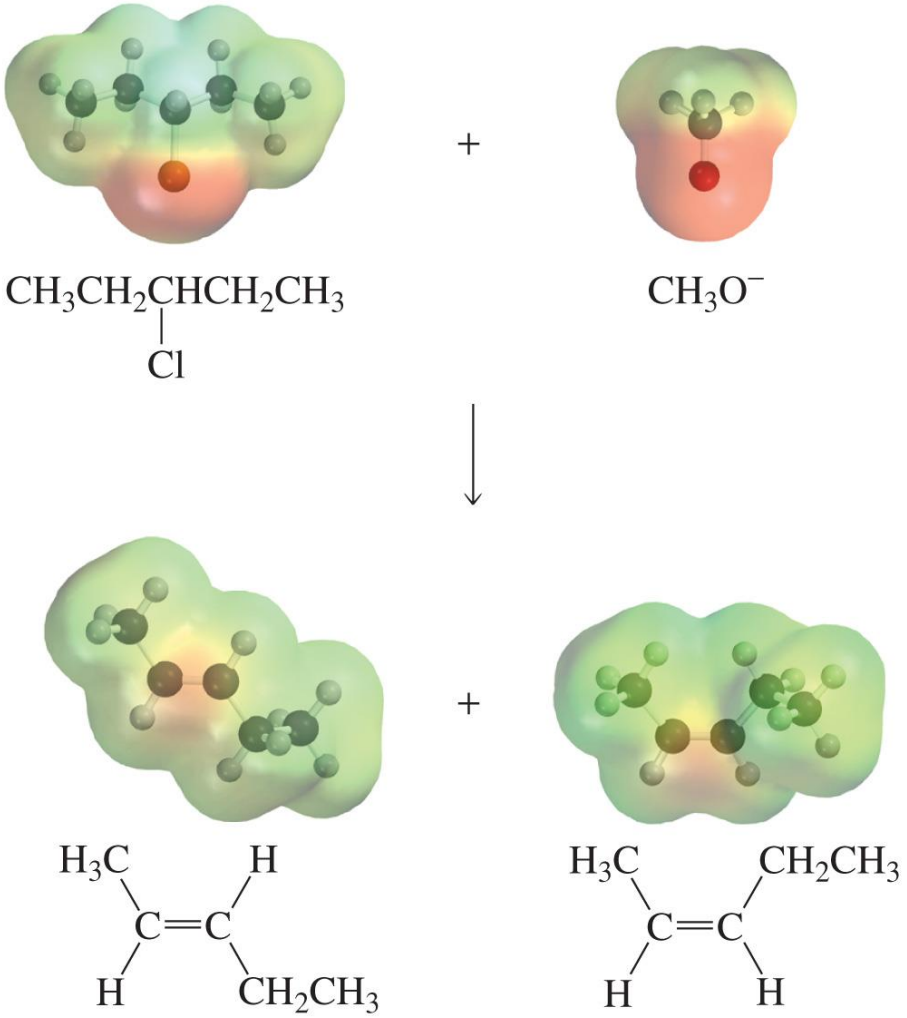
Organic Chemistry
2th Edition
Paula Yurkanis Bruice

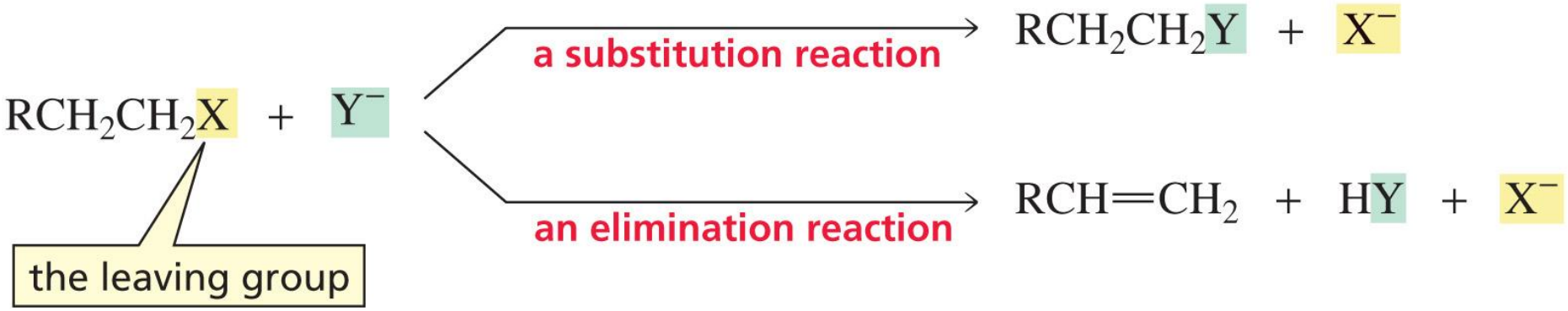


Chapter 9

Substitution and Elimination Reactions of Alkyl Halides

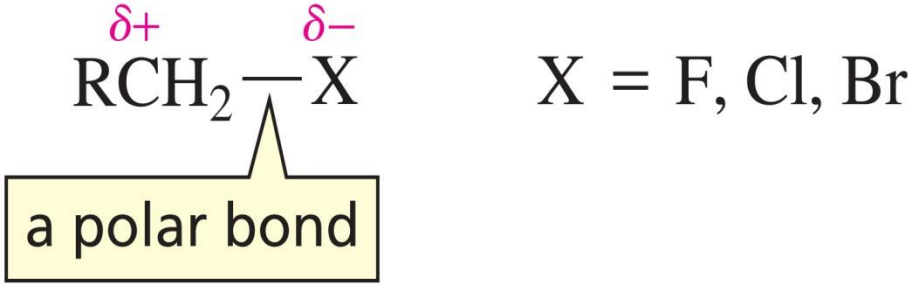
Nucleophilic Substitution

What is a Nucleophilic Substitution?

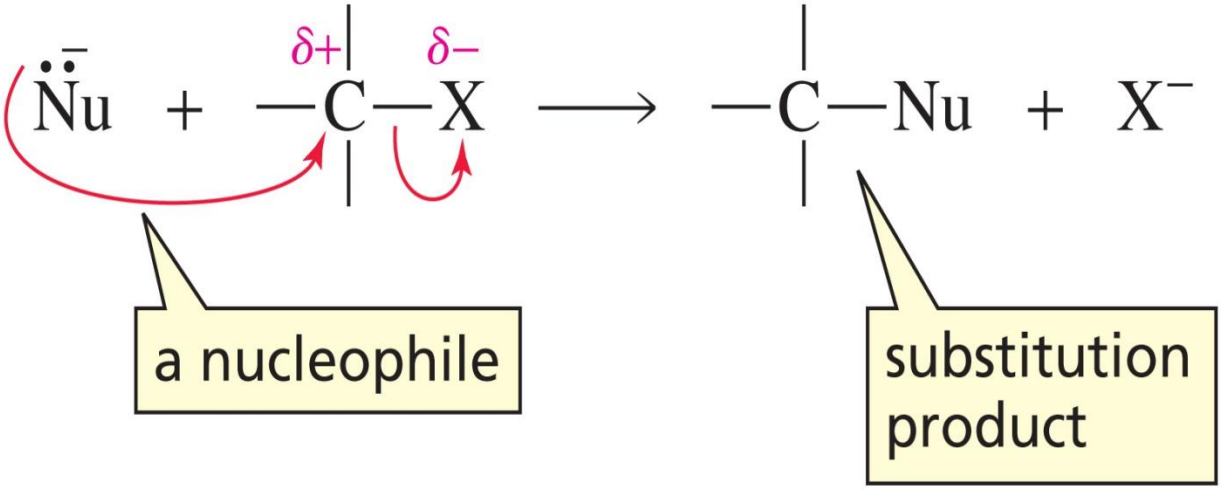


The atom or group that is substituted or eliminated in these reactions is called a leaving group

Alkyl halides have relatively good leaving groups

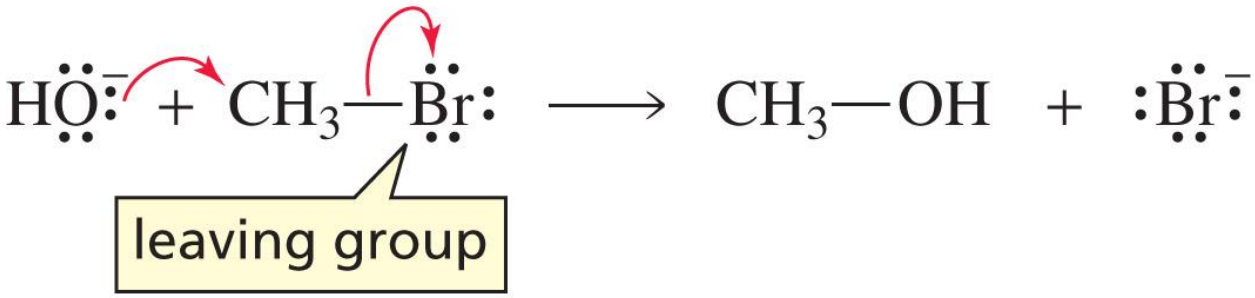


How do alkyl halides react?

