

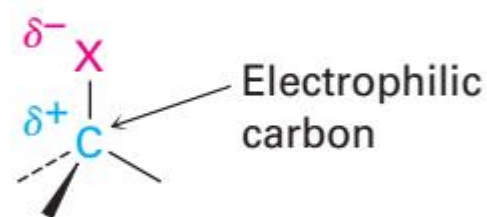
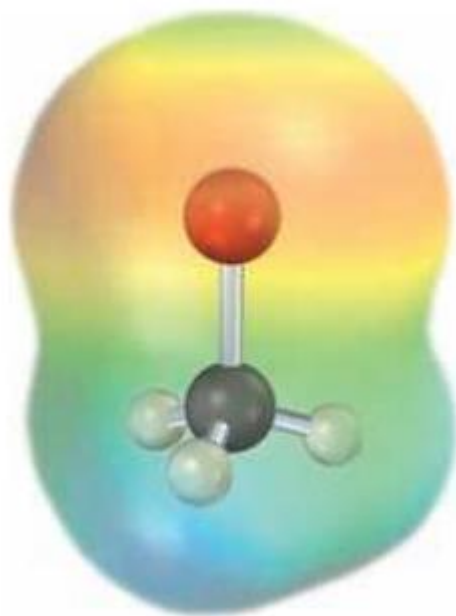
Organic Chemistry

CHE 203

Lecture 10: reactions of organohalides

Le Quoc Chon – Duy Tan University

C-X bond is polar (liên kết C-X phân cực)



C nghèo electrons nên đóng vai trò là tác nhân ái điện tử

Reactions of alkyl halides

(phản ứng của dẫn xuất halogen)

Nucleophilic substitution (SN2, SN1)

Elimination reaction (E2, E1, E1cB)

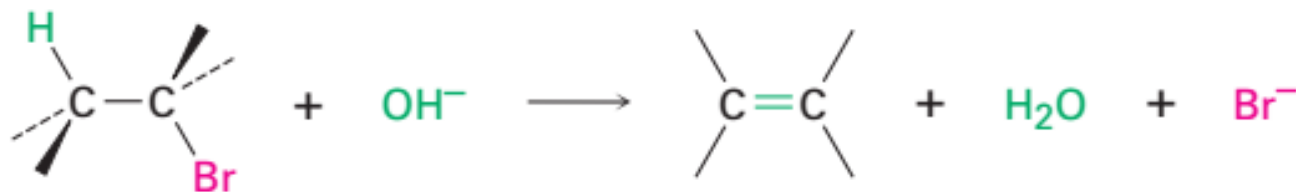
Substitution

(ví dụ)



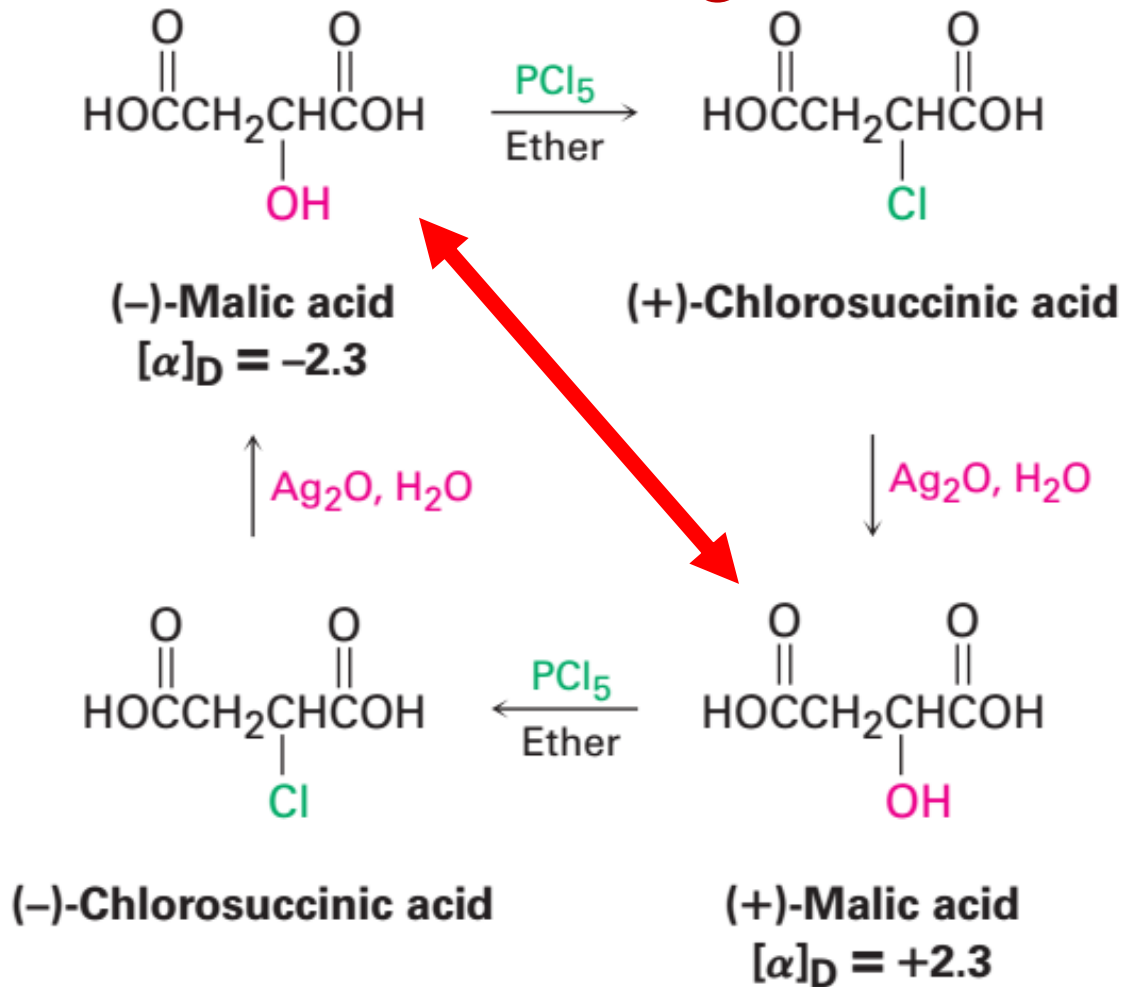
Elimination

(ví dụ)



Nucleophilic substitution reaction

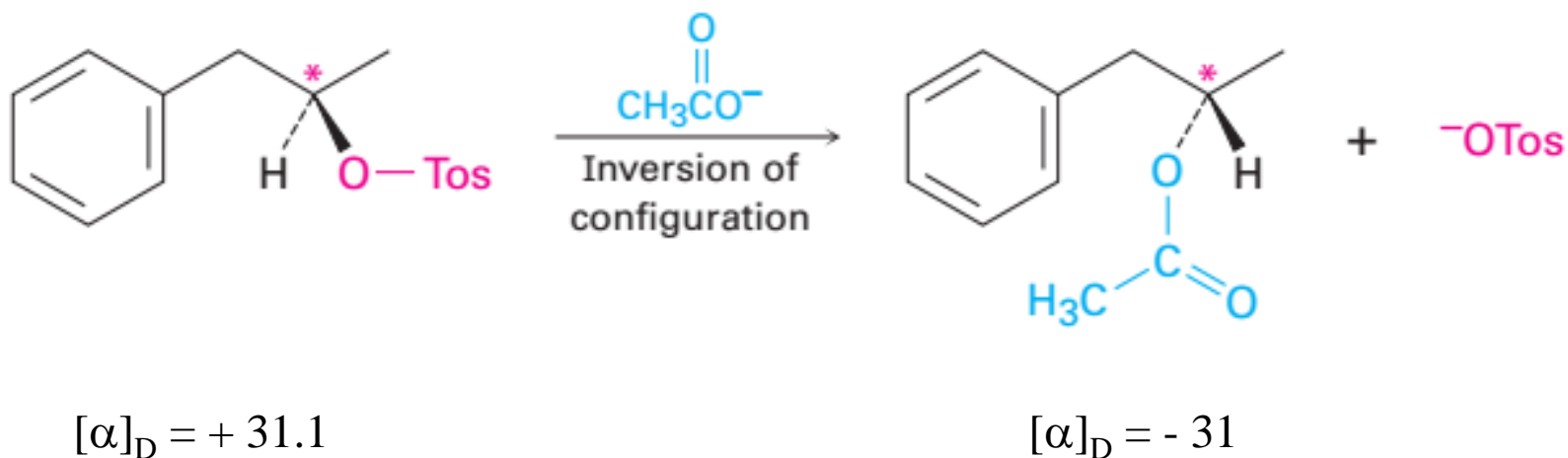
Phản ứng thế ái nhân.



discovered 1896
by Paul Walden

How?

