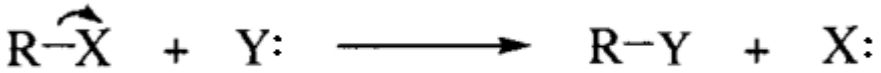
Chapter 5

Aliphatic Nucleophilic Substitution

脂肪族亲核取代反应

At saturated carbon

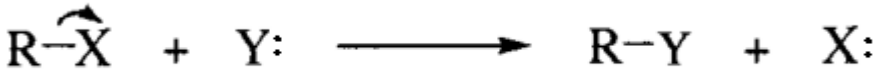


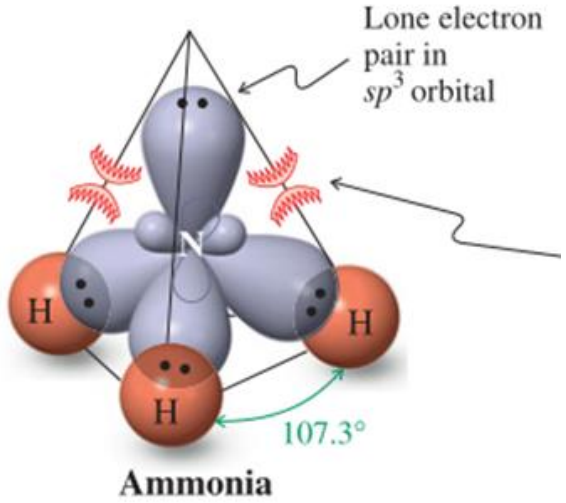
Qiong Li

March 11, 2024

5.1 Nucleophilic Substitution reaction

general equation of S_N

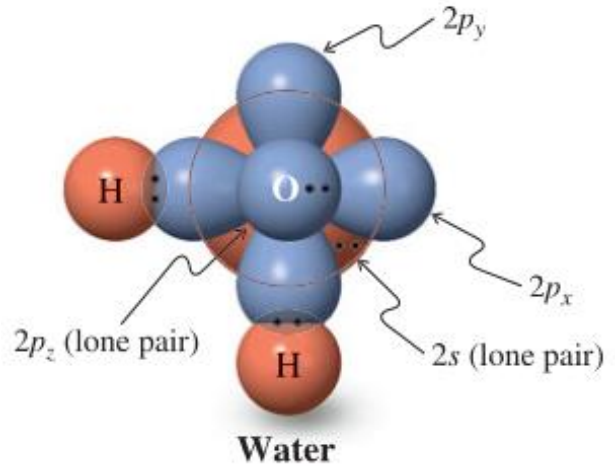




There are four charge types for the equation

nucleophile

Type I	R–I	+	OH^-	⟶	R–OH	+ I^-
Type II	R–I	+	$:NMe_3$	⟶	$R-\overset{+}{N}Me_3$	+ I^-
Type III	$R-\overset{+}{N}Me_3$	+	OH^-	⟶	R–OH	+ NMe_3
Type IV	$R-\overset{+}{N}Me_3$	+	H_2S	⟶	$R-\overset{+}{S}H_2$	+ NMe_3

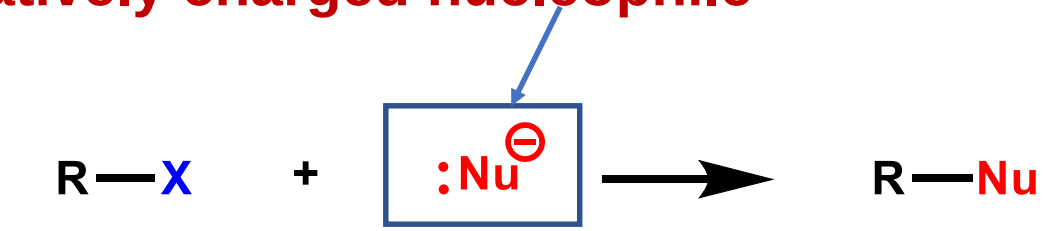


Nucleophile must have an unshared pair of electrons, it can be neutral or negatively charged.

Substrate (RX) may be neutral or positively charged.

5.1 Nucleophilic Substitution reaction

with negatively charged nucleophile



$OH^{\ominus}$	R—OH	Alcohol
$OR'^{\ominus}$	R—OR'	Ether
$SH^{\ominus}$	R—SH	Mercaptan
$SR'^{\ominus}$	R—SR'	Alkyl Sulphide
$^{\ominus}O-\overset{\overset{O}{\|\|}}{C}-R'$	$R-O-\overset{\overset{O}{\|\|}}{C}-R'$	Ester

5.1 Nucleophilic Substitution reaction

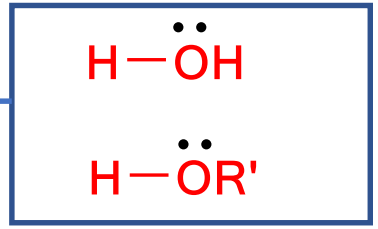
with negatively charged nucleophile

$^{\ominus}CN$	R—CN	Nitrile
$^{\ominus}C{\equiv}C-R'$	R—C≡C—R'	Alkyne
$^{\ominus}CH(CO_2Et)_2$	R—$CH(CO_2Et)_2$	Alkyl malonate
$I^{\ominus}$	R—I	Iodoalkane

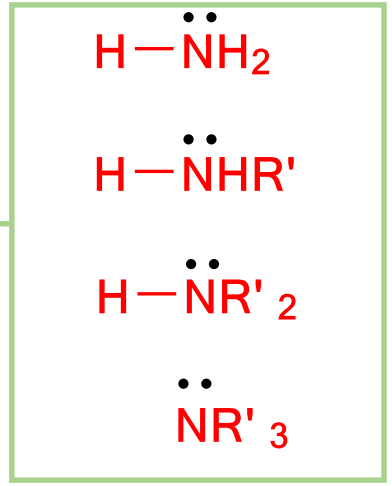
5.1 Nucleophilic Substitution reaction

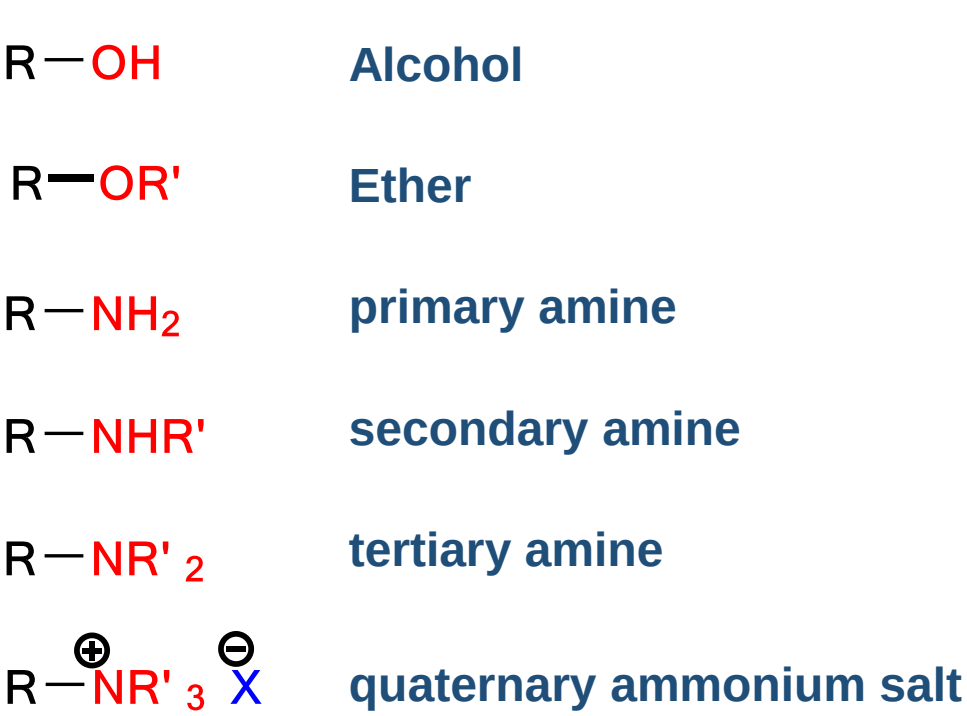
with neutral nucleophile

When HNu is a solvent, The reaction is called Solvolysis(溶剂解)



Nucleophilic substitution at an alkyl carbon is also said to alkylate the nucleophile.





5.2 Mechanisms

Several distinct mechanisms are possible for aliphatic nucleophilic substitution reactions. Depending on the substrate, nucleophile, leaving group, and reaction condition.

In all of them, Nucleophile (attacking reagent) must carry electron pair with it. it can be neutral or negatively charged.

By far the most common mechanisms that occur at a saturated carbon are the $S_N1$and S_N2 mechanisms.

Classification of the nucleophilic substitution mechanisms

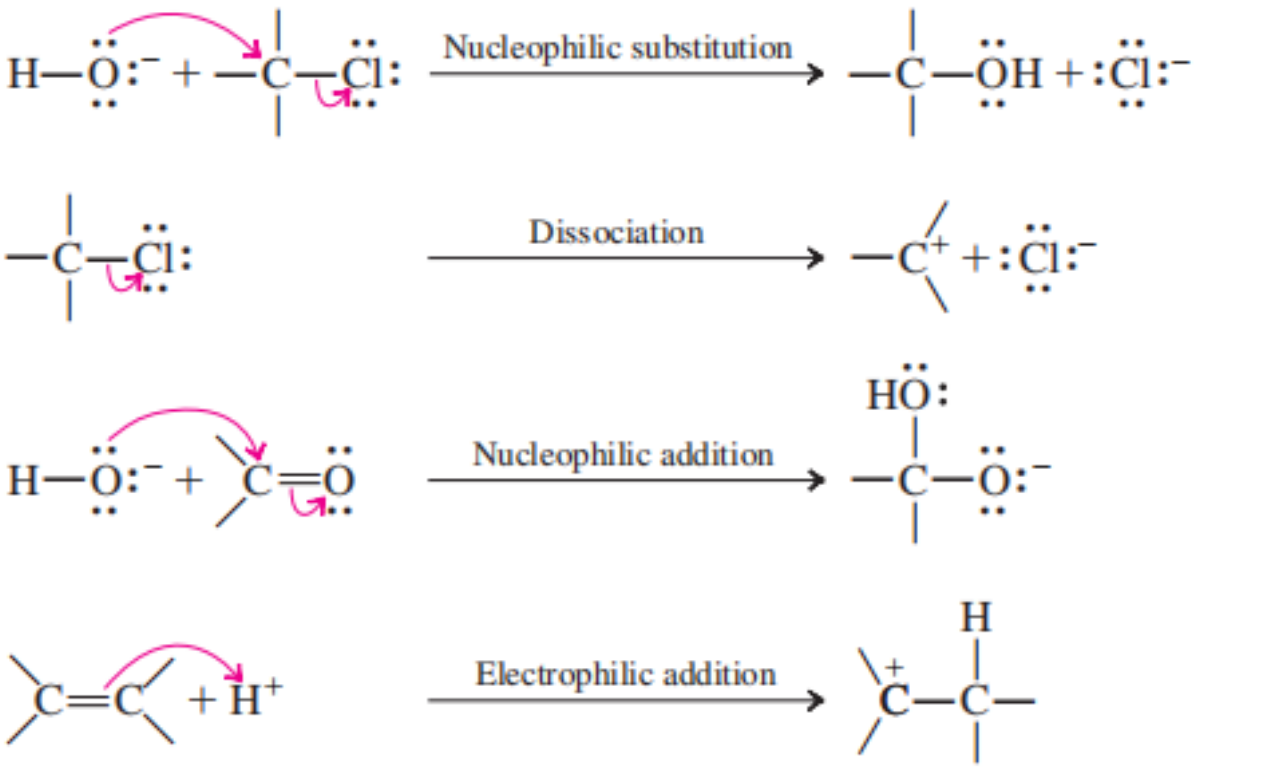
S_N1, S_N2, The neighboring-Group mechanism, S_Ni, SET

5.2 Mechanisms

Reaction Mechanisms Involving Polar Functional Groups:

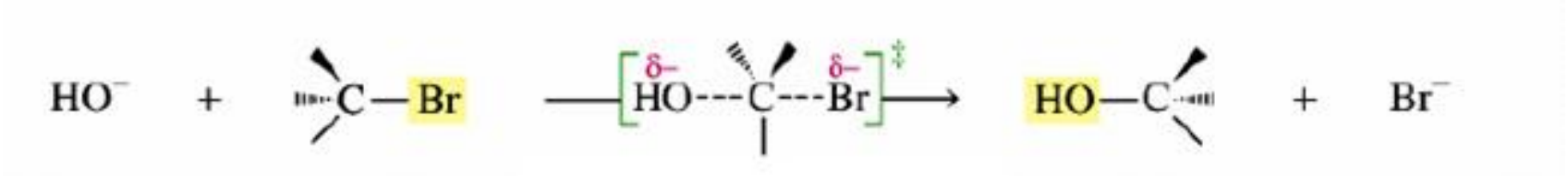
Using “Electron-Pushing” Arrows

Curved-Arrow Representations of Several Common Types of Mechanisms



5.2 Mechanisms

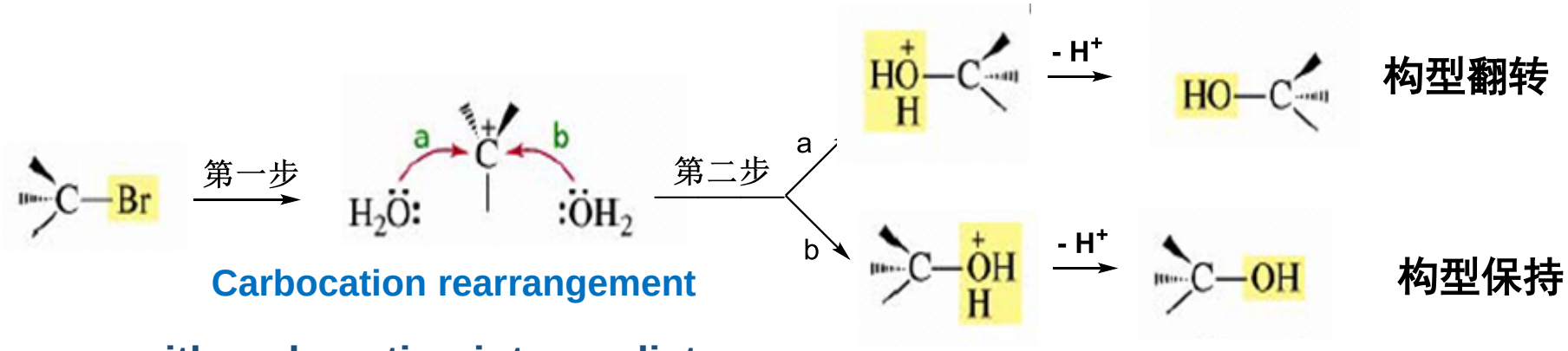
S_N2 mechanism A_ND_N Bond breaking is concurrent with bond formation $r = k[RX][Nu^-]$



one-step process with no intermediate.

Walden 翻转

S_N1 mechanism $D_N^{\ddagger}+A_N$ Bond breaking happens first, then bond formation happens $r = k[RX]$

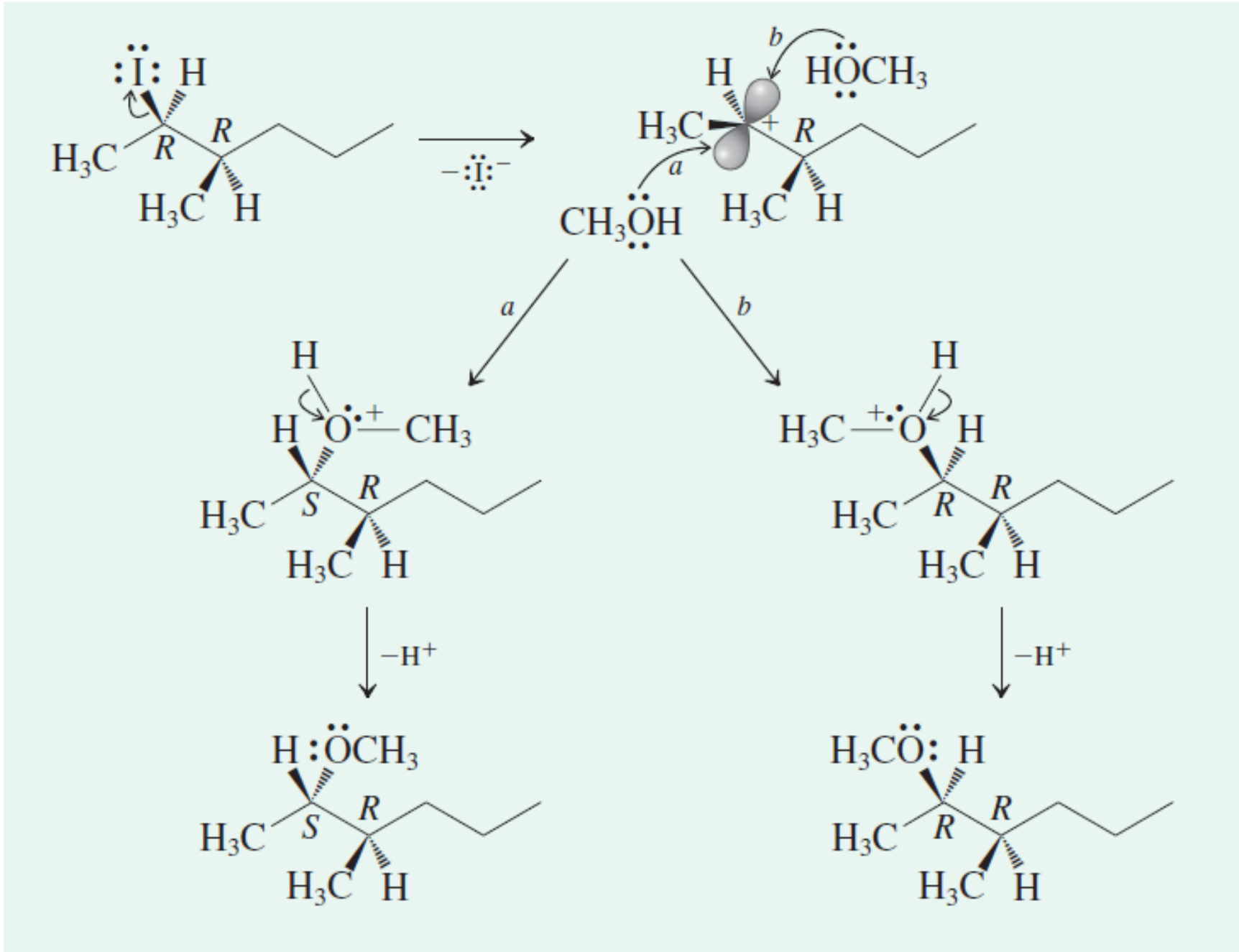


Carbocation rearrangement

two-step process with carbocation intermediate.

S_N1 Mechanism Exercise

Gentle warming of (2*R*,3*R*)-2-iodo-3-methylhexane in methanol gives two stereoisomeric methyl ethers. How are they related to each other? Explain mechanistically


b
a
a
b
−H+
−H+

5.2 Mechanisms

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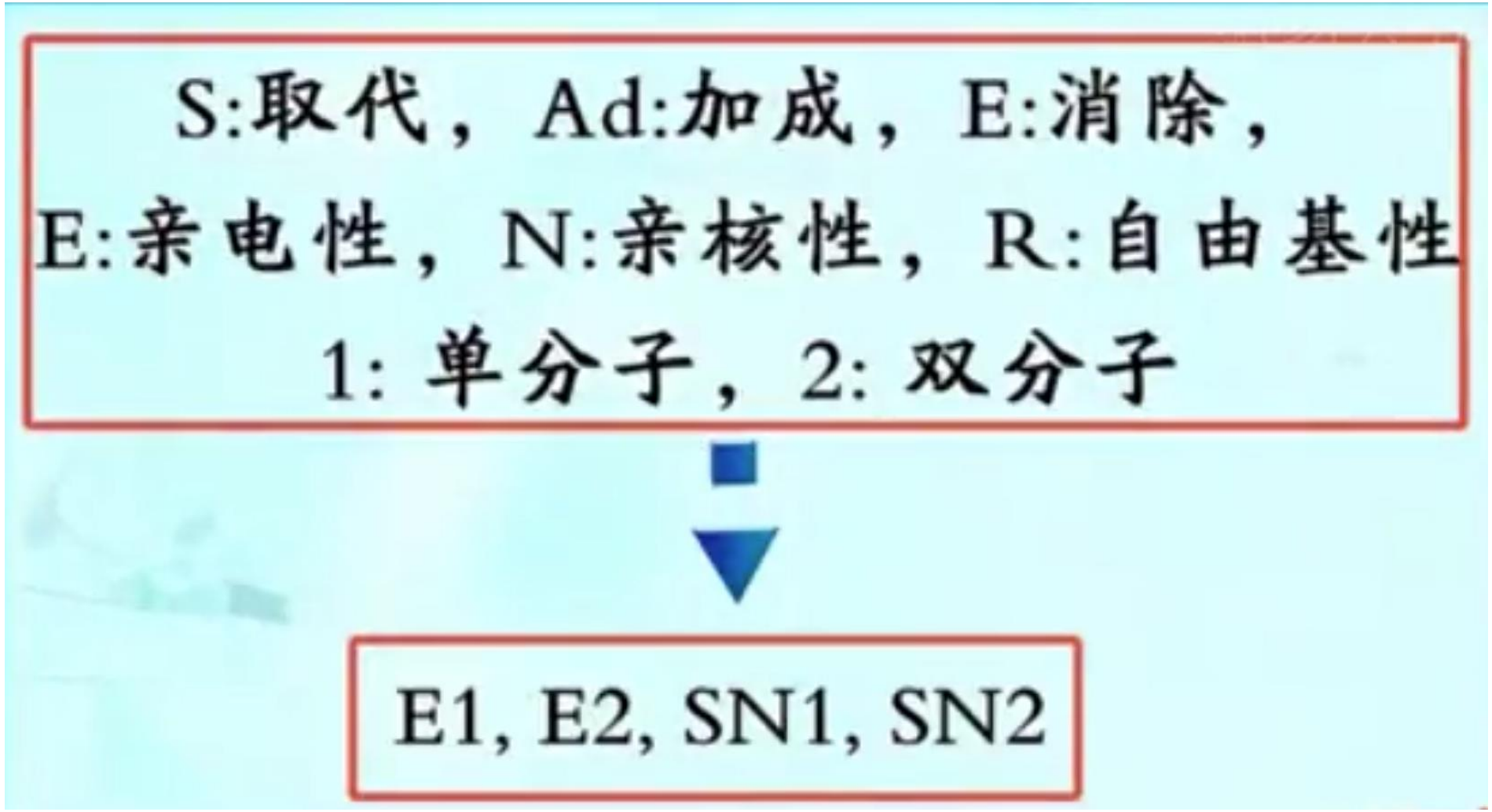

Chapter 5-2

Aliphatic Nucleophilic Substitution

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At saturated carbon

Qiong Li

March 11, 2024

Review

general equation of S_N

There are four charge types for the equation

nucleophile

Type I	R–I	+	OH^-	⟶	R–OH	+ I^-
Type II	R–I	+	NMe_3	⟶	$R-\overset{+}{N}Me_3$	+ I^-
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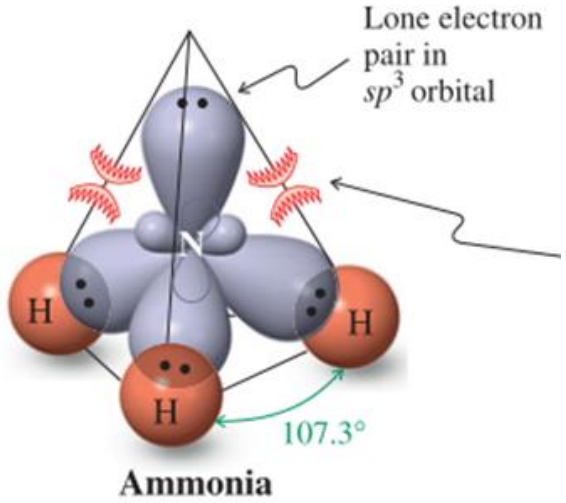
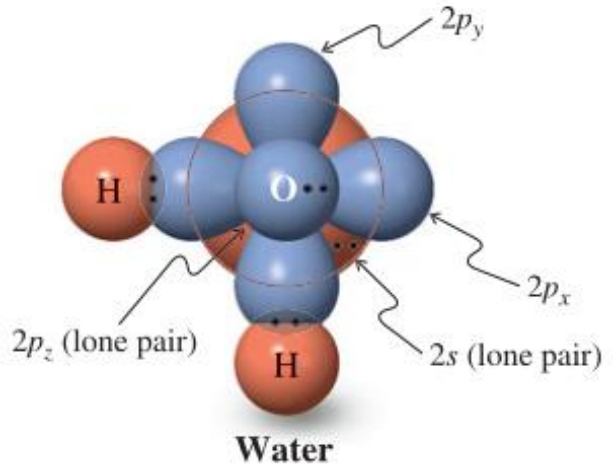


Ammonia



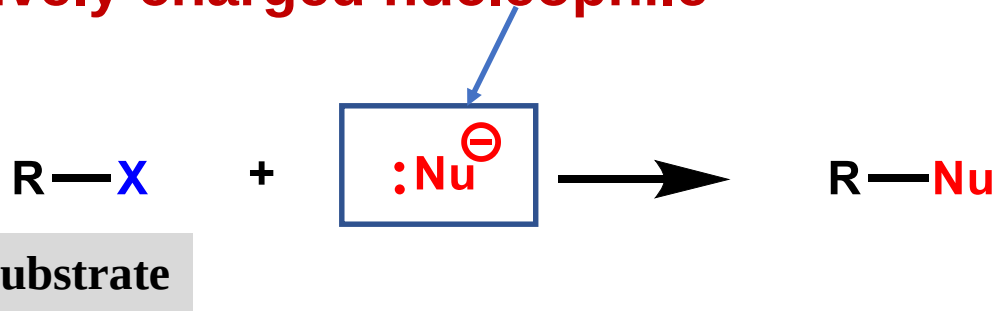
Water

Nucleophile must have an unshared pair of electrons, it can be neutral or negatively charged.