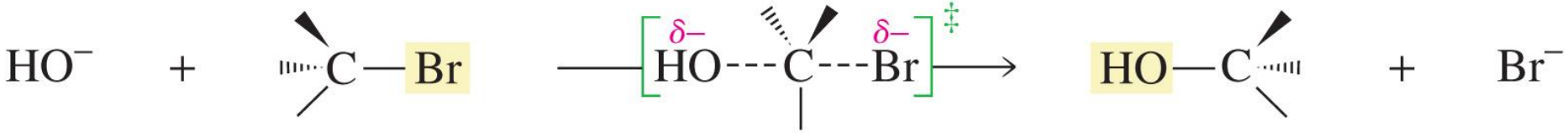


S_N2 is a one-step reaction

mechanism for the S_N2 reaction of an alkyl halide

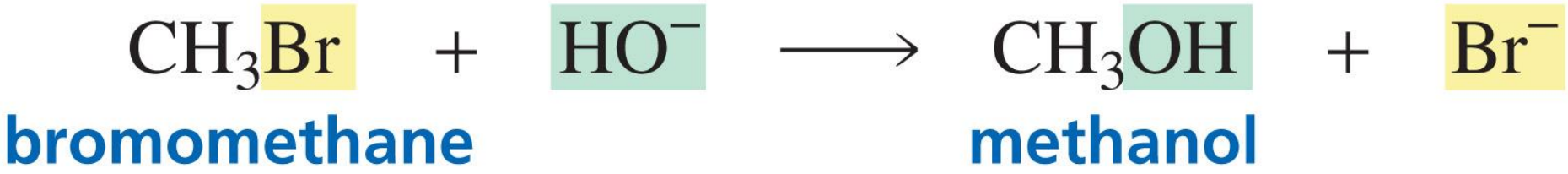


A nucleophile attacks the back side of the carbon that is bonded to the leaving group



transition state

The Mechanism of an S_N2 Reaction



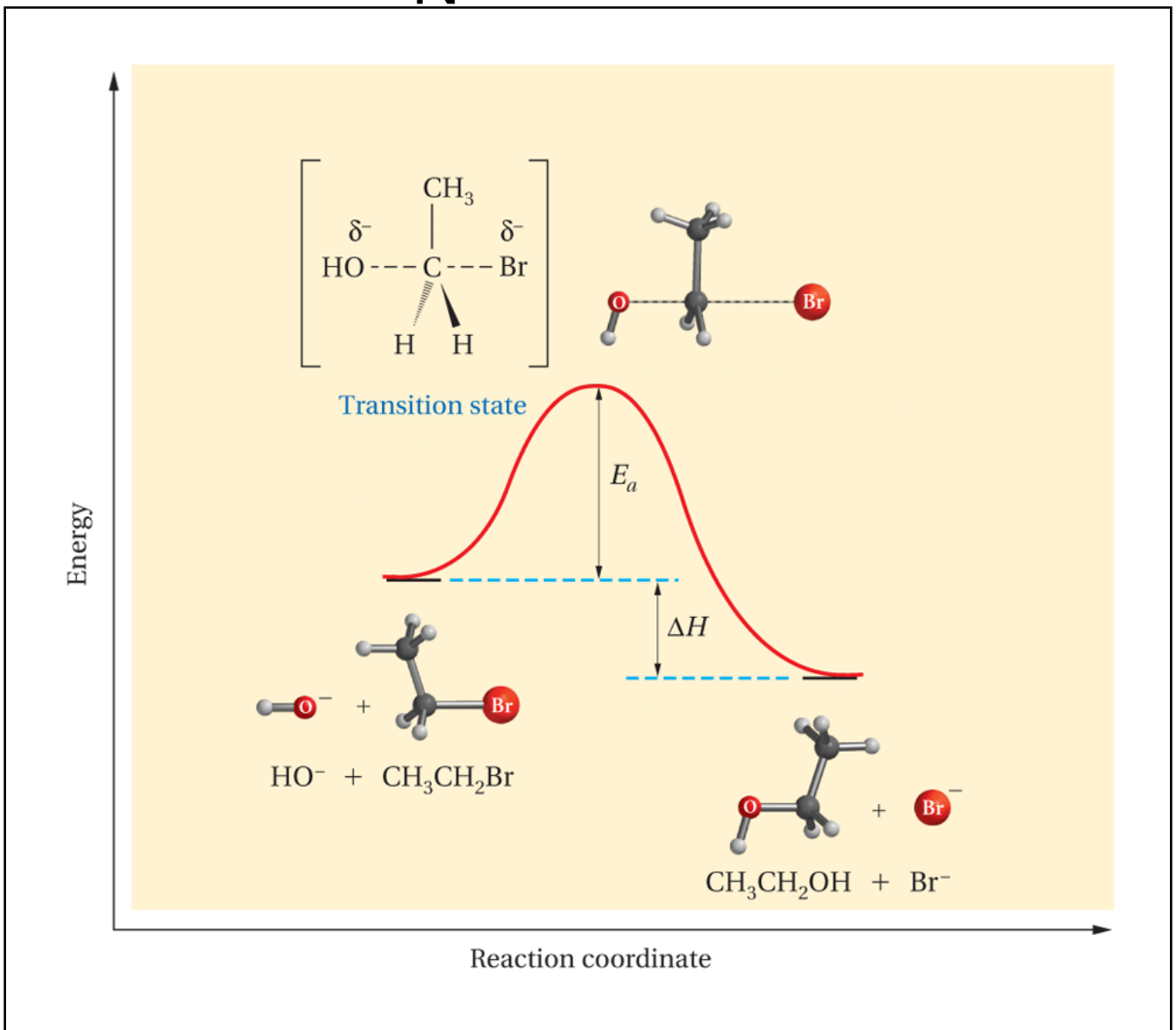
Consider the kinetic of the reaction:

$$\text{rate} = k\,[\text{alkyl halide}][\text{nucleophile}]$$

the rate constant

2 is a second-order reaction

Reaction energy diagram for an S_N2 reaction



S_N2 Reaction Mechanism

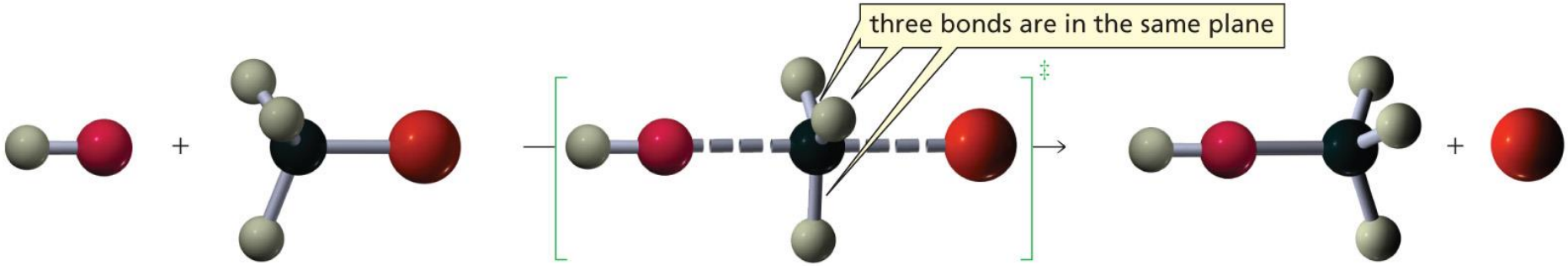
1. The rate of the reaction is dependent on the concentration of the alkyl halides and the nucleophile

