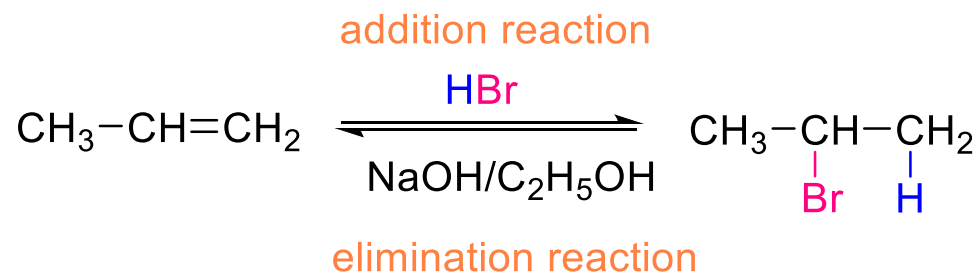


Chapter 4

Electrophilic Addition Reactions

亲电加成反应



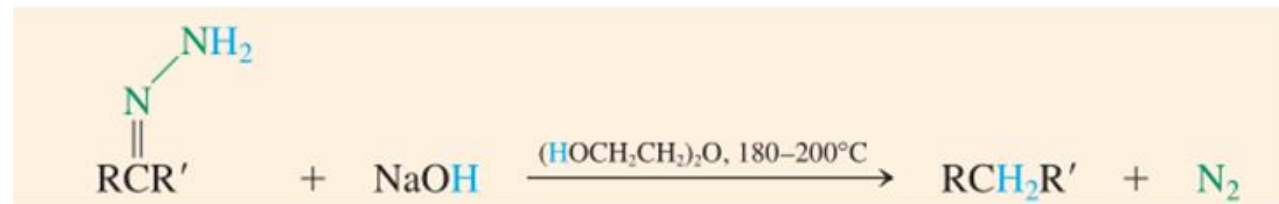
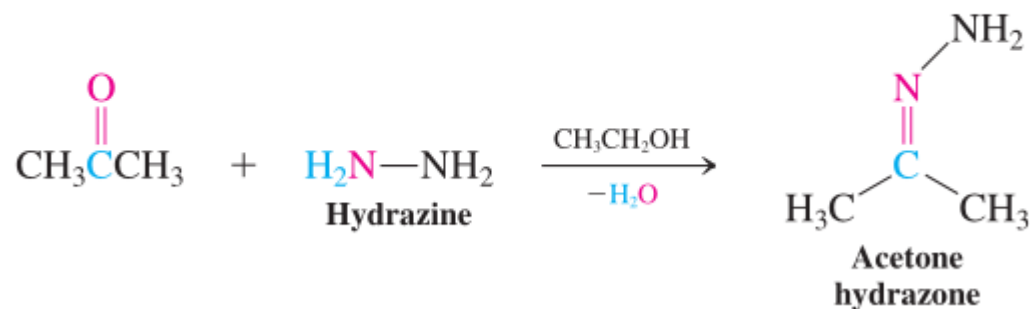
Qiong Li

May 6, 2024

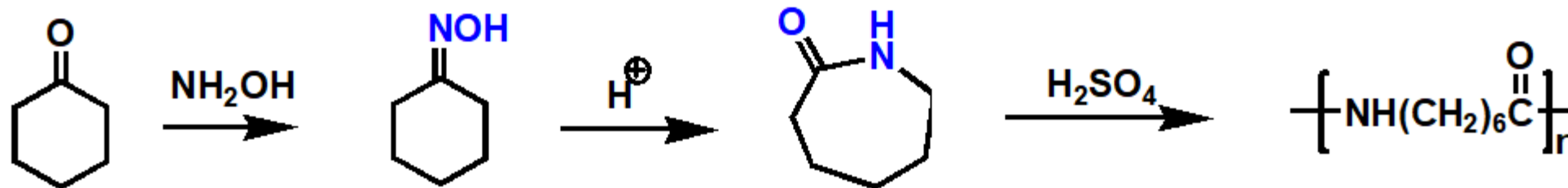
Reactions of carbonyl group

Wolff-Kishner-Huang Reduction

Synthesis of a Hydrazone

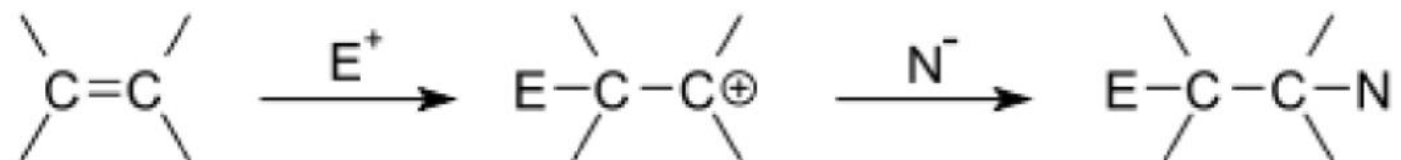


Beckmann Rearrangement

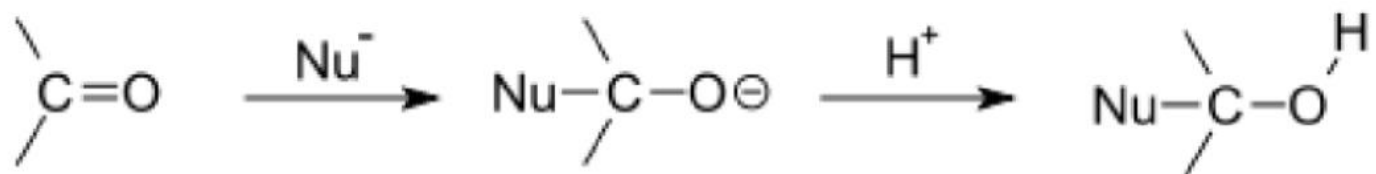


Addition Reaction

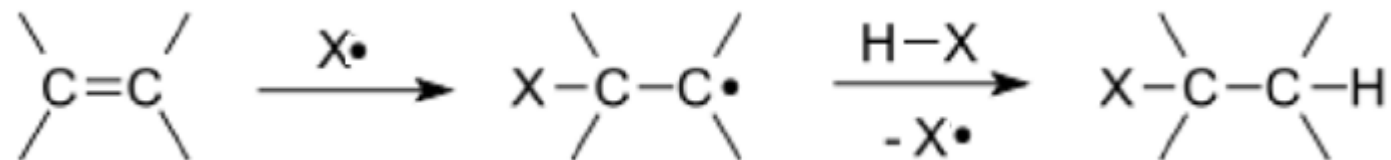
Electrophilic Addition



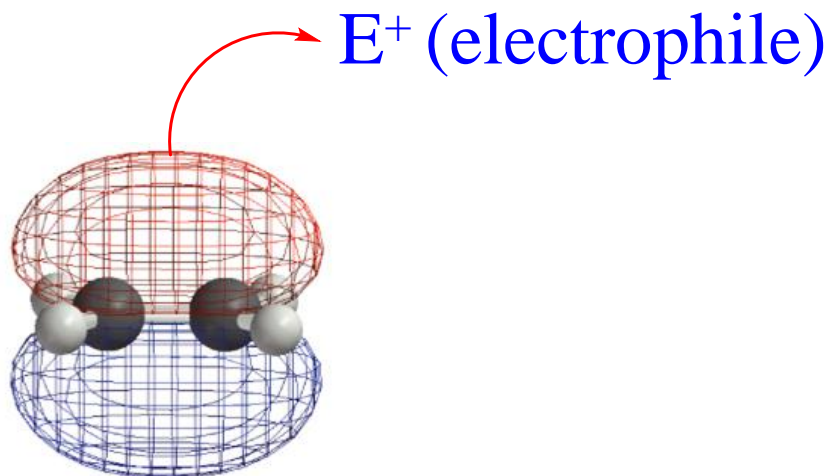
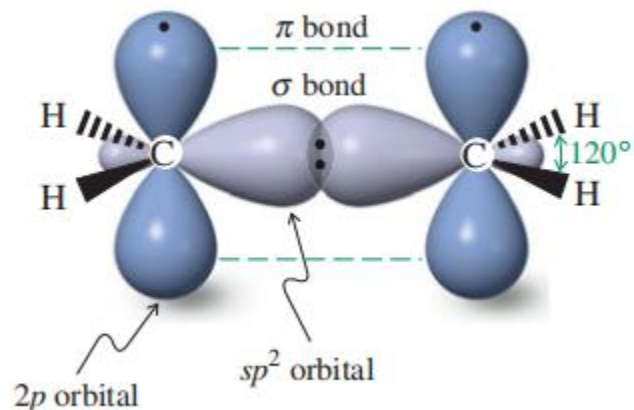
Nucleophilic Addition



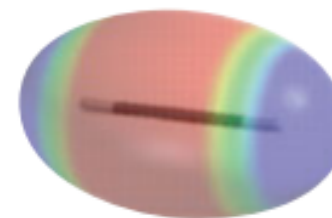
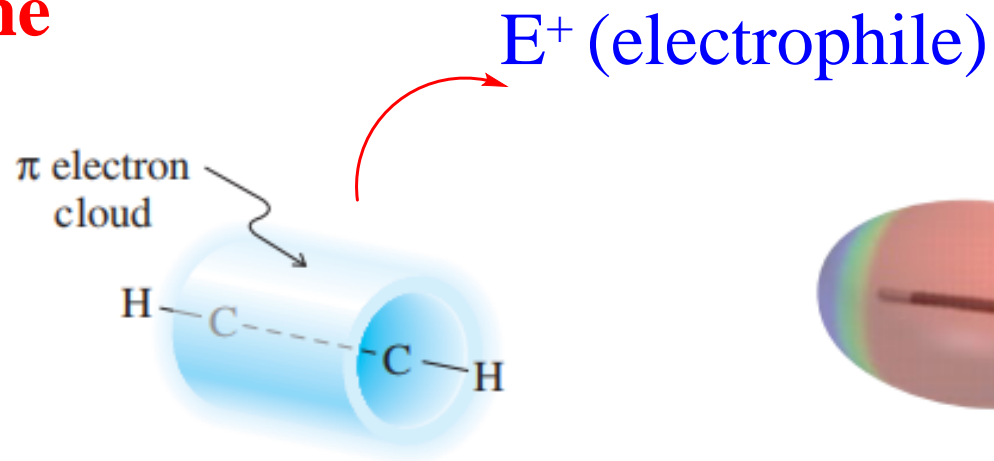
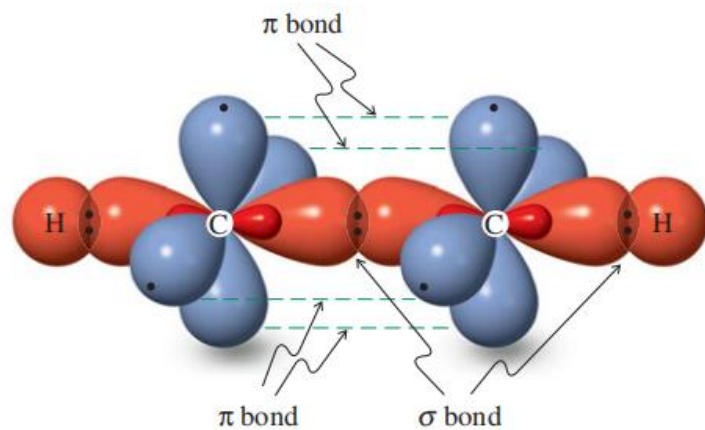
Free Radical Addition



The π electron cloud of alkene



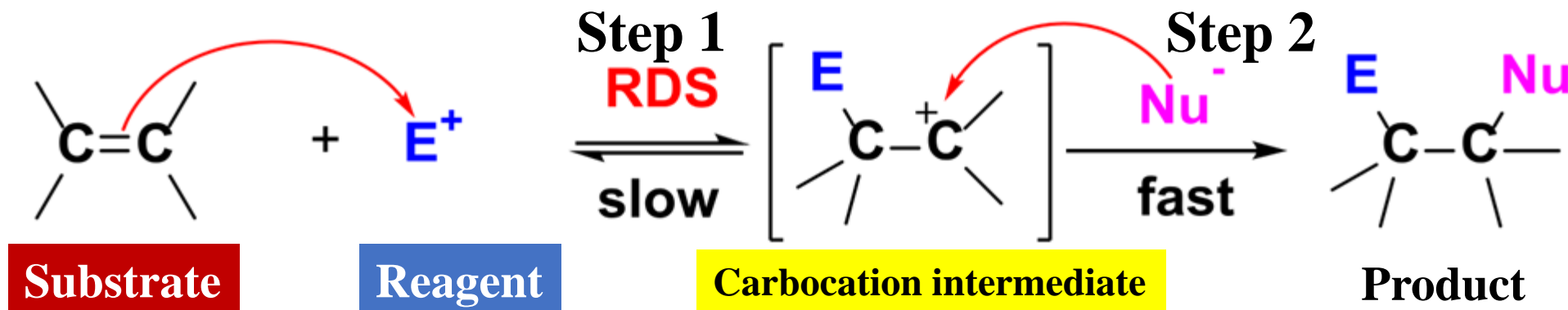
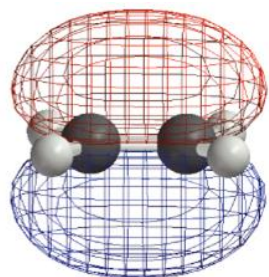
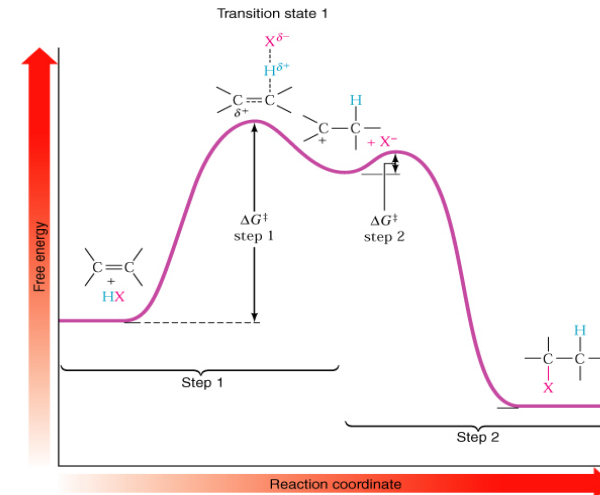
The π electron cloud of alkyne



Qiong Li

Electrophilic Addition

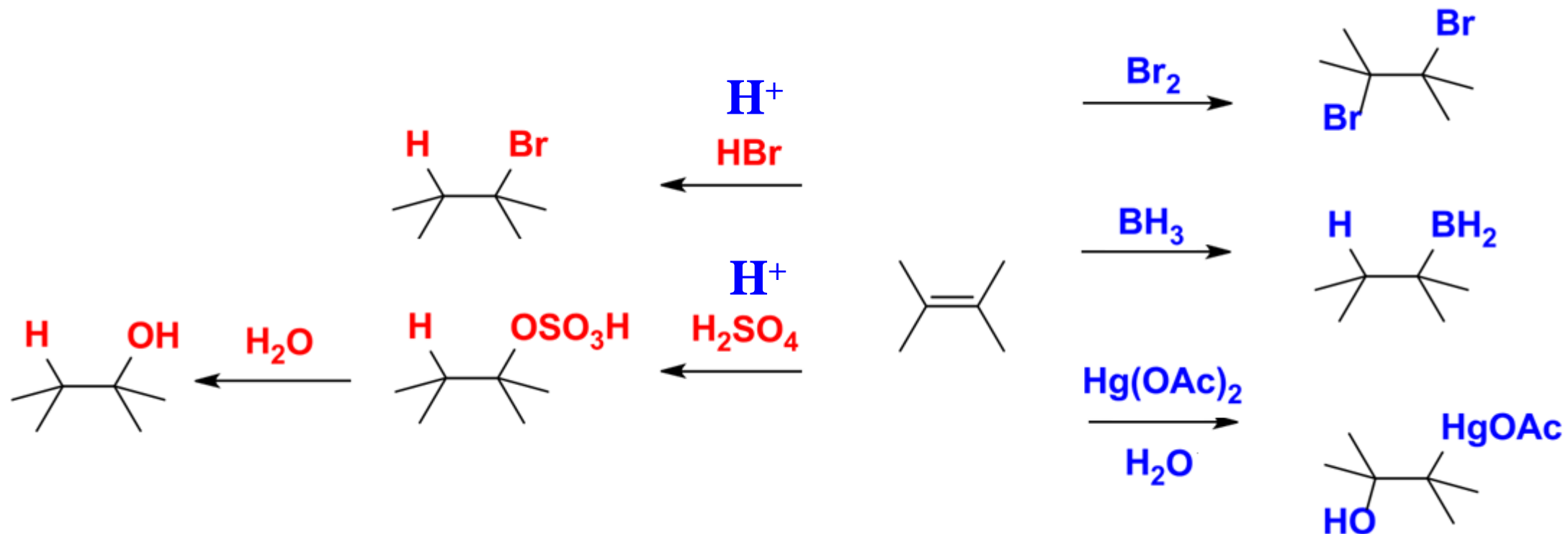
4.1 General Equation



- | | |
|--------------------------|--|
| 1. Electron-rich | 1. Electron-deficient or positively charged |
| 2. Lewis base | 2. Lewis acid |
| 3. To be oxidized | 3. To be reduced |
| 4. Nucleophile | 4. electrophile |

Electrophilic Addition

E^+ (electrophile)



Electrophiles: Electron-deficient species. Bronsted acid(H^+) or Lewis acid

Electrophilic Addition

4.2 Reactivity

Effect of substrates on reaction activity

Electro-donating groups **increase** the reactivity of a $C=C$ toward electrophilic addition, and electro-withdrawing groups **decrease** it.



Methyl is inductively donating, and hyper conjugative donating

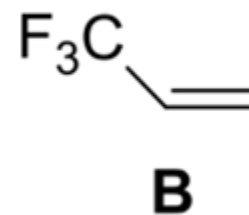
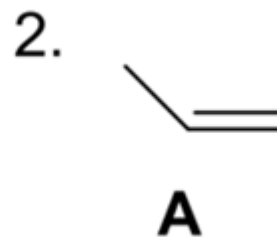
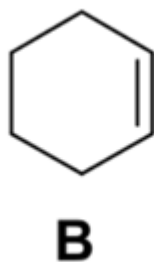
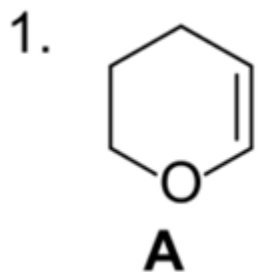
What is the Electro-donating group?

Inductive donating and conjugative donating

Qiong Li

Electrophilic Addition Exercise

Which one is faster towards electrophilic addition reaction?

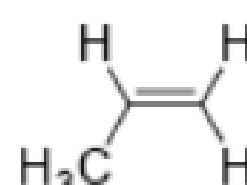
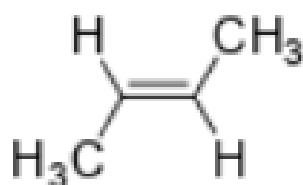
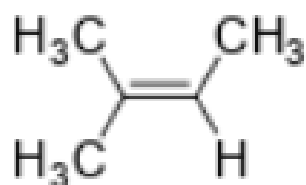
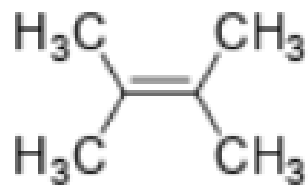


Rank the following compounds in order of decreasing reactivity toward electrophilic addition reaction.

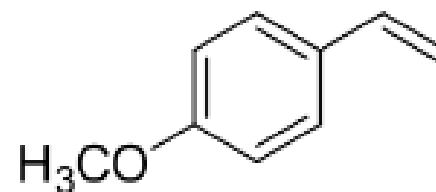
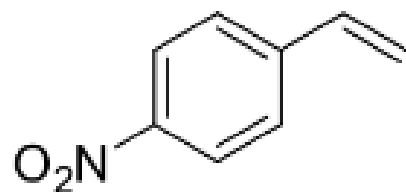


Electrophilic Addition Exercise

Rank the following compounds in order of decreasing reactivity toward electrophilic addition reaction.



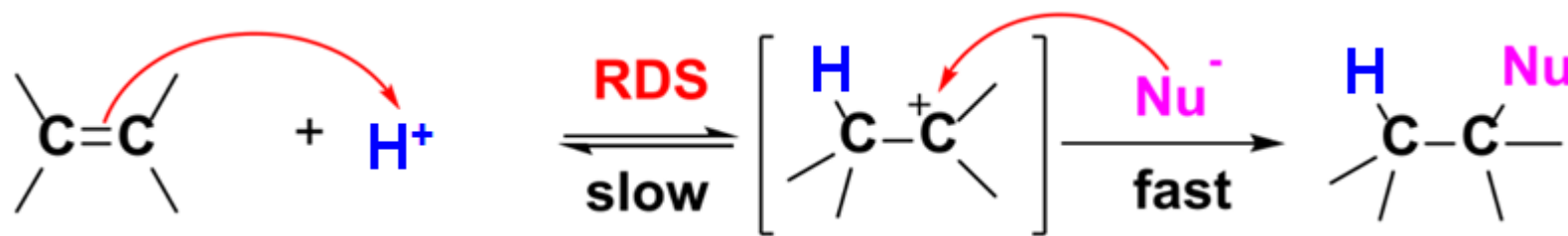
Compare the relative rates of hydration reactions of the following compounds at 25 °C in a solution of 3.5 mol/L HClO_4 .



Electrophilic Addition

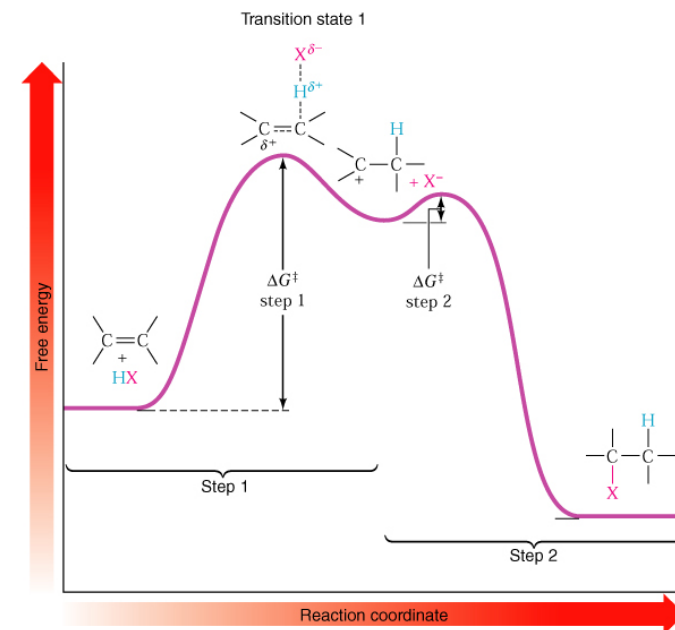
4.3 Mechanism-1 (Brønsted acid as E^+)