Substrate (RX) may be neutral or positively charged.

Review

with negatively charged nucleophile



$OH^{\ominus}$	R—OH	Alcohol
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Review

with negatively charged nucleophile

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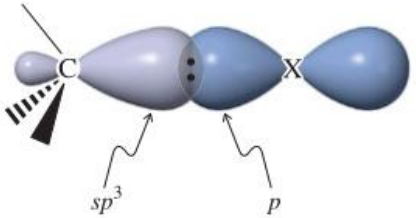
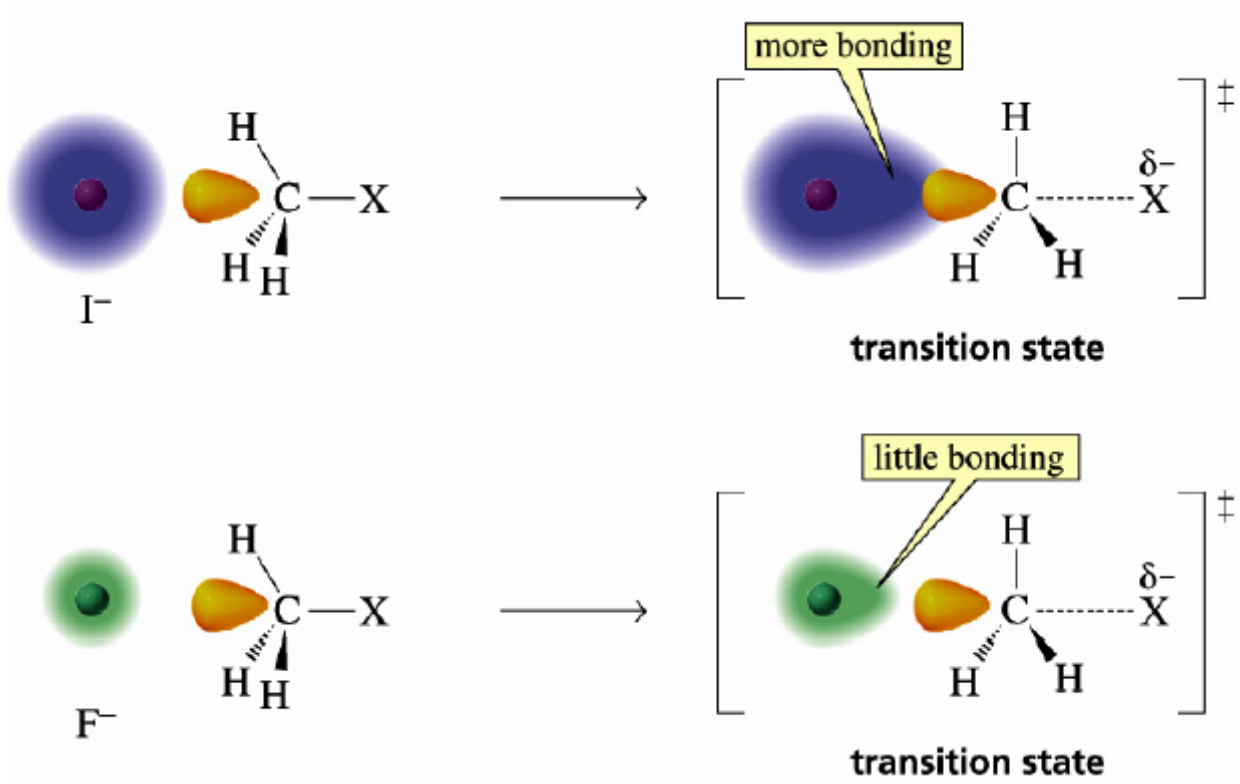
$I^{\ominus}$	R—I	Iodoalkane

1.3 Inductive and Field Effects

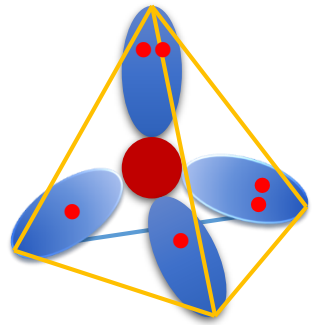
Inducted Dynamic Nuclear Polarization

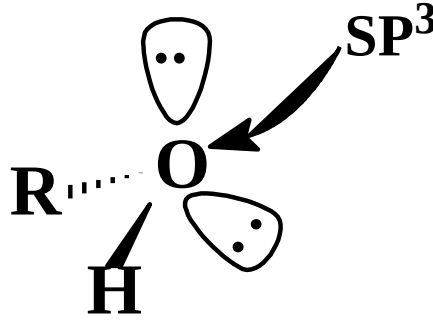


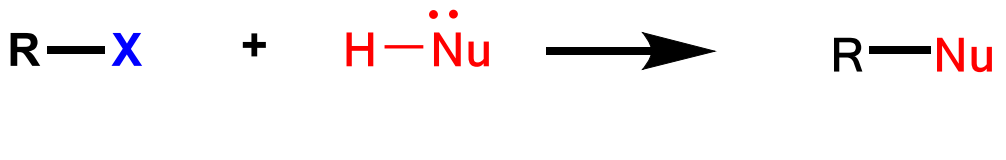


Review

with neutral nucleophile







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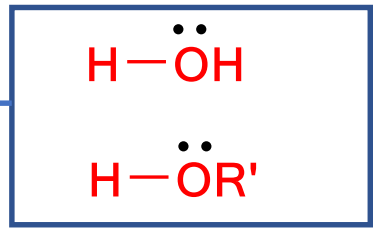
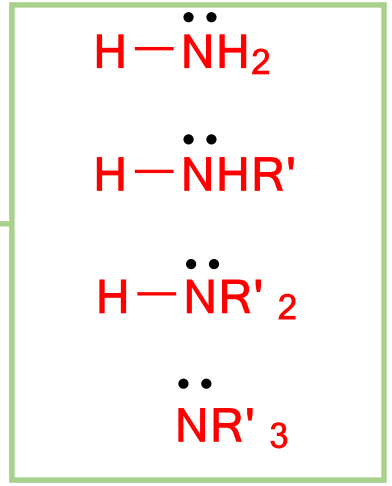


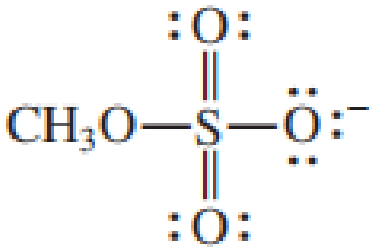
Nucleophilic substitution at an alkyl carbon is also said to alkylate the nucleophile.



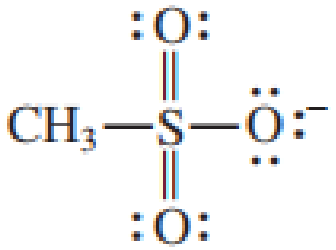
R—OH	Alcohol
R—OR'	Ether
R—NH2	primary amine
R—NHR'	secondary amine
R—NR'2	tertiary amine
R—⊕NR'3 ⊖X	quaternary ammonium salt

Review

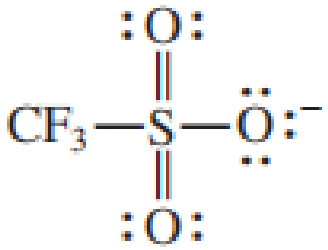
Sulfate and Sulfonate Leaving Groups



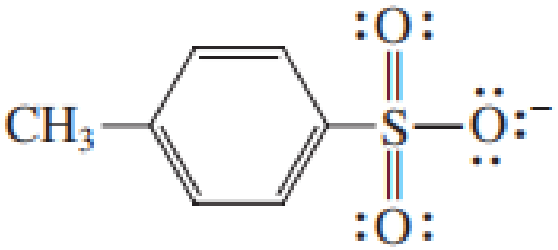
Methyl sulfate ion



Methanesulfonate ion
(Mesylate ion)



Trifluoromethanesulfonate ion
(Triflate ion)



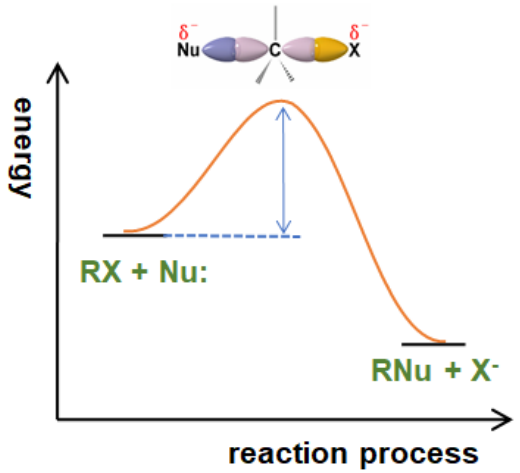
4-Methylbenzenesulfonate ion
(*p*-Toluenesulfonate ion,
tosylate ion)

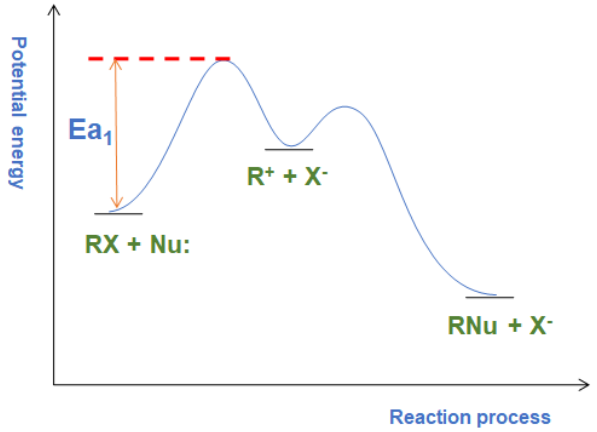
-OMs

-OTs

Classification of the nucleophilic substitution mechanisms

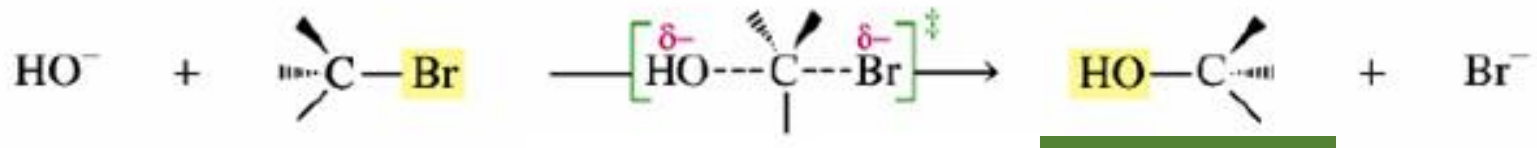
S_N2, S_N1, The neighboring-Group mechanism, S_Ni, SET



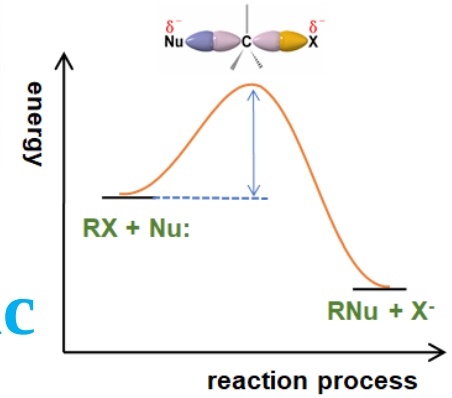


Review

S_N2 mechanism **A_ND_N** Bond breaking is concurrent with bond formation $r = k[RX][Nu^-]$

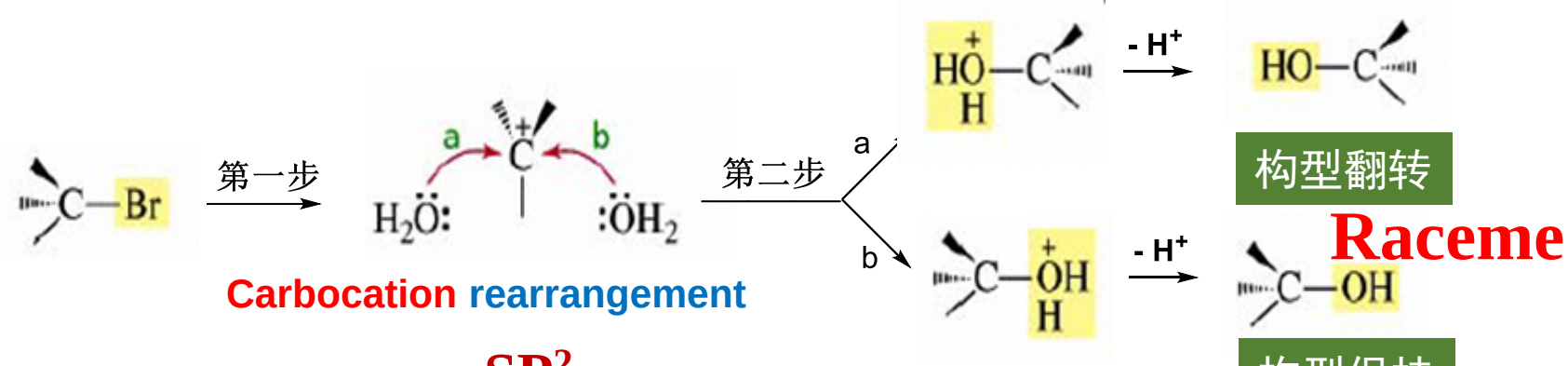


SP^3 SP^2 Walden 翻转



one-step process with no intermediate. The S_N2 reaction is **stereospecific**

S_N1 mechanism **$D_N^{\ddagger}+A_N$** Bond breaking happens first, then bond formation happens $r = k[RX]$



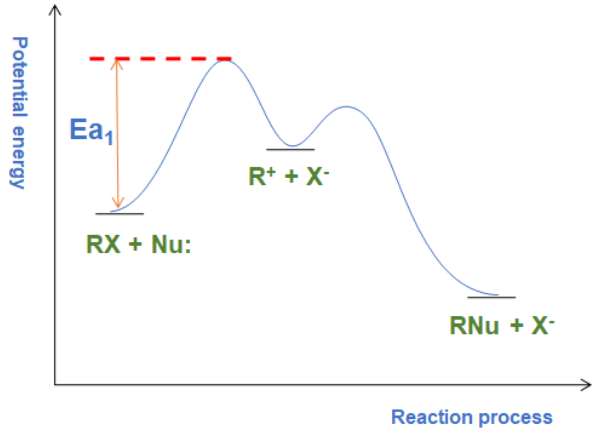
Carbocation rearrangement

构型翻转

Raceme

构型保持

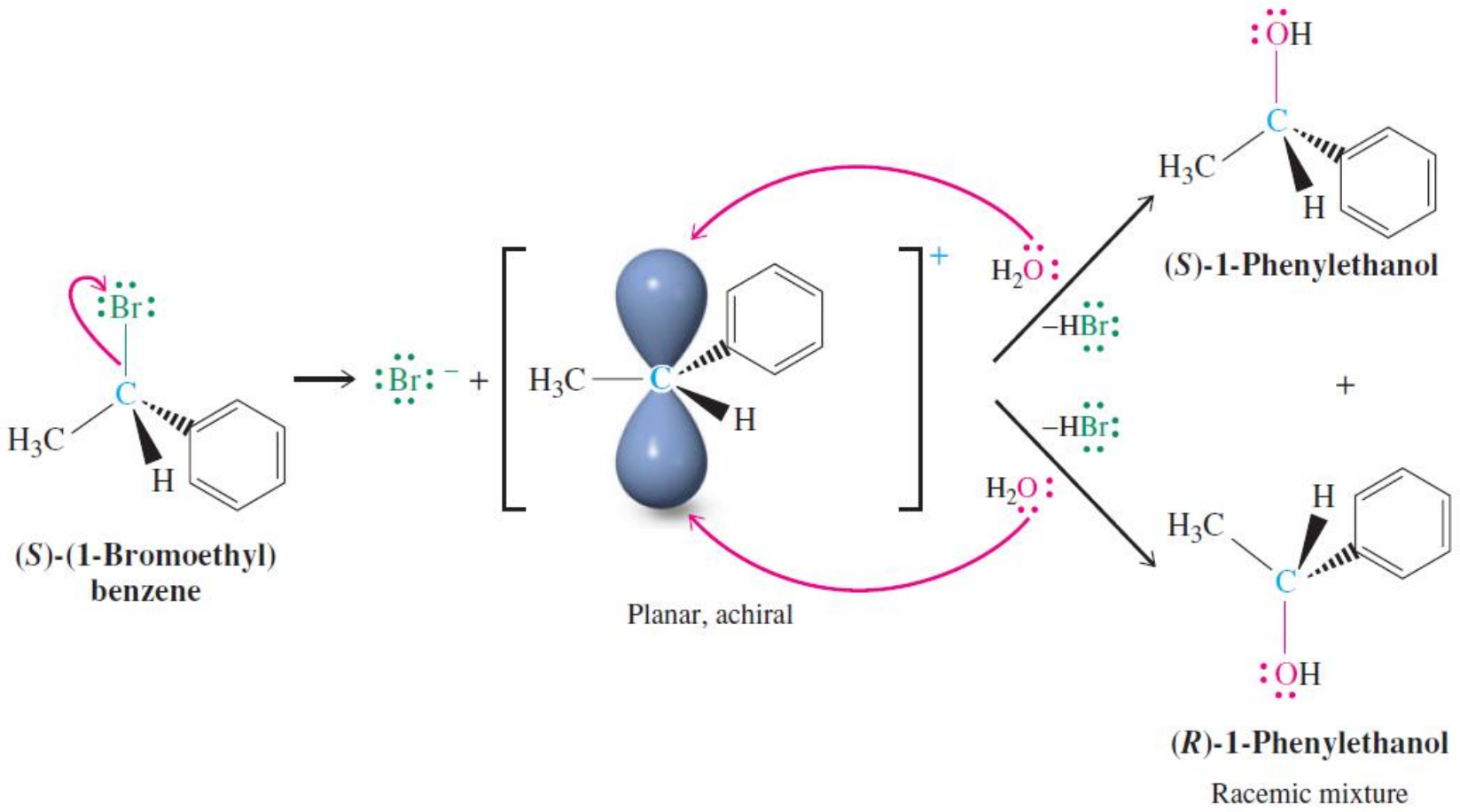
SP^2



two-step process with carbocation intermediate.

转型 > 保型？

Review



Enantiomer

对映异构体

Raceme

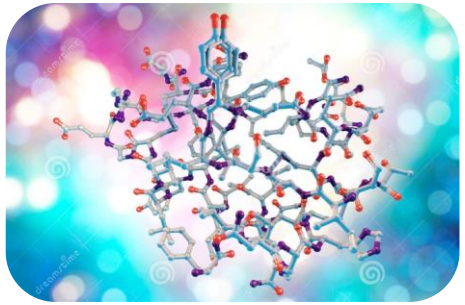
外消旋体

In general, the formation of racemic products from optically active substrates is strong evidence for the intermediate being a symmetrical, achiral specieenantiomers, such as a carbocation.

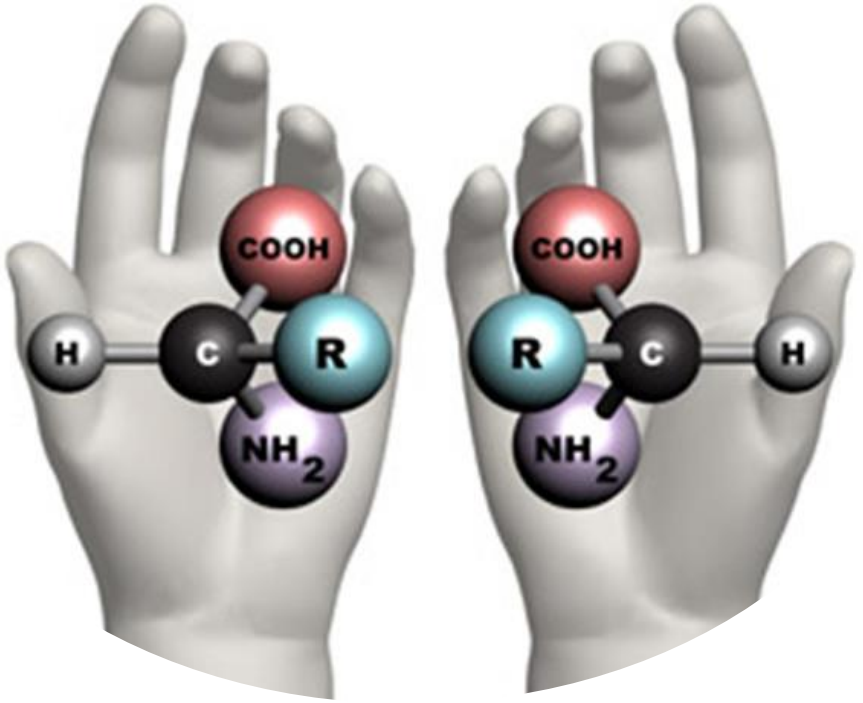
Fundamentals of Stereochemistry

Chirality

海螺



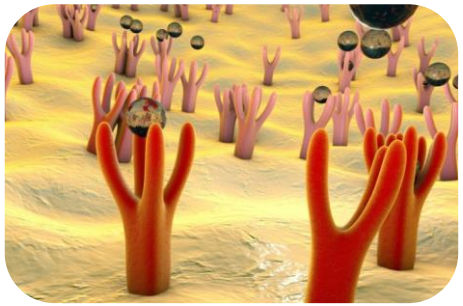
蛋白质



手性药物

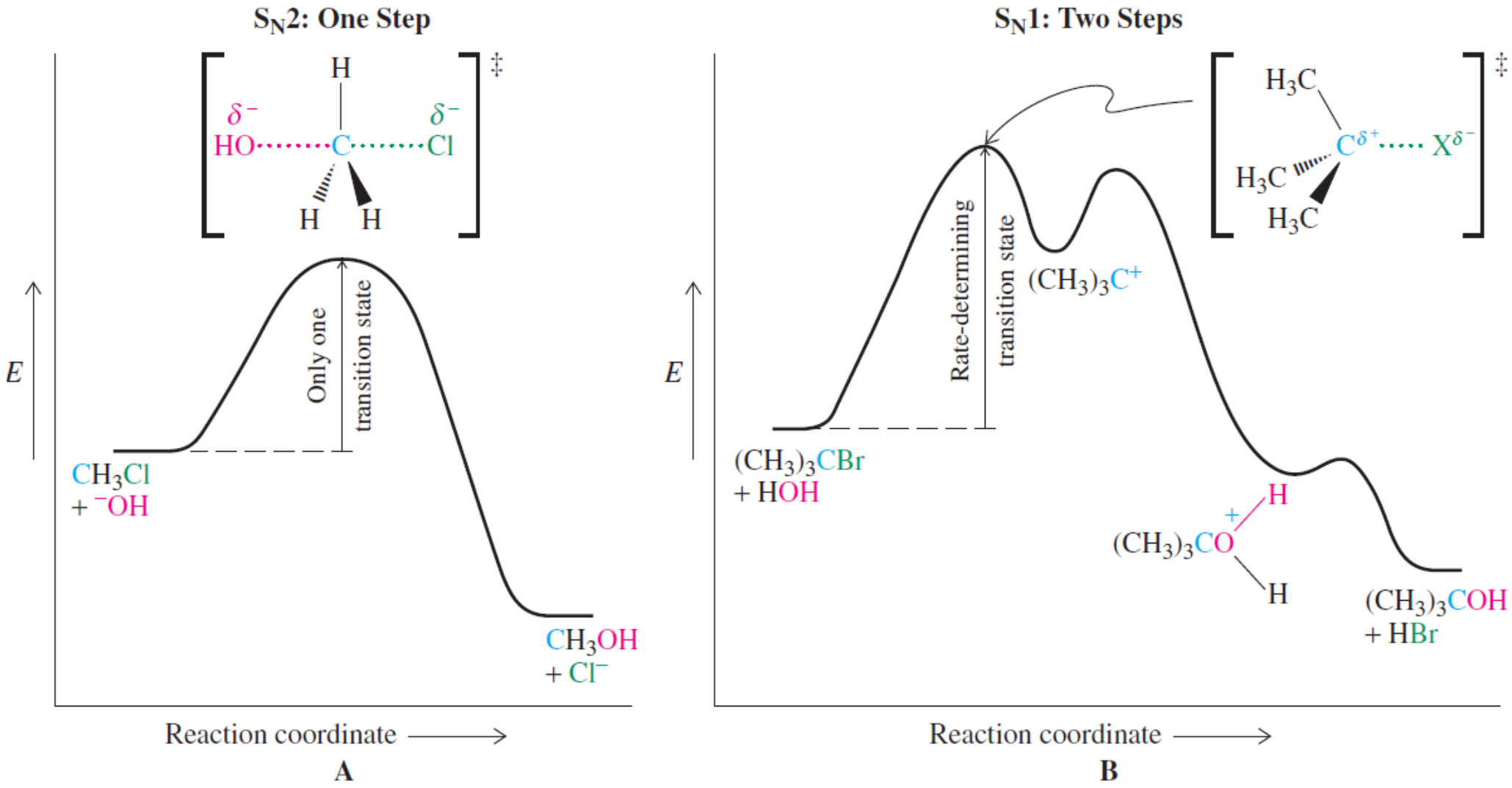
手性：左右手互为镜像但无法重叠的性质

核酸



受体

Review


SN2: One Step
H
δ−
HO
C
Cl
δ−
‡
H
H
E
Only one
transition state
CH3Cl
+ −OH
CH3OH
+ Cl−
Reaction coordinate
A
SN1: Two Steps
H3C
Cδ+
Xδ−
‡
H3C
H3C
E
Rate-determining
transition state
(CH3)3C+
(CH3)3CBr
+ HOH
(CH3)3CO
H
H
+
(CH3)3COH
+ HBr
Reaction coordinate
B