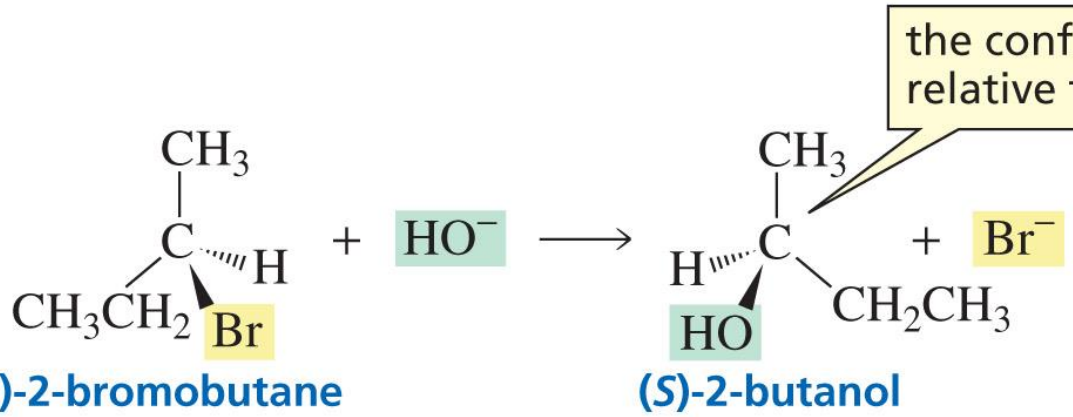
$$\text{rate} = k\,[\text{alkyl halide}][\text{nucleophile}]$$

the rate constant

2. The configuration of the substituted product is inverted compared to the configuration of the reacting chiral alkyl halide

Inversion of configuration is due to back side attack





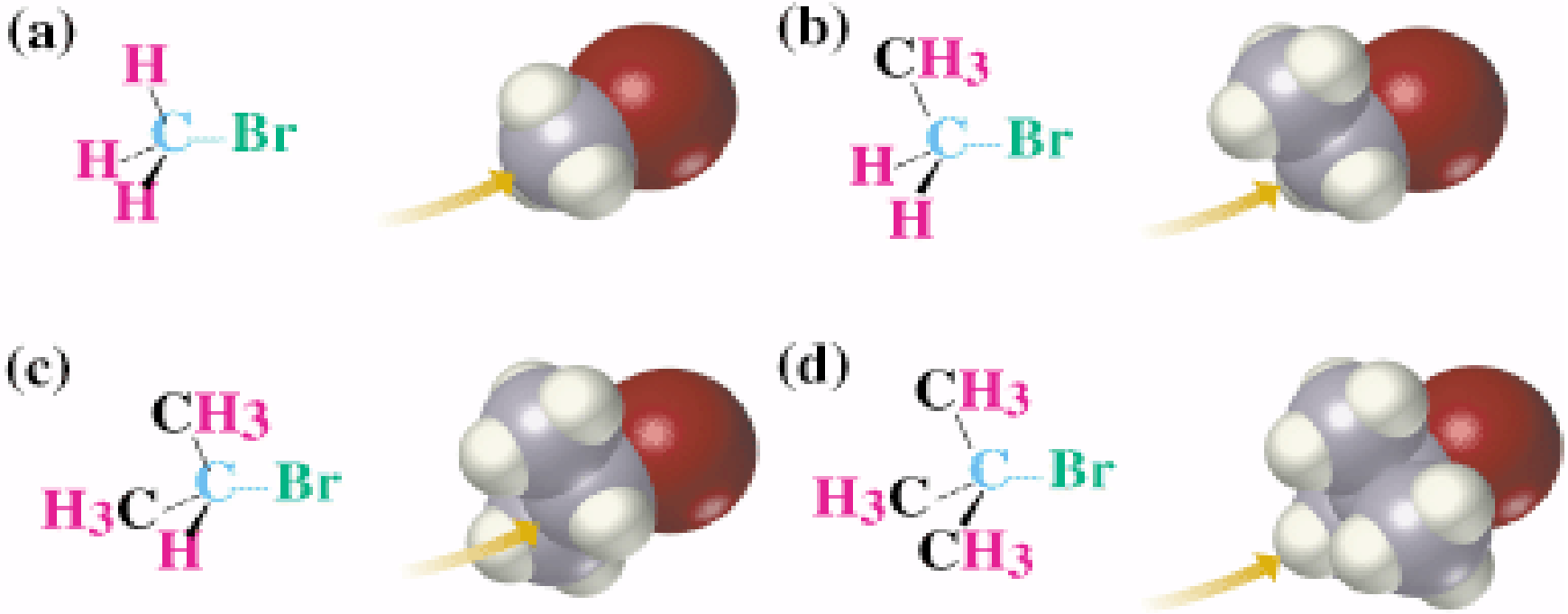
3. The rate of the reaction with a given nucleophile decreases with increasing size of the alkyl halides (steric hindrance)

Table 8.1 Relative Rates of S_N2 Reactions for Several Alkyl Halides

$$R{-}Br + Cl^- \xrightarrow{S_N2} R{-}Cl + Br^-$$

Alkyl halide	Class of alkyl halide	Relative rate
$CH_3{-}Br$	methyl	1200
$CH_3CH_2{-}Br$	primary	40
$CH_3CH_2CH_2{-}Br$	primary	16
$CH_3CH(CH_3){-}Br$	secondary	1
$CH_3C(CH_3)_2{-}Br$	tertiary	too slow to measure

Steric Effects on S_N2 Reactions



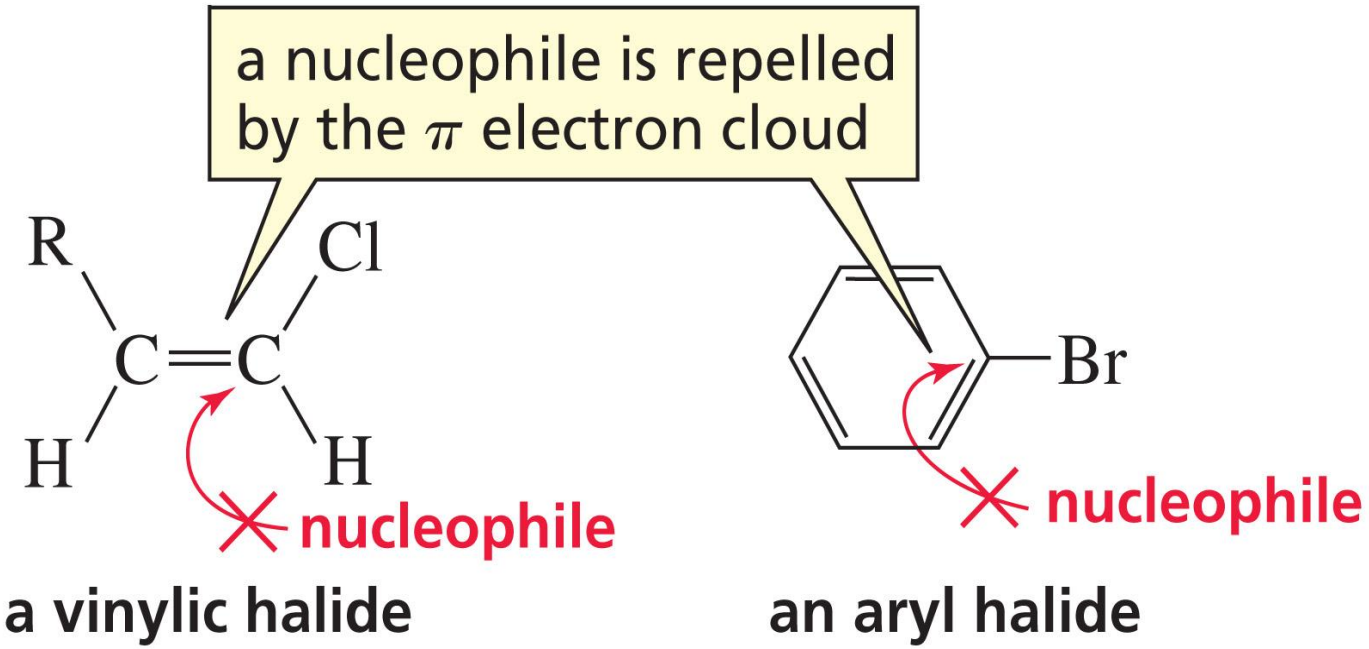
The carbon atom in (a) bromomethane is readily accessible resulting in a fast SN2 reaction. The carbon atoms in (b) bromoethane (primary), (c) 2-bromopropane (secondary), and (d) 2-bromo-2-methylpropane (tertiary) are successively more hindered, resulting in successively slower SN2 reactions.

