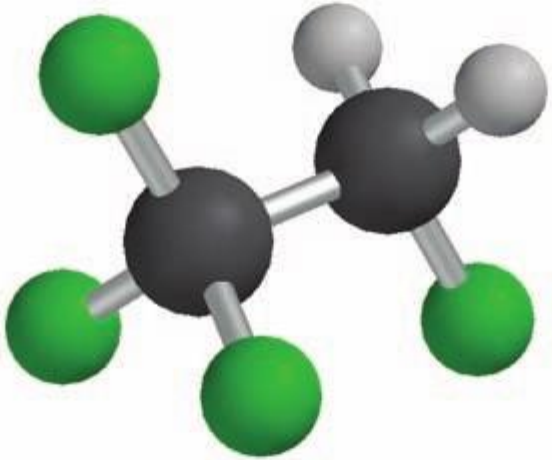
Organic Chemistry

Chapter 7

Haloalkanes



7.1 How Are Haloalkanes Named?

7.2 What Are the Characteristic Reactions of Haloalkanes?

7.3 What Are the Products of Nucleophilic Aliphatic Substitution Reactions?

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7.6 How Can S_N1 and S_N2 Be Predicted Based on Experimental Conditions?

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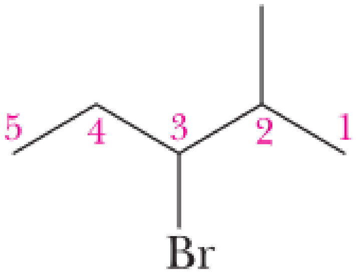
7.8 What Are the E1 and E2 Mechanisms for β-Elimination?

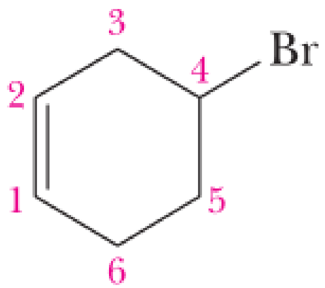
7.9 When Do Nucleophilic Substitution and β-Elimination Compete?

7.1 How Are Haloalkanes Named?

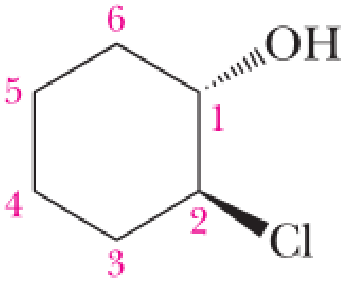
A. IUPAC Names -X作为取代基命名，母体可为烷烃、烯烃等



3-Bromo-2-methylpentane



4-Bromocyclohexene



(1*S*,2*S*)-2-Chlorocyclohexanol
or
trans-2-Chlorocyclohexanol

B. Common Names

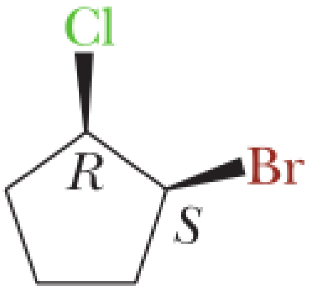
$$\overset{F}{|}\quad CH_3CHCH_2CH_3$$

2-Fluorobutane
(*sec*-Butyl fluoride)

$CH_2{=}CHCl$
Chloroethene
(Vinyl chloride)

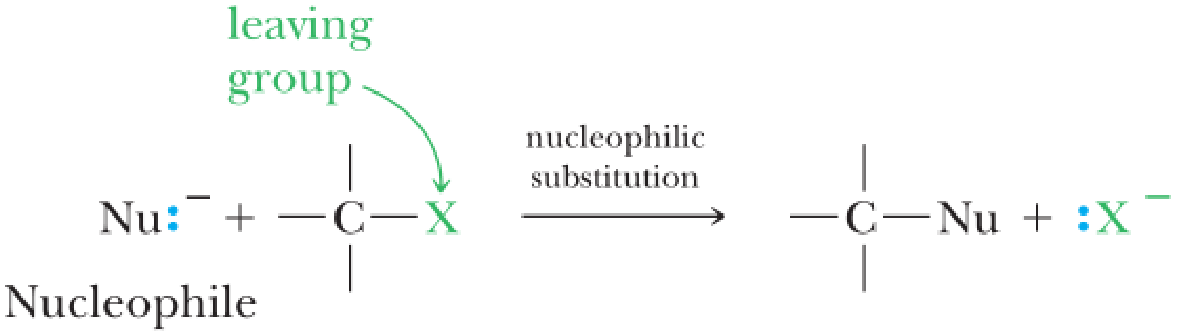
CH_2Cl_2	$CHCl_3$	CH_3CCl_3	$CCl_2{=}CHCl$
Dichloromethane	Trichloromethane	1,1,1-Trichloroethane	Trichloroethylene
(Methylene chloride)	(Chloroform)	(Methyl chloroform)	(Trichlor)
亚甲基氯	氯仿	甲基氯仿	三氯乙烯、九氯

see Chapter 6 for rules on assigning R/S configurations



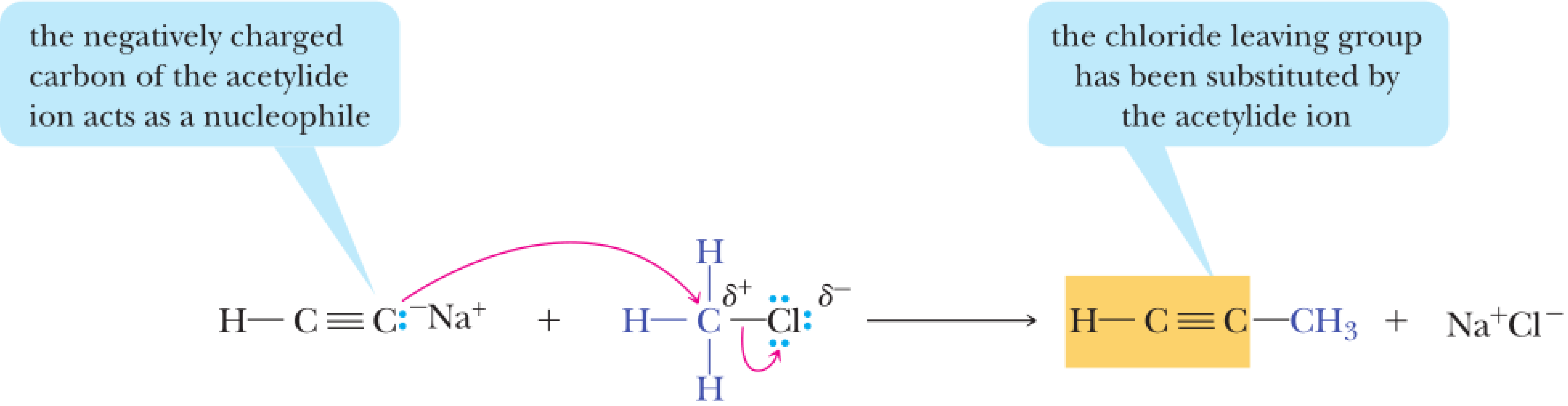
(1*S*,2*R*)-1-Bromo-2-chlorocyclopentane
or
cis -1-Bromo-2-chlorocyclopentane

7.2 What Are the Characteristic Reactions of Haloalkanes?



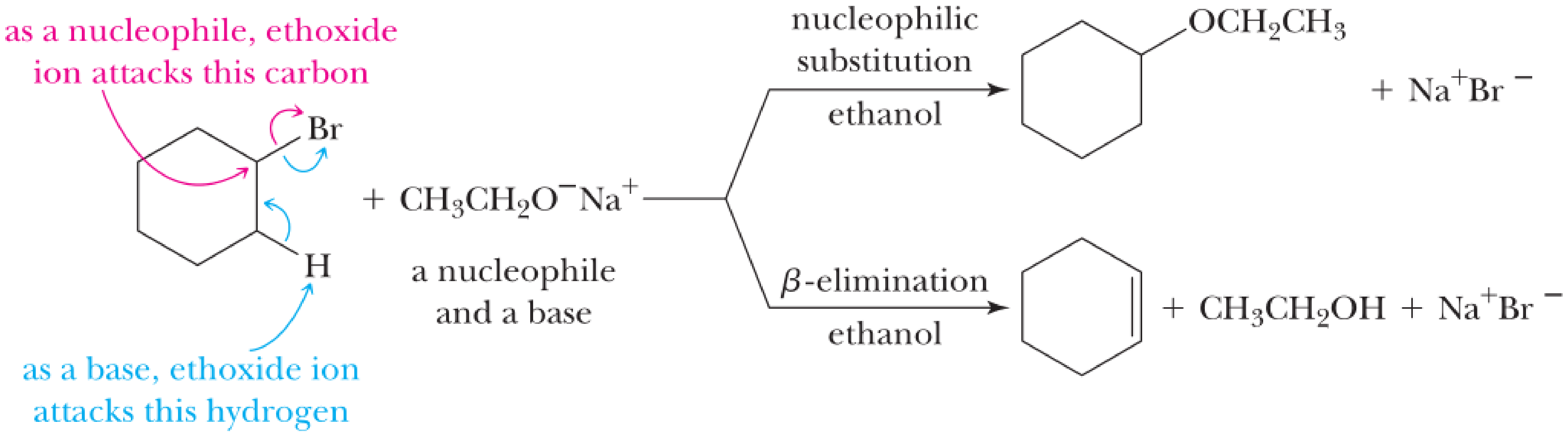
Nucleophile(亲核试剂) An atom or a group of atoms that donates a pair of electrons to another atom or group of atoms to form a new covalent bond.

Nucleophilic substitution（亲核取代） A reaction in which one nucleophile is substituted for another.


the negatively charged carbon of the acetylide ion acts as a nucleophile

the chloride leaving group has been substituted by the acetylide ion

β-Elimination reaction(β-消除反应) The removal of atoms or groups of atoms from two adjacent carbon atoms, as for example, the removal of H and X from an alkyl halide or H and OH froman alcohol to form a carbon–carbon double bond.



7.3 What are the products of Nucleophilic aliphatic Substitution reactions?

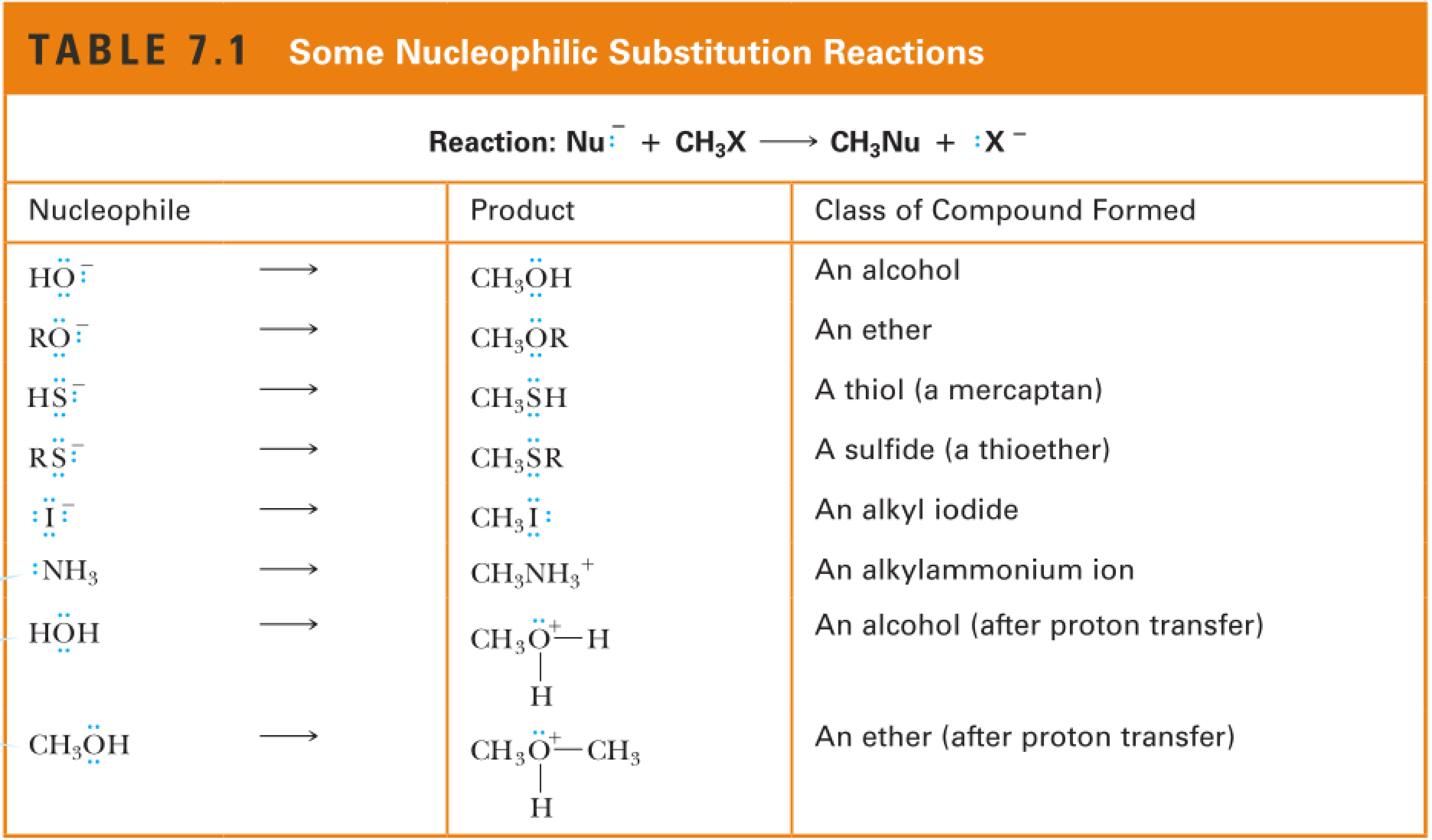
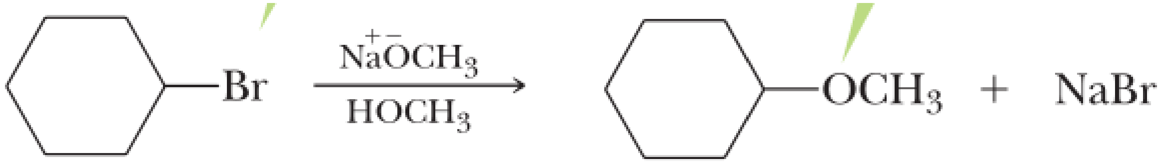


