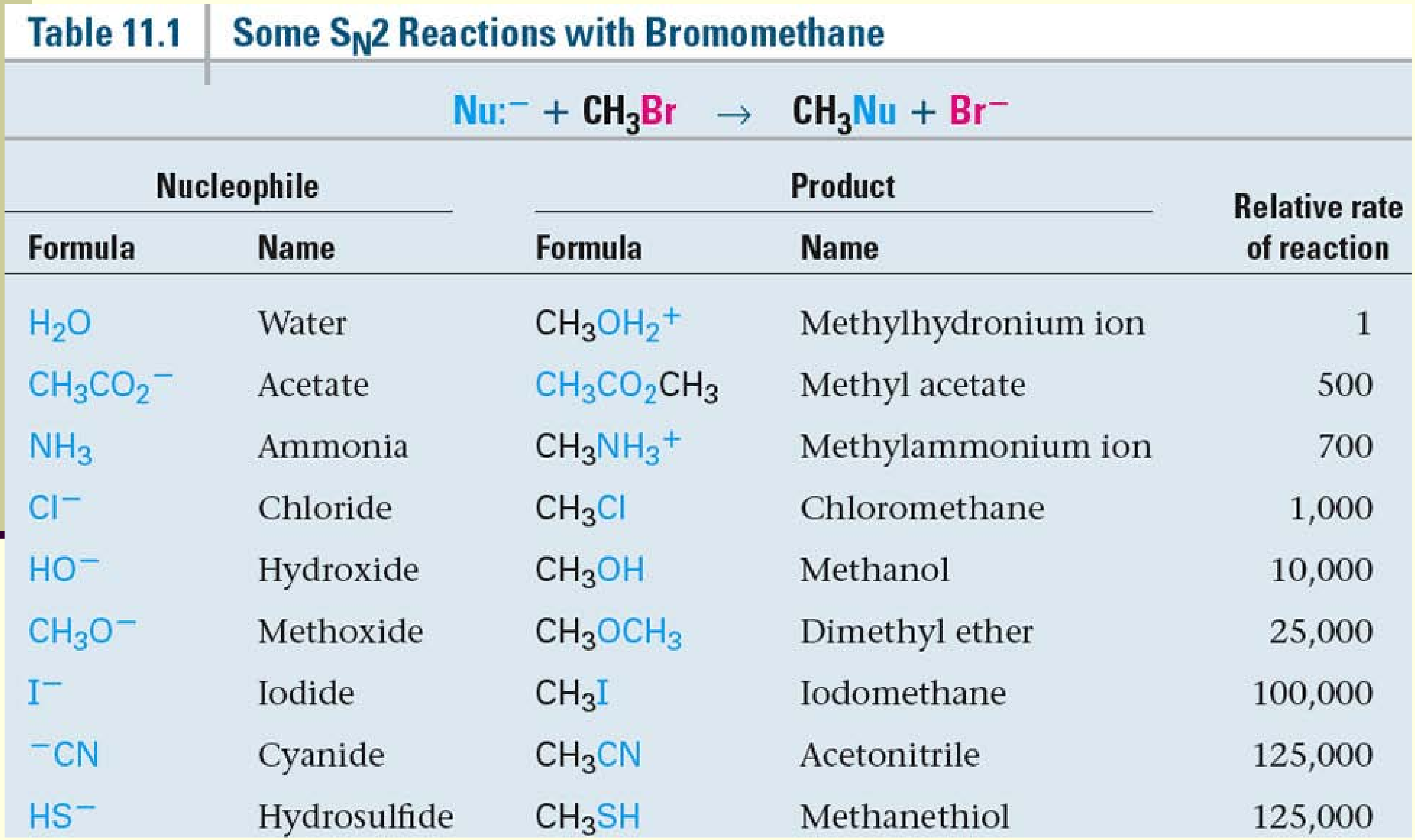


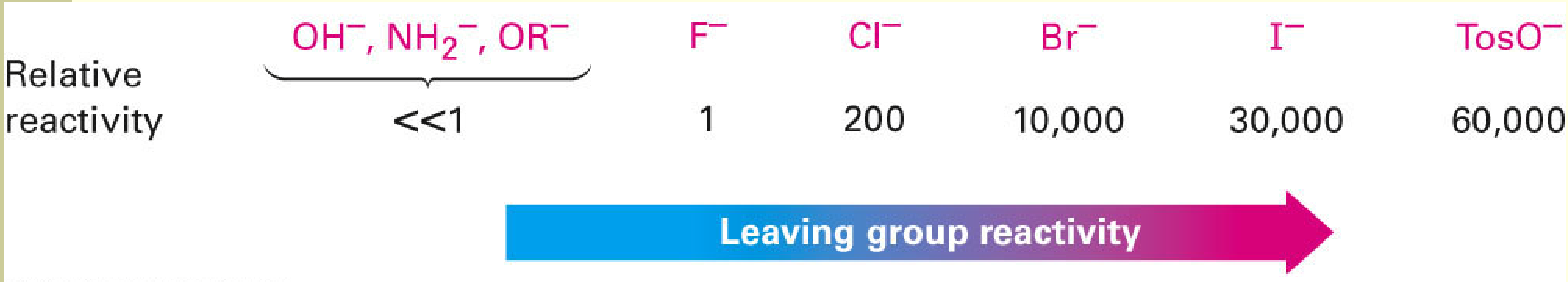
Table 11.1 **Some S_N2 Reactions with Bromomethane**

$$Nu:^- + CH_3Br \rightarrow CH_3Nu + Br^-$$

Nucleophile		Product		Relative rate of reaction
Formula	**Name**	**Formula**	**Name**	
H_2O	Water	$CH_3OH_2^+$	Methylhydronium ion	1
$CH_3CO_2^-$	Acetate	$CH_3CO_2CH_3$	Methyl acetate	500
NH_3	Ammonia	$CH_3NH_3^+$	Methylammonium ion	700
Cl^-	Chloride	CH_3Cl	Chloromethane	1,000
HO^-	Hydroxide	CH_3OH	Methanol	10,000
CH_3O^-	Methoxide	CH_3OCH_3	Dimethyl ether	25,000
I^-	Iodide	CH_3I	Iodomethane	100,000
^-CN	Cyanide	CH_3CN	Acetonitrile	125,000
HS^-	Hydrosulfide	CH_3SH	Methanethiol	125,000

The Leaving Group

- A good leaving group reduces the barrier to a reaction
- Stable anions that are weak bases are usually excellent leaving groups and can delocalize charge



	OH^-, NH_2^-, OR^-	F^-	Cl^-	Br^-	I^-	$TosO^-$
Relative reactivity	<<1	1	200	10,000	30,000	60,000

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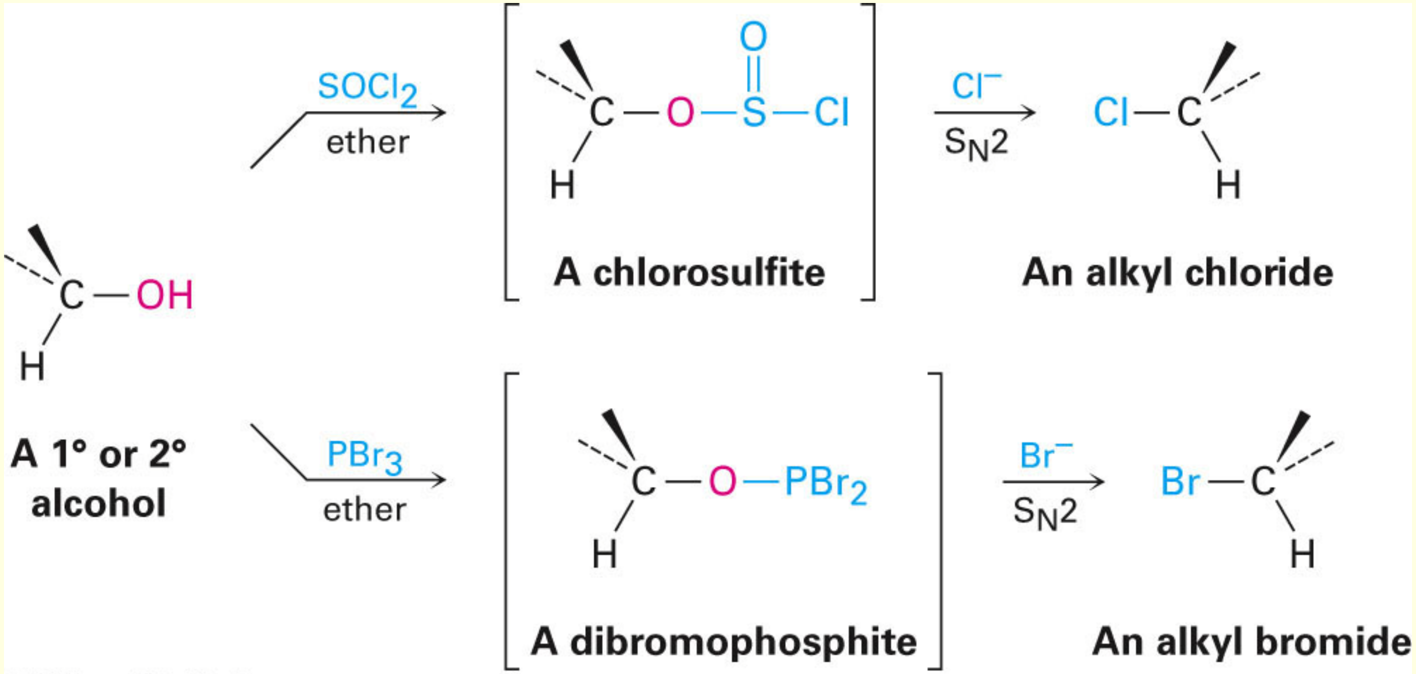

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Poor Leaving Groups

- If a group is very basic or very small, it prevents reaction

	OH^-, NH_2^-, OR^-	F^-	Cl^-	Br^-	I^-	$TosO^-$
Relative reactivity	<<1	1	200	10,000	30,000	60,000