A bulky substituent in the alkyl halide reduces the reactivity of the alkyl halide: steric hindrance

relative reactivities of alkyl halides in an S_N2 reaction

Tertiary alkyl halides cannot undergo S_N2 reactions

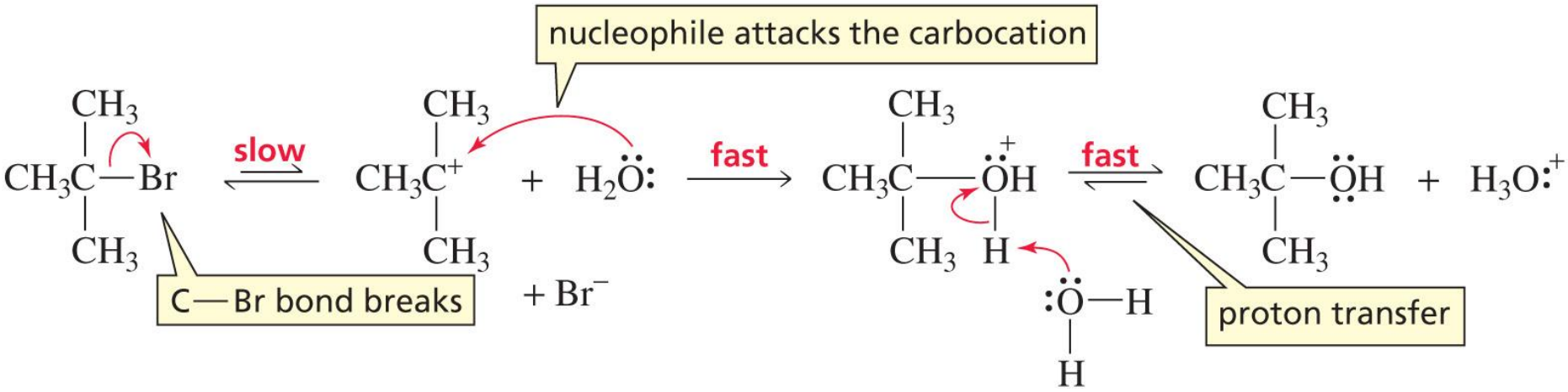
Vinyl and aryl halides do not undergo S_N2 because



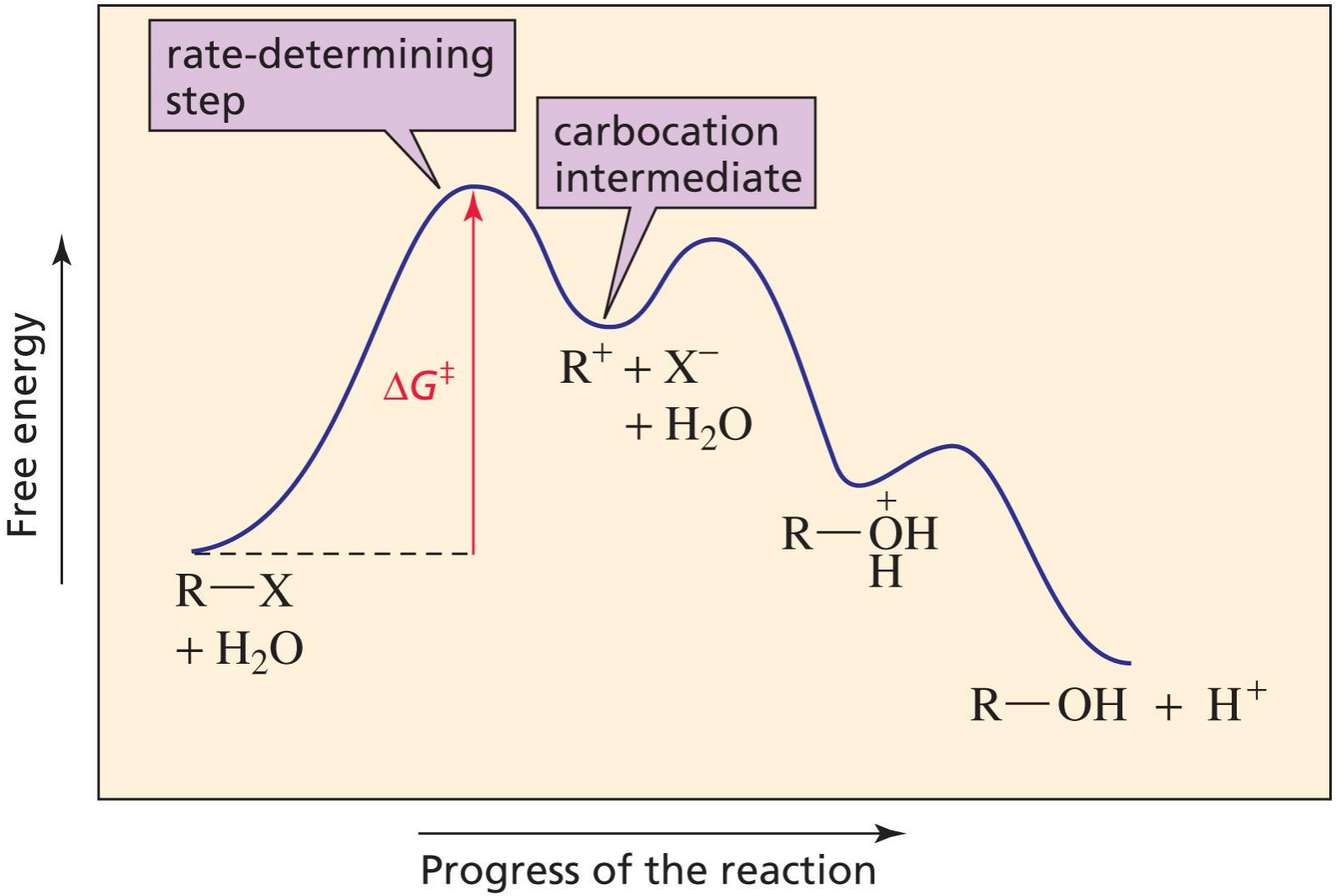
The S_N1 Mechanism

An S_N1 is a two-step reaction and the leaving group departs before the nucleophile approaches