Nucleophilic substitution reaction



Change of configuration!

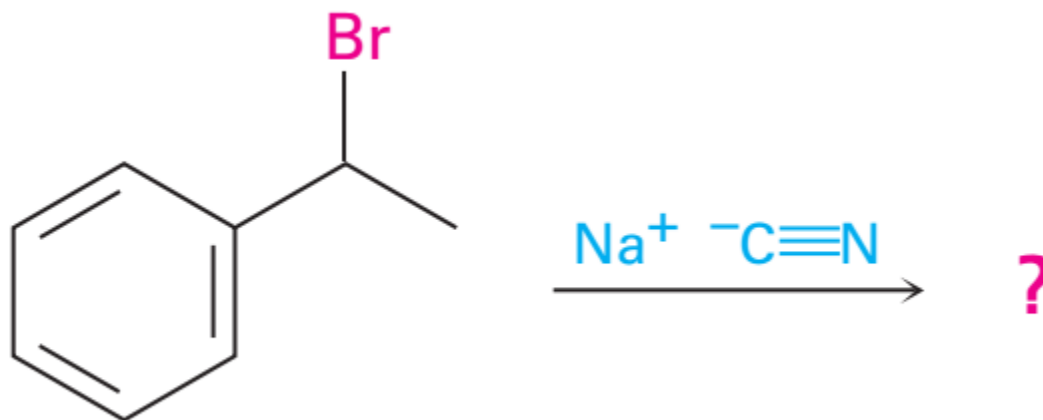
Nucleophilic substitution reaction



Change of configuration!

Problem

(viết sản phẩm phản ứng)



(S)-1-Bromo-1-phenylethane

Giả sử sự chuyển đổi cấu hình S \Rightarrow R xảy ra

S_N2 reaction

(substitution, nucleophilic, bimolecular)



(vận tốc phản ứng = vận tốc tiêu thụ chất phản ứng)

$$\begin{aligned}\text{Reaction rate} &= \text{Rate of disappearance of reactant} \\ &= k \times [\text{RX}] \times [\text{OH}^-]\end{aligned}$$

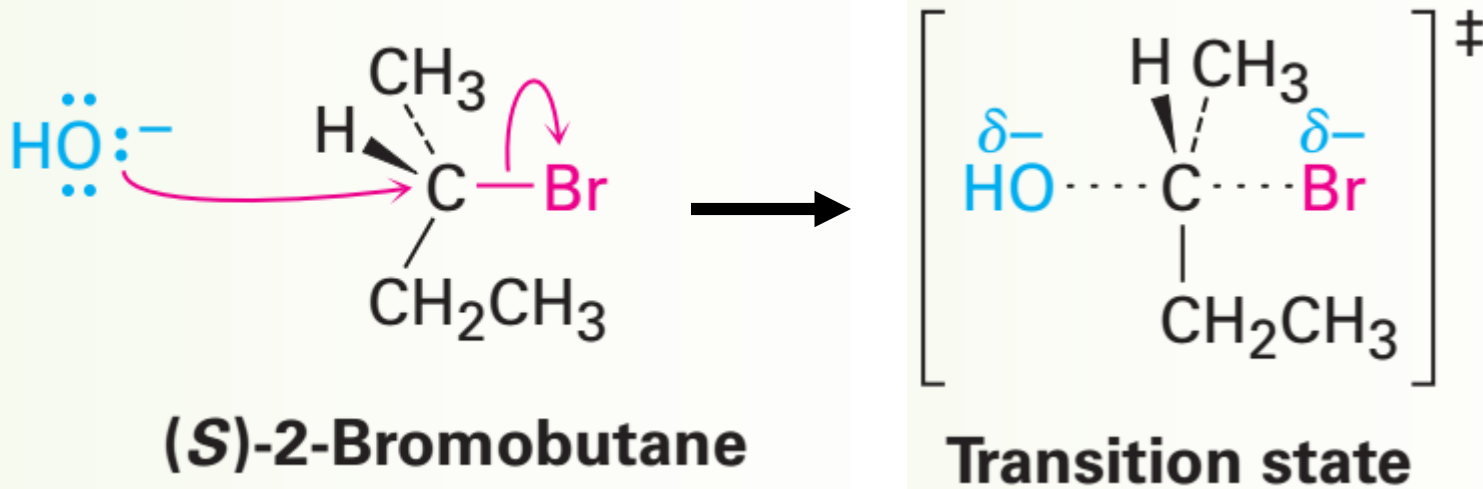
where

[RX] = CH₃Br concentration in molarity

[OH⁻] = OH⁻ concentration in molarity

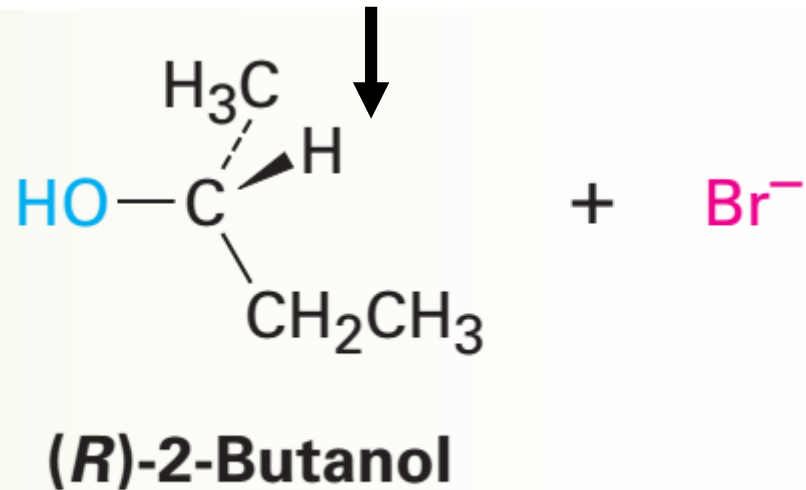
k = a constant value (the rate constant)

S_N2 mechanism (cơ chế phản ứng S_N2)