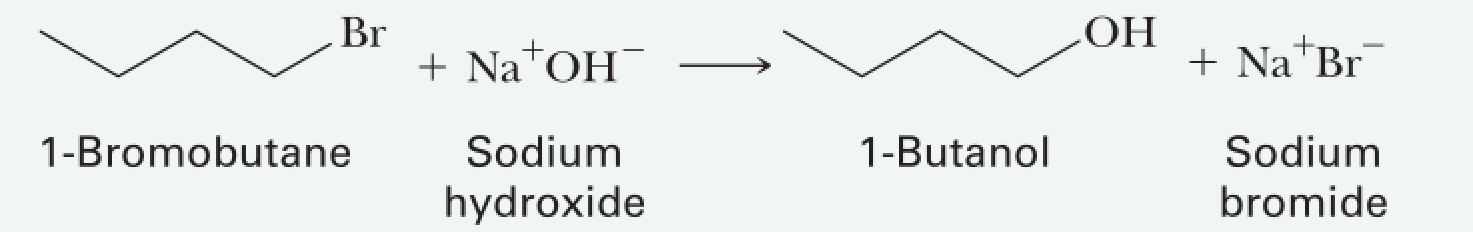
TABLE 7.1 Some Nucleophilic Substitution Reactions

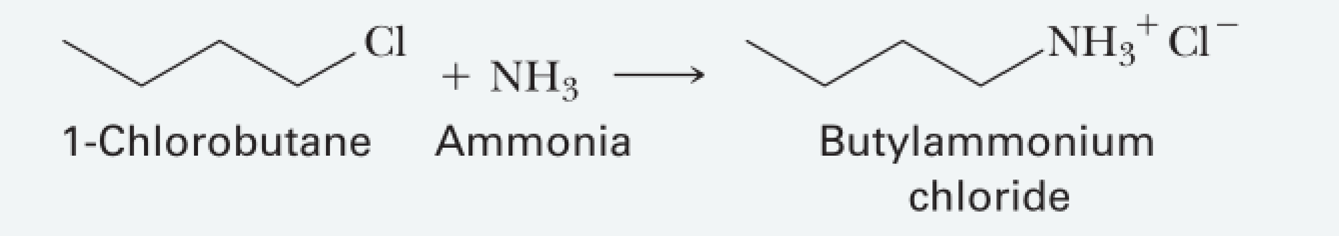
Reaction: $Nu{:}^- + CH_3X \longrightarrow CH_3Nu + {:}X^-$

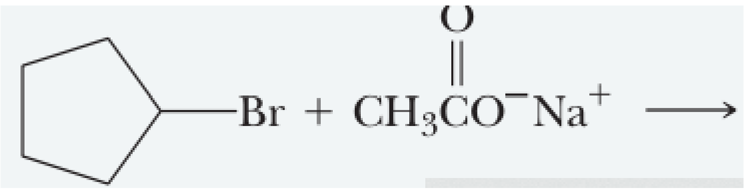
Nucleophile		Product	Class of Compound Formed
$H\ddot{O}{:}^-$	$\longrightarrow$	$CH_3\ddot{O}H$	An alcohol
$R\ddot{O}{:}^-$	$\longrightarrow$	$CH_3\ddot{O}R$	An ether
$H\ddot{S}{:}^-$	$\longrightarrow$	$CH_3\ddot{S}H$	A thiol (a mercaptan)
$R\ddot{S}{:}^-$	$\longrightarrow$	$CH_3\ddot{S}R$	A sulfide (a thioether)
${:}\ddot{I}{:}^-$	$\longrightarrow$	$CH_3\ddot{I}{:}$	An alkyl iodide
${:}NH_3$	$\longrightarrow$	$CH_3NH_3^+$	An alkylammonium ion
$H\ddot{O}H$	$\longrightarrow$	$CH_3\overset{+}{\underset{\underset{H}{\vert}}{\ddot{O}}}-H$	An alcohol (after proton transfer)
$CH_3\ddot{O}H$	$\longrightarrow$	$CH_3\overset{+}{\underset{\underset{H}{\vert}}{\ddot{O}}}-CH_3$	An ether (after proton transfer)

notice that a nucleophile does not need to be negatively charged


Br
$\overset{+}{Na}\overset{-}{O}CH_3$
$HOCH_3$
OCH_3
+
NaBr


Br
+ Na^+OH^-
OH
+ Na^+Br^-
1-Bromobutane
Sodium hydroxide
1-Butanol
Sodium bromide


Cl
+ NH_3
$NH_3^+\ Cl^-$
1-Chlorobutane
Ammonia
Butylammonium chloride


Br + $CH_3\overset{O}{\overset{\|}{C}}O^-Na^+$

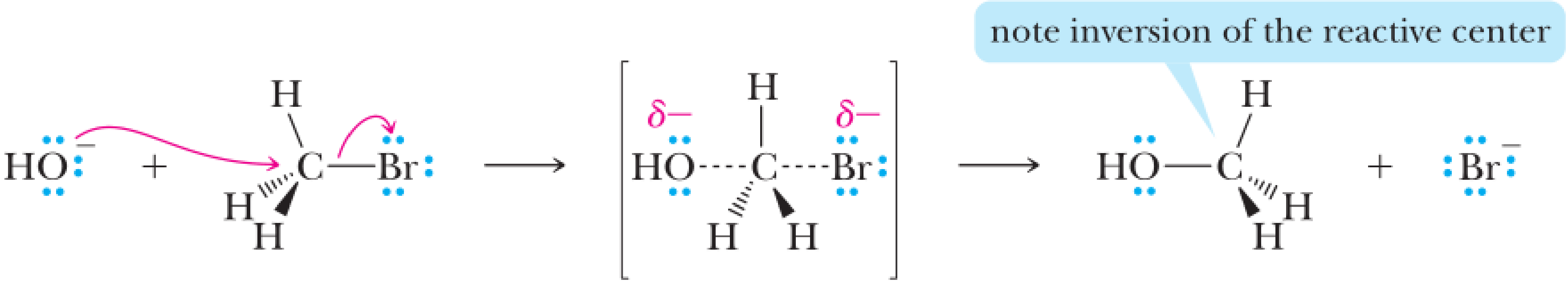
7.4 What are the S_N2 and S_N1 Mechanisms for NucleophilicSubstitution?

A. S_N2 Mechanism

Bimolecular reaction （双分子亲核取代）A reaction in which two species are involved in the reaction leading to the transition state of the rate-determining step.

k is the rate constant for the reaction

$$\text{Rate} = k[\text{haloalkane}][\text{nucleophile}]$$



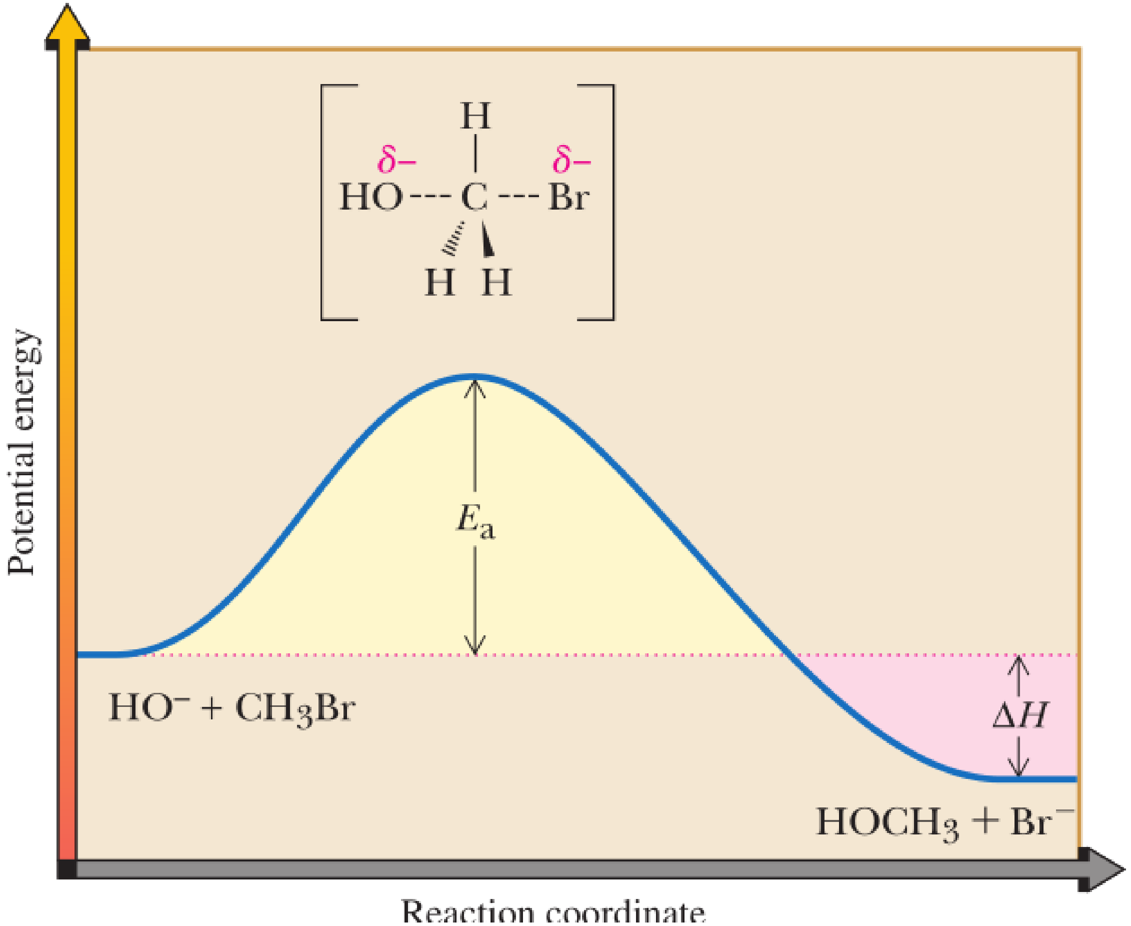
note inversion of the reactive center

Reactants

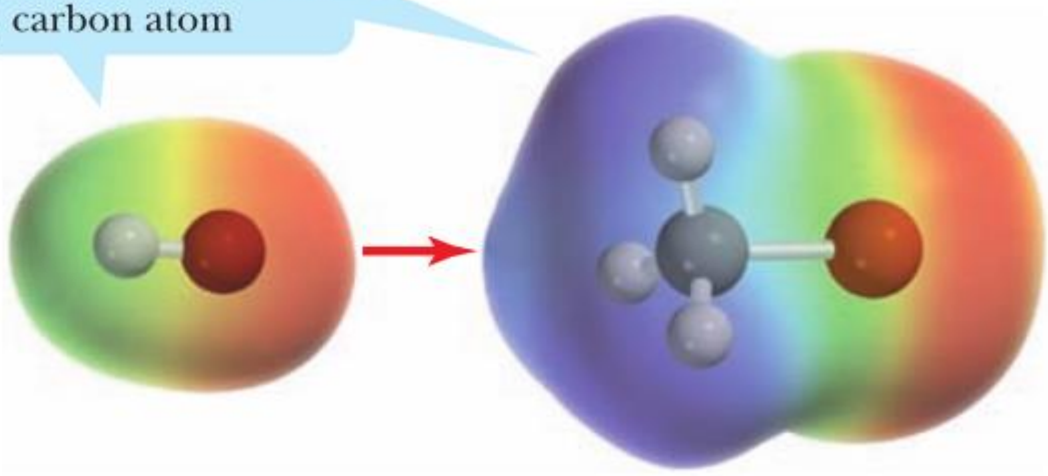
Transition state with simultaneous bond breaking and bond forming