mechanism for the S_N1 reaction of an alkyl halide



Reaction Coordinate Diagram for an S_N1 Reaction

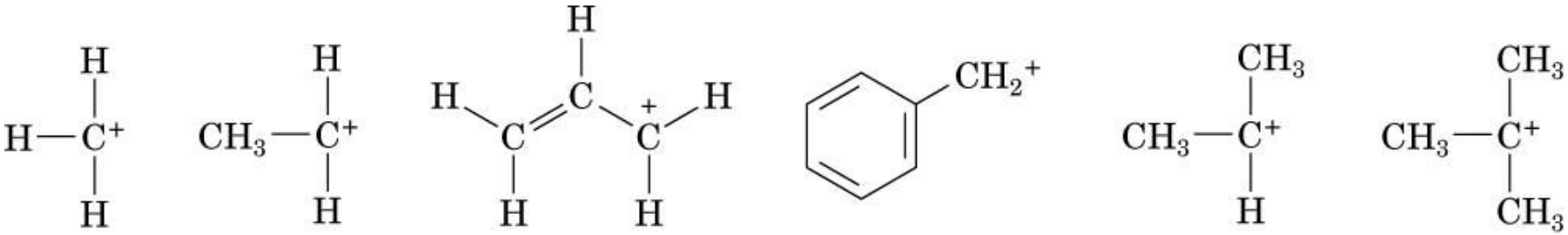


S_N1 Reaction Mechanism

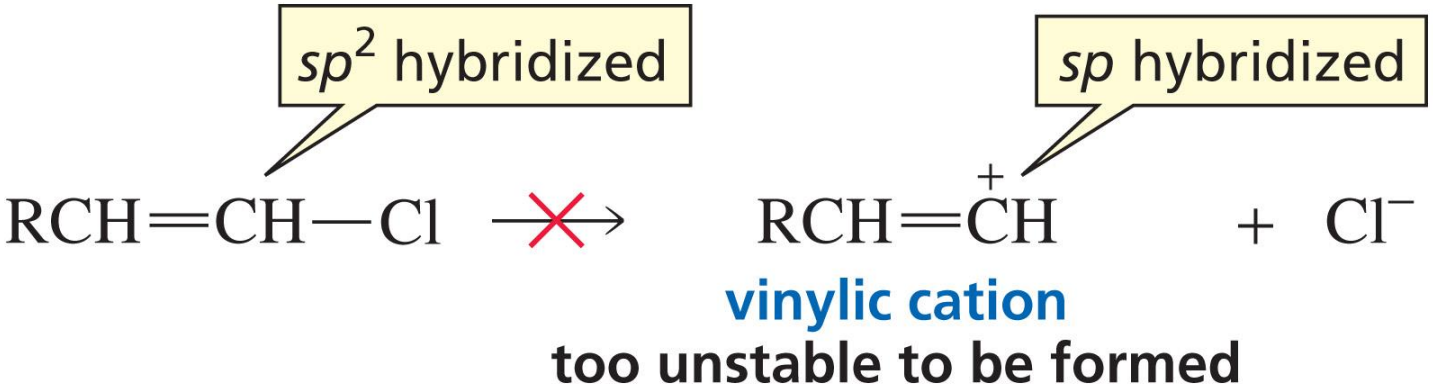
1. **The rate of the reaction depends only on the concentration of the alkyl halide**

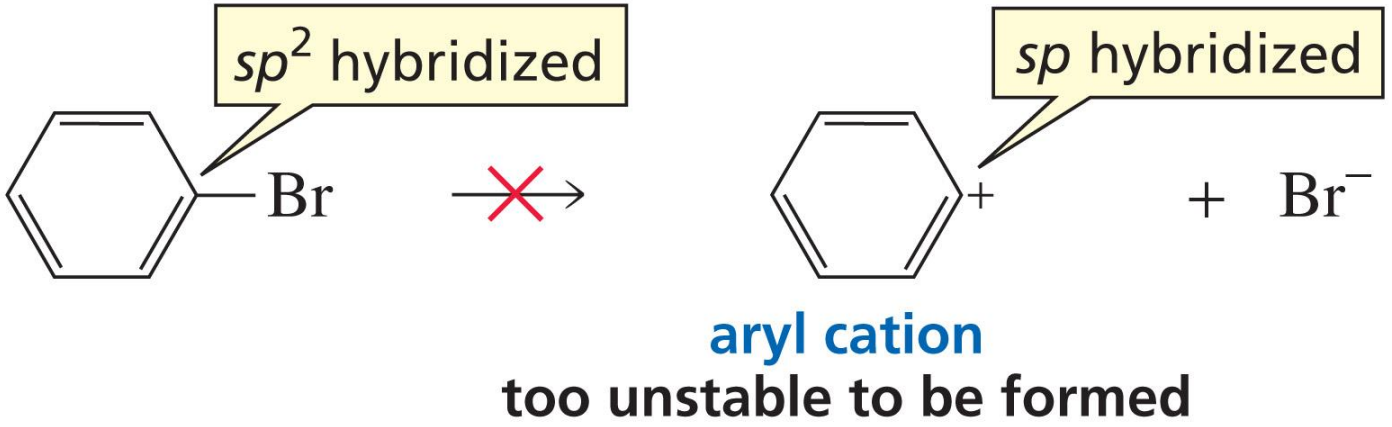
$$\text{rate} = k[\text{alkyl halide}]$$