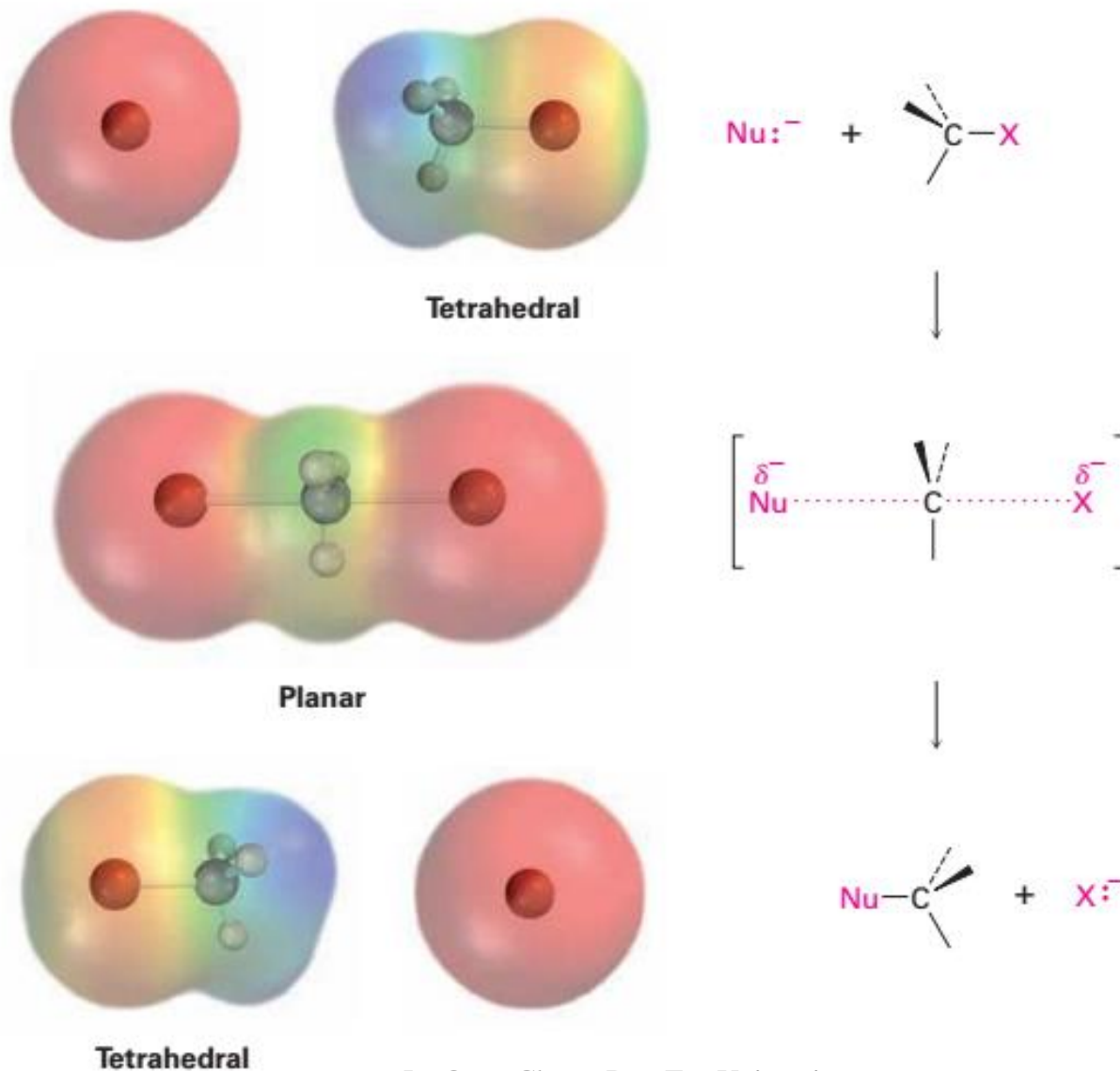


Configuration?

$^-$ OH phản ứng theo hướng ngược với Br



S_N2 mechanism



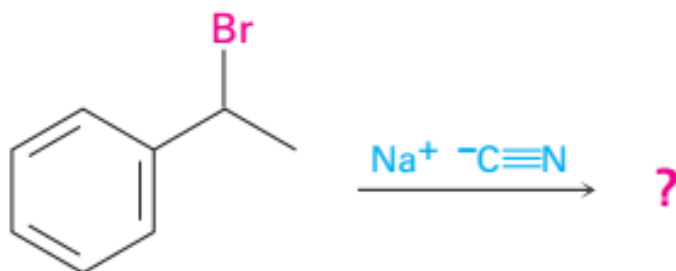
Ingold and Hughes

Prof Edward D Hughes



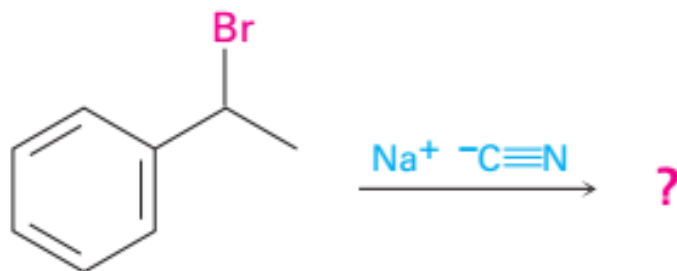
Problem 1

What product would you expect from a nucleophilic substitution reaction of (*R*)-1-bromo-1-phenylethane with cyanide ion, ${}^{-}\text{C}\equiv\text{N}$, as nucleophile? Show the stereochemistry of both reactant and product, assuming that inversion of configuration occurs.



Problem 1

What product would you expect from a nucleophilic substitution reaction of (*R*)-1-bromo-1-phenylethane with cyanide ion, ${}^{-}\text{C}\equiv\text{N}$, as nucleophile? Show the stereochemistry of both reactant and product, assuming that inversion of configuration occurs.



Solution



(*R*)-1-Bromo-1-phenylethane

(*S*)-2-Phenylpropanenitrile

Problem

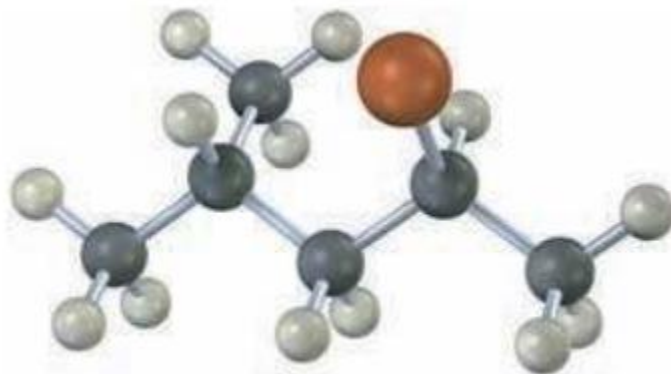
PROBLEM 11-2

What product would you expect to obtain from S_N2 reaction of OH^- with (*R*)-2-bromobutane? Show the stereochemistry of both the reactant and product.

Problem

PROBLEM 11-3

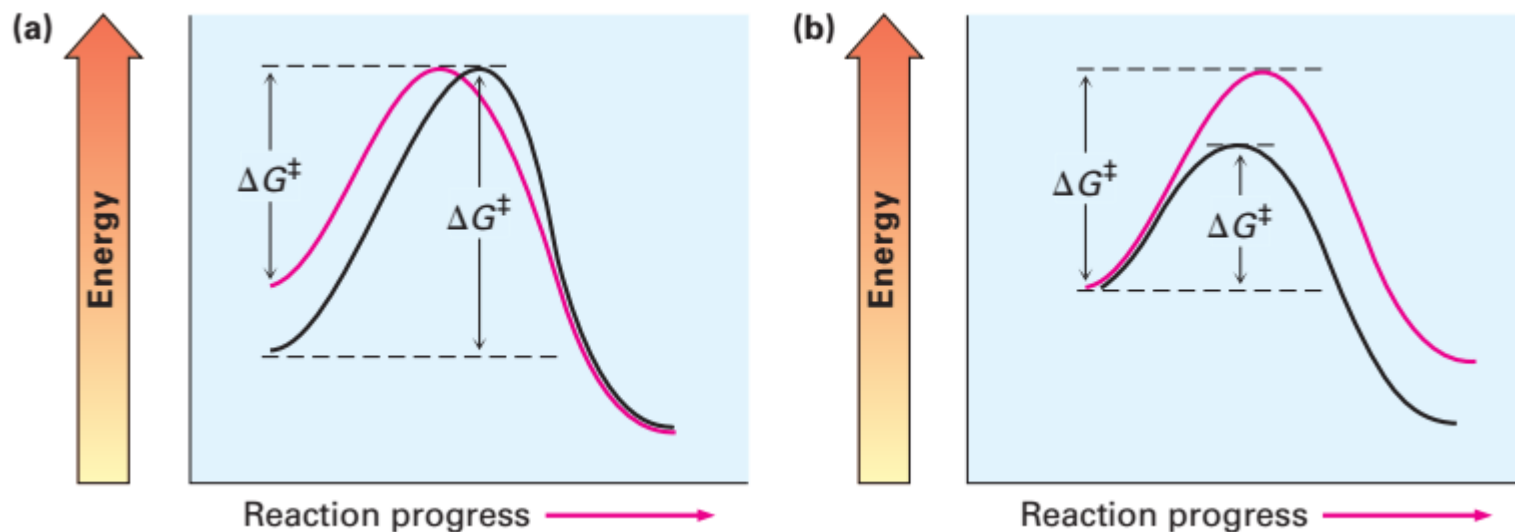
Assign configuration to the following substance, and draw the structure of the product that would result from nucleophilic substitution reaction with HS^- (reddish brown = Br):