4.3.1 $A_E + A_N$ ($A_H + A_N$) mechanism



Electron-rich

Carbocation Intermediate

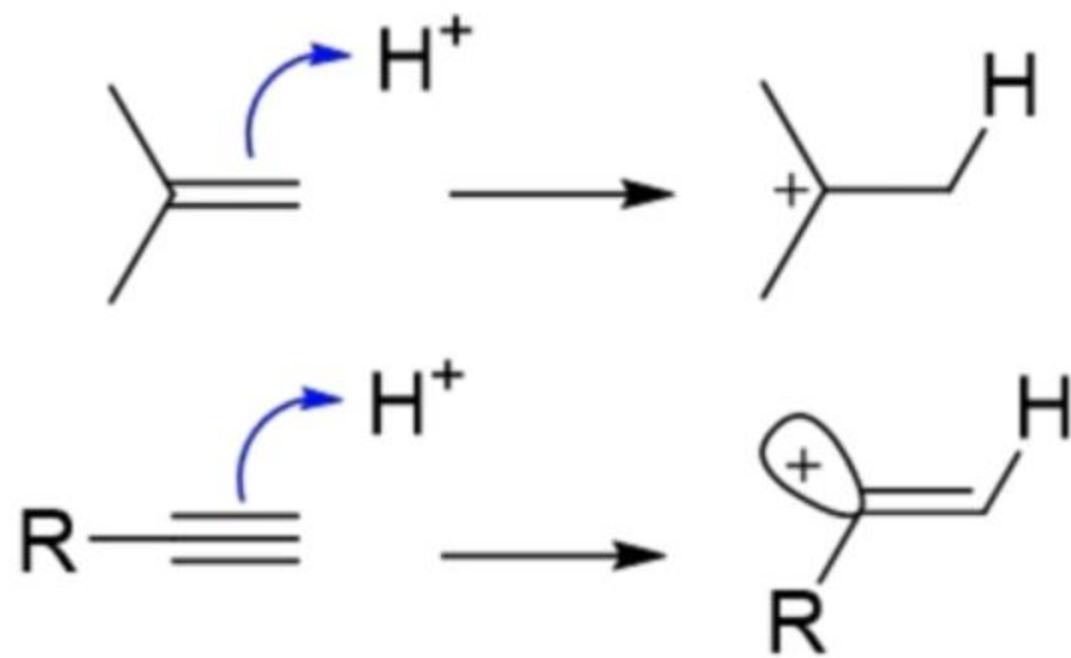


π -bond of the substrate: Brønsted base, Nucleophile, To be oxidized

E^+ : Brønsted acid(H^+), Electrophile, To be reduced

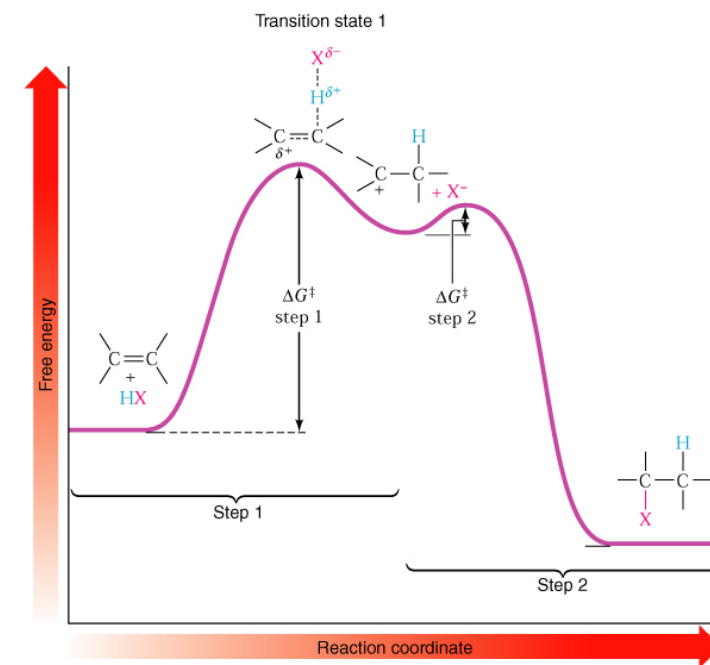
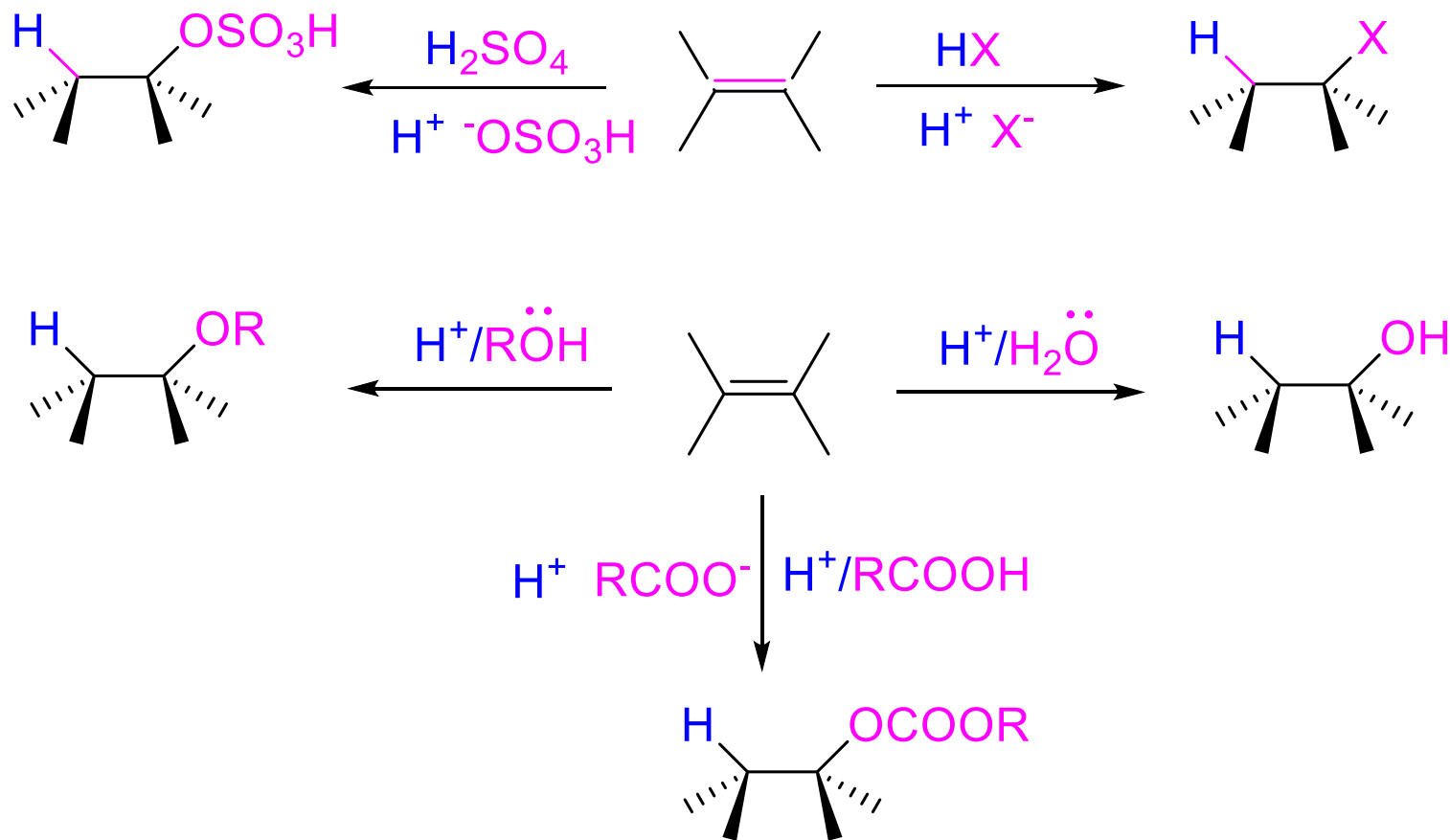
Rate-determining step (RDS): **Step 1** the formation of carbocation intermediate

Intermediate: carbocation



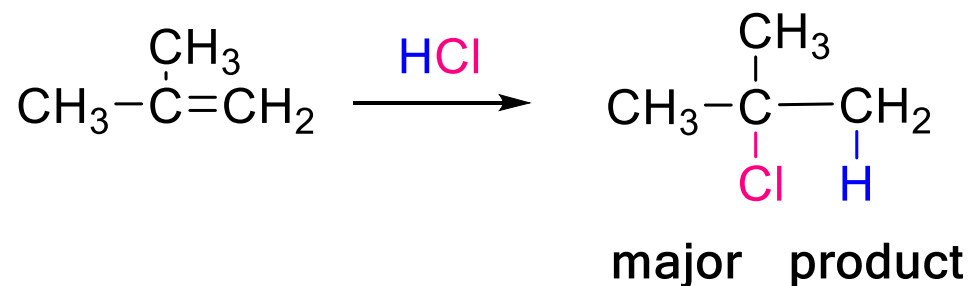
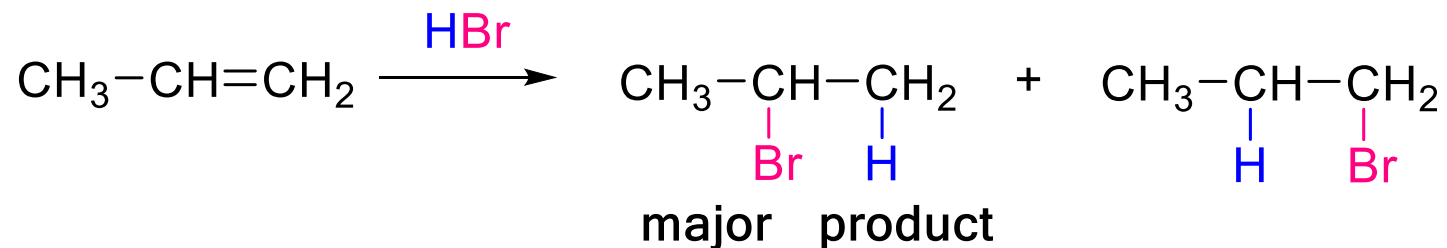
Electrophilic Addition

A. Reactions that undergo $A_H + A_N$ mechanism. (Carbocation Intermediate)



Electrophilic Addition

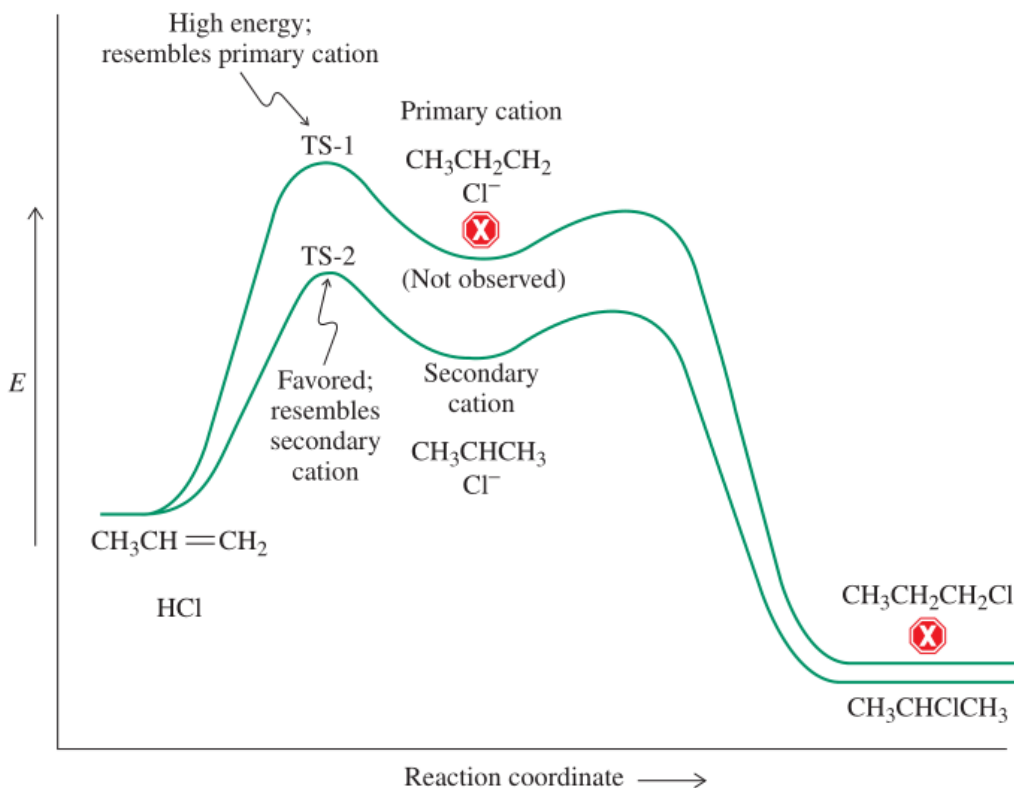
B. Regioselectivity: Markovnikov's Rule (1865)



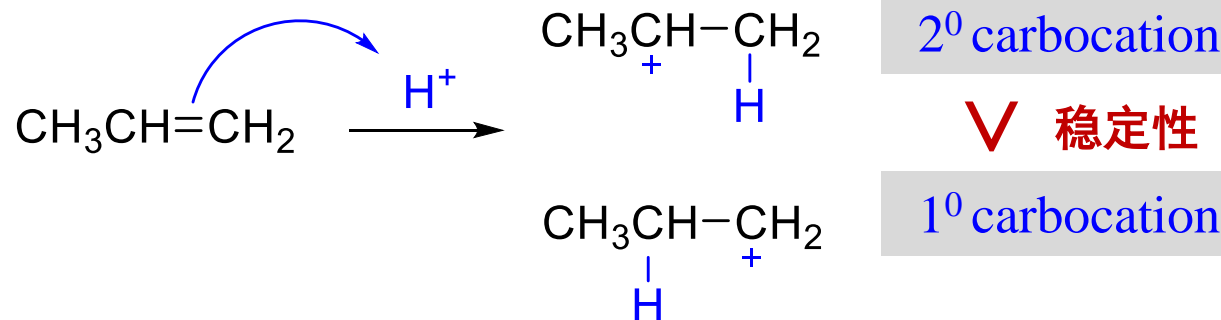
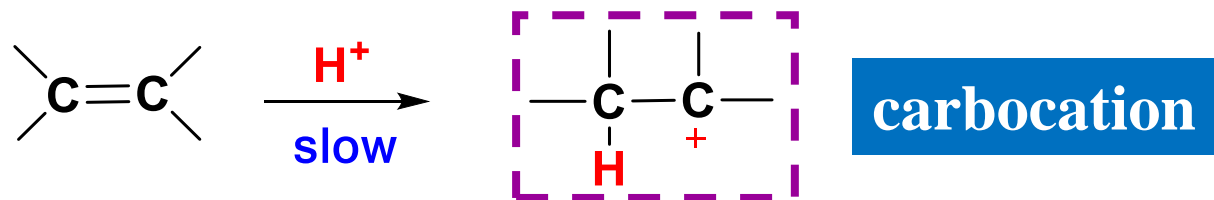
Vladimir Vasilevich Markovnikov

Electrophilic Addition

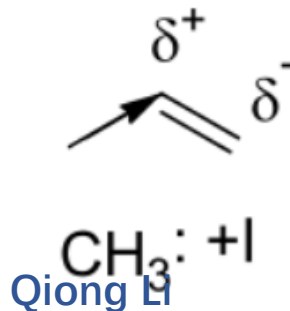
Why Markovnikov's Rule?



1. From the stability of the carbocation intermediate

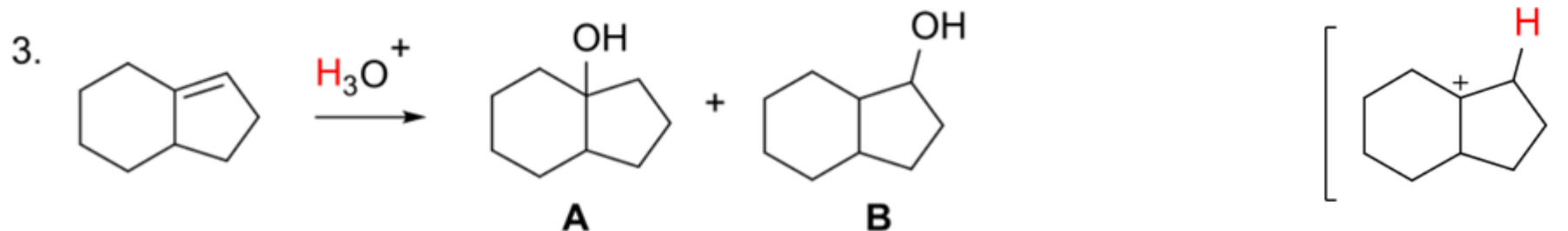
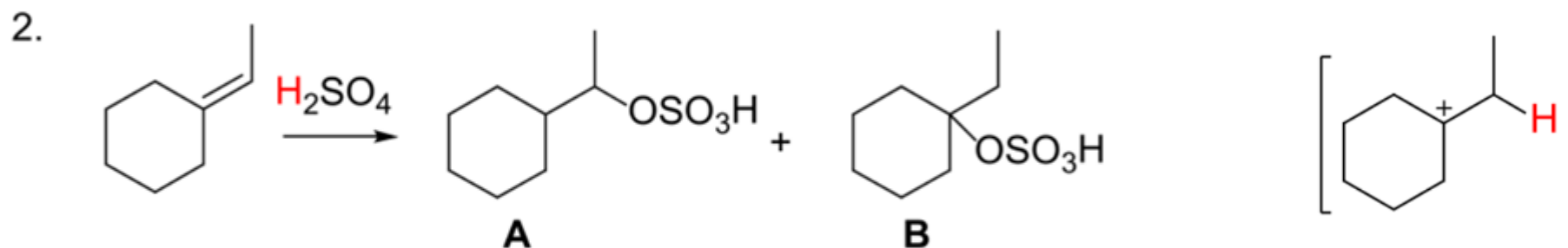
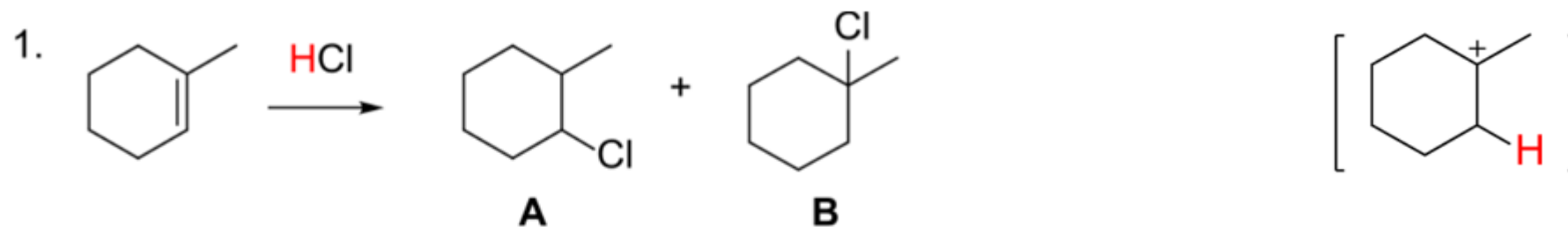


2. From the structure of the substrate



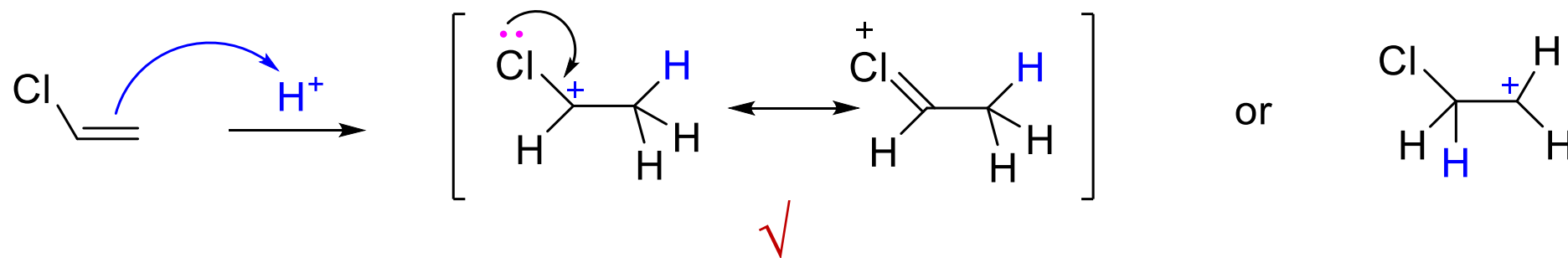
Electrophilic Addition

Determine the regioselectivity of the following reactions



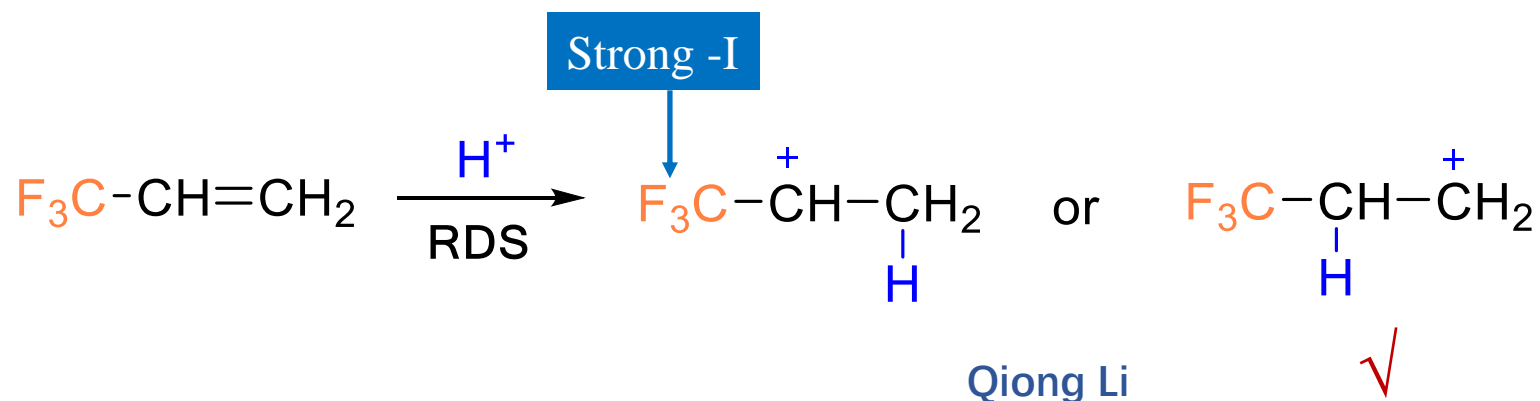
Electrophilic Addition

Markovnikov's Rule



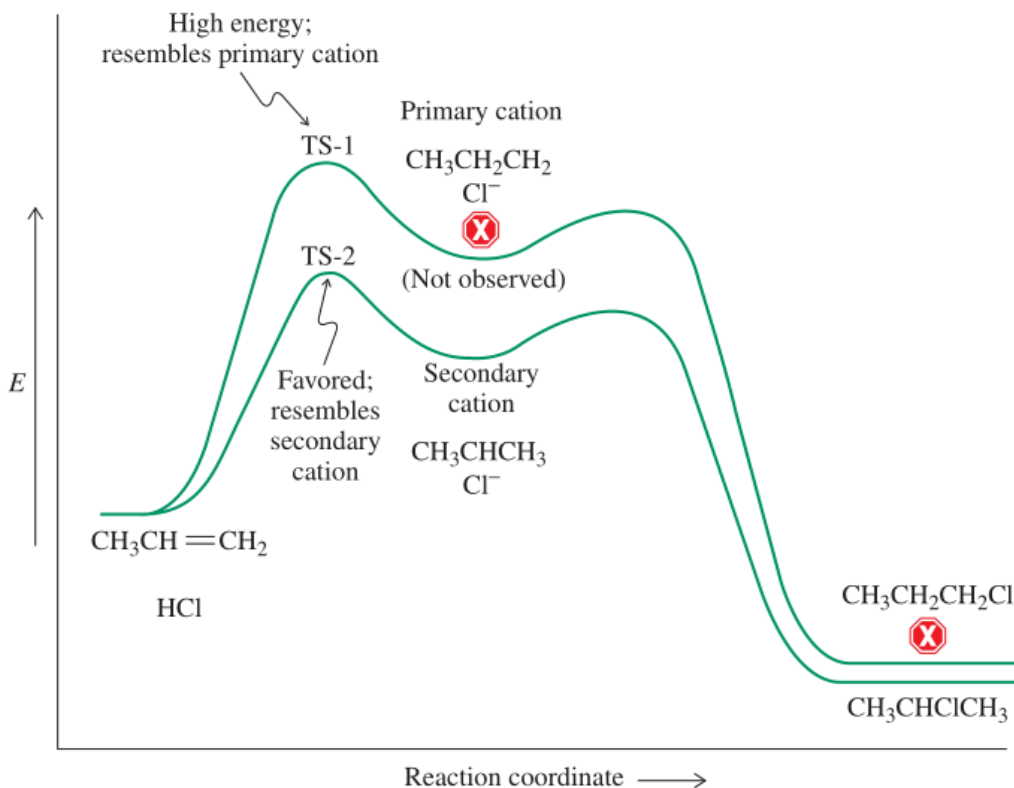
the halogen is inductively electron withdrawing(-I),
resonance with the lone electron pairs allows the charge to be delocalized

Alkenes containing strong electron-withdrawing groups may violate Markovnikov's Rule

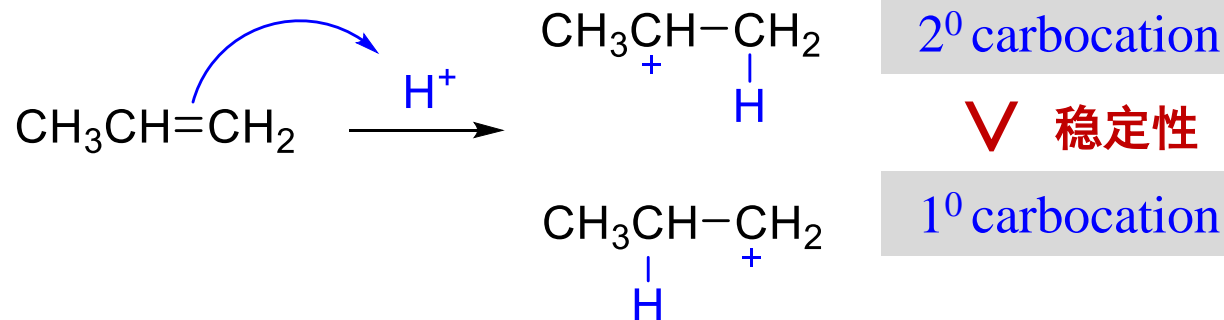
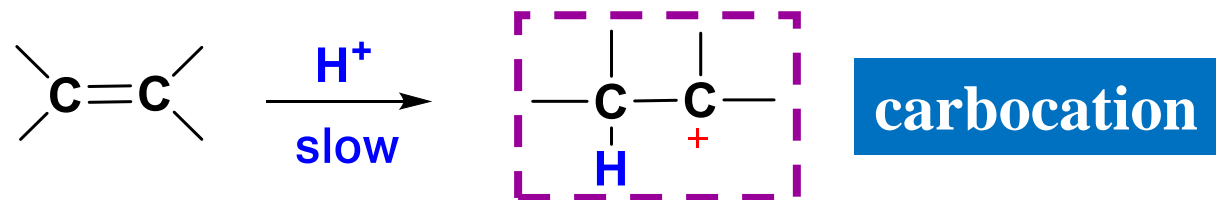


Electrophilic Addition

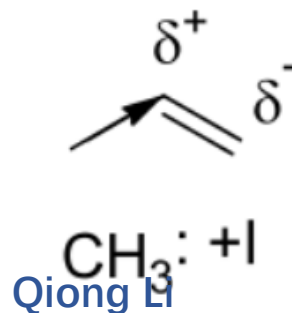
Why Markovnikov's Rule?