Review

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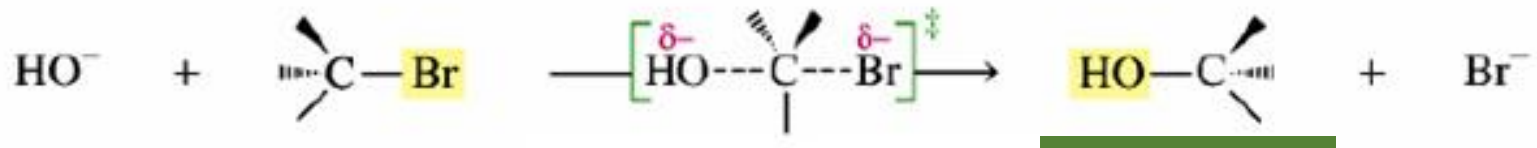
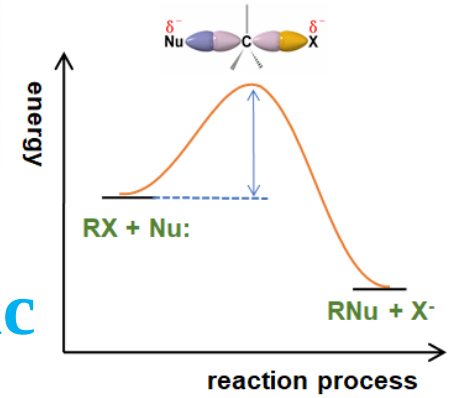
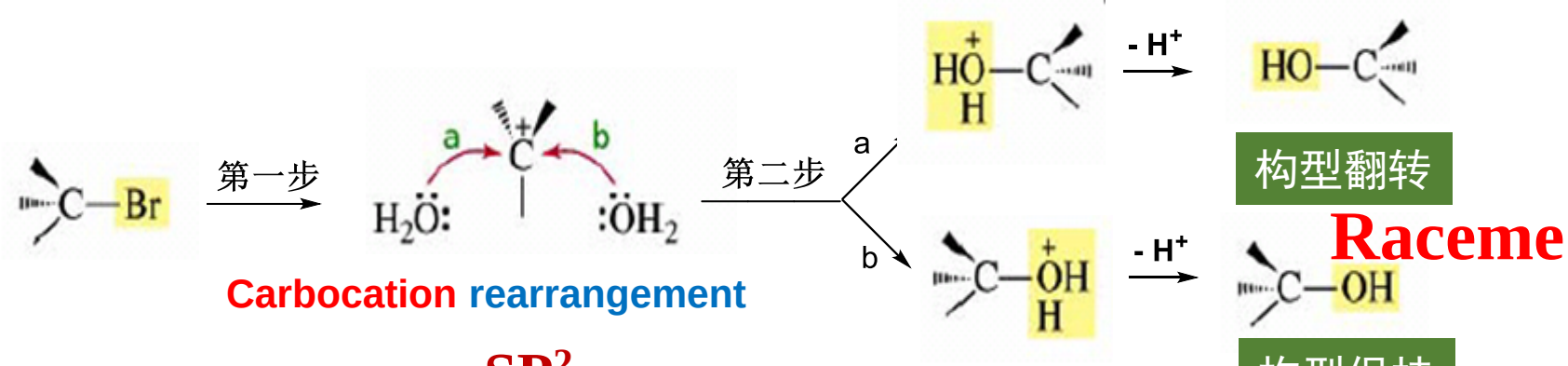


SP^3 SP^2 Walden 翻转



one-step process with no intermediate. The S_N2 reaction is **stereospecific**

S_N1 mechanism **$D_N^{\ddagger}+A_N$** Bond breaking happens first, then bond formation happens $r = k[RX]$



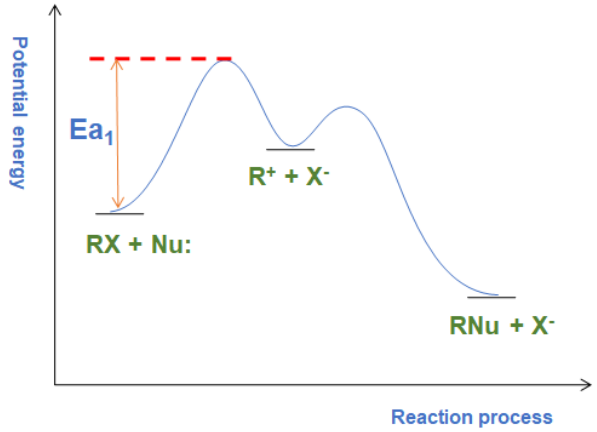
Carbocation rearrangement

构型翻转

Raceme

构型保持

SP^2

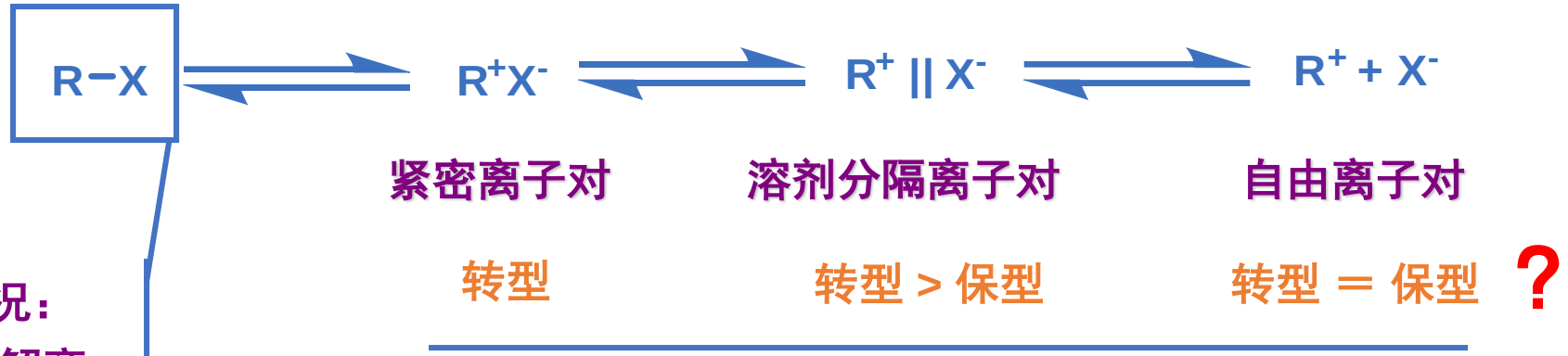


two-step process with carbocation intermediate.

转型 > 保型？

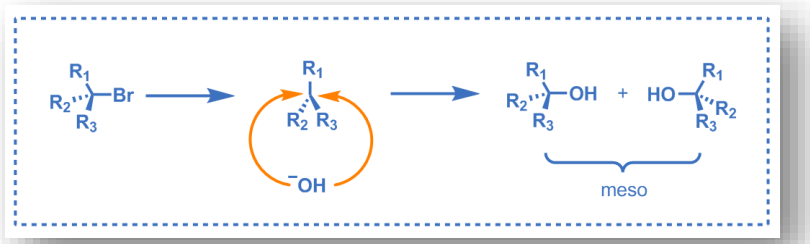
Review

Ion Pair Theory 离子对理论　　描述S_N1过程



极端情况：
RX难以解离
反应在此步
发生

总结果：转型 > 保型



S_N2反应！

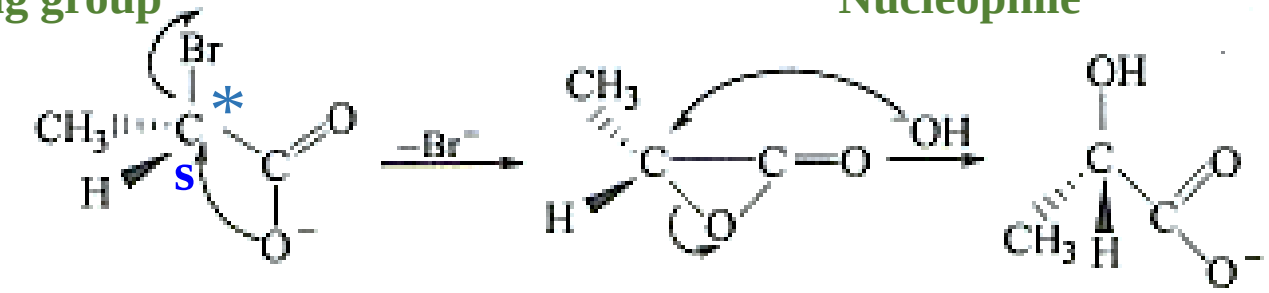
Winstein S.

5.4 The Neighboring-Group Mechanism 邻基参与机理

(S)-α -溴代丙酸盐的水解反应

Leaving group

Nucleophile



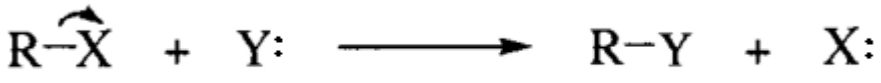
substrate

构型保持

The configuration at the chiral carbon is retained. and not inverted or racemized why?

5.4 The Neighboring-Group Mechanism

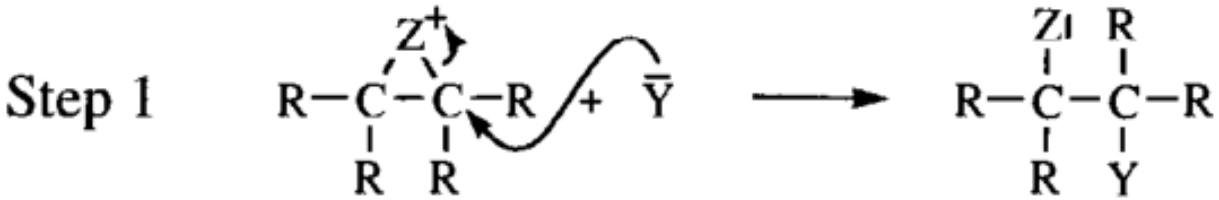
5.4.1 The structure of the substrates



There is usually a group with an unshared pair of electrons β to the leaving group

在离去基团的β-位通常连有一个带有未共用电子对的基团

intramolecular S_N2



intermolecular S_N2

5.4 The Neighboring-Group Mechanism

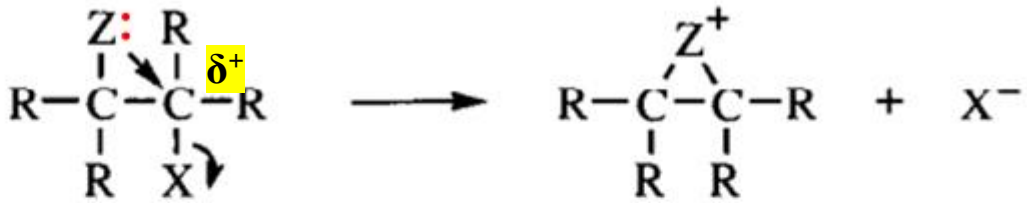
5.4.2 the characteristics of the neighboring-group mechanism

1. **The configuration at a chiral carbon is retained**
2. **The rate of reaction is greater than expected**

The rate law followed in the neighboring-group mechanism is the first-order law, $\text{Rate} = k[\text{RX}]$

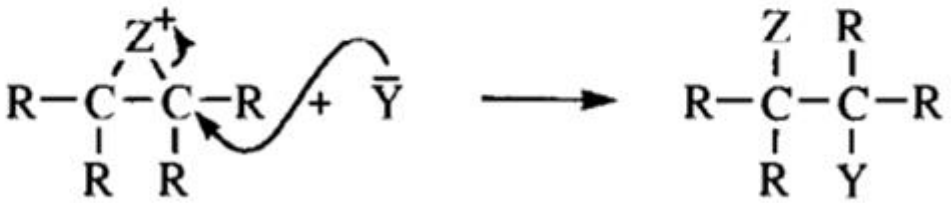
Y does not take part in the rate-determining step.

Step 1



intramolecular S_N2
rate-determining step

Step 1

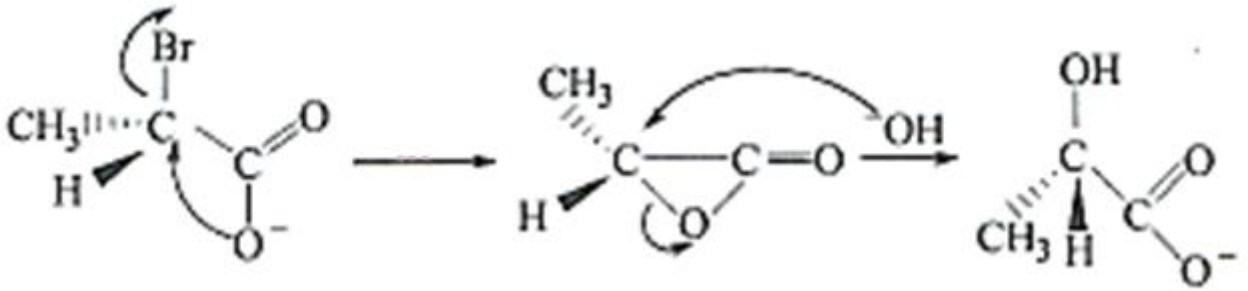


intermolecular S_N2

5.4 The Neighboring-Group Mechanism

The first important evidence for the existence of this mechanism was the demonstration that retention of configuration can occur if the substrate is suitable.

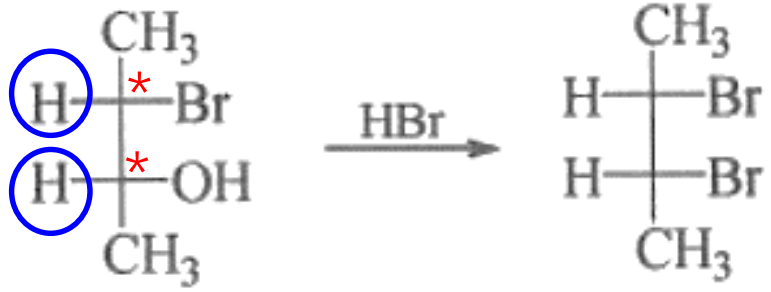
例1 （S）-α -溴代丙酸盐的水解反应（O负离子作为邻近基团）



5.4 The Neighboring-Group Mechanism

例2：3-溴-丁-2-醇与HBr的反应（Br作为邻近基团）

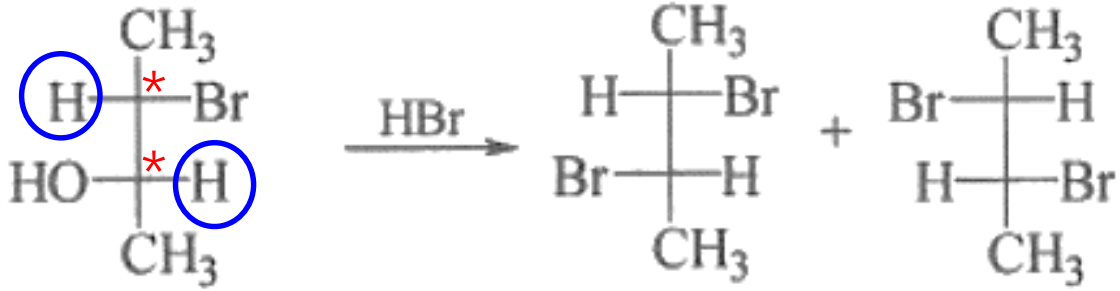
reaction



erythro 赤式

Chiral compound 有旋光性的

内消旋体 **Meso**



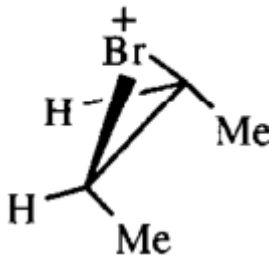
threo 苏式

Chiral compound 有旋光性的

外消旋体

5.4 The Neighboring-Group Mechanism

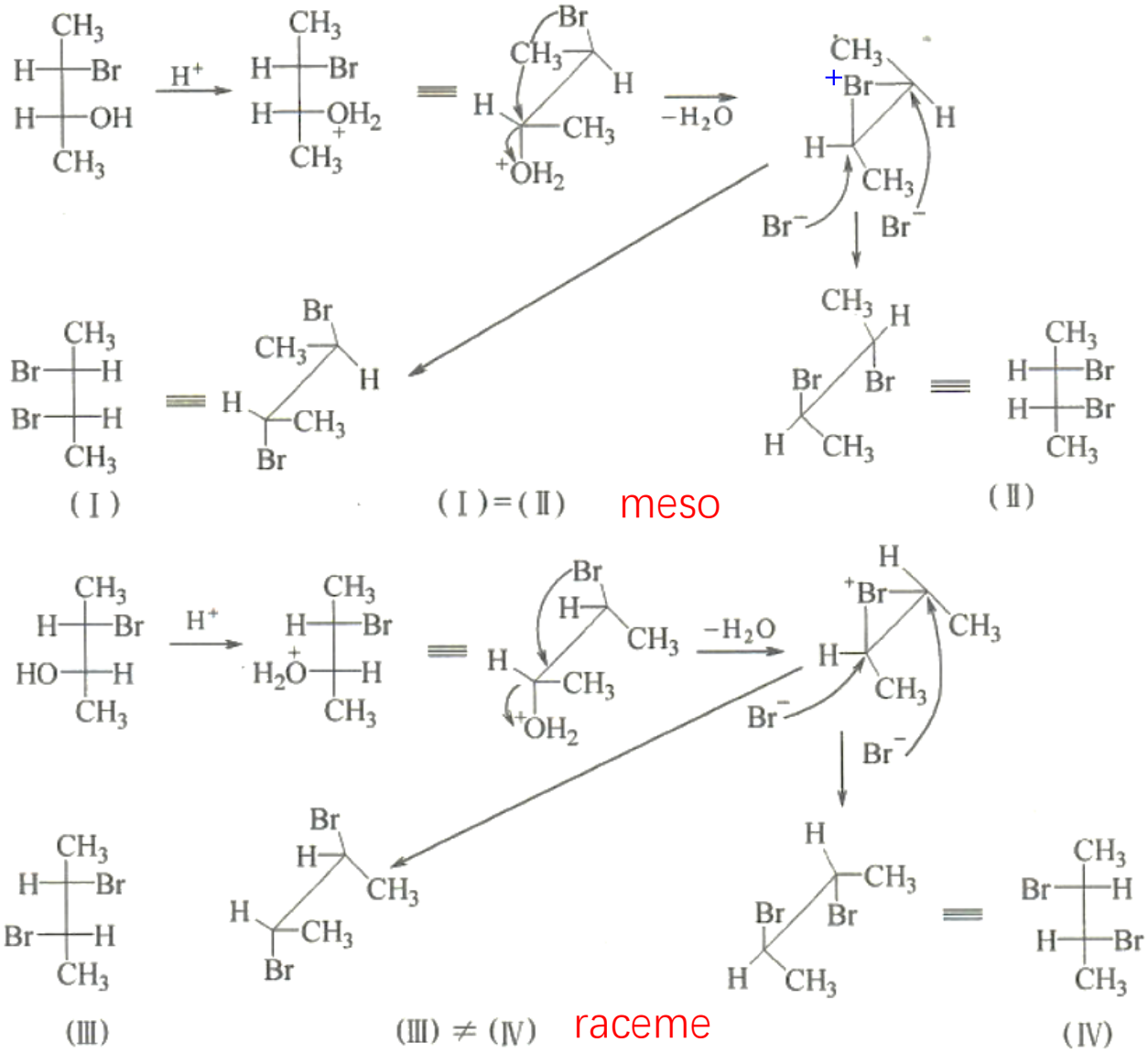
mechanism ★



symmetric

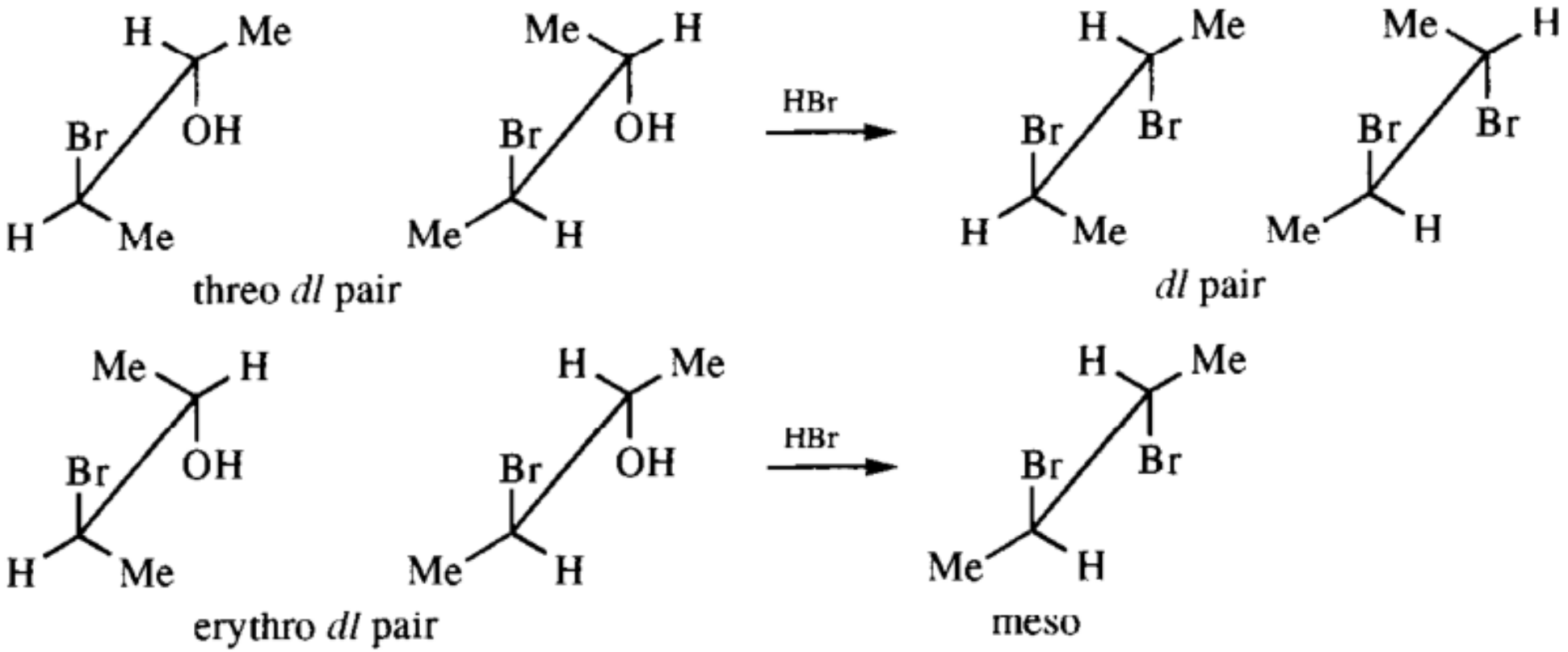
Product of the intramolecular S_N2

反式共平面



5.4 The Neighboring-Group Mechanism

Stereochemistry



raceme

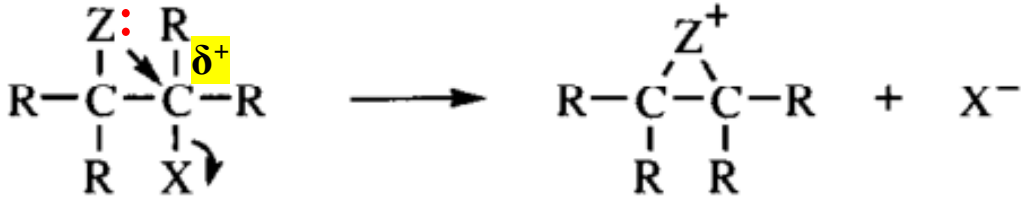
Review （The Neighboring-Group Mechanism）

The structure of the substrates

There is usually a group with an unshared pair of electrons β to the leaving group

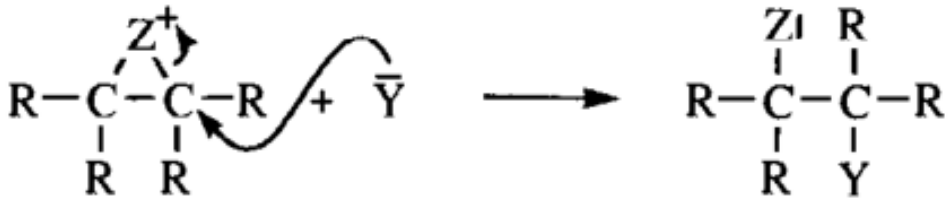
在离去基团的β-位通常连有一个带有未共用电子对的基团

Step 1



intramolecular S_N2

Step 1



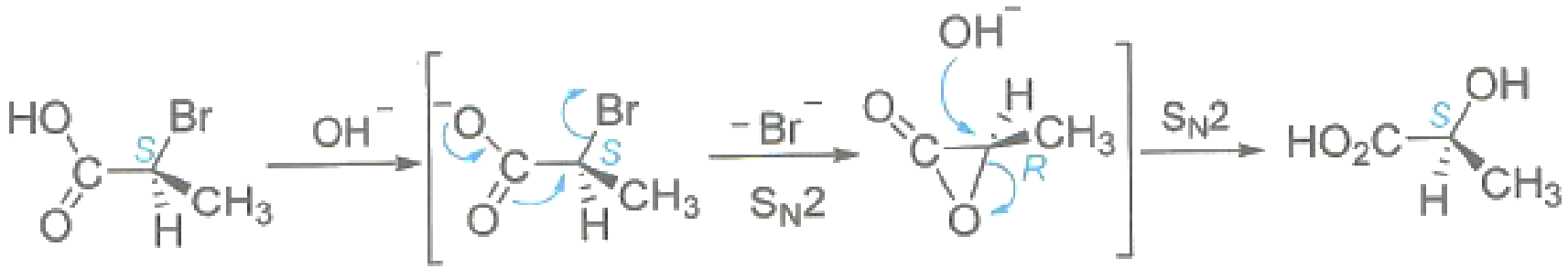
intermolecular S_N2

Review （The Neighboring-Group Mechanism）

the characteristics of the neighboring-group mechanism

1. **The configuration at a chiral carbon is retained**
2. **The rate of reaction is greater than expected**
3. **Carbon skeleton reconstruction may occur**

例1 （S）-α -溴代丙酸盐的水解反应（O负离子作为邻近基团）



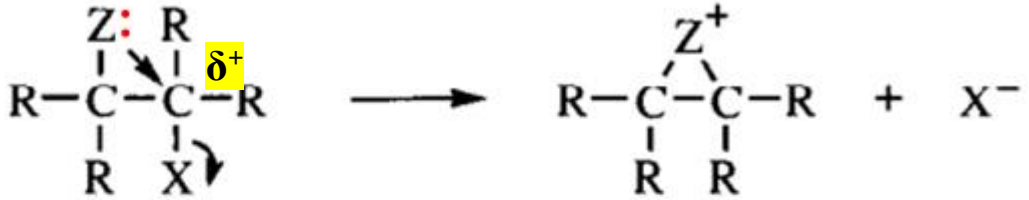
Review （The Neighboring-Group Mechanism）

1. **The configuration at a chiral carbon is retained**
2. **The rate of reaction is greater than expected**
3. **Carbon skeleton reconstruction may occur**

The rate law followed in the neighboring-group mechanism is the first-order law,
Y does not take part in the rate-determining step.