Variables affect S_N2

(các yếu tố ảnh hưởng đến phản ứng S_N2)

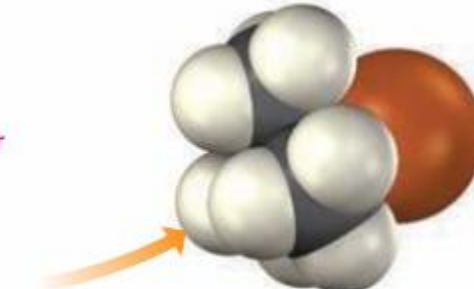
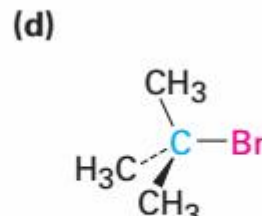
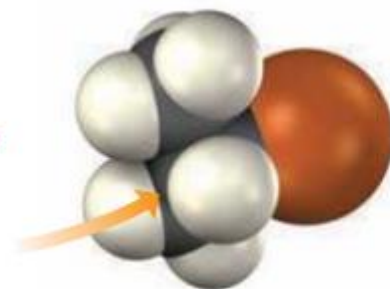
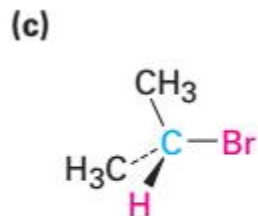
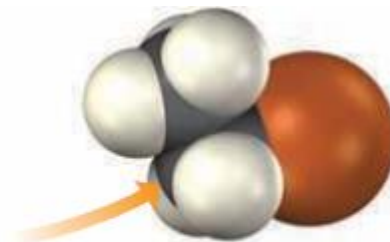
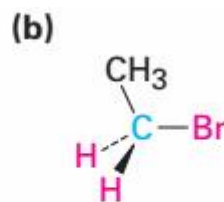
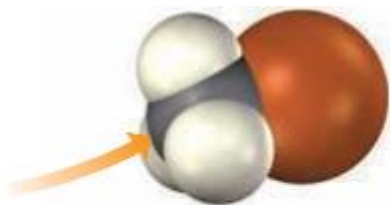
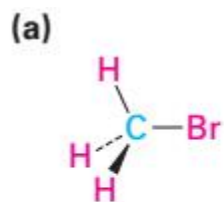
Năng lượng hoạt hóa, kích thước chất tham gia phản ứng...



Variables affect S_N2

(các yếu tố ảnh hưởng đến phản ứng S_N2)

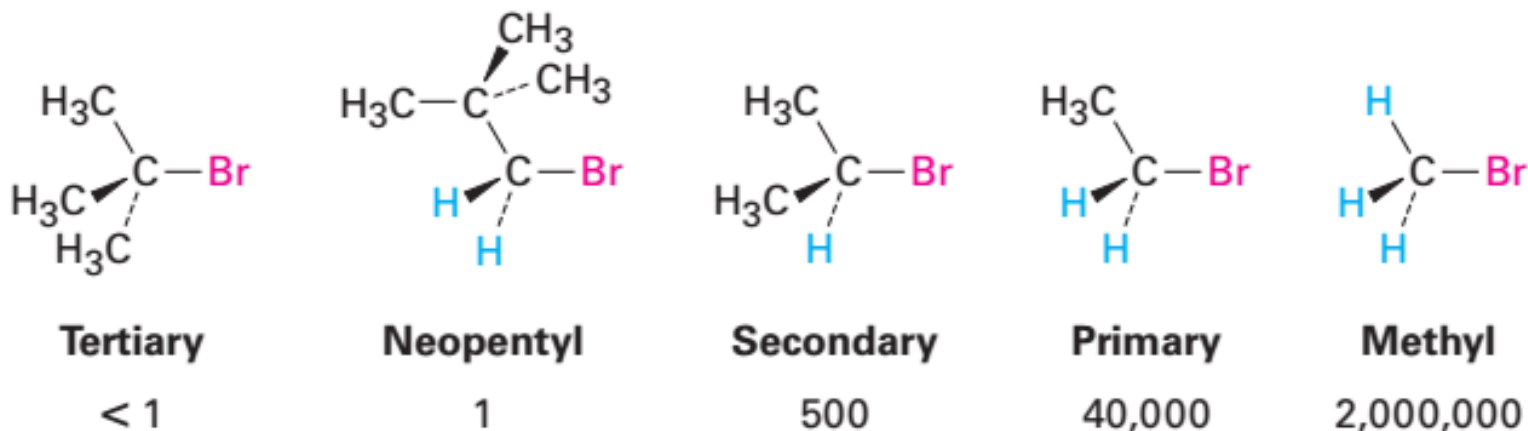
Năng lượng hoạt hóa, kích thước chất tham gia phản ứng...



Variables affect S_N2

(các yếu tố ảnh hưởng đến phản ứng S_N2)

Năng lượng hoạt hóa, kích thước chất tham gia phản ứng...



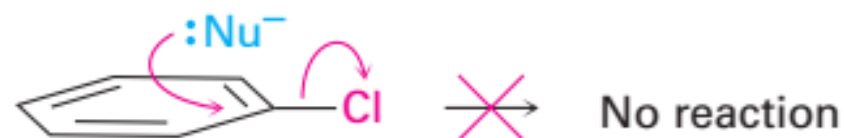
Variables affect S_N2

(các yếu tố ảnh hưởng đến phản ứng S_N2)



Nu:⁻

Vinylic halide



Aryl halide

Variables affect S_N2

TABLE 11-1 Some S_N2 Reactions with Bromomethane

$$\text{Nu:}^- + \text{CH}_3\text{Br} \rightarrow \text{CH}_3\text{Nu} + \text{Br}^-$$

Nucleophile		Product		Relative rate of reaction
Formula	Name	Formula	Name	
H ₂ O	Water	CH ₃ OH ₂ ⁺	Methylhydronium ion	1
CH ₃ CO ₂ ⁻	Acetate	CH ₃ CO ₂ CH ₃	Methyl acetate	500
NH ₃	Ammonia	CH ₃ NH ₃ ⁺	Methylammonium ion	700
Cl ⁻	Chloride	CH ₃ Cl	Chloromethane	1,000
HO ⁻	Hydroxide	CH ₃ OH	Methanol	10,000
CH ₃ O ⁻	Methoxide	CH ₃ OCH ₃	Dimethyl ether	25,000
I ⁻	Iodide	CH ₃ I	Iodomethane	100,000
⁻ CN	Cyanide	CH ₃ CN	Acetonitrile	125,000
HS ⁻	Hydrosulfide	CH ₃ SH	Methanethiol	125,000

Variables affect S_N2

Leaving group (nhóm rời đi)