1. From the stability of the carbocation intermediate

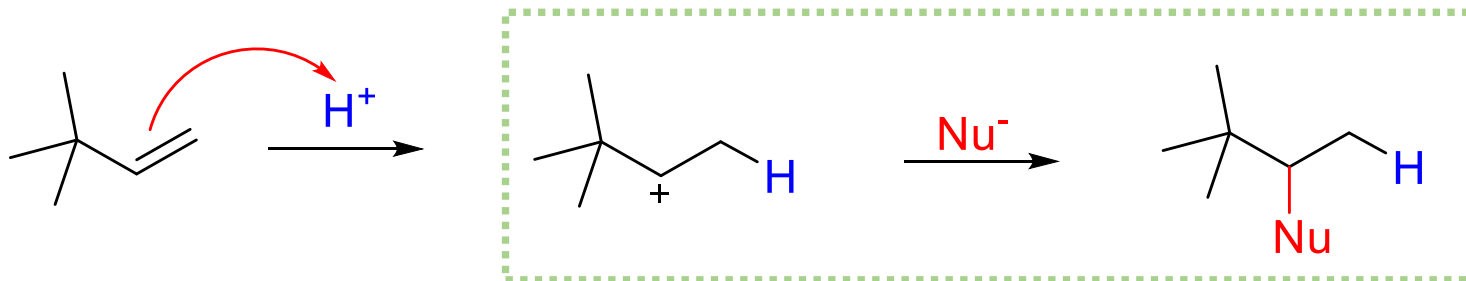


2. From the structure of the substrate



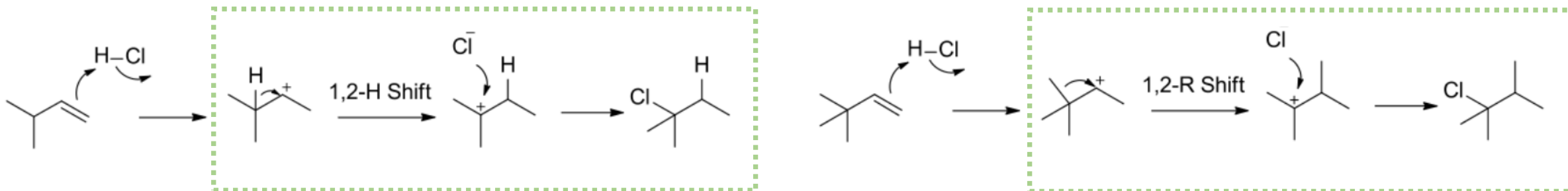
Electrophilic Addition

碳正离子命运-1 The carbocation and the nucleophile combine to form a new σ -bond



碳正离子命运-2 Carbocation undergo rearrangement

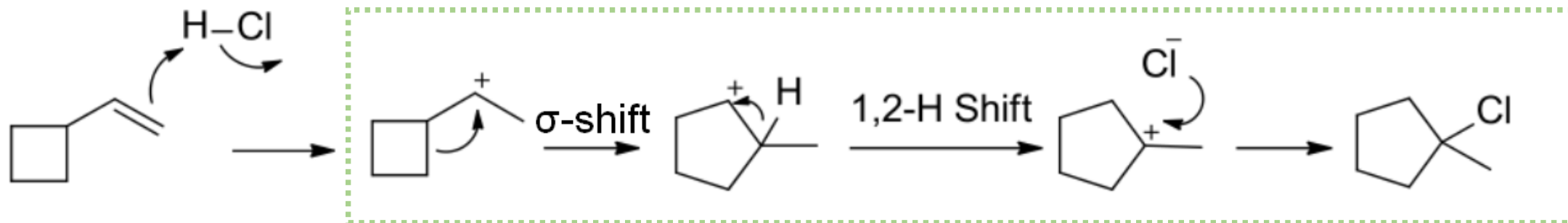
Driving Force 1 Converts the initial carbocation into a more stable carbocation



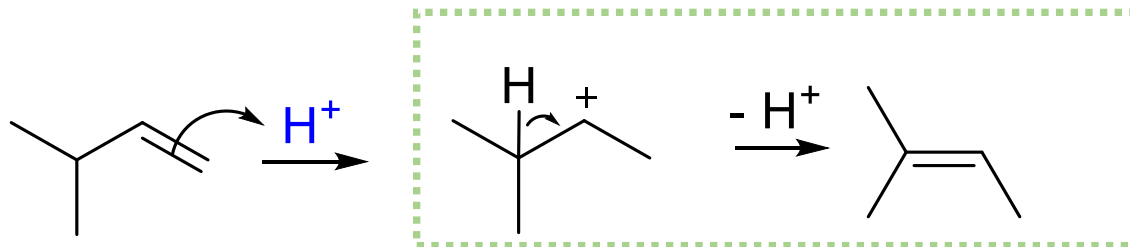
Electrophilic Addition

Driving Force 2

Reduce ring strain

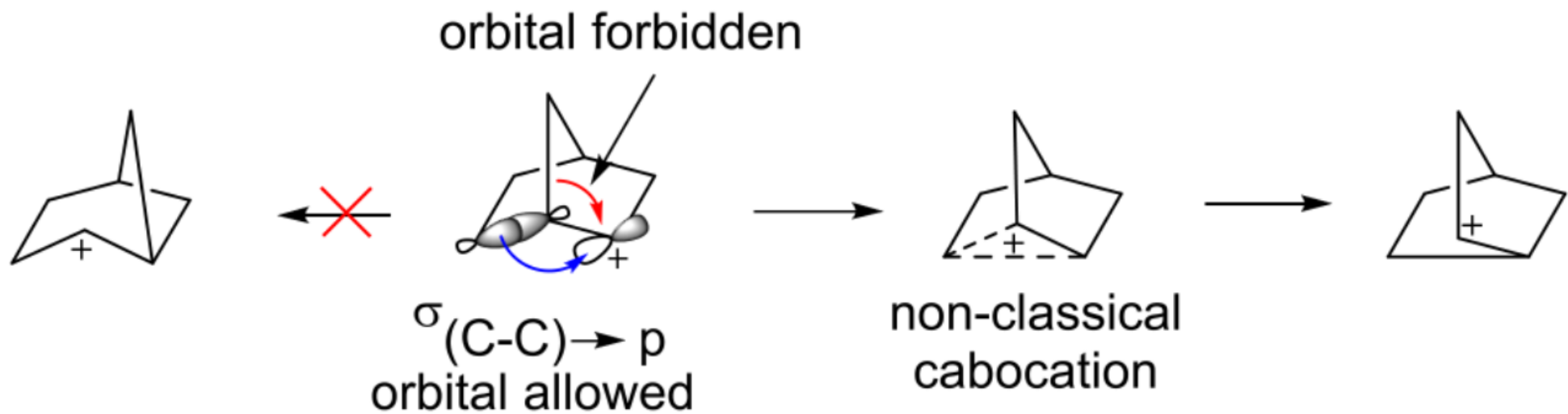


碳正离子命运-3 The protons leave to form a double bond



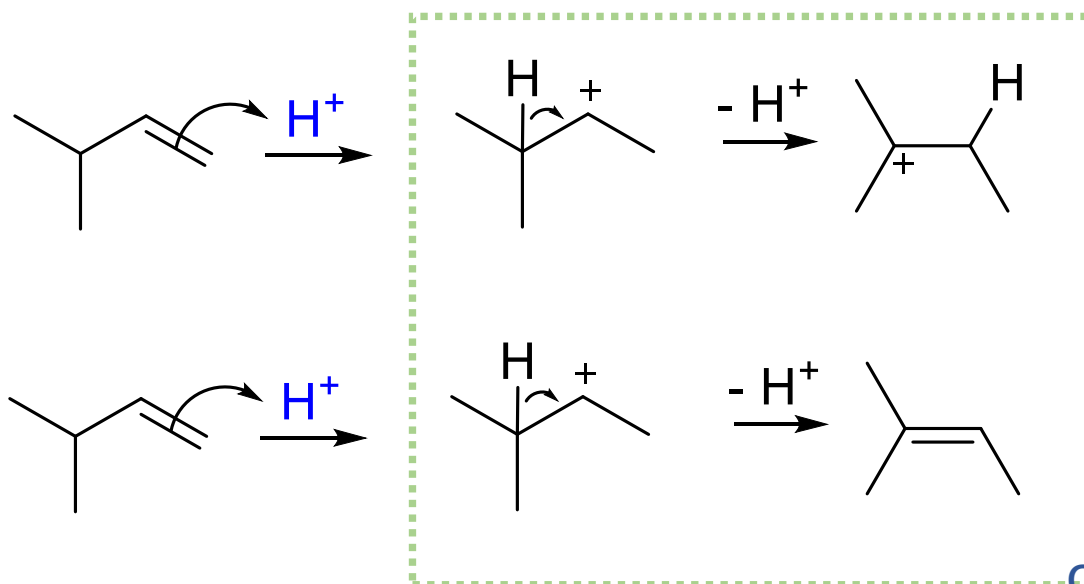
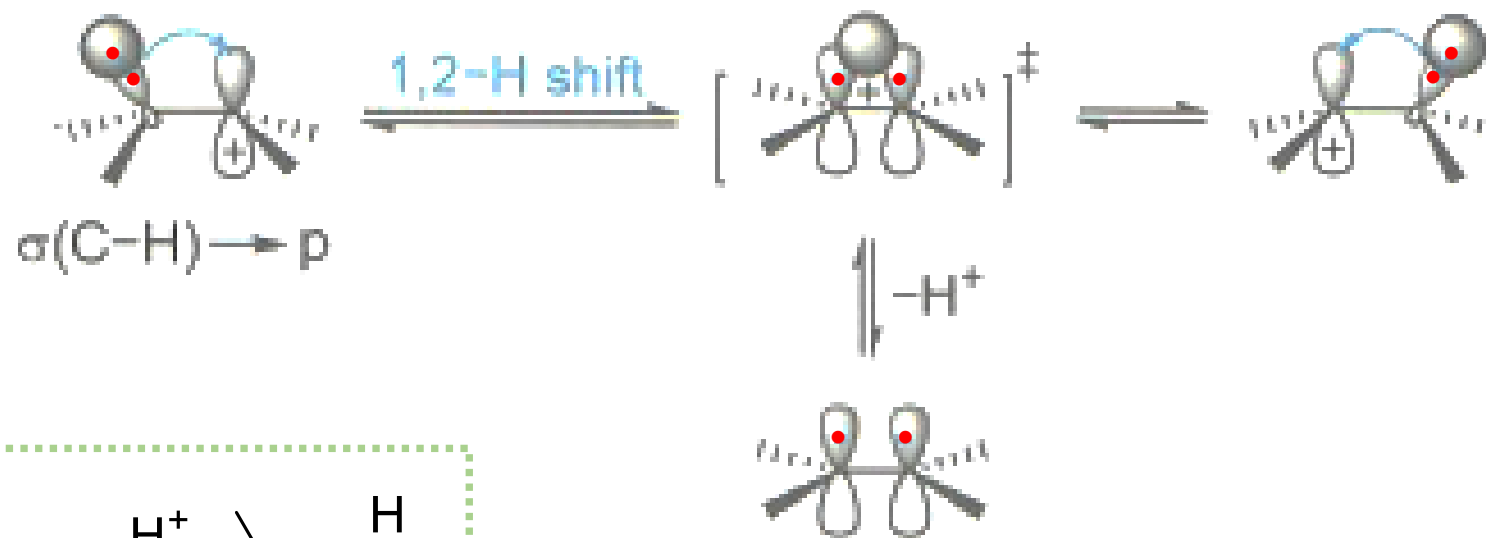
Electrophilic Addition

Orbital directionality of carbocation rearrangement

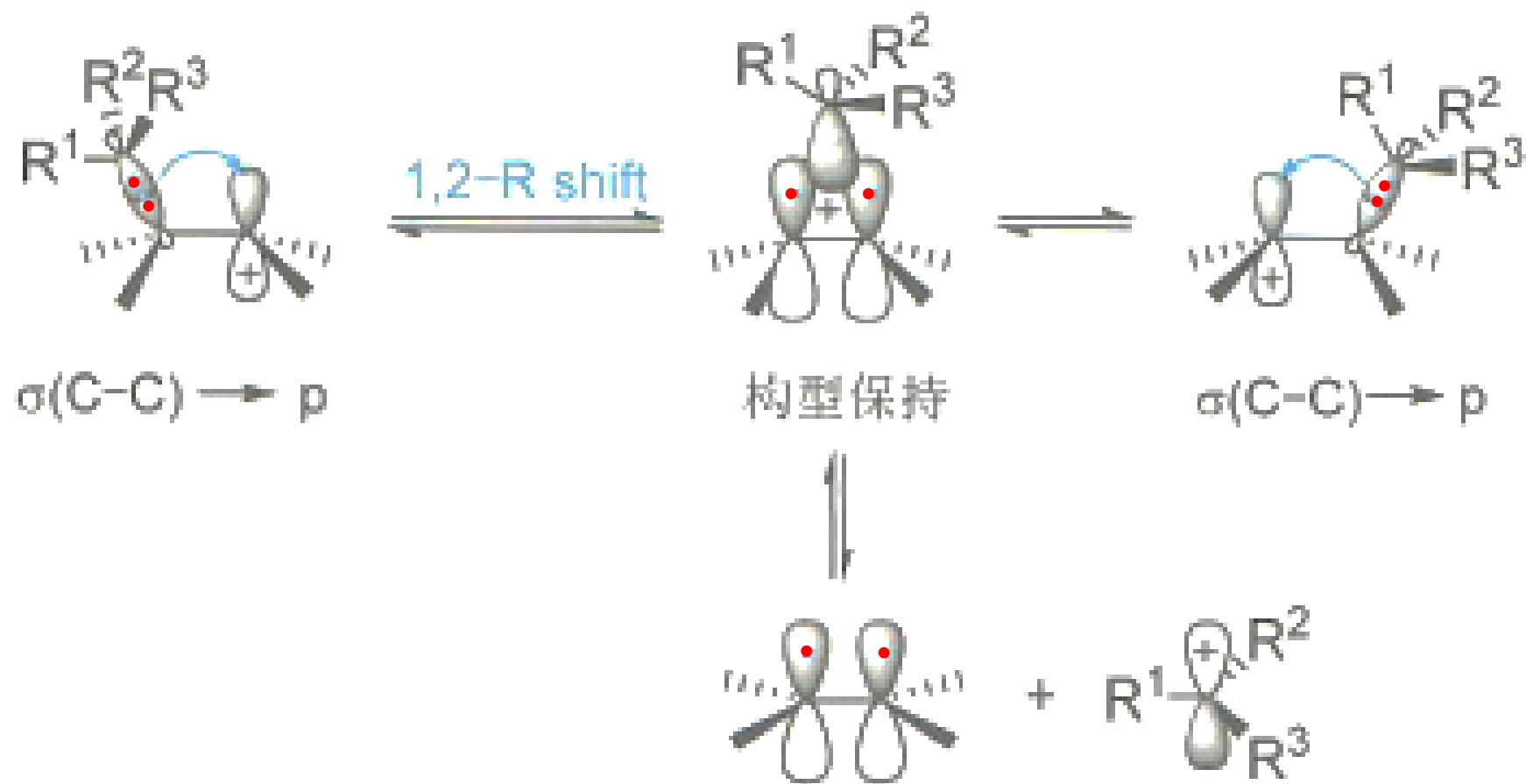


Electrophilic Addition

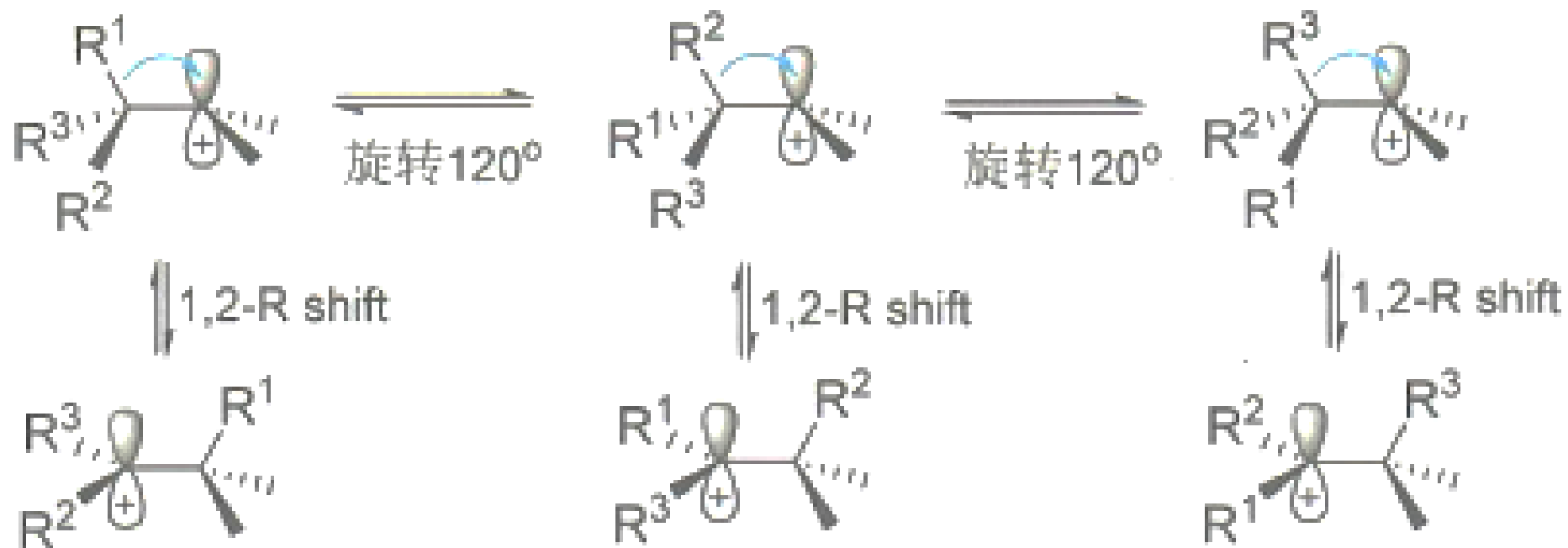
Orbital directionality of carbocation rearrangement



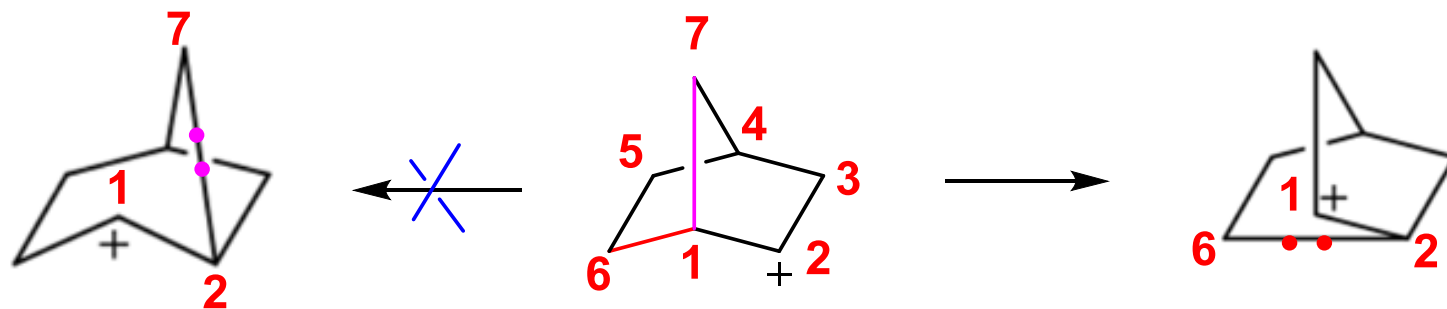
Electrophilic Addition



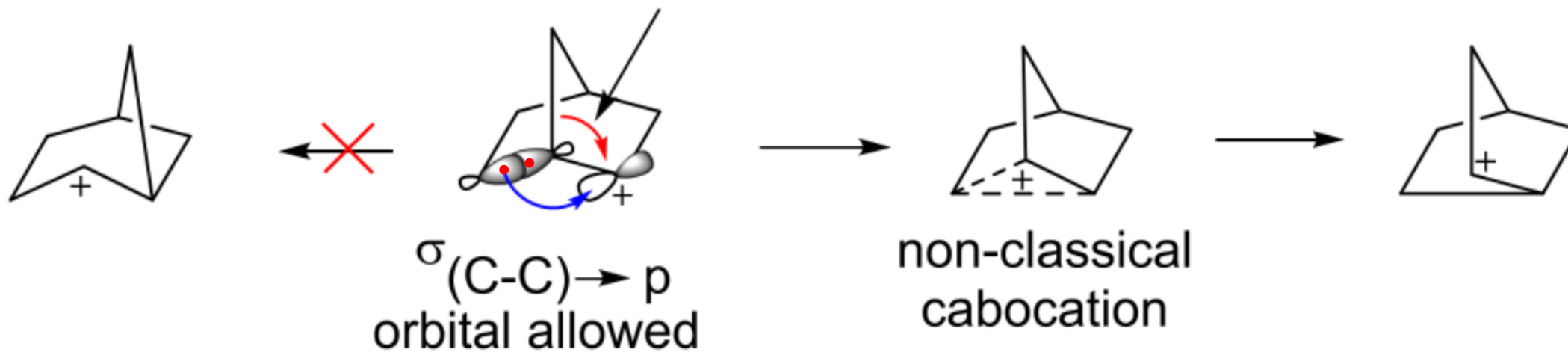
Electrophilic Addition



Electrophilic Addition

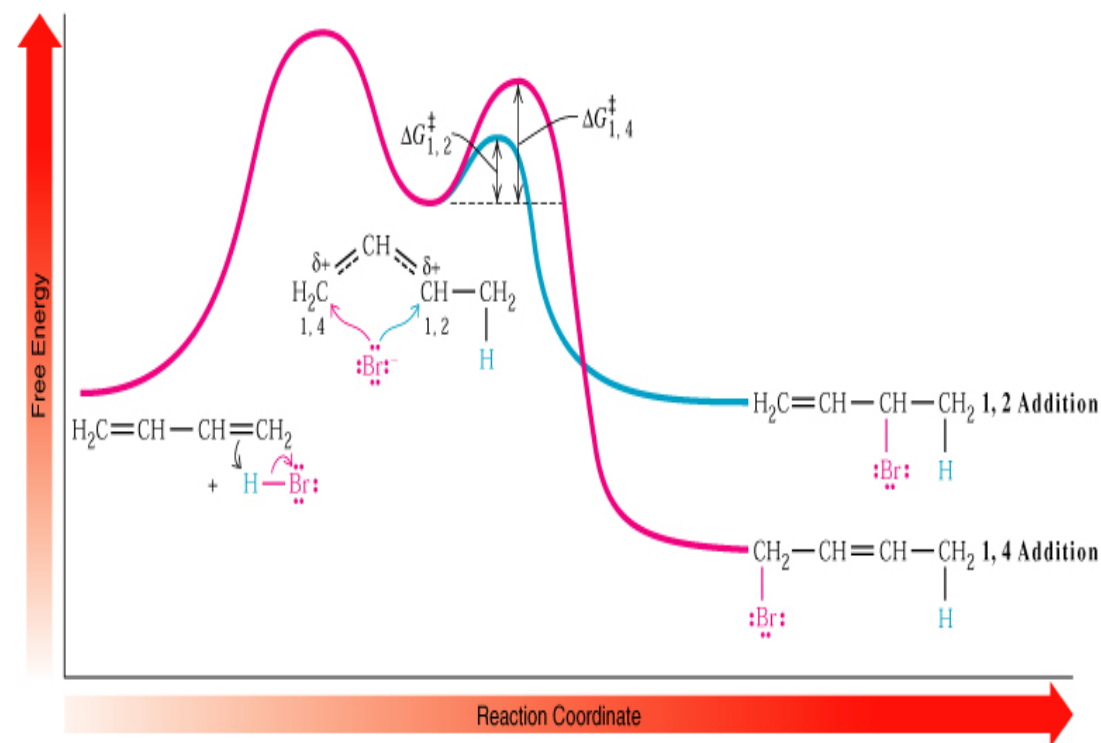
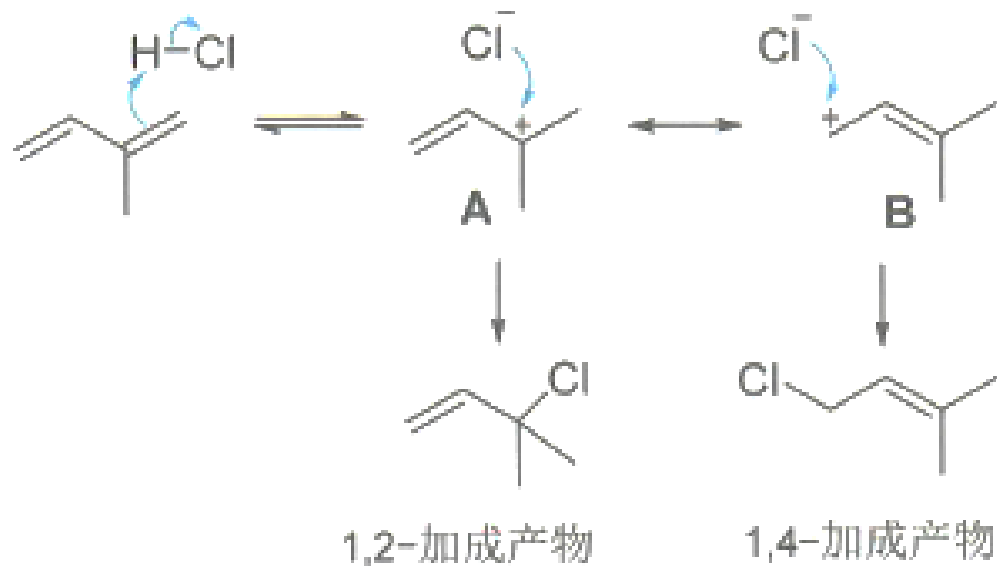


orbital forbidden



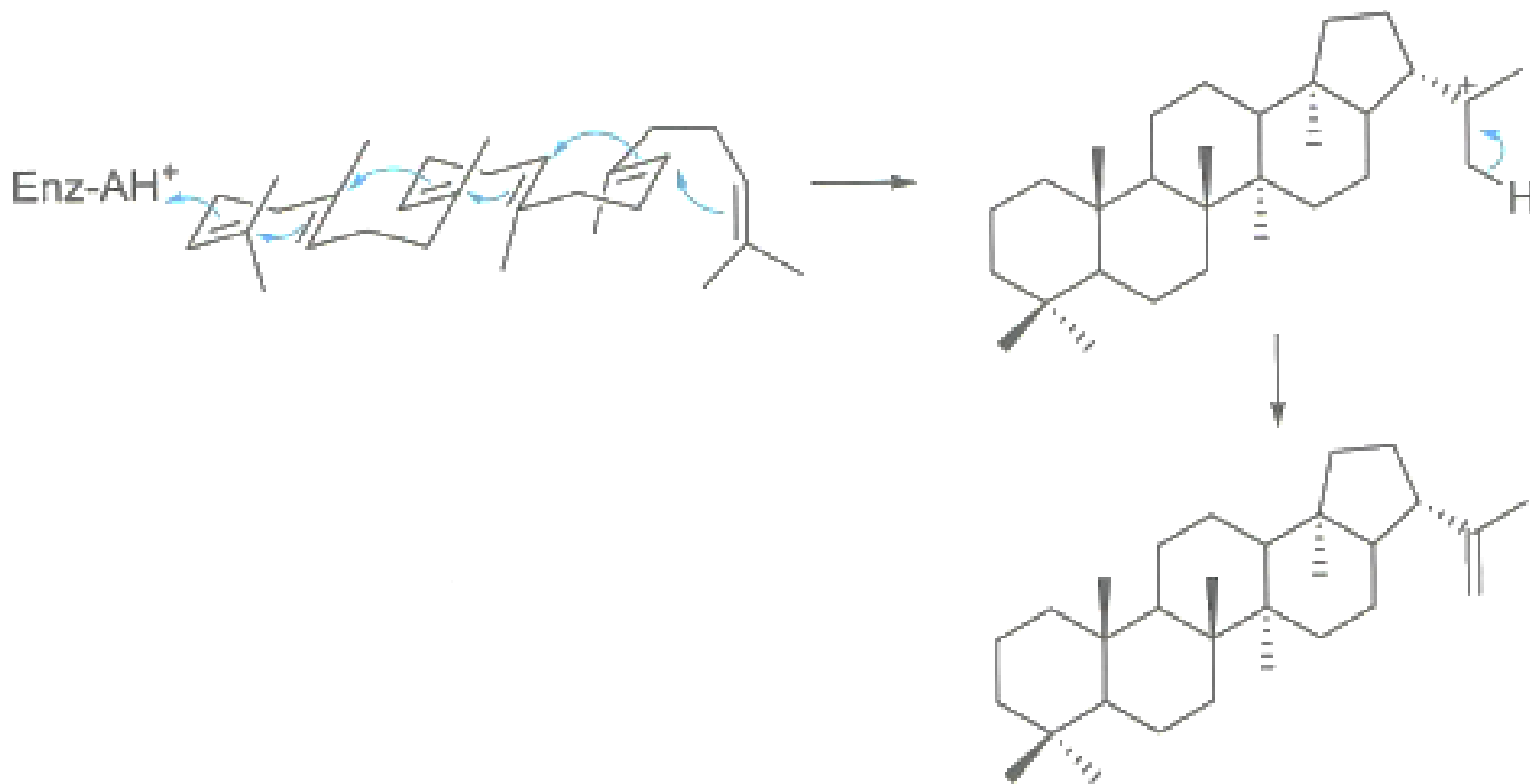
Electrophilic Addition

Electrophilic Attack on Conjugated Dienes: Kinetic and Thermodynamic Control



Electrophilic Addition

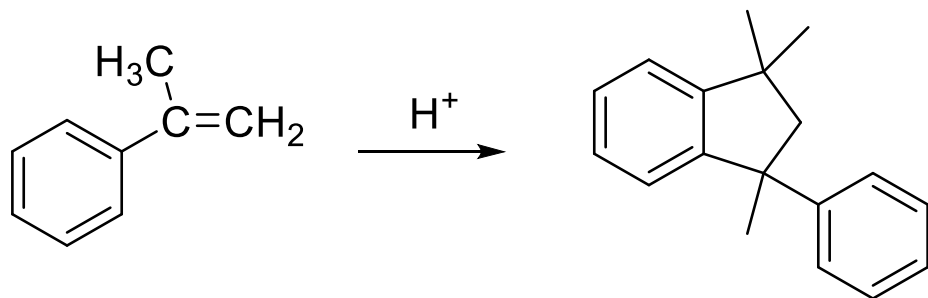
角鲨烯在 H^+ 条件下发生亲电环化反应，生成甾体化合物。（碳正离子本身也是亲电试剂）