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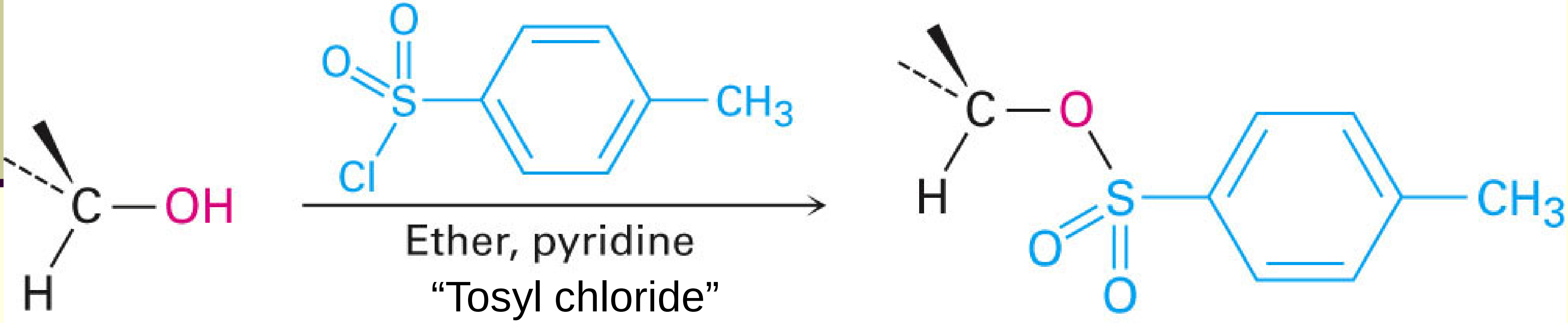
- Alkyl fluorides, alcohols, ethers, and amines do not typically undergo S_N2 reactions.
- Poor Leaving groups can be made into good leaving groups



Ether, pyridine

“Tosyl chloride”

A 1° or 2° alcohol

A tosylate

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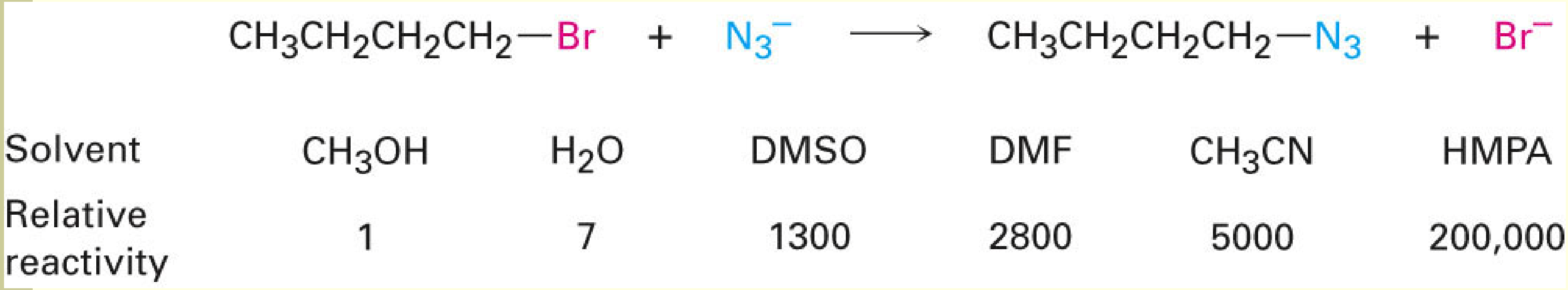
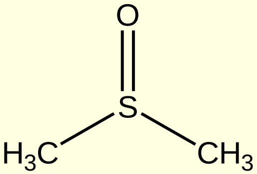
The Solvent

- Solvents that can donate hydrogen bonds (-OH or –NH) slow S_N2 reactions by associating with reactants
- Energy is required to break interactions between reactant and solvent
- Polar aprotic solvents (no NH, OH, SH) form weaker interactions with substrate and permit faster reaction

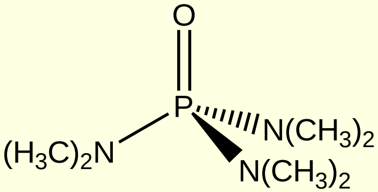


$$CH_3CH_2CH_2CH_2{-}Br + N_3^- \longrightarrow CH_3CH_2CH_2CH_2{-}N_3 + Br^-$$

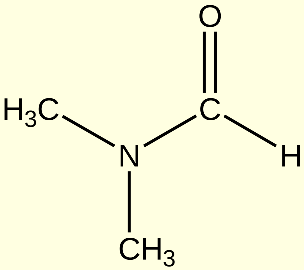
Solvent	CH_3OH	H_2O	DMSO	DMF	CH_3CN	HMPA
Relative reactivity	1	7	1300	2800	5000	200,000



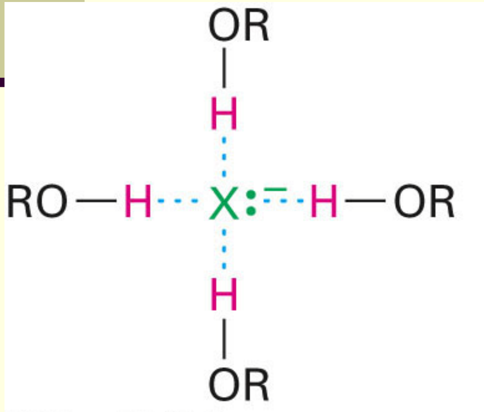
DMSO
Dimethyl Sulfoxide



HMPA
Hexamethylphosphoramide



DMF
Dimethylformamide



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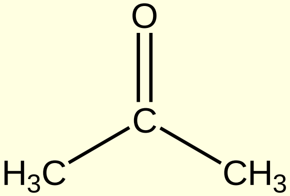
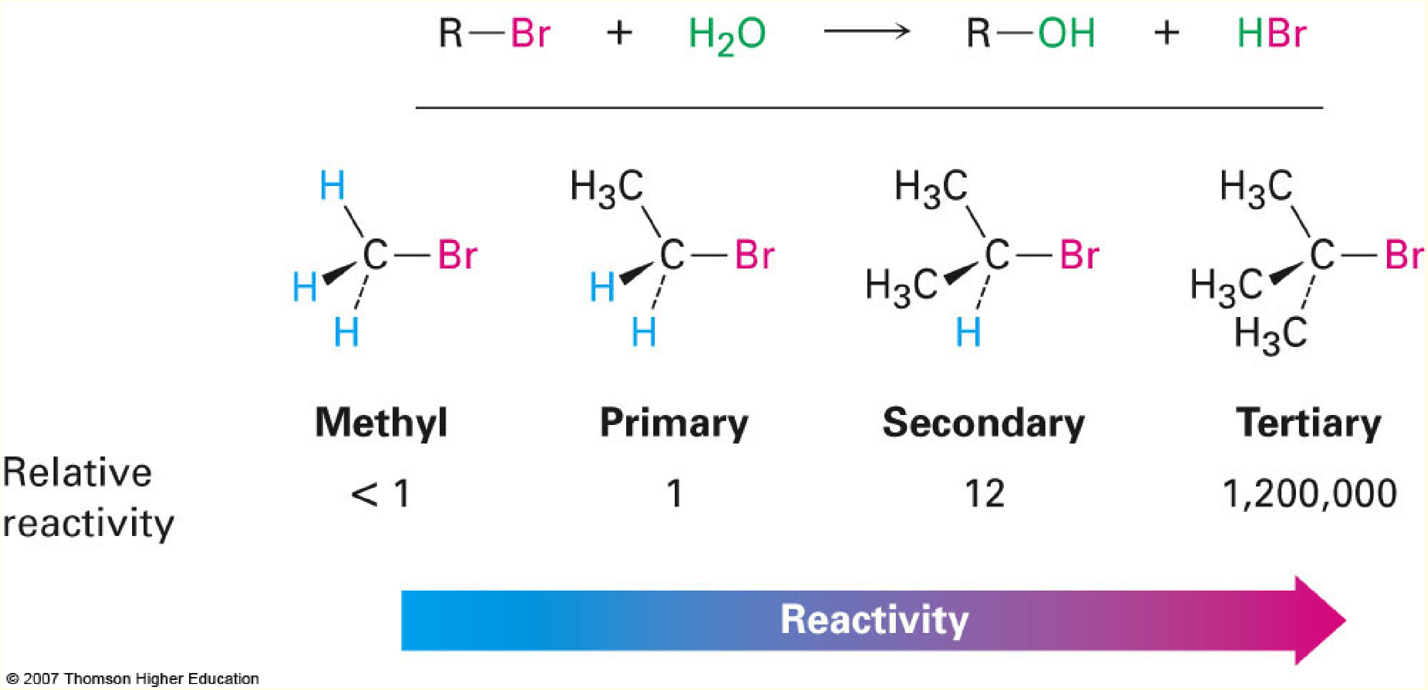


Acetone

11.4 The S_N1 Reaction

- Tertiary alkyl halides react rapidly in protic solvents by a mechanism that involves departure of the leaving group prior to addition of the nucleophile
- Called an S_N1 reaction – occurs in two distinct steps while S_N2 occurs with both events in same step
- If nucleophile is present in reasonable concentration (or it is the solvent), then ionization is the slowest step