2. The rate of the reaction is favored by the bulkiness of the alkyl substituent

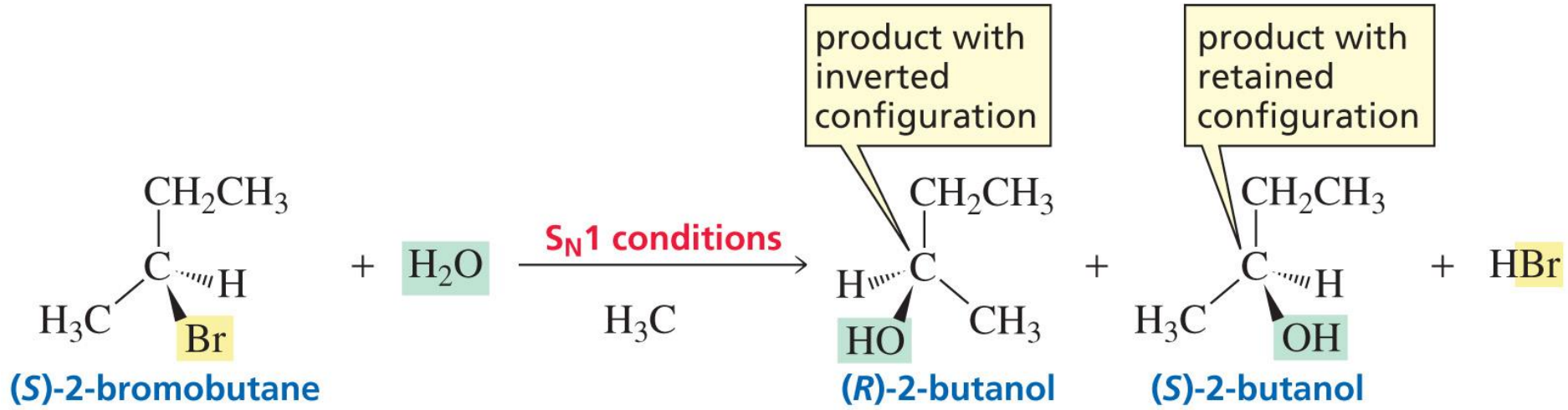


Vinyl and aryl halides do not undergo S_N1 because





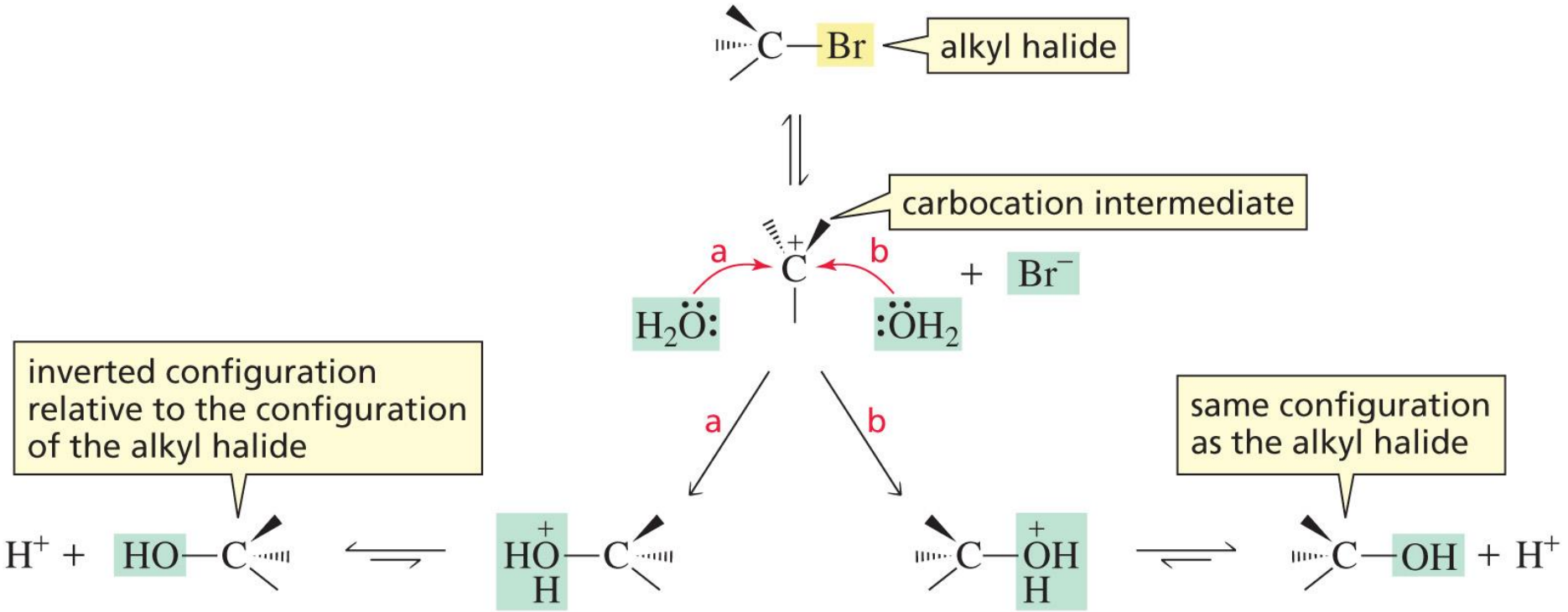
3.The Stereochemistry of S_N1Reactions



%50 : %50

Racemic mixture

The carbocation reaction intermediate leads to the formation of two stereoisomeric products



S_N1 and S_N2 Reactions Are Affected by the Leaving Group

most reactive — RI > RBr > RCl > RF — least reactive

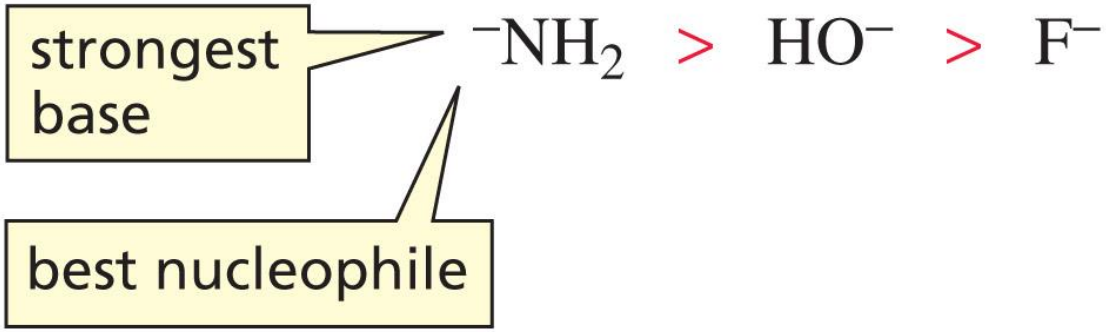
When comparing molecules with the same attacking atom

stronger base, better nucleophile		weaker base, poorer nucleophile
OH^-	>	H_2O
CH_3O^-	>	CH_3OH
$^-NH_2$	>	NH_3
$CH_3CH_2NH^-$	>	$CH_3CH_2NH_2$

When comparing molecules with attacking atoms of approximately the same size, the stronger bases are the better nucleophiles

relative acid strengths

relative base strengths and relative nucleophilicities



Size ⟵

C->N- >O->F-

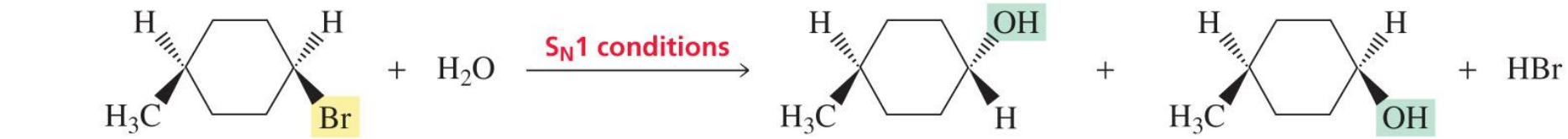
EN ⟶

I^{-}>Br^{-} >Cl^{-}>F^{-} ⟵

The products resulting from substitution of cyclic compounds

cis-1-bromo-4-methylcyclohexane

trans-4-methylcyclohexanol

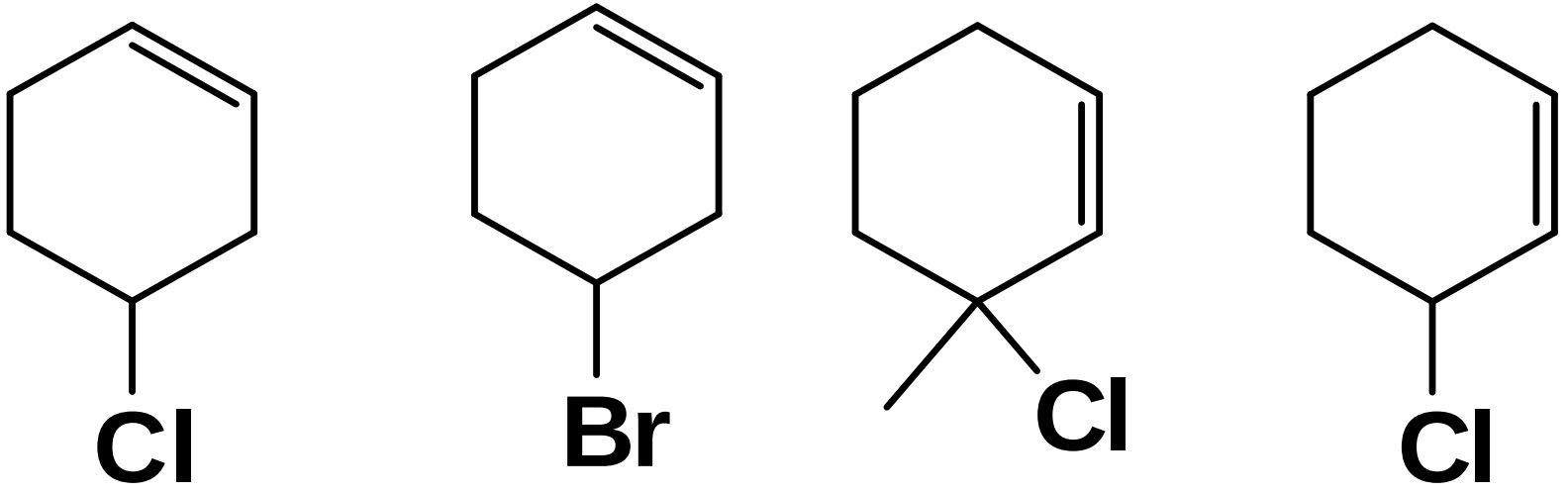


cis-1-bromo-4-methylcyclohexane

trans-4-methylcyclohexanol

cis-4-methylcyclohexanol

Arrange the following compounds in order of increasing reactivity toward SN1 reaction?