Products

nversion of configuration（构型翻转） The reversal of the arrangement of atoms or groups of atoms about a reaction center in an S_N2 reaction.



the negatively charged (red) oxygen atom is attracted to the electropositive (blue) carbon atom



Nucleophilic attack from the side opposite the leaving group

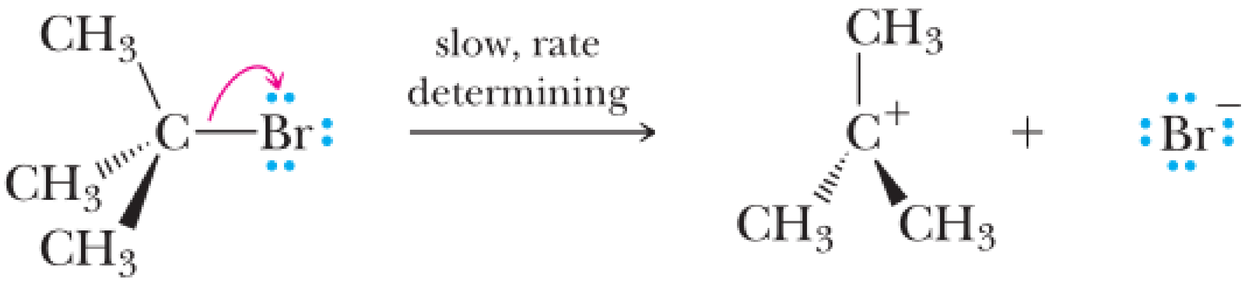
B. S_N1 Mechanism

Unimolecular reaction（单分子亲核取代） A reaction in which only one species is involved in the reaction leading to the transition state of the rate-determining step.

$$\boxed{\text{Rate} = k[\text{haloalkane}]}$$

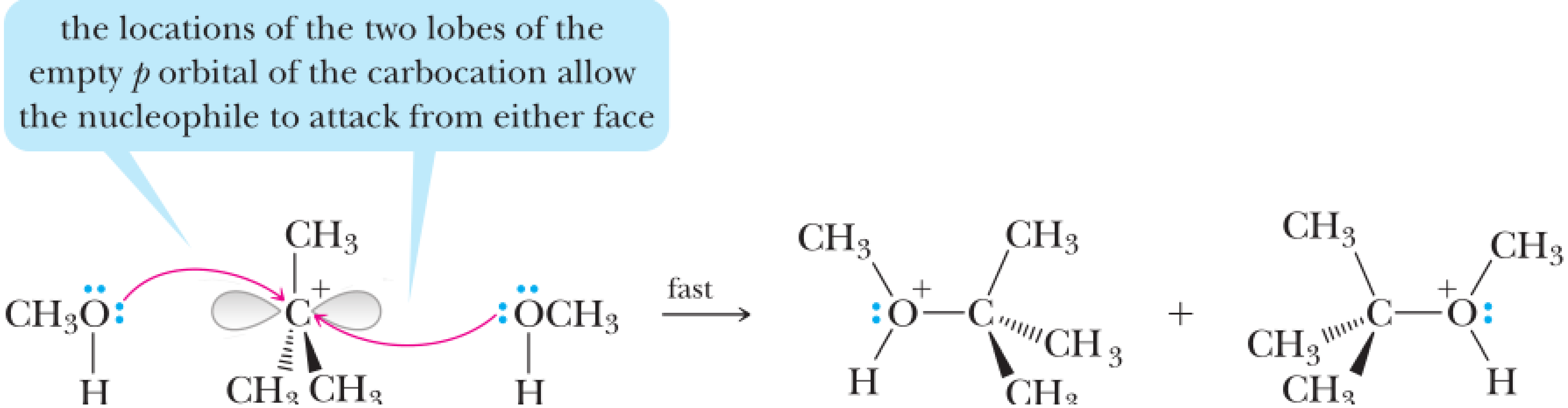
An S_N1 Reaction

STEP 1: Break a bond to form a more stable ion or molecule. The ionization of a C—X bond forms a 3° carbocation intermediate:

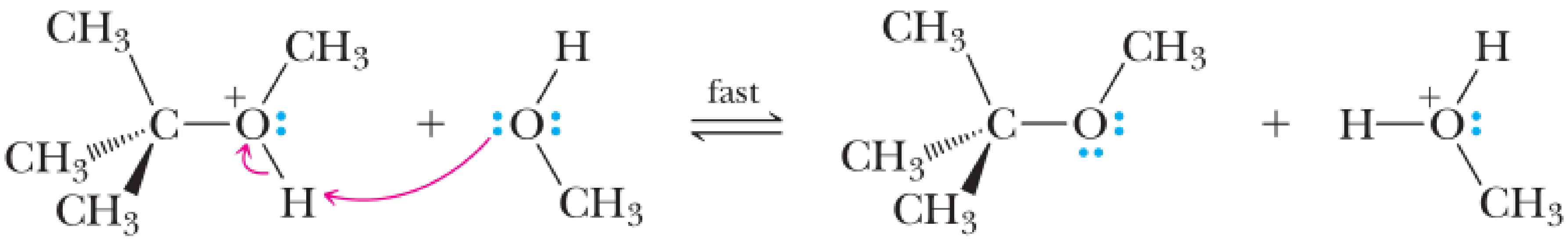


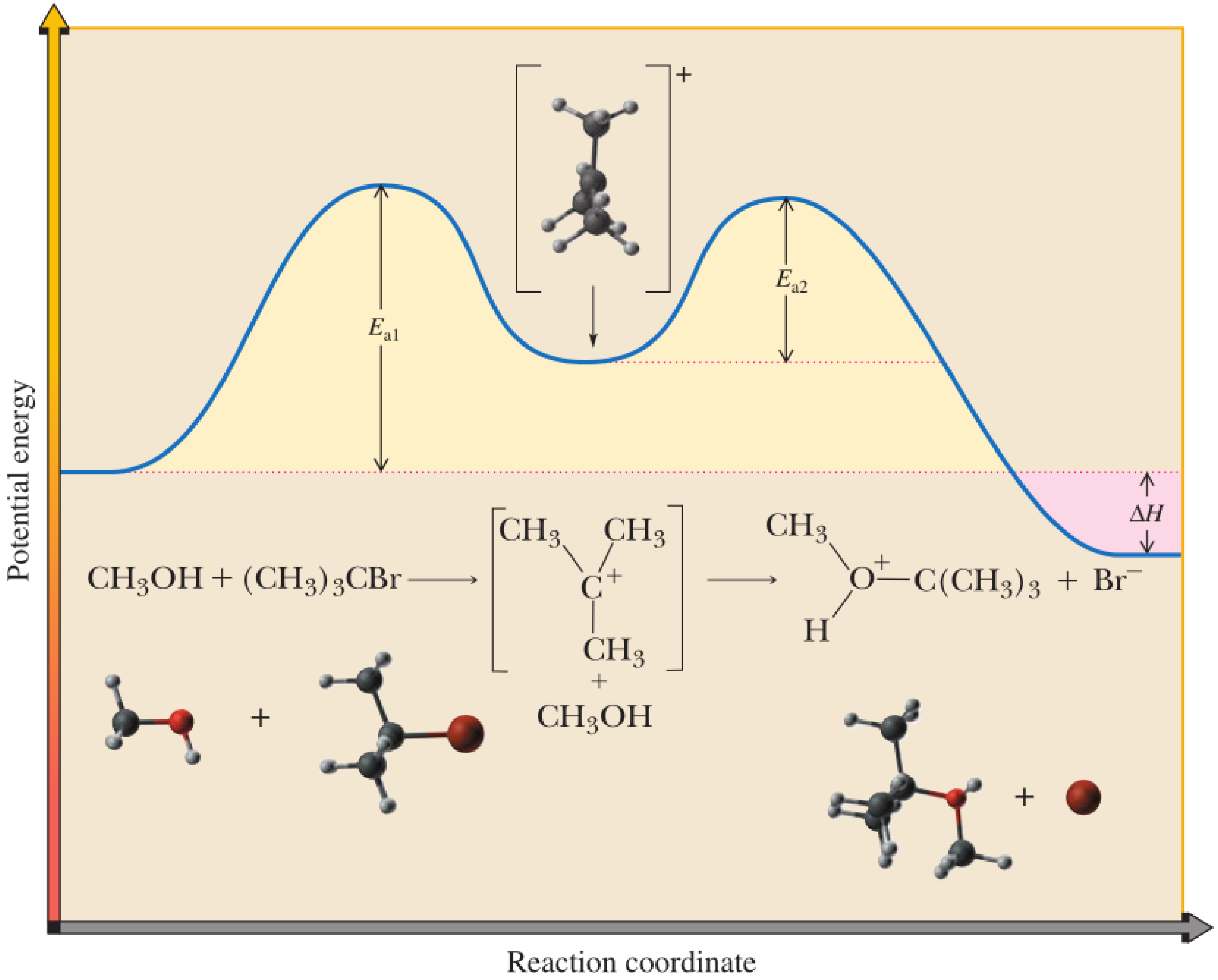
A carbocation intermediate; carbon is trigonal planar

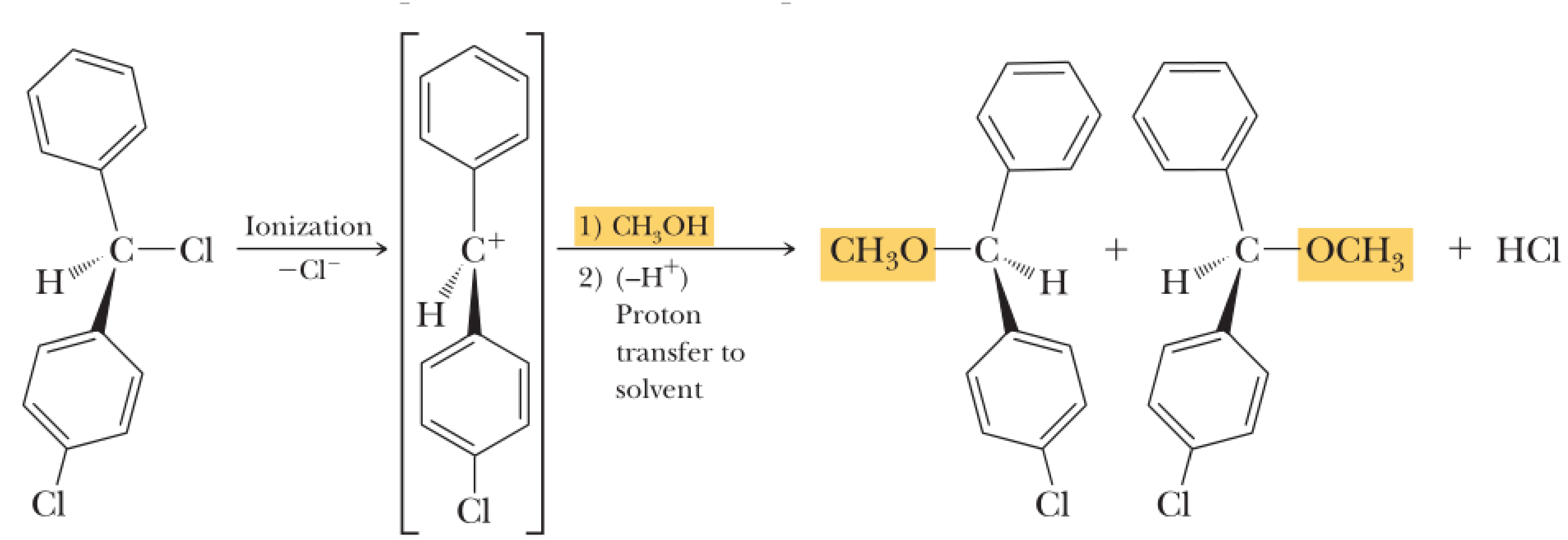
STEP 2: Reaction of a nucleophile and an electrophile to form a new covalent bond. Reaction of the carbocation intermediate (an electrophile) with methanol (a nucleophile) gives an oxonium ion. Attack by the nucleophile occurs with equal probability from either face of the planar carbocation intermediate.