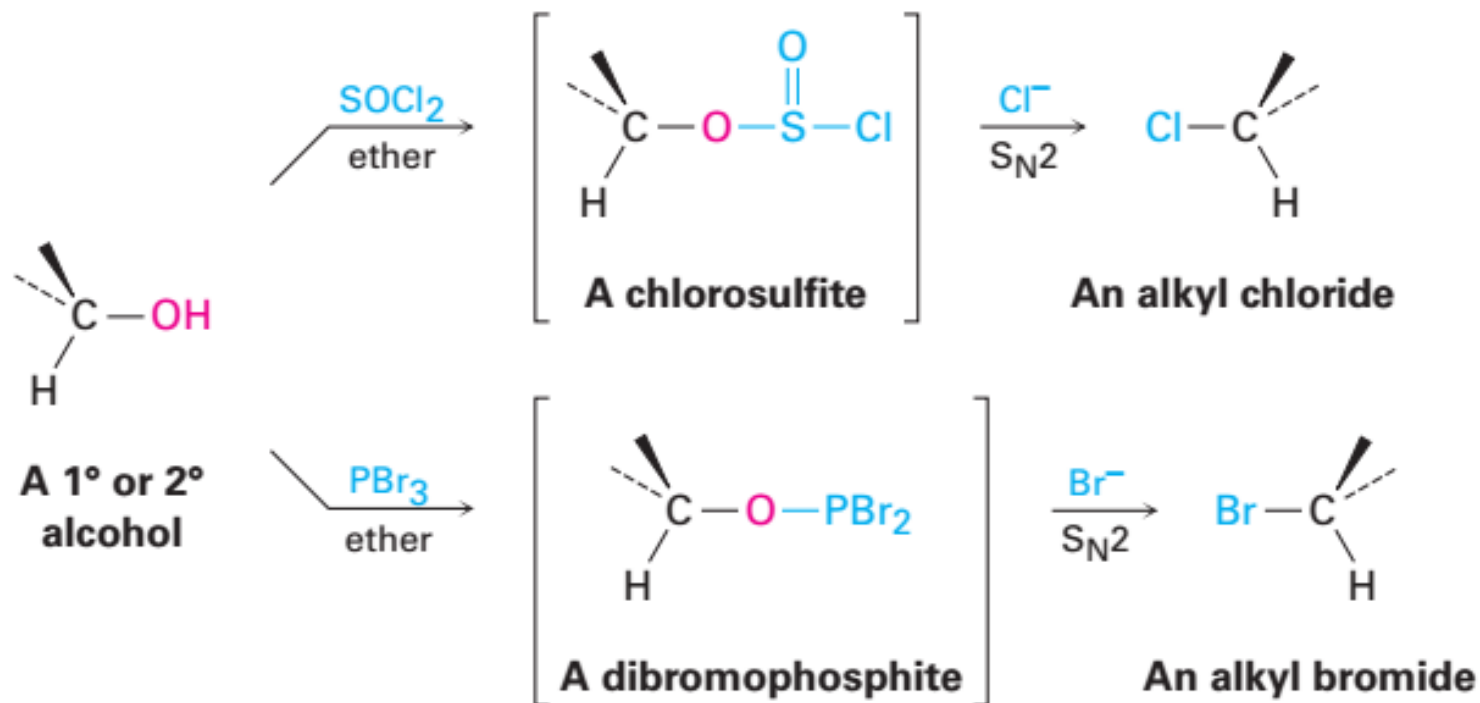
Relative reactivity	OH^- , NH_2^- , OR^-	F^-	Cl^-	Br^-	I^-	TosO^-
	$\ll 1$	1	200	10,000	30,000	60,000

Leaving group reactivity 

Variables affect S_N2

Leaving group (nhóm rời đi)

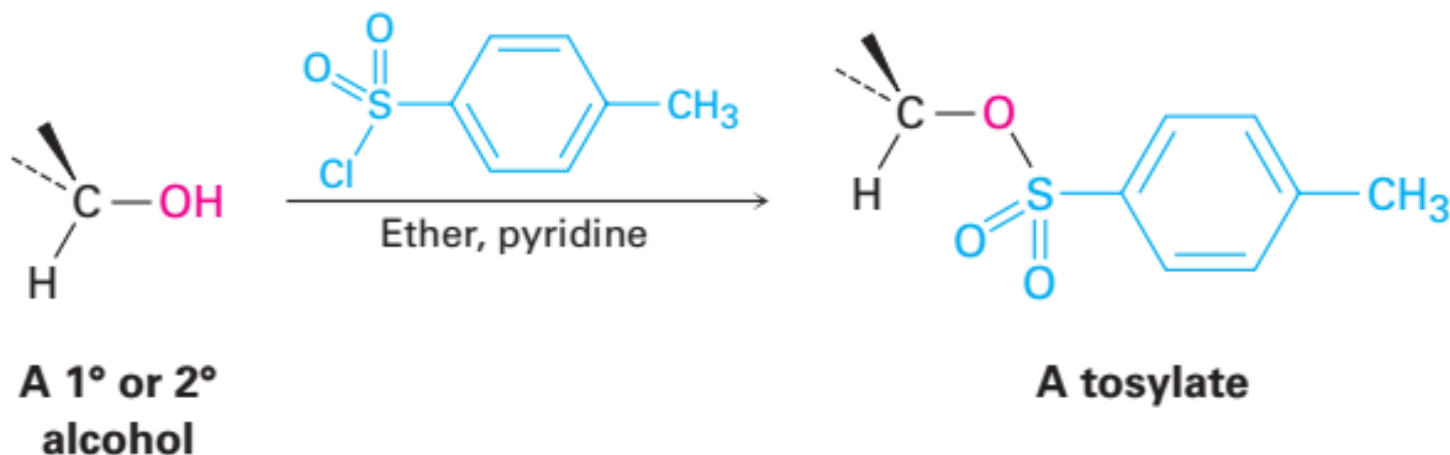
Chuyển alcohol về alkyl halide để phản ứng tốt hơn
(vì -OH không phải là nhóm rời tốt cho phản ứng S_N2)



Variables affect S_N2

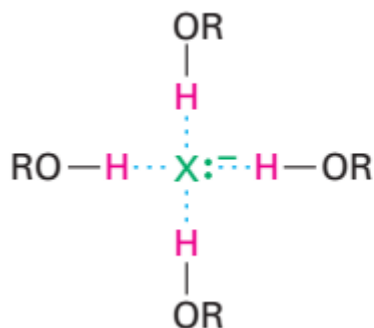
Leaving group (nhóm rời đi)

Thay nhóm –OH bằng tosylate để phản ứng tốt hơn (vì –OH không phải là nhóm rời tốt cho phản ứng S_N2)



Variables affect S_N2

Solvent (dung môi)



A solvated anion
(reduced nucleophilicity due to
enhanced ground-state stability)



Solvent	CH ₃ OH	H ₂ O	DMSO	DMF	CH ₃ CN	HMPA
Relative reactivity	1	7	1300	2800	5000	200,000



