Lecture 5

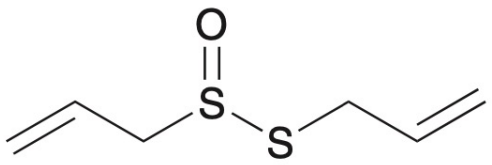
β – Eliminations

А.И.Соч

2021/12/9

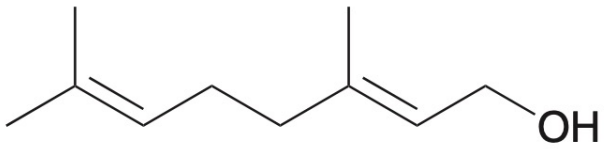
Alkenes

Nomenclature of Alkenes, Basic Physical & Chemical Properties



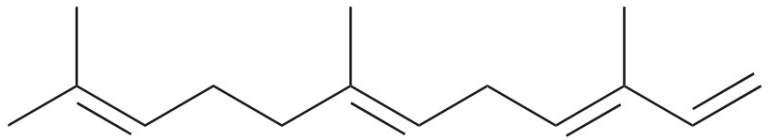
Allicin
Responsible for
the odor of garlic

大蒜素



Geraniol
Isolated from roses
and used in perfumes

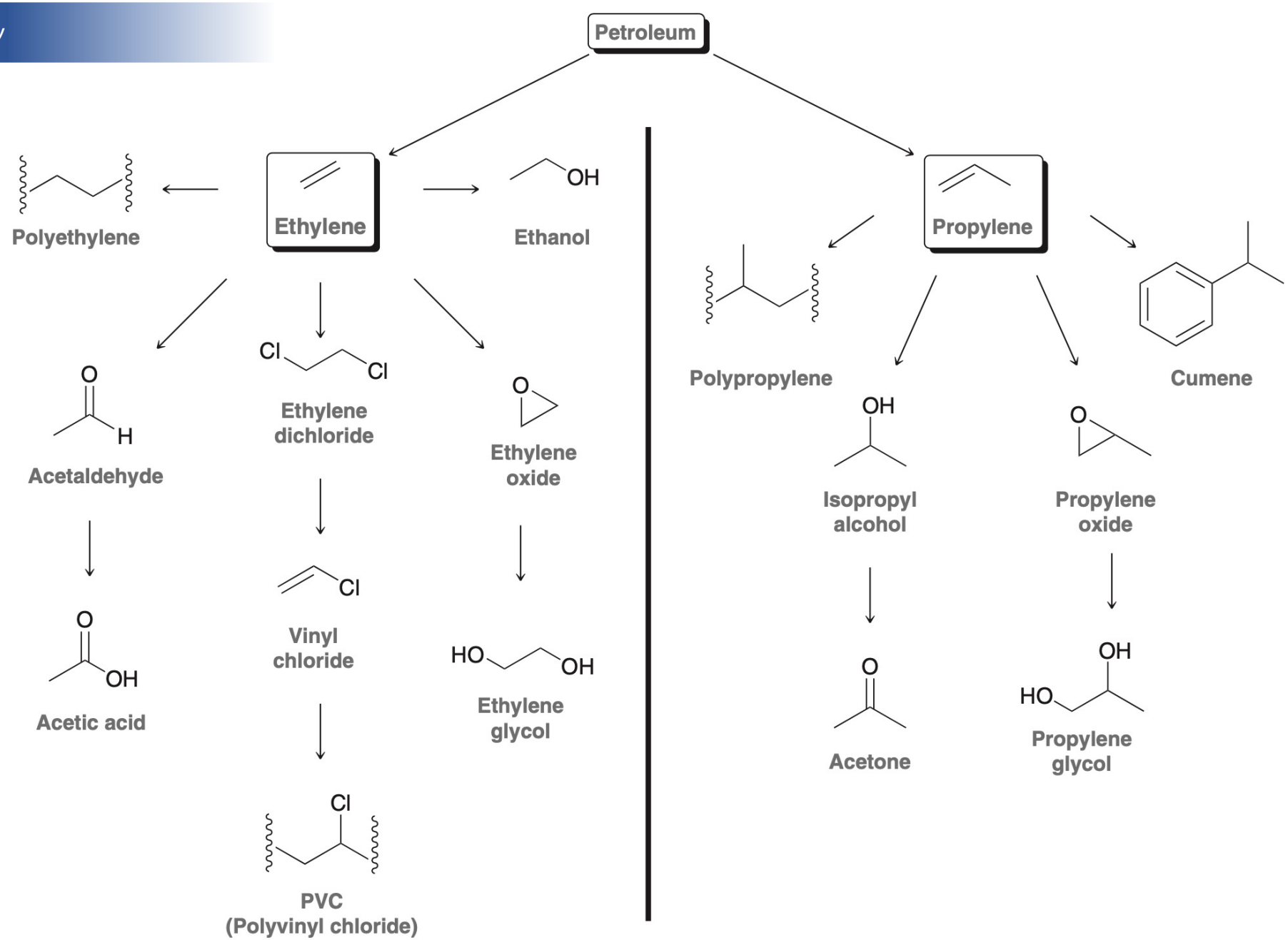
香叶醇



α-Farnesene
Found in the natural waxy coating
on apple skins

金合欢烯

Alkenes in Industry

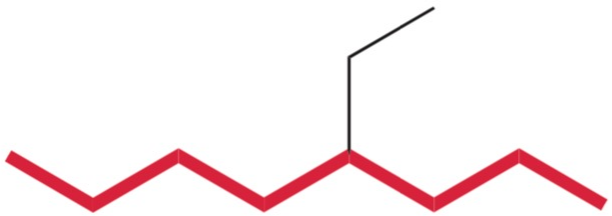


- 烯烃的命名
  - 烯烃的命名法与烷烃大致相同
  - 将烷烃的后缀(-ane)换成-ene

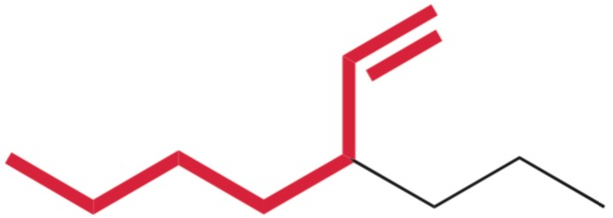
Pentane

Pentene

- 选择含有双键的最长链作为主链

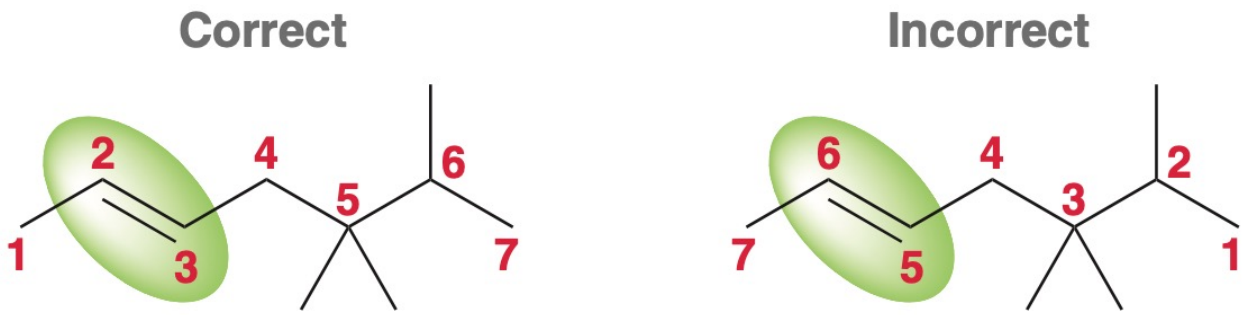


Parent = octane



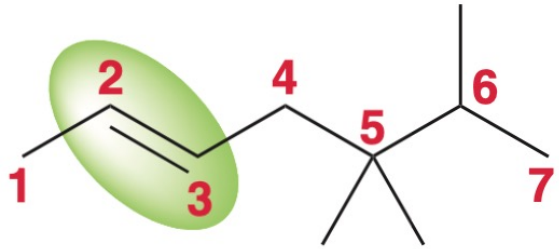
Parent = heptene

- 标记位序时，双键的序号要尽量最小



编号时，首先考虑双键的位序，忽略其它取代基的字母顺序

- 以下两种命名均可（但推荐后一种）

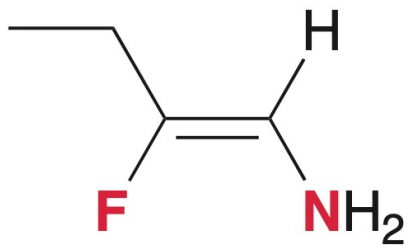


5,5,6-Trimethyl-2-heptene
or
5,5,6-Trimethylhept-2-ene

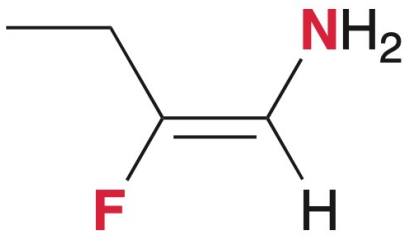
指代双键位置的编号可放在烯烃主链名称的前面

也可以放在后缀(-ene)的前面

- 立体异构必须指明



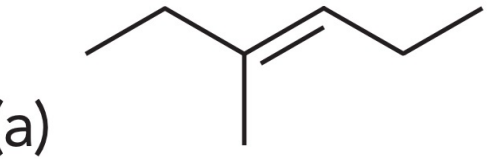
Z

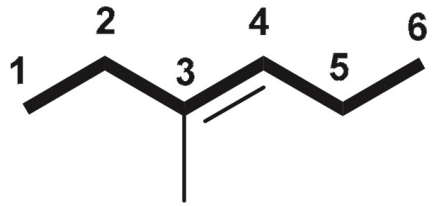


E

- Practice: provide a systematic name for each of the following compounds:

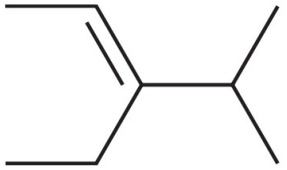
(a)

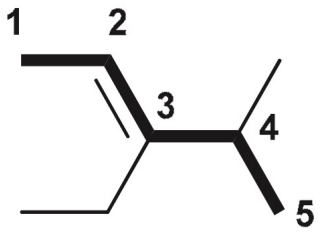




(*E*)-3-methyl-3-hexene

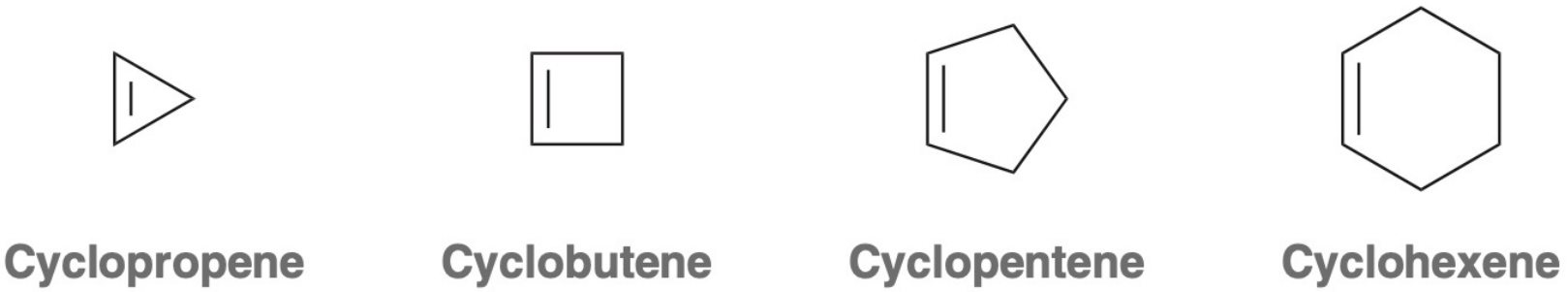
(b)





(*E*)-3-ethyl-4-methyl-2-pentene

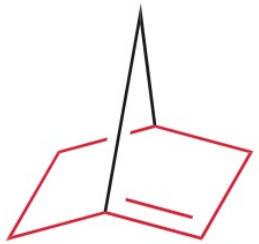
- 小环烯烃不利于形成反式构型



所以 对于3～6个碳的环烯烃来说
命名的时候就不用标*E/Z*和*cis-/trans-*啦(´▽｀)

- Bredt's rule

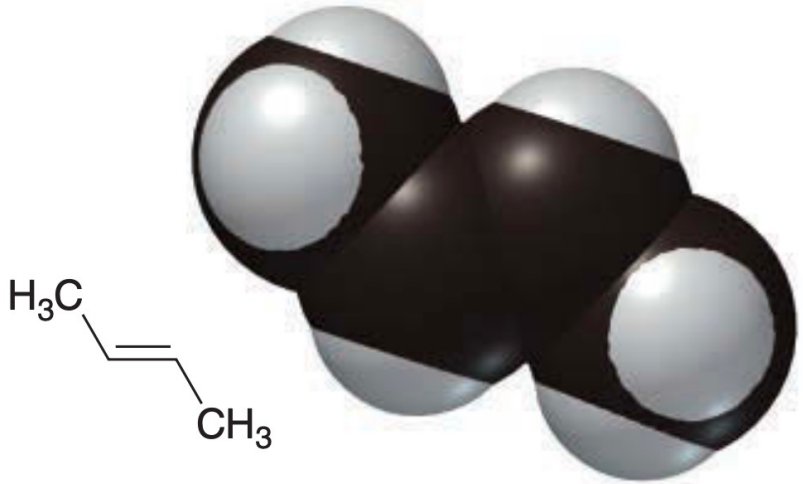
"…it is not possible for a bridgehead carbon of a bicyclic system to possess a C=C double bond if it involves a *trans* π bond being incorporated in a small ring."



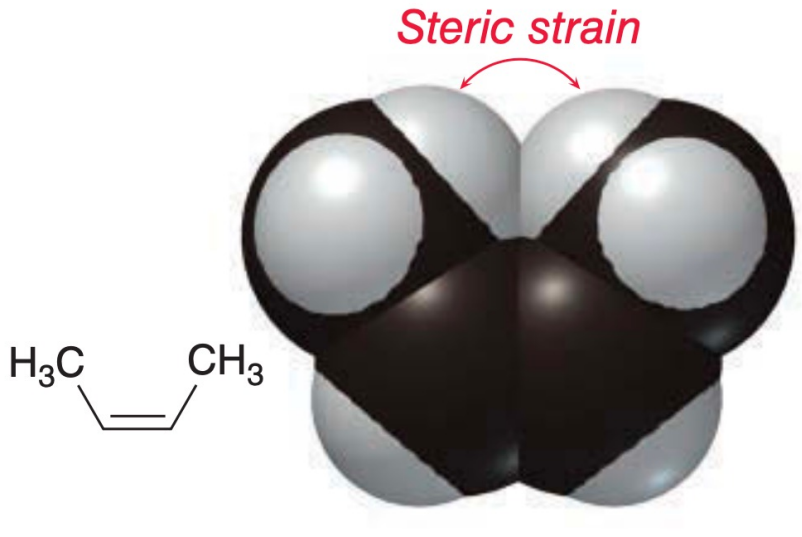
This compound is not stable

This compound is stable

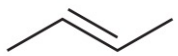
- 反式烯烃更稳定



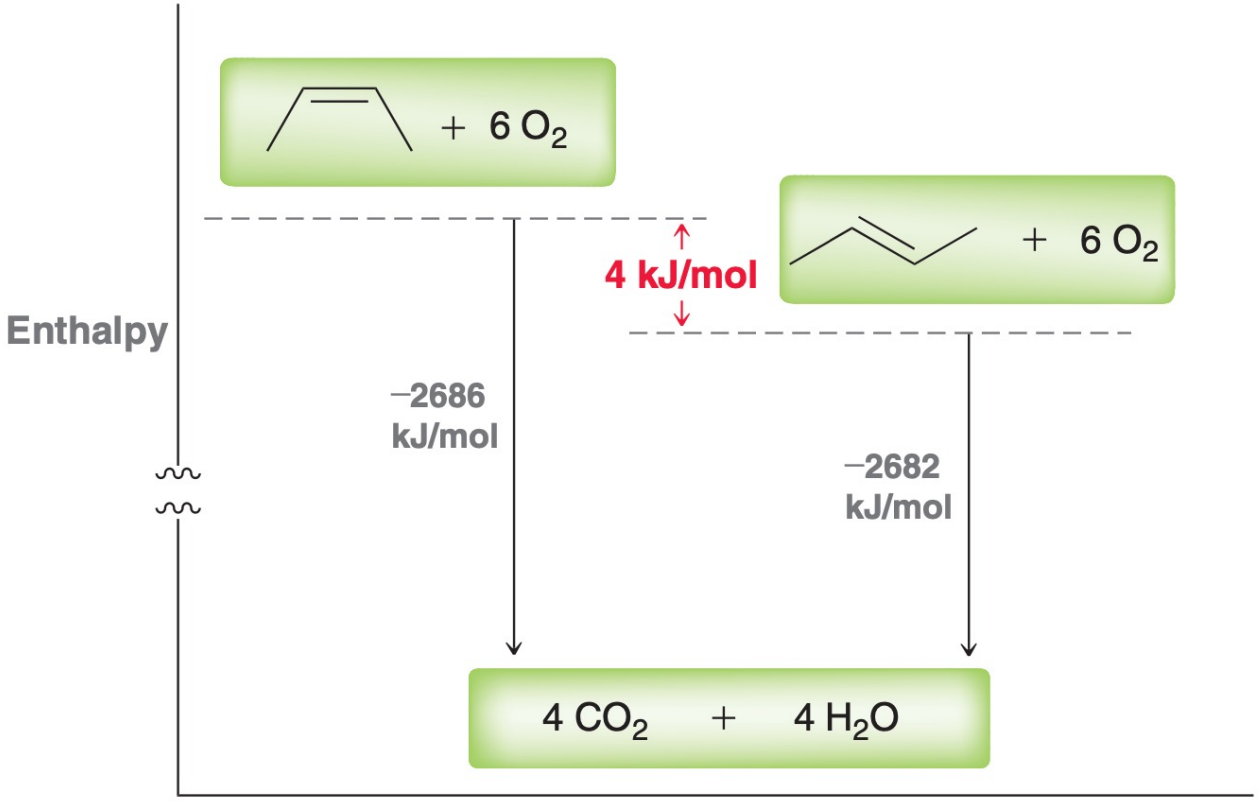
trans-2-Butene



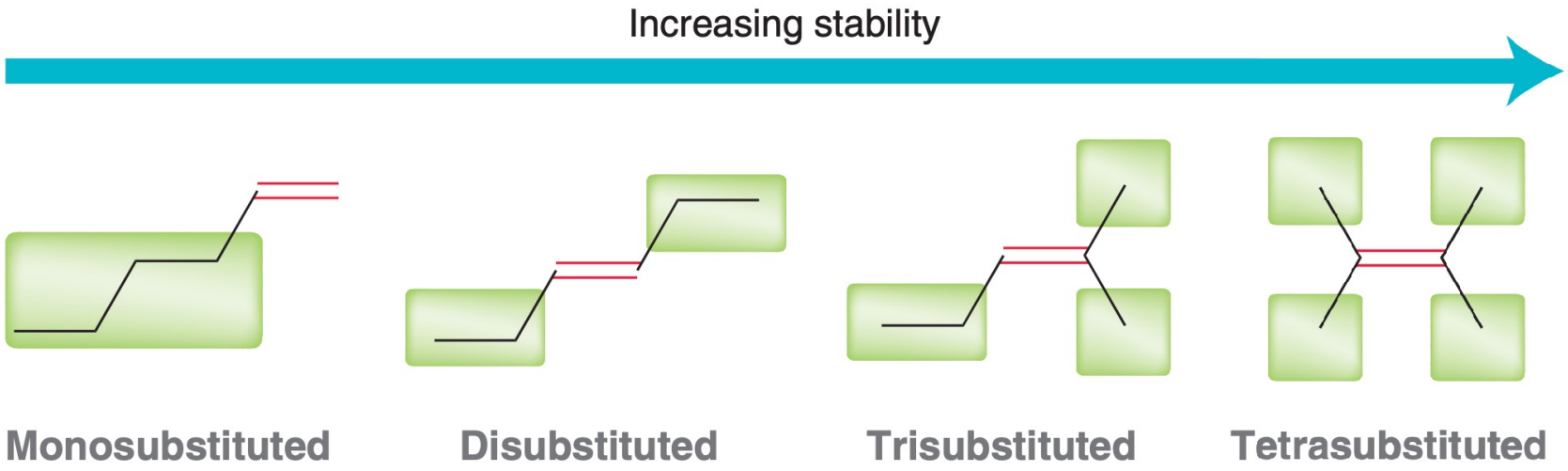
cis-2-Butene


+ 6 O_2 ⟶ 4 CO_2 + 4 H_2O $\Delta H° = -2682$ kJ/mol


+ 6 O_2 ⟶ 4 CO_2 + 4 H_2O $\Delta H° = -2686$ kJ/mol

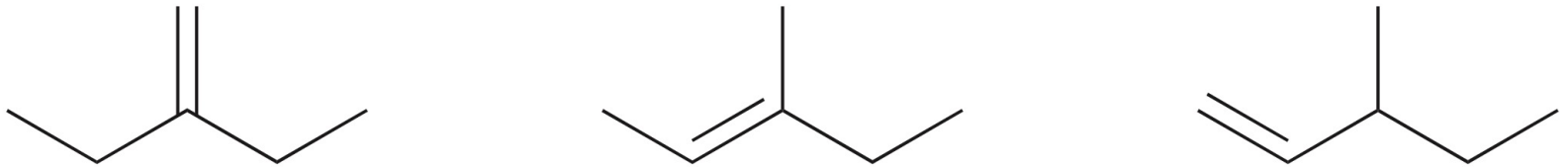


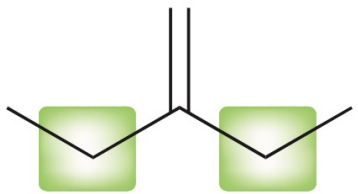
- 多取代烯烃更稳定



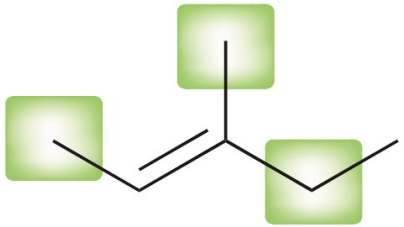
hyperconjugation

- Practice: arrange the following isomeric alkenes in order of stability:



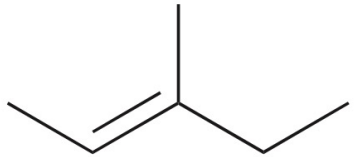


Disubstituted



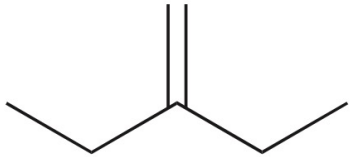
Trisubstituted

Monosubstituted



Most stable

>



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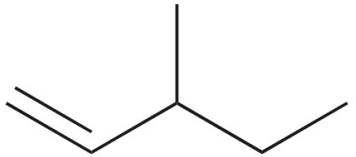
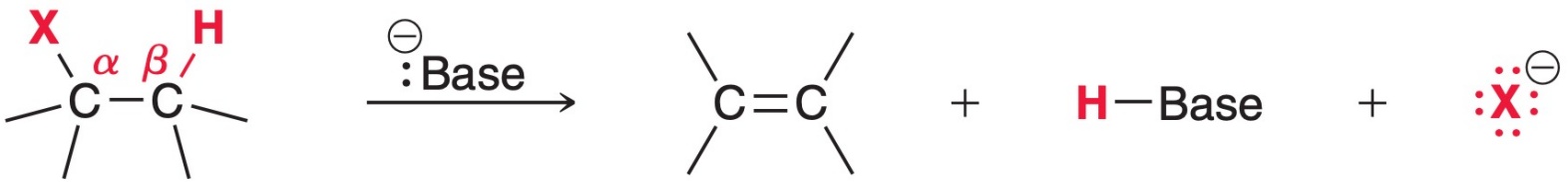


Least stable

β – Eliminations

E2 Reactions, E1 Reactions

- 消除反应

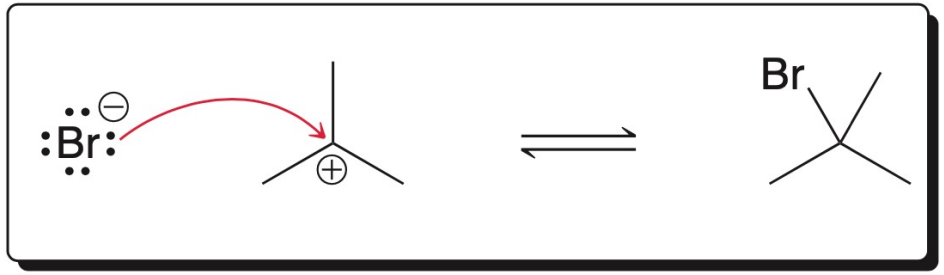


因为消除了β位的H

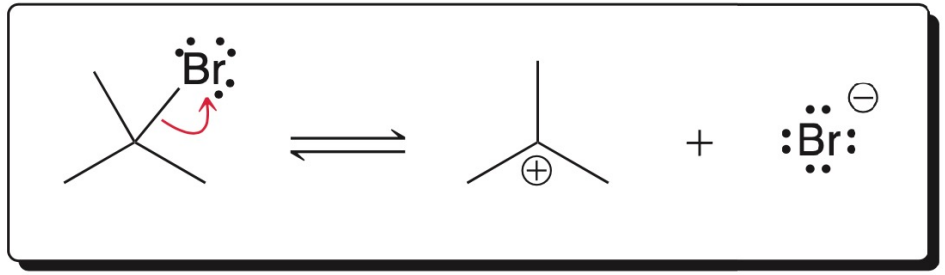
所以也叫β-消除反应

- 回顾：取代反应中的四种基本机理

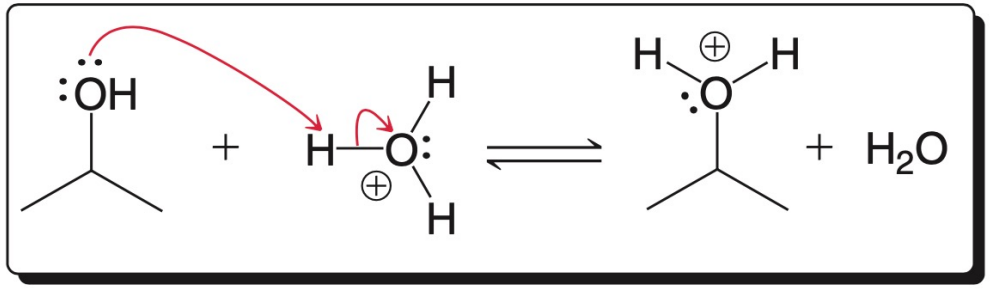
Nucleophilic attack



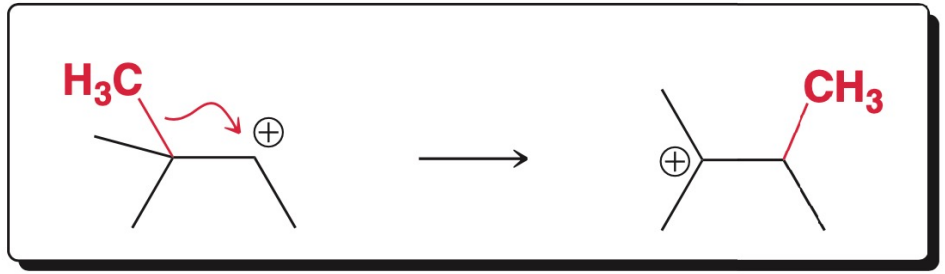
Loss of a leaving group



Proton transfer

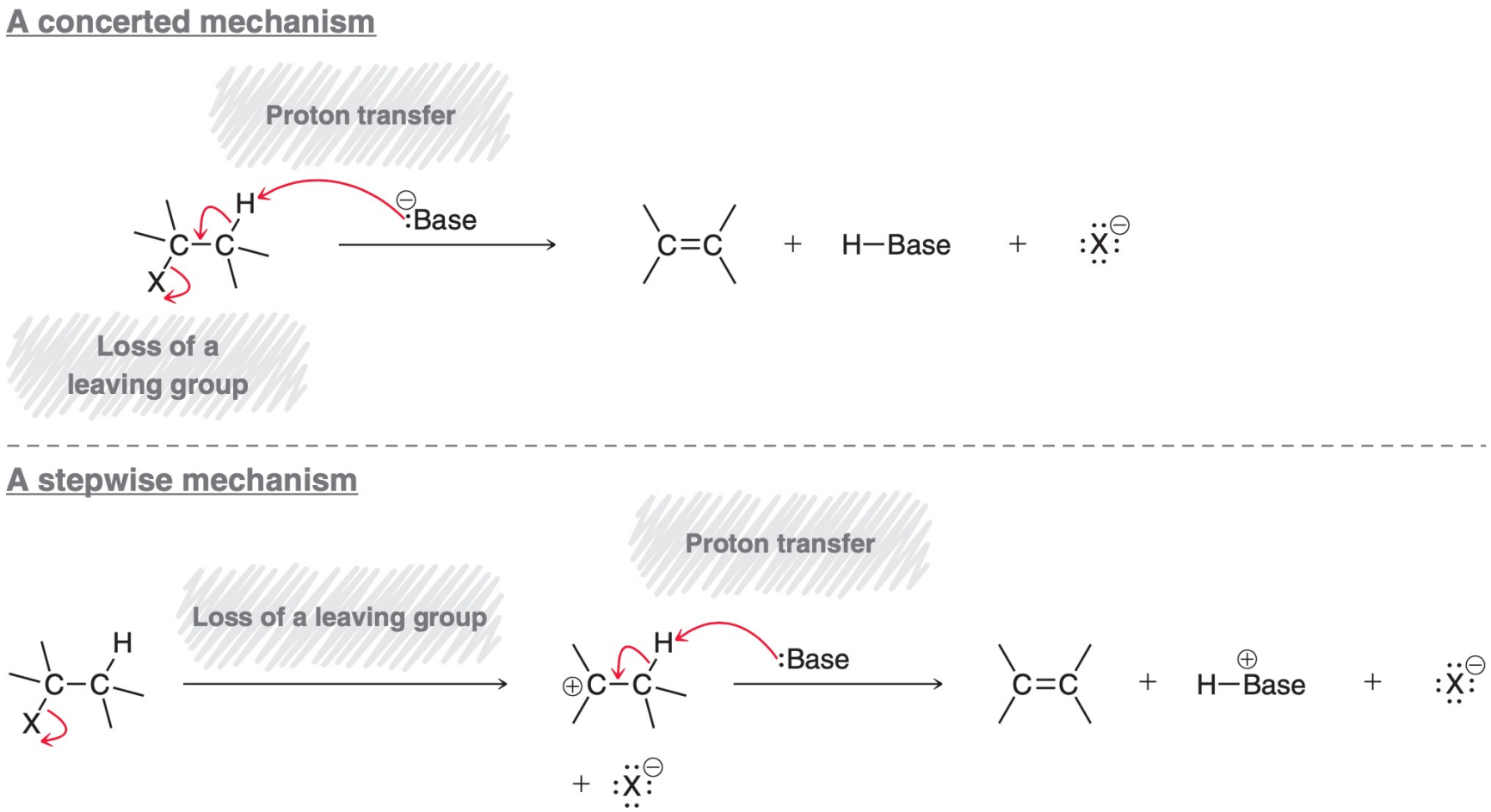


Rearrangement

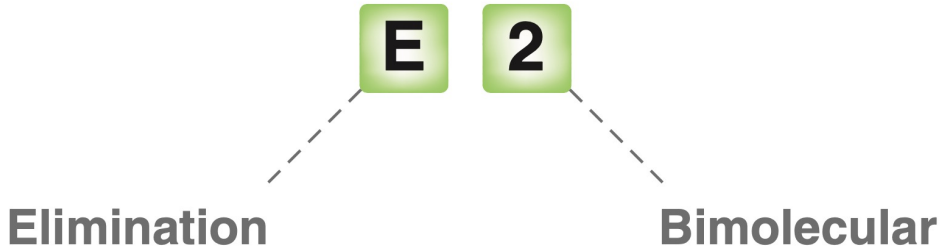


- Possible mechanisms

E2 reaction

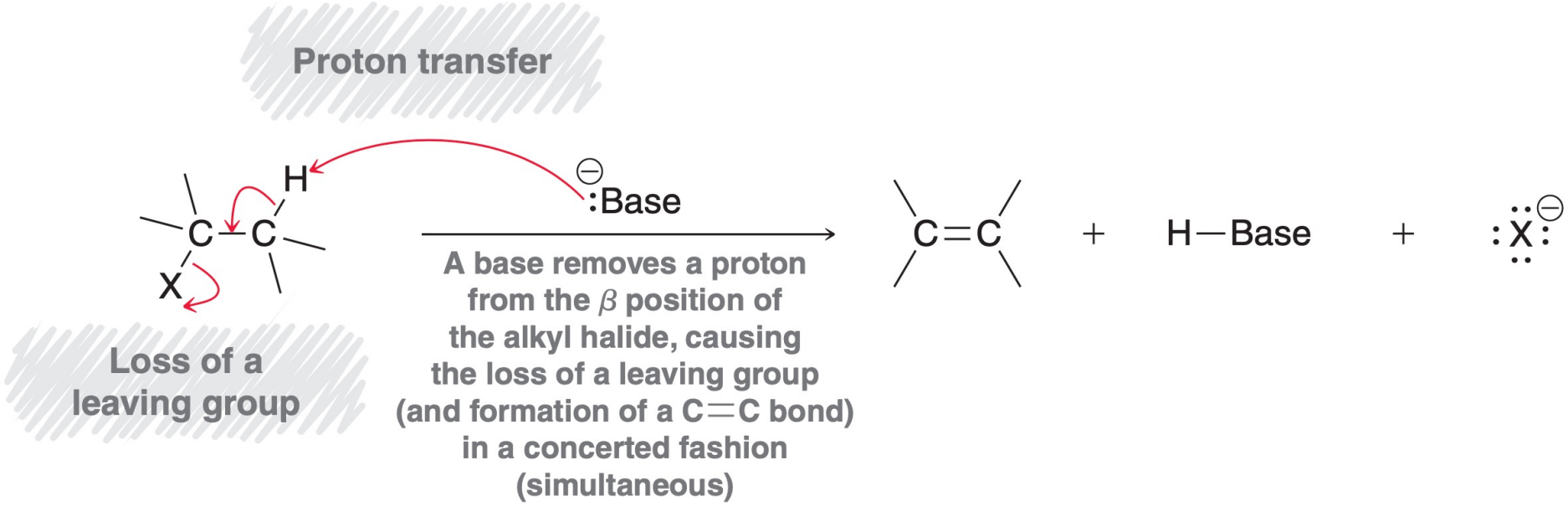


- What is E2?

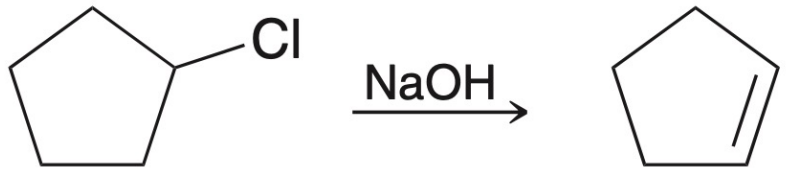


$$\text{Rate} = k\,[\text{alkyl halide}]\,[\text{base}]$$

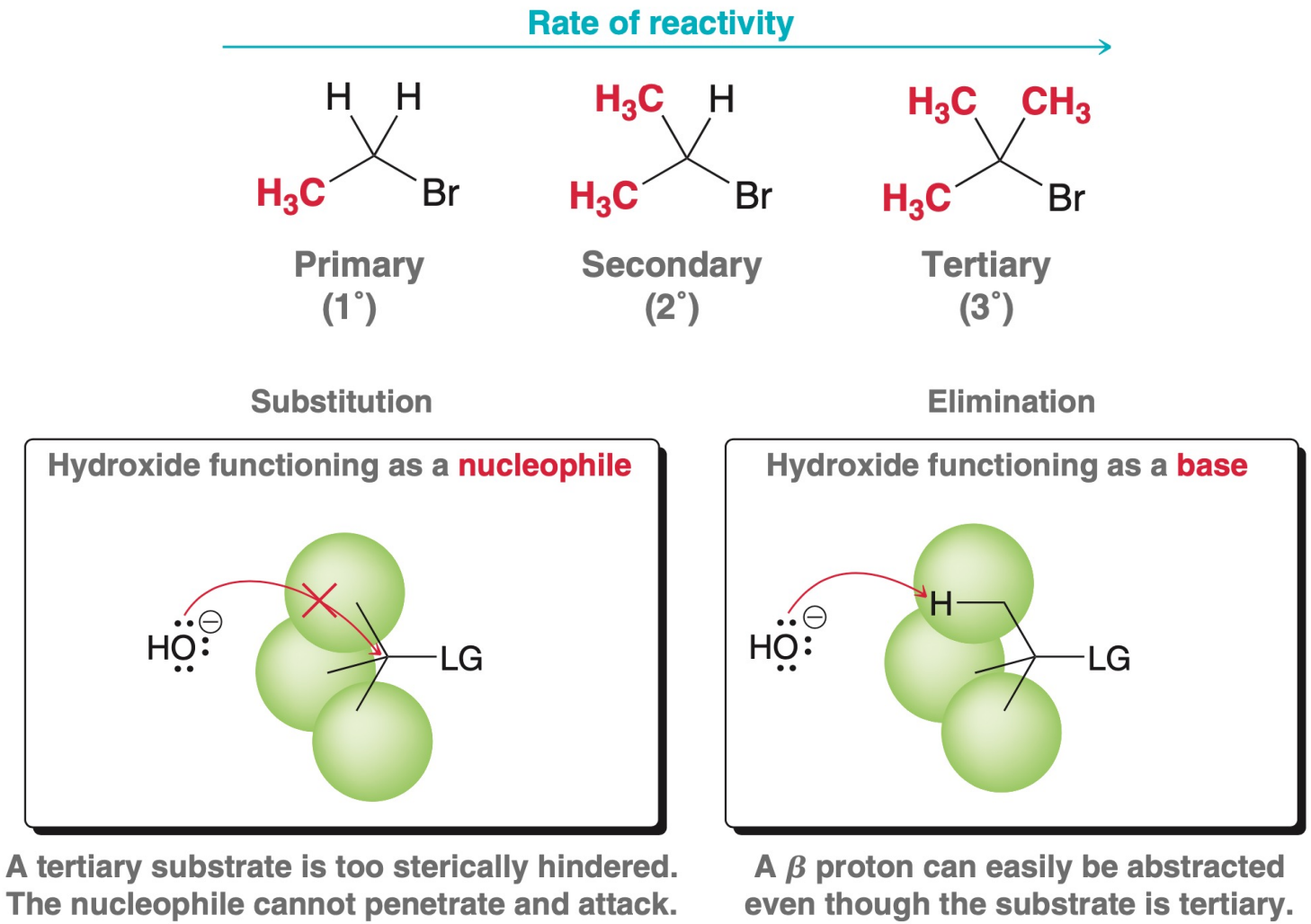
- **The E2 Mechanism**



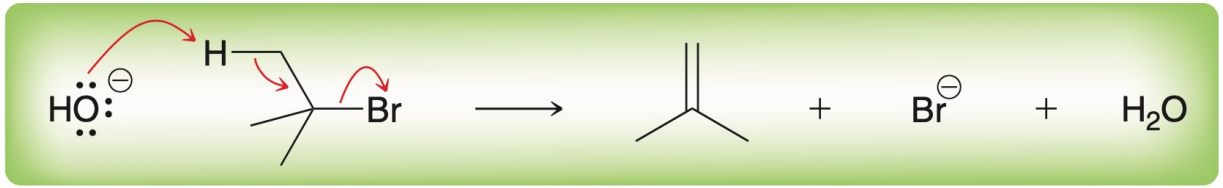
- Practice: identify the base and substrate, then draw a mechanism for the following E2 reaction:

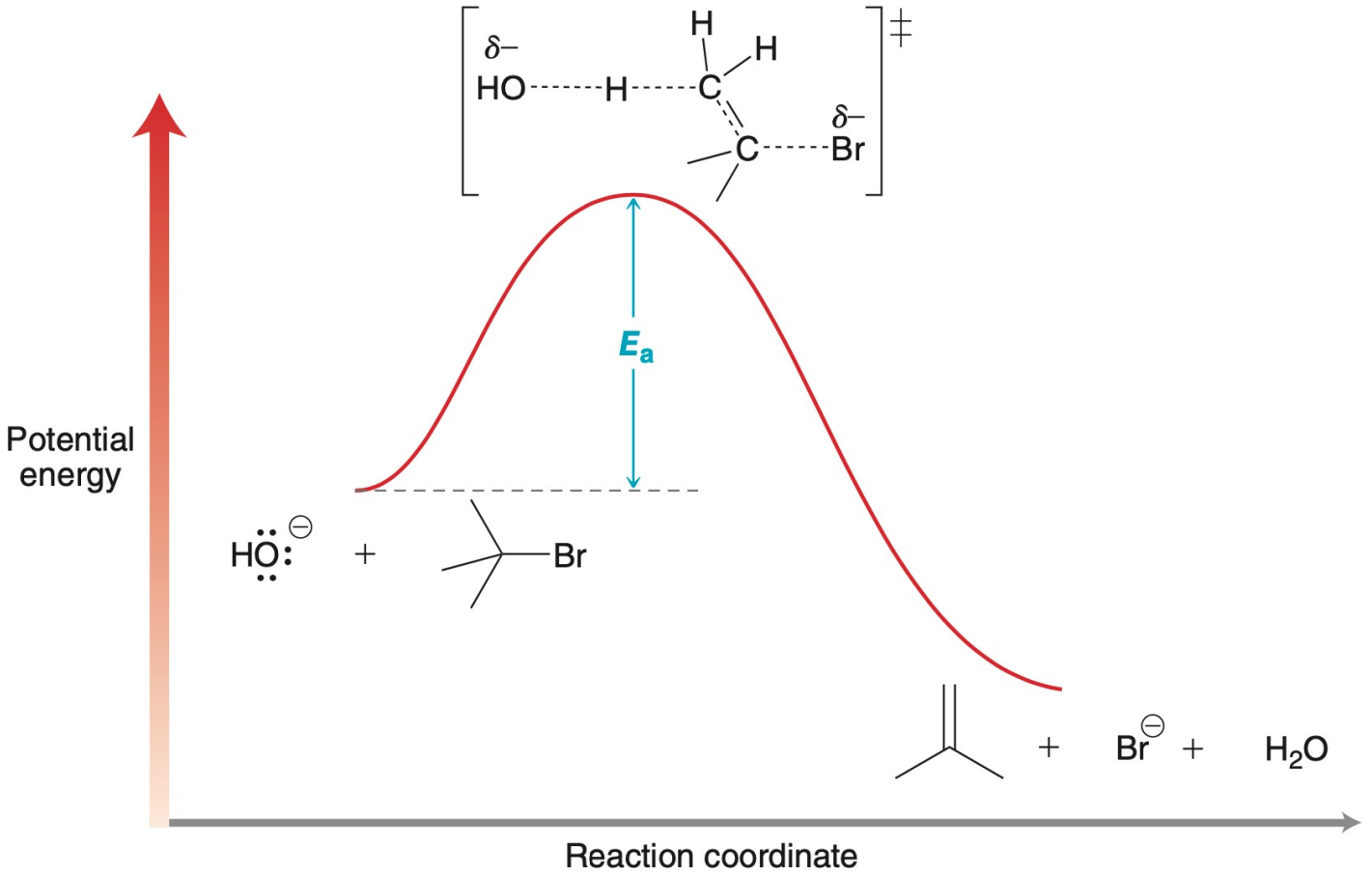


- E2的反应性与S_N2相反

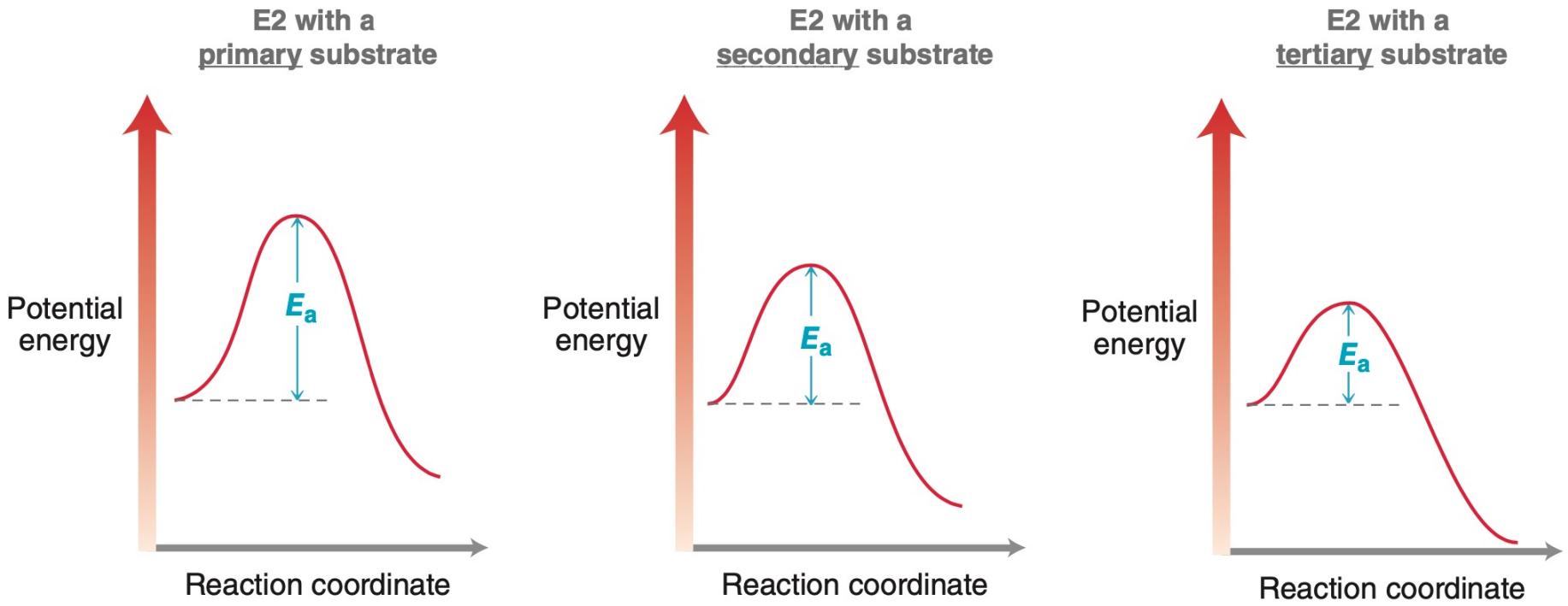


- 反应历程


HO
H
Br
Br
H2O


δ–
HO
H
H
H
C
C
δ–
Br
‡
Ea
Potential energy
HO
Br
Br
H2O
Reaction coordinate

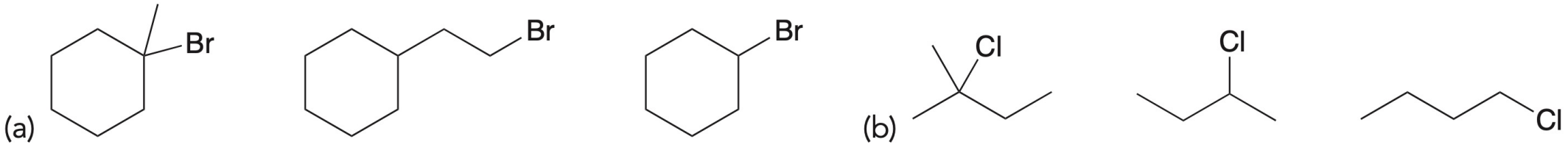
- 过渡态决定消除反应的产物（热力学+动力学均有利）



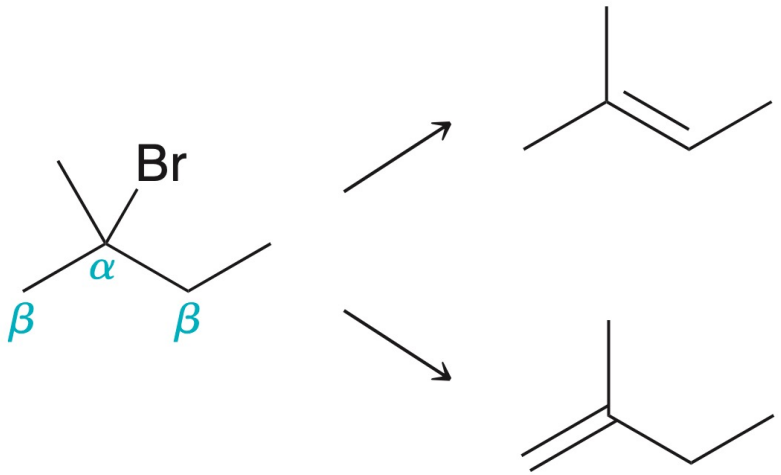
过渡态有部分双键的性质

形成的双键取代越多，过渡态能量越低

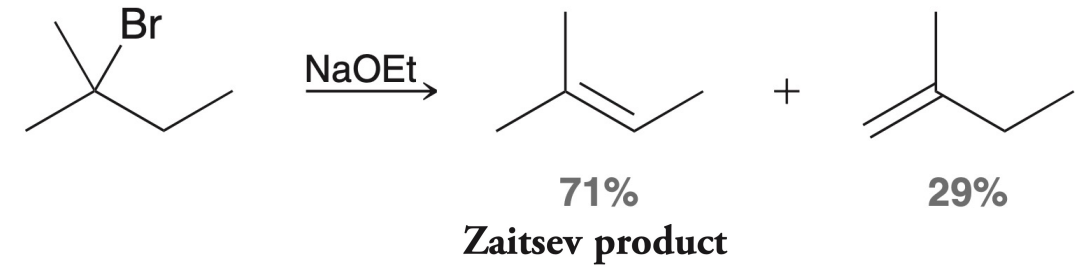
- Practice: arrange each set of compounds in order of reactivity toward an E2 process:

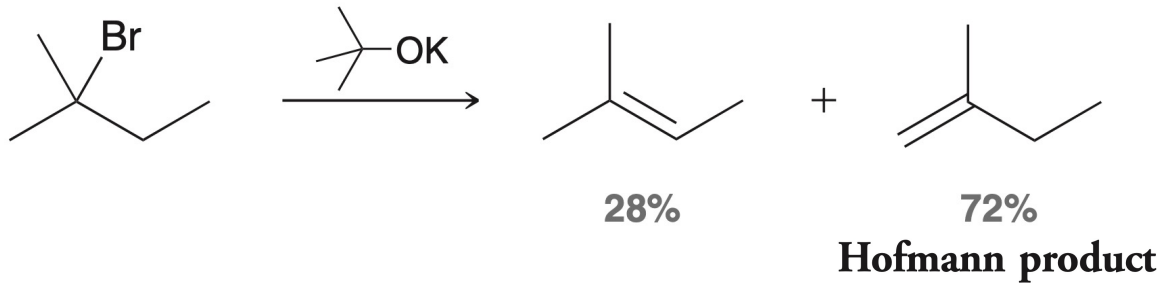


- E2反应的**区域选择性(regioselectivity)**

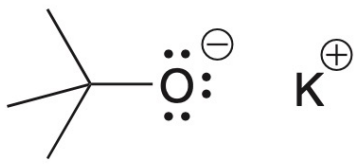


- 扎伊采夫(Zaitsev)产物和霍夫曼(Hofmann)产物——热力学vs动力学

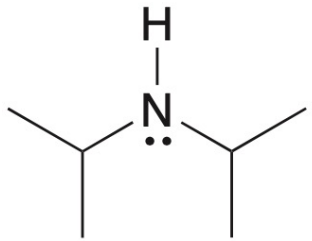




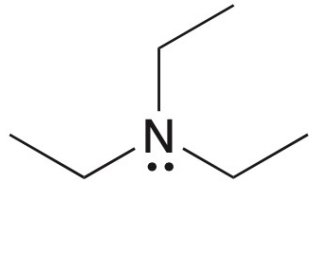
- 大位阻的碱有利于生成少取代烯烃(Hofmann product)



Potassium *tert*-butoxide
(*t*-BuOK)

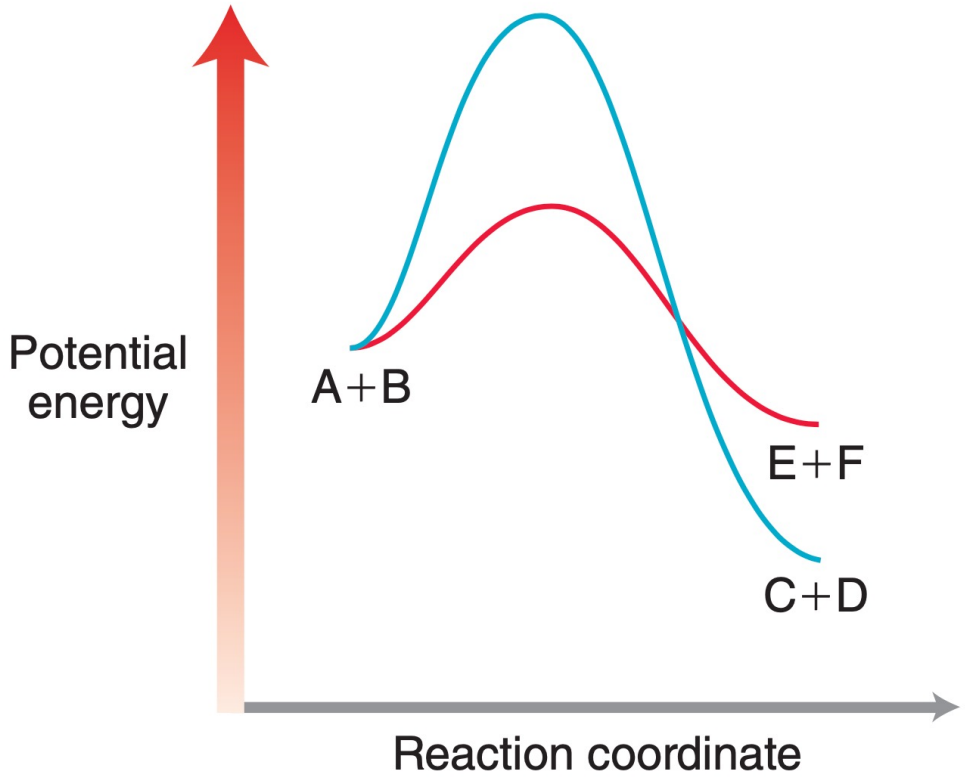


Diisopropylamine



Triethylamine

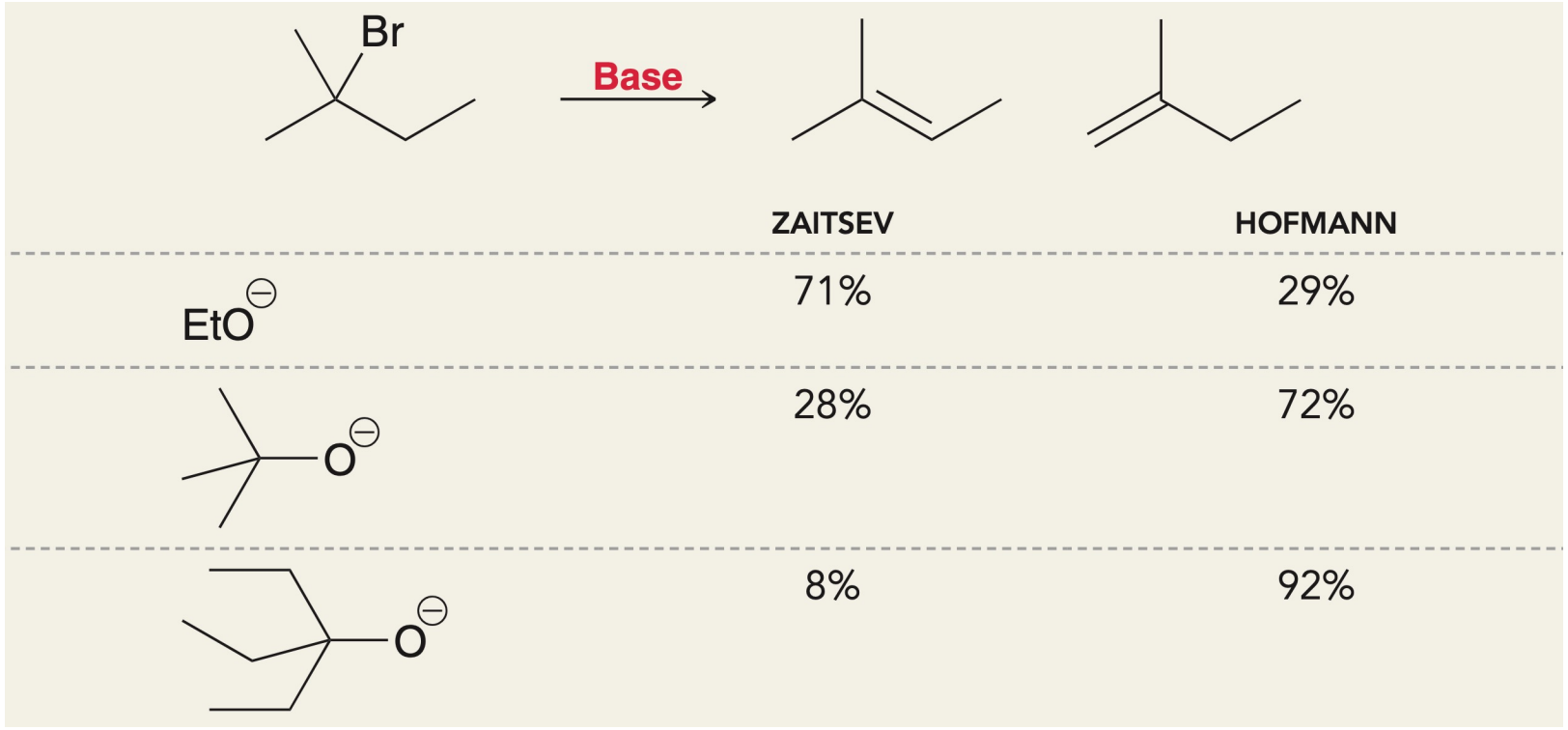
- 热力学控制与动力学控制



热力学：C+D有利(Zaitsev product)

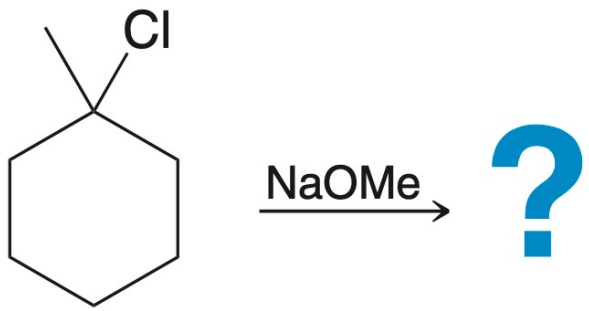
动力学：E+F有利(Hofmann product)

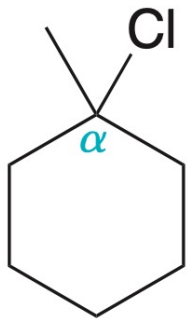
- 不同碱对E2反应区域选择性的影响



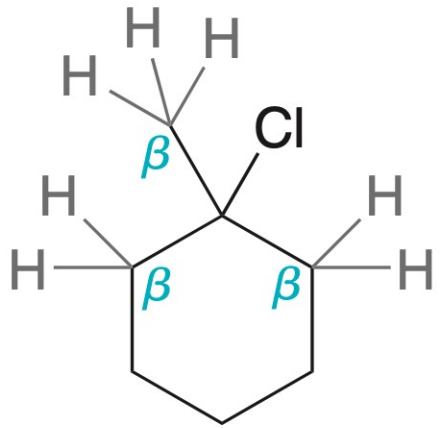
	ZAITSEV	HOFMANN
EtO⊖	71%	29%
O⊖	28%	72%
O⊖	8%	92%

- Practice: identify the major and minor products of the following E2 reaction:

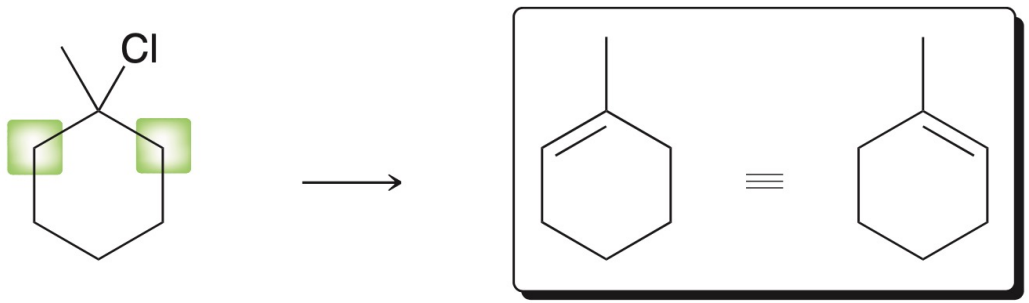




找到α位

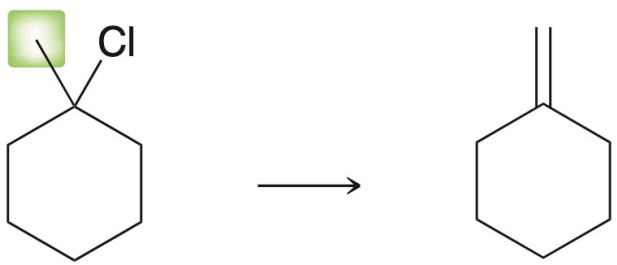


找到β位



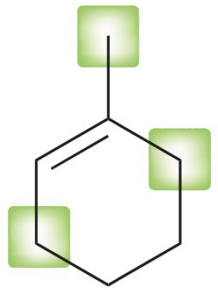
Abstracting a proton from either of these two positions affords the same product

These two drawings represent the same product

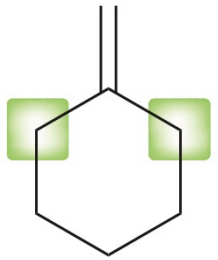


Abstracting a proton from this position...

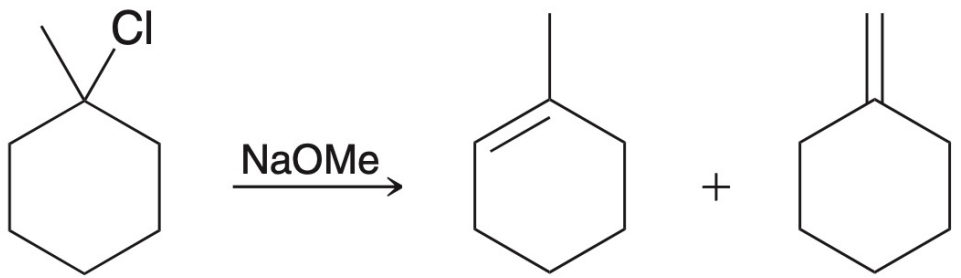
...affords this product



Trisubstituted
(Zaitsev)



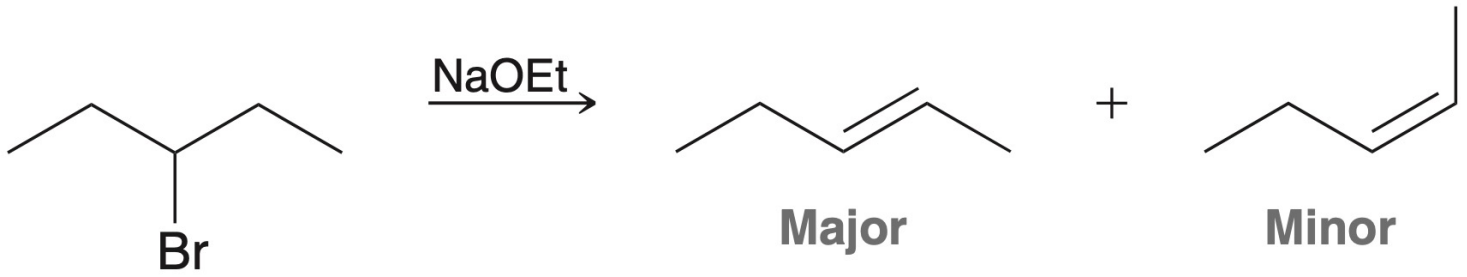
Disubstituted
(Hofmann)