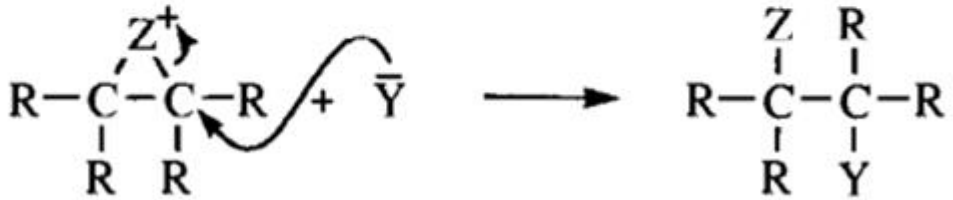
$$\text{Rate} = k[\text{RX}]$$

Step 1



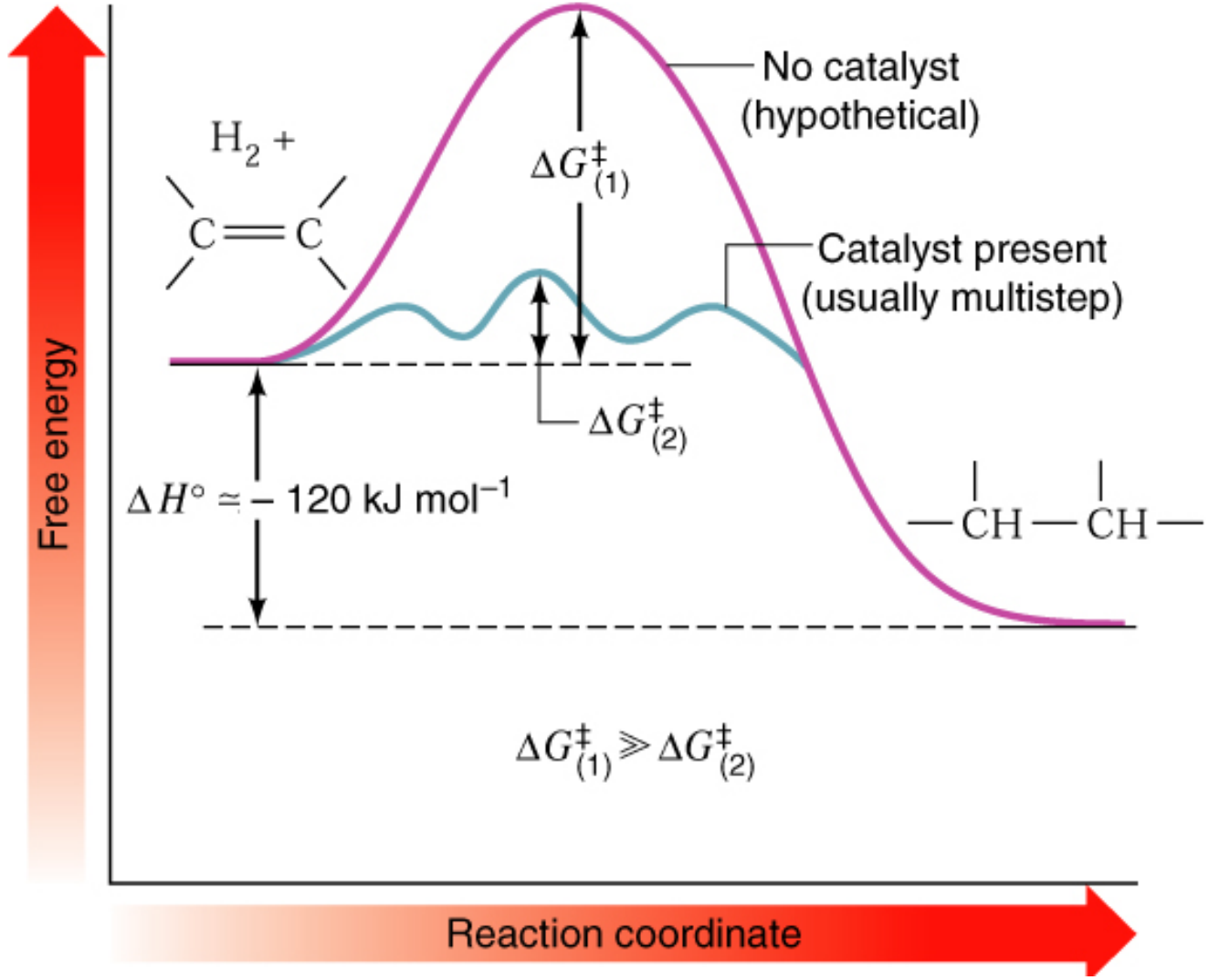
intramolecular S_N2
rate-determining step

Step 1



intermolecular S_N2

5.4 The Neighboring-Group Mechanism



Chapter 5

Aliphatic Nucleophilic Substitution

脂肪族亲核取代反应

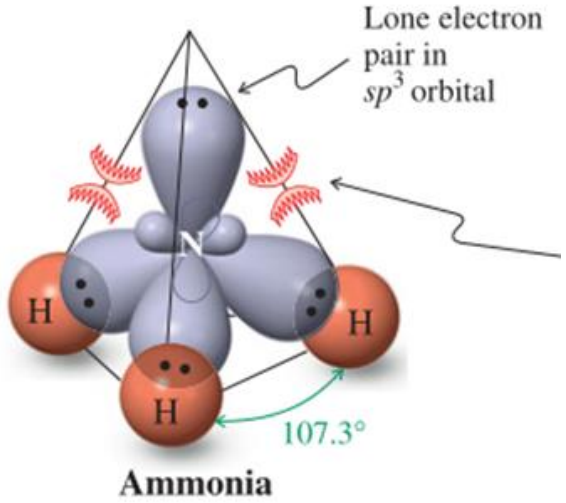
At saturated carbon

Qiong Li

March 18, 2024

Review

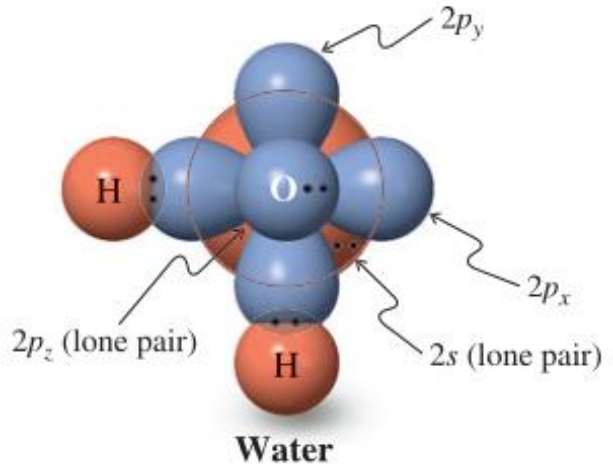
general equation of S_N



There are four charge types for the equation

nucleophile

Type I	R–I	+	OH^-	⟶	R–OH	+ I^-
Type II	R–I	+	NMe_3	⟶	$R-\overset{+}{N}Me_3$	+ I^-
Type III	$R-\overset{+}{N}Me_3$	+	OH^-	⟶	R–OH	+ NMe_3
Type IV	$R-\overset{+}{N}Me_3$	+	H_2S	⟶	$R-\overset{+}{S}H_2$	+ NMe_3

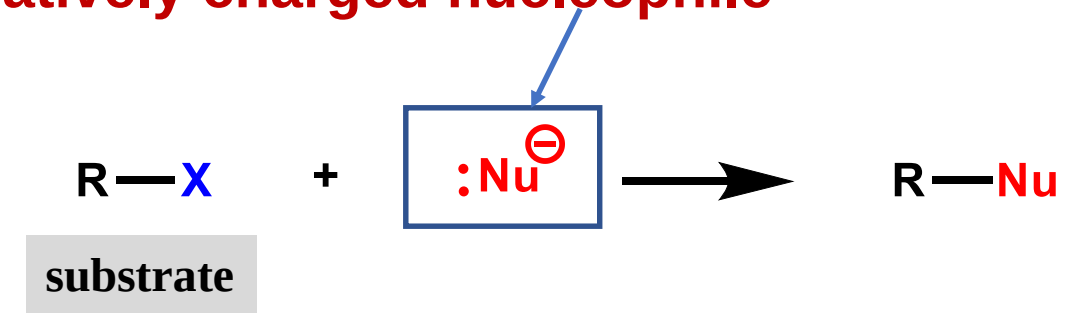


Nucleophile must have an unshared pair of electrons, it can be neutral or negatively charged.

Substrate (RX) may be neutral or positively charged.

Review

with negatively charged nucleophile



$OH^{\ominus}$	R—OH	Alcohol
$OR'^{\ominus}$	R—OR'	Ether
$SH^{\ominus}$	R—SH	Mercaptan
$SR'^{\ominus}$	R—SR'	Alkyl Sulphide
$^{\ominus}O-\overset{\overset{O}{\|\|}}{C}-R'$	$R-O-\overset{\overset{O}{\|\|}}{C}-R'$	Ester

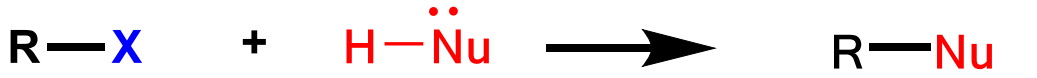
Review

with negatively charged nucleophile

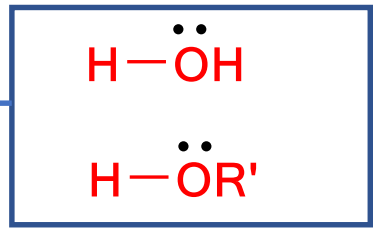
$^{\ominus}CN$	R—CN	Nitrile
$^{\ominus}C{\equiv}C-R'$	R—C≡C—R'	Alkyne
$^{\ominus}CH(CO_2Et)_2$	R—$CH(CO_2Et)_2$	Alkyl malonate
$I^{\ominus}$	R—I	Iodoalkane

Review

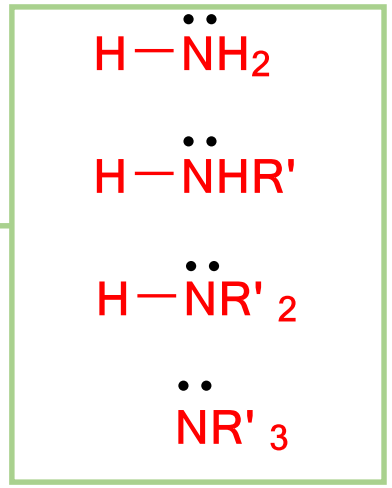
with neutral nucleophile

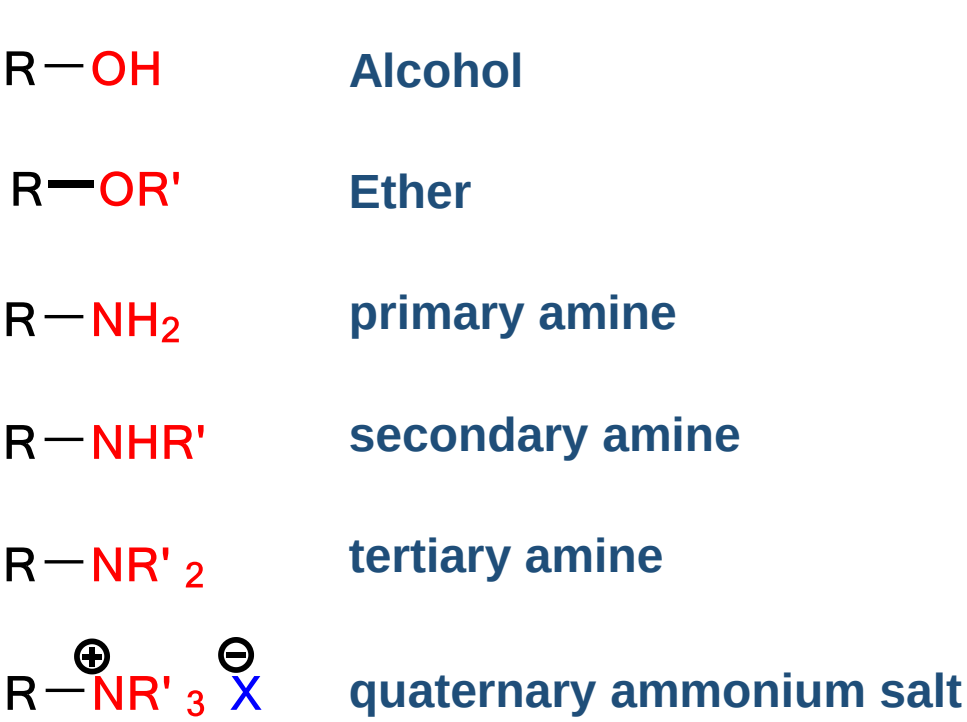


When HNu is a solvent,
The reaction is called
Solvolysis(溶剂解)



Nucleophilic substitution at an alkyl carbon is also said to alkylate the nucleophile.





Review

Several distinct mechanisms are possible for aliphatic nucleophilic substitution reactions. Depending on the substrate, nucleophile, leaving group, and reaction condition.

In all of them, Nucleophile (attacking reagent) must carry electron pair with it. it can be neutral or negatively charged.

By far the most common mechanisms that occur at a saturated carbon are the $S_N1$and S_N2 mechanisms.

Classification of the nucleophilic substitution mechanisms

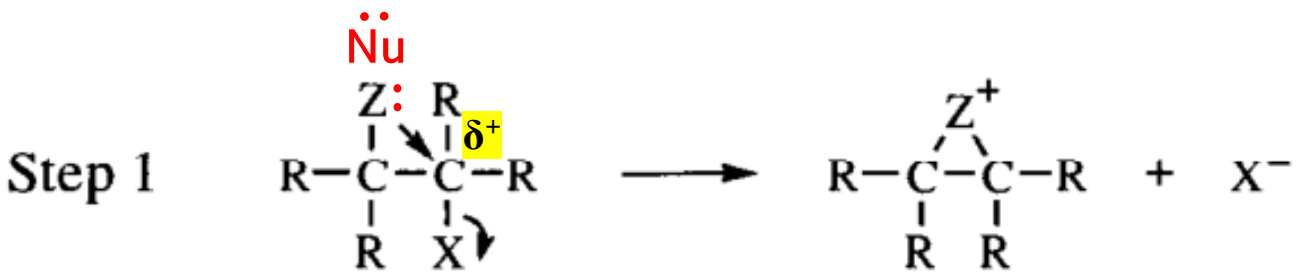
S_N1, S_N2, The neighboring-Group mechanism, S_Ni

Review （The Neighboring-Group Mechanism）

The structure of the substrates

There is usually a group with an unshared pair of electrons β to the leaving group

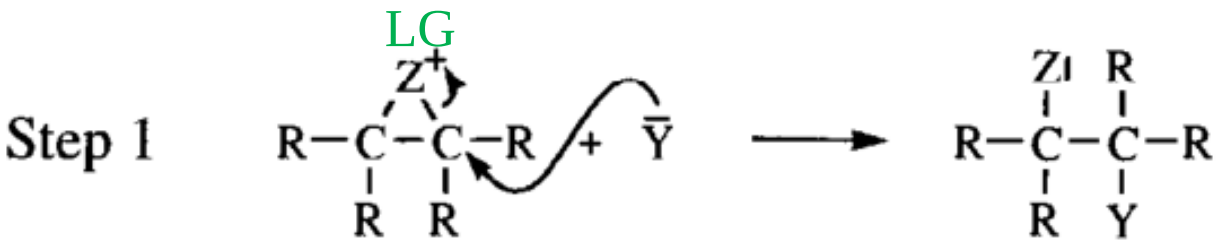
在离去基团的β-位通常连有一个带有未共用电子对的基团



$$\text{Rate} = k[\text{RX}]$$

intramolecular S_N2

rate-determining step



intermolecular S_N2

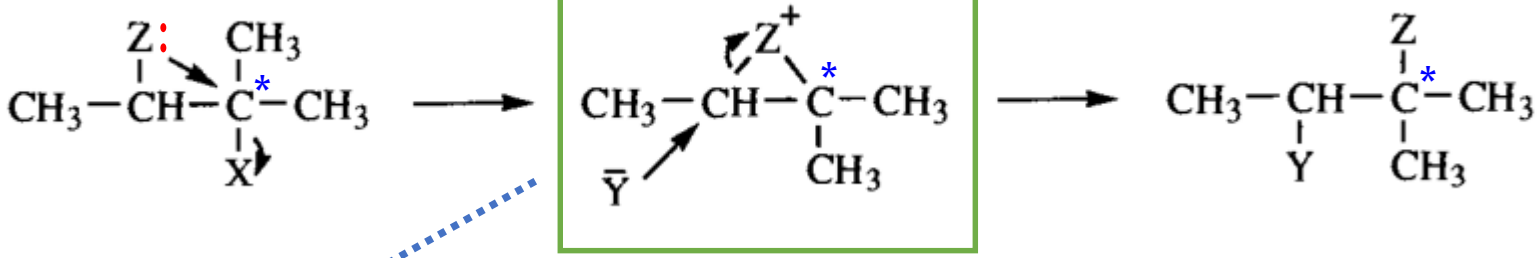
Review （The Neighboring-Group Mechanism）

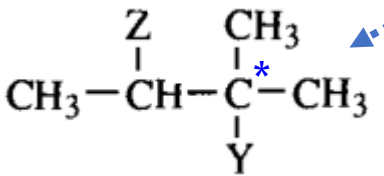
the characteristics of the neighboring-group mechanism

1. The configuration at a chiral carbon is retained
2. The rate of reaction is greater than expected
3. Carbon skeleton reconstruction may occur

In such cases, substitution and rearrangement products are often produced together.

rearrangement





Product of the intramolecular S_N2

asymmetric

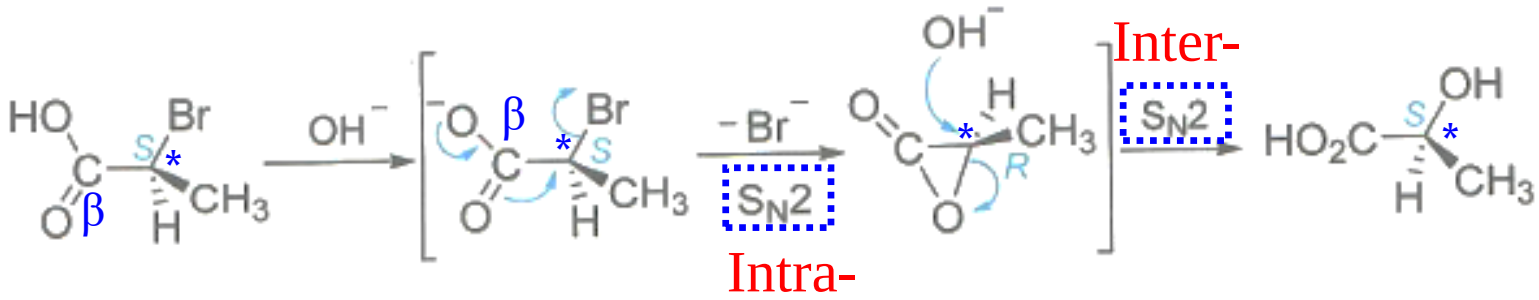
通过邻基参与发生重排反应

5.4 The Neighboring-Group Mechanism

5.4.3 Some of the more important neighboring groups

a. Neighboring group participation by O atom (-COO$^-$)

例1 （S）-α -溴代丙酸盐的碱性水解反应（O负离子作为邻近基团）



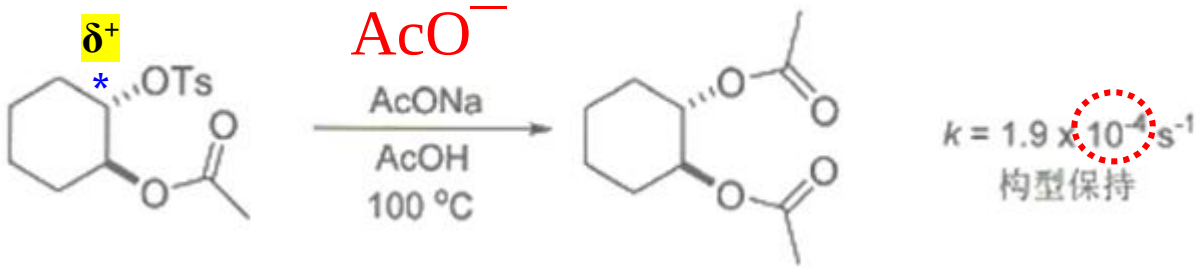
Unstable α-lactone intermediate

5.4 The Neighboring-Group Mechanism

Neighboring group participation by O atom (-COOR)

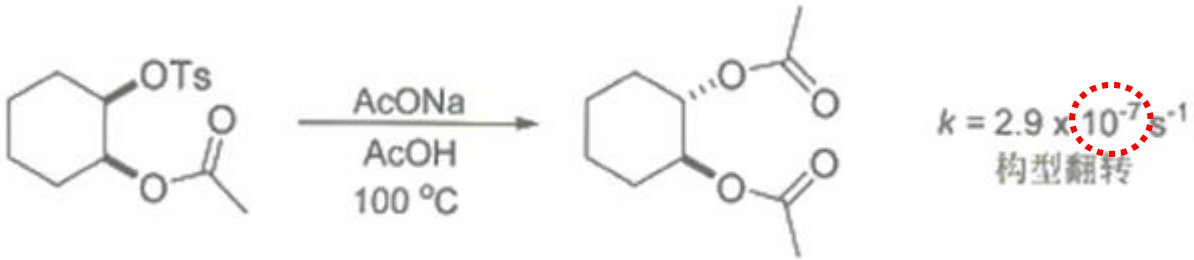
例2：acetolysis of anti isomer of 2-(tosyloxy)cyclohexyl acetate （酯基氧原子作为邻近基团）