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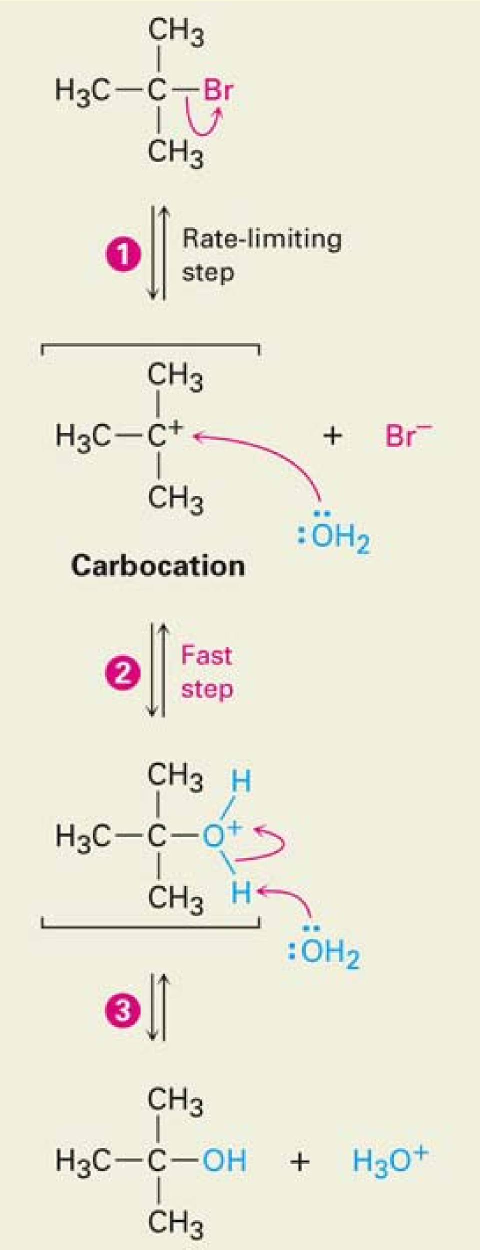
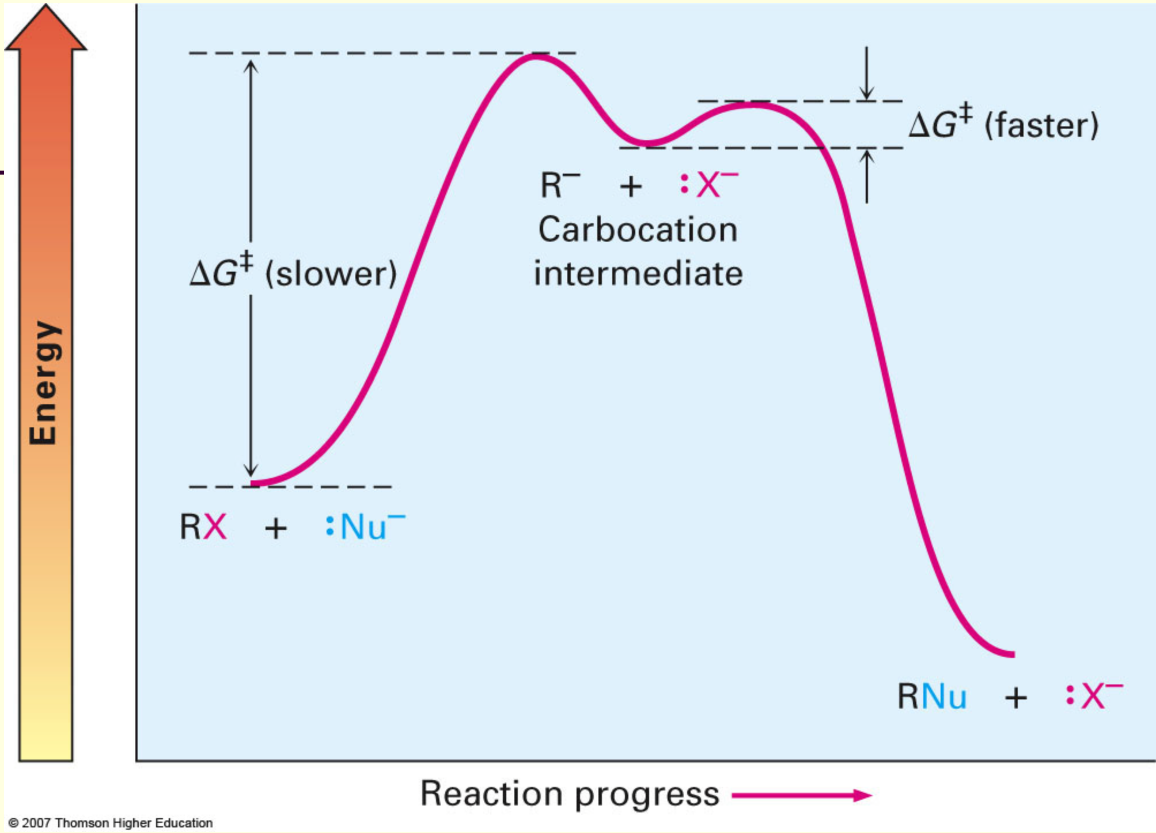
S_N1 Energy Diagram and Mechanism





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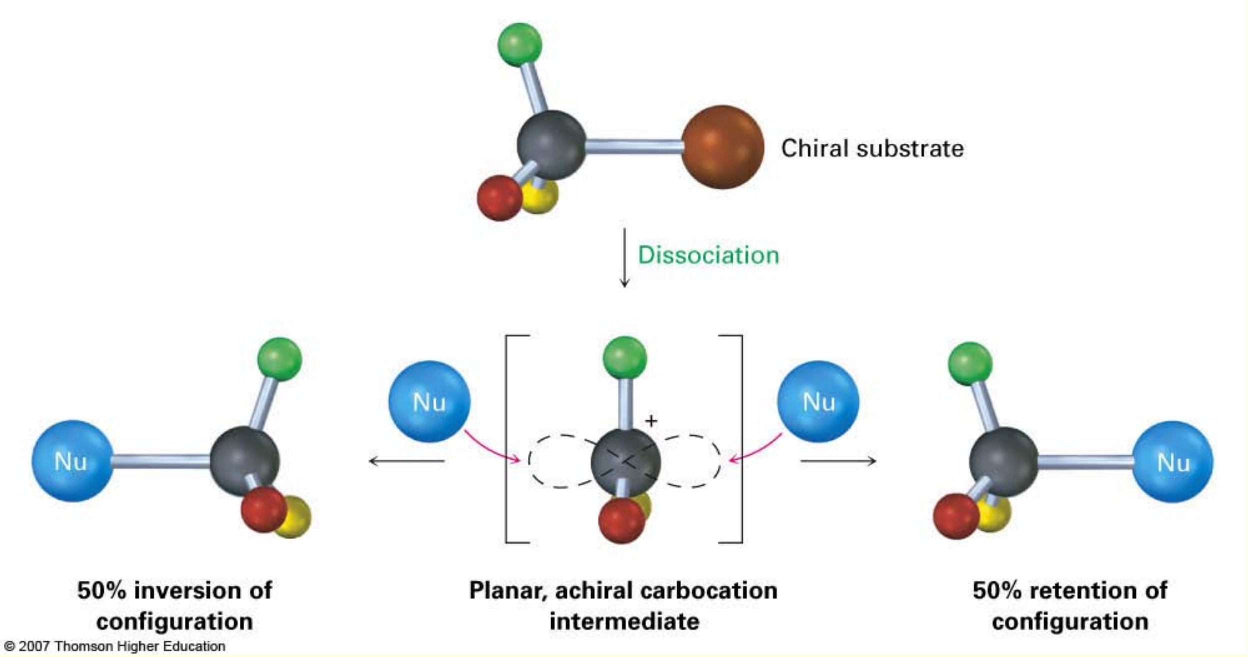
- Rate-determining step is formation of carbocation
- rate = k[RX]

Stereochemistry of S_N1 Reaction

- The planar intermediate leads to loss of chirality
  - A free carbocation is achiral
- Product is racemic or has some inversion



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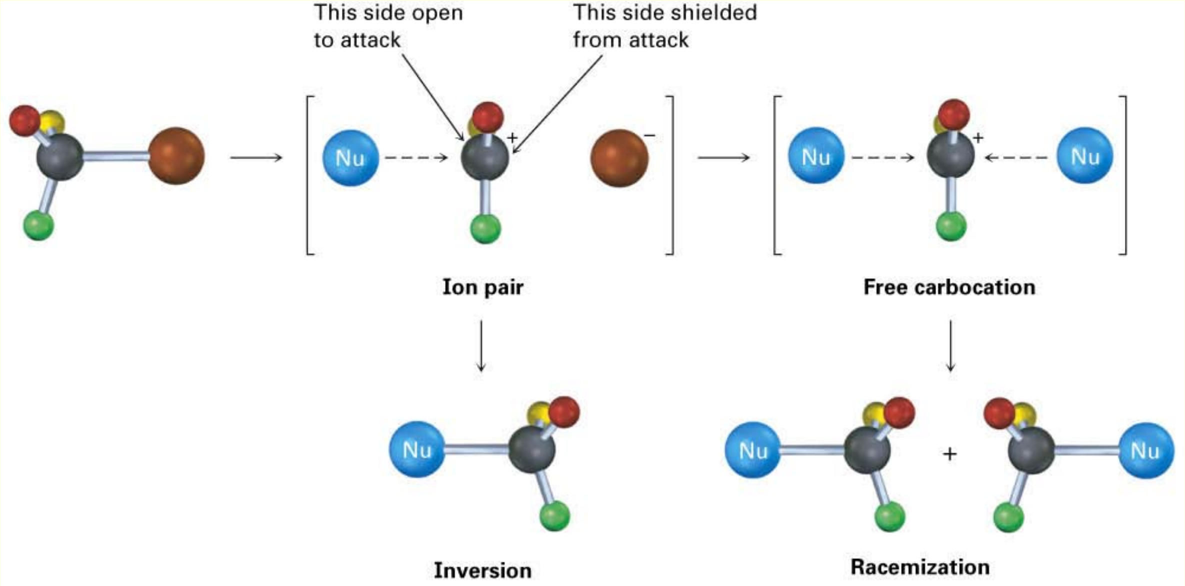
S_N1 in Reality

- Carbocation is biased to react on side opposite leaving group
- Suggests reaction occurs with carbocation loosely associated with leaving group during nucleophilic addition (Ion Pair)
- Alternative that S_N2 is also occurring is unlikely



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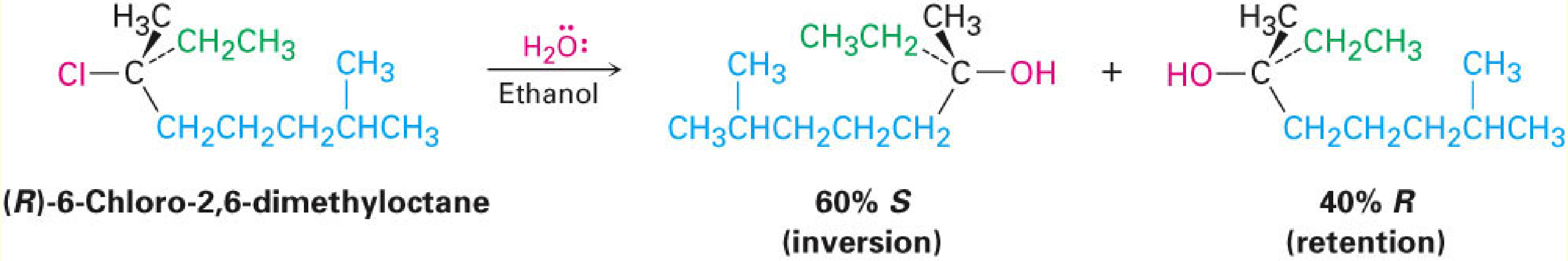