the locations of the two lobes of the empty *p* orbital of the carbocation allow the nucleophile to attack from either face

STEP 3: Take a proton away. Proton transfer from the oxonium ion to methanol (the solvent) completes the reaction and gives *tert*-butyl methyl ether:




Potential energy
Reaction coordinate
E_{a1}
E_{a2}
ΔH
+
$CH_3OH + (CH_3)_3CBr \longrightarrow$
$[(CH_3)_3C^+]$
+
CH_3OH
$\longrightarrow$
$CH_3(H)O^+{-}C(CH_3)_3 + Br^-$
+
+



R enantiomer

Planar carbocation
(achiral)

S enantiomer R enantiomer

A racemic mixture

（外消旋化）

S_N1反应特点

1、两步完成

2、反应速度只与RX有关

3、中间体C^+(重排产物)

4、产物可能存在外消旋化

S_N2反应特点：

1、一步完成

2、反应速度和RX、亲核试剂有关

3、无中间体

4、产物构型翻转（瓦尔登转化）

7.5 What Determines Whether S_N1 or S_N2 Predominates?

A. Structure of the Nucleophile

$$CH_3CH_2Br + NH_3 \longrightarrow CH_3CH_2NH_3^+ + Br^-$$

亲核试剂主要影响双分子亲核取代（S_N2）反应

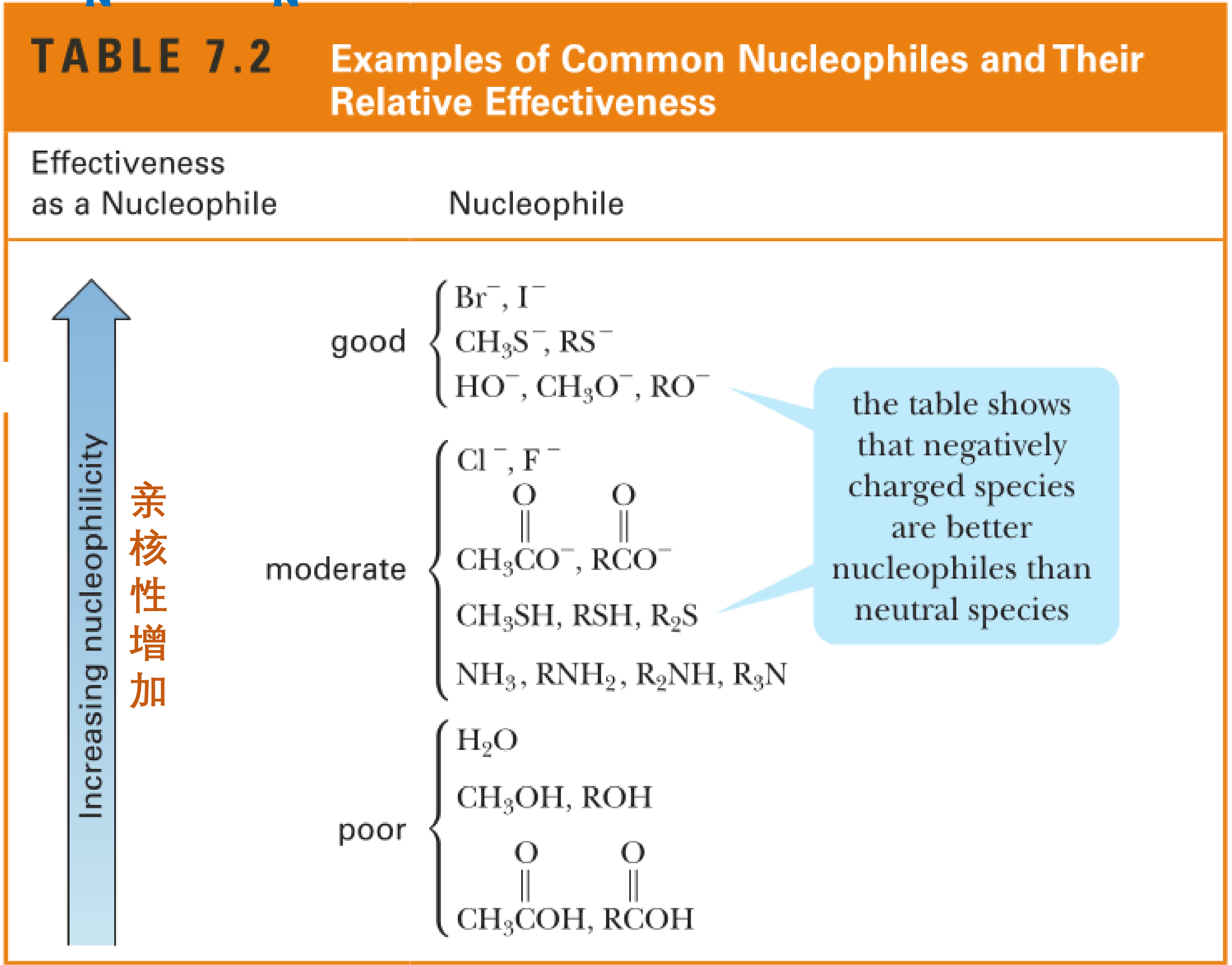


TABLE 7.2 Examples of Common Nucleophiles and Their Relative Effectiveness

Effectiveness as a Nucleophile	Nucleophile
good	Br^-, I^-
	CH_3S^-, RS^-
	HO^-, CH_3O^-, RO^-
moderate	Cl^-, F^-
	$CH_3\overset{\overset{O}{\Vert}}{C}O^-$, $R\overset{\overset{O}{\Vert}}{C}O^-$
	CH_3SH, RSH, R_2S
	NH_3, RNH_2, R_2NH, R_3N
poor	H_2O
	CH_3OH, ROH
	$CH_3\overset{\overset{O}{\Vert}}{C}OH$, $R\overset{\overset{O}{\Vert}}{C}OH$

the table shows that negatively charged species are better nucleophiles than neutral species

B. Structure of the Haloalkane

S_N1：电子效应

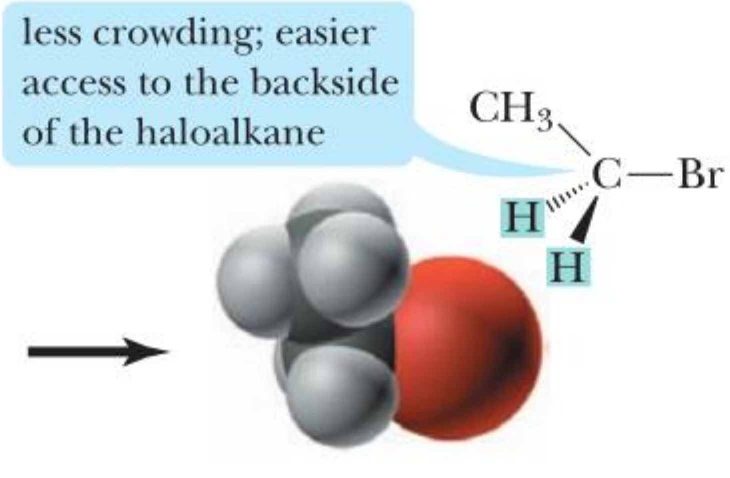
S_N2：空间效应

1. Relative stabilities of carbocations（碳正离子稳定性）.

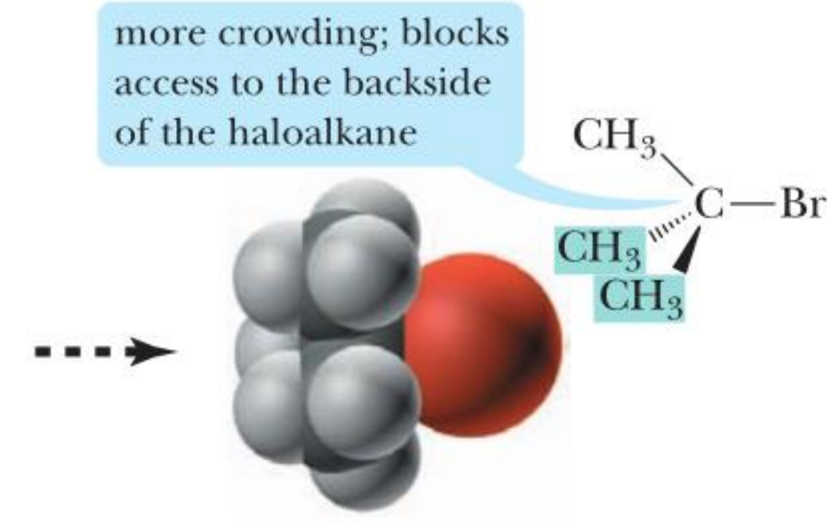
碳正离子越稳定越倾向于S_N1反应

2. Steric hindrance（空间位阻）.

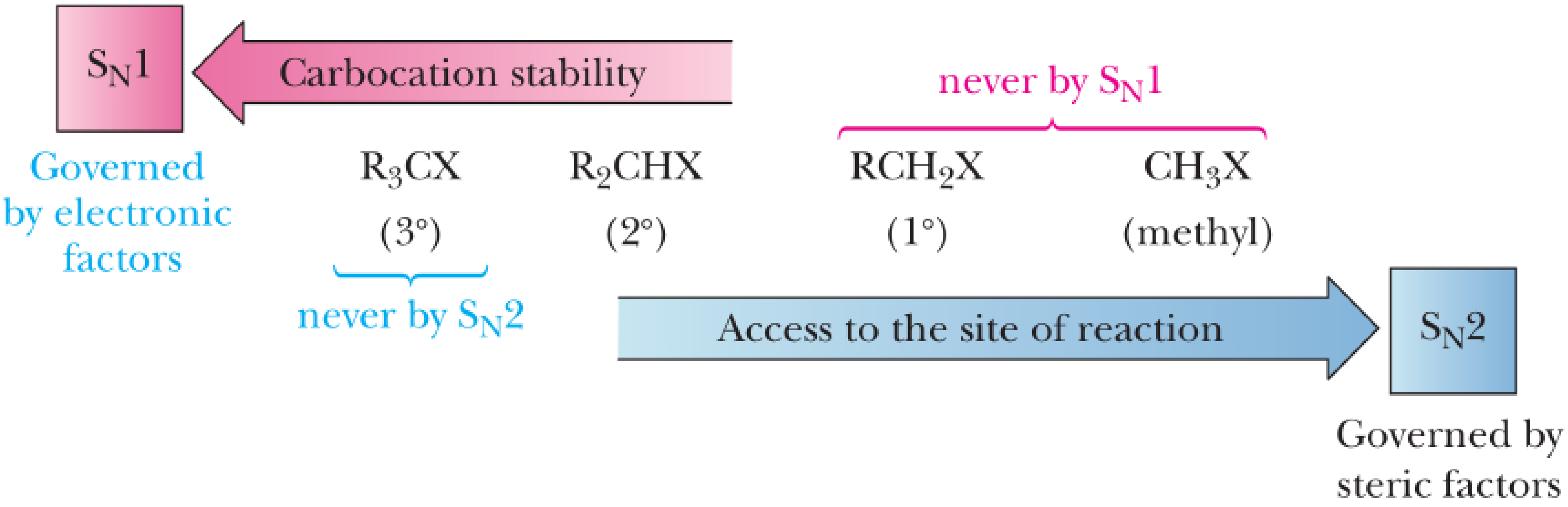
RX结构越简单越倾向于SN2



Bromoethane (Ethyl bromide)



2-Bromo-2-methylpropane (*tert*-Butyl bromide)