I II III IV

Q2 Which of the following molecules is best for SN1 reaction :

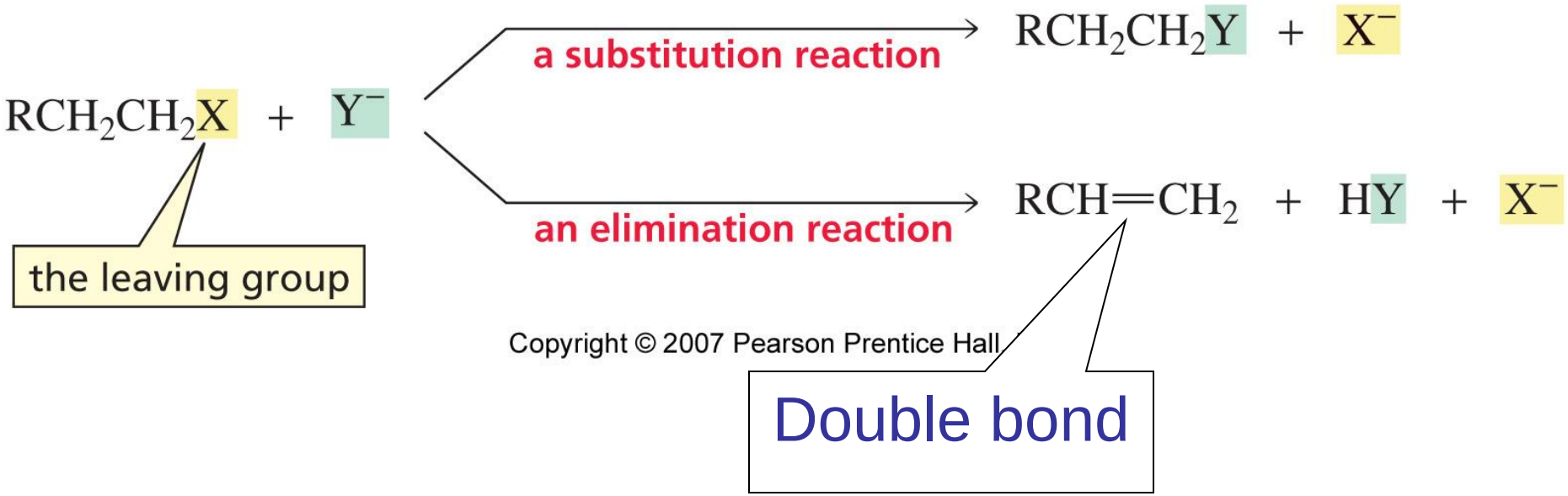
(A) ethanol (B)DMF (C) DMSO (D) acetone

Q3 **Which of the following Nucleophils is the strongest.**

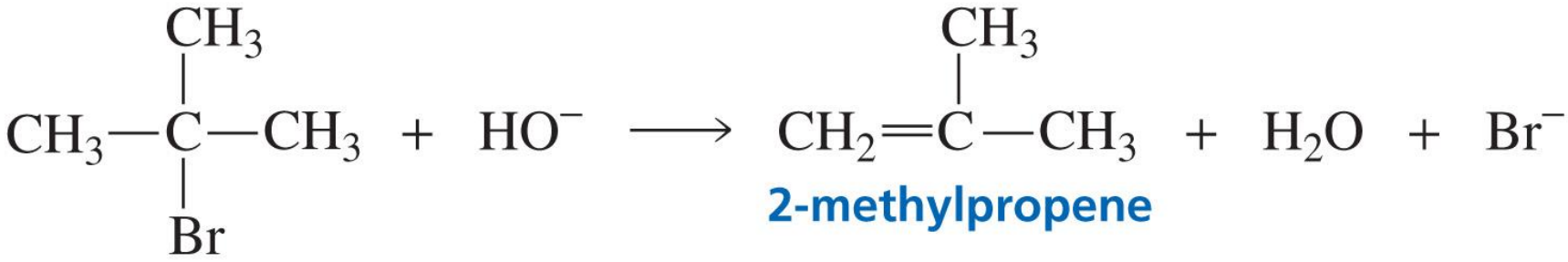
(A) NaCN (B) NaNH2 (C) NaOCH3 (D) NaSH E) NaF