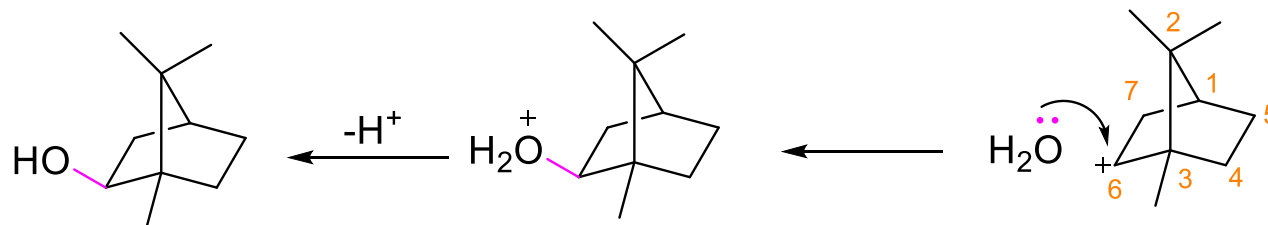
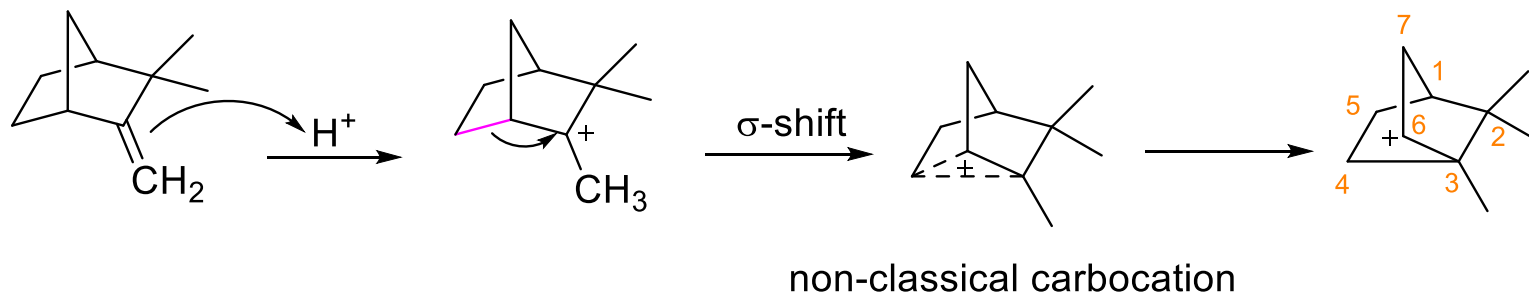
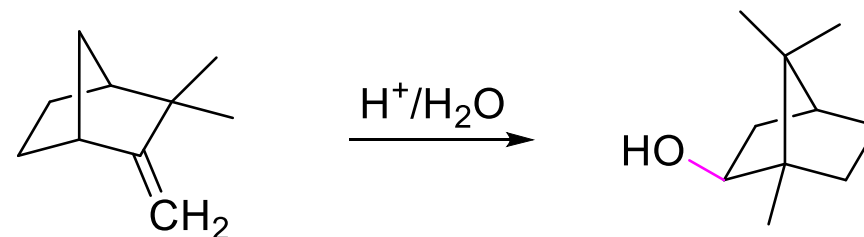
Exercise 1

Draw the complete mechanism for the reactions below

1)



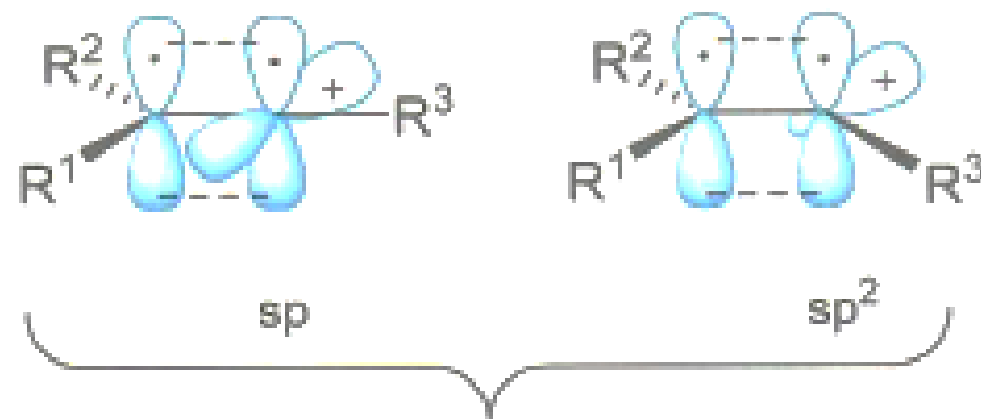
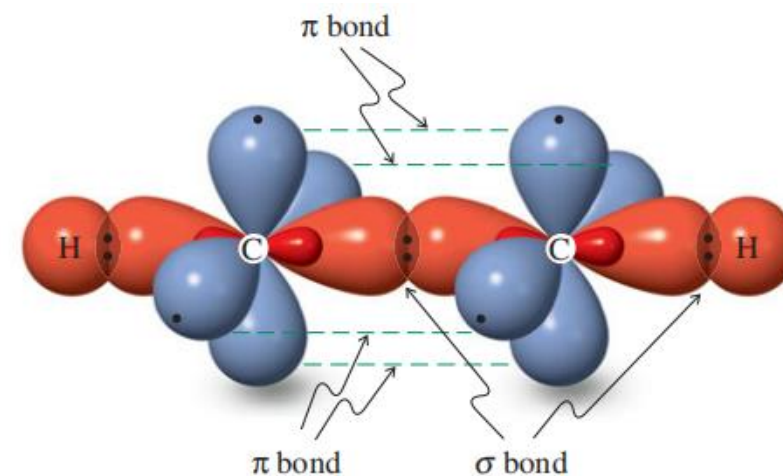
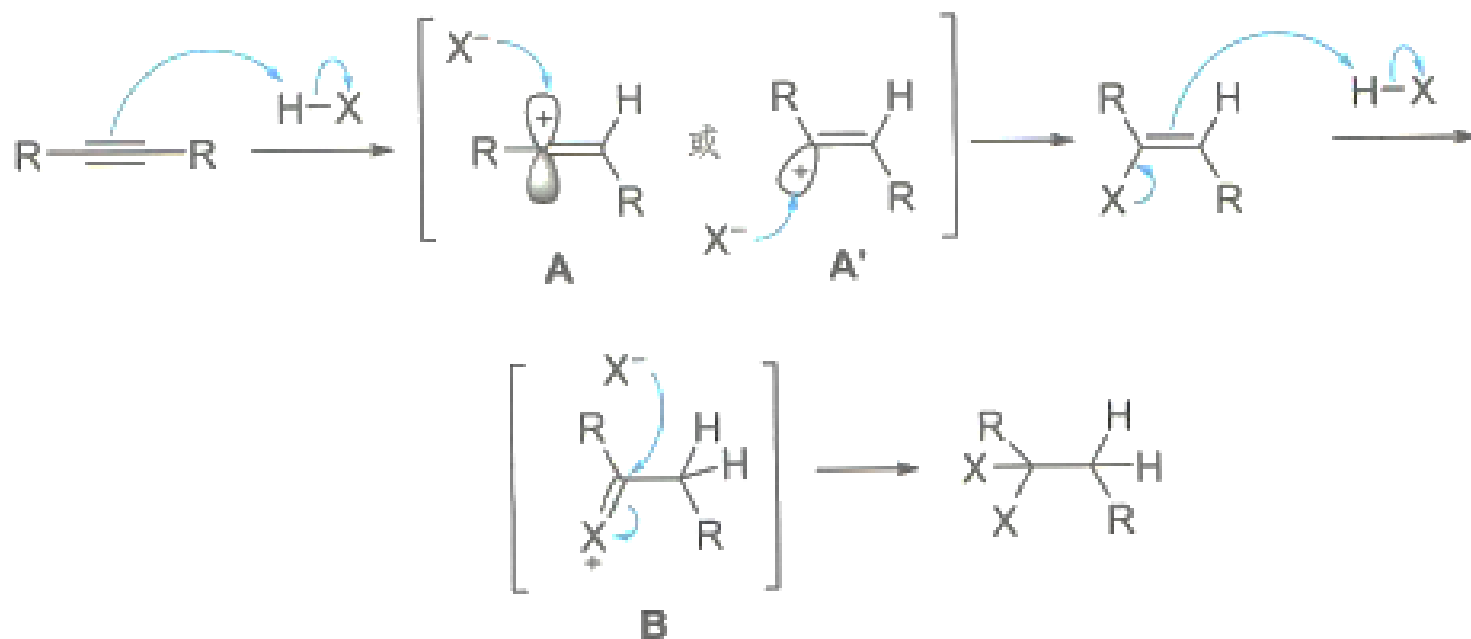
2)



Qiong Li

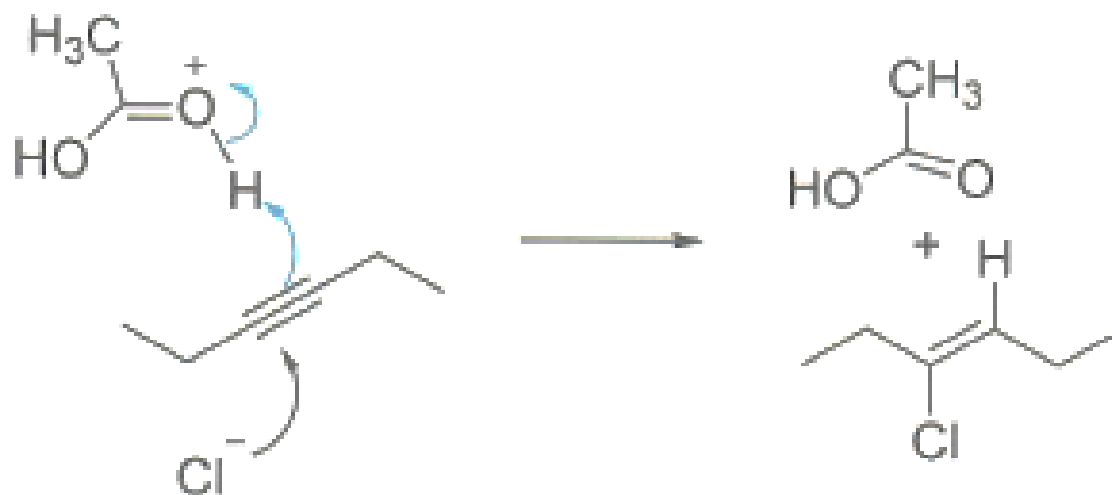
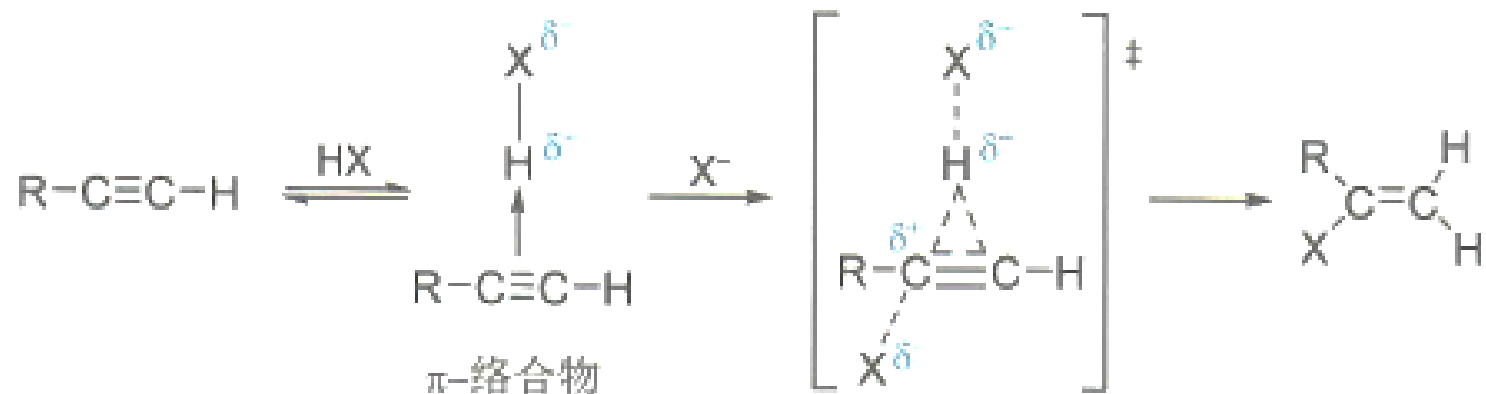
Electrophilic Addition

4.3.1' Electrophilic Addition of alkynes (了解)



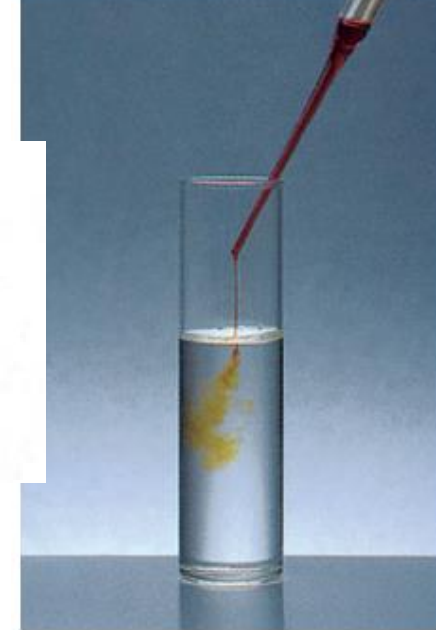
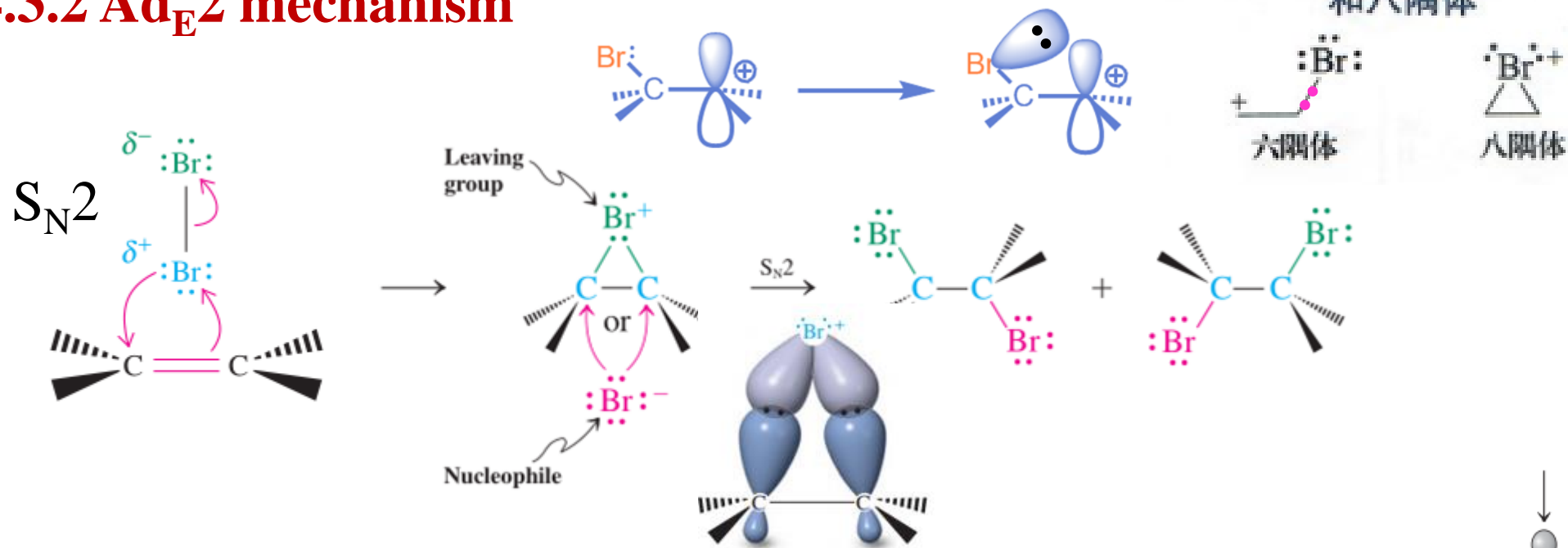
Electrophilic Addition

协同的三分子亲电加成机理（了解）



Electrophilic Addition

4.3.2 $\text{Ad}_{\text{E}}2$ mechanism



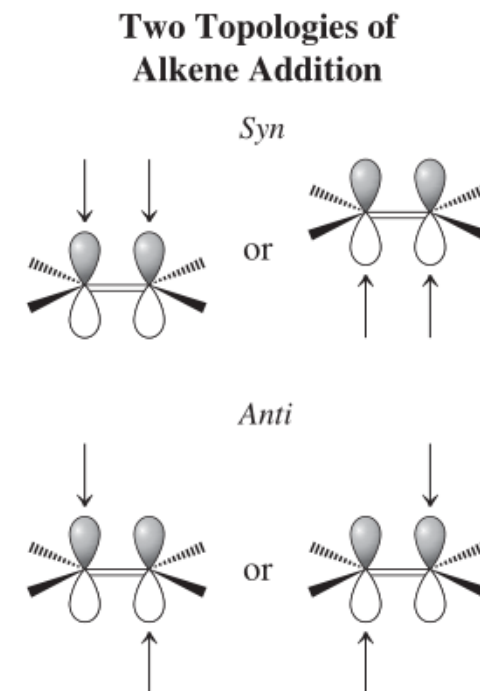
π -bond of the substrate: **Lewis base**, Nucleophile, To be oxidized

$\text{E}^{\delta+}$: **Lewis acid**, Electrophile, To be reduced

Topologies of Addition: **anti-addition**

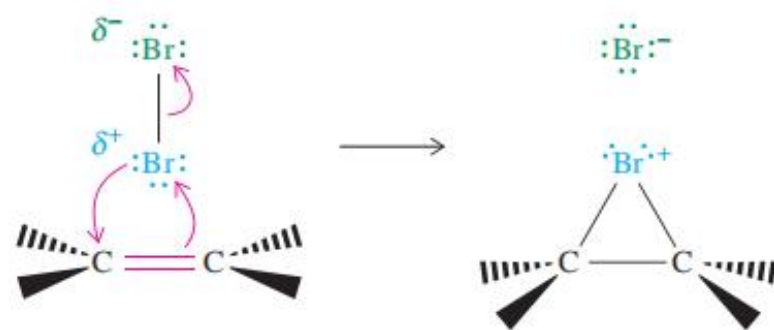
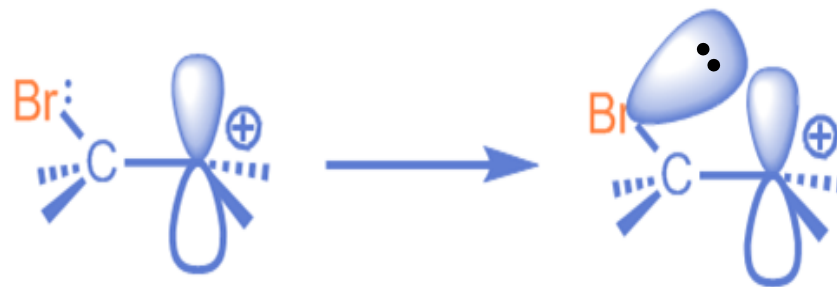
Stereospecific and Regiospecific