S_N1 ← Carbocation stability

Governed by electronic factors

never by S_N1

R_3CX	R_2CHX	RCH_2X	CH_3X
(3°)	(2°)	(1°)	(methyl)

never by S_N2

Access to the site of reaction → S_N2

Governed by steric factors

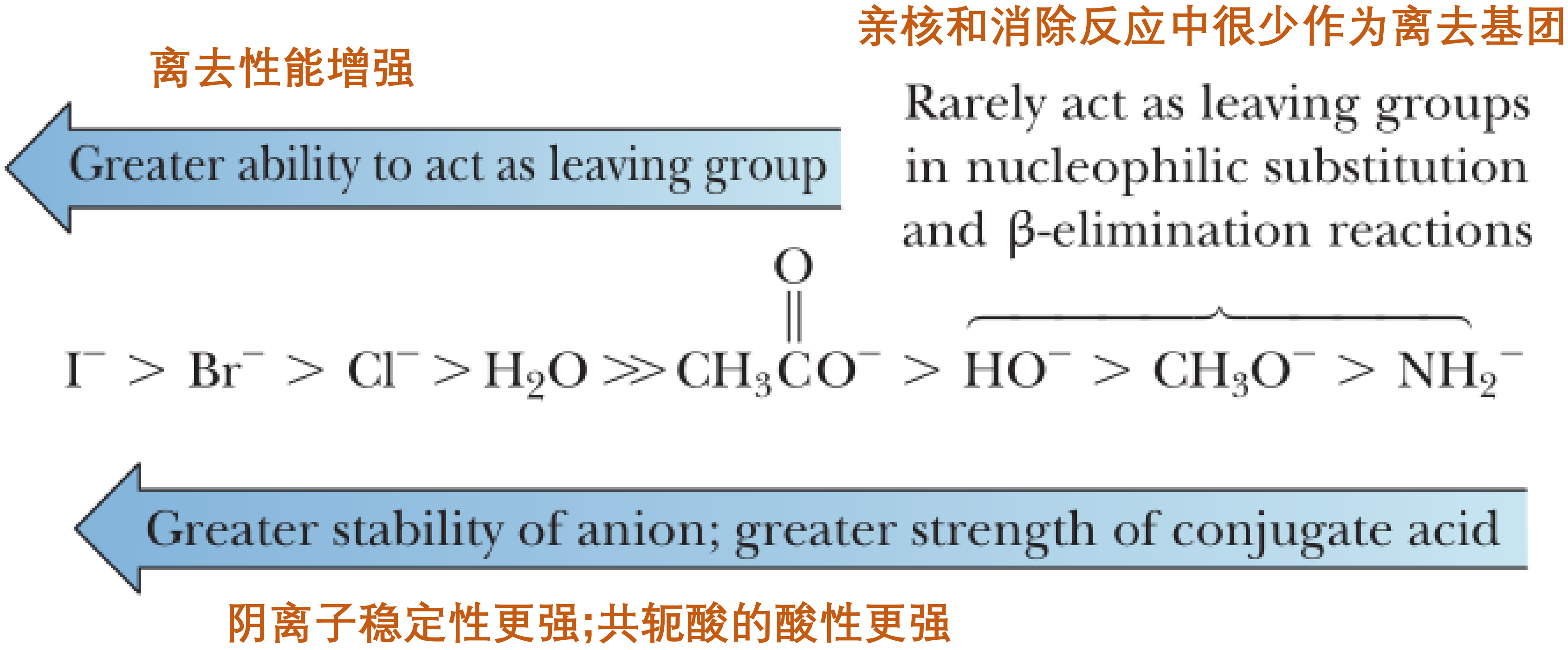
小结: 普通卤代烃的S_N反应

对S_N1反应： 3ºRX > 2ºRX > 1ºRX

对S_N2反应： 1º RX > 2ºRX > 3ºRX

叔卤代烷主要进行S_N1反应，伯卤代烷主要进行S_N2反应，仲卤代烷两种历程均可，由反应条件决定。

C. The leaving group



离去性能增强

Greater ability to act as leaving group

亲核和消除反应中很少作为离去基团

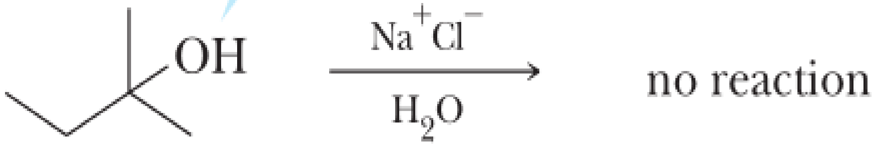
Rarely act as leaving groups in nucleophilic substitution and β-elimination reactions

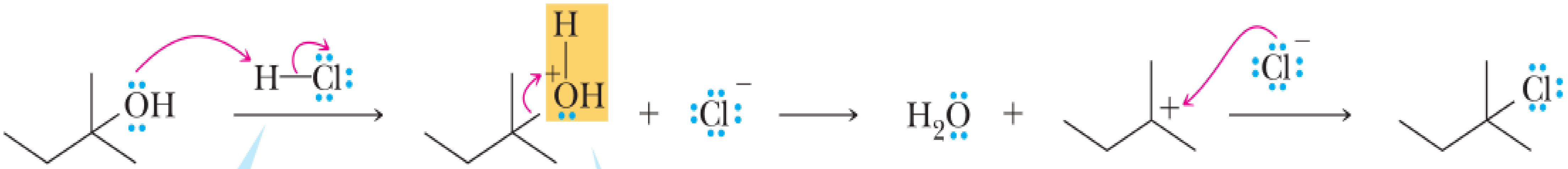
$$I^- > Br^- > Cl^- > H_2O \gg CH_3\overset{\overset{O}{\|}}{C}O^- > \overbrace{HO^- > CH_3O^- > NH_2^-}$$

Greater stability of anion; greater strength of conjugate acid

阴离子稳定性更强;共轭酸的酸性更强

an —OH group is a poor leaving group and does not undergo substitution





a strong acid can protonate the —OH group

H_2O is a good leaving group because it is a stable, neutral molecule

D. The Solvent

Protic solvent（质子溶剂）： A hydrogen bond donor solvent as（氢键的供体）, for example, water, ethanol, and acetic acid. We define hydrogen bond donors as compounds containing hydrogens that can participate in H-bonding（含有H并能参与氢键的形成）.

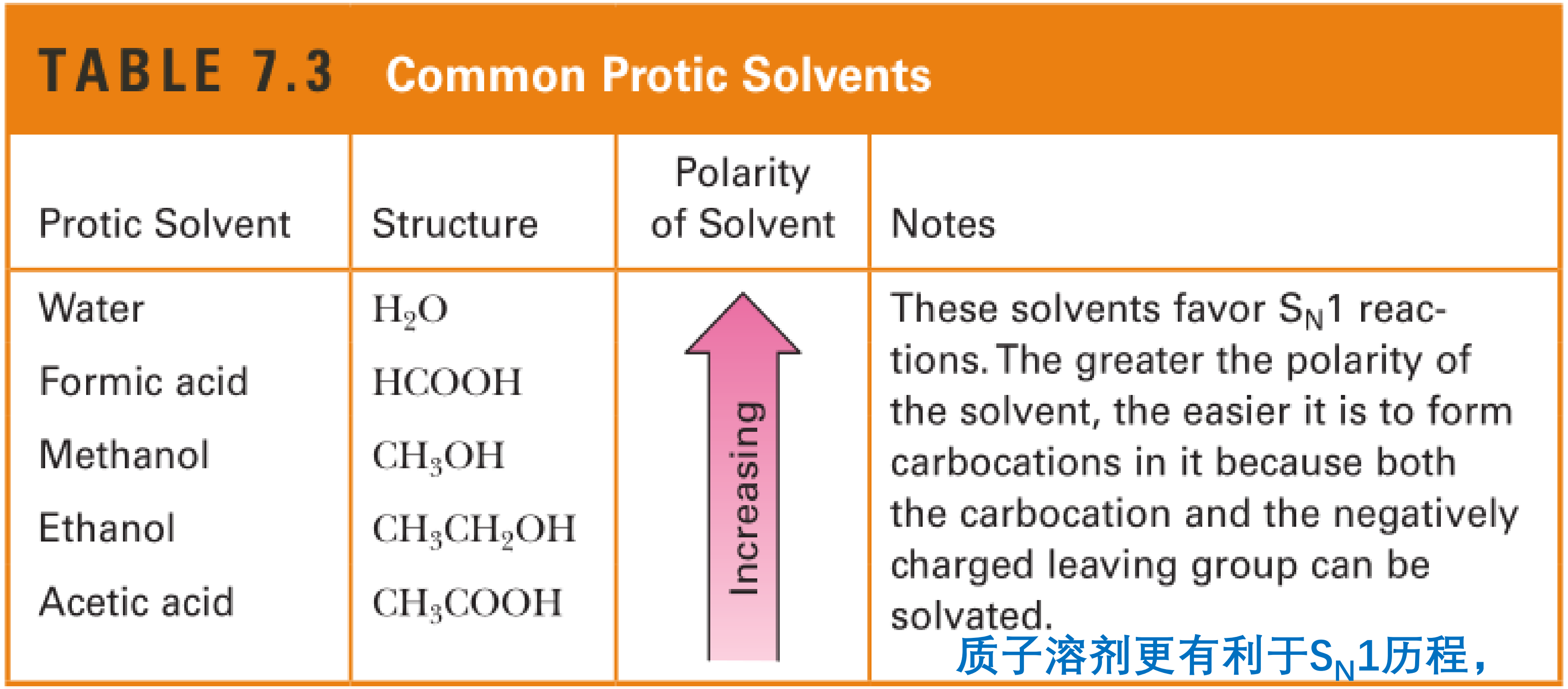
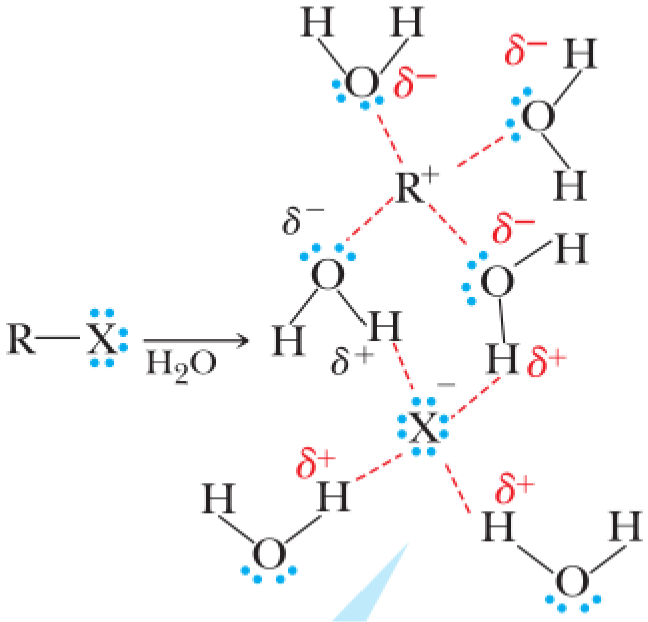


TABLE 7.3 Common Protic Solvents

Protic Solvent	Structure	Polarity of Solvent	Notes
Water	H_2O	Increasing	These solvents favor S_N1 reactions. The greater the polarity of the solvent, the easier it is to form carbocations in it because both the carbocation and the negatively charged leaving group can be solvated.
Formic acid	$HCOOH$		
Methanol	CH_3OH		
Ethanol	CH_3CH_2OH		
Acetic acid	CH_3COOH		

质子溶剂更有利于S_N1历程，



Aprotic solvent A solvent that cannot serve as a hydrogen bond donor as, for example, acetone, diethyl ether(乙醚), and dichloromethane（CH_2Cl_2）.