例2 1-乙酰氧基-2对甲苯磺酰氧基环己烷的乙酸解反应（羰基氧原子作为邻近基团）



anti-isomer **Configuration retained**

anti-2-(tosyloxy)cyclohexyl acetate



syn-isomer **Configuration inverted**

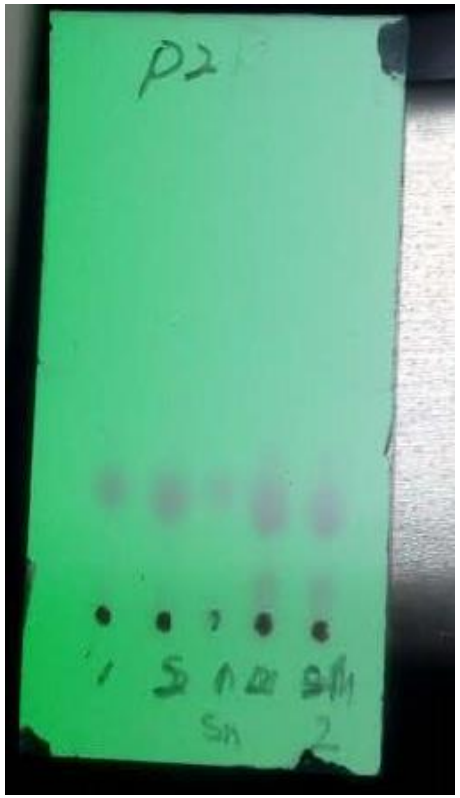
syn-2-(tosyloxy)cyclohexyl acetate

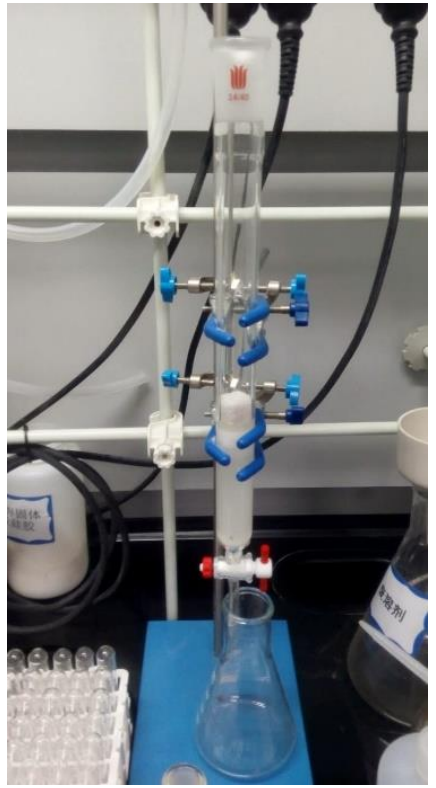
The Neighboring-Group Mechanism

intramolecular S_N2 + intermolecular S_N2

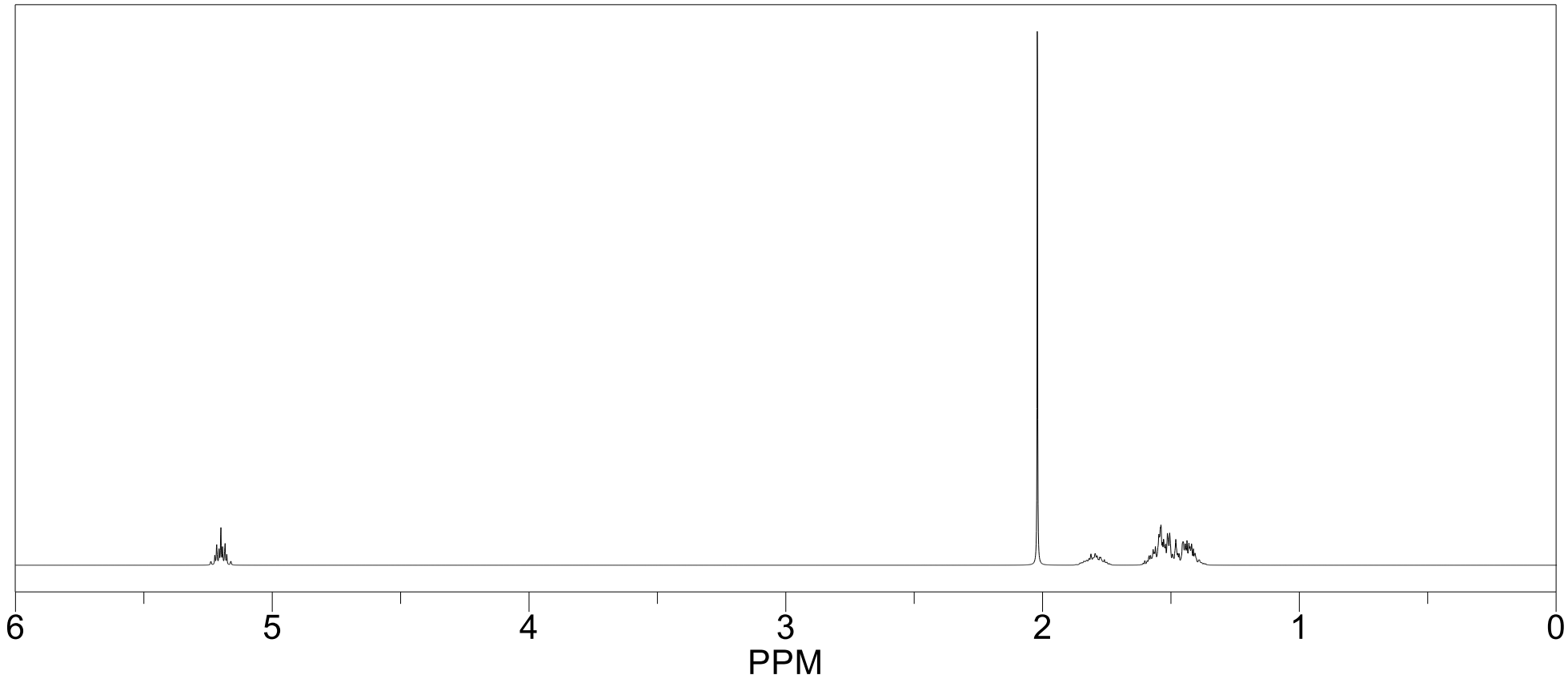
anti-isomer is about 10^3 times faster than that of syn-isomer

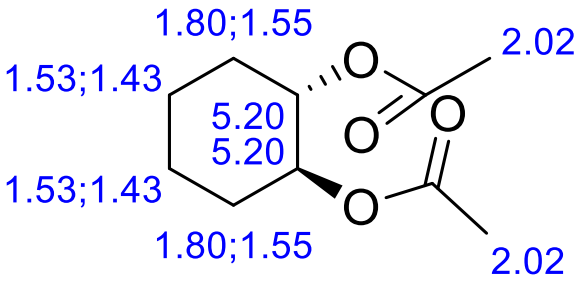
5.4 The Neighboring-Group Mechanism





5.4 The Neighboring-Group Mechanism



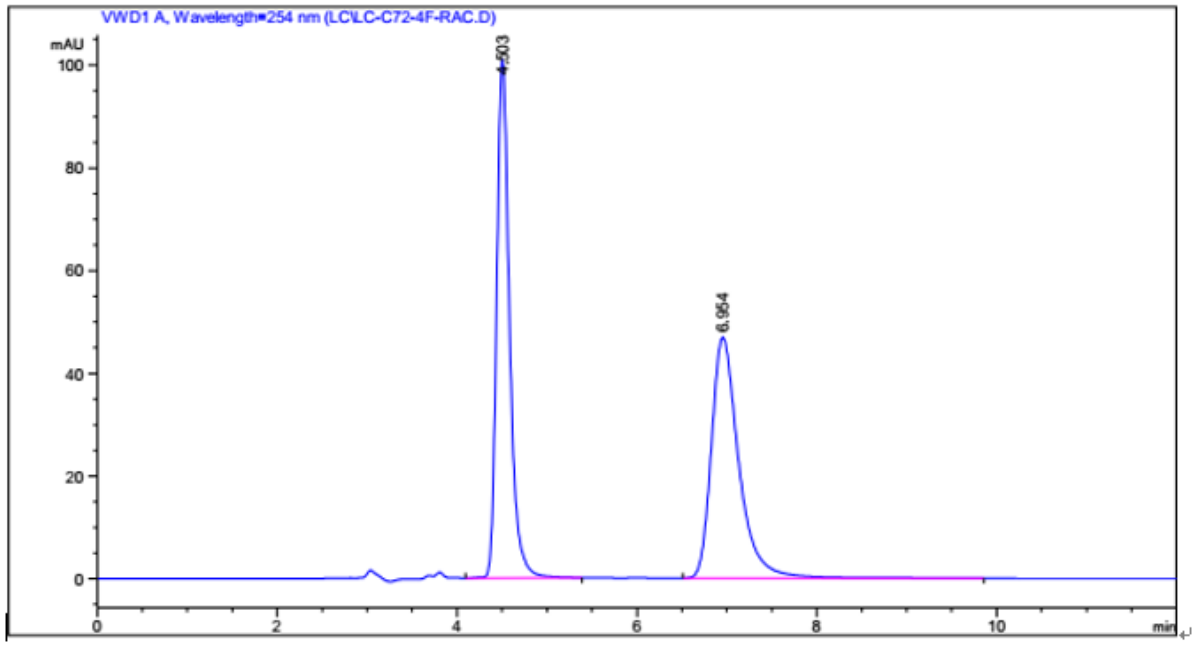


5.4 The Neighboring-Group Mechanism

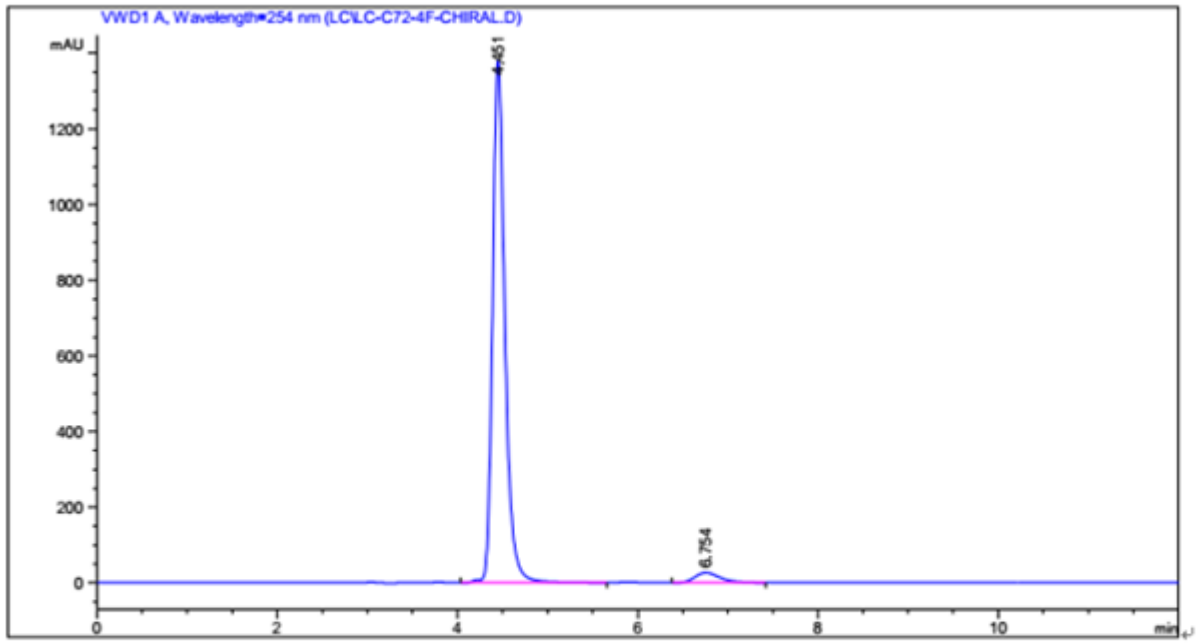
HPLC

GC

5.4 The Neighboring-Group Mechanism



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.503	BB	0.1516	997.78448	100.74065	50.1051
2	6.954	BB	0.3213	993.59680	46.88333	49.8949

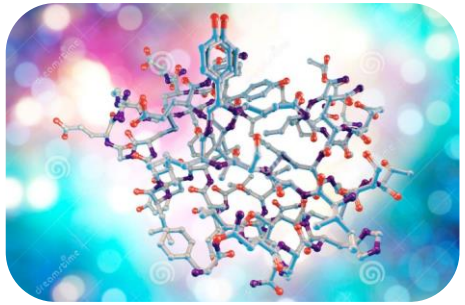


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.451	VB R	0.1450	1.31675e4	1380.53625	96.2340
2	6.754	BB	0.2948	515.29236	26.73674	3.7660