Qiong Li

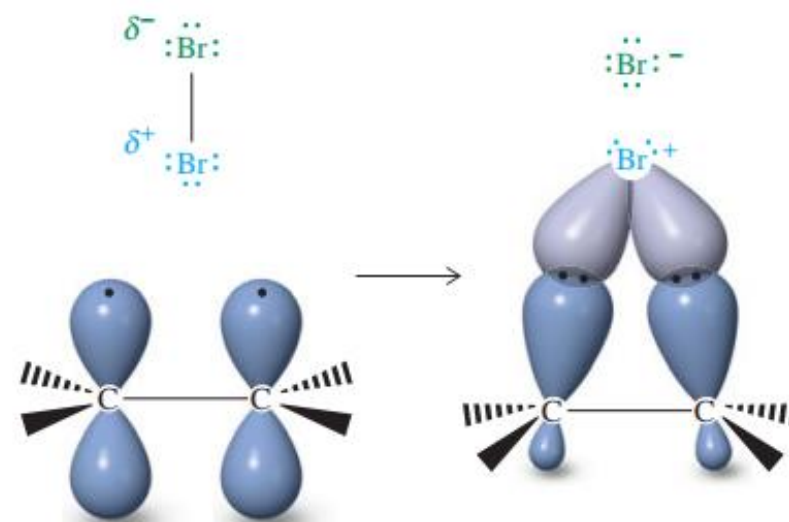


Electrophilic Addition

环状鎇离子的电子六隅体和八隅体



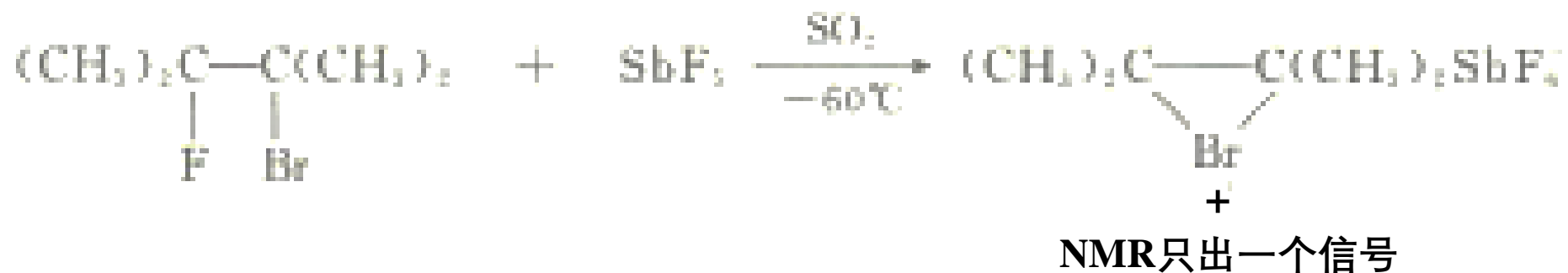
A



B

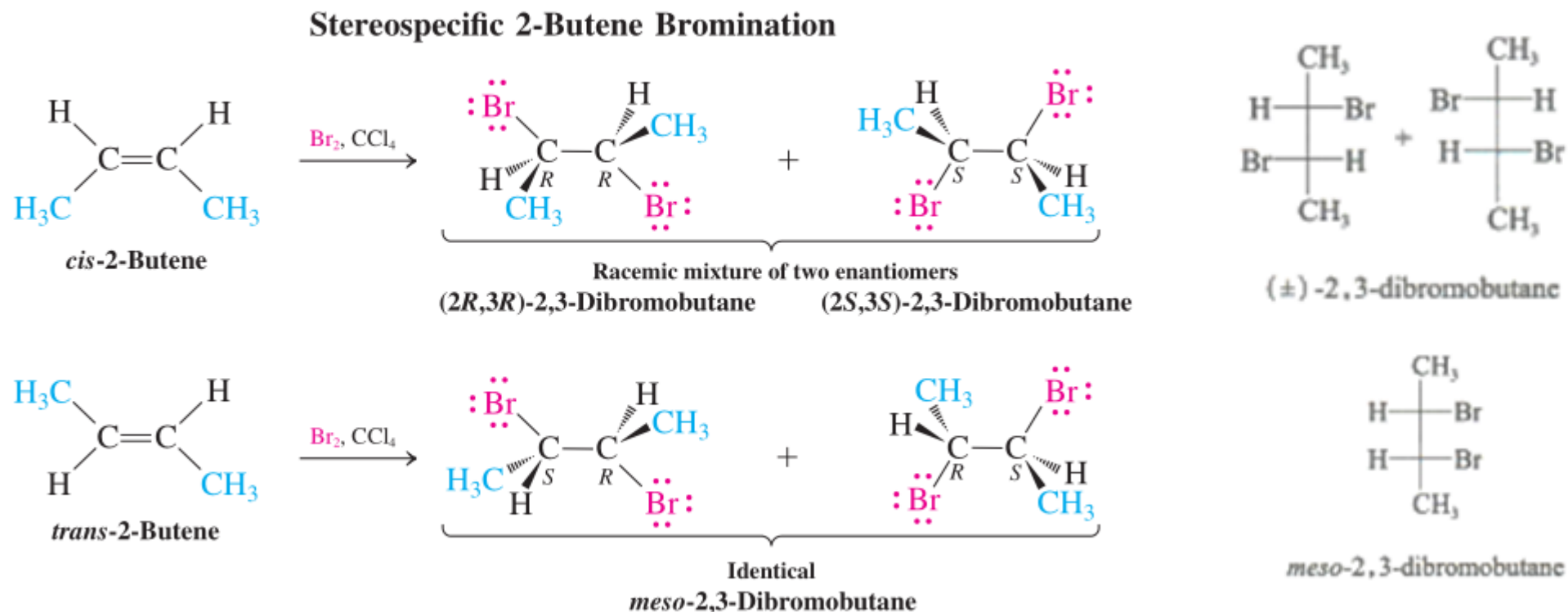
Electrophilic Addition

环溴鎓离子最初作为立体化学的一种合理解释而提出；但随后就发现了确切的证据。

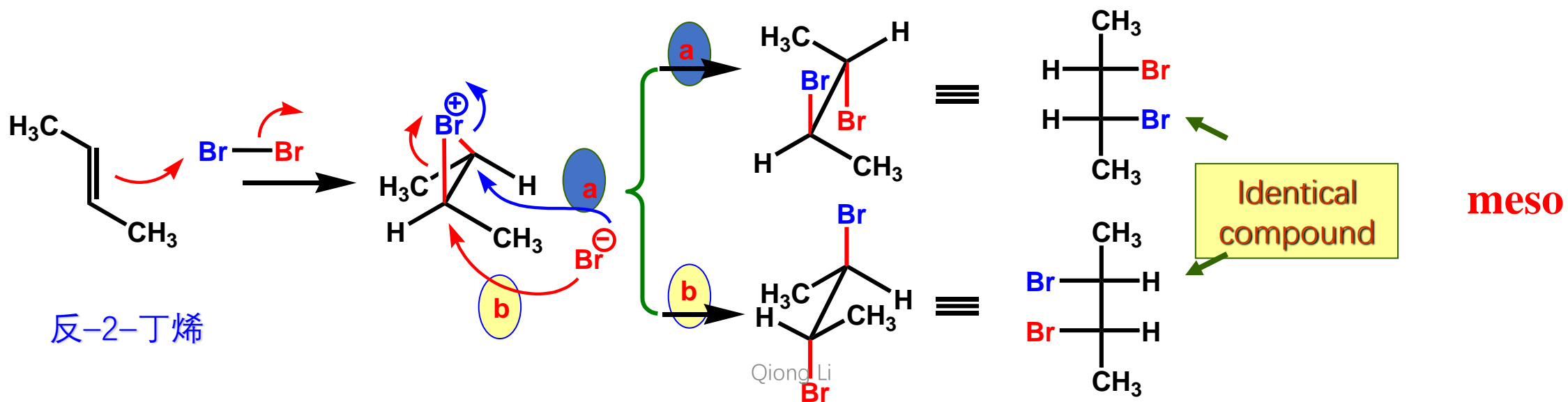
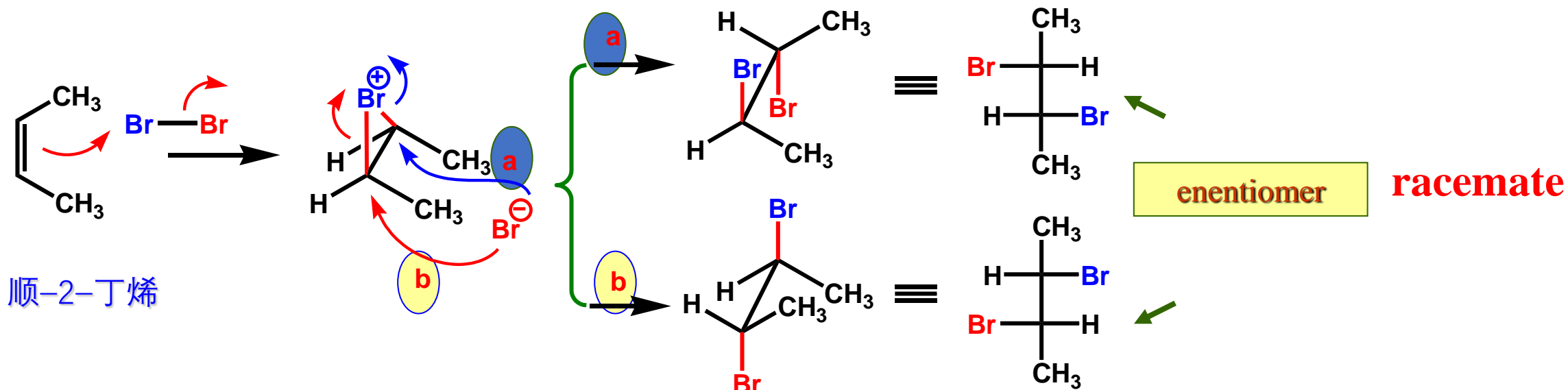


Exercise 2

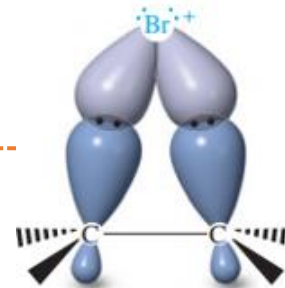
Give mechanisms to account for the stereochemistry of the products observed from the addition of bromine to *cis*- and *trans*-but-2-ene. Why are two products formed from *cis* isomer but only one from the *trans*?



➤ Cis -或trans-but-2-ene 加Br₂的立体化学

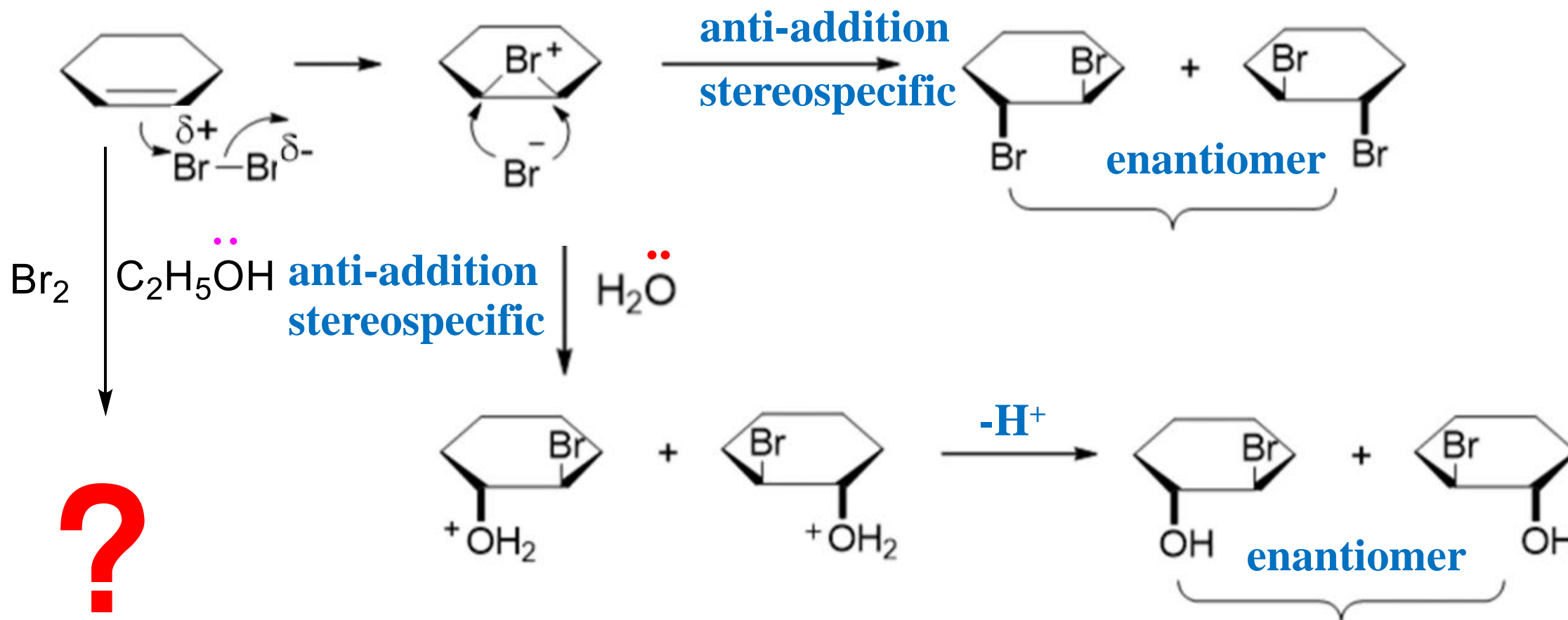


Electrophilic Addition



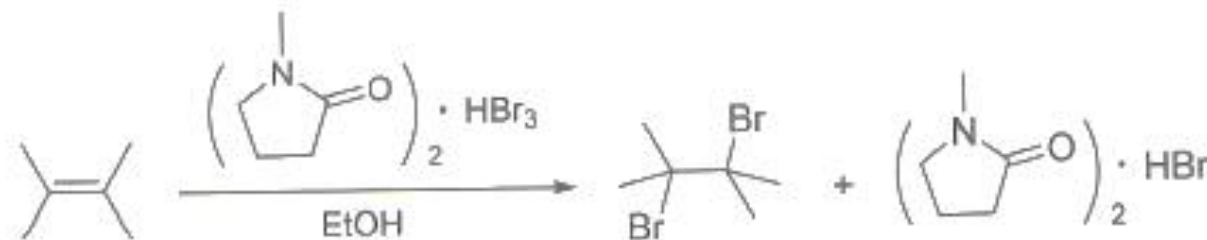
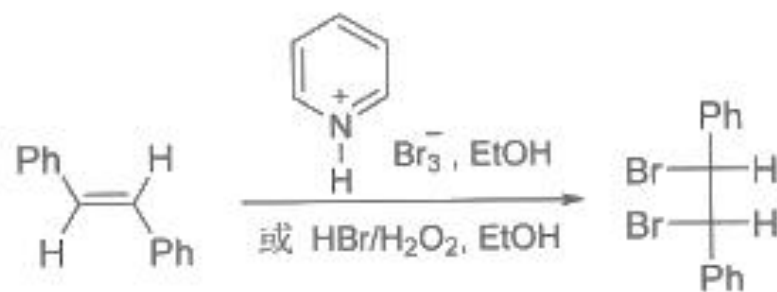
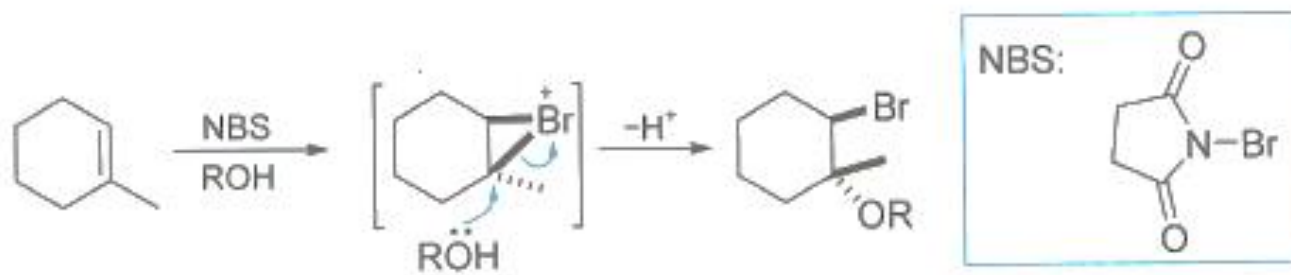
A. The Generality of Electrophilic Addition

The bromonium ion can be trapped by other nucleophiles



Electrophilic Addition

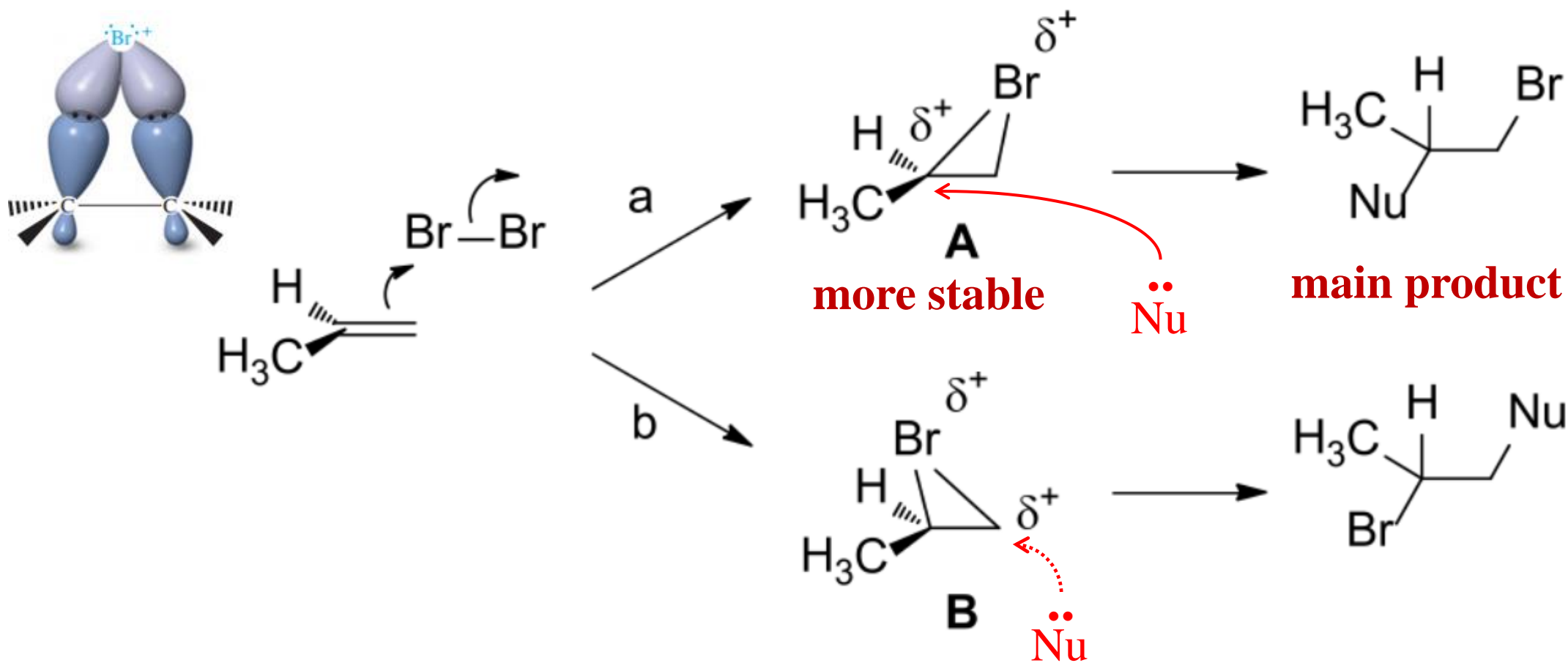
Other bromo-containing electrophiles



https://www.bilibili.com/video/BV1iv411P7Ms/?spm_id_from=333.337.search-card.all.click&vd_source=a1de320a3341bd841e2e169885958e16

Electrophilic Addition

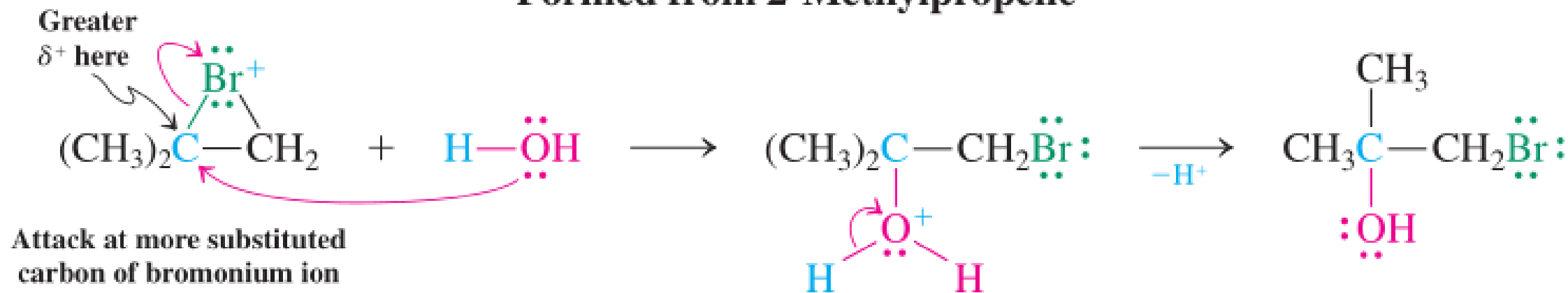
B. Regioselectivity when the substrate alkene is unsymmetric



the nucleophile attacks the more highly substituted carbon of the ring, because this carbon is more positively polarized than the other.

Electrophilic Addition

Regioselective Opening of the Bromonium Ion Formed from 2-Methylpropene



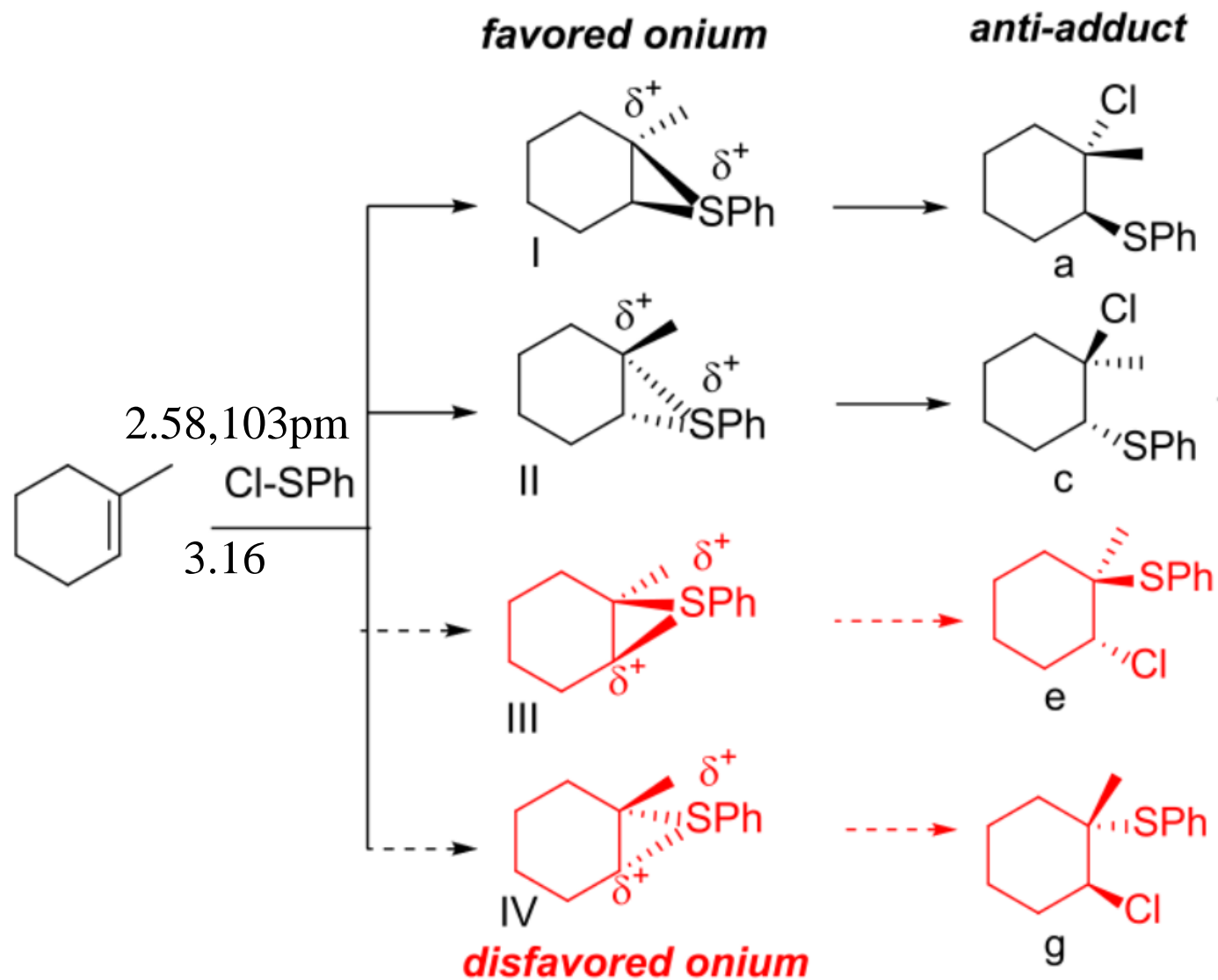
Electrophilic Addition

In general, alkenes can undergo **stereo-** and **regiospecific addition** reactions with reagents of the type **A-B**, in which the **A-B bond is polarized** such that A acts as the electrophile **A⁺** and B as the nucleophile **B⁻**.

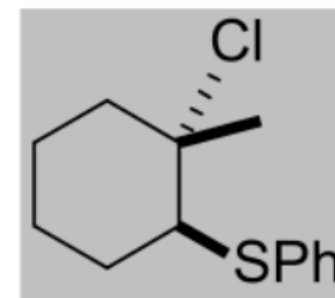
Reagents A-B That Add to Alkenes by Electrophilic Attack

$ \begin{array}{c} \text{H} & & \text{CH}_3 \\ & \diagdown & / \\ & \text{C} = \text{C} \\ & / & \diagdown \\ \text{H} & & \text{CH}_3 \end{array} + \delta^+ \text{A} - \text{B}^{\delta-} \longrightarrow \begin{array}{c} \text{H} & \text{CH}_3 \\ & \\ \text{H}-\text{C} & - & \text{C}-\text{CH}_3 \\ & \\ \text{A} & \text{B} \end{array} $		
Name	Structure	Addition product to 2-methylpropene
Bromine chloride	$\text{:}\ddot{\text{Br}}-\ddot{\text{Cl}}\text{:}$	$\text{:}\ddot{\text{Br}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{Cl}}\text{:}$
Cyanogen bromide	$\text{:}\ddot{\text{Br}}-\text{CN}\text{:}$	$\text{:}\ddot{\text{Br}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{CN}\text{:}$
Iodine chloride	$\text{:}\ddot{\text{I}}-\ddot{\text{Cl}}\text{:}$	$\text{:}\ddot{\text{I}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{Cl}}\text{:}$
Sulfenyl chlorides	$\text{R}\ddot{\text{S}}-\ddot{\text{Cl}}\text{:}$	$\text{R}\ddot{\text{S}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{Cl}}\text{:}$
Mercuric salts	$\text{XHg}-\text{X}^a; \text{H}\ddot{\text{O}}\text{H}$	$\text{XHgCH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{O}}\text{H}$
^a X here denotes acetate.		