(*R*)-6-Chloro-2,6-dimethyloctane

60% *S* (inversion)

40% *R* (retention)

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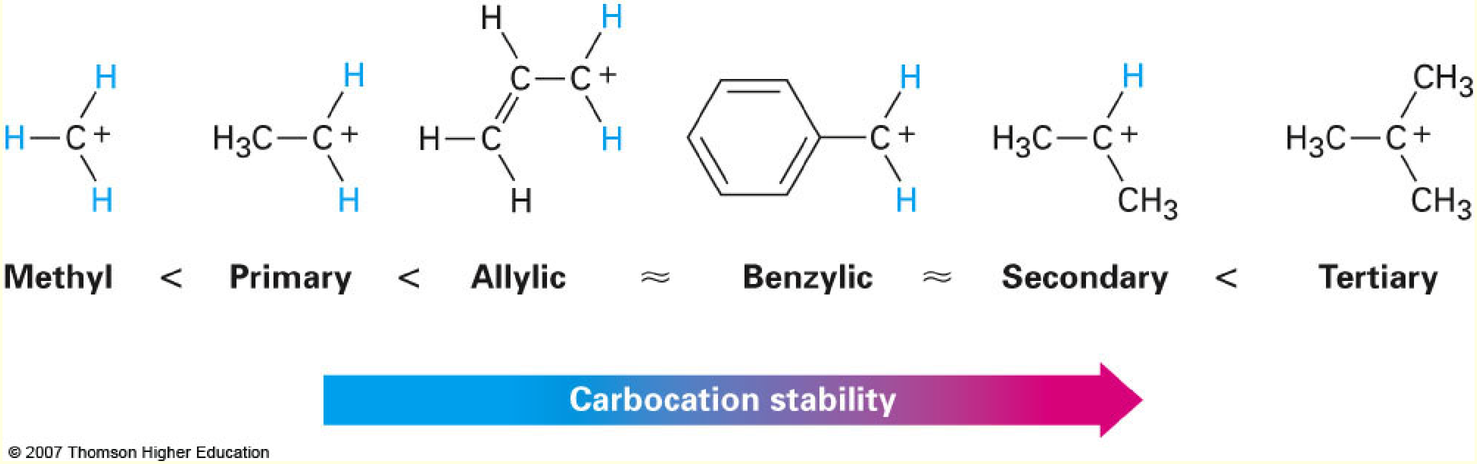
11.5 Characteristics of the S_N1 Reaction

Substrate

- Tertiary alkyl halide is most reactive by this mechanism
  - Controlled by stability of carbocation
  - Remember Hammond postulate,"Any factor that stabilizes a high-energy intermediate stabilizes transition state leading to that intermediate"



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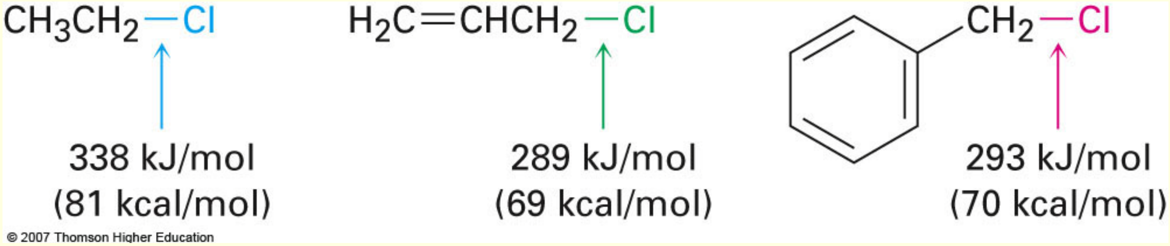
- Allylic and benzylic intermediates stabilized by delocalization of charge
  - Primary allylic and benzylic are also more reactive in the S_N**2** mechanism



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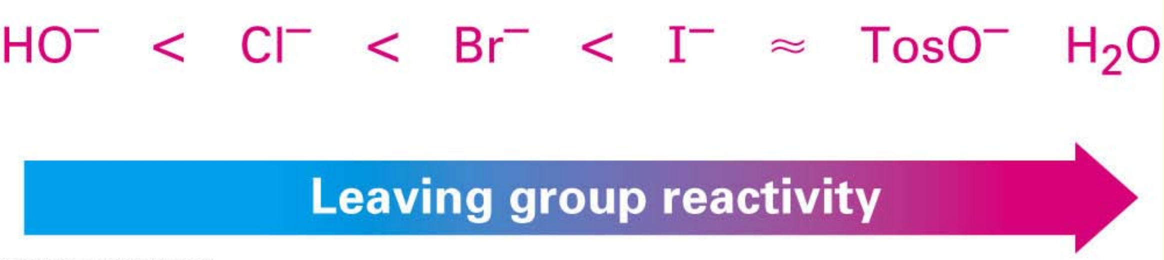
Effect of Leaving Group on S_N1

- Critically dependent on leaving group
  - Reactivity: the larger halides ions are better leaving groups
- In acid, OH of an alcohol is protonated and leaving group is H_2O, which is still less reactive than halide
- p-Toluensulfonate ($TosO^-$) is excellent leaving group



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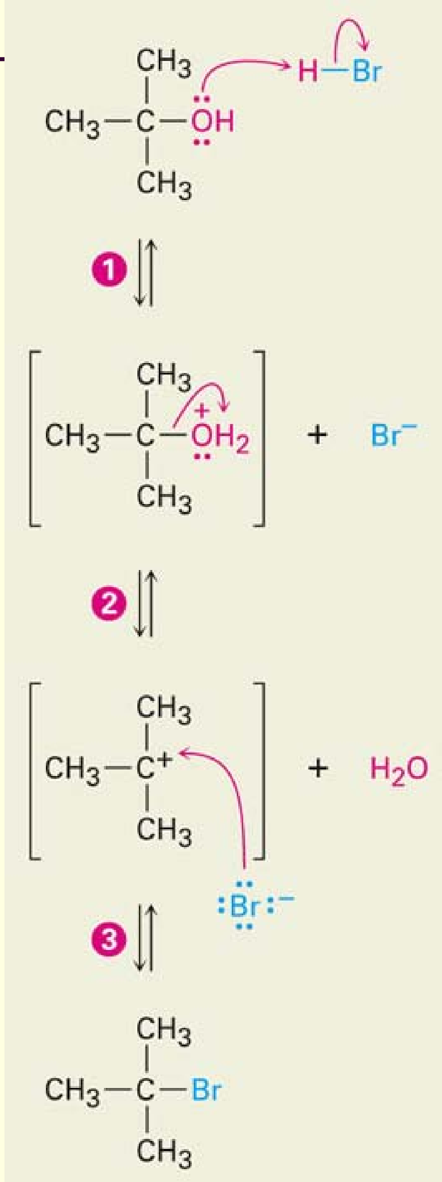
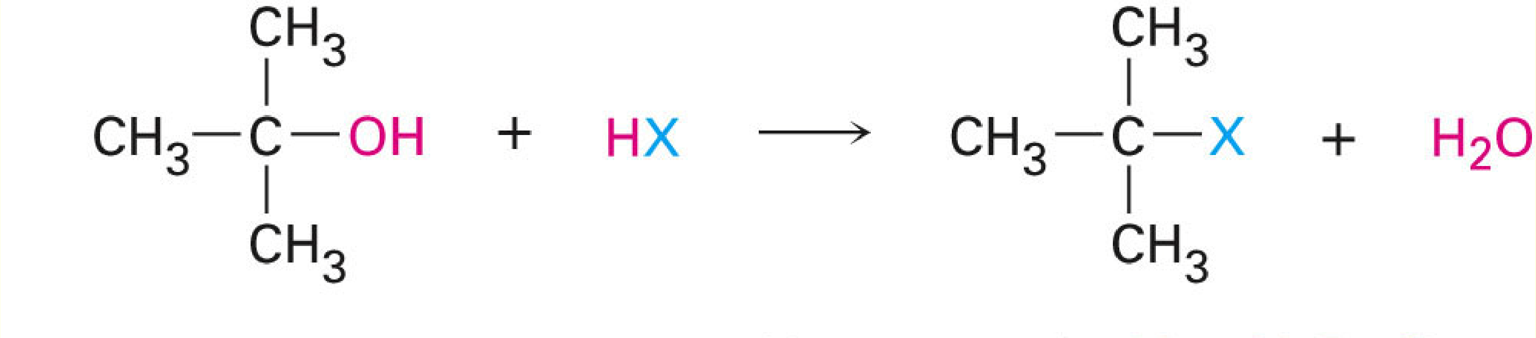


Nucleophiles in S_N1

- Since nucleophilic addition occurs *after* formation of carbocation, reaction rate is not normally affected by nature or concentration of nucleophile



$$(CH_3)_3C{-}OH + HX \longrightarrow (CH_3)_3C{-}X + H_2O$$

2-Methyl-2-propanol

(Same rate for X = Cl, Br, I)

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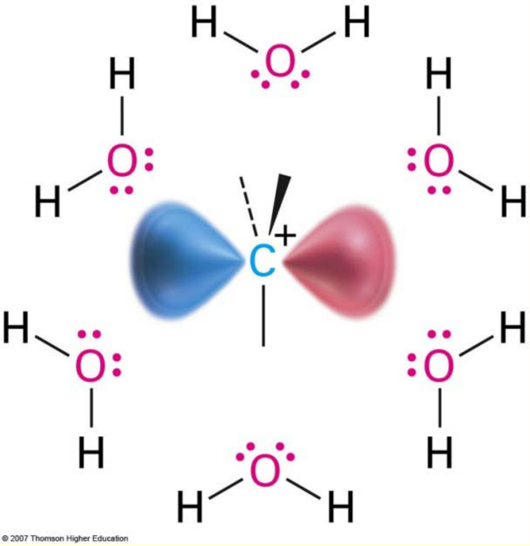
Solvent in S_N1