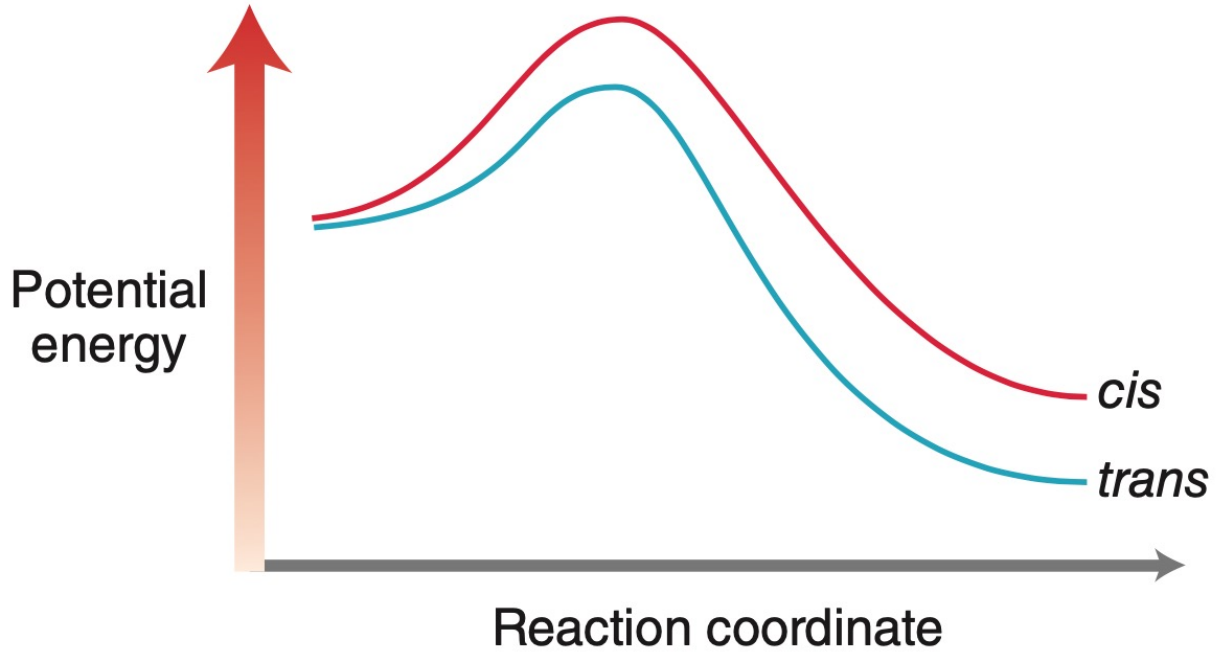
Major

Minor

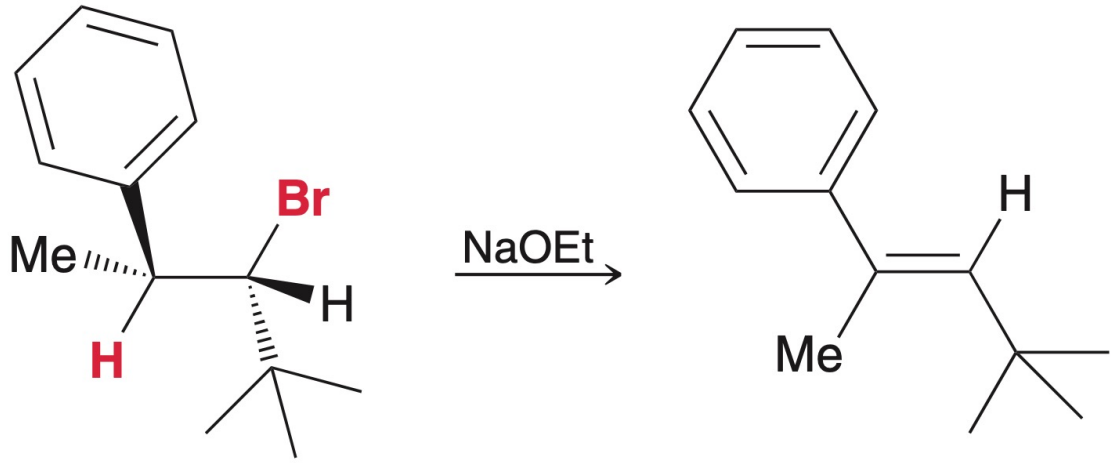
- E2反应的**立体选择性(stereoselectivity)**



- 生成反式烯烃更稳定：热力学+动力学均有利



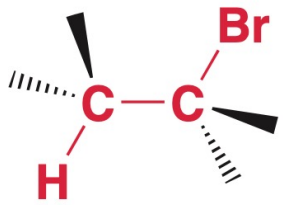
- E2反应的**立体专一性(stereospecificity)**



只会生成一种产物

（反式产物）

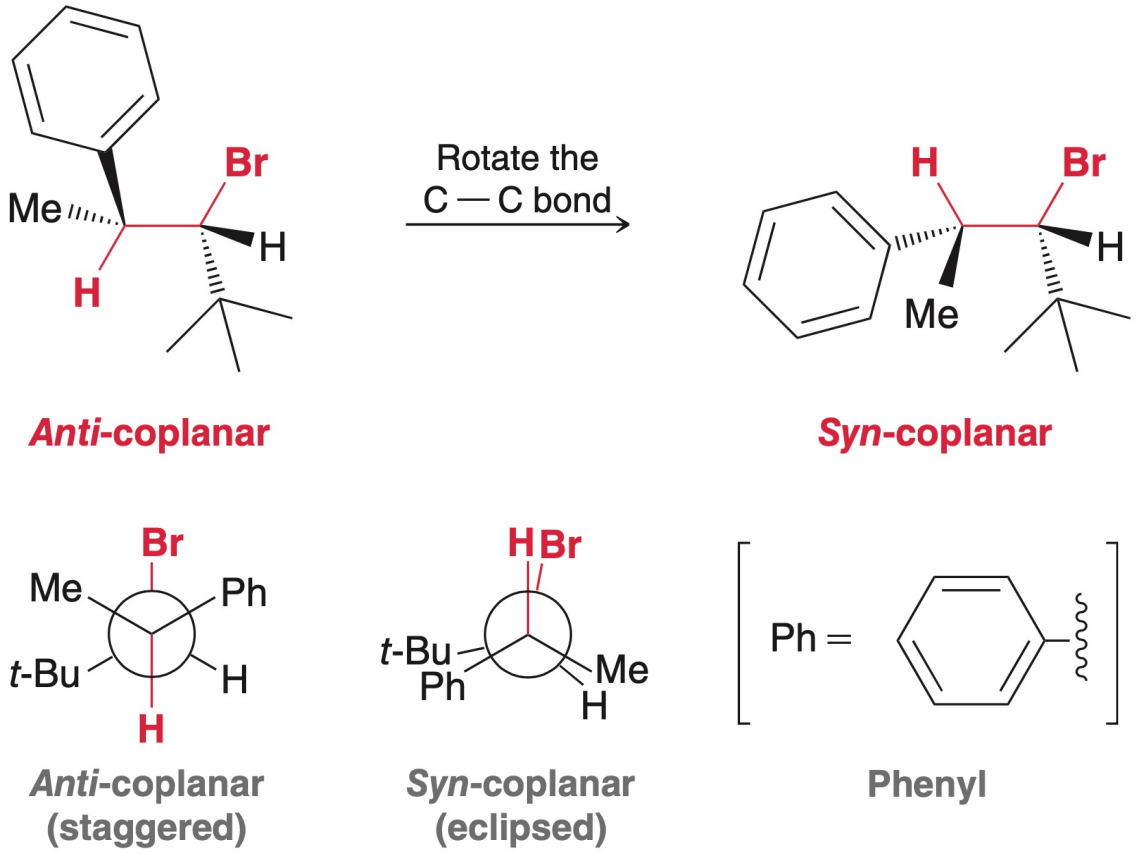
- 发生消除时，以下四个原子必须共面



These four atoms (shown in red)
must all lie in the same plane

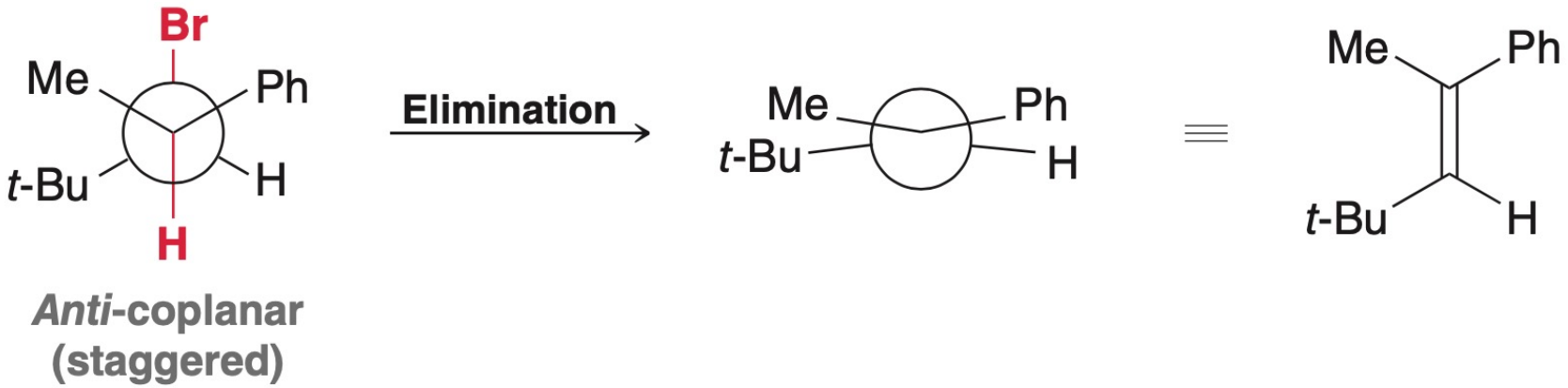
π键的形成要求碳原子的p轨道重叠

- 反式共平面(*anti*-coplanar)与顺式共平面(*syn*-coplanar)

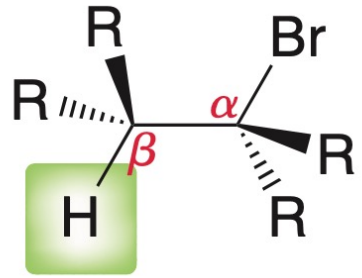


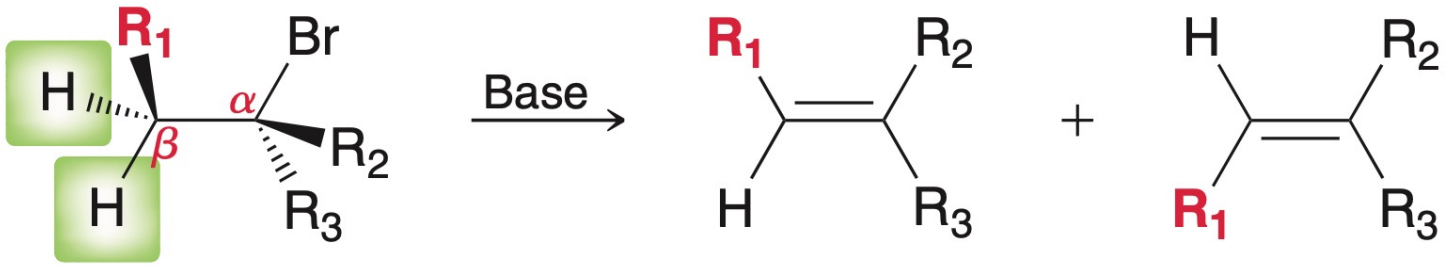
反式共平面为交叉式，势能更低

- E2反应为反式共平面消除



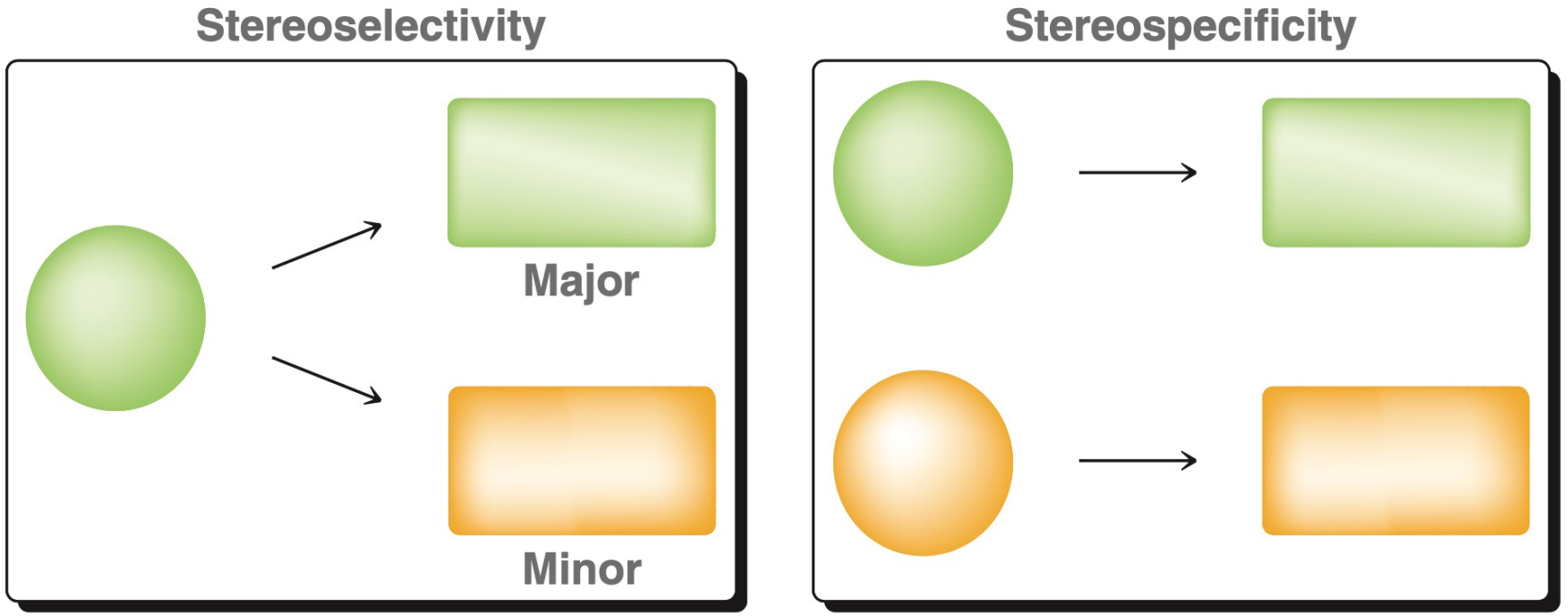
- 立体专一性只考虑β位有一个H的情况





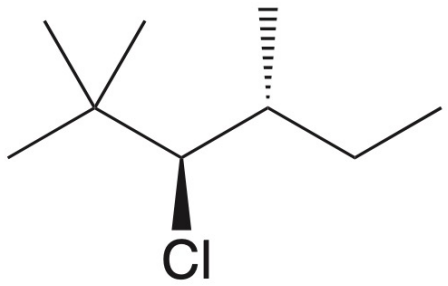
β位有两个H时，可生成两种产物（反应不再具有立体专一性）

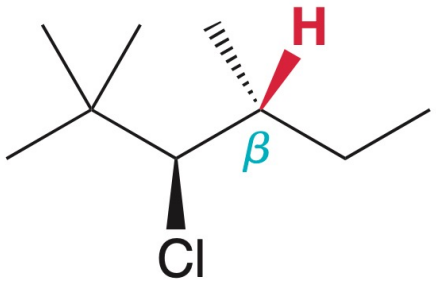
- 区域选择性、立体选择性与立体专一性
- **Regioselectivity**: a reaction that can produce **two or more constitutional isomers** but nevertheless produces **one as the major product**.
- **Stereoselectivity**: a reaction in which **one substrate** produces **two stereoisomers** in **unequal amounts**.
- **Stereospecificity**: a reaction in which **the (stereo)configuration of the product** is **dependent** on **the (stereo)configuration of the starting material**.



- In a *stereoselective* E2 reaction: The substrate itself is not necessarily stereoisomeric; nevertheless, this substrate can produce two stereoisomeric products, and it is found that one stereoisomeric product is formed in higher yield.
- In a *stereospecific* E2 reaction: The substrate is stereoisomeric, and the stereochemical outcome is dependent on which stereoisomeric substrate is used.

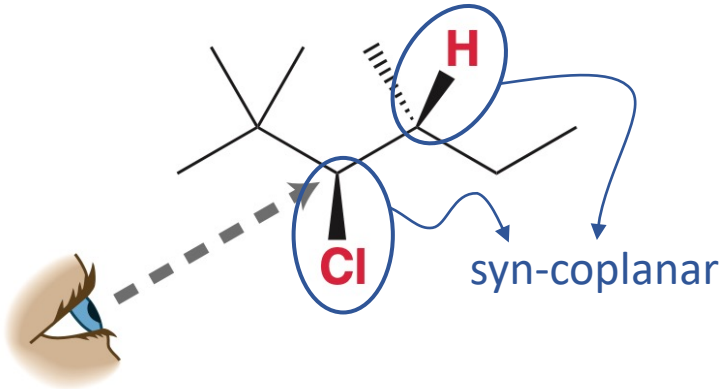
- Practice: identify the major and minor products for the E2 reaction that occurs when the following substrate is treated with a strong base:

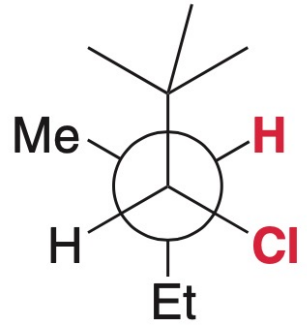




只有一个β-H

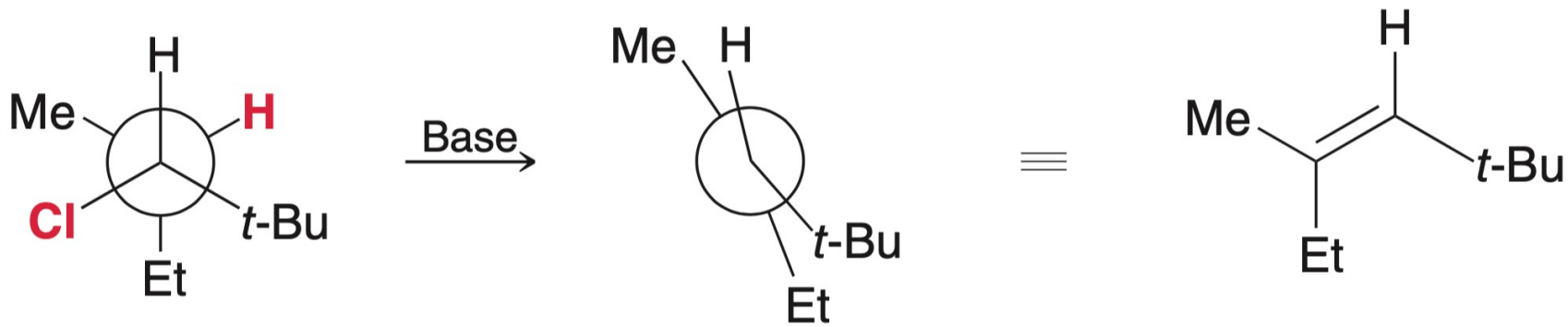
不用考虑区域选择性



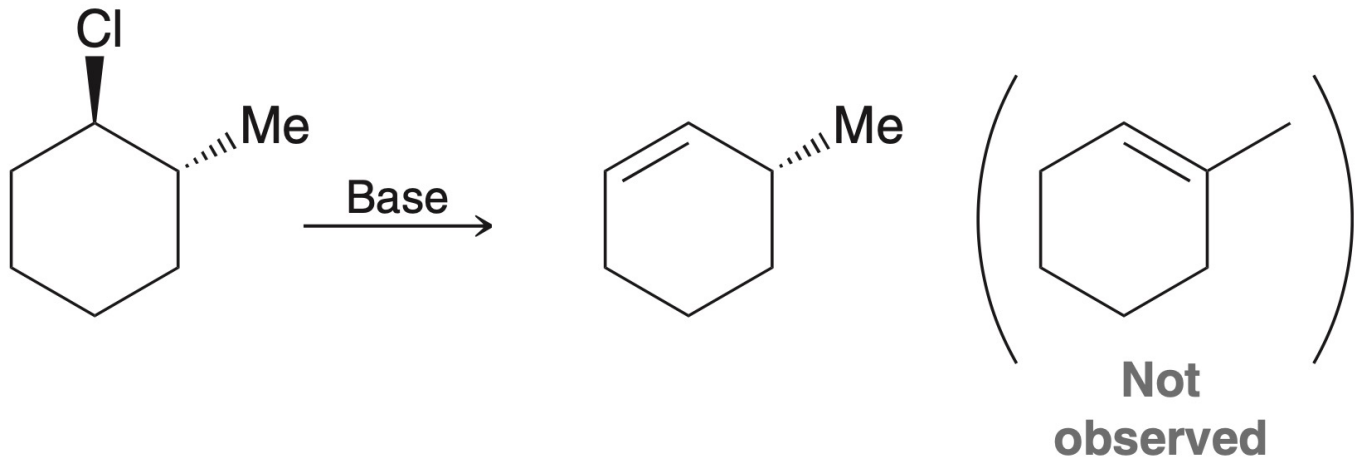


但Cl和H处于顺式共平面

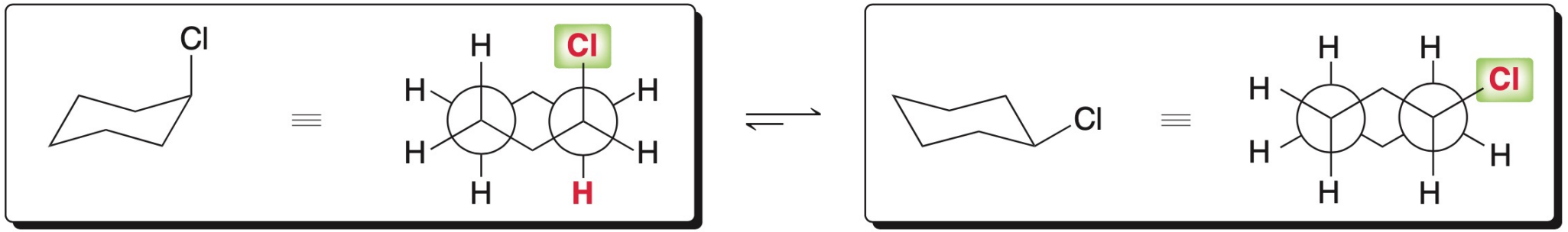
需转化为反式共平面进行反应


H
Me
H
Cl
t-Bu
Et
Base
Me
H
t-Bu
Et
H
Me
t-Bu
Et

- 环己烷上的E2消除反应

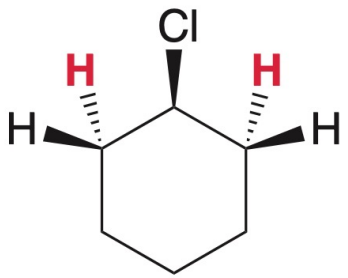


- 复习：取代环己烷的两种构象



When Cl is axial,
it can be *anti*-periplanar
with a neighboring hydrogen atom

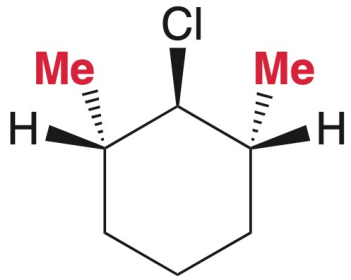
When Cl is equatorial,
it cannot be *anti*-periplanar with any
of its neighboring hydrogen atoms



Only the two hydrogen atoms shown in red can participate in an E2 reaction

β位与LG的反式共面上有H时

可完成E2消除

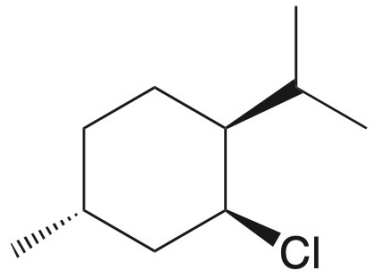


This compound will not undergo an E2 reaction

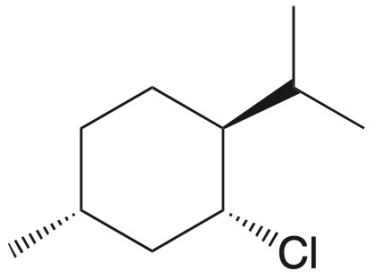
β位与LG的反式共面上无H时

不能完成E2消除

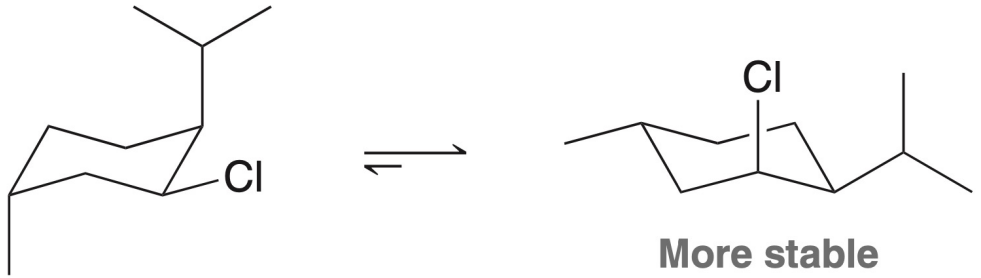
- LG处于A键和E键时的稳定性决定环己烷E2反应的速率



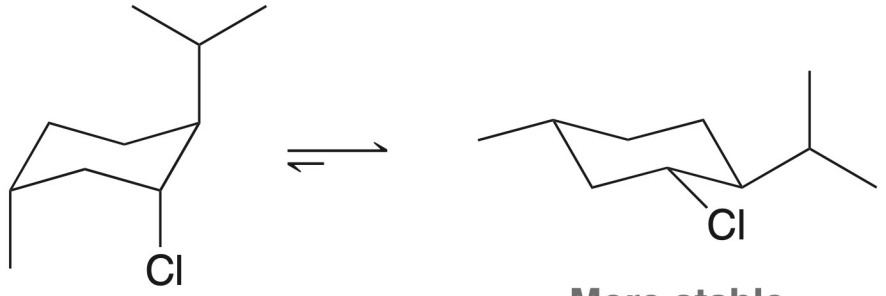
Neomenthyl chloride



Menthyl chloride



More stable



More stable

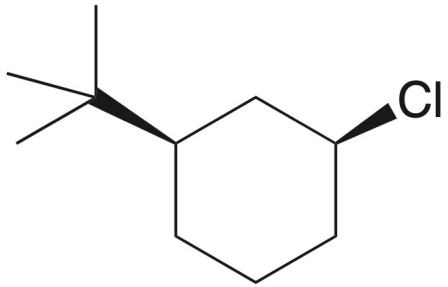
该物质的LG处于A键时更稳定

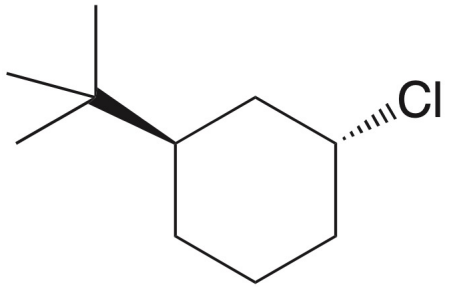
A键的LG可以完成E2反应

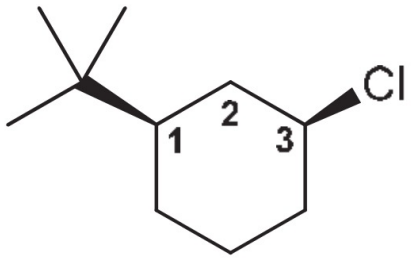
该物质的LG处于E键时更稳定

然而……E键的LG不能完成E2反应

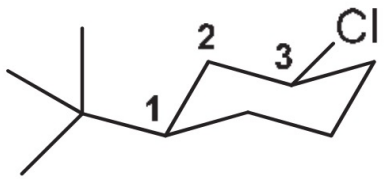
- Practice: predict which of the following two compounds will undergo an E2 reaction more rapidly:

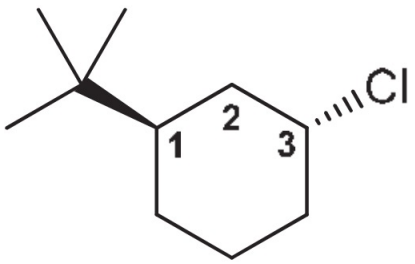




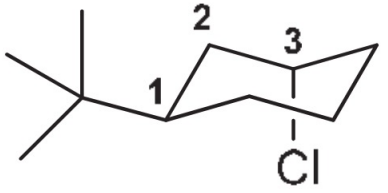


≡





≡

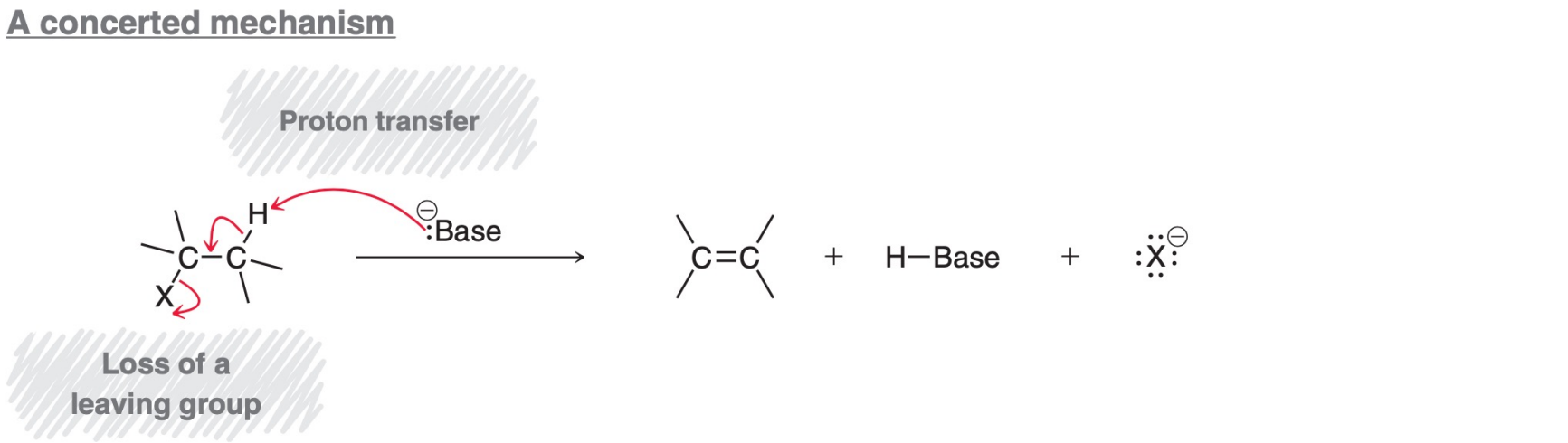


- Additional steps for E2

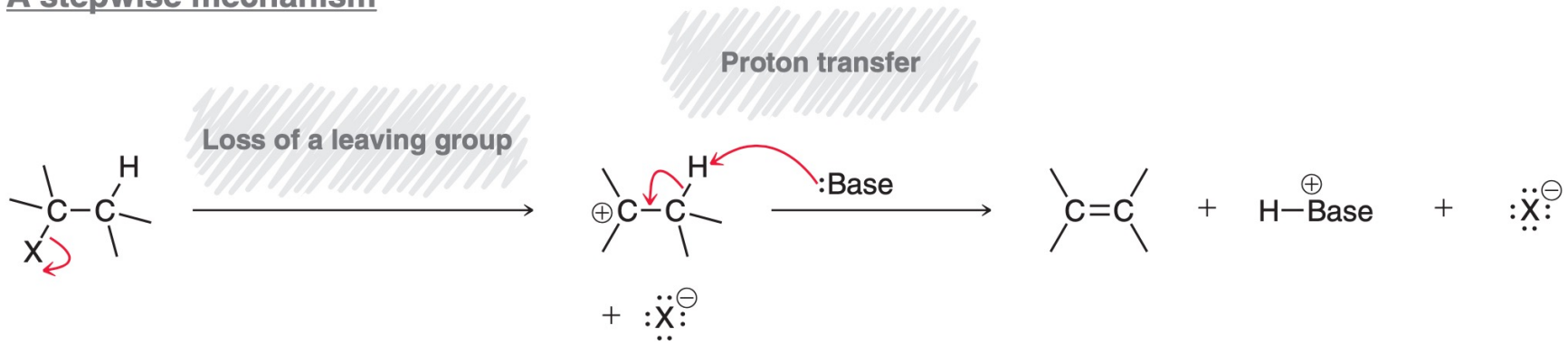
…an E2 process consists of one concerted step and **is rarely accompanied by any other steps**. A carbocation is never formed, and therefore, there is no possibility for a carbocation rearrangement. In addition, E2 conditions generally require the use of a strong base, and an OH group cannot be protonated under such conditions. It is therefore not common to see an E2 process with a proton transfer at the beginning of the mechanism.

- Possible mechanisms

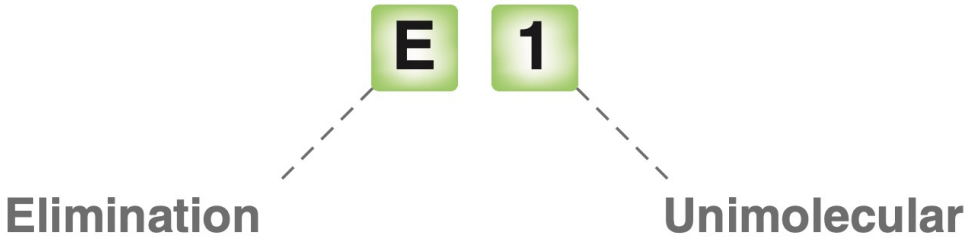
E2 reaction



E1 reaction

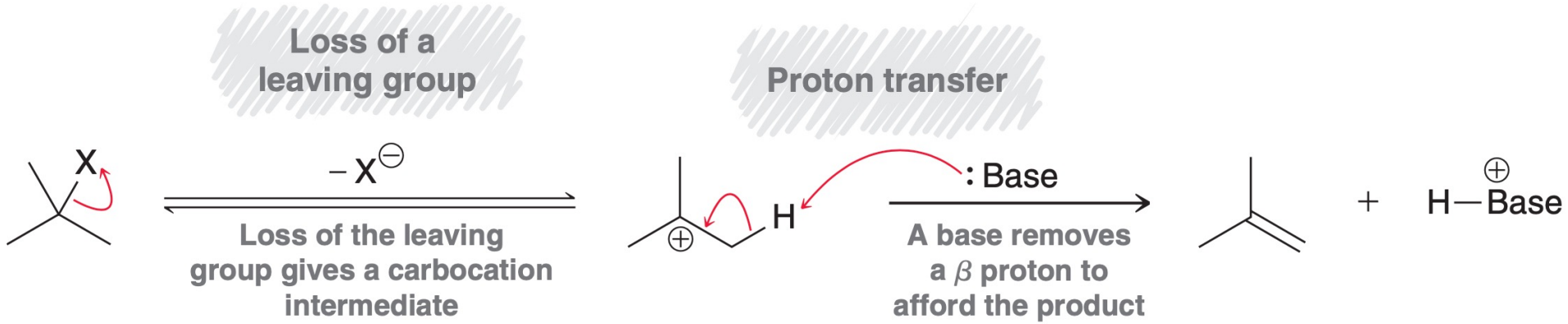


- What is E1?

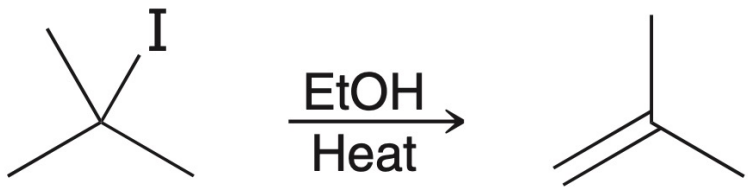


$$\text{Rate} = k\,[\text{substrate}]$$

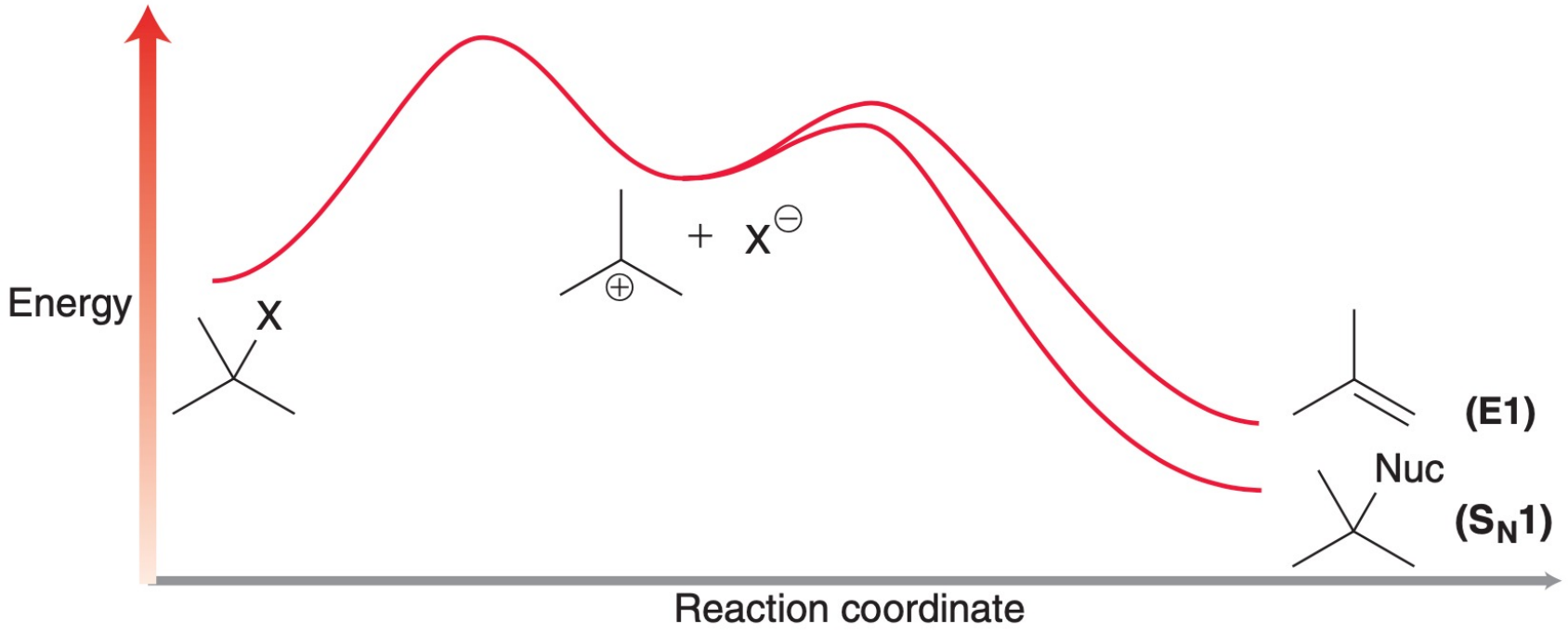
- **The E1 Mechanism**



- Practice: draw a mechanism for the following E1 reaction:

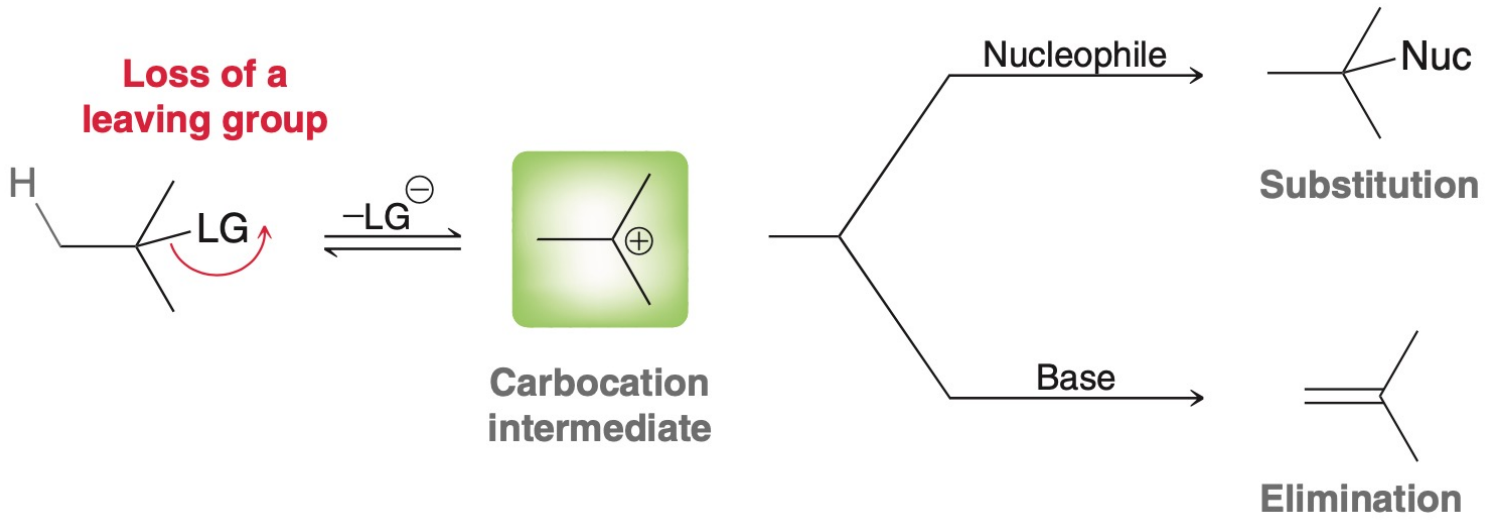


- 反应历程



E1反应产物的能量通常比S_N1反应产物的能量高

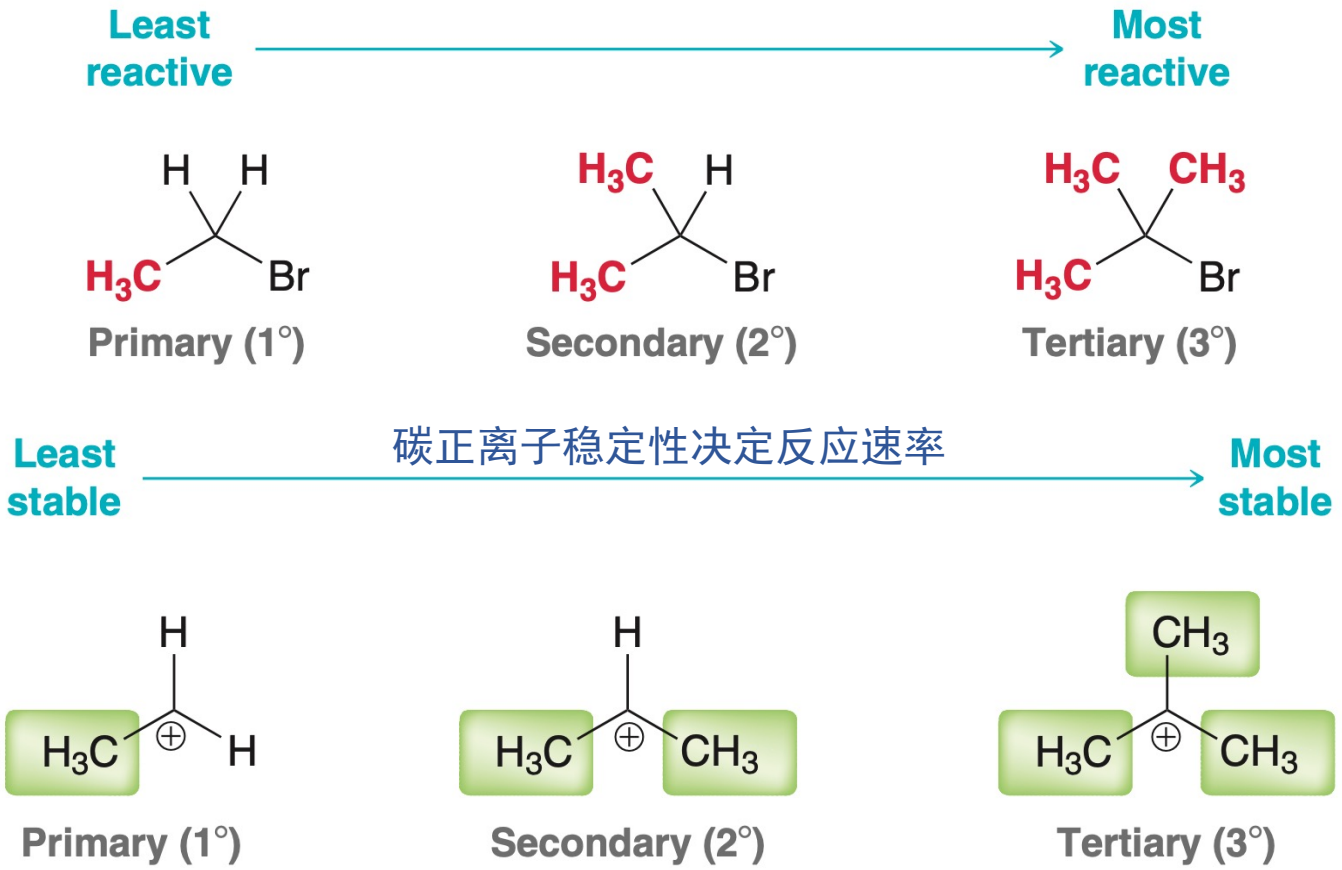
- E1与S_N1的竞争



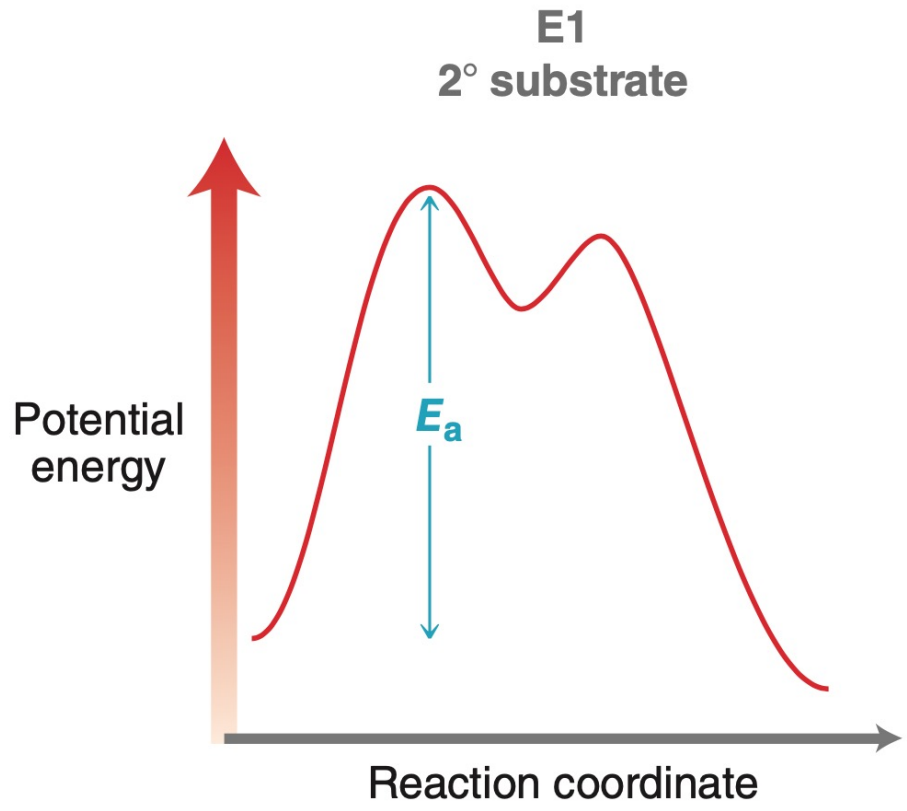
E1与S_N1为竞争反应

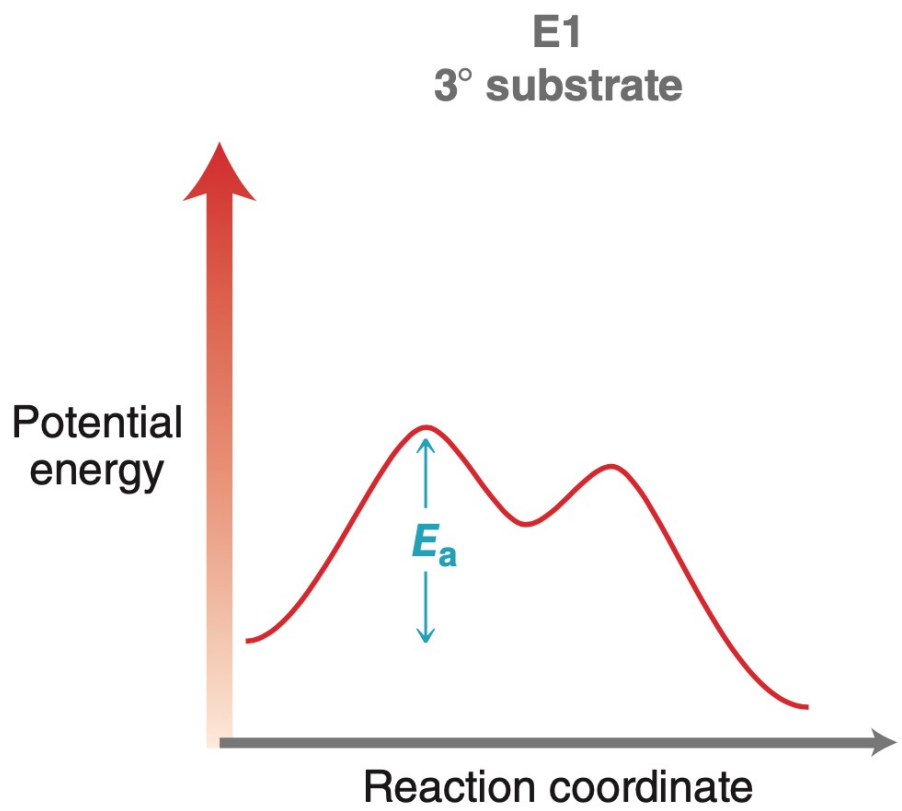
通常得到两者的混合物

- E1的反应性与S_N1相同

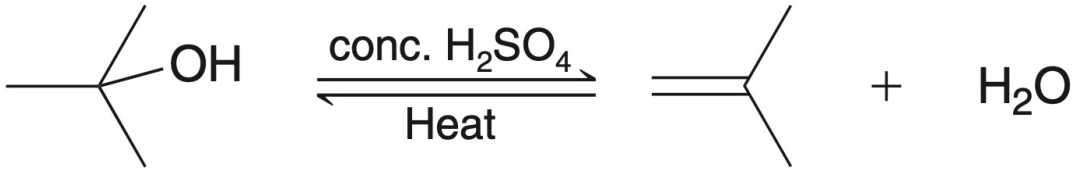


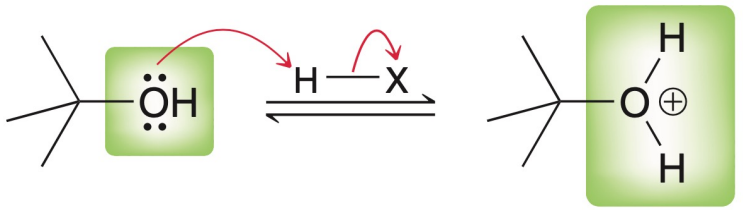
- 二级底物和三级底物的势能比较



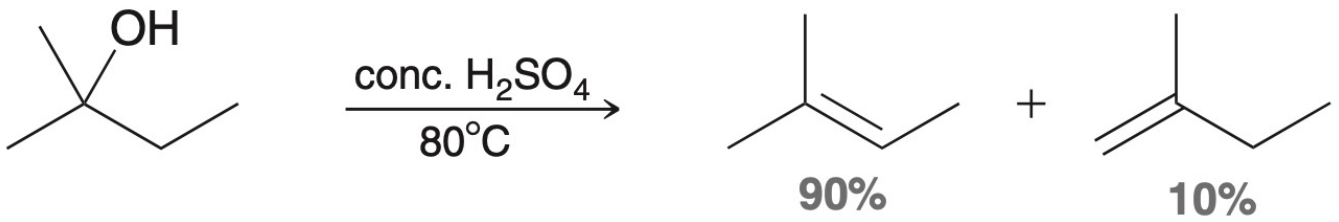


- 浓硫酸催化的E1反应
  - 在**LG为羟基**时，**选用酸**而不选用碱来完成消除反应

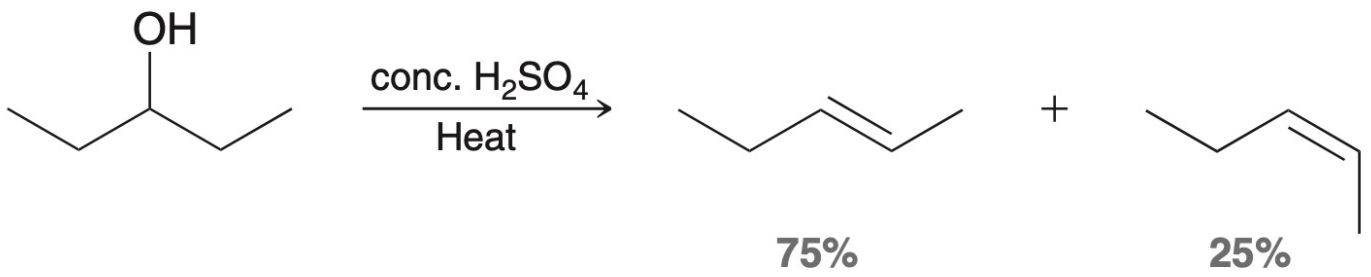




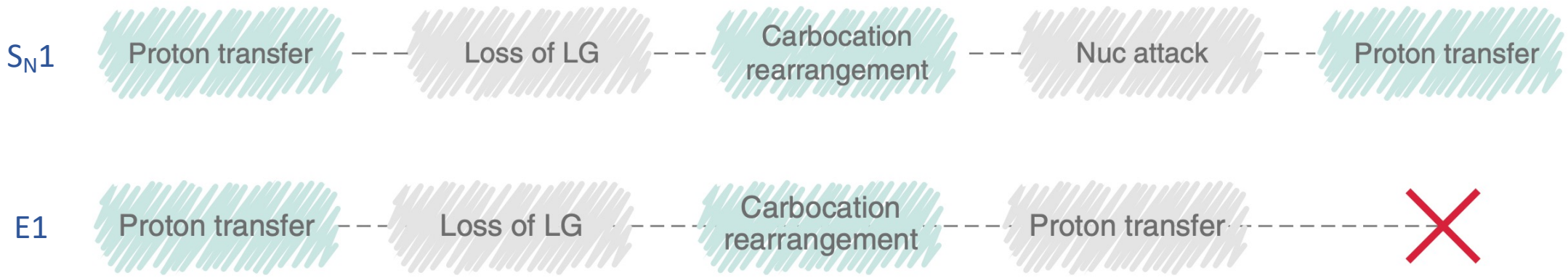
- E1反应的**区域选择性(regioselectivity)**



- E1反应的**立体选择性(stereoselectivity)**

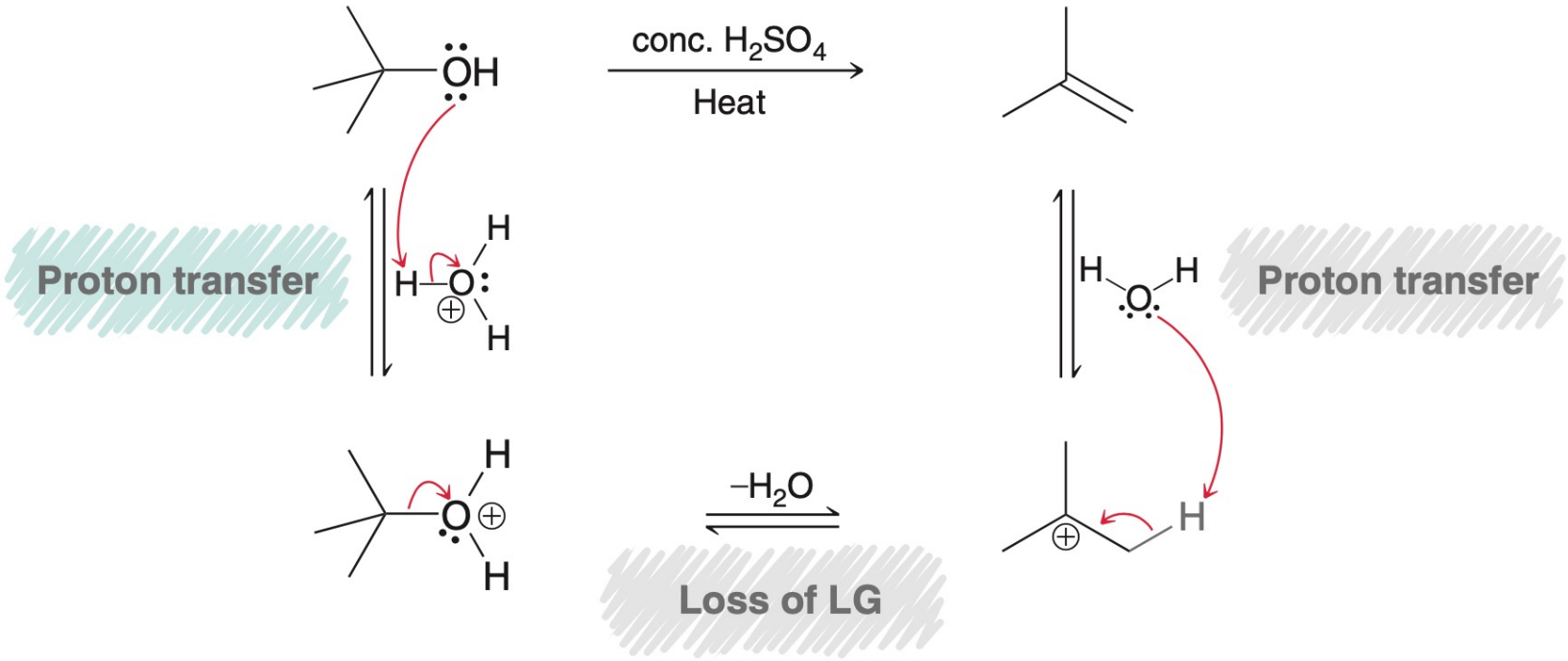


- Additional steps for E1

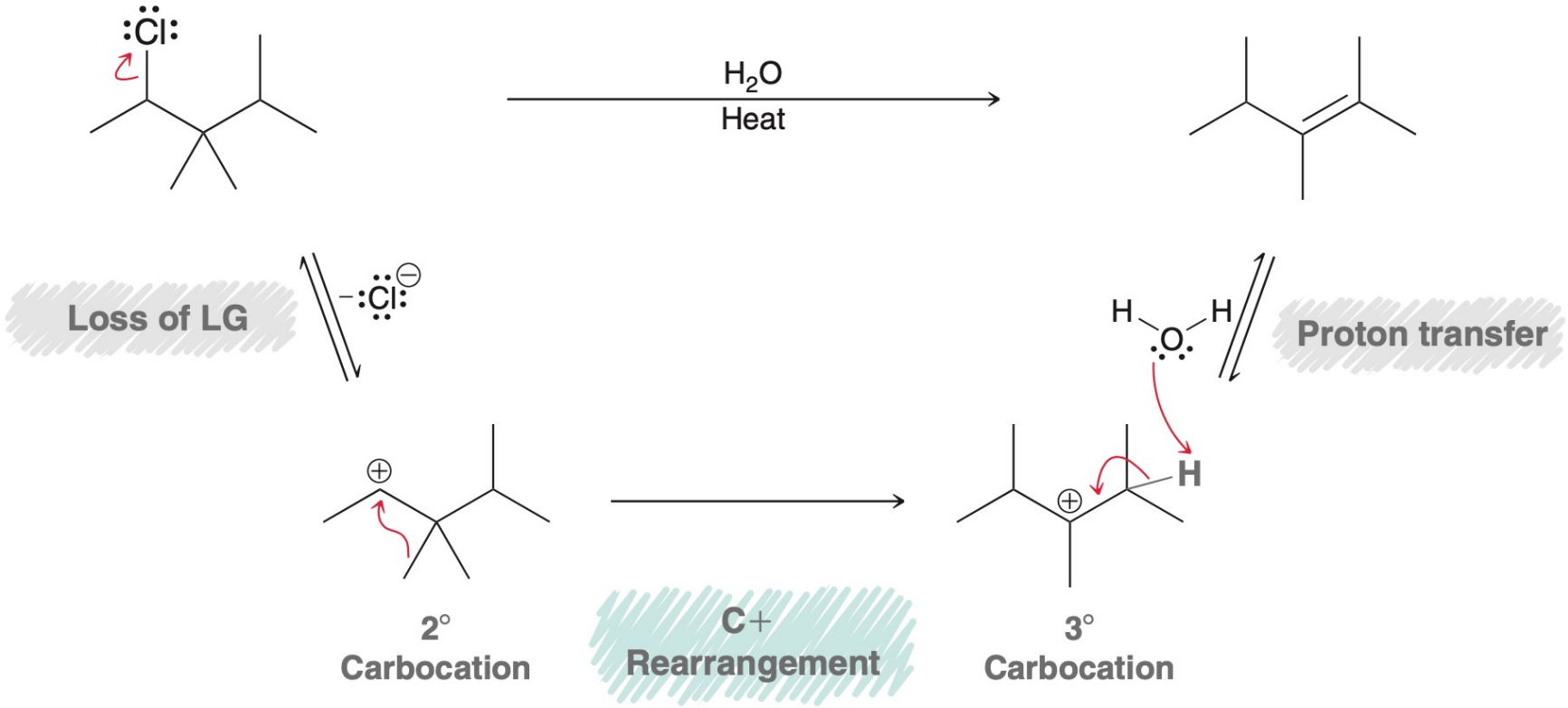


+H+ --- –LG --- –H+

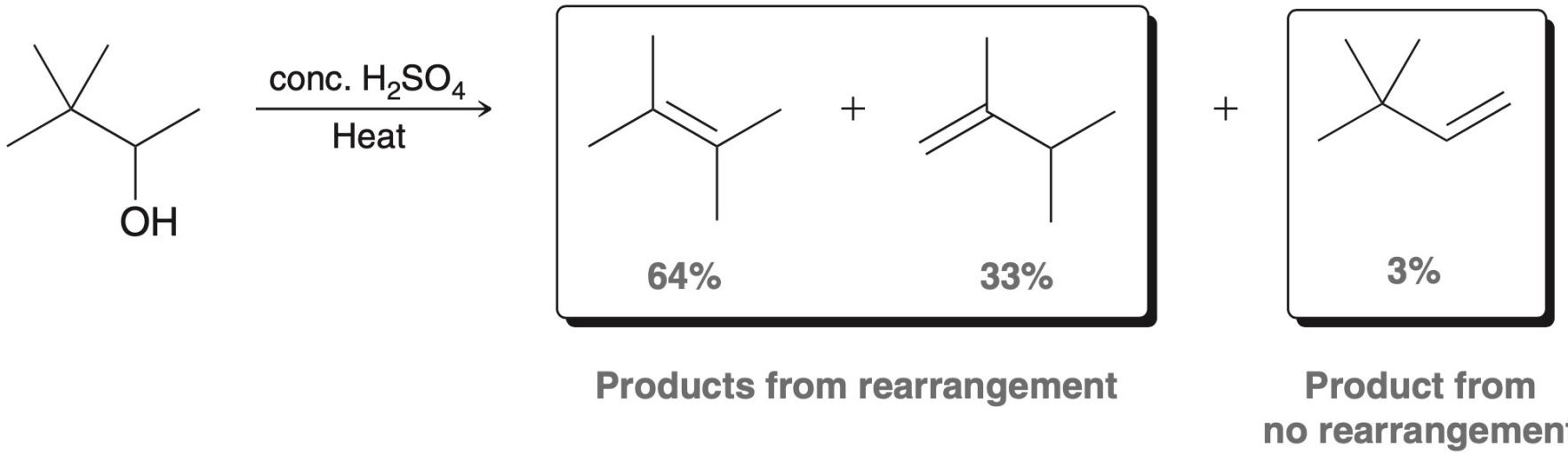
- Proton transfer at the beginning



- Carbocation rearrangement

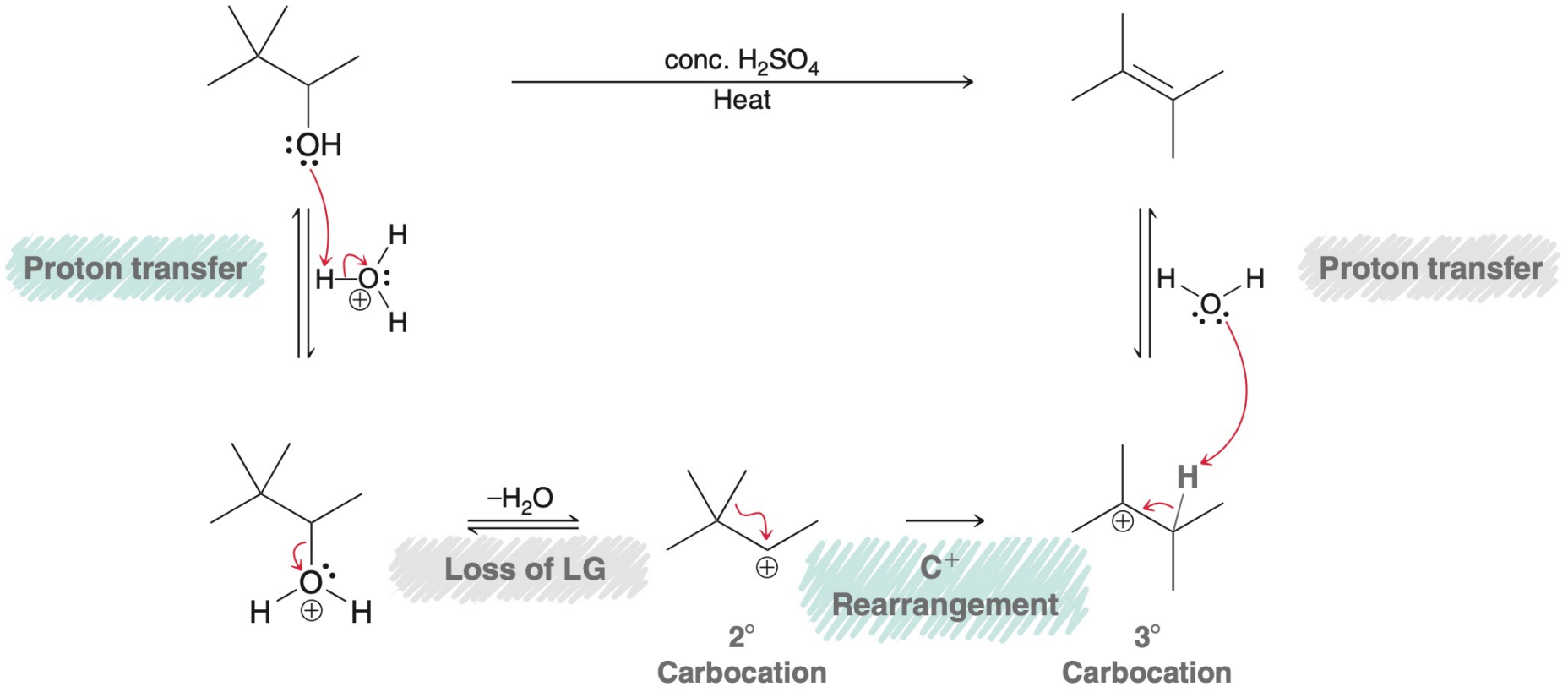


- Rearrangement results mixtures



+H+ --- –LG --- C+ Rearrangement --- –H+

- Multistep E1 mechanisms

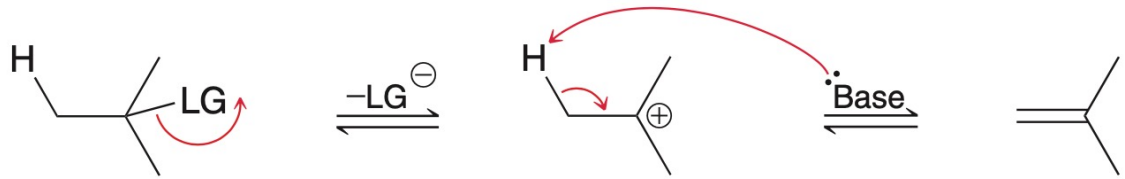


- The complete E1 process

Two core steps

Loss of LG

Proton transfer



The first core step of an E1 process involves loss of a leaving group to form an intermediate carbocation

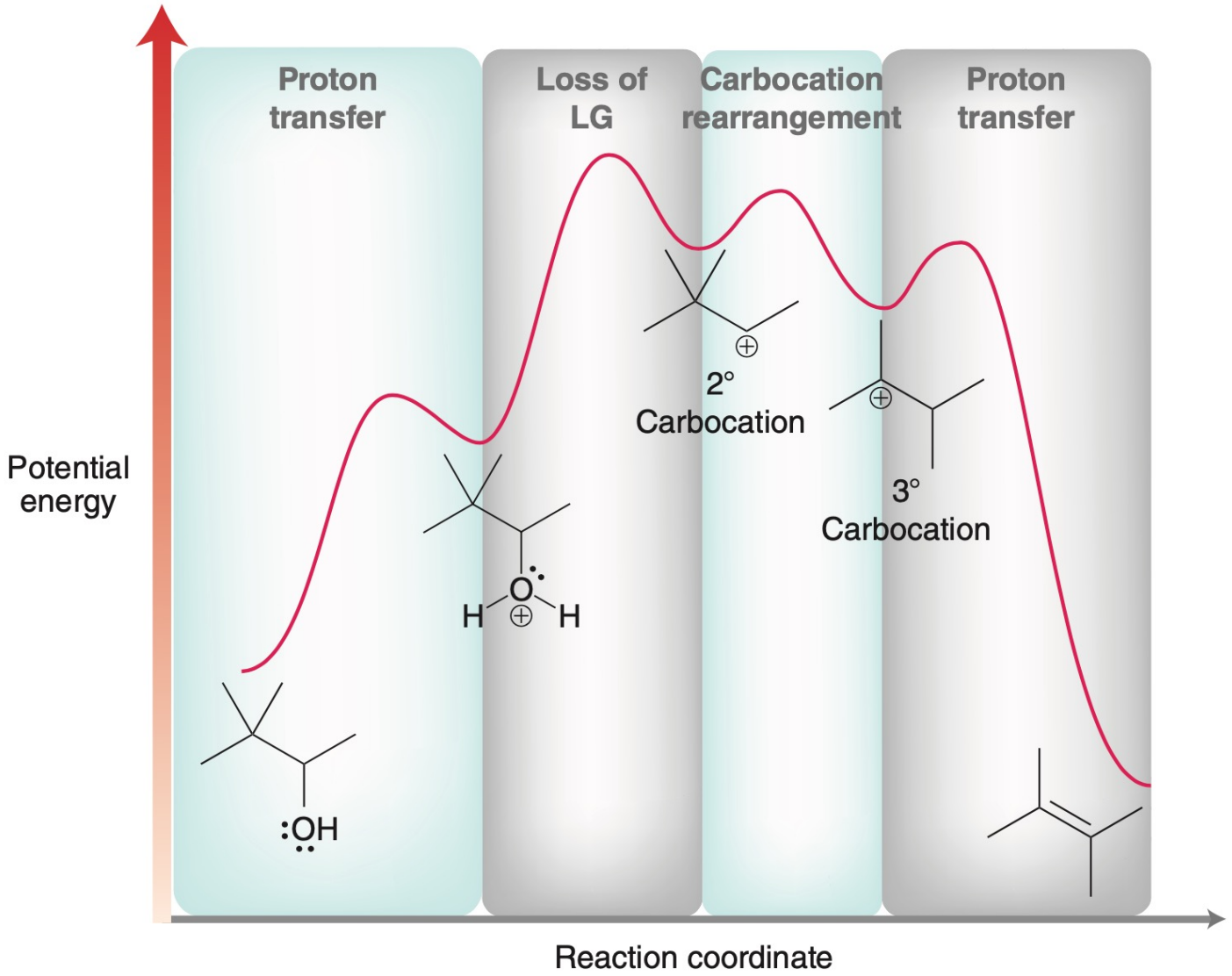
The second core step of an E1 process is a proton transfer to form an alkene