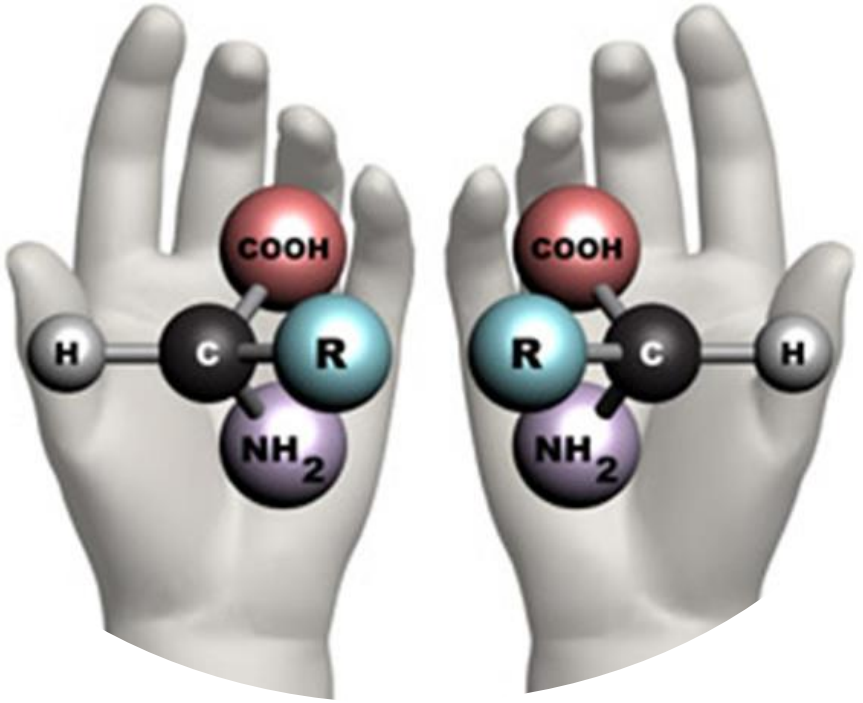
Fundamentals of Stereochemistry

Chirality

海螺



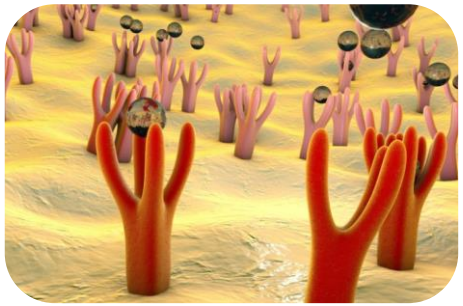
蛋白质



手性药物

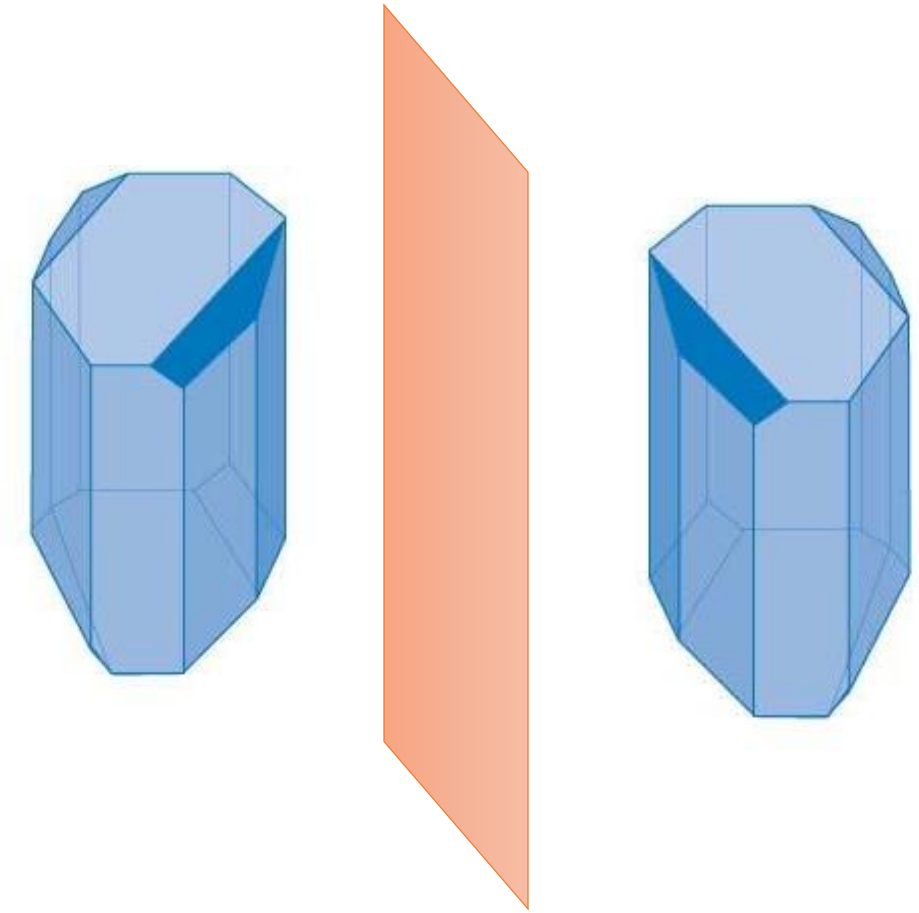
手性：左右手互为镜像但无法重叠的性质

核酸

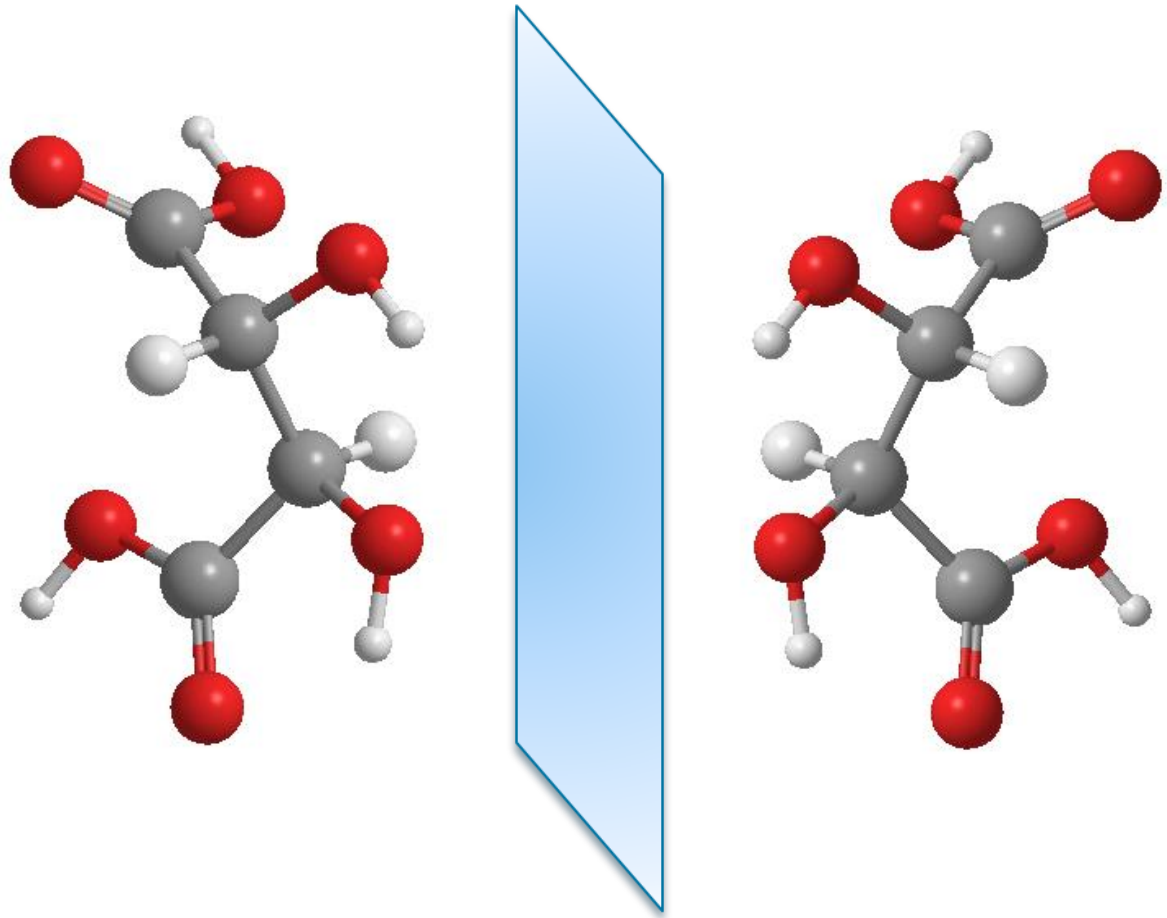


受体

Fundamentals of Stereochemistry

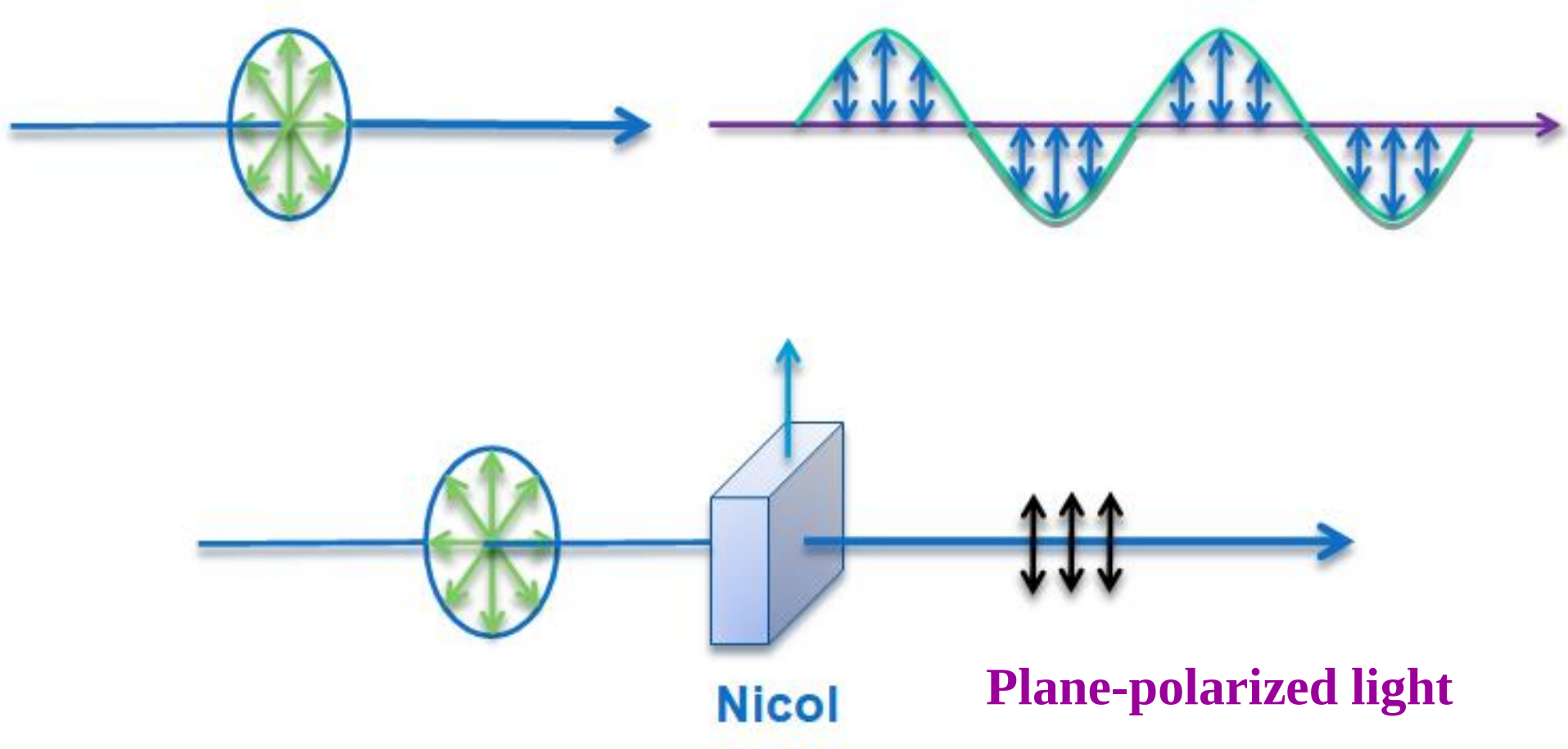


Chirality 手性



Chirality 手性

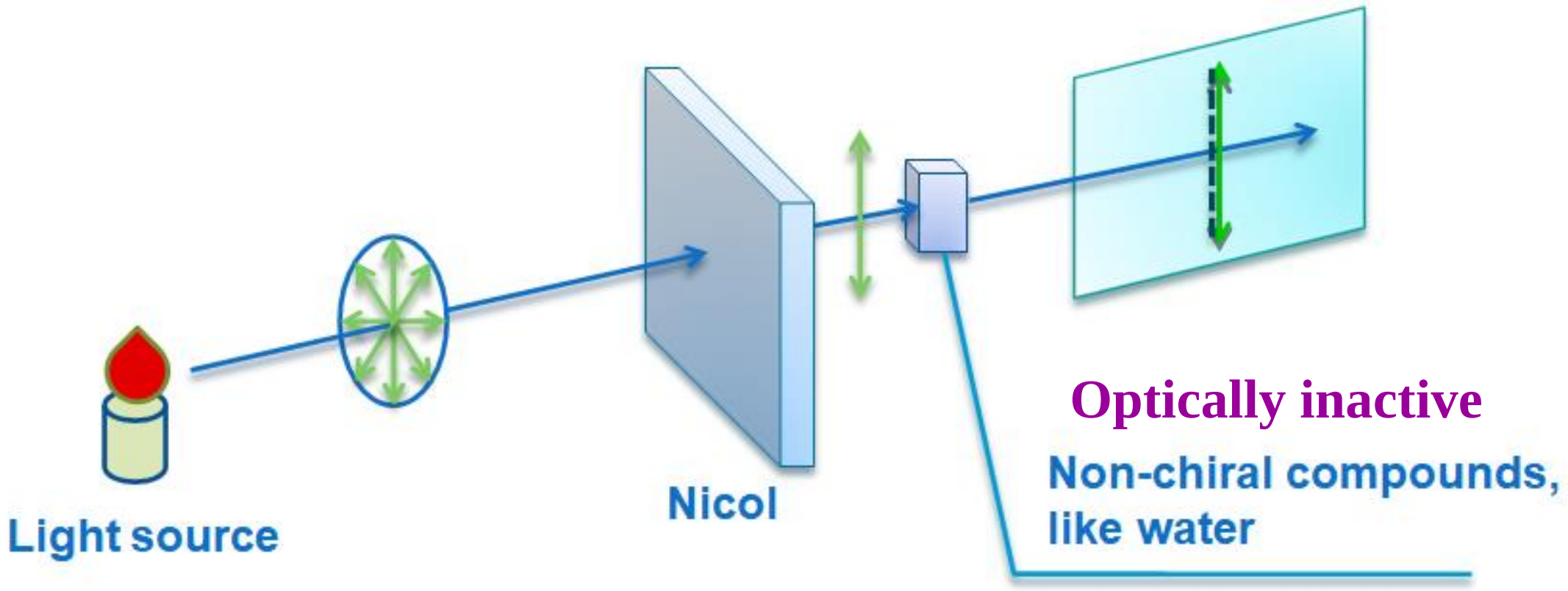
1. Optical Activity and Chirality



Plane-polarized light

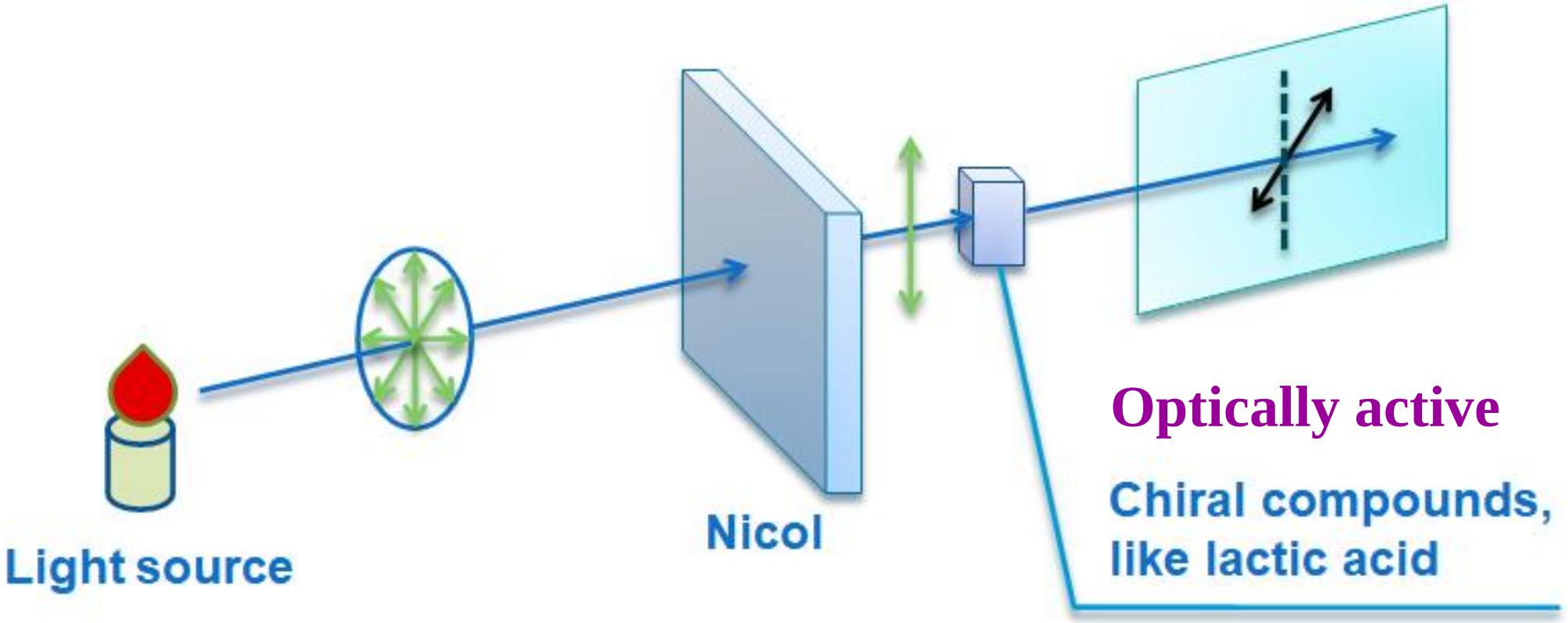
平面偏振光（偏振光）

Fundamentals of Stereochemistry



该化合物具没有“光学活性”、没有“旋光性”

Fundamentals of Stereochemistry



该化合物具有“光学活性”、“旋光性”

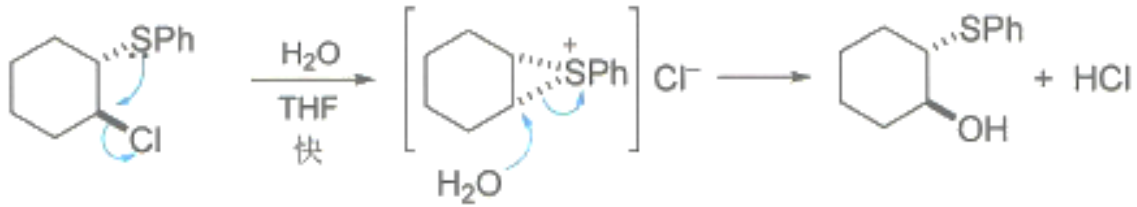
5.4 The Neighboring-Group Mechanism

b. Neighboring group participation by S atom

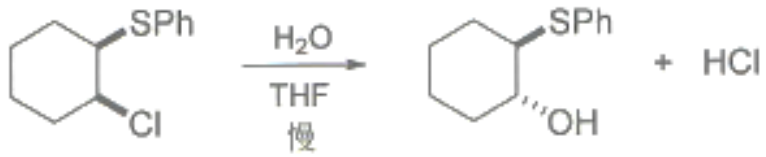
例3：hydrolysis of anti isomer of 1-chloro-2-thiophenyl cyclohexane（S原子作为邻近基团）

例3 反式-1-氯-2-苯硫基环己烷的水解反应（ S原子作为邻近基团）

anti-isomer

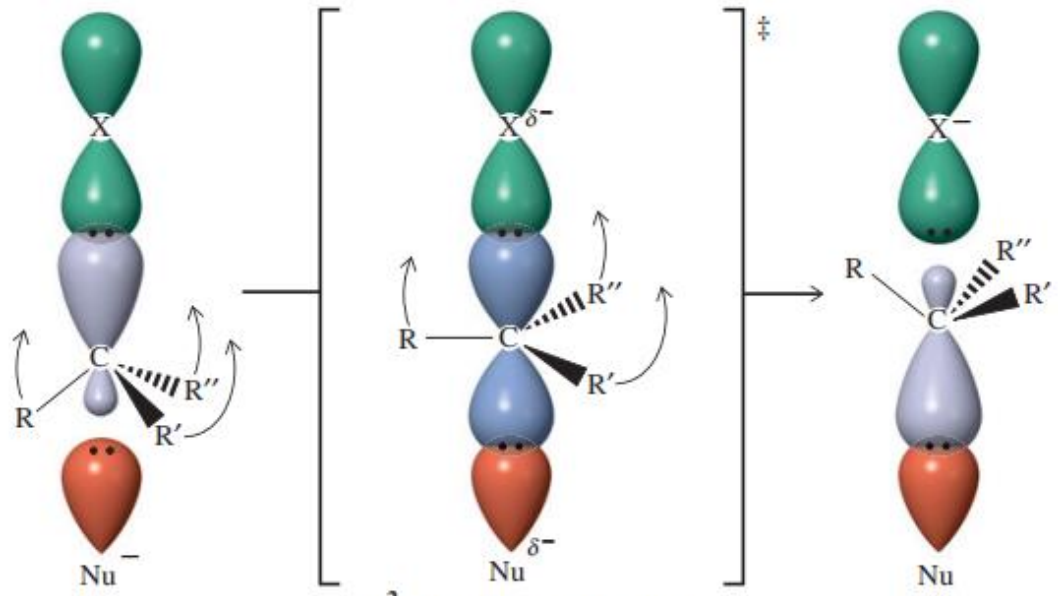


syn-isomer

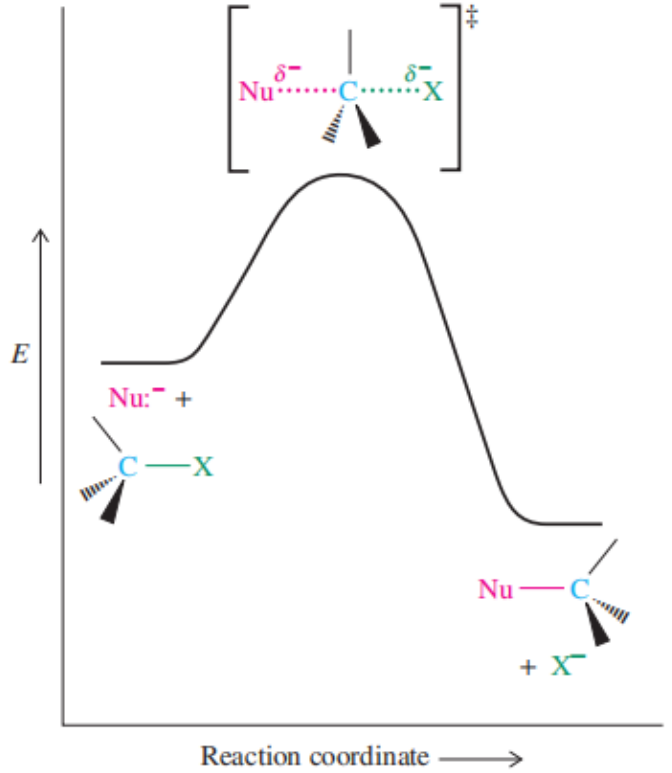


anti-isomer is 10^5 times faster than that of syn-isomer

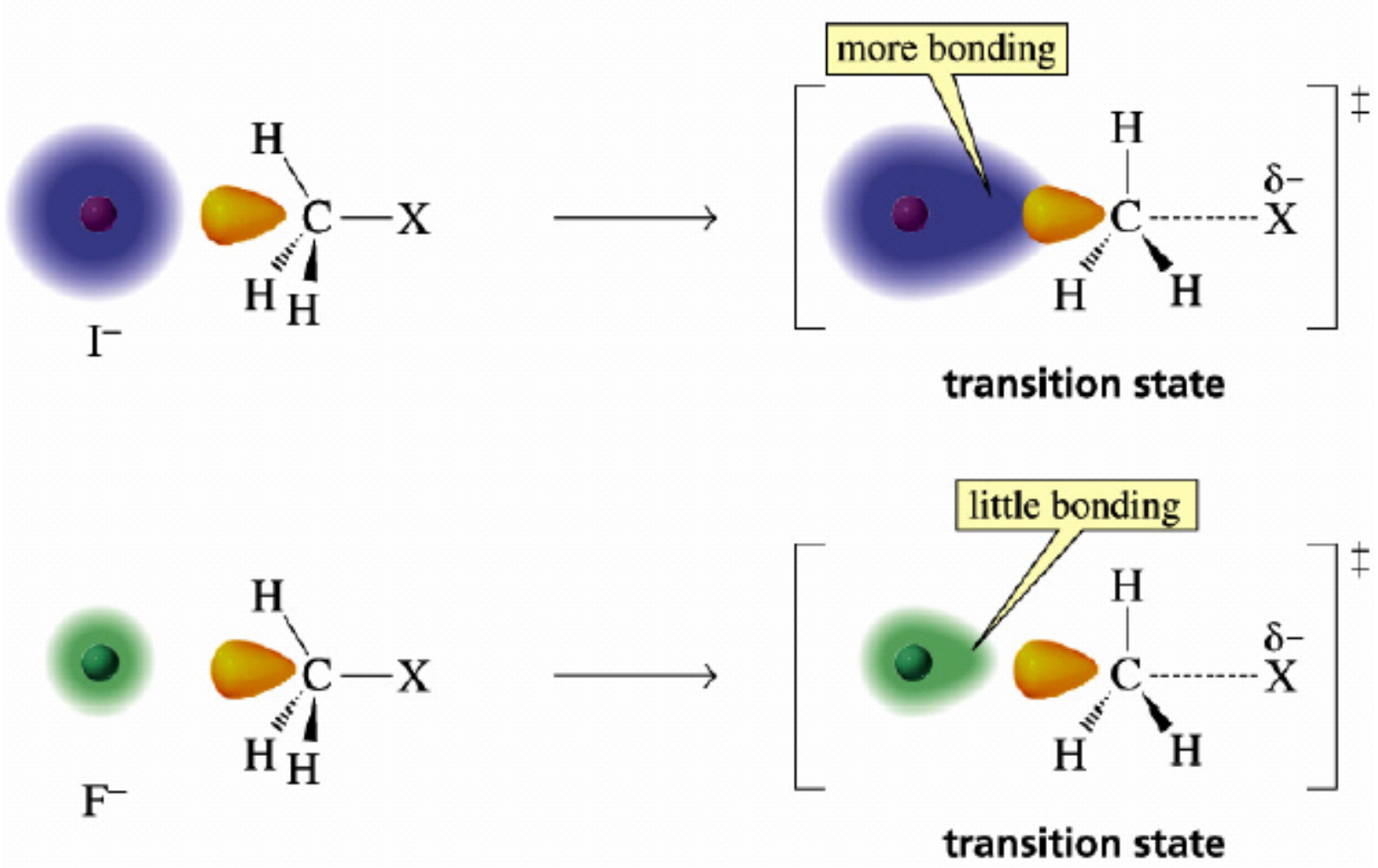
Transition State of S_N2 Reation



sp^2 hybridization at carbon



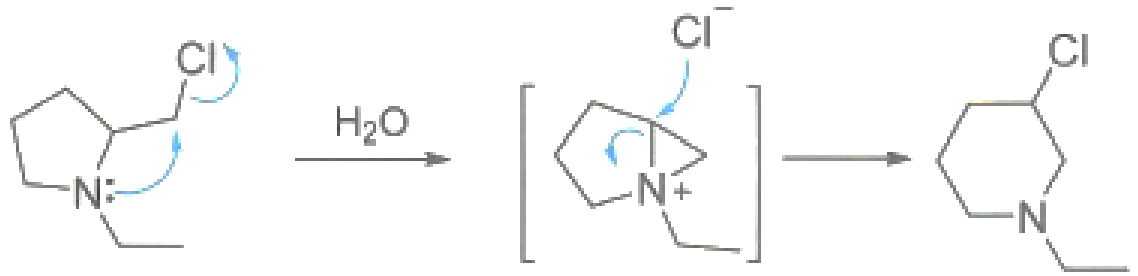
Inducted Dynamic Nuclear Polarization



5.4 The Neighboring-Group Mechanism

c. Neighboring group participation by N atom

例4 2-氯甲基-N-乙基吡咯烷通过N邻基参与发生扩环（N原子作为邻近基团，**碳骨架重构**）



2-(chloromethyl)-N-ethylpyrrolidine **3-chloro-1-ethylpiperidine**

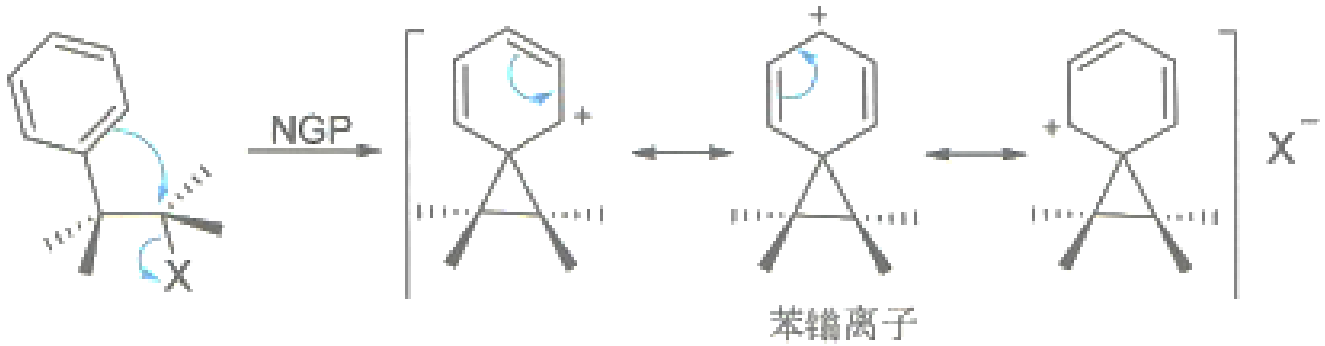
1. **The configuration at a chiral carbon is retained**
2. **The rate of reaction is greater than expected**
3. **Carbon skeleton reconstruction may occur**

5.4 The Neighboring-Group Mechanism Homework

5.4 The Neighboring-Group Mechanism

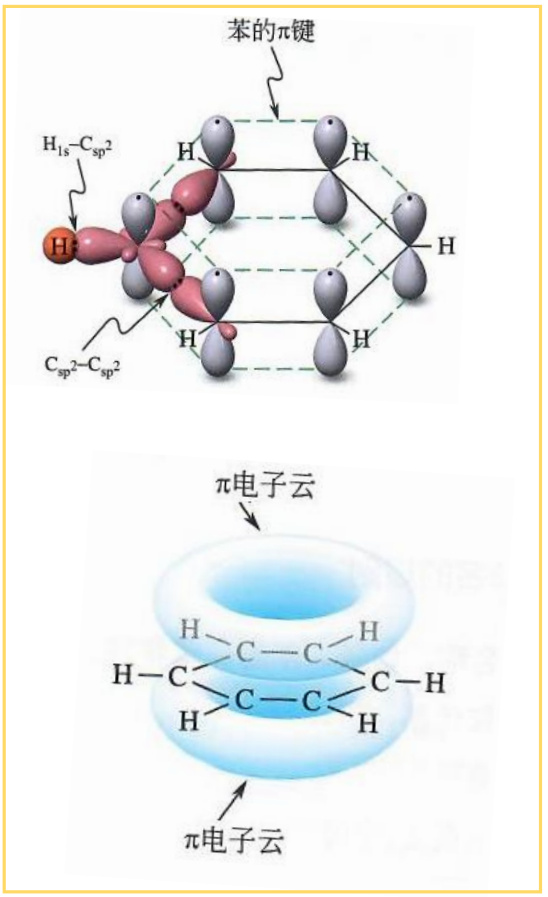
d. Neighboring group participation by aromatic ring

具有6π电子的苯环是常见的邻基参与基团

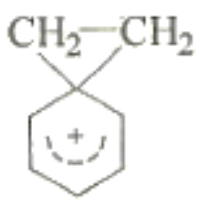


Phenonium ion intermediate

resonance stabilization



5.4 The Neighboring-Group Mechanism



(Ⅳ)

(Ⅵ)

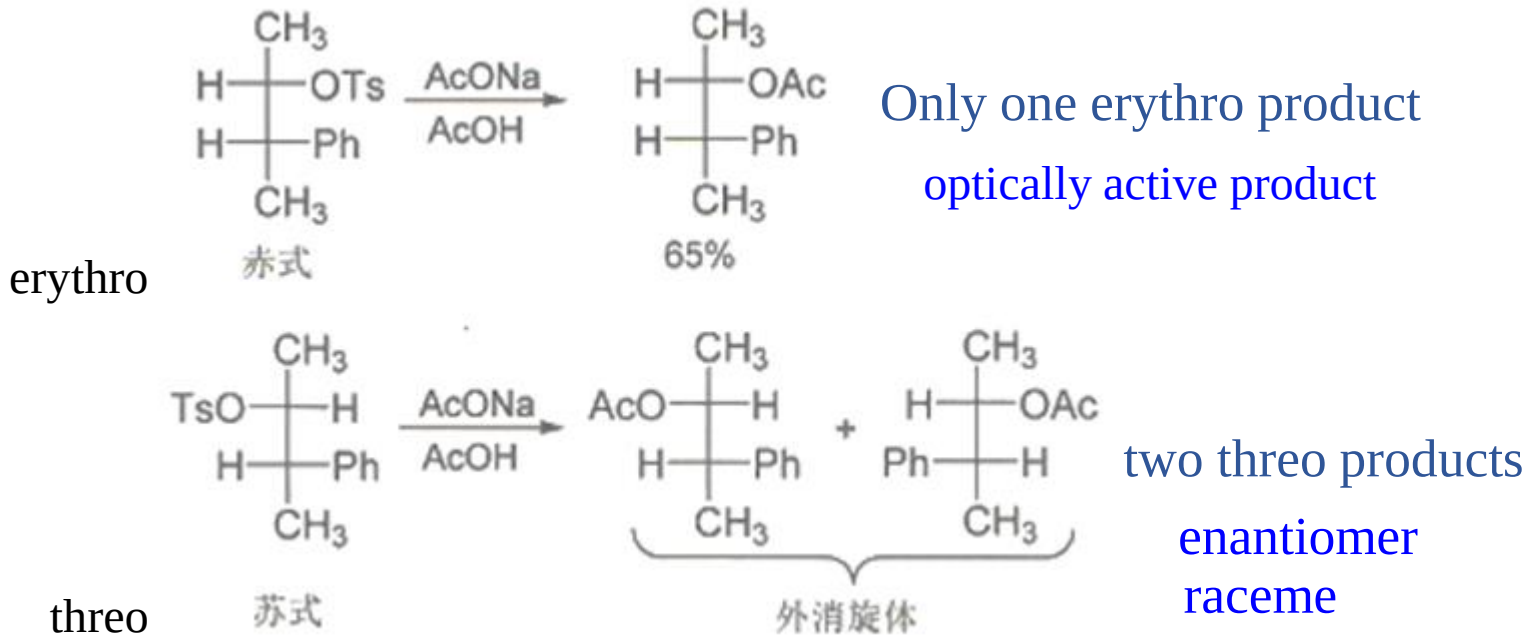
NMR证实，苯鎓离子IV结构和苯环方向亲电取代反应中间体σ-络合物VI是相似的。