- Stabilizing carbocation also stabilizes associated transition state and controls rate
- Protic solvents favoring the S_N1 reaction are due largely to stabilization of the transition state
- Protic solvents disfavor the S_N2 reaction by stabilizing the ground state
- Polar, protic and unreactive Lewis base solvents facilitate formation of R^+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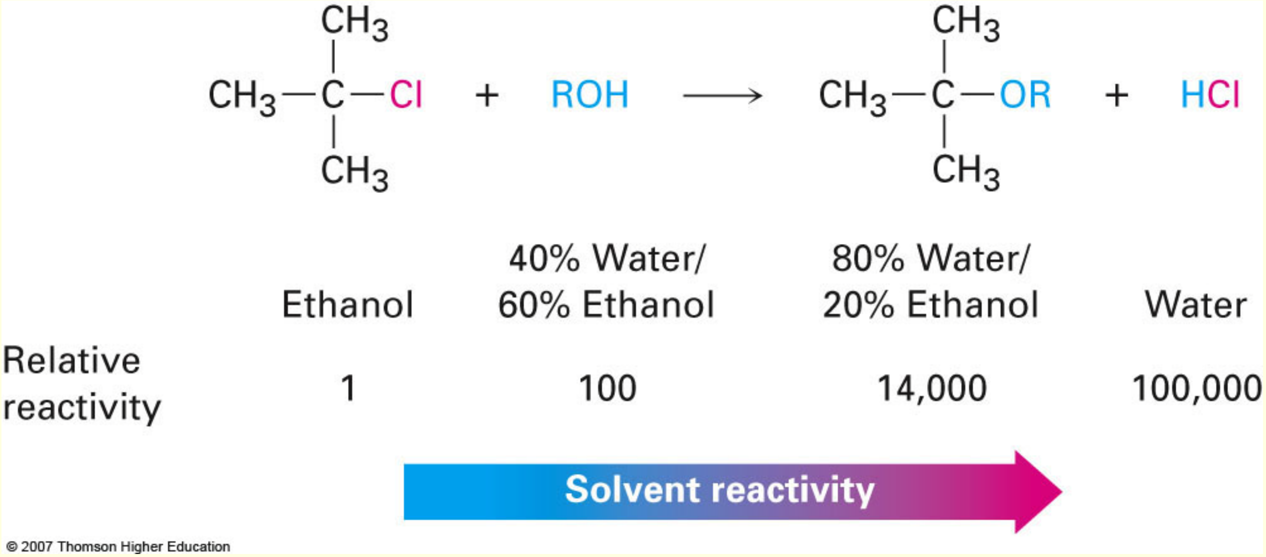

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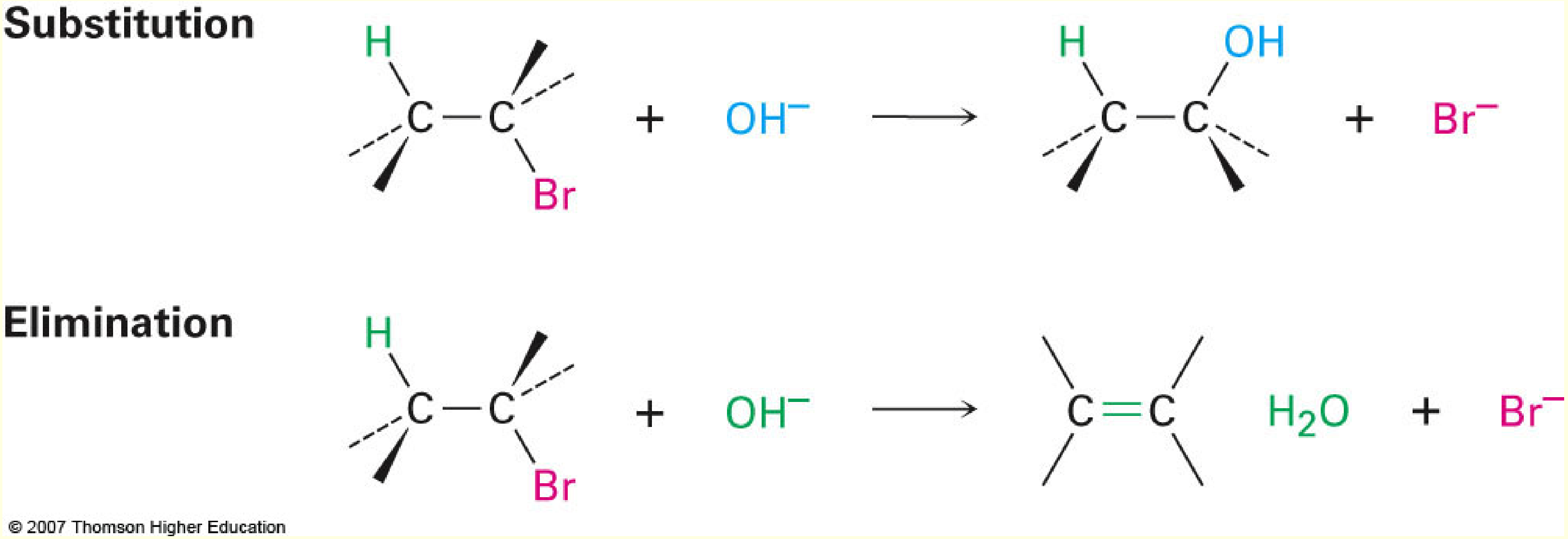
11.7 Elimination Reactions of Alkyl Halides: Zaitsev's Rule

- Elimination is an alternative pathway to substitution
- Opposite of addition
- Generates an alkene
- Can compete with substitution and decrease yield, especially for S_N1 processes



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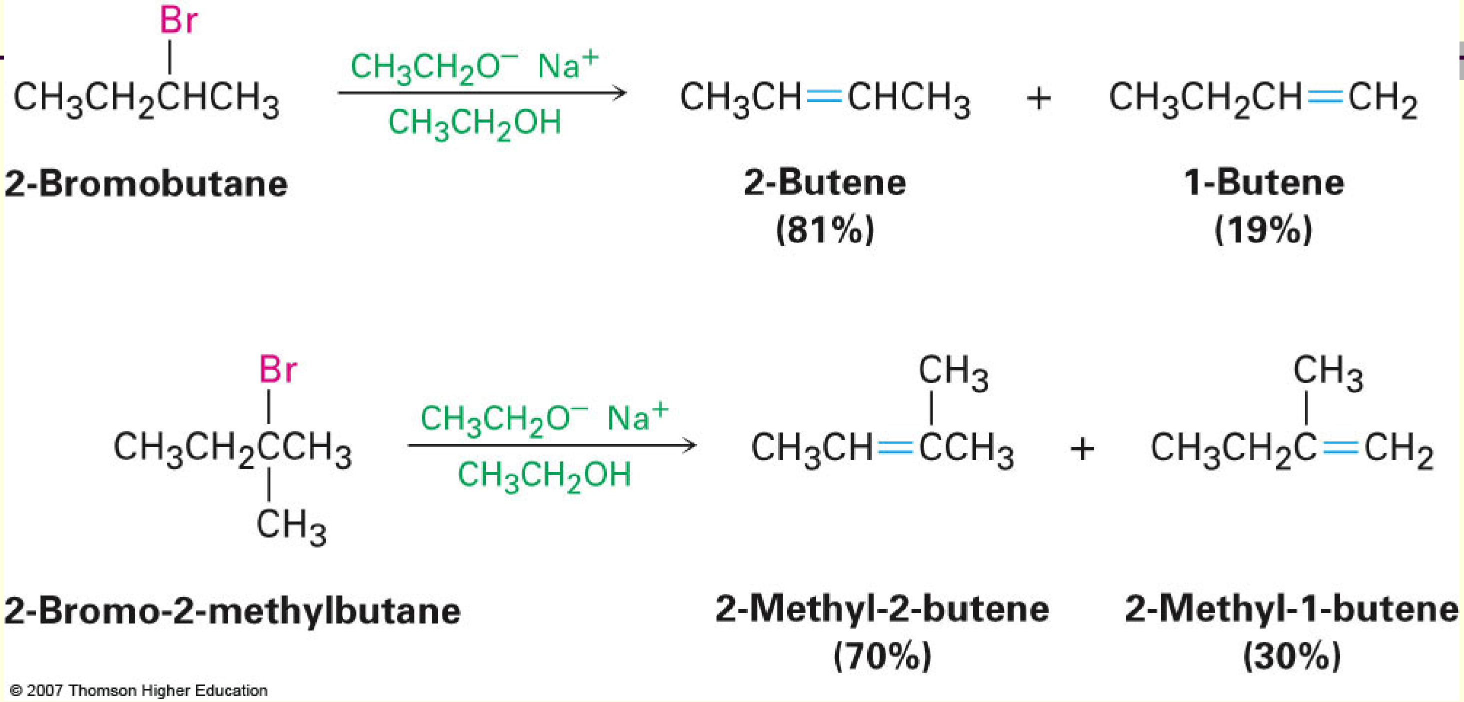
Zaitsev's Rule for Elimination Reactions

- In the elimination of HX from an alkyl halide, the more highly substituted alkene product predominates