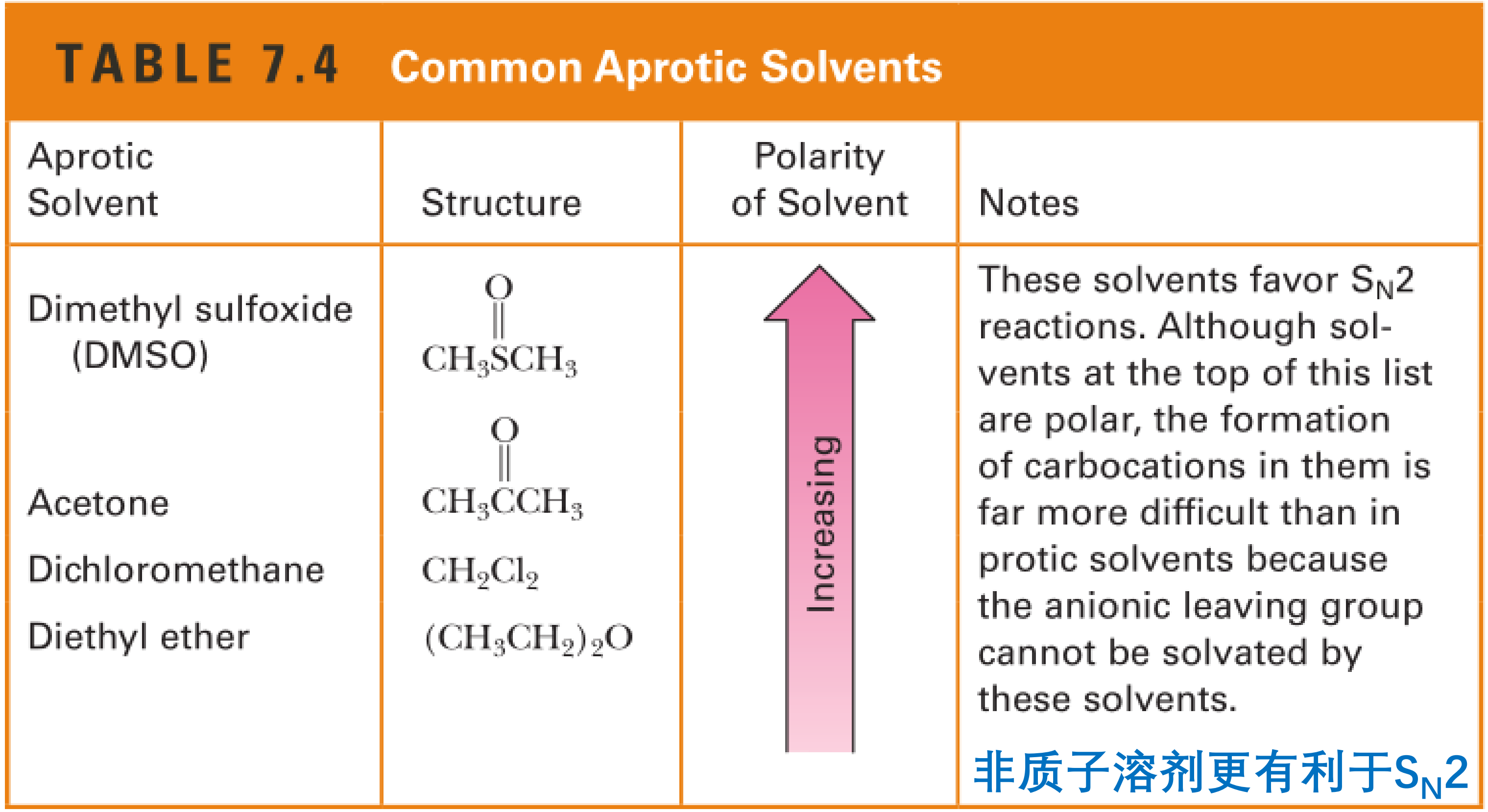


TABLE 7.4 Common Aprotic Solvents

Aprotic Solvent	Structure	Polarity of Solvent	Notes
Dimethyl sulfoxide (DMSO)	$CH_3\overset{\overset{O}{\|}}{S}CH_3$	↑ Increasing	These solvents favor S_N2 reactions. Although solvents at the top of this list are polar, the formation of carbocations in them is far more difficult than in protic solvents because the anionic leaving group cannot be solvated by these solvents. 非质子溶剂更有利于S_N2
Acetone	$CH_3\overset{\overset{O}{\|}}{C}CH_3$		
Dichloromethane	CH_2Cl_2		
Diethyl ether	$(CH_3CH_2)_2O$		

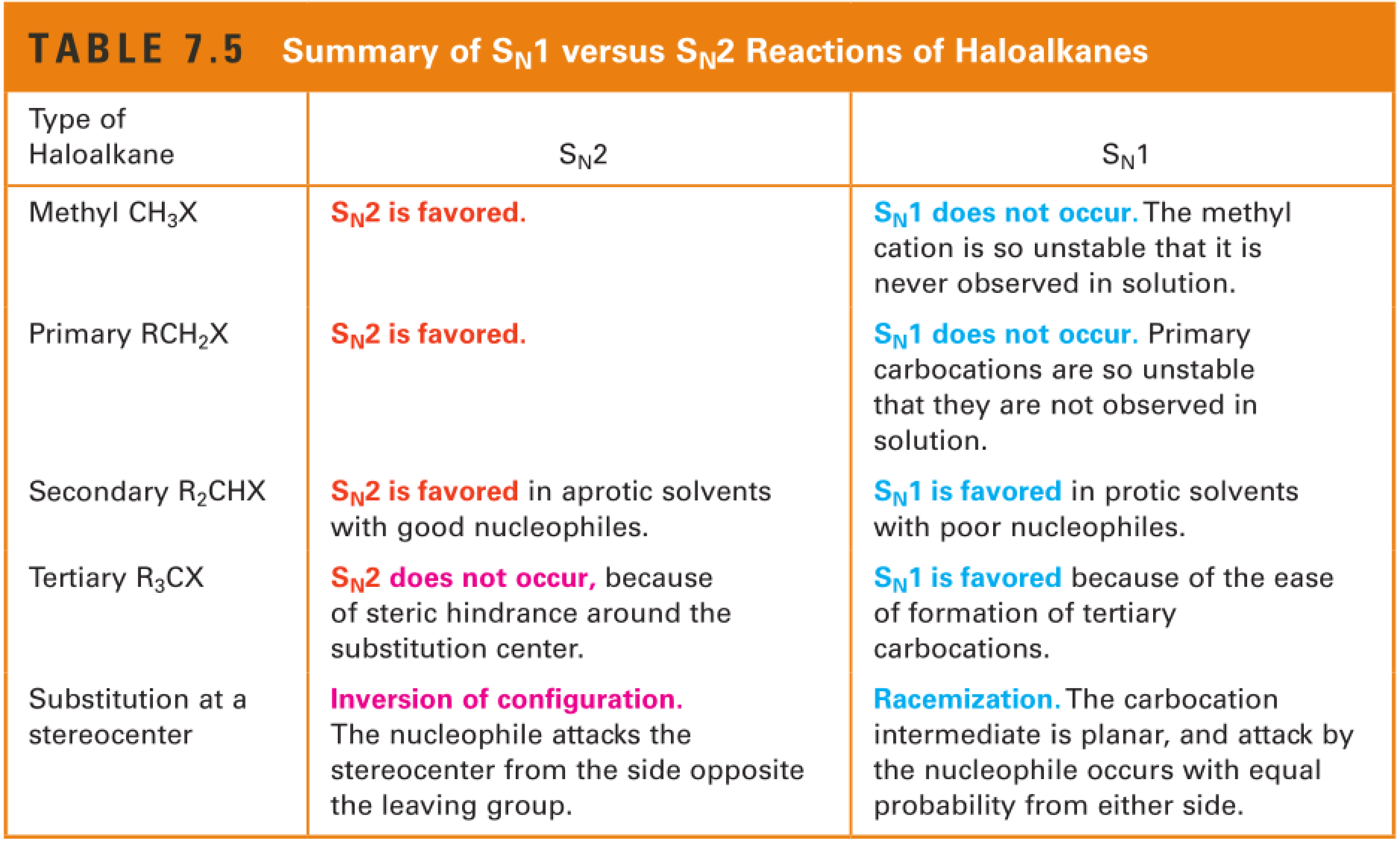
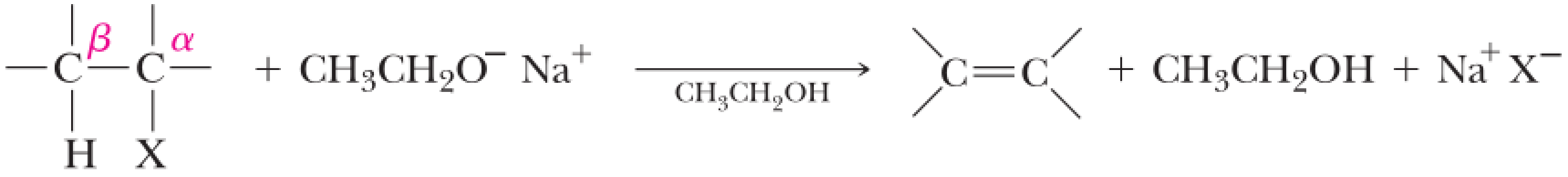


TABLE 7.5 Summary of S_N1 versus S_N2 Reactions of Haloalkanes

Type of Haloalkane	S_N2	S_N1
Methyl CH_3X	**S_N2 is favored.**	**S_N1 does not occur.** The methyl cation is so unstable that it is never observed in solution.
Primary RCH_2X	**S_N2 is favored.**	**S_N1 does not occur.** Primary carbocations are so unstable that they are not observed in solution.
Secondary R_2CHX	**S_N2 is favored** in aprotic solvents with good nucleophiles.	**S_N1 is favored** in protic solvents with poor nucleophiles.
Tertiary R_3CX	**S_N2 does not occur,** because of steric hindrance around the substitution center.	**S_N1 is favored** because of the ease of formation of tertiary carbocations.
Substitution at a stereocenter	**Inversion of configuration.** The nucleophile attacks the stereocenter from the side opposite the leaving group.	**Racemization.** The carbocation intermediate is planar, and attack by the nucleophile occurs with equal probability from either side.

7.7 What Are the Products of Β-Elimination?

Dehydrohalogenation（脱HX） Removal of -H and -X from adjacent carbons; a type of β-elimination.

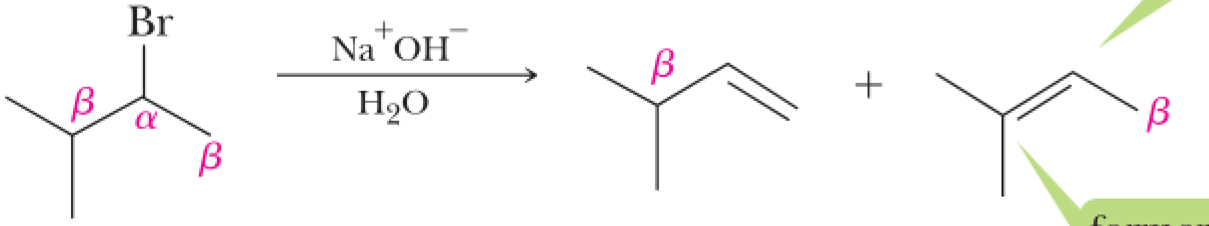


$$-\overset{|}{\underset{\underset{H}{|}}{C}}^{\beta}-\overset{|}{\underset{\underset{X}{|}}{C}}^{\alpha}- + CH_3CH_2O^- Na^+ \xrightarrow[CH_3CH_2OH]{} \rangle C{=}C\langle + CH_3CH_2OH + Na^+X^-$$

A haloalkane

Base

An alkene



formerly the α-carbon

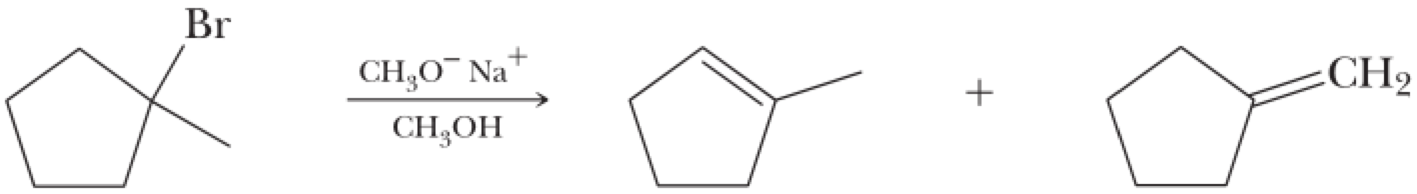
formerly a β-carbon

Zaitsev's rule A rule stating that the major product from a β-elimination reaction is the most stable alkene; that is, the major product is the alkene with the greatest number of substituents on the carbon–carbon double bond（双键上连有较多取代基的烯烃）.