Electrophilic Addition



Final product: a + c



Regiospecific

I, II 优于 III, IV

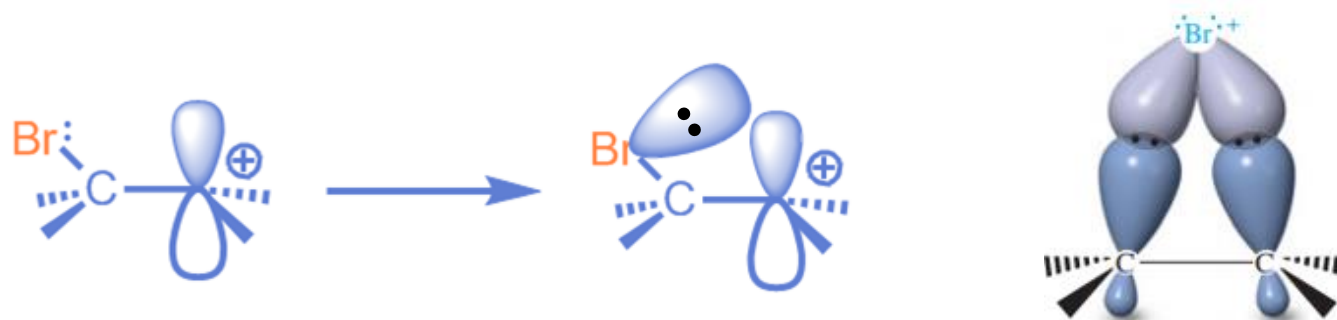
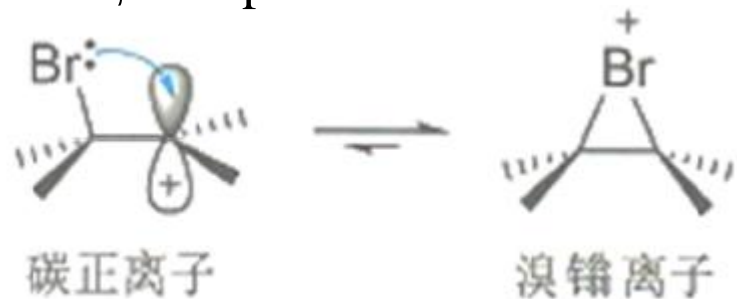
Stereospecific

anti-addition

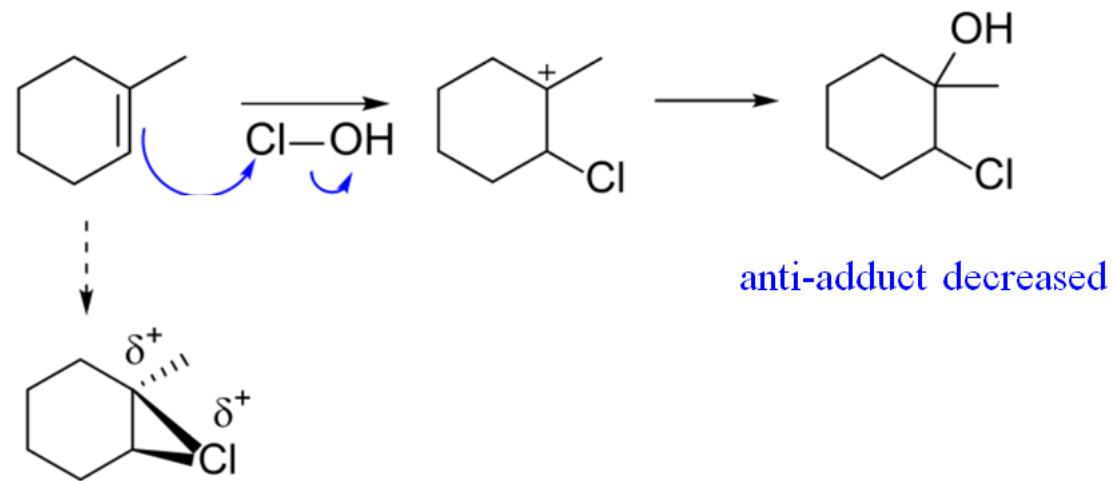
Qiong Li

Electrophilic Addition

2.96, 114pm



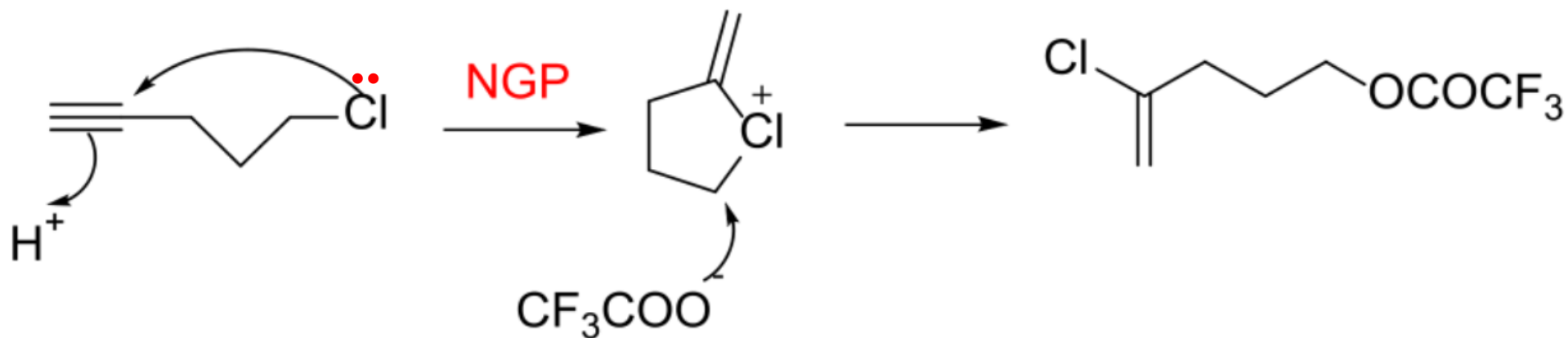
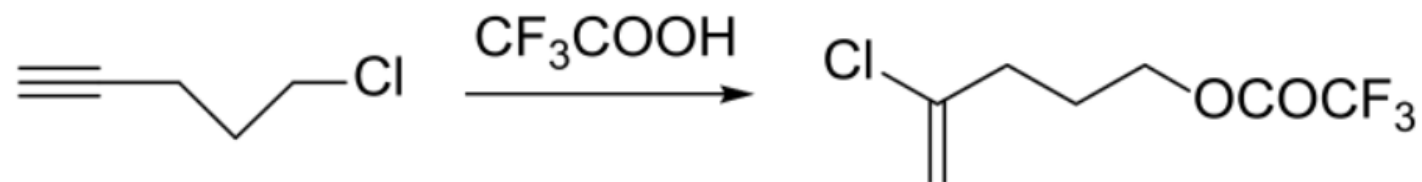
3.16, 99pm



和原子半径有关；和电负性有关；

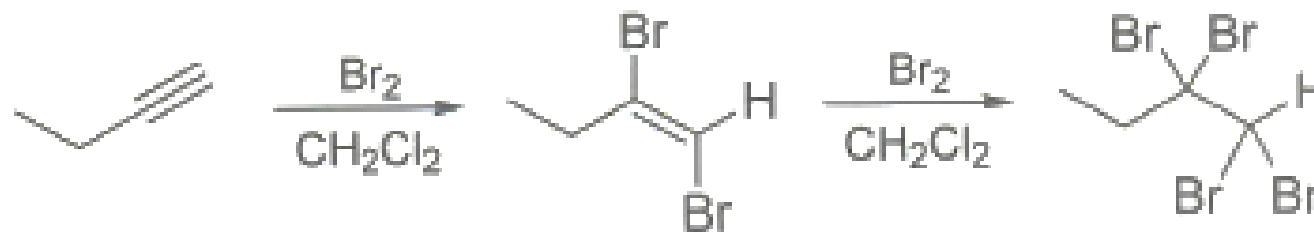
Exercise 3

Draw the complete mechanism for the reactions below

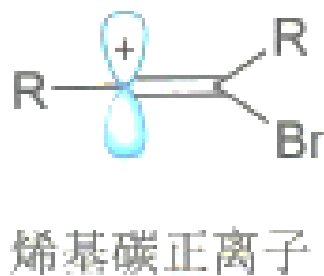
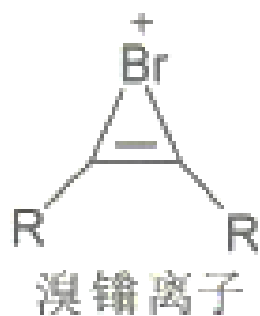


Electrophilic Addition

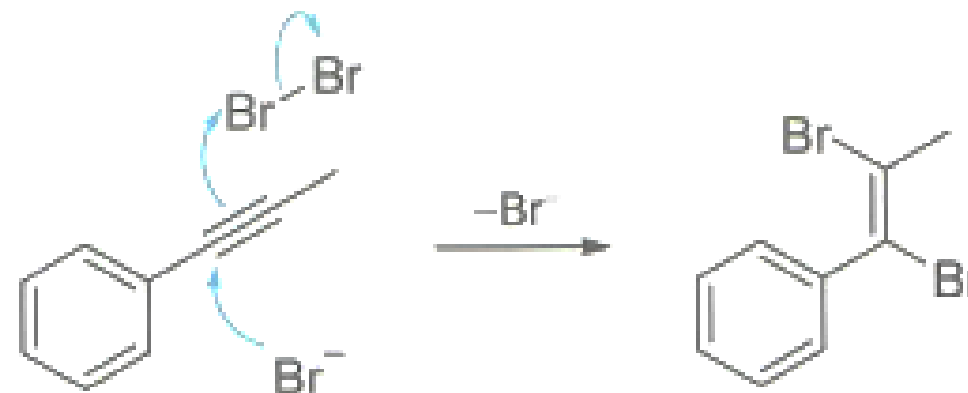
4.3.2' Ad_E2 mechanism of alkynes (了解)



Ad_E2



Ad_E3



Electrophilic Addition

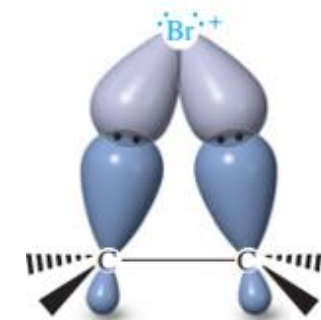
In general, alkenes can undergo **stereo-** and **regiospecific addition** reactions with reagents of the type **A-B**, in which the **A-B bond is polarized** such that A acts as the electrophile **A⁺** and B as the nucleophile **B⁻**.

Reagents A-B That Add to Alkenes by Electrophilic Attack

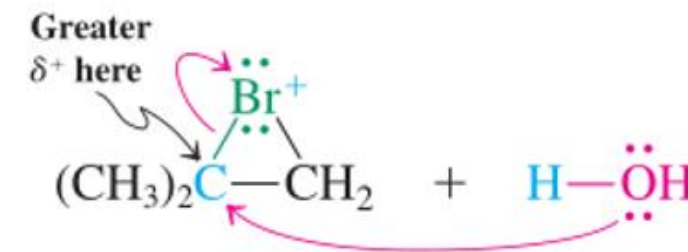
$ \begin{array}{c} \text{H} & & \text{CH}_3 \\ & \backslash & / \\ & \text{C} = \text{C} \\ & / & \backslash \\ \text{H} & & \text{CH}_3 \end{array} + \delta^+ \text{A} - \text{B}^{\delta-} \longrightarrow \begin{array}{c} \text{H} & \text{CH}_3 \\ & \\ \text{H}-\text{C} & - & \text{C}-\text{CH}_3 \\ & \\ \text{A} & \text{B} \end{array} $		
Name	Structure	Addition product to 2-methylpropene
Bromine chloride	$\text{:}\ddot{\text{Br}}-\ddot{\text{Cl}}\text{:}$	$\text{:}\ddot{\text{Br}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{Cl}}\text{:}$
Cyanogen bromide	$\text{:}\ddot{\text{Br}}-\text{CN}\text{:}$	$\text{:}\ddot{\text{Br}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{CN}\text{:}$
Iodine chloride	$\text{:}\ddot{\text{I}}-\ddot{\text{Cl}}\text{:}$	$\text{:}\ddot{\text{I}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{Cl}}\text{:}$
Sulfenyl chlorides	$\text{R}\ddot{\text{S}}-\ddot{\text{Cl}}\text{:}$	$\text{R}\ddot{\text{S}}\text{CH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{Cl}}\text{:}$
Mercuric salts	$\text{XHg}-\text{X}^a; \text{H}\ddot{\text{O}}\text{H}$	$\text{XHgCH}_2\text{C}(\text{CH}_3)_2$ $\text{:}\ddot{\text{O}}\text{H}\text{:}$

^aX here denotes acetate.

Qiong Li



anti-addition

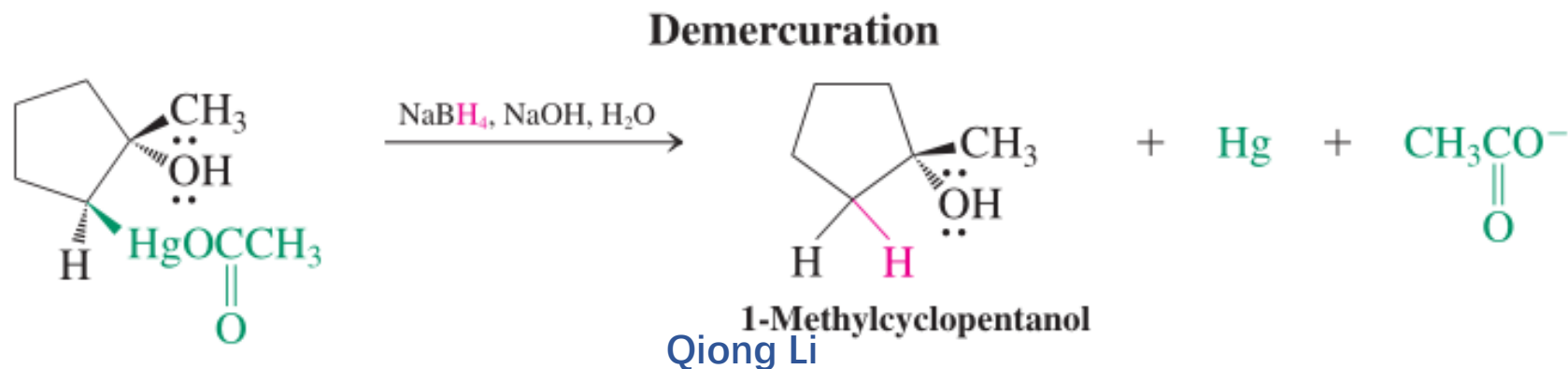
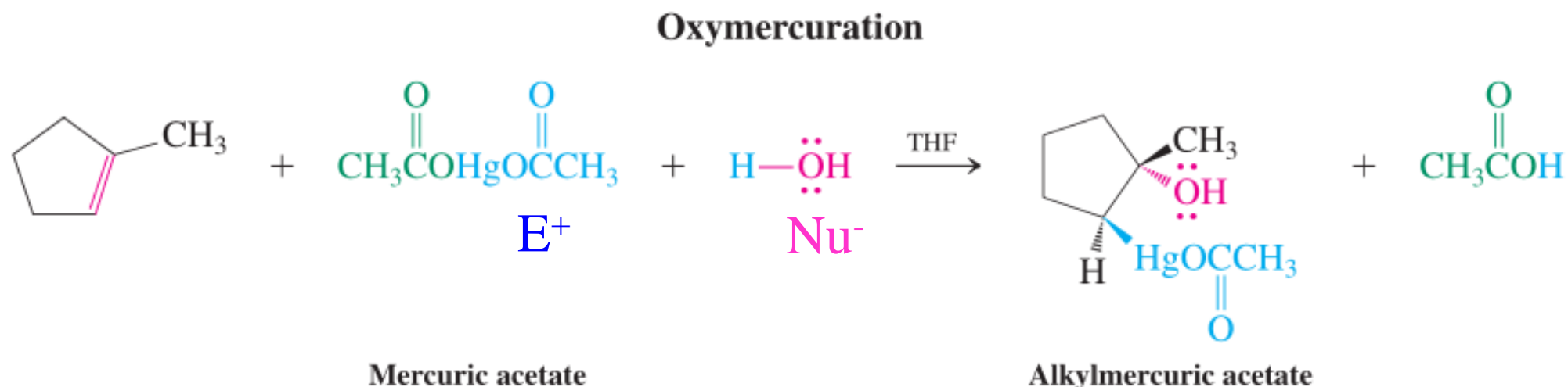


Attack at more substituted carbon of bromonium ion

Electrophilic Addition

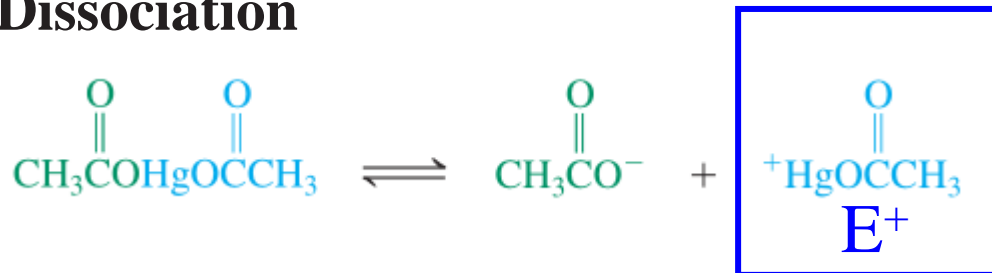
4.3.3 Mechanism of Oxymercuration-Demercuration: A Special Electrophilic Addition

Oxymercuration is anti-stereospecific and regioselective.

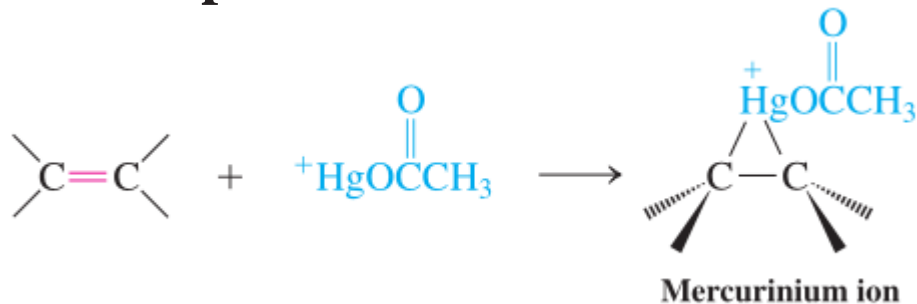


Electrophilic Addition

Step 1. Dissociation

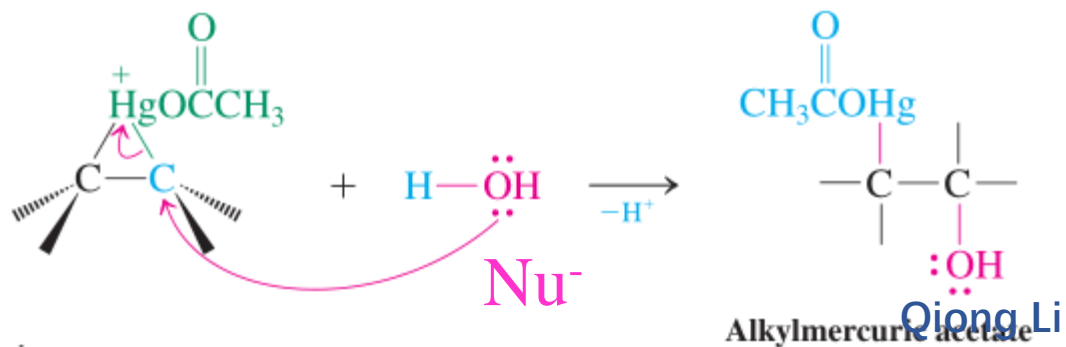


Step 2. Electrophilic attack



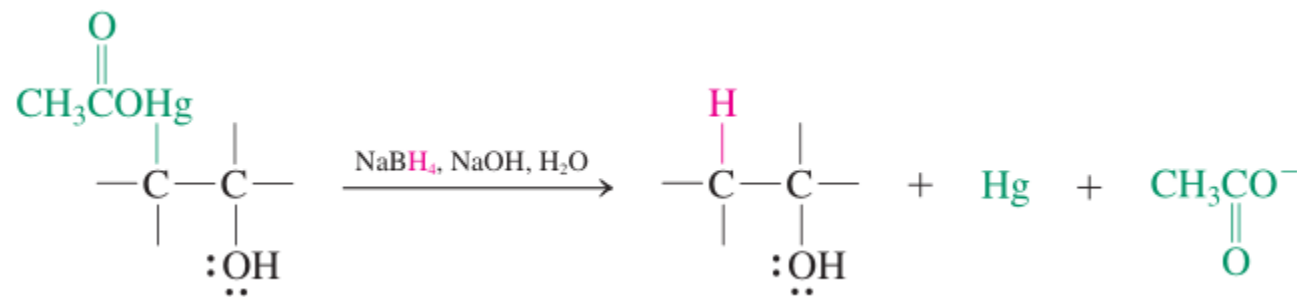
anti-stereospecific and regioselective.

Step 3. Nucleophilic opening (Markovnikov regioselectivity)



Electrophilic Addition

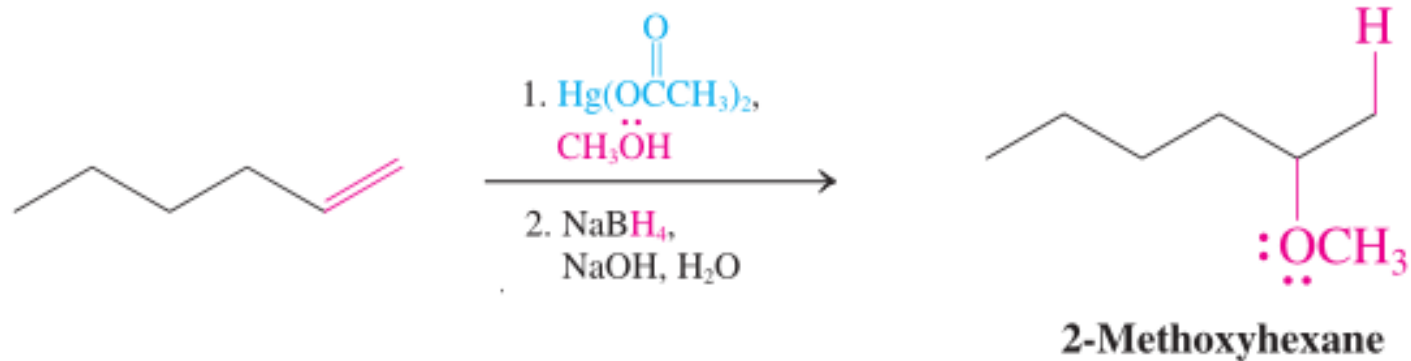
Step 4. Reduction



Oxymercuration – demercuration is a synthetically useful method for converting alkenes regioselectively (following the Markovnikov rule) into alcohols or ethers. Carbocations are not involved; therefore, rearrangements do not occur.

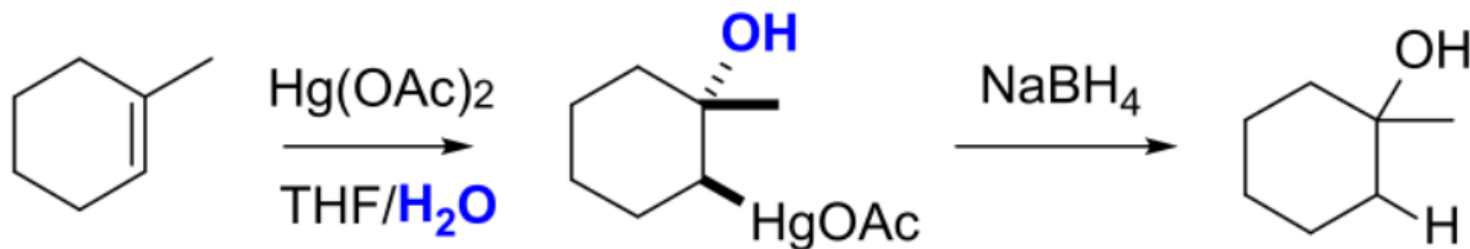
Exercise 4

What product will we get When the oxymercuration of an alkene is executed in an alcohol solvent and then demercuration with $\text{NaBH}_4/\text{NaOH}/\text{H}_2\text{O}$?

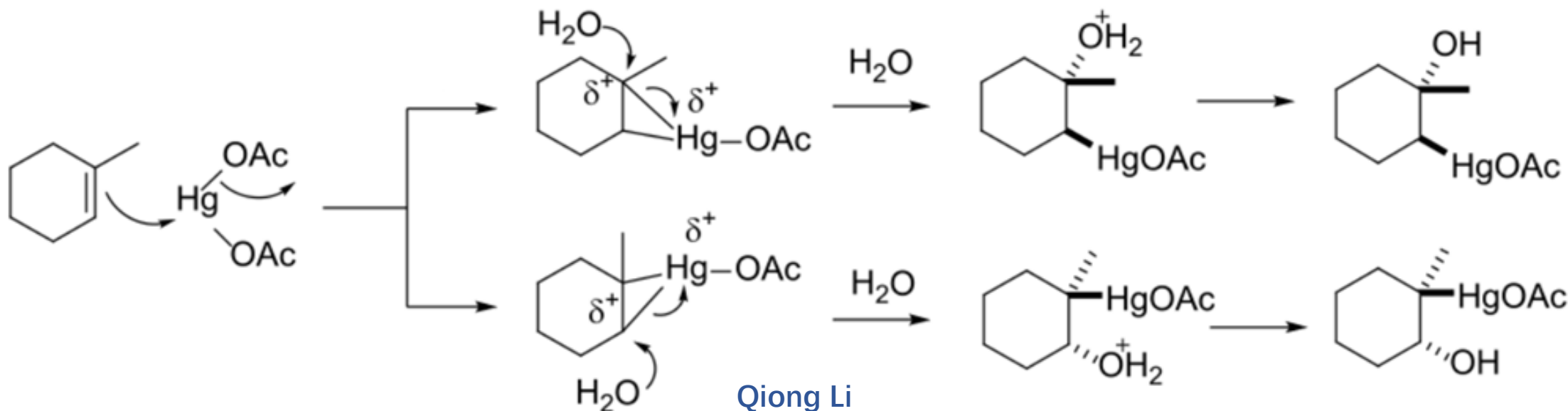


Electrophilic Addition

Stereospecific: anti-addition

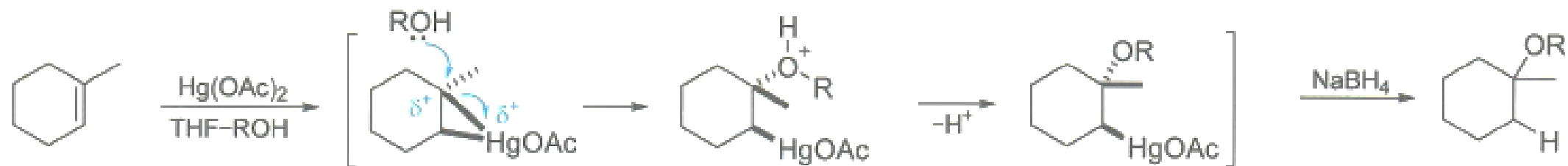


Regioselective



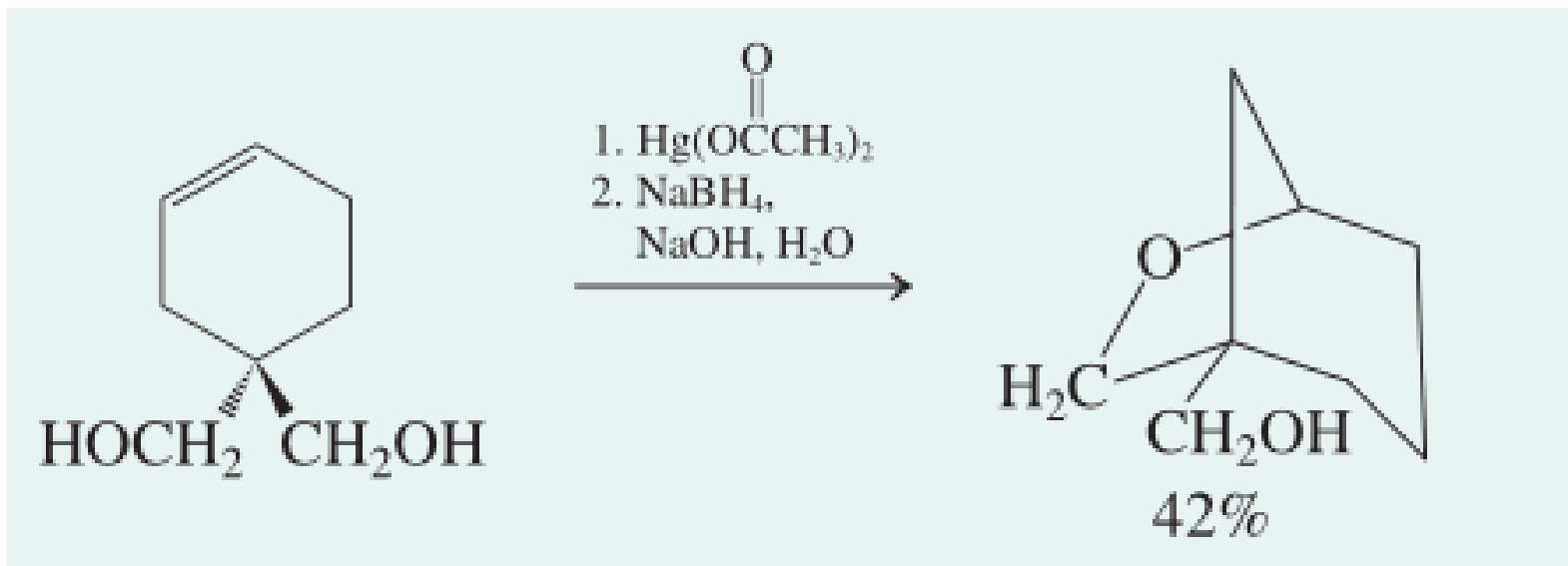
Qiong Li

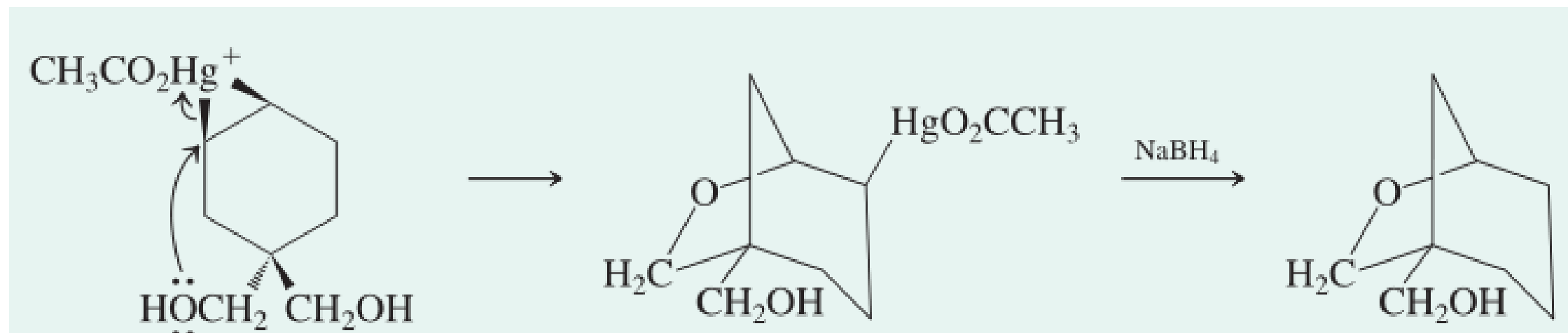
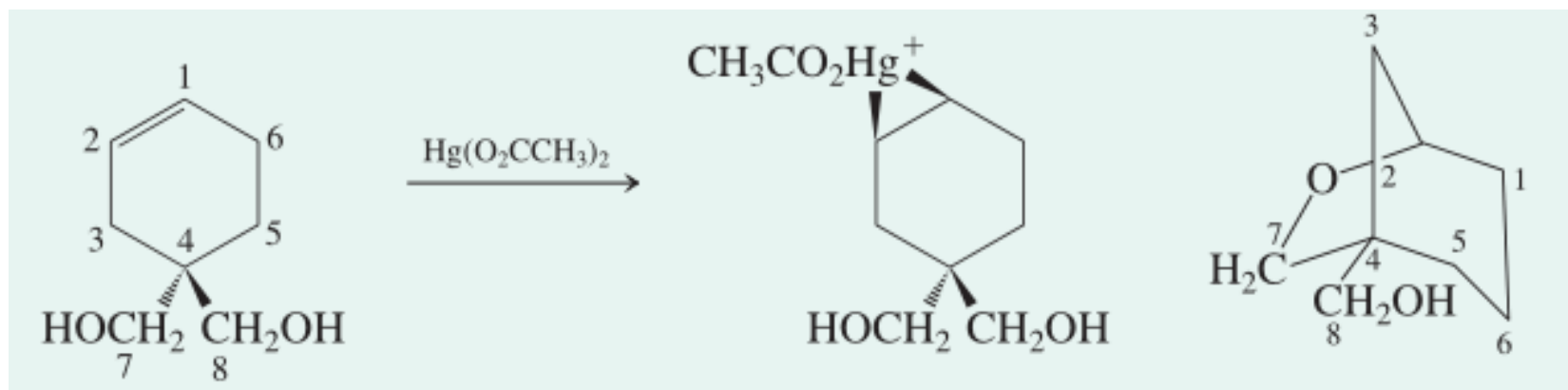
Electrophilic Addition