Possible additional steps

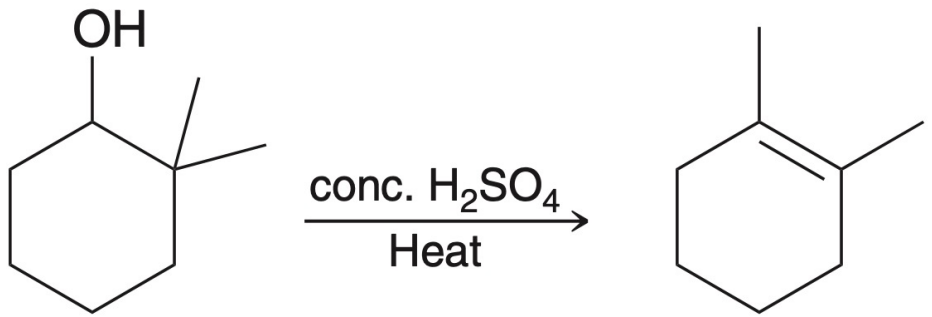
Proton transfer — Loss of LG — C^+ Rearrangement — Proton transfer

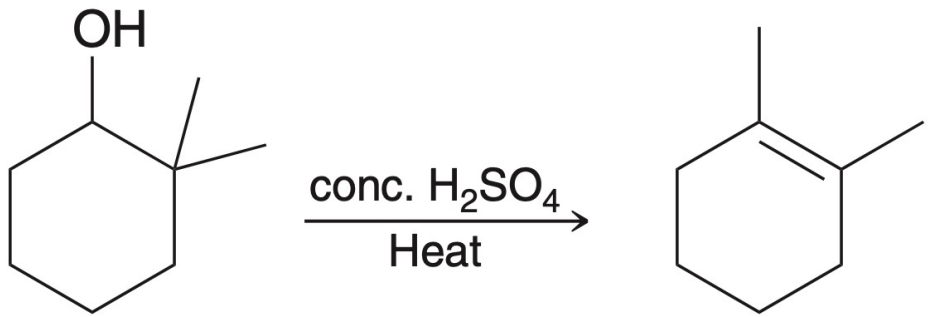
If the leaving group is an OH group, it must be protonated before it can leave

If the carbocation initially formed can rearrange to generate a more stable carbocation, then a carbocation rearrangement will occur


Proton transfer
Loss of LG
Carbocation rearrangement
Proton transfer
Potential energy
2° Carbocation
3° Carbocation
:OH
H
O
H
Reaction coordinate

- Practice: draw a mechanism for the following E1 process:

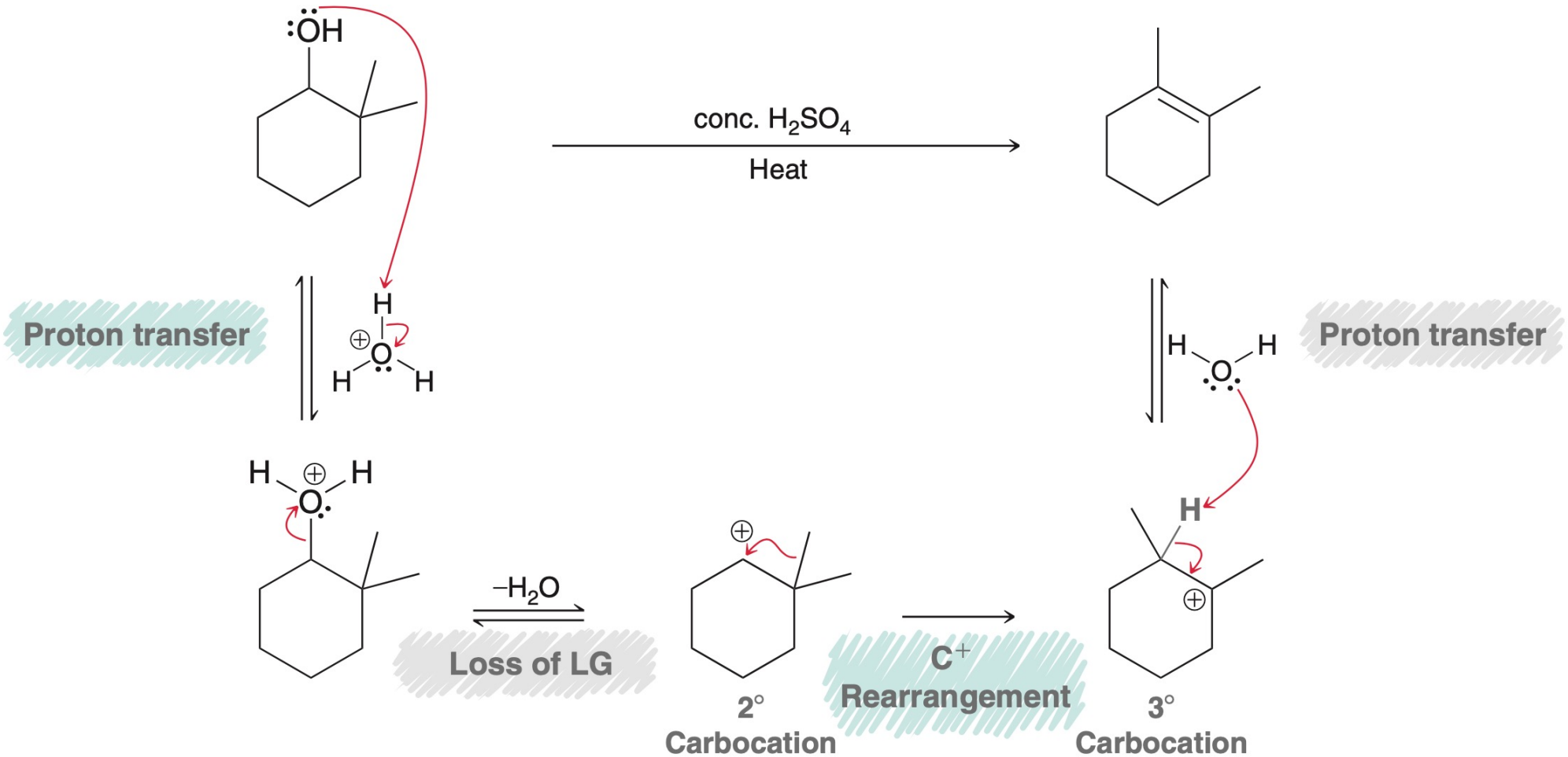




Proton transfer — Loss of LG — Carbocation rearrangement — Proton transfer

Does the LG need to be protonated before it can leave?
—**Yes.** Hydroxide is a bad LG and must be protonated.

Has the carbon skeleton changed?
—**Yes.** This indicates a carbocation rearrangement.

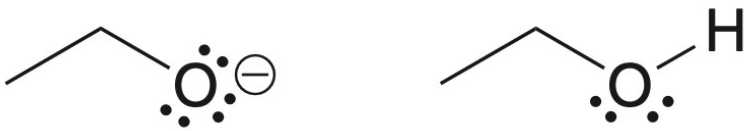

:ÖH
conc. H2SO4
Heat
Proton transfer
H
H
H
H
H
H
H
Proton transfer
–H2O
Loss of LG
2°
Carbocation
C+
Rearrangement
H
3°
Carbocation

Substitution vs. Elimination

Identify Reagents, Identify Mechanisms, Analyze Regio&Stereochemical Outcomes, Synthesis Strategies

- 亲核性(nucleophilicity)

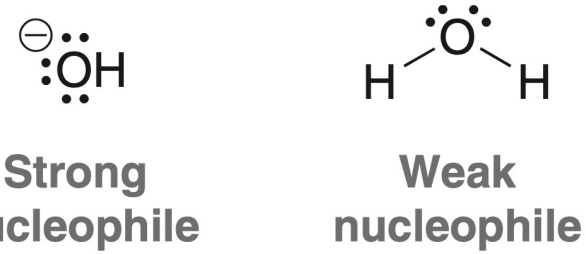
Nucleophilicity is a **kinetic** concept that refers to the **rate** at which a particular nucleophile will attack an electrophile.



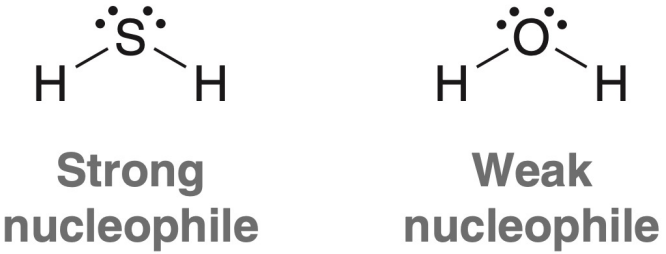
Ethoxide Ethanol

ethoxide reacts faster than ethanol in a nucleophilic reaction

- 影响因素
  - Charge: more negative, more nucleophilic

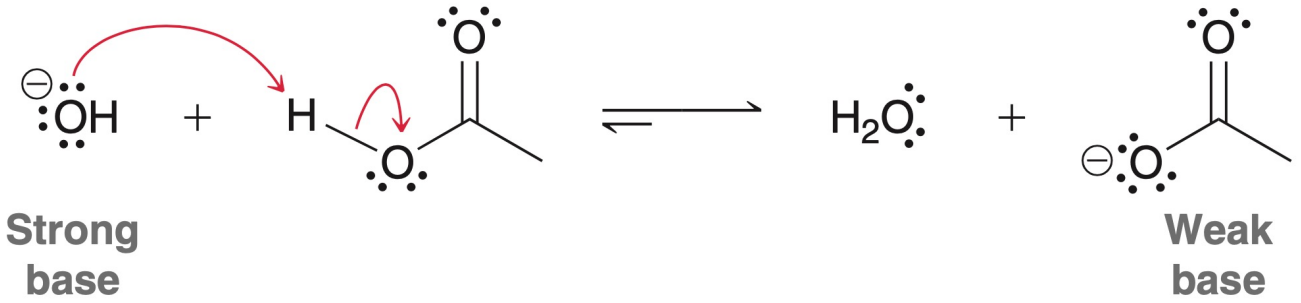


  - Polarizability: more polarizable, more nucleophilic



- 碱性(basicity)

Basicity is a **thermodynamic** concept that refers to the position of **equilibrium**:



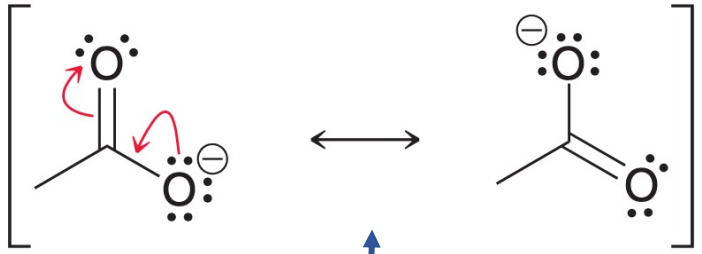
In a proton transfer process, the equilibrium will favor the weaker base.

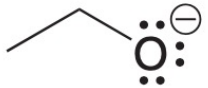
- 酸碱性的定性分析：电负性

H所连的原子电负性越大，酸性越强

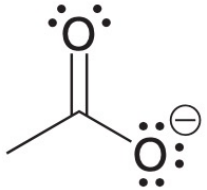
对应的共轭碱碱性越弱

- 酸碱性的定性分析：共振





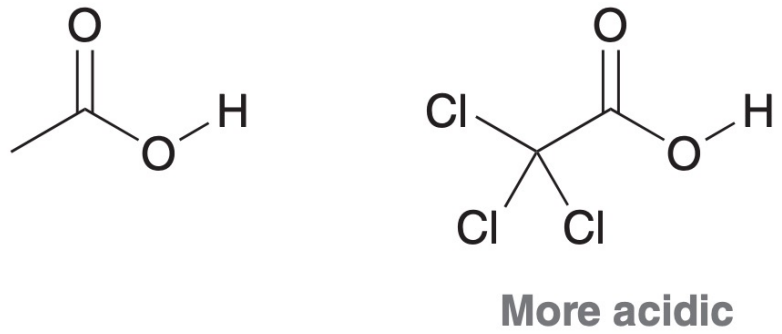
Charge is localized
(less stable)



Charge is delocalized
(more stable)

存在共振式的共轭碱更稳定（碱性越弱）

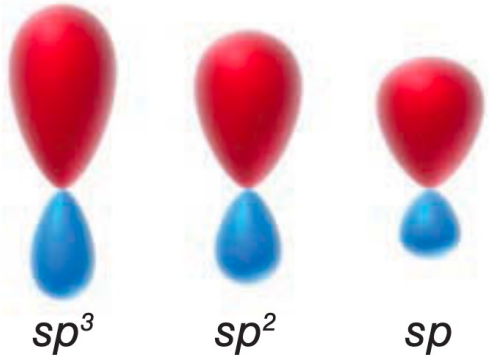
- 酸碱性的定性分析：诱导效应



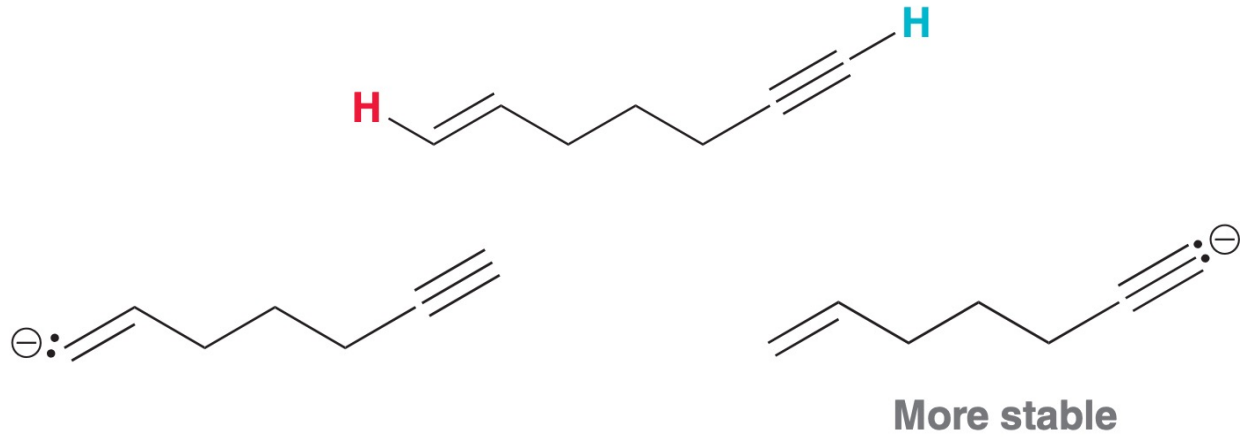
More acidic

诱导效应使得三氯乙酸的酸性增强

对应的共轭碱碱性随之变弱



- 酸碱性的定性分析：轨道
  - 在sp杂化中，s轨道成分占比越大，轨道越收缩，即越靠近原子核
  - 越靠近核的轨道上的电子受到核的静电引力越大，因此越稳定

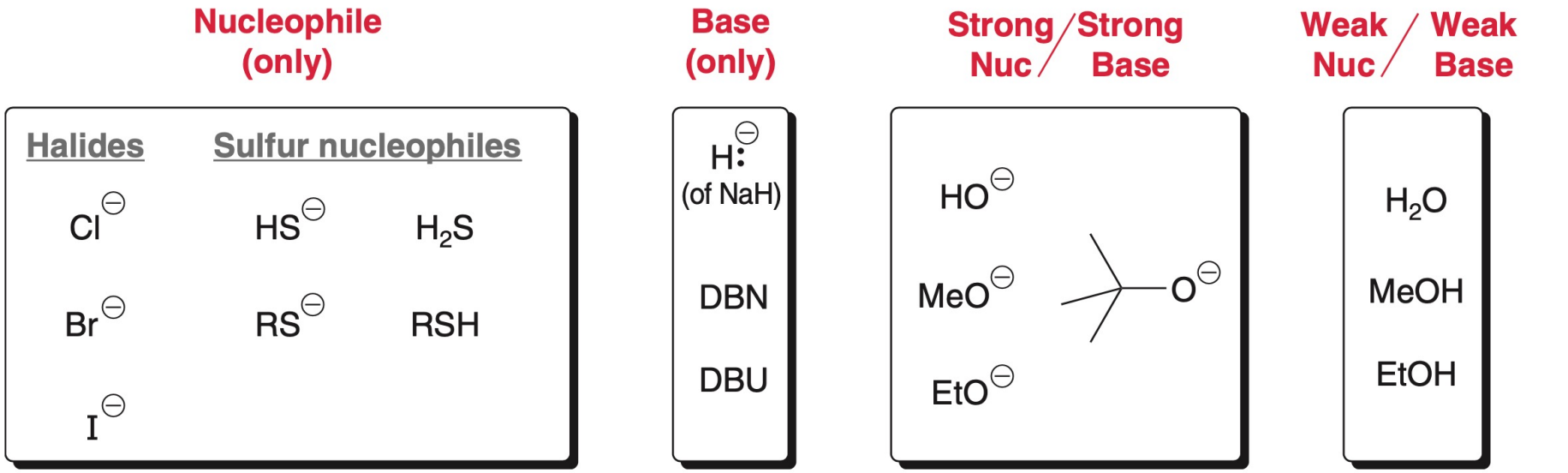


炔基负离子相对更稳定（碱性越弱）

- 软硬酸碱理论(HSAB)
  - 硬酸：体积小、正电荷数高、可极化性低的中心原子
  - 硬碱：电负性高、可极化性低、难被氧化的配位原子
  - 软酸：体积大、正电荷数（相对）低、可极化性高的中心原子
  - 软碱：电负性（相对）低、可极化性高、易被氧化的配位原子

“硬酸碰硬碱，软酸碰软碱”

- 亲核试剂与碱的分类



弱碱、强亲核试剂（仅做亲核试剂）

强碱、弱亲核试剂（仅做碱）

强碱、强亲核试剂

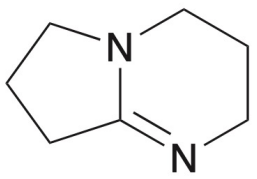
弱碱、弱亲核试剂

- 弱碱、强亲核试剂（仅做亲核试剂）
  - 碱性弱
  - 极化性强
  - “软碱”——亲碳正（软酸）
  - 主要表现为亲核性
  - 作为取代反应(S_N2, S_N1)的试剂

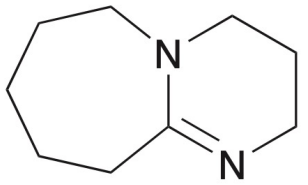
Halides	Sulfur nucleophiles	
$Cl^{\ominus}$	$HS^{\ominus}$	H_2S
$Br^{\ominus}$	$RS^{\ominus}$	RSH
$I^{\ominus}$		

- 强碱、弱亲核试剂（仅做碱）
  - 碱性强
  - 极化性弱
  - “硬碱”——亲质子（硬酸）
  - 主要表现为碱性
  - 作为取代反应(E2, E1)的试剂

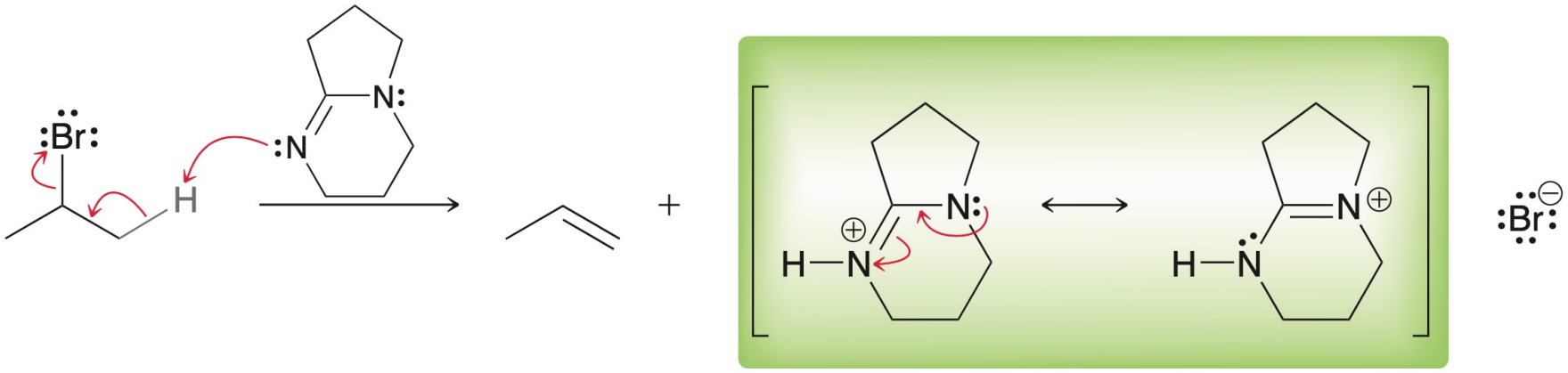
- DBN与DBU



1,5-Diazabicyclo[4.3.0]non-5-ene
(DBN)

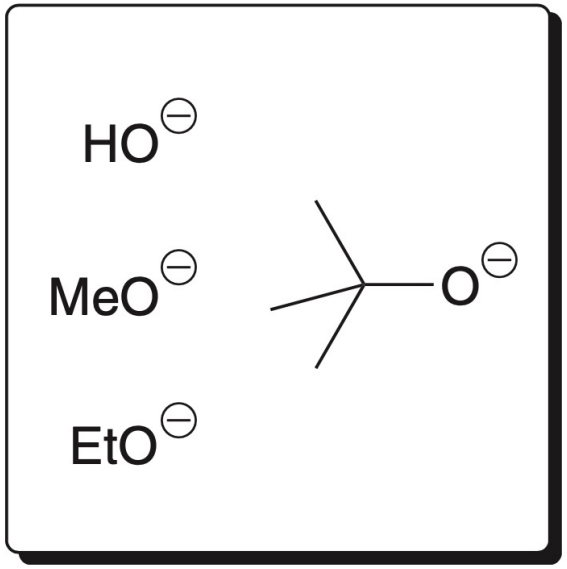


1,8-Diazabicyclo[5.4.0]undec-7-ene
(DBU)

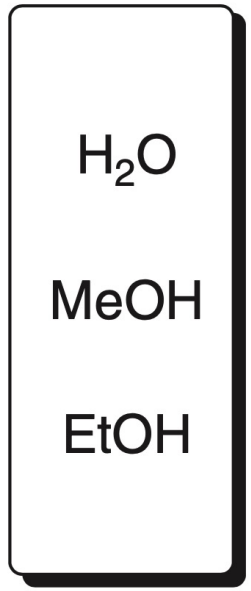


Resonance stabilized

- 强碱、强亲核试剂
  - 碱性强
  - 带负电荷，极化能力强
  - 表现为强碱及强亲核性
  - 作为S_N2和E2的试剂



- 弱碱、弱亲核试剂
  - 碱性弱
  - 无电荷，极化能力弱
  - 表现为弱碱及弱亲核性
  - 作为S_N1和E1的试剂



	Strong base Weak nucleophile	Strong base Strong nucleophile	Weak base Strong nucleophile	Weak base Weak nucleophile
1°	E2	E2 / S_N2	S_N2	✗
2°	E2	E2 / S_N2	S_N2	✗
3°	E2	E2	S_N1	S_N1 / E1