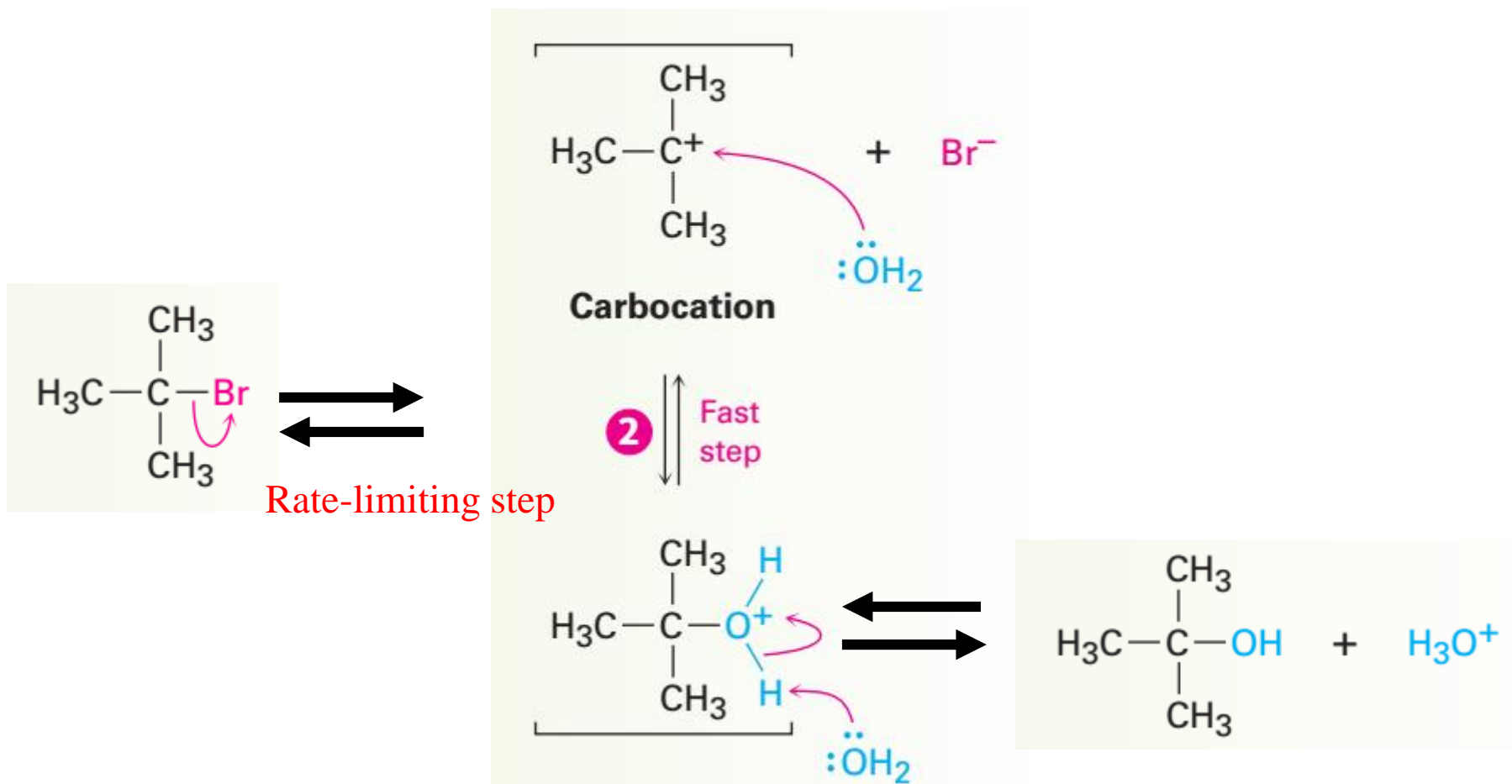
S_N1 reaction

substitution, nucleophilic, unimolecular.