Exercise 5

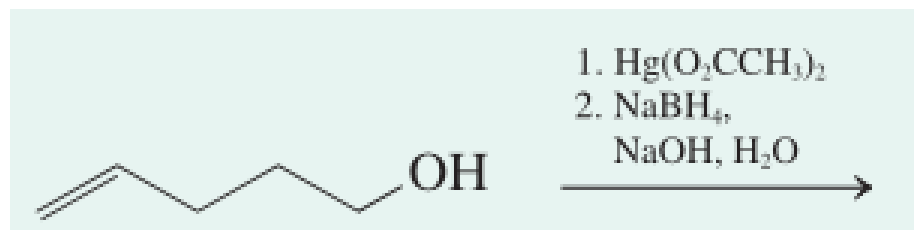
Draw the complete mechanism for the reactions below





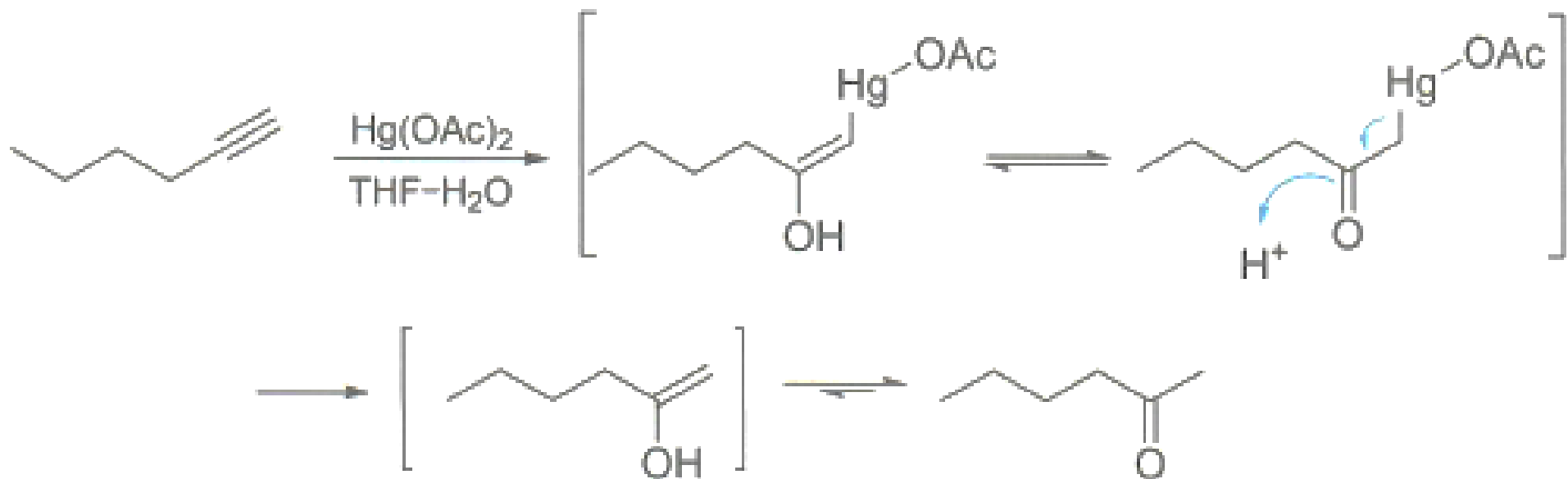
Exercise 6

The reaction below proceeds to a cyclic product that is an isomer of the starting material. Suggest a structure for it.



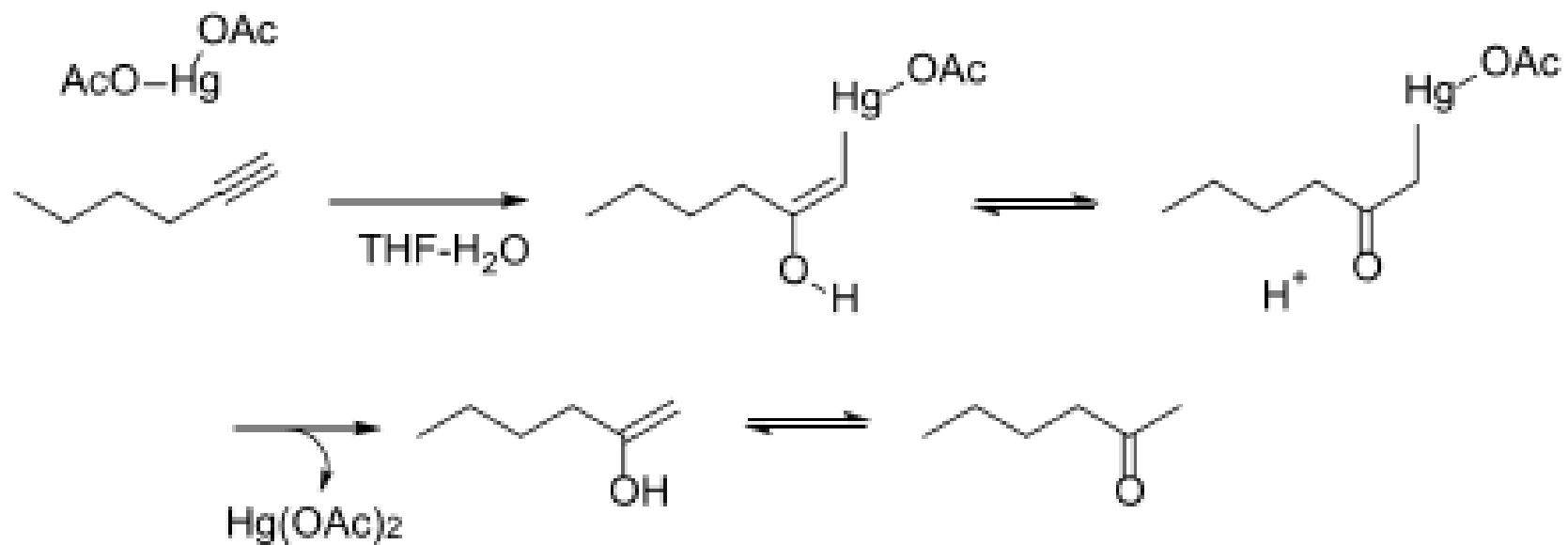
Electrophilic Addition

4.3.3' Oxymercuration reactions of alkynes



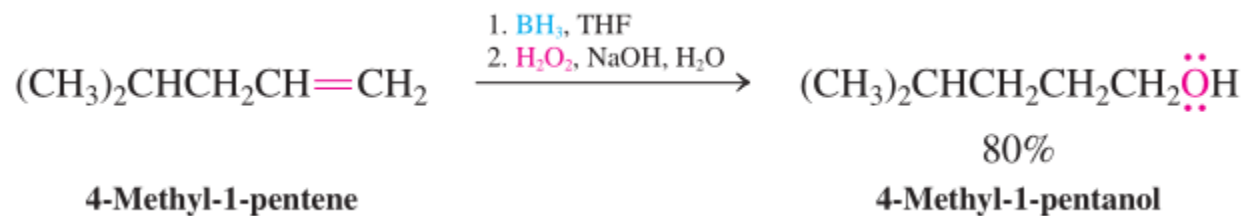
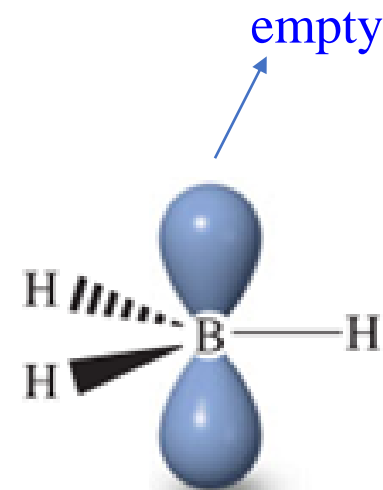
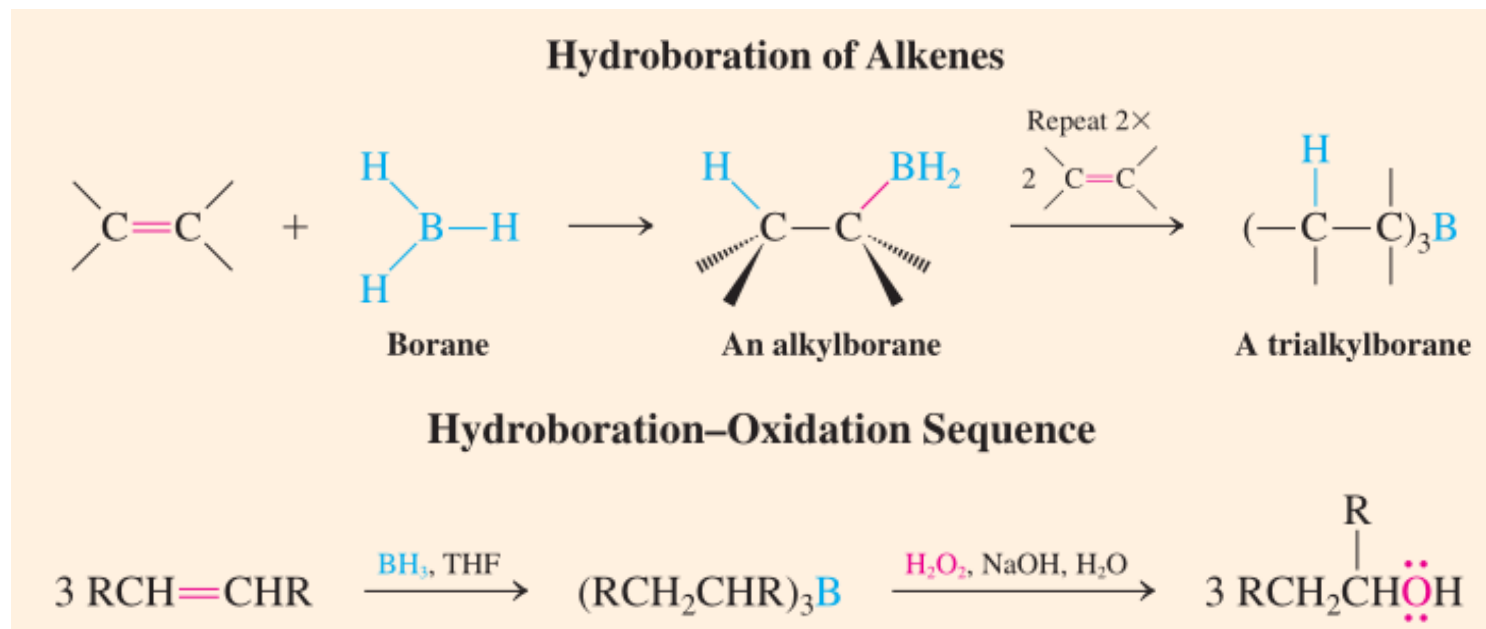
1. 只需要催化量的汞盐；
2. 不需要还原剂脱汞；
3. 具有区域选择性

Electrophilic Addition



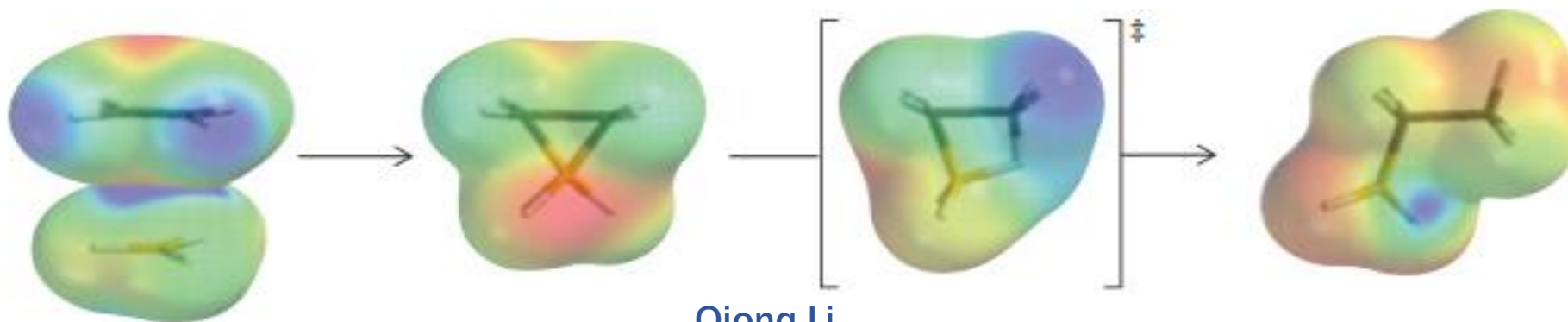
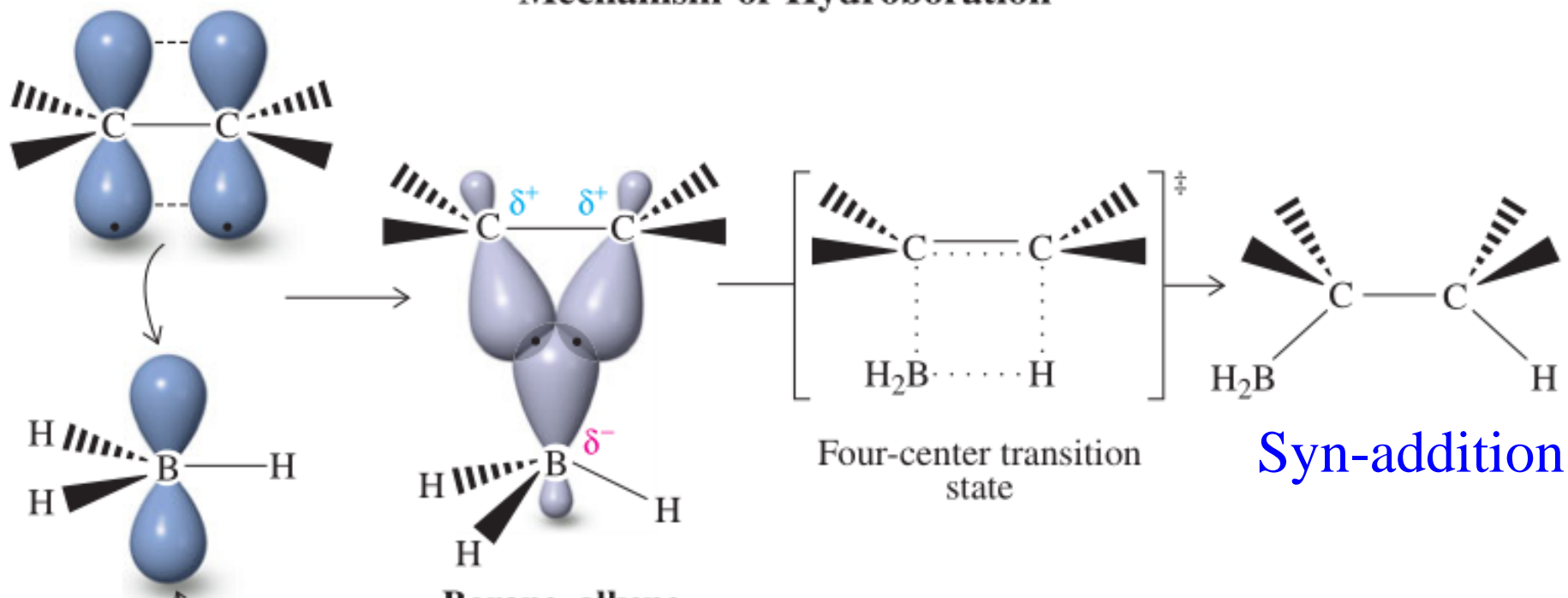
Electrophilic Addition

4.3.4 Mechanism of Hydroboration-Oxidation : A Stereospecific, Anti-Markovnikov Hydration



Electrophilic Addition

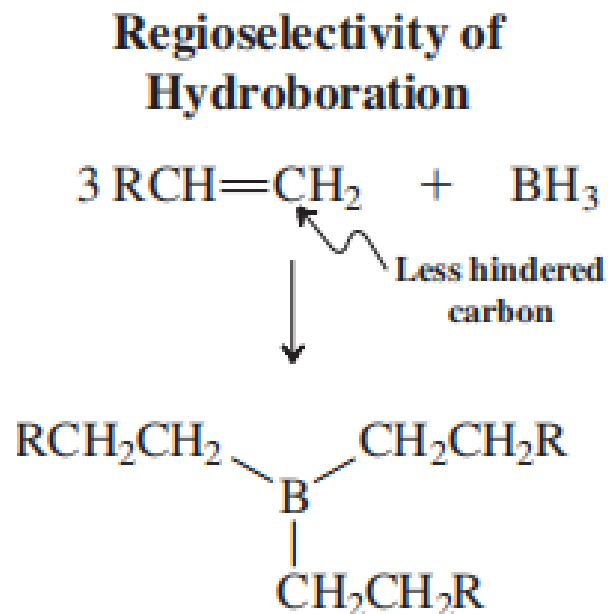
Mechanism of Hydroboration



Qiong Li

Electrophilic Addition

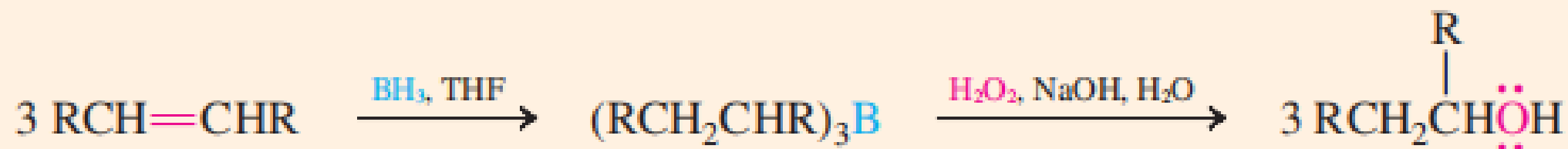
Steric factors primarily control the regioselectivity: The boron binds to the less hindered (less substituted) carbon.



Electrophilic Addition

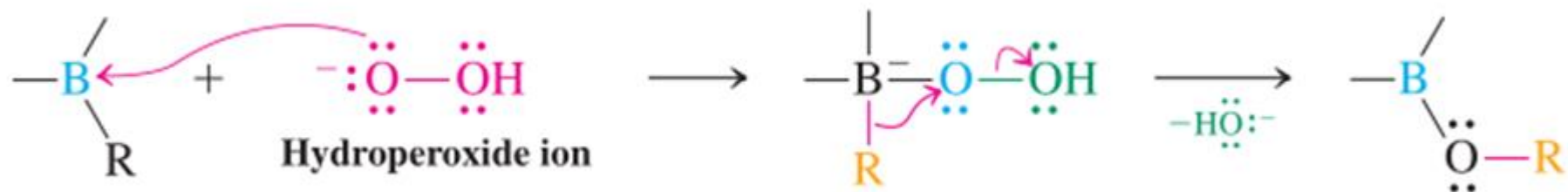
The oxidation of alkylboranes gives alcohols

Hydroboration–Oxidation Sequence

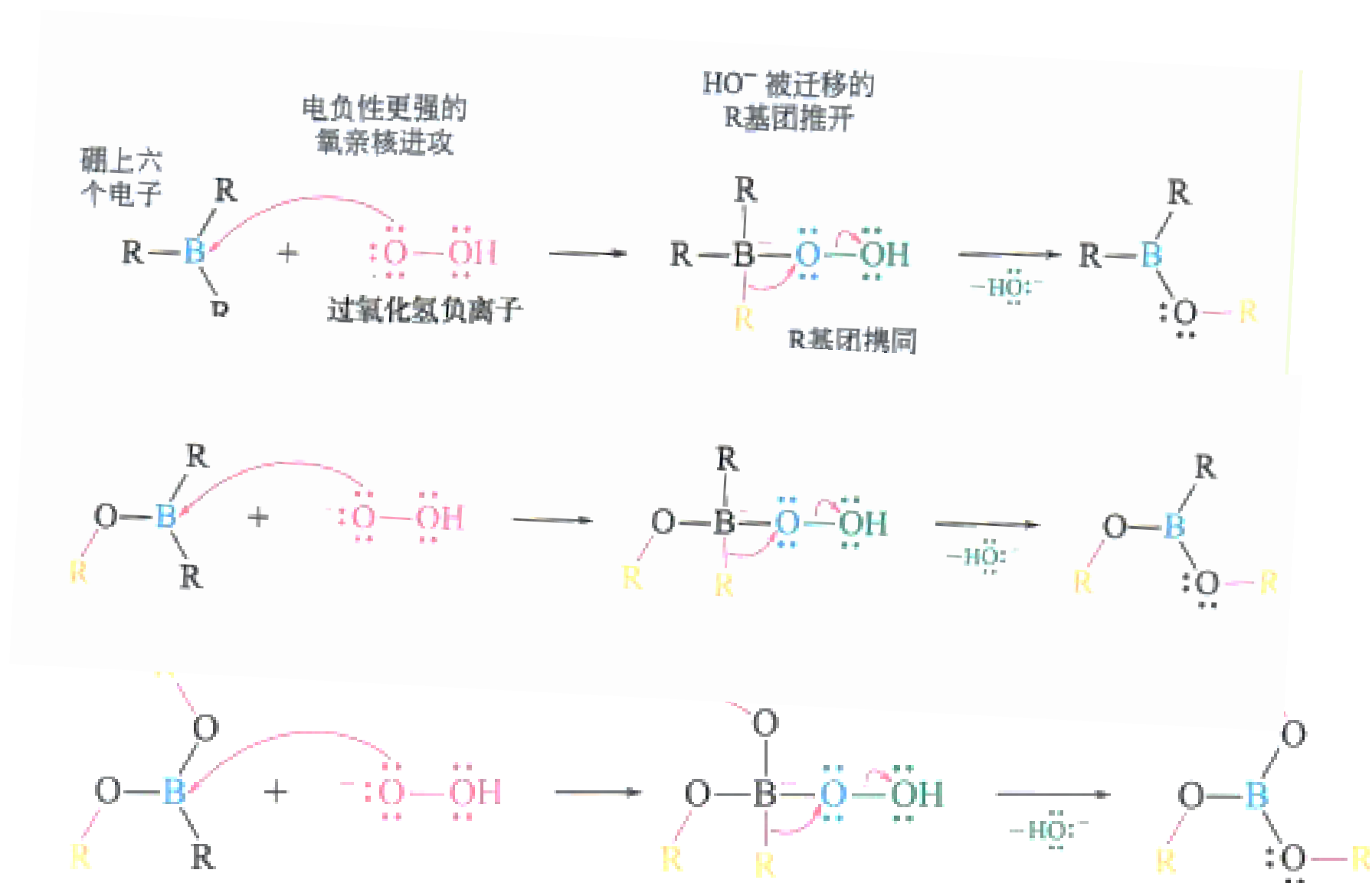


Electrophilic Addition

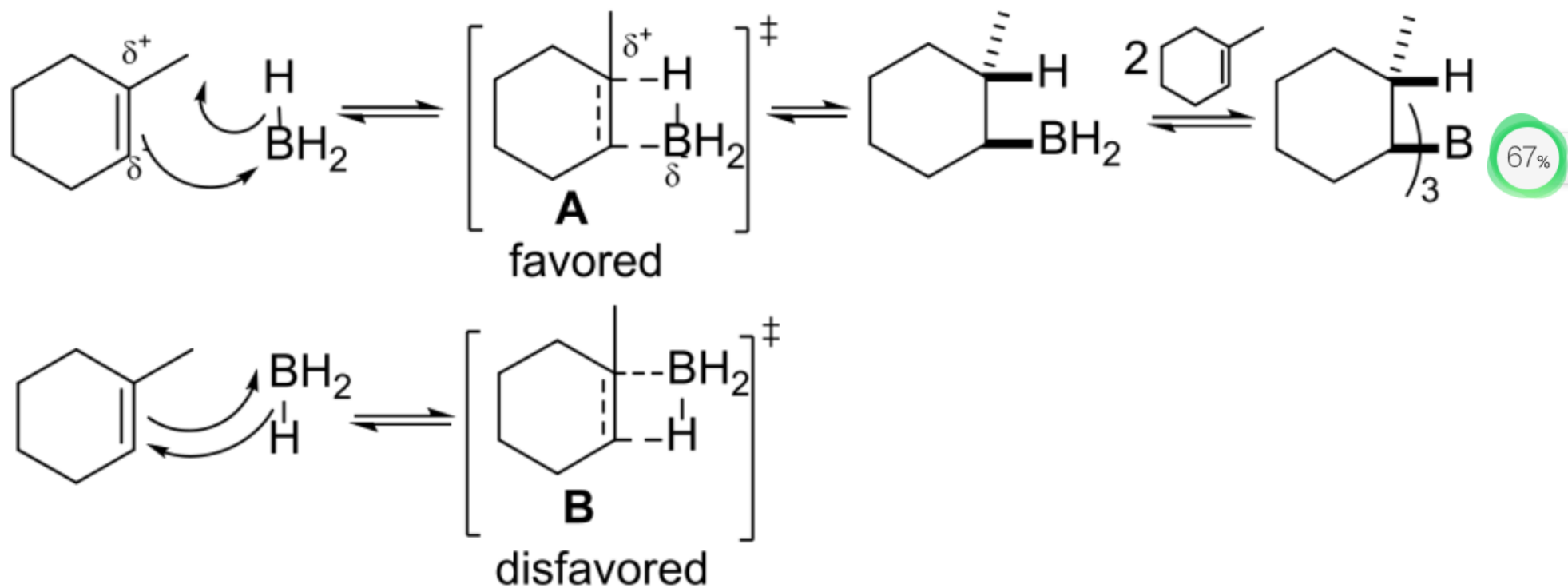
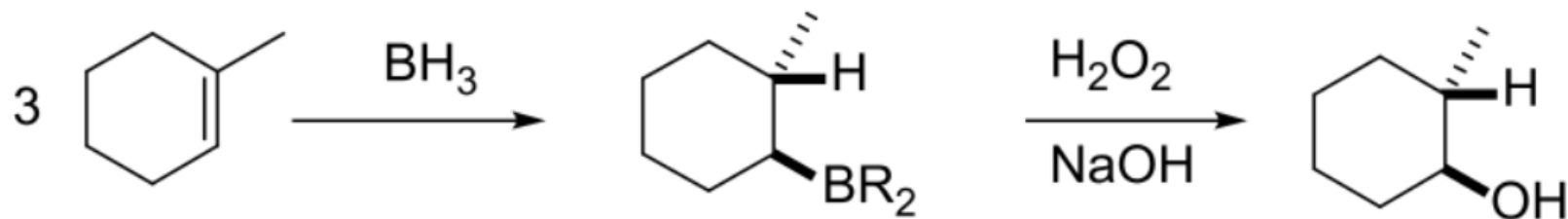
Mechanism of Alkylborane Oxidation