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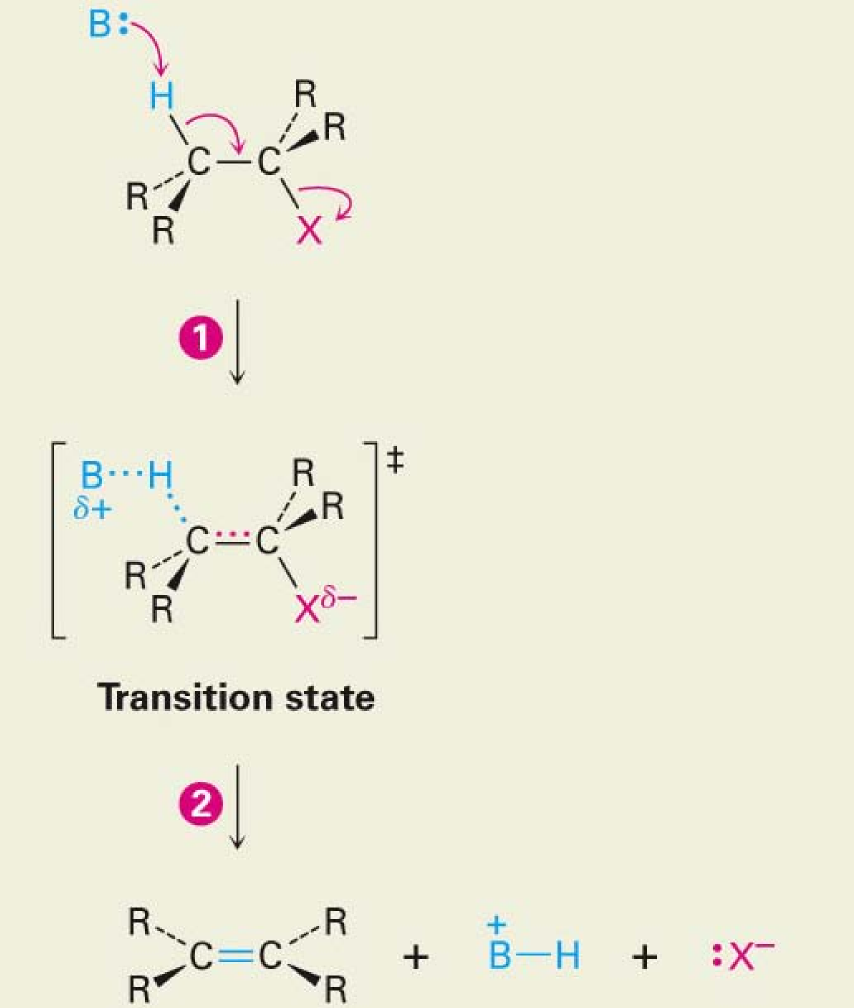
- Mechanisms of Elimination Reactions
  - E1: X^- leaves first to generate a carbocation
    - a base abstracts a proton from the carbocation
  - E2: Concerted transfer of a proton to a base and departure of leaving group

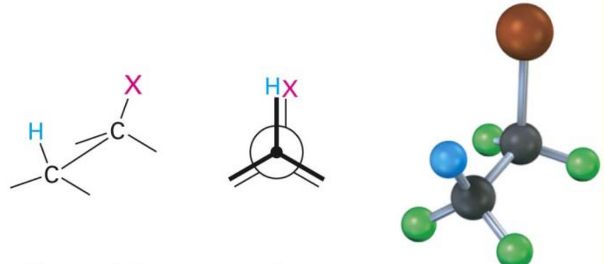
11.8 The E2 Reaction

- A proton is transferred to base as leaving group begins to depart
- Transition state combines leaving of X and transfer of H
- Product alkene forms stereospecifically
- Rate = k[RX][B]

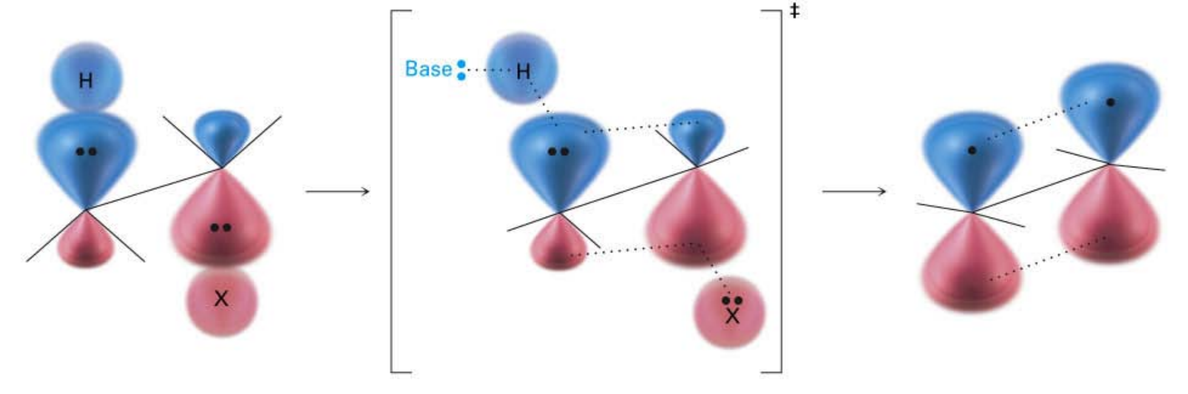


Geometry of Elimination – E2

- Syn arrangement requires eclipsed conformation = disfavored
- Anti arrangement allows orbital overlap and minimizes steric interactions
- Overlap of the developing π orbital in the transition state requires periplanar geometry, anti arrangement



Syn periplanar geometry
(eclipsed, higher energy)



Anti periplanar reactant

Anti transition state

Alkene product

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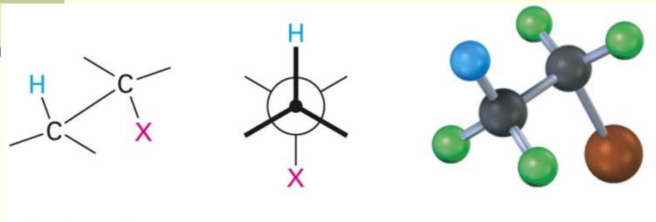

Anti periplanar geometry
(staggered, lower energy)

S_N2 reaction
(backside attack)

E2 reaction
(anti periplanar)

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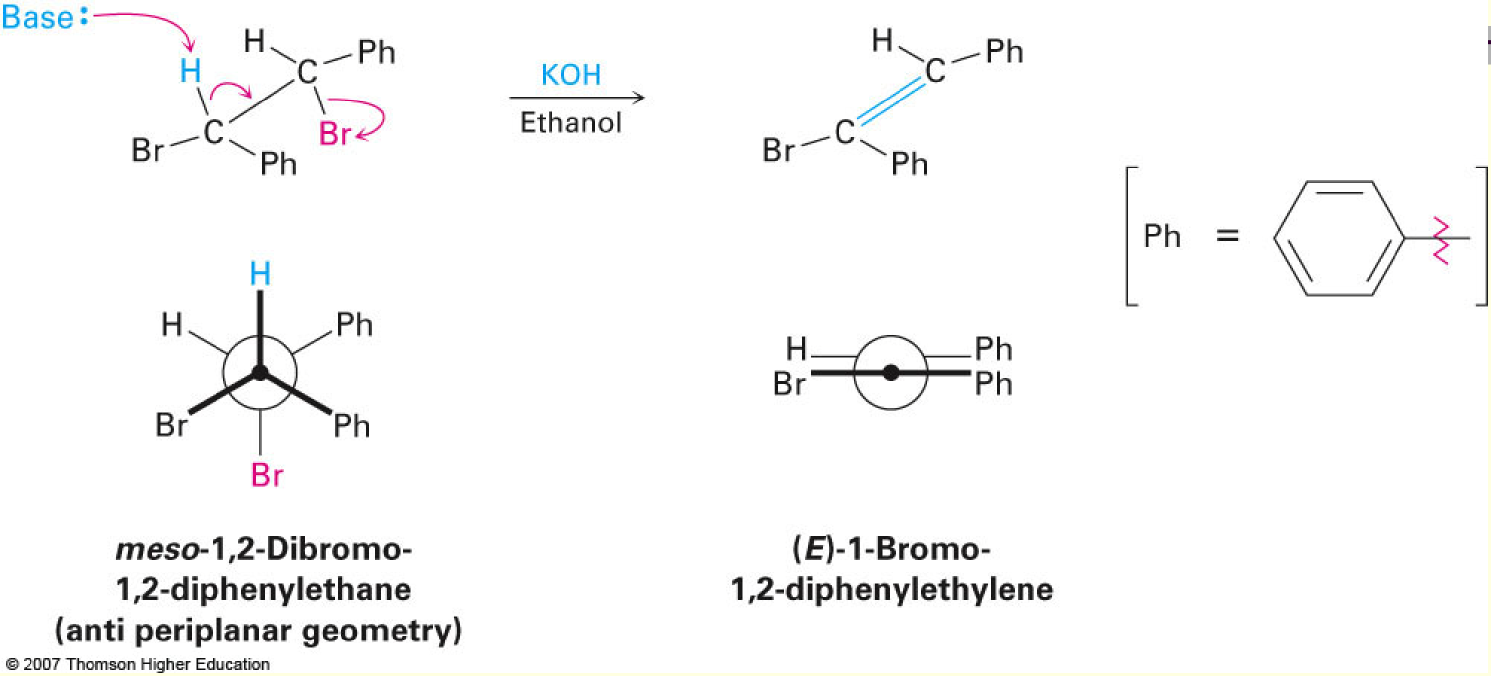
Predicting Product

- E2 is stereospecific
- Meso-1,2-dibromo-1,2-diphenylethane with base gives cis-1,2-diphenyl



meso-1,2-Dibromo-1,2-diphenylethane (anti periplanar geometry)

(*E*)-1-Bromo-1,2-diphenylethylene

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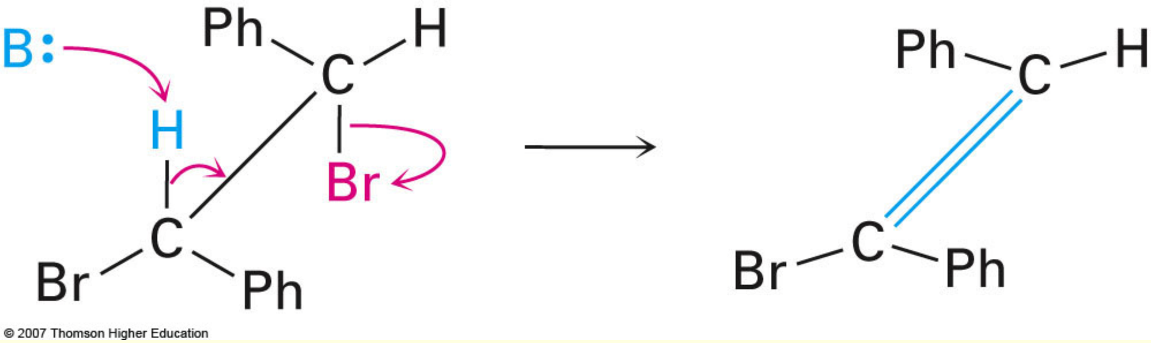
- RR or SS 1,2-dibromo-1,2-diphenylethane gives trans 1,2-diphenyl