5.4 The Neighboring-Group Mechanism

例5：acetolysis of 3-phenylbutan-2-yl 4-methylbenzenesulfonate（苯基作为邻近基团）

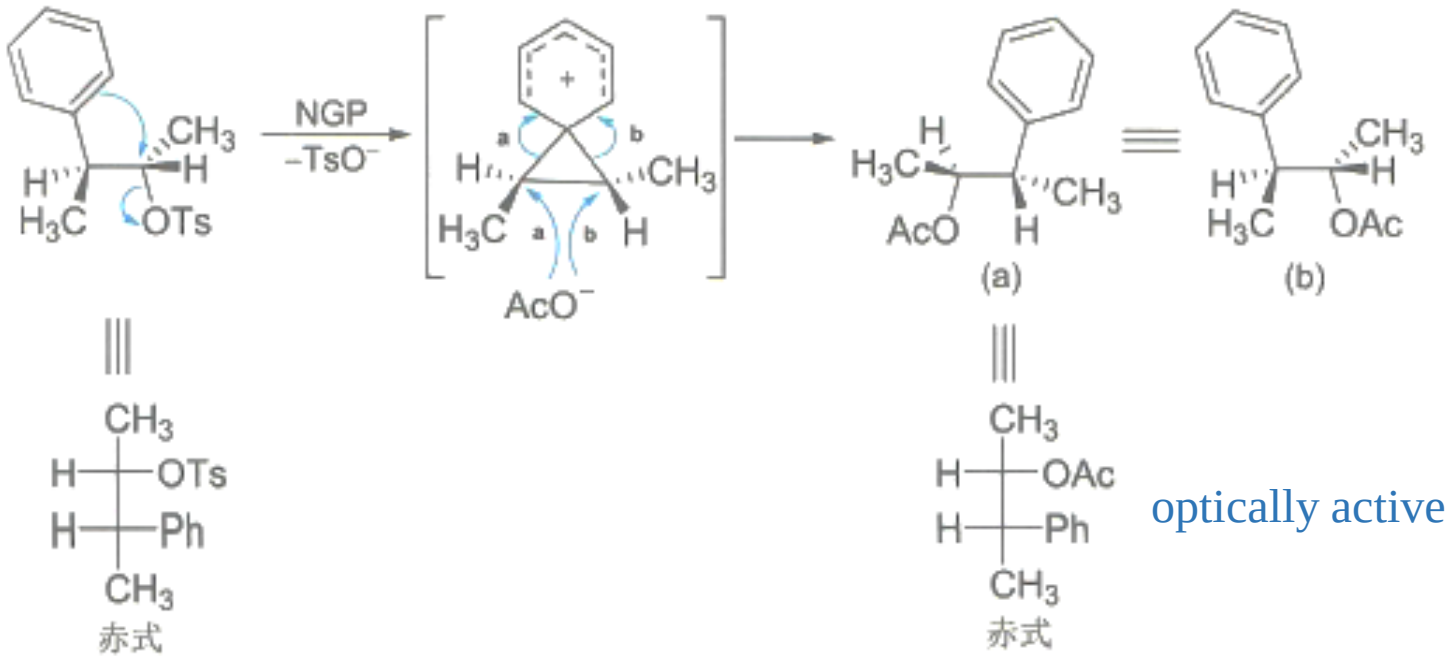
例5：3-苯基丁-2-醇对甲苯磺酸酯的乙酸解（苯基作为邻近基团）

Results of stereochemical studies



5.4 The Neighboring-Group Mechanism

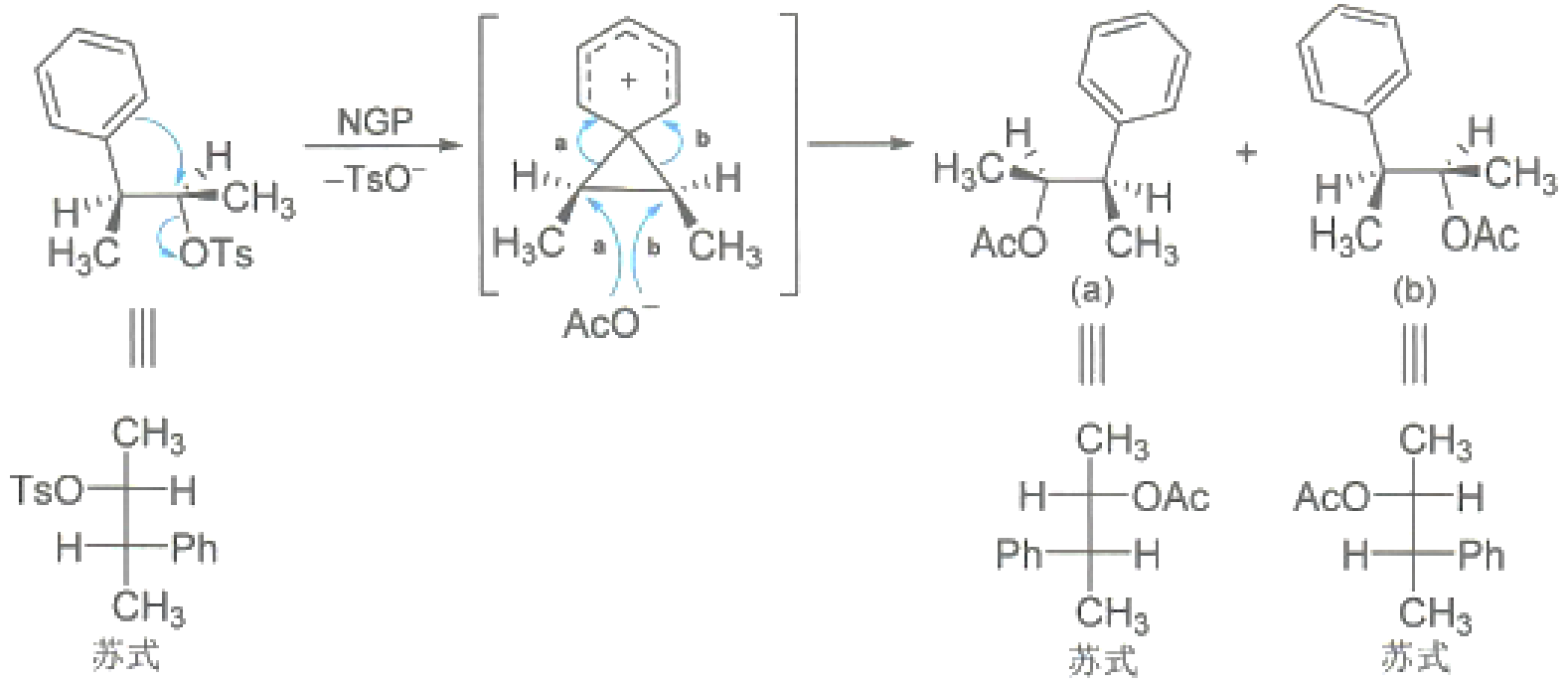
identical compound



optically active 光学活性

erythro

5.4 The Neighboring-Group Mechanism



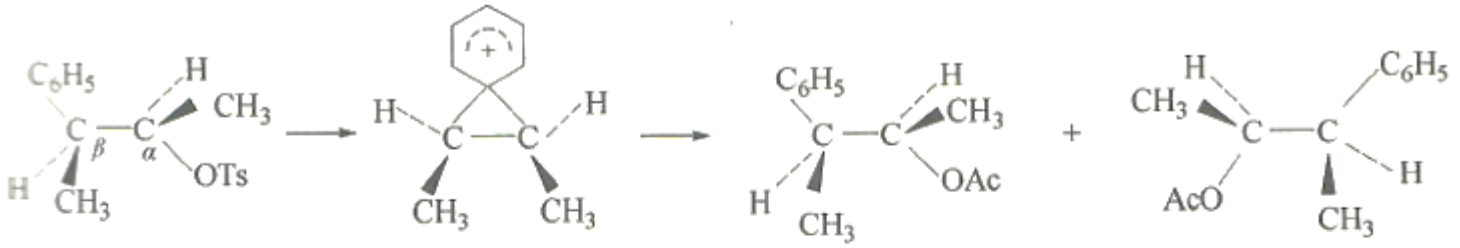
threo

Threo product 1　　Threo product 2

enantiomer

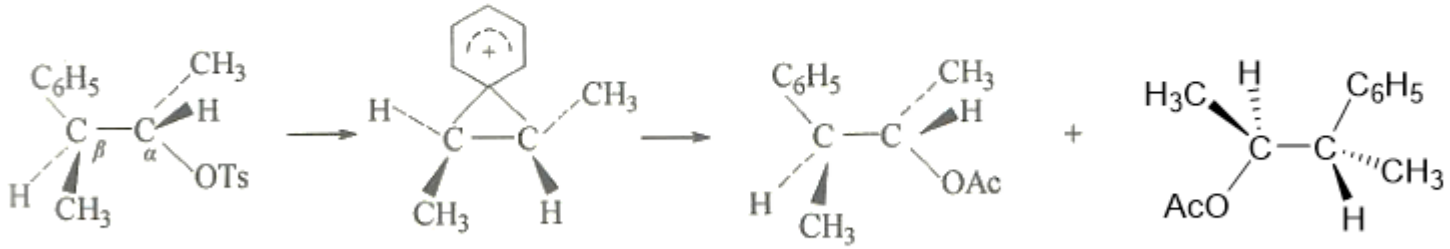
raceme

5.4 The Neighboring-Group Mechanism



threo Phenonium ion 苯鎓离子 D- enantiomer L- raceme

(Ⅰ) (Ⅱ) (Ⅲ)

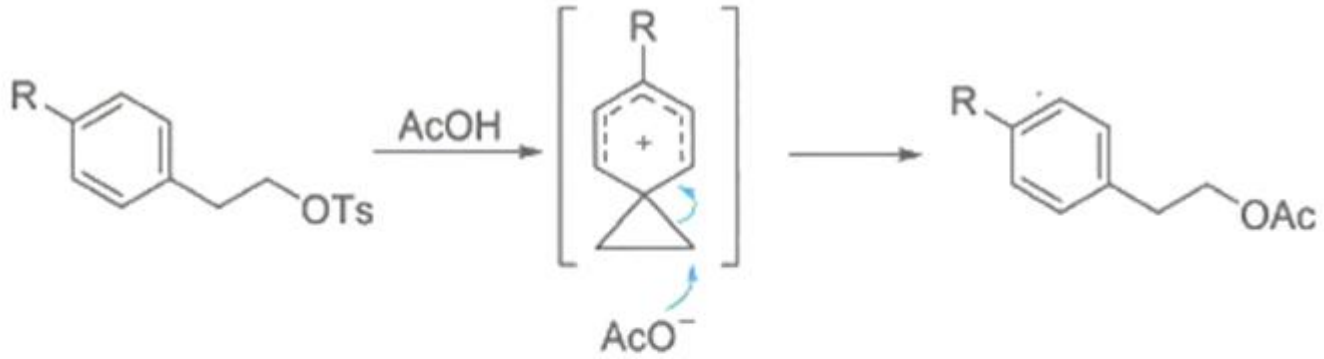


erythro Phenonium ion 苯鎓离子 L- identical compound

(Ⅰ′) (Ⅱ′) (Ⅲ′) optically active 光学活性

5.4 The Neighboring-Group Mechanism

Exercise: which of the following compounds is the most reactive towards acetolysis reaction?

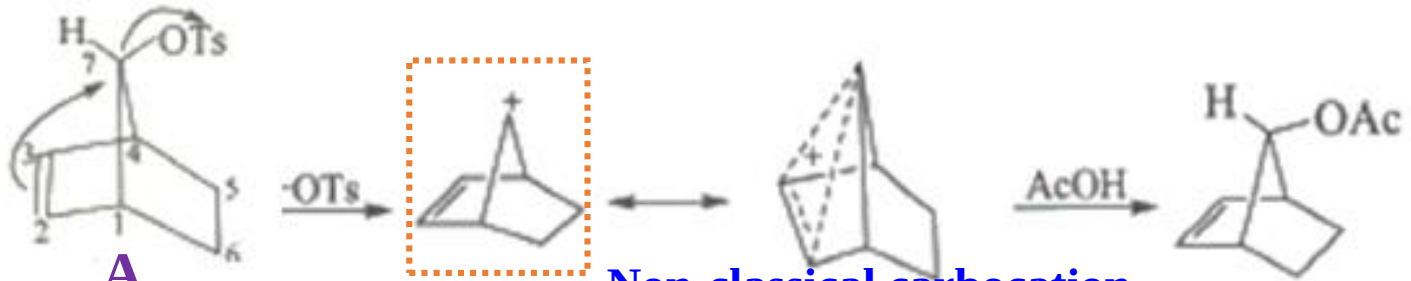


R	yield / %
NO_2	0
CF_3	0
Cl	0
H	38
CH_3	71
OCH_3	94

5.4 The Neighboring-Group Mechanism

e. Neighboring group participation by π bonds π-electrons of C=C can act as a neighboring group

例6：acetolysis of anti isomer of 7-norbornenyl tosylate（π-bond作为邻近基团）



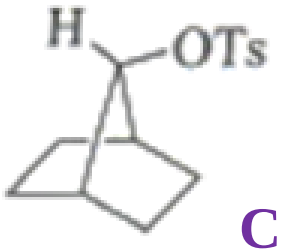
A

anti-7-norbornenyl tosylate

Non-classical carbocation

7-norbornenyl cation

1. retention of configuration

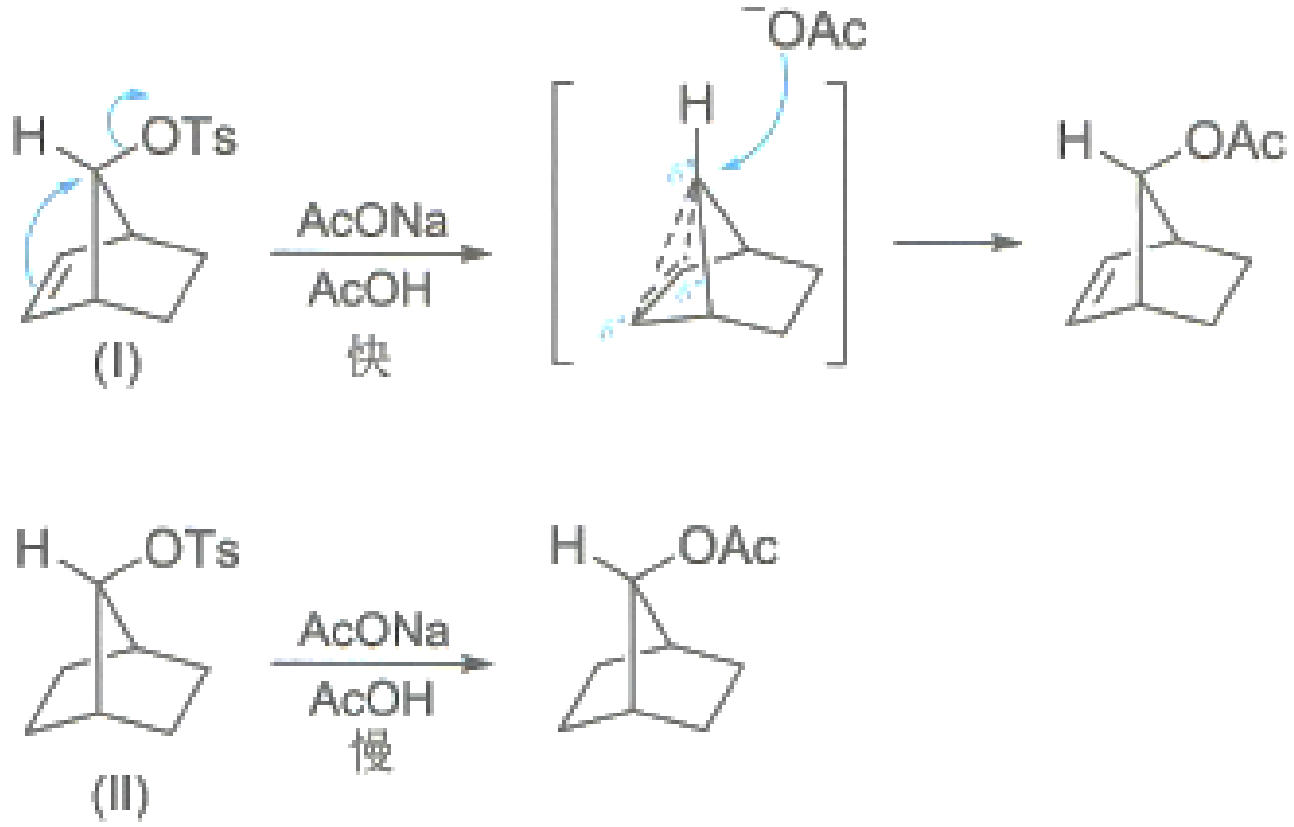


C

bicyclo[2.2.1]heptan-7-yl-4-methylbenzenesulfonate

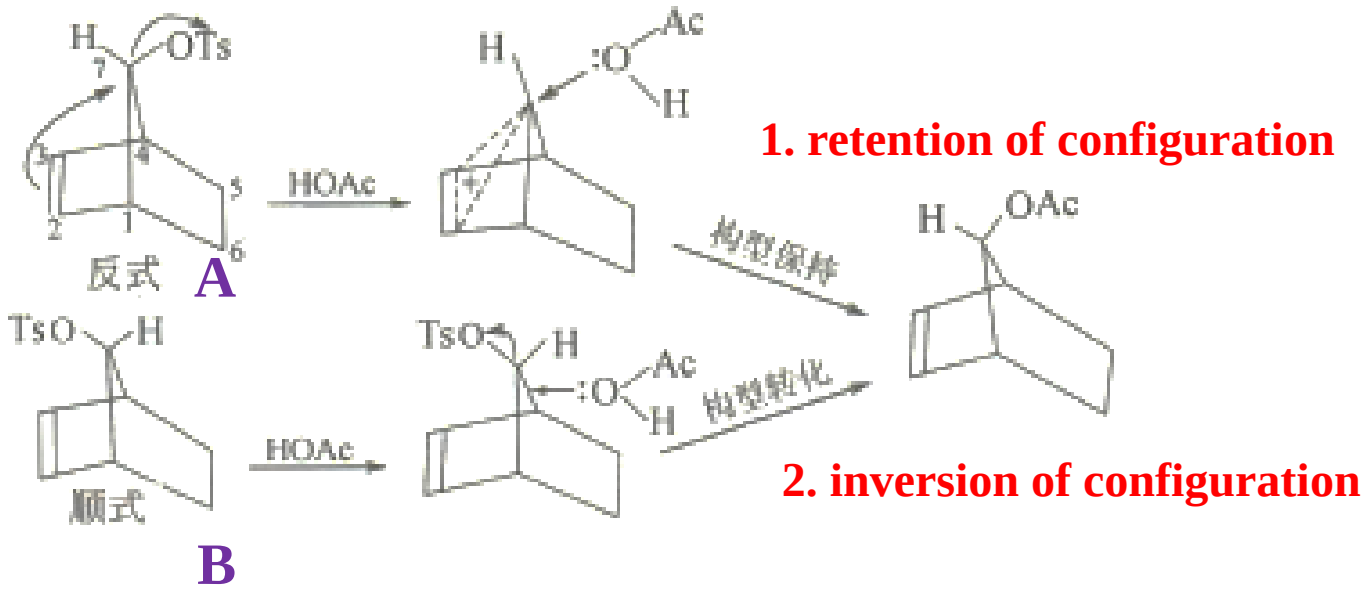
2. anti isomer of 7-norbornenyl tosylate A is 10^{11} times faster than that of saturated analog C

5.4 The Neighboring-Group Mechanism



2. anti isomer of 7-norbornenyl tosylate A is 10^{11} times faster than that of saturated analog C

5.4 The Neighboring-Group Mechanism



3. The syn-isomer B, where the double bond is not in a position to participate in the ionization step, reacts 10^{11} times slower than the anti-isomer A

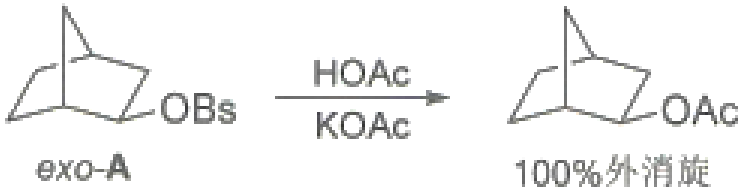
5.4 The Neighboring-Group Mechanism

f. Neighboring group participation by σ bonds

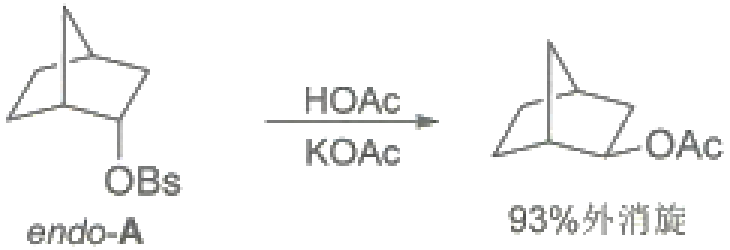
Non-classical carbocation by neighboring-group participation by C=C π-bonds and C–C and C–H σ-bonds, are called non-classical(or bridged) carbocations

例7：acetolysis（σ-bond作为邻近基团）

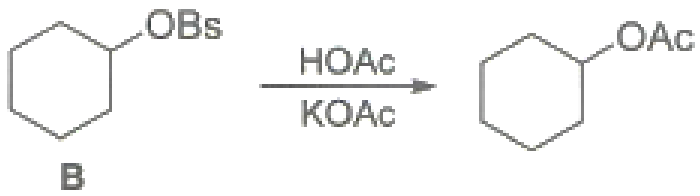
reaction rate



exo-A　　100%外消旋　　350



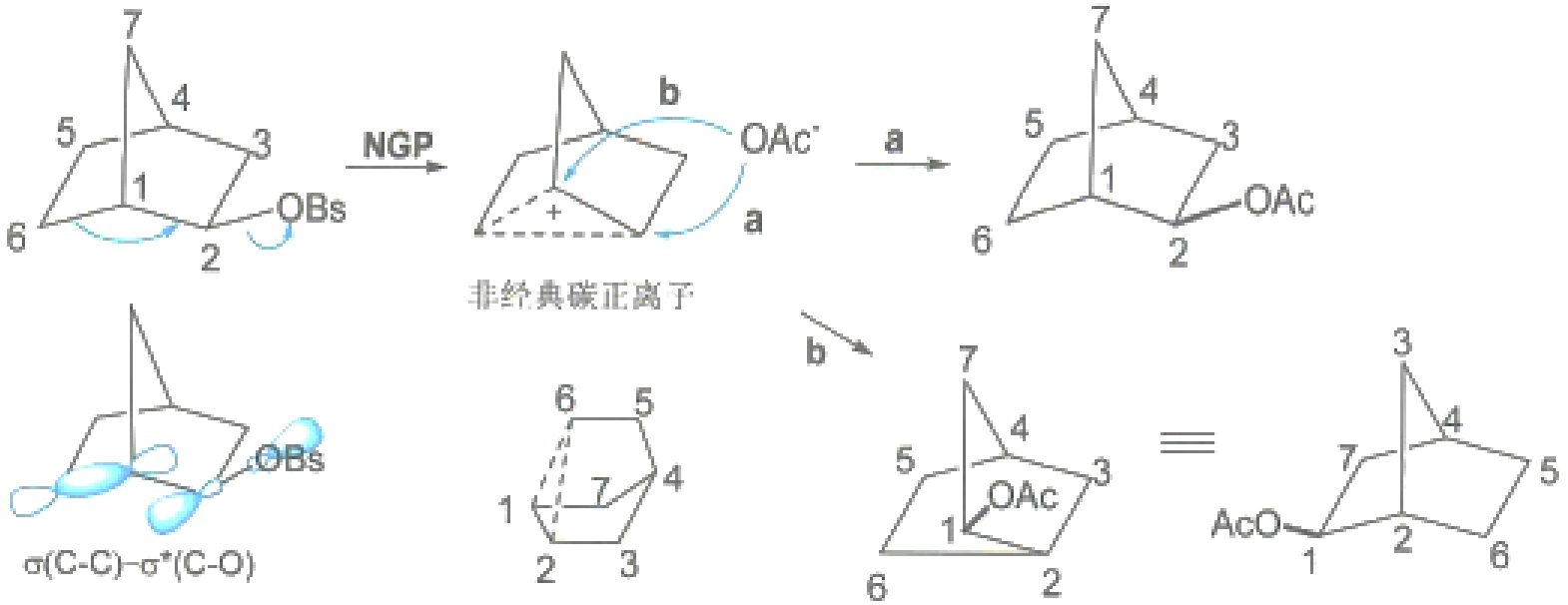
endo-A　　93%外消旋　　1



B　　1

5.4 The Neighboring-Group Mechanism

f. Neighboring group participation by σ bonds

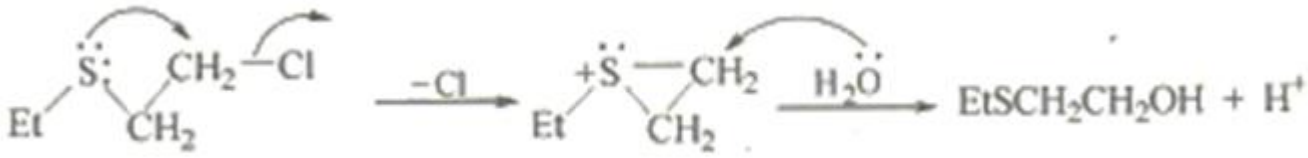


5.4 The Neighboring-Group Mechanism

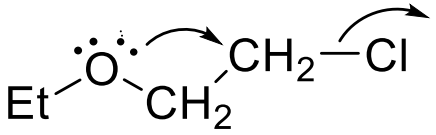
Conclusion the characteristics of the neighboring-group mechanism

1. The rate of reaction is greater than expected. 反应速率明显增快

Exercise A比B发生水解反应的速率快10^4倍 **Why?**



A

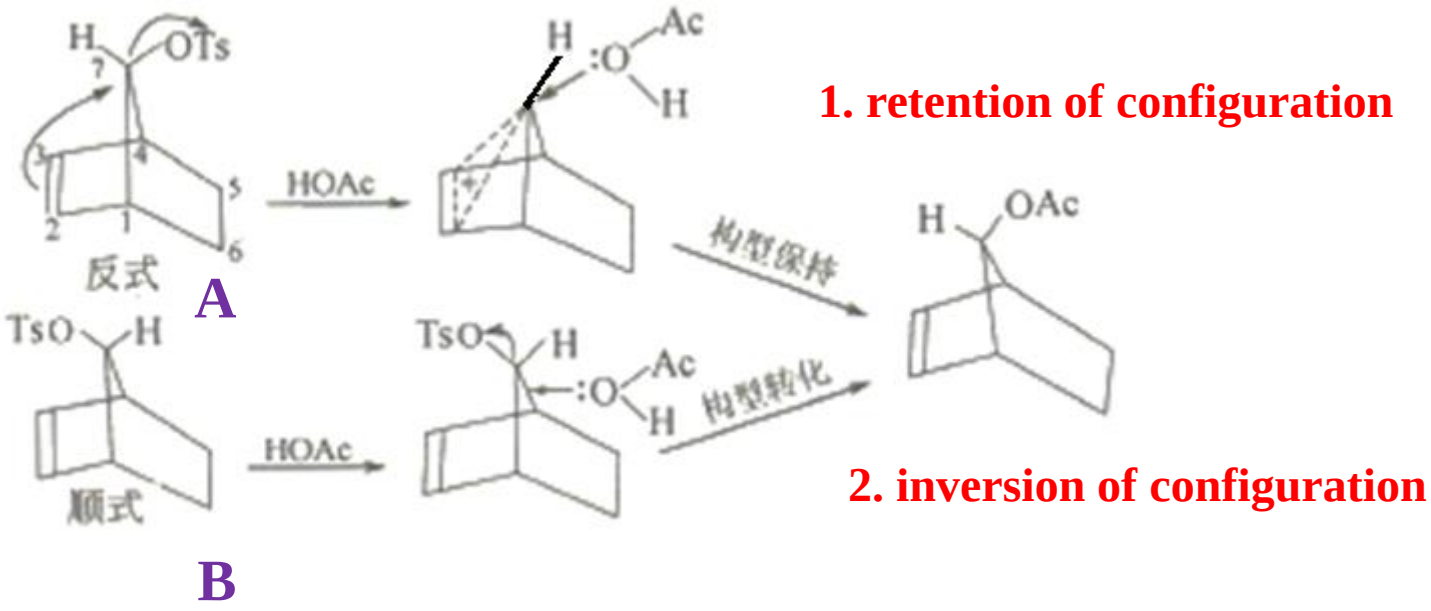


B

5.4 The Neighboring-Group Mechanism

2. The configuration at a chiral carbon is retained 反应物中的手性碳反应前后构型保持

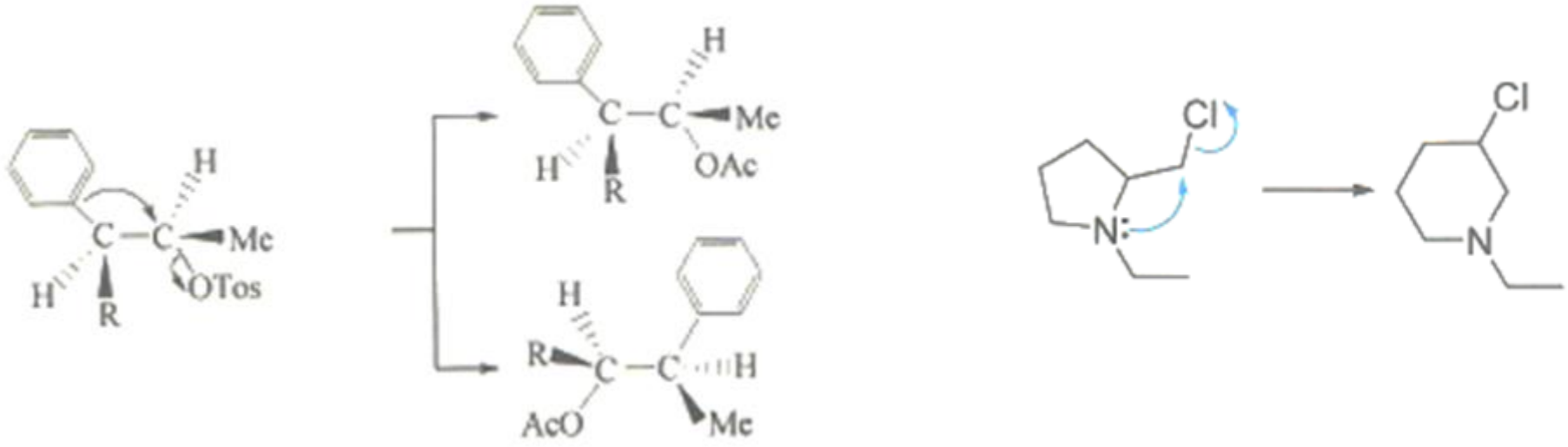
Exercise A得到构型保持的乙酸解产物B得到构型反转产物 **Why?**