Dehydrohalogenation, an Elimination Reaction; The E2 and E1 Mechanisms

In addition to substitution, an alkyl halide can undergo an elimination reaction

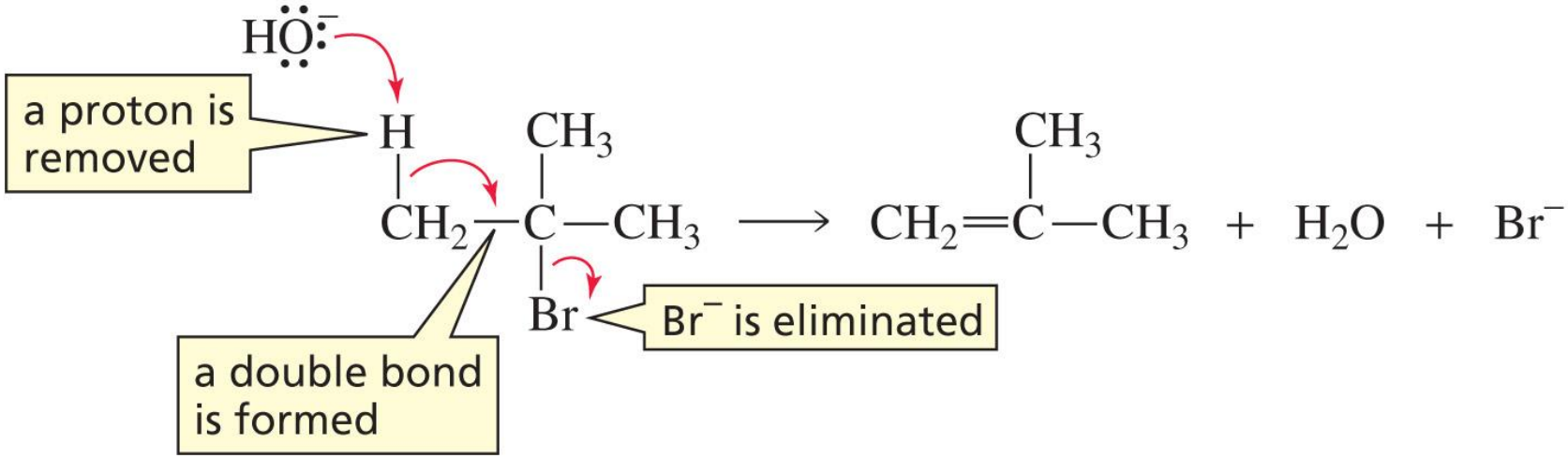


The E2 Reaction



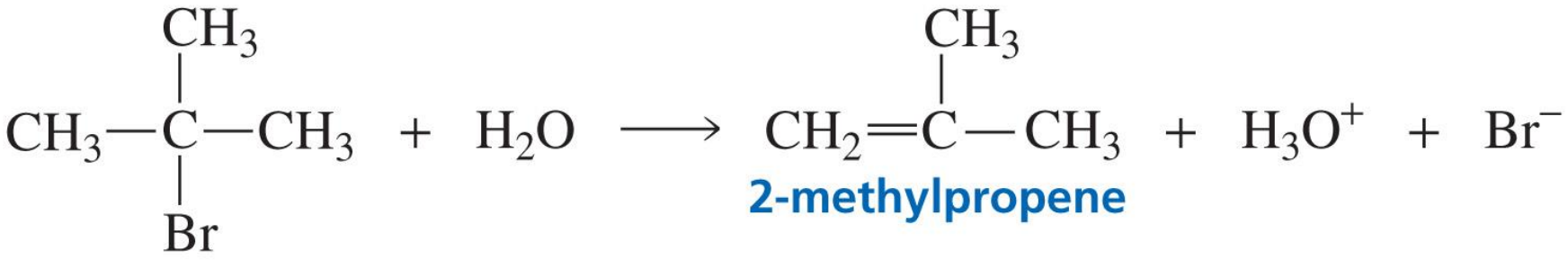
2-methylpropene

mechanism of the E2 reaction



$$\text{rate} = k[\text{alkyl halide}][\text{base}]$$

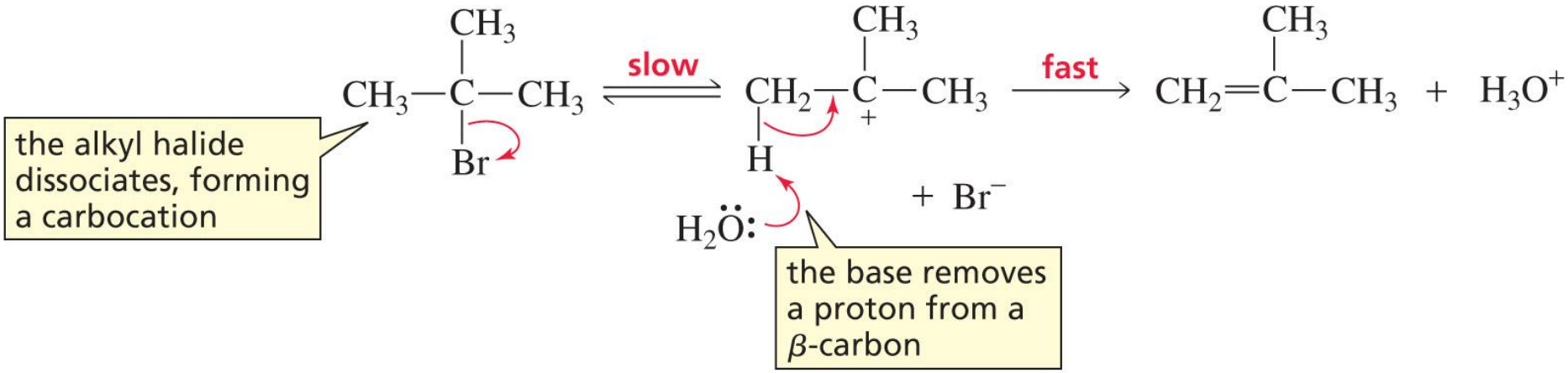
The E1 Reaction



2-methylpropene

2-bromo-2-methylpropane

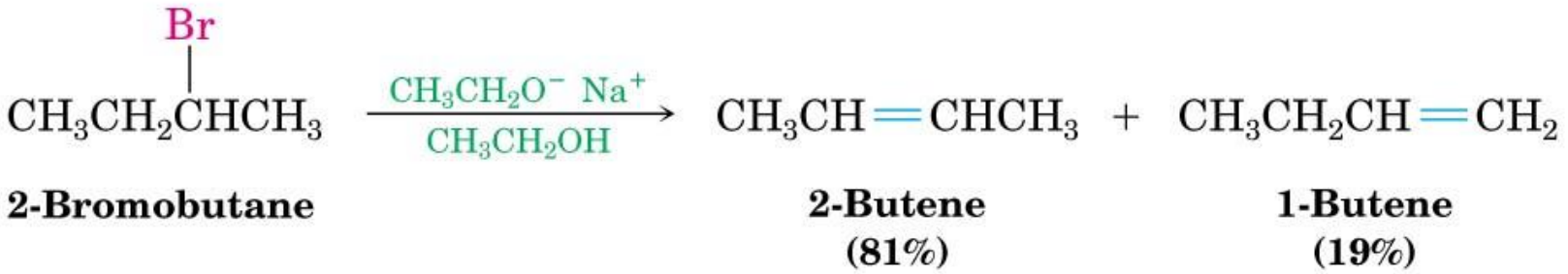
mechanism of the E1 reaction

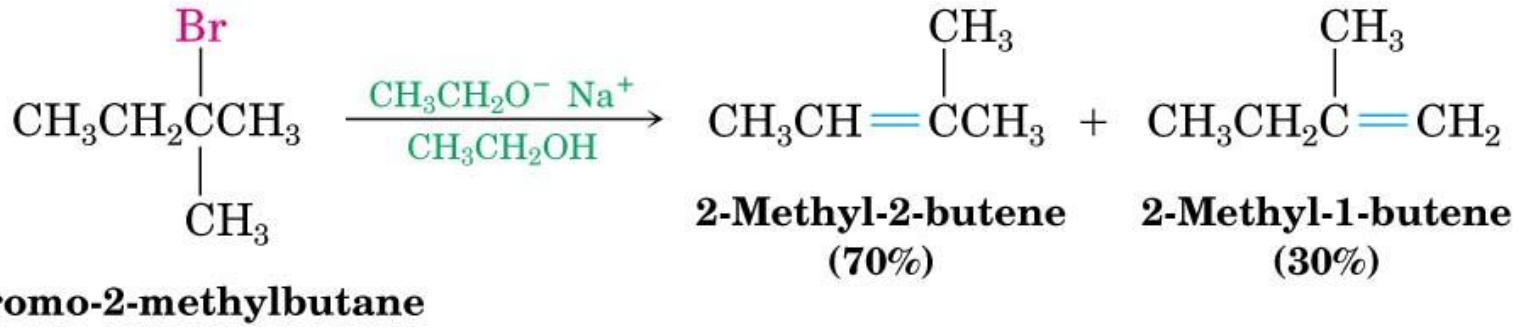


$$\text{rate} = k[\text{alkyl halide}]$$

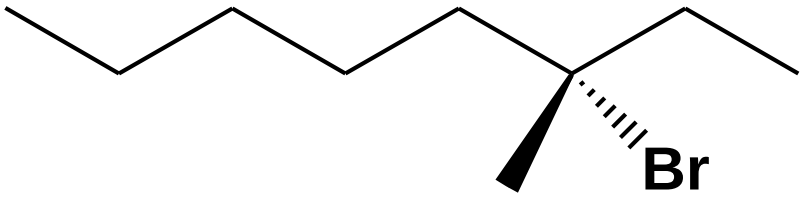
The Regioselectivity of the E1 & E2 Reaction

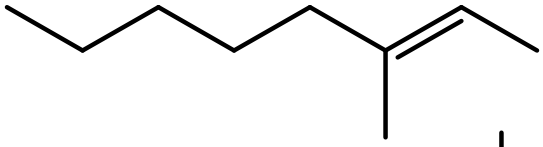
The major product of an elimination reaction is the most stable alkene. (Zaitsev's Rule)

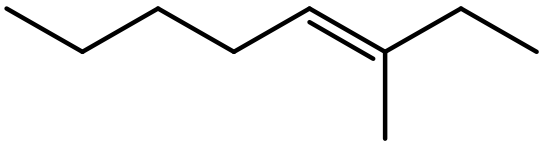


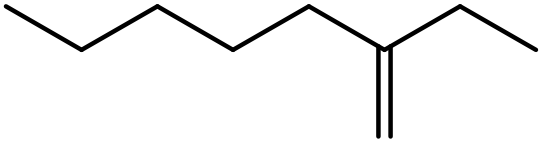


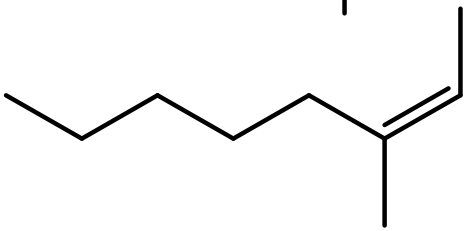
How many distinct alkene products are possible when the alkyl iodide below undergoes elimination?

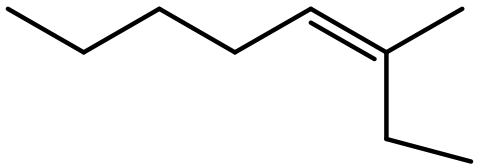


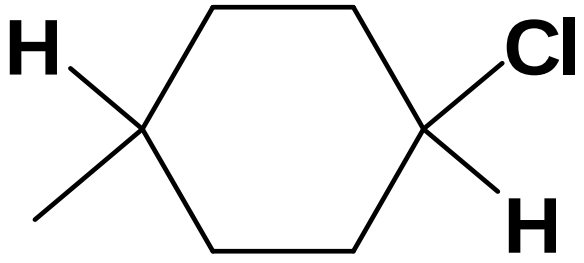




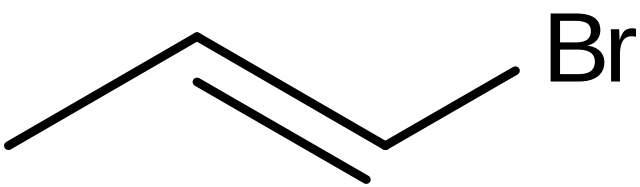




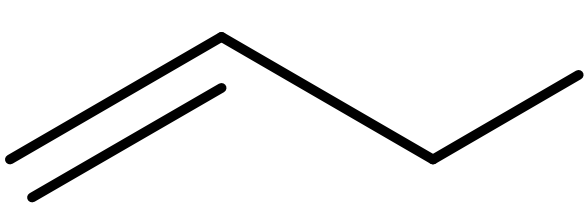




CH_3CH_2OH ?



CH_3SNa



CH_3SNa

Arrange the following compound according to decreasing their reactivity toward SN2 reaction