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E2 Reactions and Cyclohexene Formation

- Abstracted proton and leaving group should align trans-diaxial to be anti periplanar (*app*) in approaching transition state

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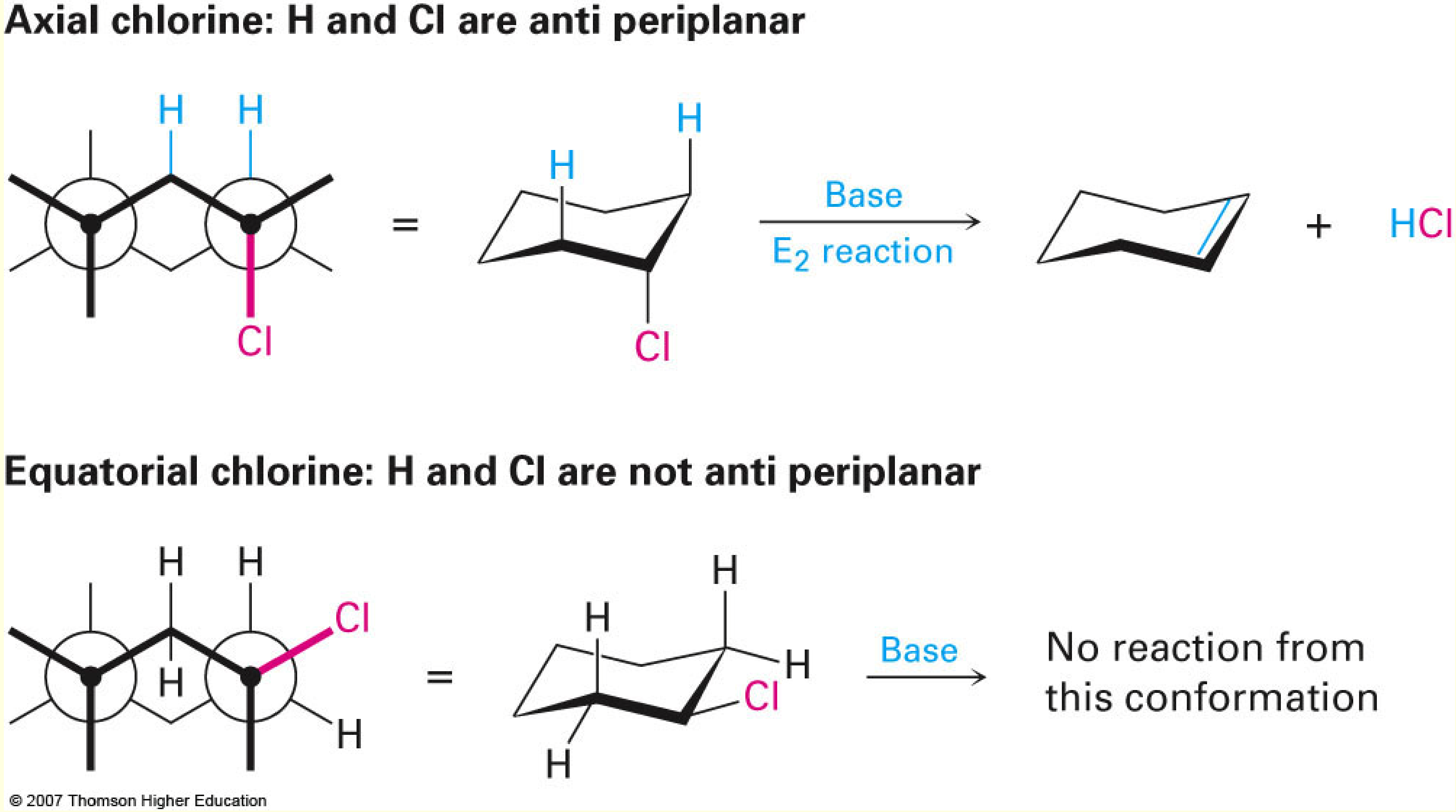
- Equatorial groups are not in proper alignment



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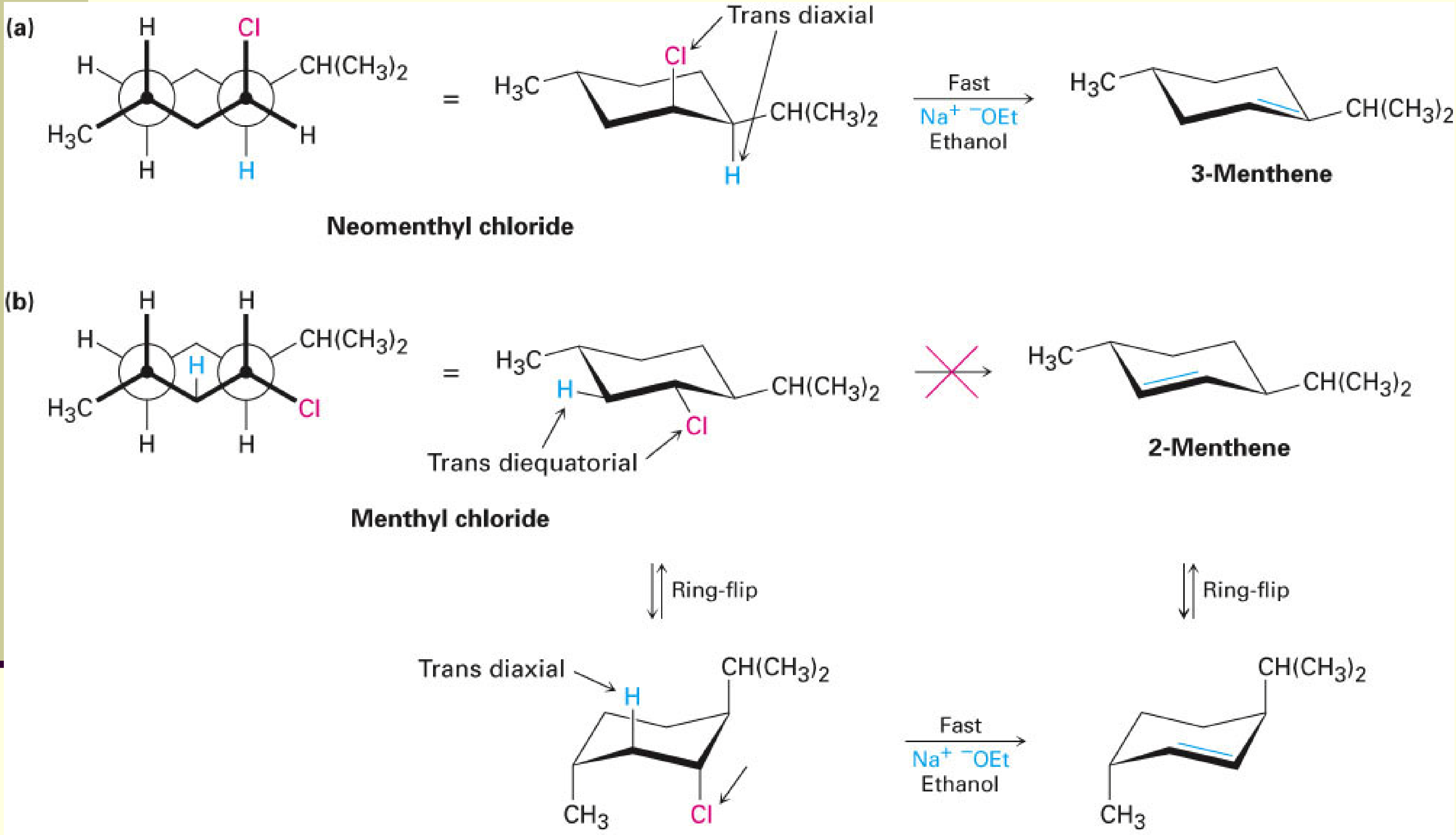

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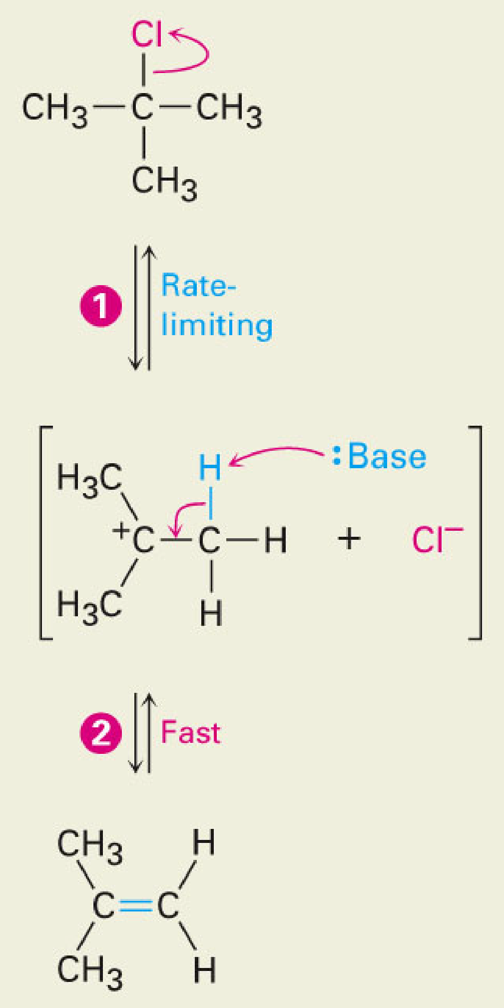
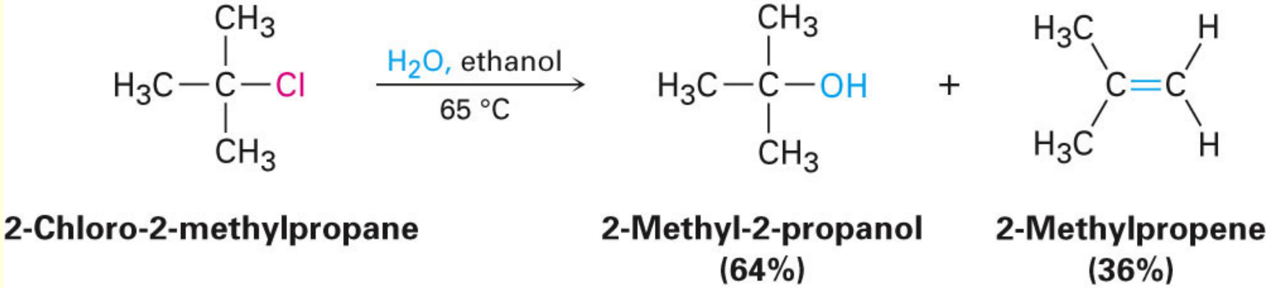
11.10 The E1 Reaction