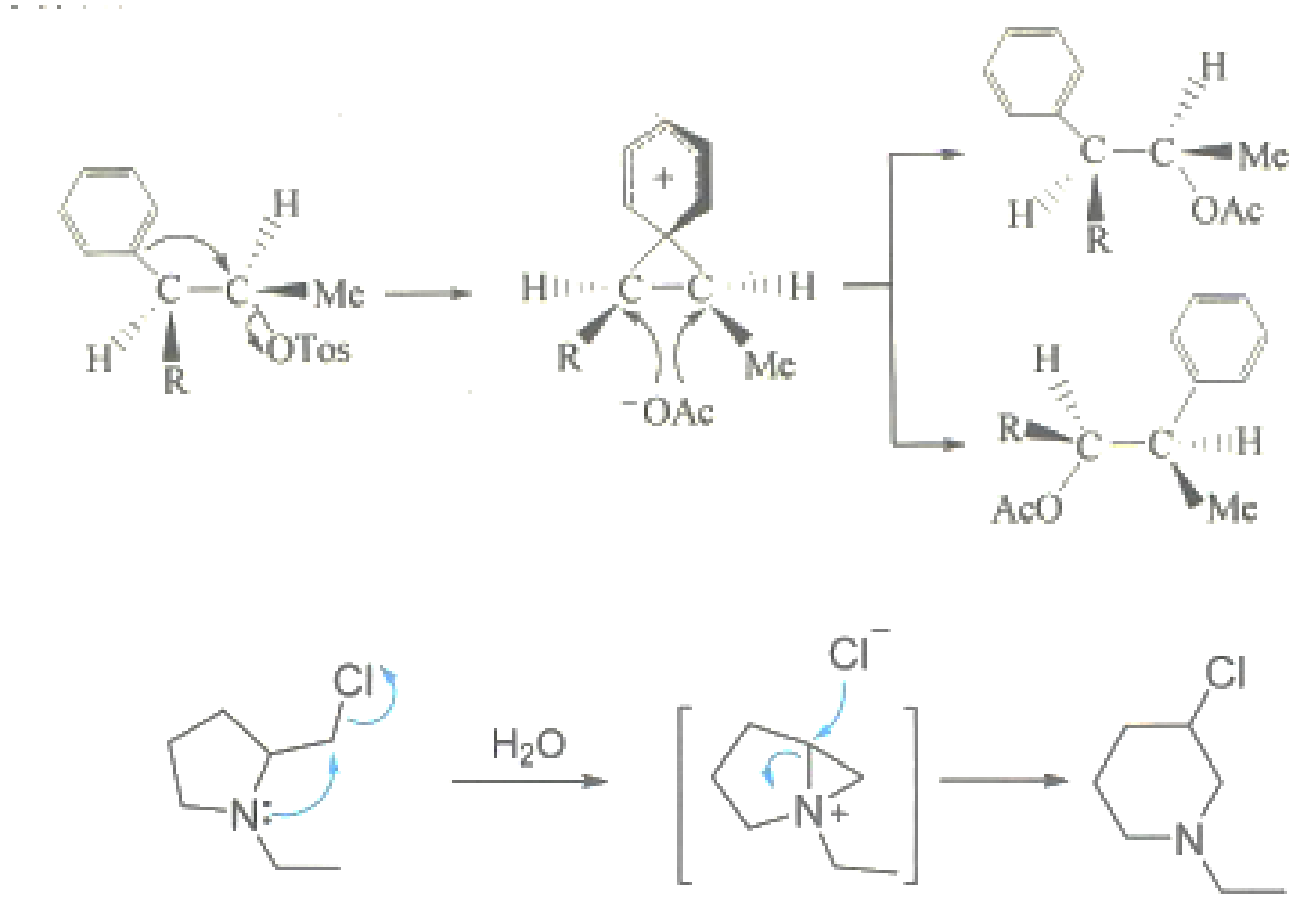
5.4 The Neighboring-Group Mechanism

3. There may be intramolecular rearrangement products through the neighboring-group Particapation. 邻基参与作用可导致生成分子内重排产物。

Exercise 反应得到了骨架重构的产物 **Why?**



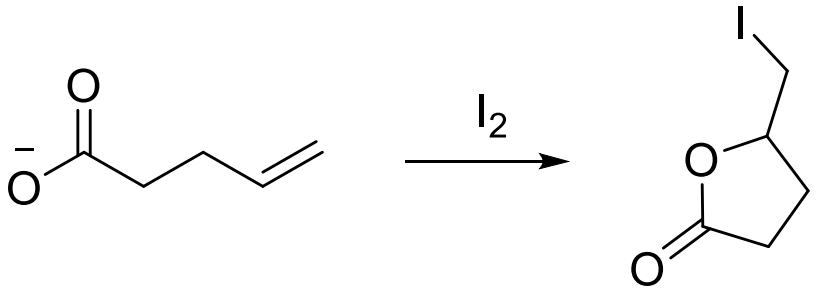
5.4 The Neighboring-Group Mechanism

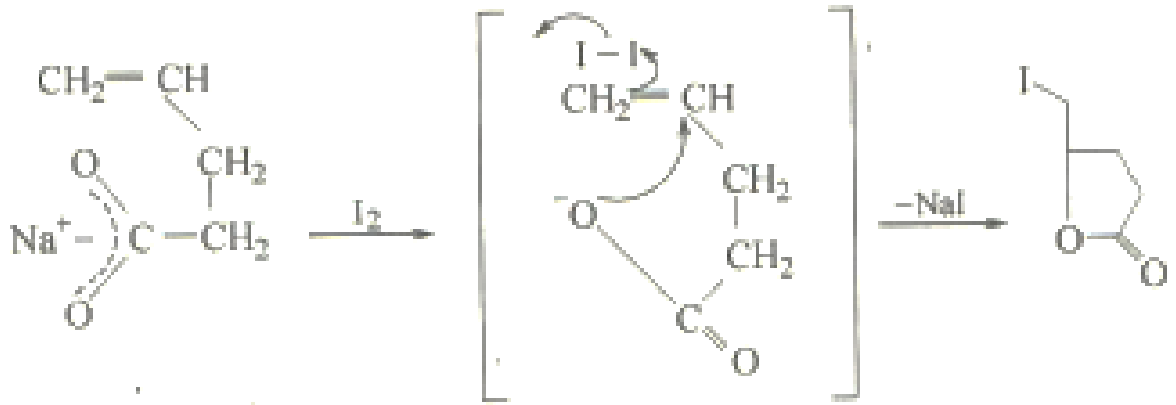


5.4 The Neighboring-Group Mechanism

4. There may be cyclic products through the neighboring-group participation.

邻基参与作用可导致易生成环状化合物。



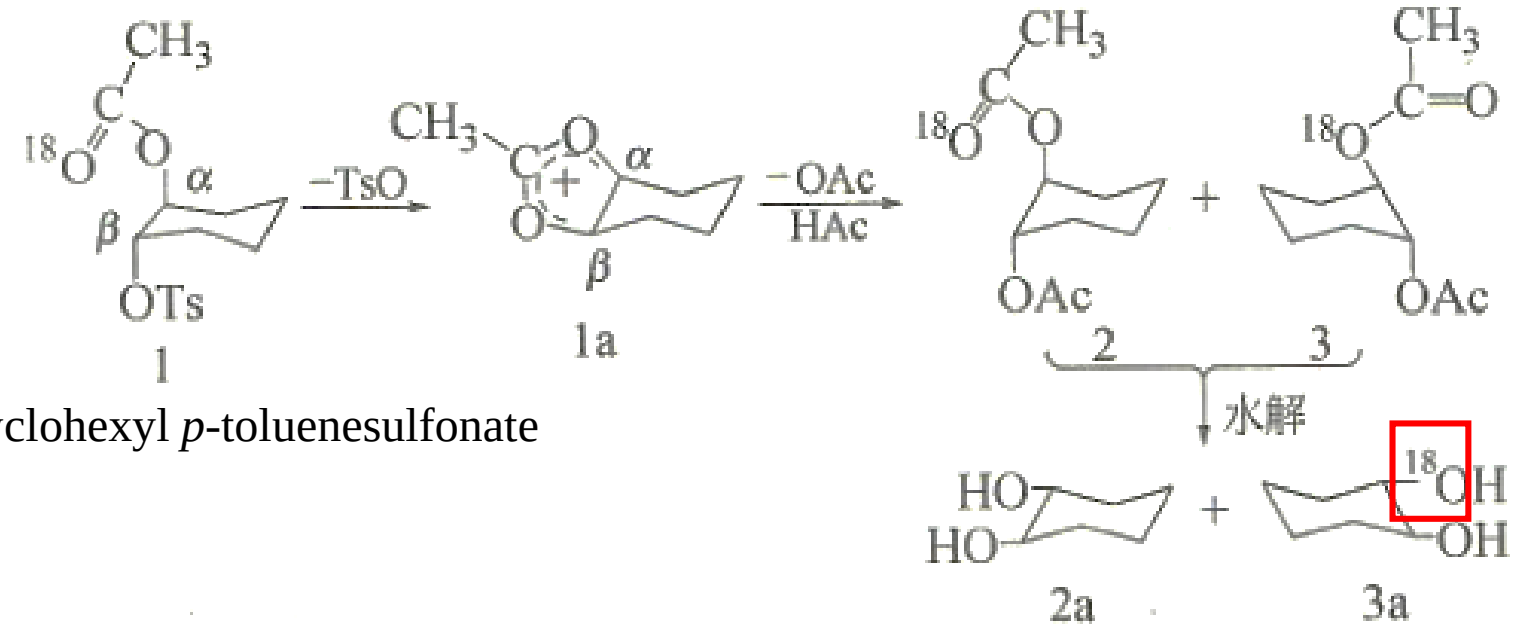


4-戊烯酸钠　　$-COO^-$ 参与形成五元环　　碘内酯

5.4 The Neighboring-Group Mechanism

例3：1-O-乙酰基-2-O-对甲苯磺酰基-反-1，2-环己醇的乙酸解（同位素标记）（羰基作为邻近基团）

Solvolysis of 2-acetoxy cyclohexyl p-toluenesulfonate

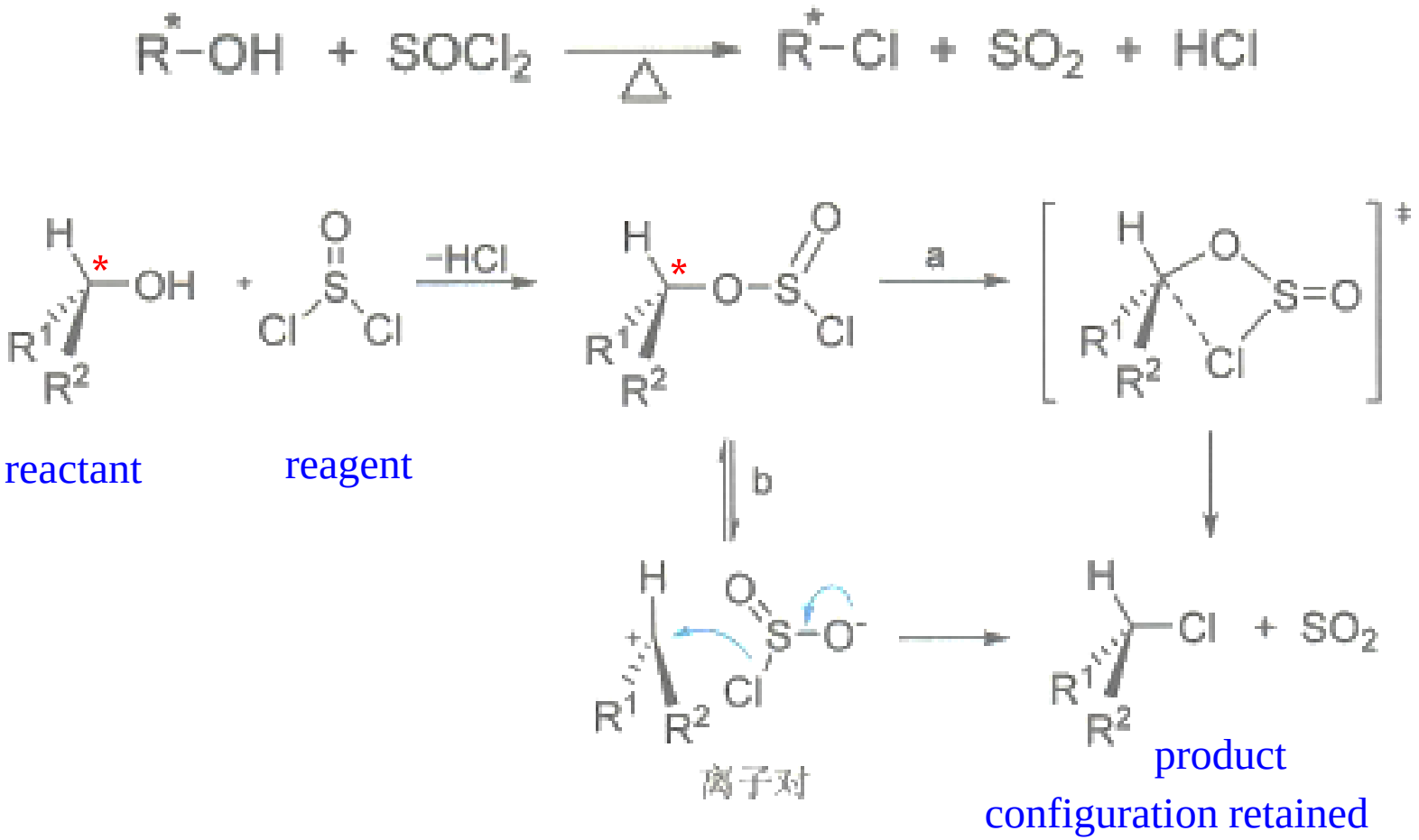


2-acetoxy cyclohexyl *p*-toluenesulfonate

The rates of solvolysis of the cis and trans isomer of 2-acetoxy cyclohexyl p-toluenesulfonate differ by a factor of about 670, the trans isomer being be more reactive .

5.5 S_Ni mechanism Internal Nucleophilic Substitution 内部亲核取代反应

In a few reactions, nucleophilic substitution proceeds with retention of configuration, even where there is no possibility of a neighboring-group effect.



5.5 S_Ni mechanism Internal Nucleophilic Substitution 内部亲核取代反应

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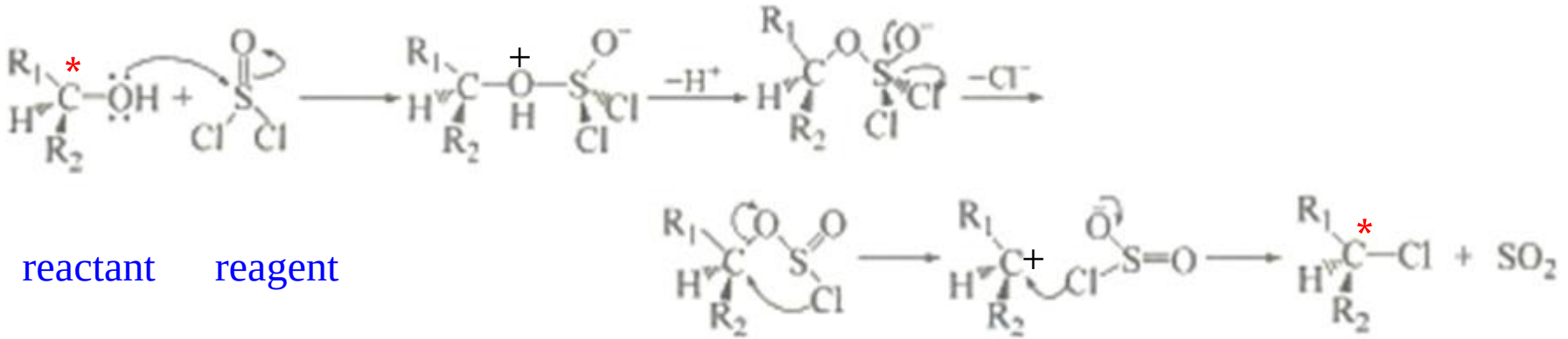
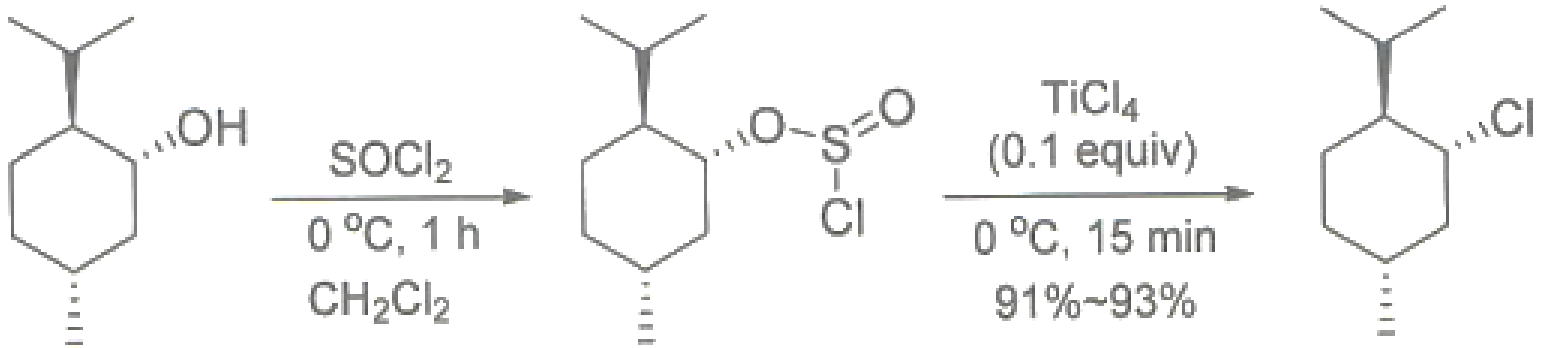
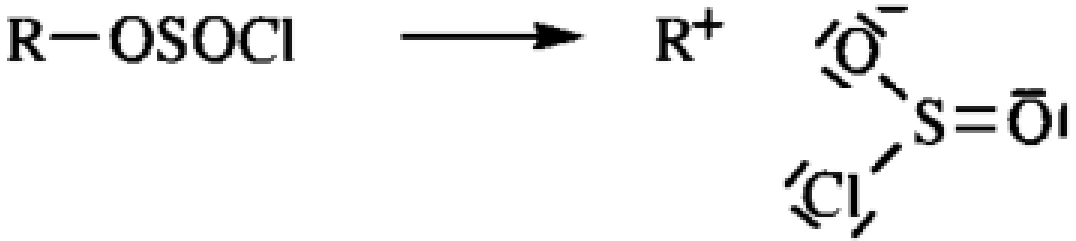


5.5 S_Ni mechanism

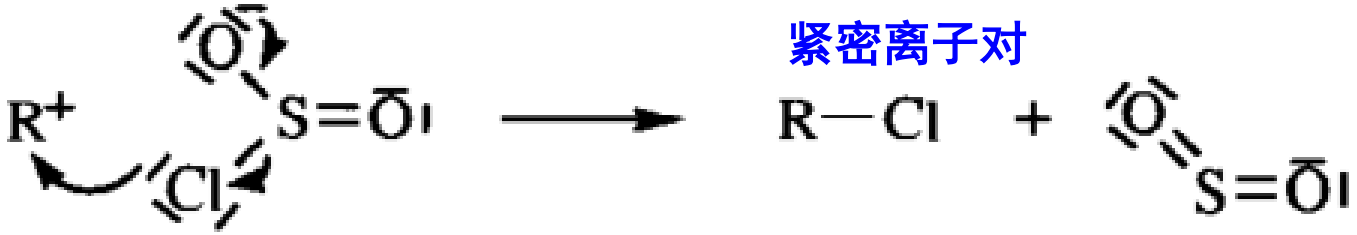


5.5 S_Ni mechanism

Step 1



Step 2

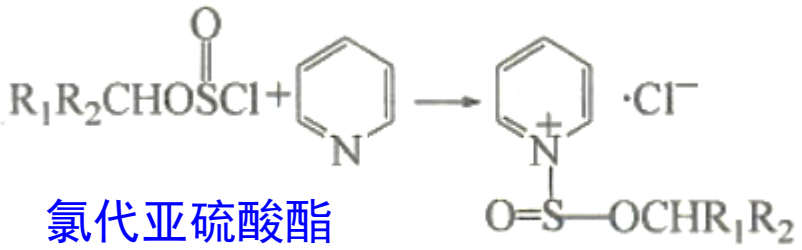


紧密离子对

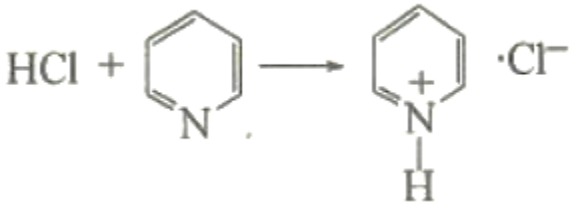
5.5 S_Ni mechanism

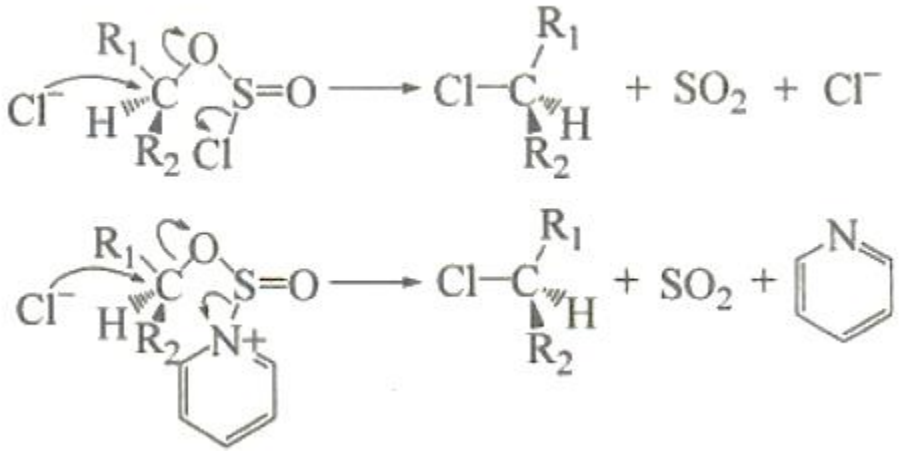
Evidence for this mechanism :

If addition of pyridine to the mixture of alcohol and thionyl chloride.

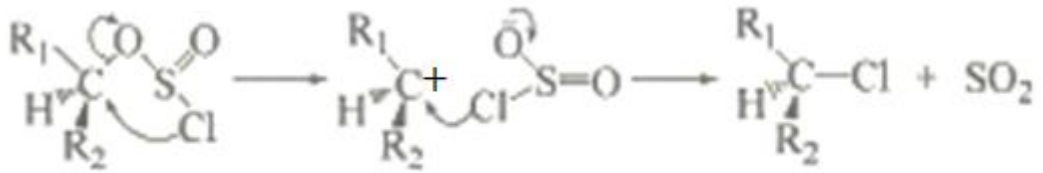


氯代亚硫酸酯





S_Ni mechanism



亲核试剂的类型和反应

① 含氧亲核试剂，含氧亲核试剂有 H_2O、ROH、OH^- 和 RO^-，它们的反应包括各种水解反应和醇解反应。

② 含硫亲核试剂，含硫亲核试剂有 H_2S、S_2^{2-}、RS^-、RSO_2^-、$S_2O_3^{2-}$ 等。

③ 含氮亲核试剂，含氮亲核试剂有 NH_3、RNH_2、R_2NH、R_3N、$ClSO_2NCO$、Li_3N、NO_2^-、NaN_3、NCO^-、NCS^- 等。

④ 卤素亲核试剂，含卤素的亲核试剂有 HX、X^-、LiI、$SOCl_2$、  等。

⑤ 负氢离子，能提供负氢离子作为亲核试剂的化合物有 $LiAlH_4$、AlH_3、$NaBH_4$、$LiAlH(O\text{-}t\text{-}Bu)_3$ 等。

⑥ 碳亲核试剂，碳亲核试剂有 RMgX、R_2CuLi、RLi、叶立德、R_3B、$RC{\equiv}C^-$、R_3Al、ArCu及各种活泼亚甲基产生的负碳离子。

⑦ 溶剂解（Solvolysis），溶剂作为亲核试剂的亲核取代反应，称为溶剂解或溶剂解反应。所用的溶剂有水、乙醇、乙酸等。

Fundamentals of Stereochemistry