2-Bromo-2-methylbutane

2-Methyl-2-butene (major product)

2-Methyl-1-butene



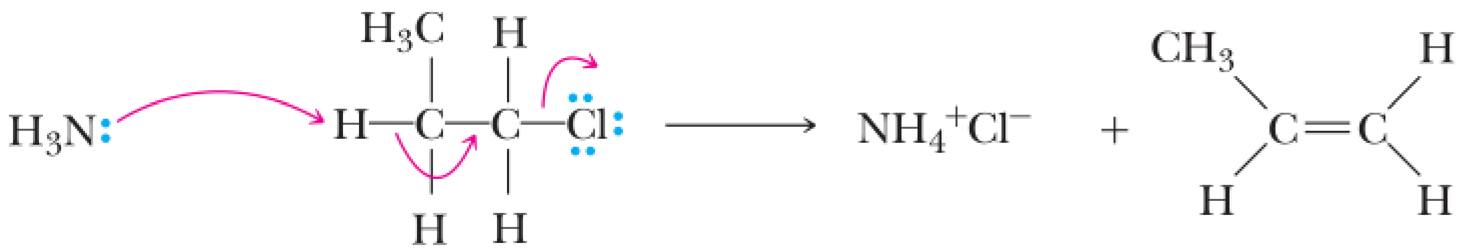
1-Bromo-1-methylcyclopentane

1-Methylcyclopentene (major product)

Methylenecyclopentane

7.8 What Are the E1 and E2 Mechanisms for β-Elimination?

Correct use of curved arrows...

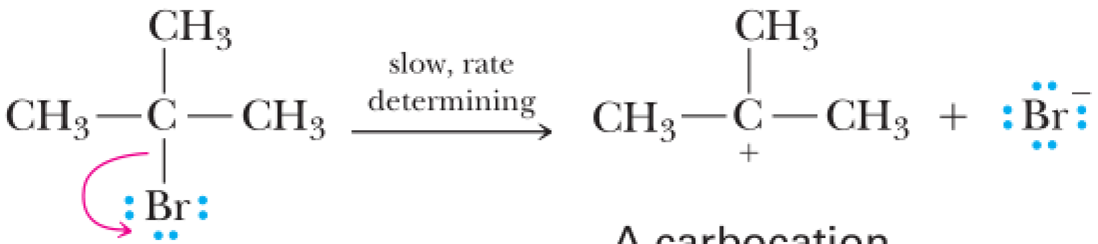


A. E1 Mechanism

$$\boxed{\text{Rate} = k[\text{haloalkane}]}$$

E1 reaction of 2-bromo-2-methylpropaneE

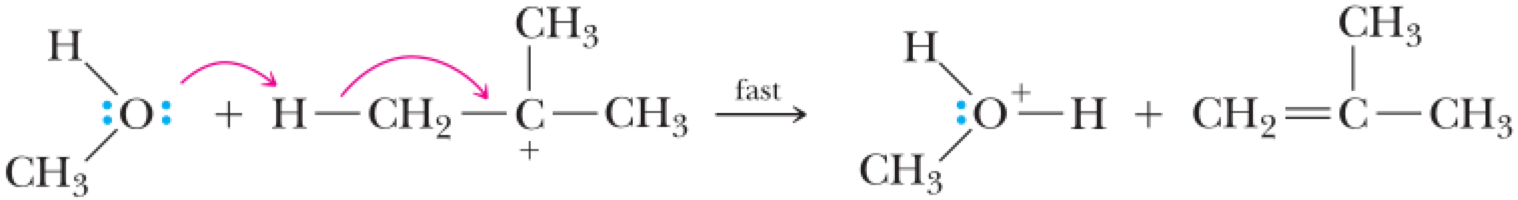
STEP 1: Break a bond. Rate-determining ionization of the C—Br bond gives a carbocation intermediate:



$$CH_3-\overset{CH_3}{\underset{Br}{C}}-CH_3 \xrightarrow[\text{determining}]{\text{slow, rate}} CH_3-\overset{CH_3}{\underset{+}{C}}-CH_3 + Br^-$$

A carbocation intermediate

STEP 2: Take away a proton. Proton transfer from the carbocation intermediate to methanol (which in this instance is both the solvent and a reactant) gives the alkene:



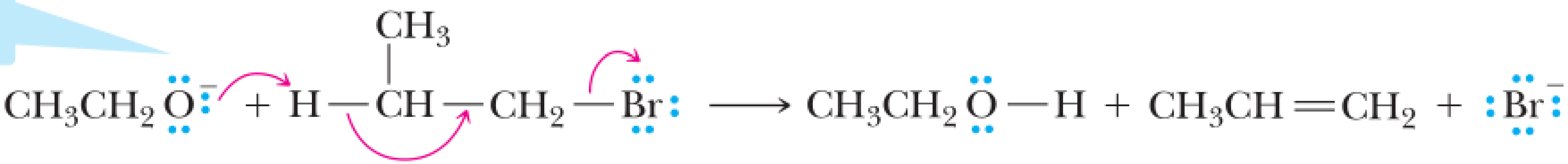
$$CH_3-O-H + H-CH_2-\overset{CH_3}{\underset{+}{C}}-CH_3 \xrightarrow{\text{fast}} CH_3-\overset{+}{O}H-H + CH_2=\overset{CH_3}{C}-CH_3$$

B. E2 Mechanism

$$\boxed{\text{Rate} = k[\text{haloalkane}][\text{base}]}$$

E2 reaction of 1-bromopropane

the E2 mechanism is concerted



$$CH_3CH_2\ddot{\underset{\cdot\cdot}{O}}{:}^- + H-\overset{\displaystyle CH_3}{\overset{|}{CH}}-CH_2-\ddot{\underset{\cdot\cdot}{Br}}{:} \longrightarrow CH_3CH_2\ddot{\underset{\cdot\cdot}{O}}-H + CH_3CH{=}CH_2 + {:}\ddot{\underset{\cdot\cdot}{Br}}{:}^-$$

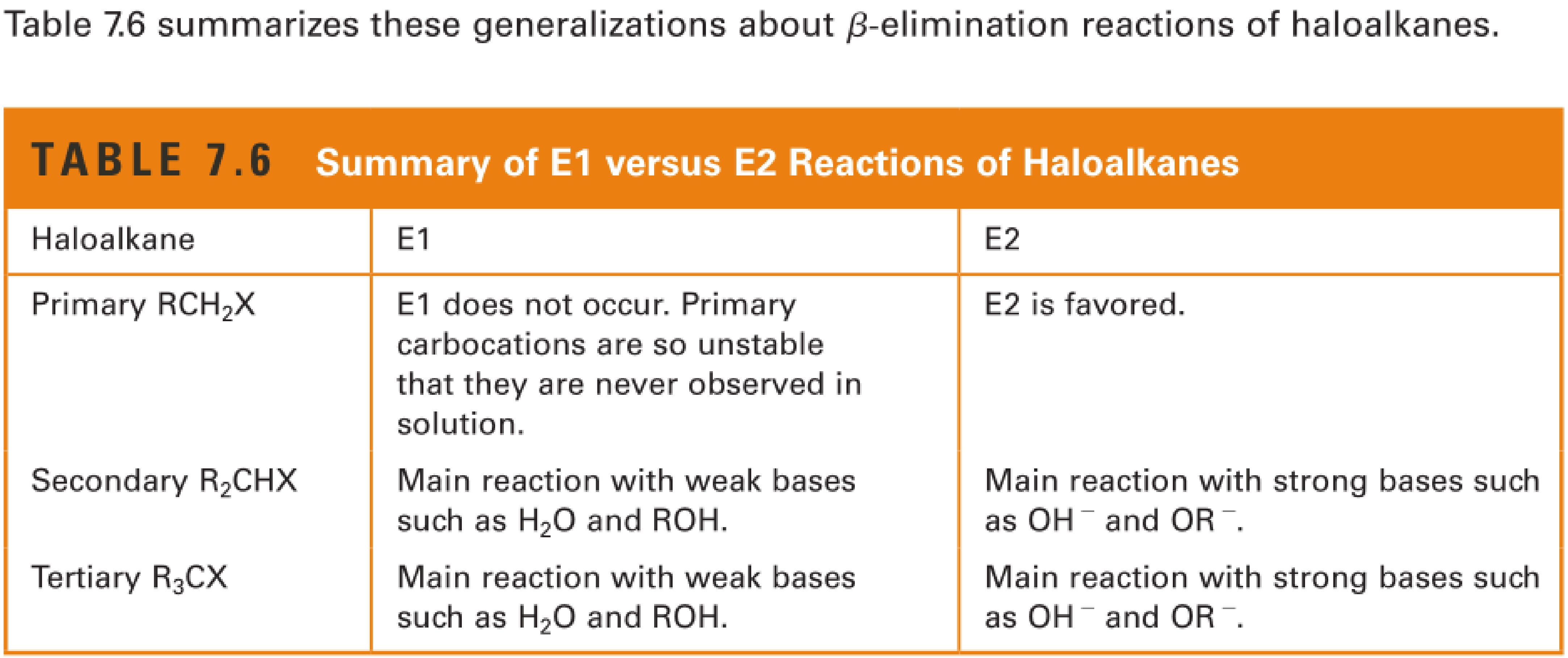


Table 7.6 summarizes these generalizations about β-elimination reactions of haloalkanes.

TABLE 7.6 Summary of E1 versus E2 Reactions of Haloalkanes

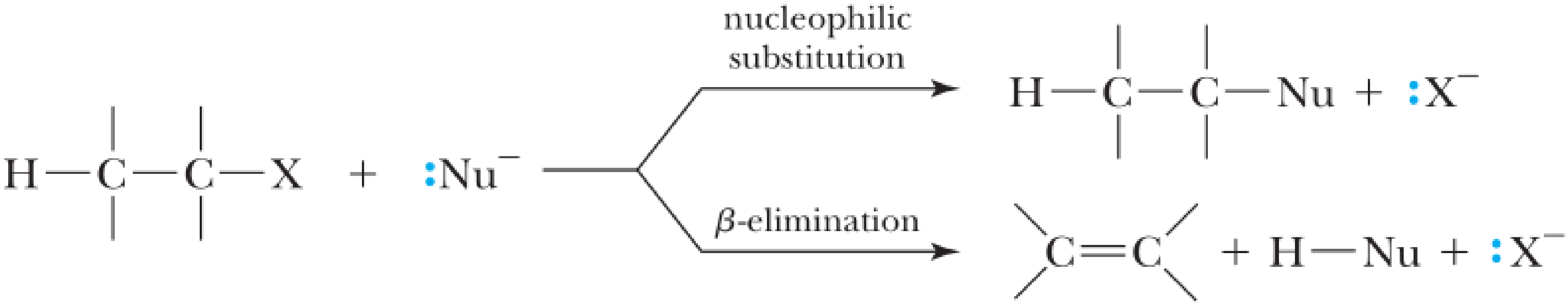
Haloalkane	E1	E2
Primary RCH_2X	E1 does not occur. Primary carbocations are so unstable that they are never observed in solution.	E2 is favored.
Secondary R_2CHX	Main reaction with weak bases such as H_2O and ROH.	Main reaction with strong bases such as OH^- and OR^-.
Tertiary R_3CX	Main reaction with weak bases such as H_2O and ROH.	Main reaction with strong bases such as OH^- and OR^-.