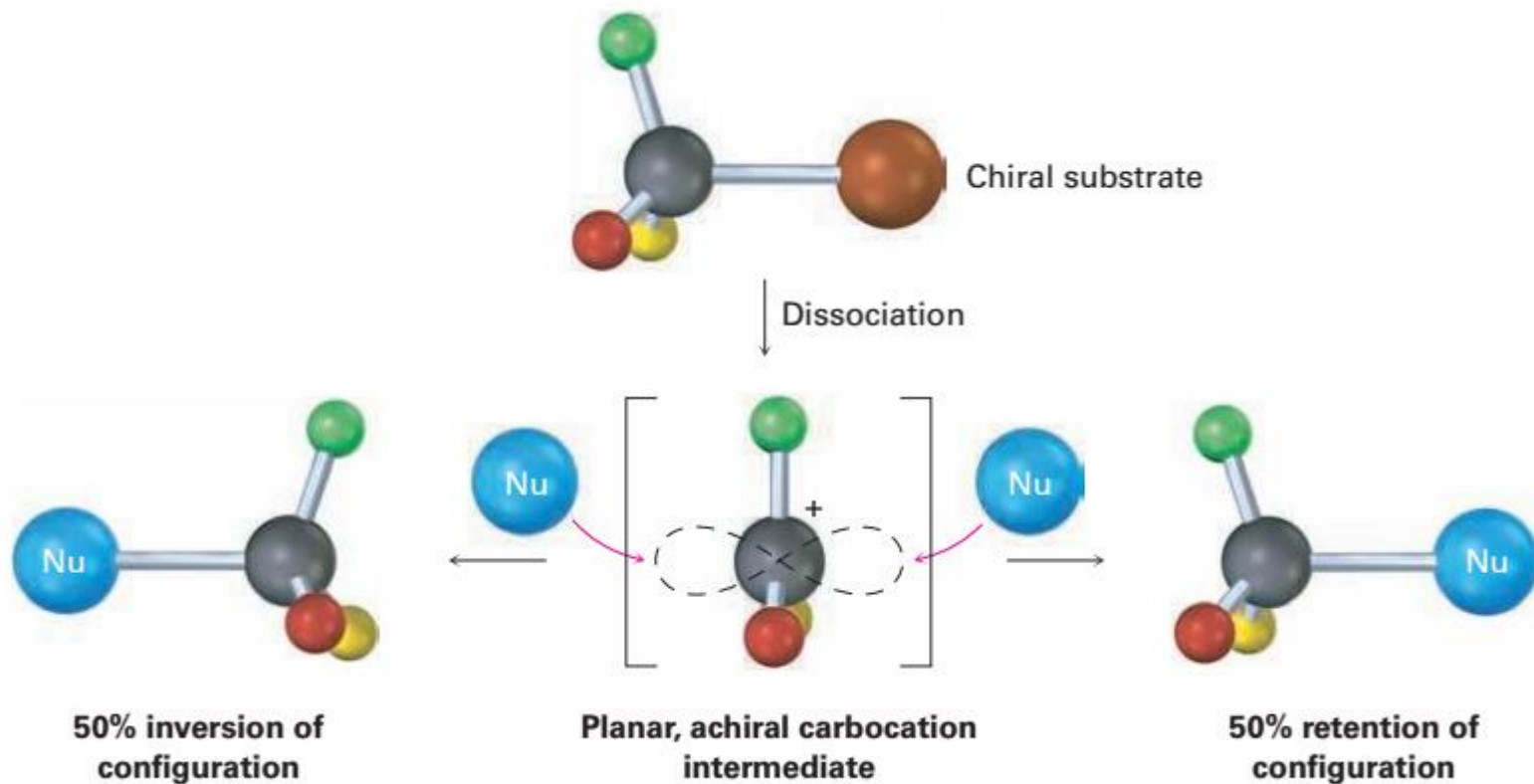


Reaction rate = Rate of disappearance of alkyl halide
 $= k \times [\text{RX}]$

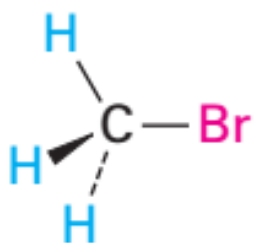
S_N1 mechanism



Stereochemistry of S_N1

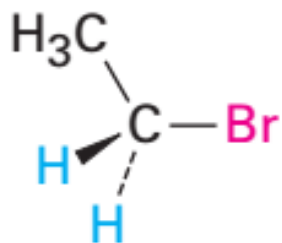


S_N1 reaction



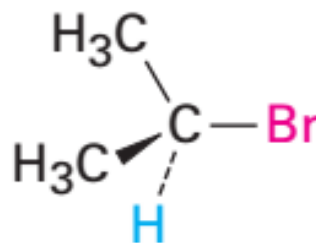
Methyl

< 1



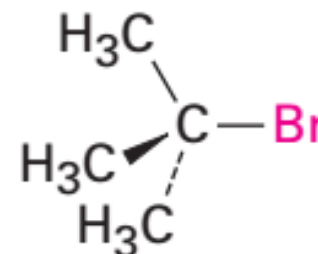
Primary

1



Secondary

12



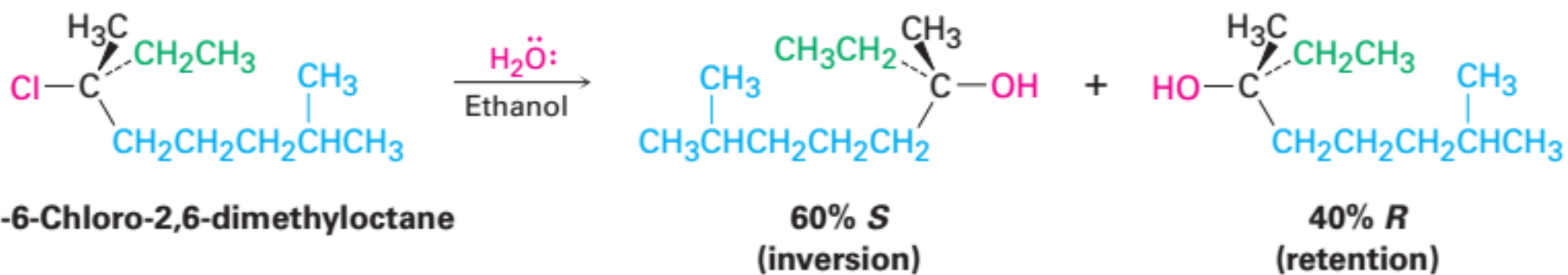
Tertiary

1,200,000



(different vs S_N2)
Le Quy Chon N Tay Tan University

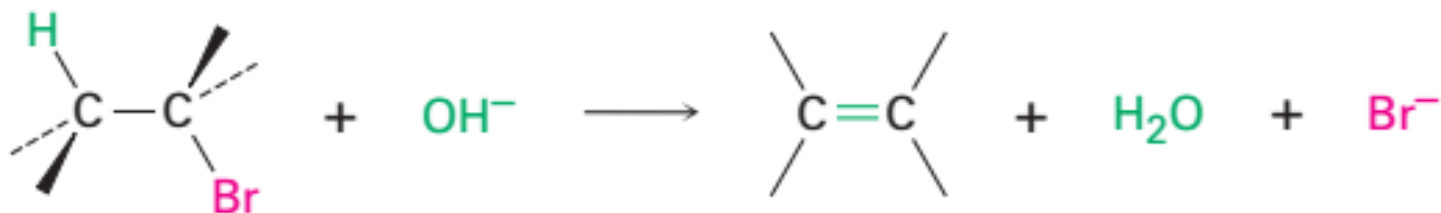
Example: S_N1



S_N1 characteristics

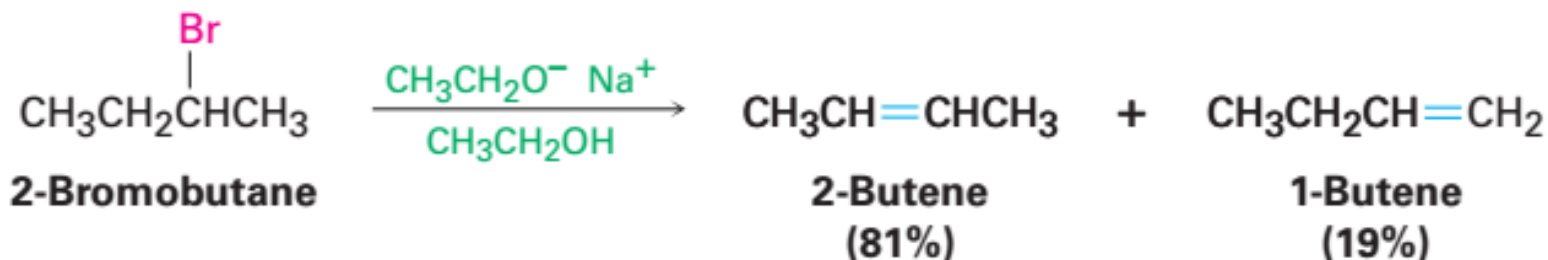
- Substrate** The best substrates yield the most stable carbocations. As a result, S_N1 reactions are best for tertiary, allylic, and benzylic halides.
- Leaving group** Good leaving groups increase the reaction rate by lowering the energy level of the transition state for carbocation formation.
- Nucleophile** The nucleophile must be nonbasic to prevent a competitive elimination of HX (**Section 11-7**), but otherwise does not affect the reaction rate. Neutral nucleophiles work well.
- Solvent** Polar solvents stabilize the carbocation intermediate by solvation, thereby increasing the reaction rate.

Elimination reactions and Zaitsev's rules (phân tách và quy tắc Zaitzev)



ZAITSEV'S RULE

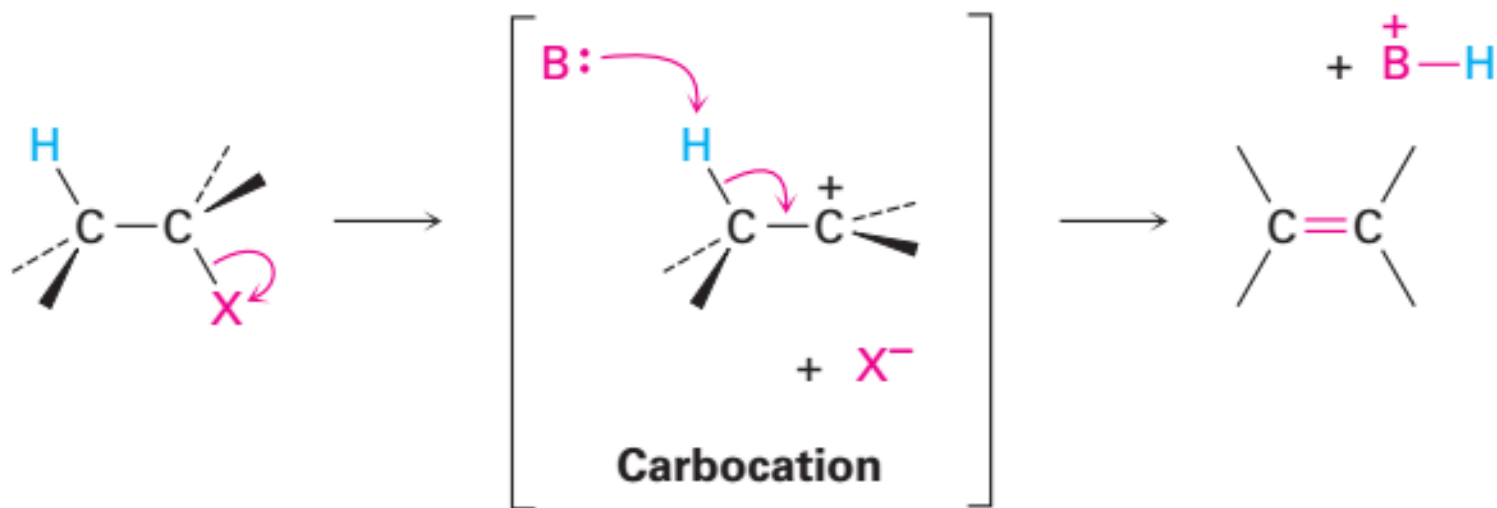
In the elimination of HX from an alkyl halide, the more highly substituted alkene product predominates.



Common mechanism: E1, E2 and E1cB

E1 reaction

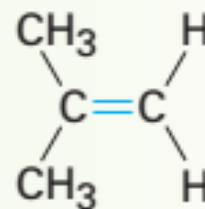
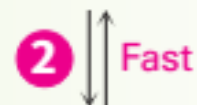
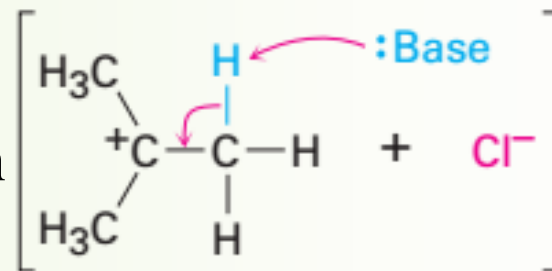
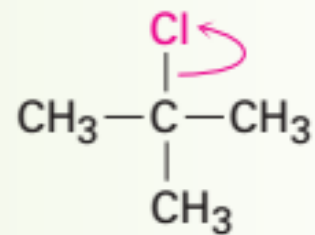
E1 Reaction: C–X bond breaks first to give a carbocation intermediate, followed by base removal of a proton to yield the alkene.



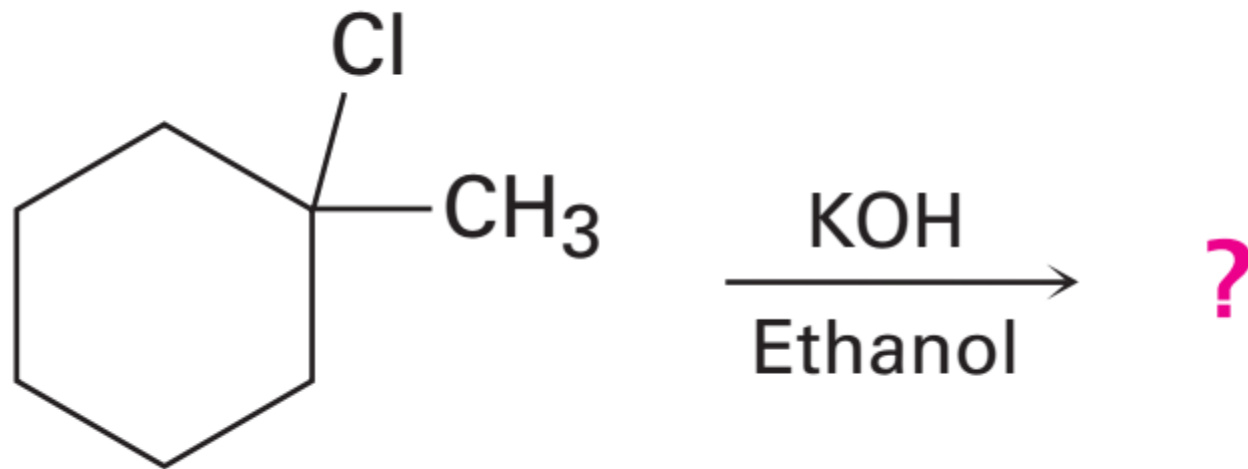
E1 reaction

elimination, unimolecular

Carbocation



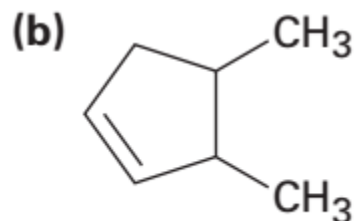
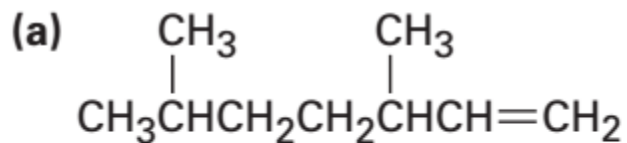
Dự đoán sản phẩm phản ứng sau