- Competes with S_N1 and E2 at 3° centers
- Rarely have “clean” S_N2 or E1 single products
- Rate = k [RX], same as S_N1





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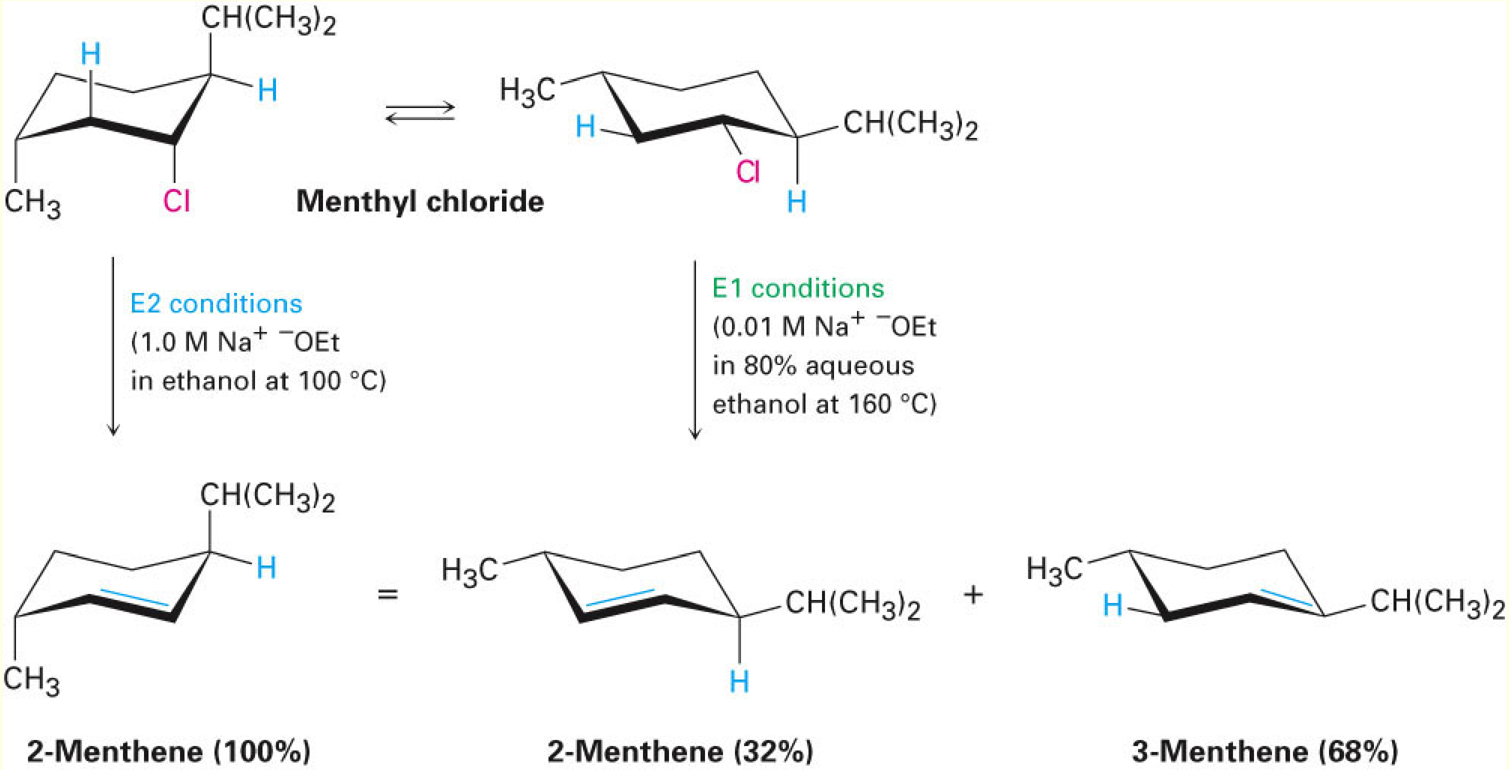
Comparing E1 and E2

- Strong base is needed for E2 but not for E1
- E2 is stereospecifc, E1 is not
- E1 gives Zaitsev orientation



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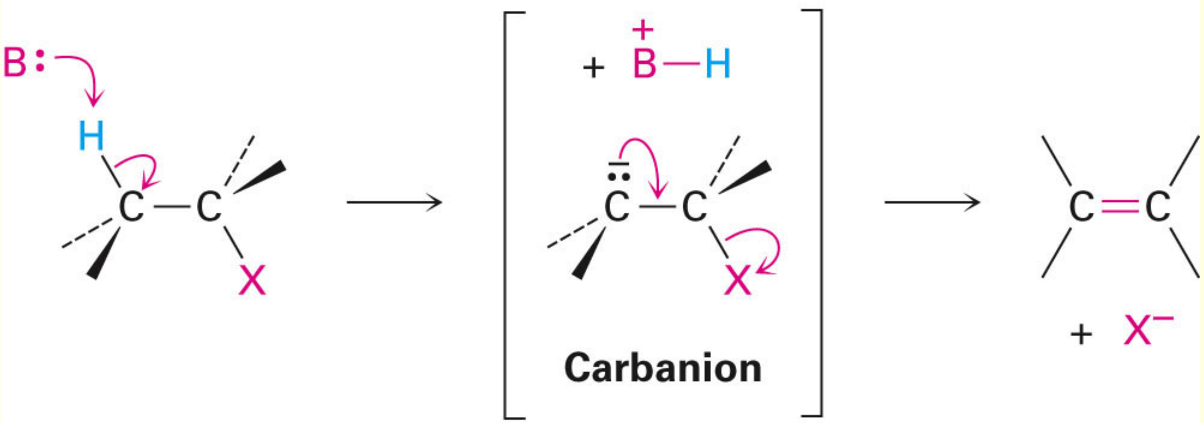
E1cB Reaction

- Takes place through a carbanion intermediate
  - Common with very poor leaving group (OH-)
  - HO-C-C=O fragment often involved

E1cB Reaction: C–H bond breaks first, giving a carbanion intermediate that loses X⁻ to form the alkene.



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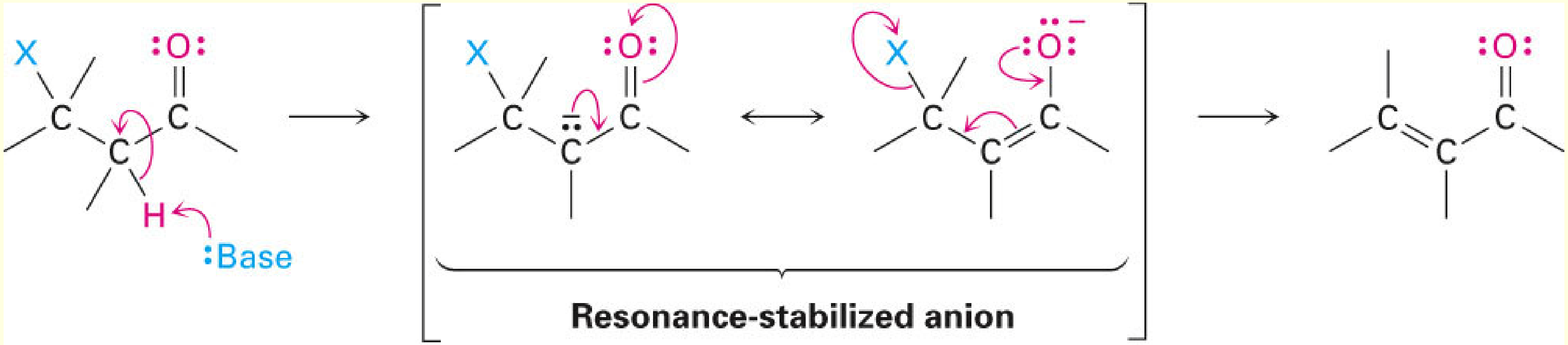

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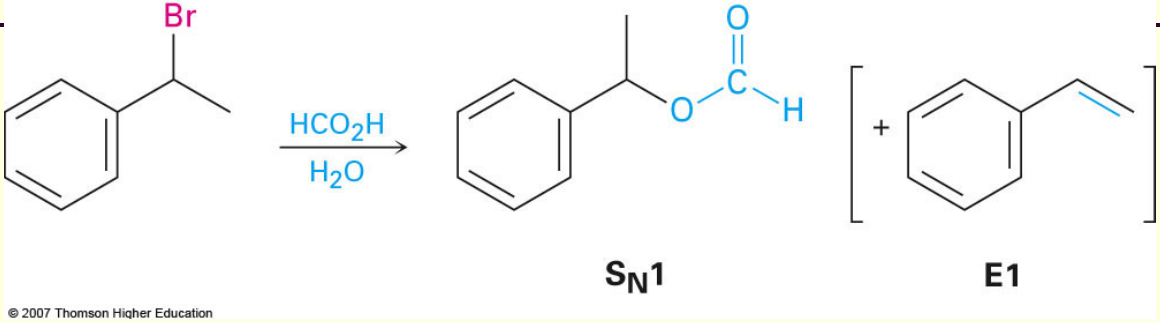
Summary of Reactivity: S_N2, S_N1, E1, E2

- Alkyl halides undergo different reactions in competition, depending on the reacting molecule and the conditions
- Based on patterns, we can predict likely outcomes



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Good L.G.
2^o alkyl halide
Poor Nucleophile
Polar Protic Solvent
S_N1 and E1 products

- Primary Haloalkanes
  - S_N2 with any fairly good nucleophile
  - E2 only if Bulky, strong base

- Secondary Haloalkanes
  - S_N2 with good nucleophiles, weak base, Polar Aprotic Solvent
  - S_N1/E1 with good LG, weak Nu, Polar Protic Solvent
  - E2 with strong base

- Tertiary Haloalkane
  - S_N1/E1 with good LG, no base (solvolysis)
  - E2 with strong base