Electrophilic Addition

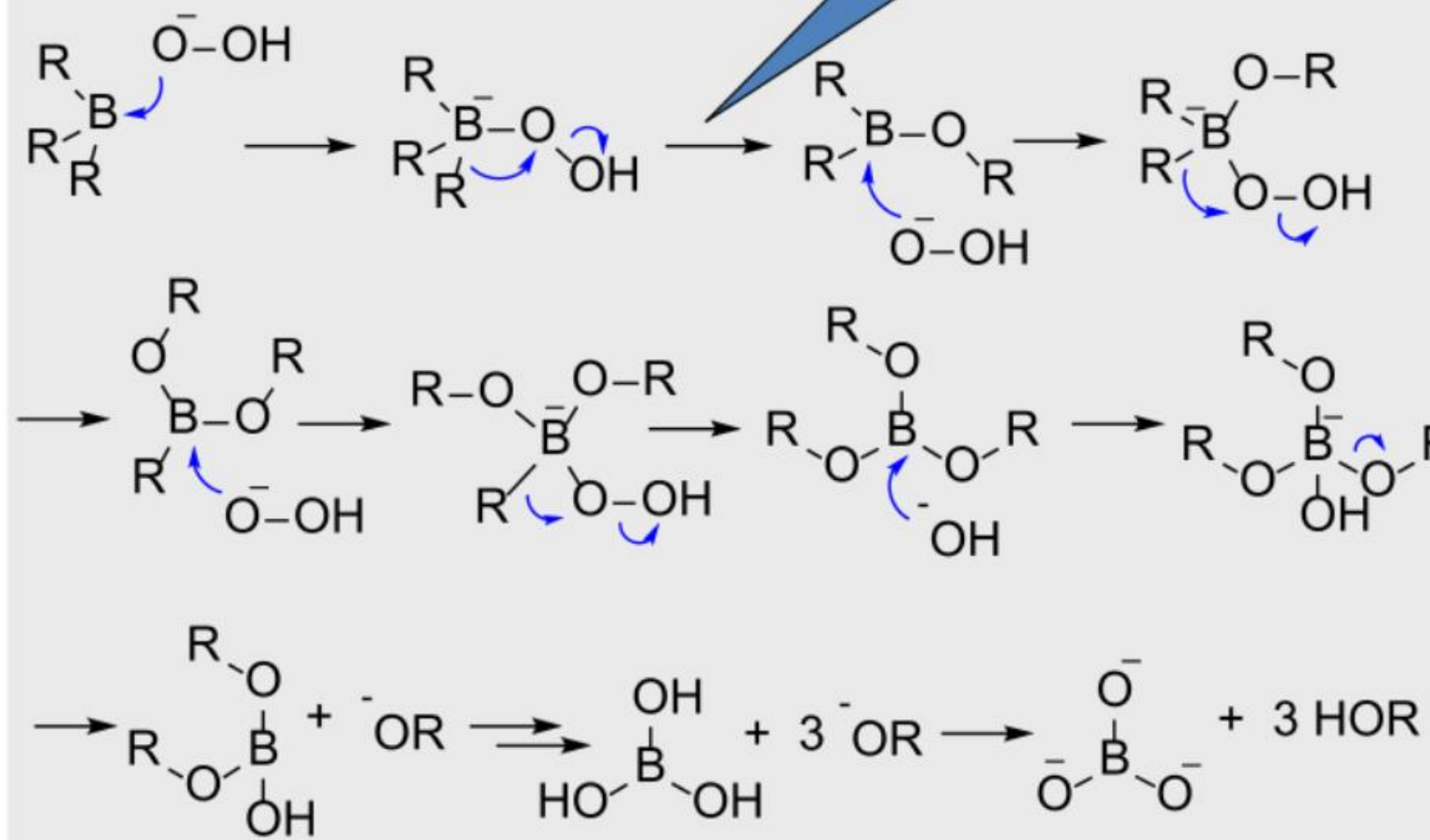


Electrophilic Addition



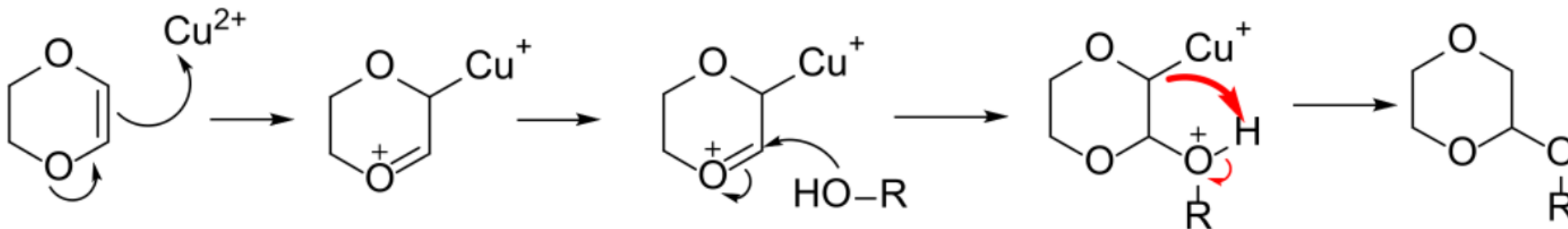
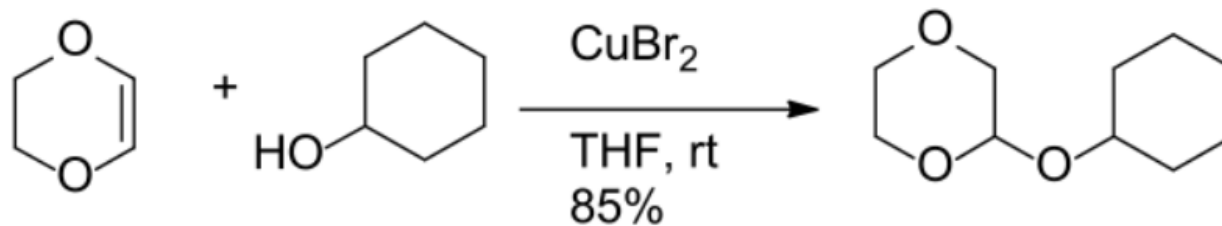
Electrophilic Addition

立体专一性得以保留



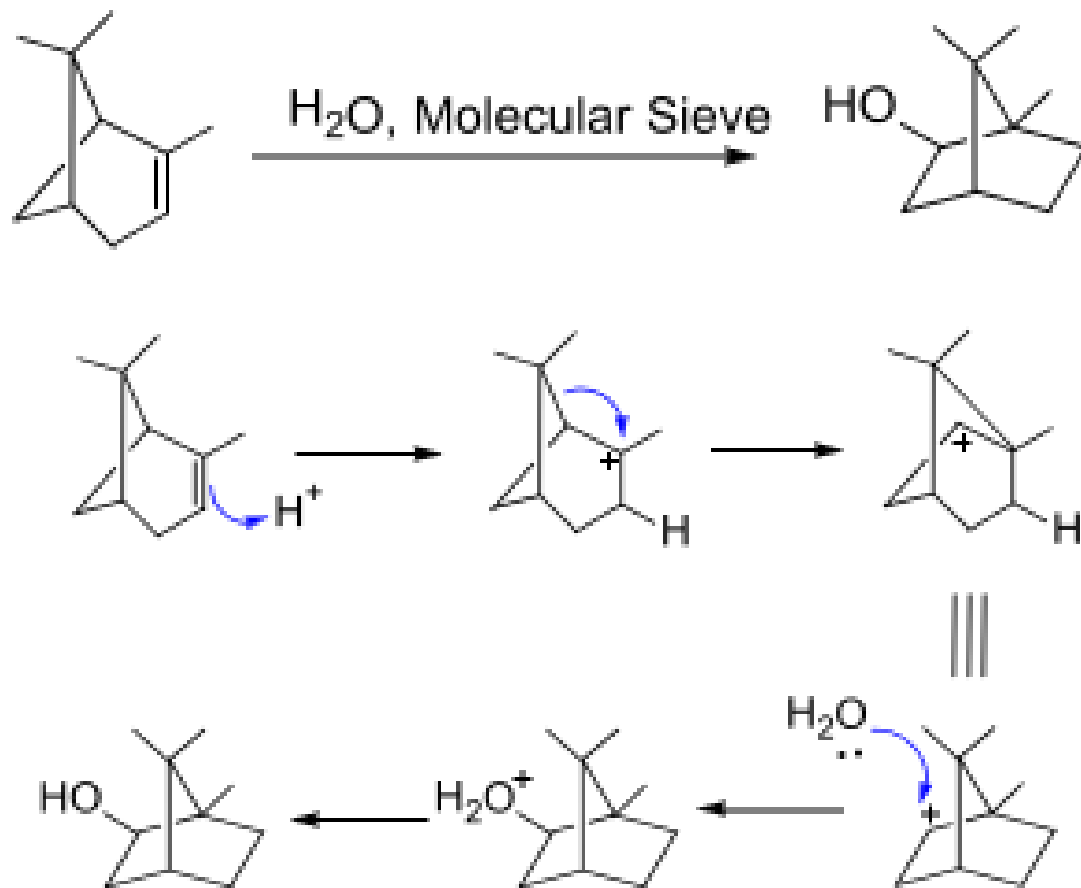
Exercise 7

Draw the complete mechanism for the reaction below



Exercise 8

Draw the complete mechanism for the reaction below

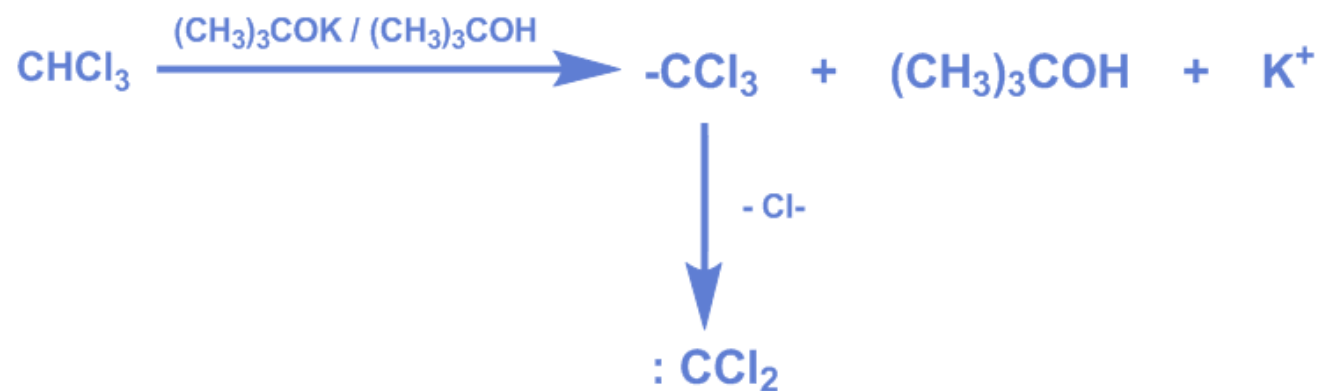


Electrophilic Addition

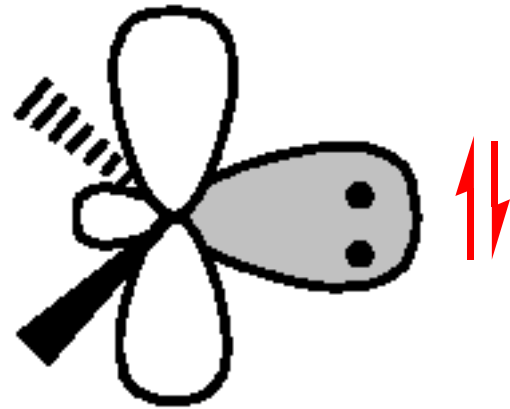
7.3.5 Carbene: :CR_2

碳周围只有6个电子的活性中间体

Preparation: 多卤代烷在碱的作用下，消除 α -氢，得到不稳定的多卤代烷负离子，再消除一个卤原子，得卡宾。

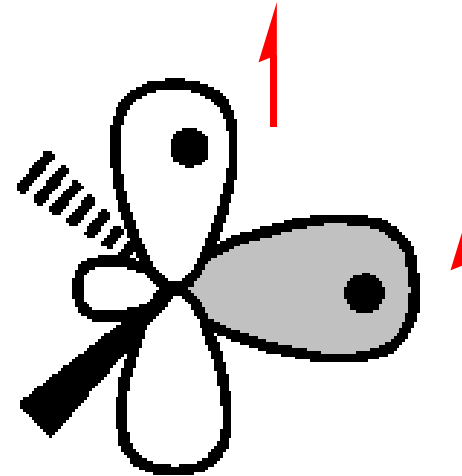


Electrophilic Addition



Singlet carbene

单线态



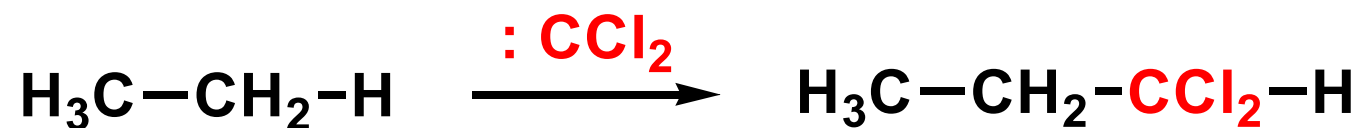
Triplet carbene

三线态

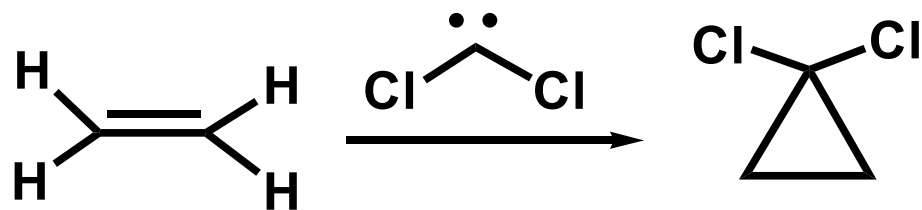
Electrophilic Addition

Reactions:

- 插入C—H键



- 与C=C双键反应

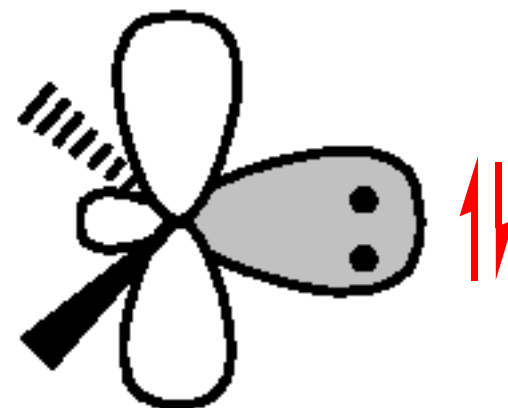
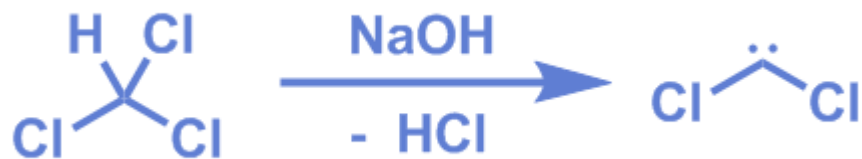


制备环丙烷衍生物

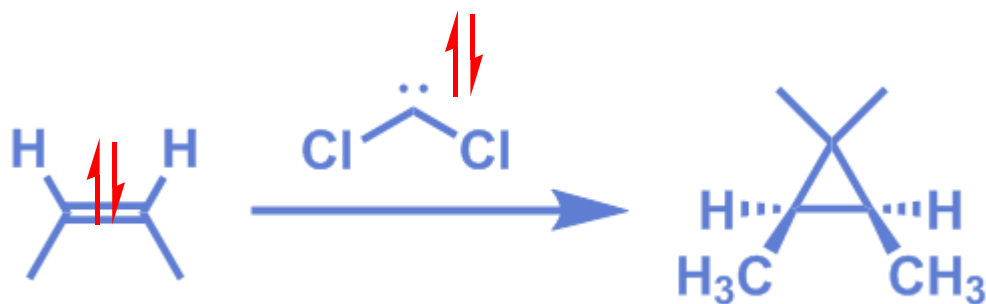
立体选择性？是否是立体专一性的？

Electrophilic Addition

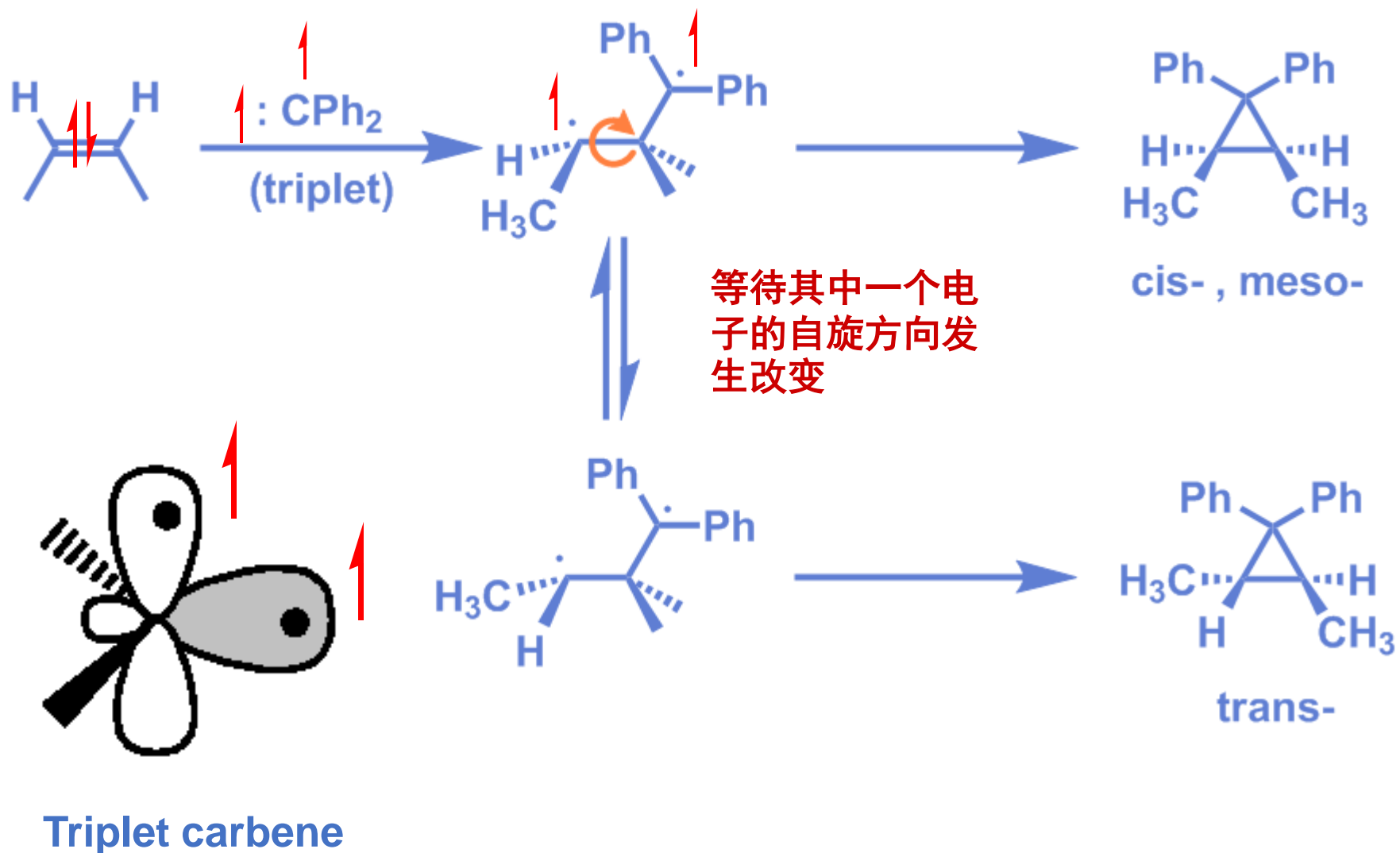
Stereochemistry



Singlet carbene



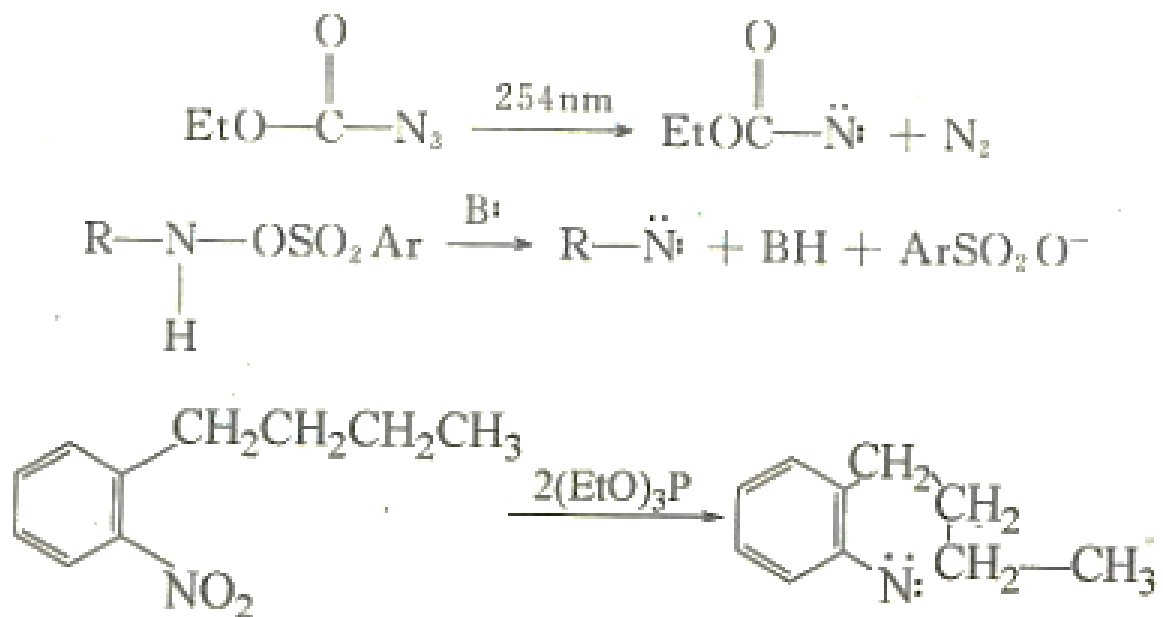
Electrophilic Addition



Electrophilic Addition

7.3.6 氮烯（氮宾或乃春）（Nitrenes） 缺电子的一价氮活性中间体

Preparation: 叠氮化合物的热或光分解、 α -消除和氧化还原反应产生。



Electrophilic Addition

Reaction and Stereochemistry

与碳烯相同