Problem

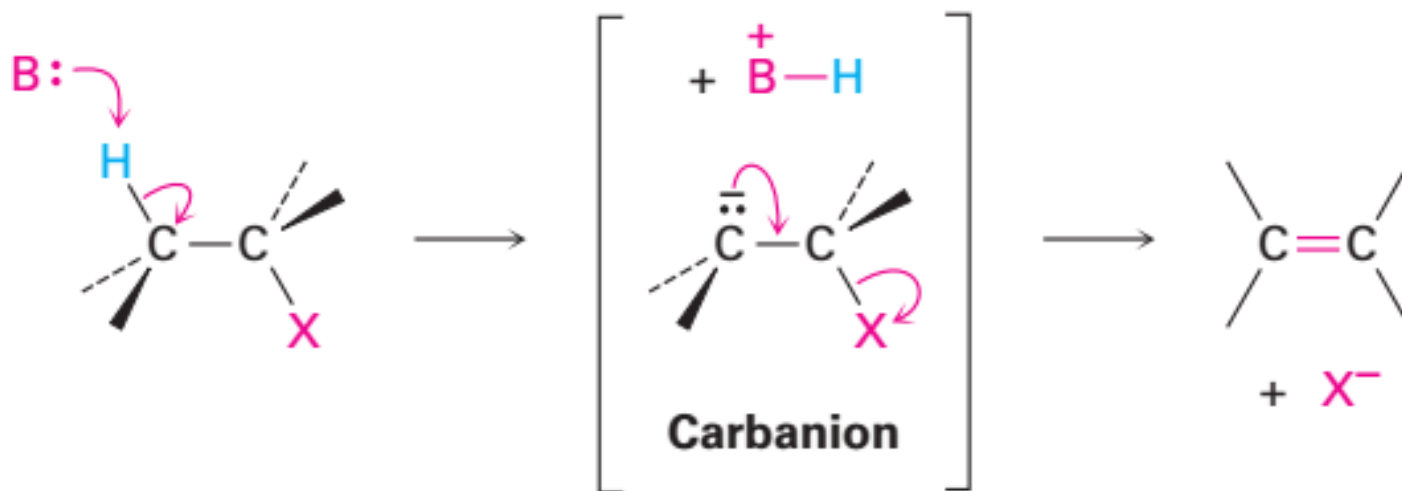
PROBLEM 11-16

What alkyl halides might the following alkenes have been made from?



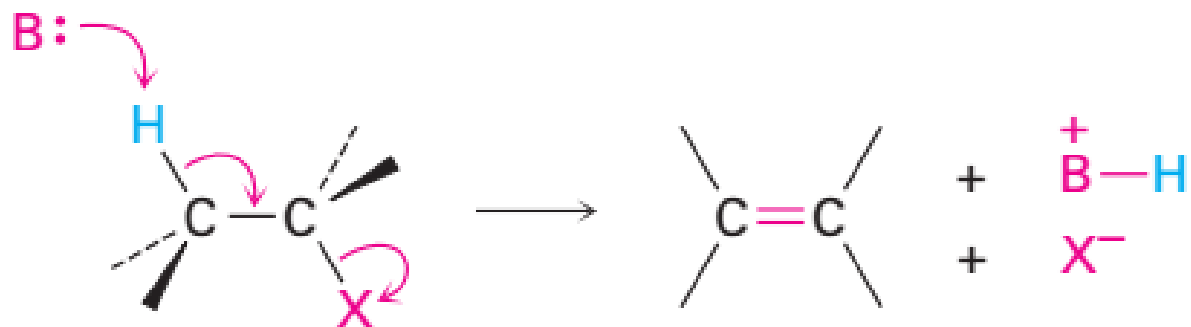
E1cB reaction

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



E2 reaction

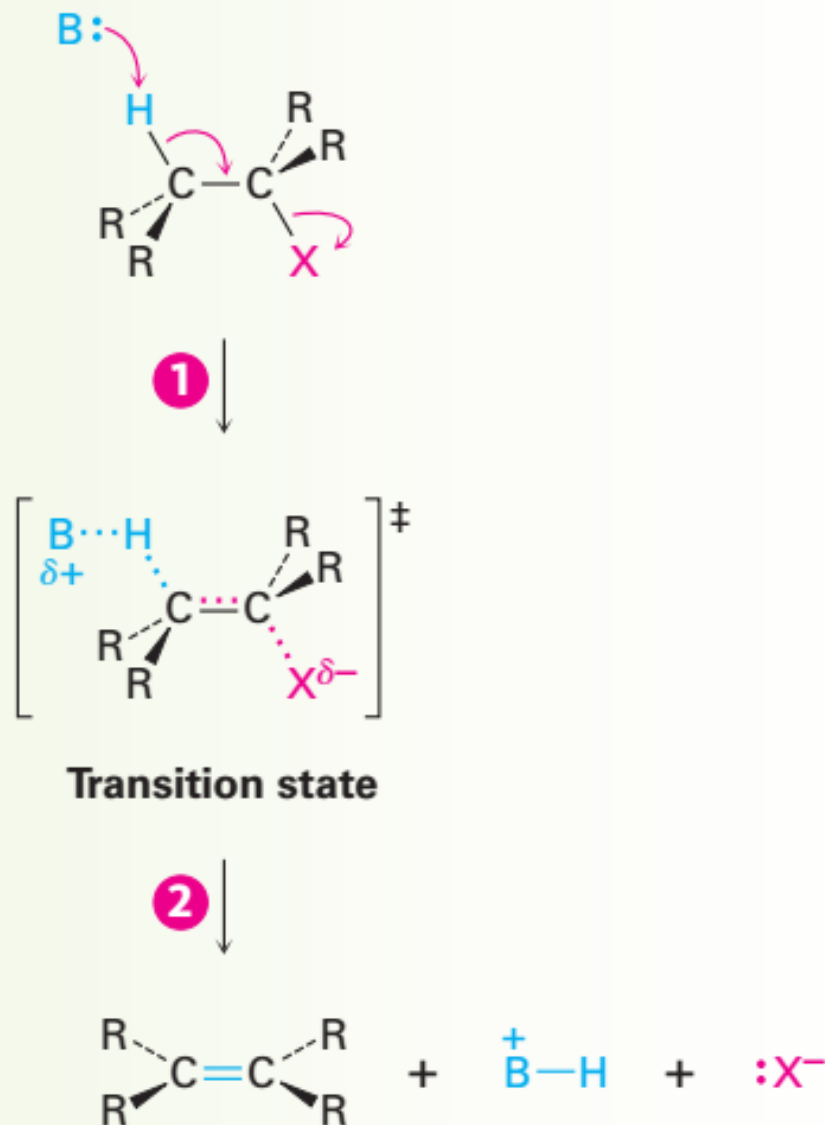
E2 Reaction: C-H and C-X bonds break simultaneously, giving the alkene in a single step without intermediates.



E2 reaction

elimination, bimolecular

Most common
for elimination
reactions





More details: read books