Predict the Type of Β-Elimination Reaction a Haloalkane Will Undergo

(a) Classify the structure of the haloalkane. Primary haloalkanes will not undergo E1 reactions. Secondary and tertiary haloalkanes will undergo both E1 and E2 reactions.（伯卤代烷不发生E1反应；仲、叔卤代烷可以发生E1和E2反应）

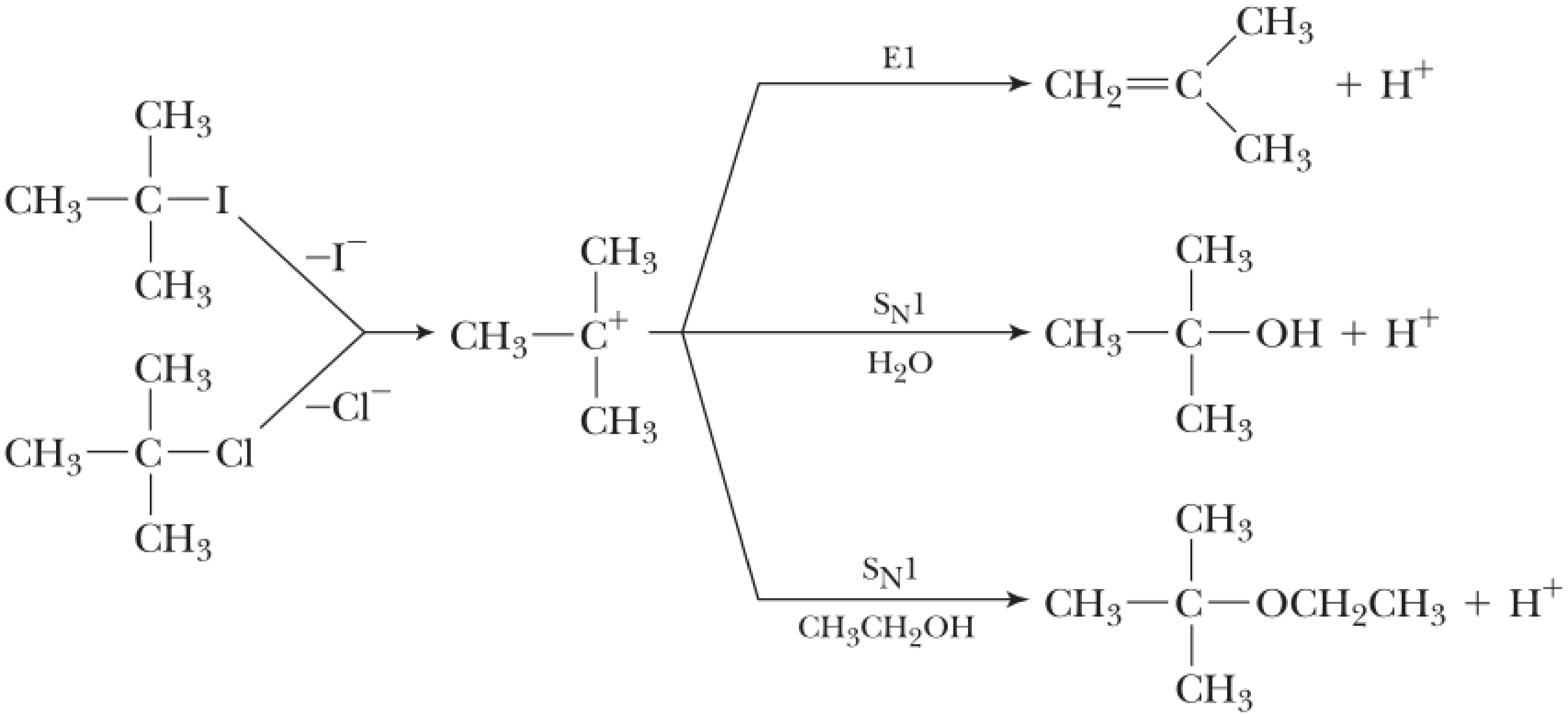
(b) Identify and assess the base. E2 reactions are favored with strong bases and rarely occur with weak bases. E2 reactions can occur in any solvent. E1 reactions can occur with both weak and strong bases, but require polar protic solvents to stabilize the carbocation formed in the first step of the reaction.（强碱更有利于E2， E2 可以发生在任何溶剂中；E1在弱碱和强碱中都能发生，但是需要极性的质子化溶剂）

7.9 When Do Nucleophilic Substitution and β-Elimination Compete?



取代和消除反应同时存在、相互竞争

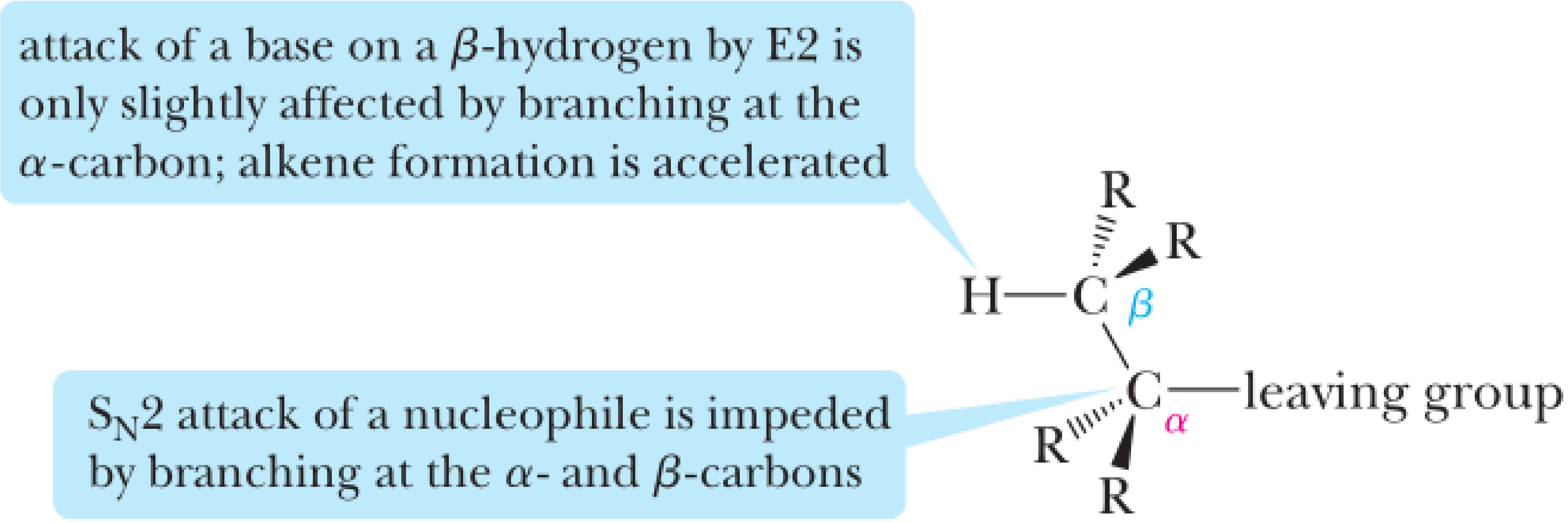
A. S_N 1-versus-E1 Reactions


$(CH_3)_3C-I$
$-I^-$
$(CH_3)_3C-Cl$
$-Cl^-$
$(CH_3)_3C^+$
E1
$CH_2=C(CH_3)_2 + H^+$
S_N1
H_2O
$(CH_3)_3C-OH + H^+$
S_N1
CH_3CH_2OH
$(CH_3)_3C-OCH_2CH_3 + H^+$

B. S_N2-versus-E2 Reactions

1. Branching at the α-carbon or β-carbon(s) increases steric hindrance about the α-carbon and significantly retards S_N2 reactions. By contrast, branching at the α-carbon or β-carbon(s) increases the rate of E2 reactions because of the increased stability of the alkene product.
（α-C/ β-C(s)上支链增加，位阻增加，烯烃稳定性增加，更有利于E2）

2. The greater the nucleophilicity of the attacking reagent, the greater is the S_N2-to-E2 ratio. Conversely, the greater the basicity of the attacking reagent, the greater is the E2-to-S_N2 ratio. （亲核性强有利于SN2，碱性强有利于E2）


attack of a base on a *β*-hydrogen by E2 is only slightly affected by branching at the *α*-carbon; alkene formation is accelerated

S_N2 attack of a nucleophile is impeded by branching at the *α*- and *β*-carbons

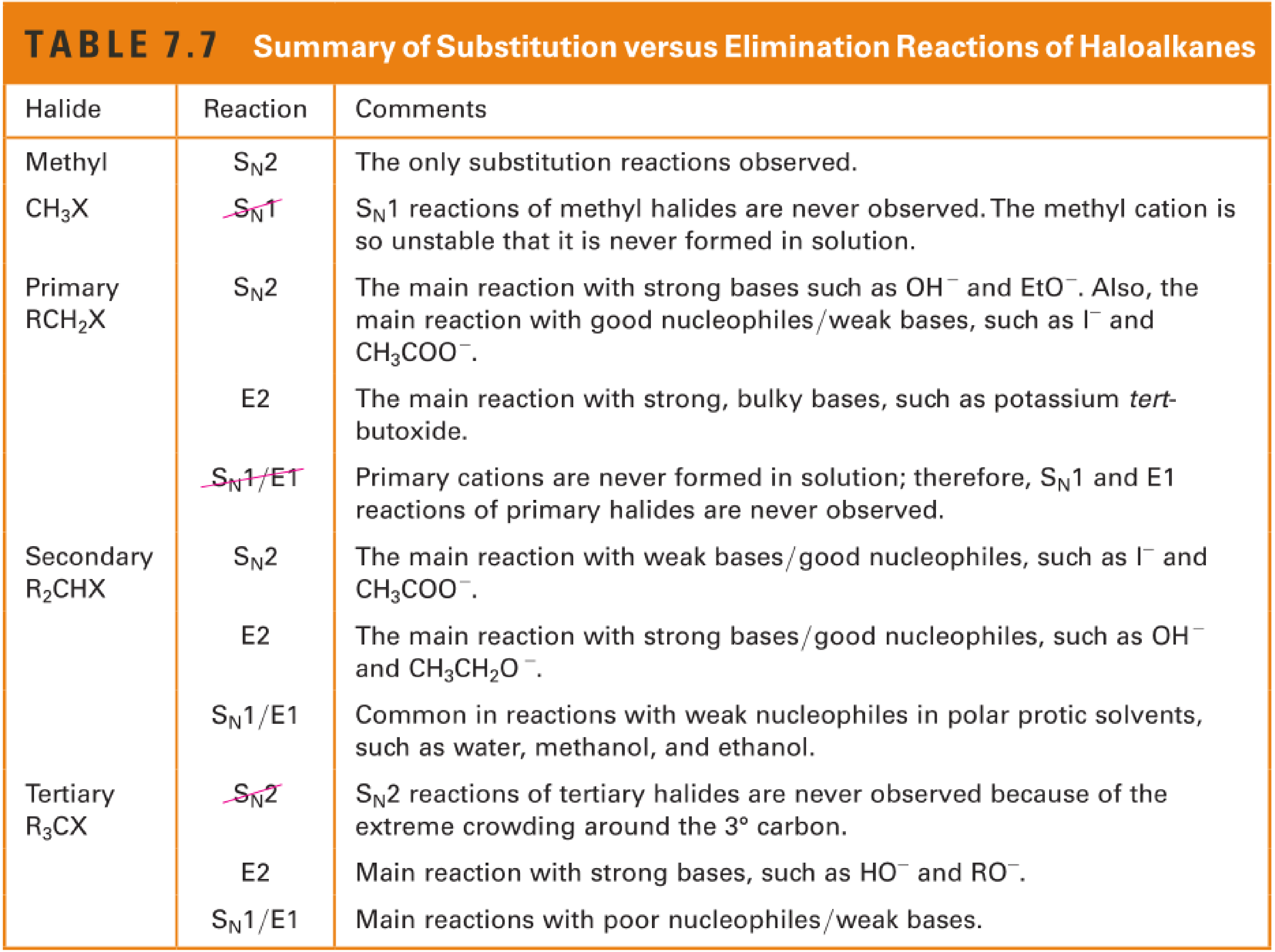


TABLE 7.7 Summary of Substitution versus Elimination Reactions of Haloalkanes

Halide	Reaction	Comments
Methyl	S_N2	The only substitution reactions observed.
CH_3X	~~S_N1~~	S_N1 reactions of methyl halides are never observed. The methyl cation is so unstable that it is never formed in solution.
Primary RCH_2X	S_N2	The main reaction with strong bases such as OH^- and EtO^-. Also, the main reaction with good nucleophiles/weak bases, such as I^- and CH_3COO^-.
	E2	The main reaction with strong, bulky bases, such as potassium *tert*-butoxide.
	~~S_N1/E1~~	Primary cations are never formed in solution; therefore, S_N1 and E1 reactions of primary halides are never observed.
Secondary R_2CHX	S_N2	The main reaction with weak bases/good nucleophiles, such as I^- and CH_3COO^-.
	E2	The main reaction with strong bases/good nucleophiles, such as OH^- and $CH_3CH_2O^-$.
	S_N1/E1	Common in reactions with weak nucleophiles in polar protic solvents, such as water, methanol, and ethanol.
Tertiary R_3CX	~~S_N2~~	S_N2 reactions of tertiary halides are never observed because of the extreme crowding around the 3° carbon.
	E2	Main reaction with strong bases, such as HO^- and RO^-.
	S_N1/E1	Main reactions with poor nucleophiles/weak bases.

作　业

7.9 、7.10（a、c、e）、7.19、7.20、7.21、7.22（a、b、c、e）、7.25、7.26、7.29、7.36