- Practice

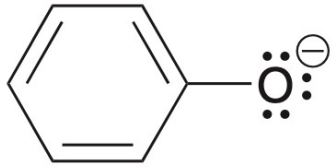
Consider the phenolate ion. We will explore the reactivity of this ion in Chapter 19. From the following list, identify the category to which the phenolate ion belongs:

(a) Strong nucleophile and weak base

(b) Weak nucleophile and strong base

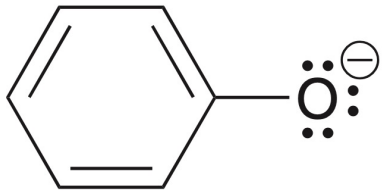
(c) Strong nucleophile and strong base

(d) Weak nucleophile and weak base



Phenolate

- For nucleophilicity…

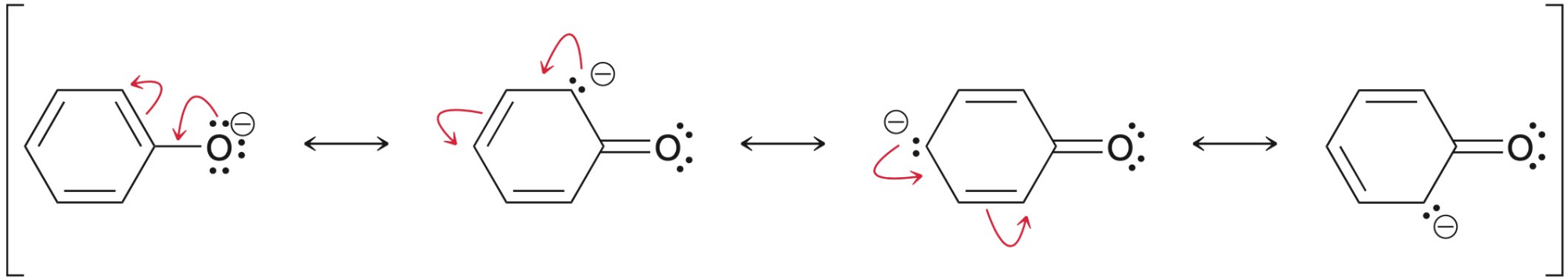


Phenolate

- contains negative charge – strong nucleophile
- oxygen atom - not highly polarizable, but it is also not small enough of an atom (like hydrogen) to render it non-nucleophilic

strong nucleophile

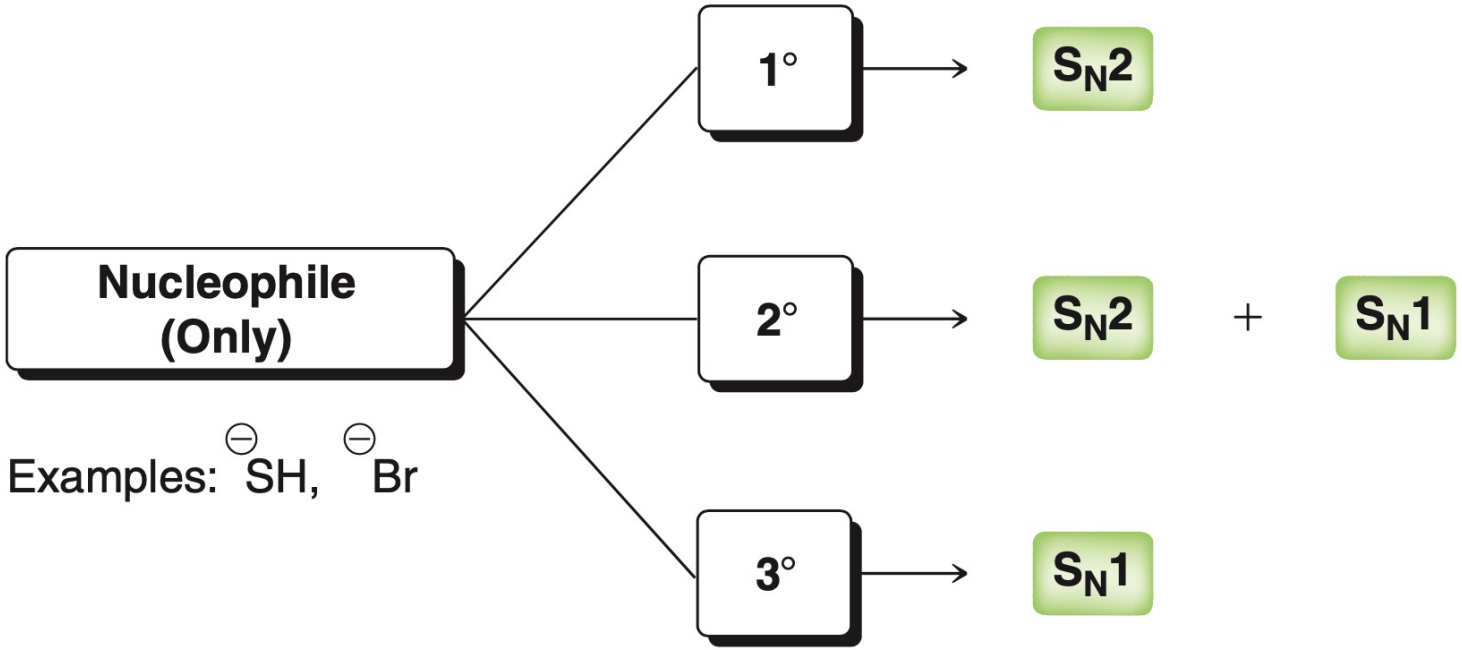
- For basicity…



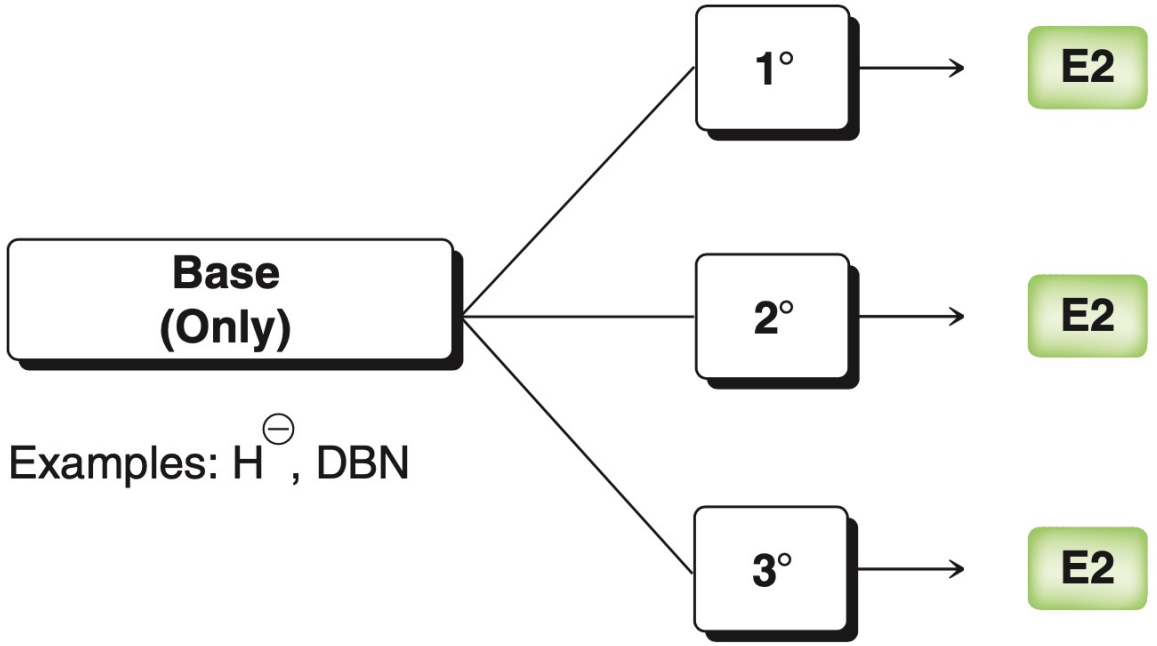
  - phenolate ion can be resonance stabilized
  - resonance stabilized – more stable – fairly weak base

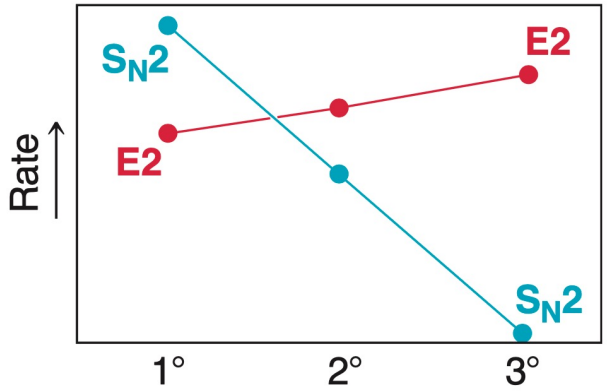
weak base

- 弱碱强亲核（亲核试剂）

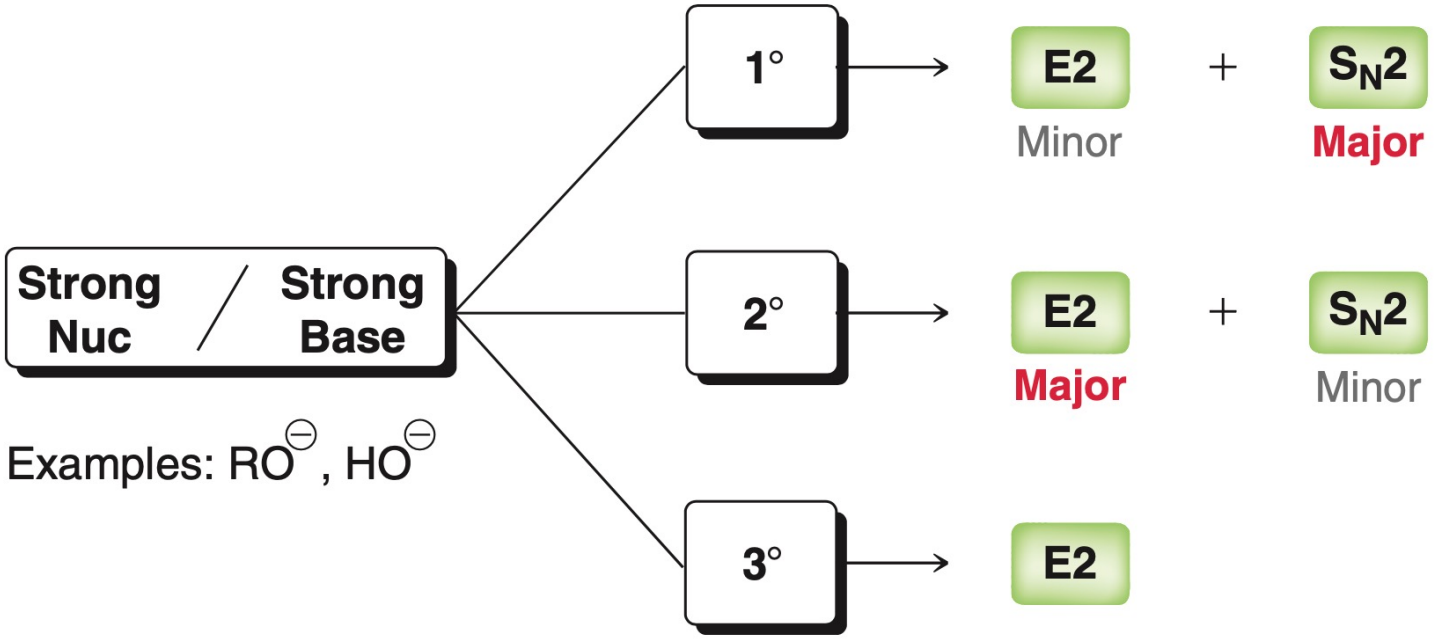


- 强碱弱亲核（碱）

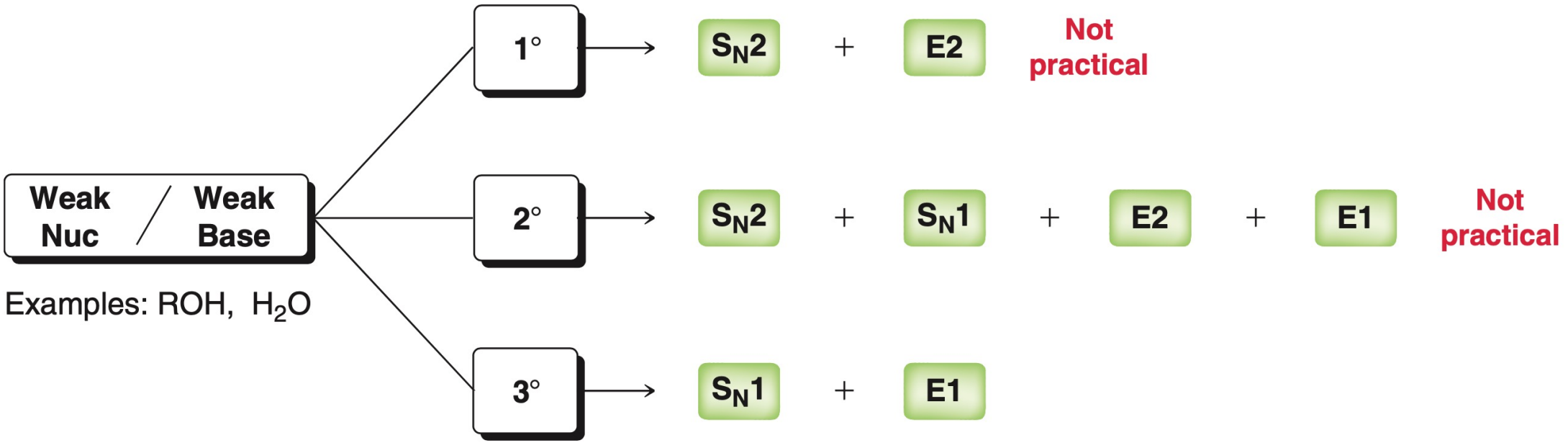



Rate
SN2
E2
E2
SN2
1°
2°
3°

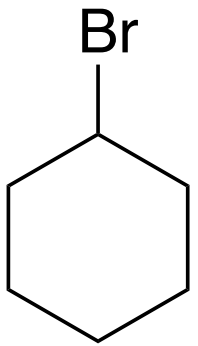
- 强碱强亲核


Strong Nuc / Strong Base
Examples: RO⊖, HO⊖
1°
2°
3°
E2
Minor
+
SN2
Major
E2
Major
+
SN2
Minor
E2

- 弱碱弱亲核


Weak Nuc / Weak Base
Examples: ROH, H_2O
1°
2°
3°
S_N2 + E2 Not practical
S_N2 + S_N1 + E2 + E1 Not practical
S_N1 + E1

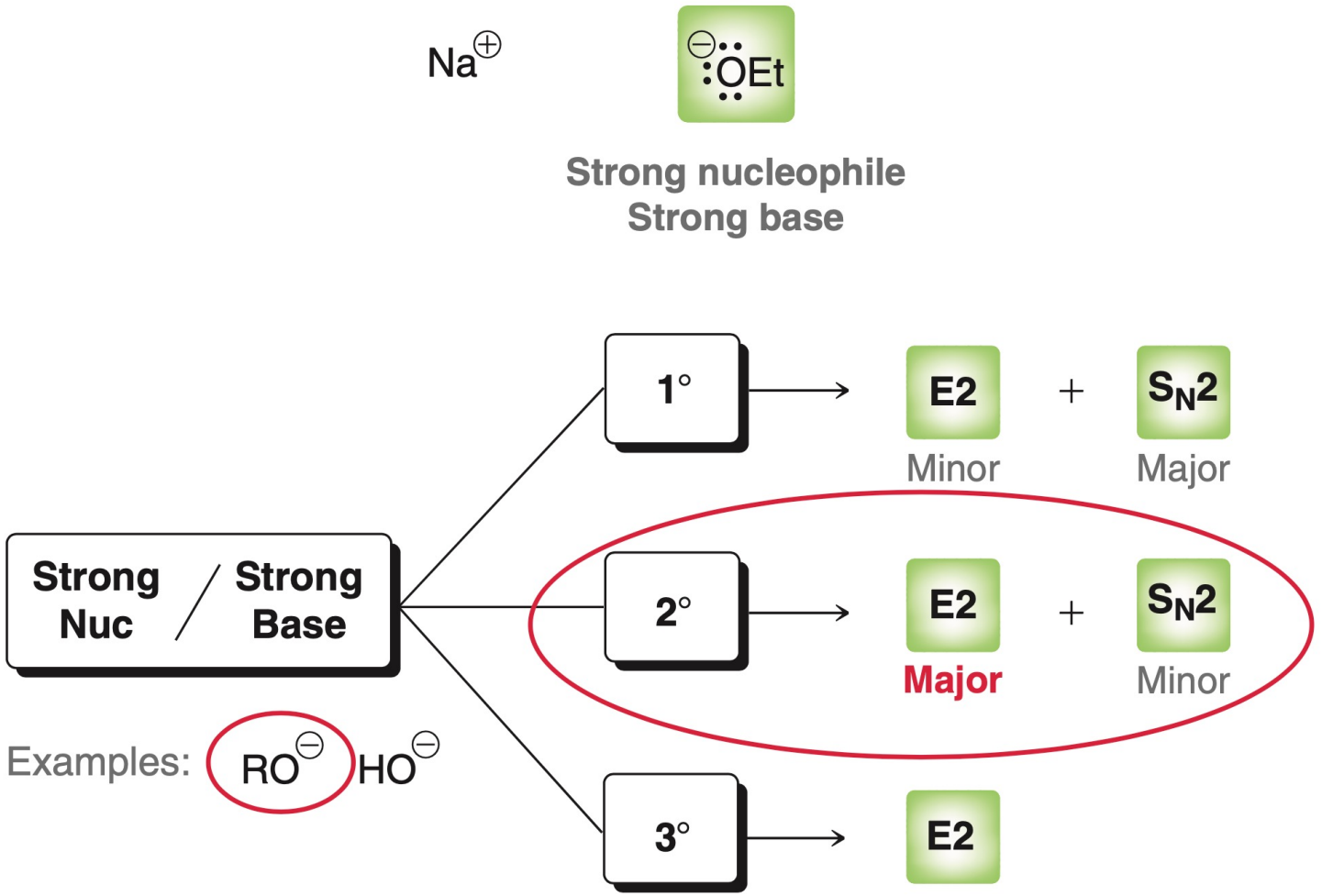
- Practice: identify the mechanism(s) expected to occur when bromocyclohexane is treated with sodium ethoxide.



bromocyclohexane

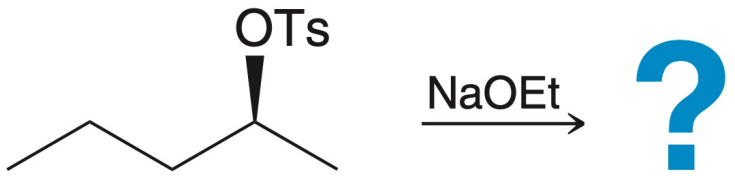
NaOEt

sodium ethoxide

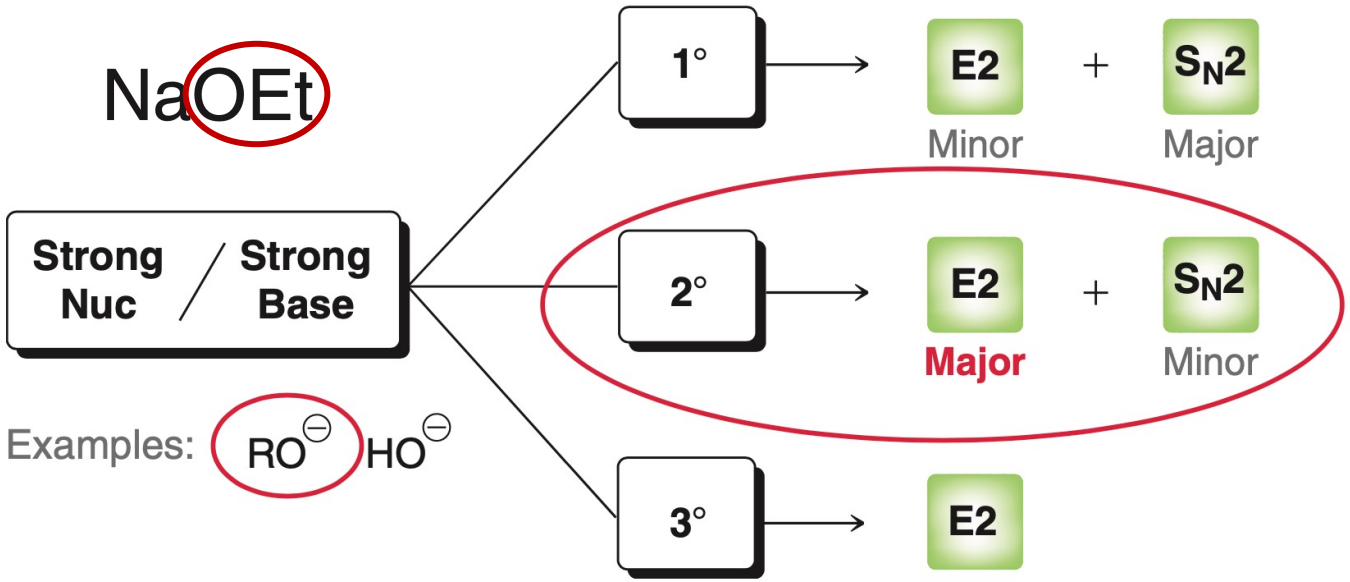

Na⊕
⊖:ÖEt
Strong nucleophile
Strong base
Strong Nuc / Strong Base
1°
2°
3°
E2
Minor
+
SN2
Major
E2
Major
+
SN2
Minor
E2
Examples:
RO⊖
HO⊖

	Regiochemistry	Stereochemistry
S_N2	亲核试剂进攻α碳	立体专一性：构型翻转
E2	通常生成扎伊采夫产物（热力学控制） 使用大位阻碱时，生成霍夫曼产物（动力学控制）	立体选择性：生成反式烯烃更稳定 立体专一性：反式共平面消除
S_N1	亲核试剂进攻碳正离子 可能发生碳正离子重排	生成接近消旋的产物 Winstein离子对机理：构型翻转产物多于构型保持产物
E1	倾向于生成扎伊采夫产物 可能发生碳正离子重排	立体选择性：生成反式烯烃更稳定

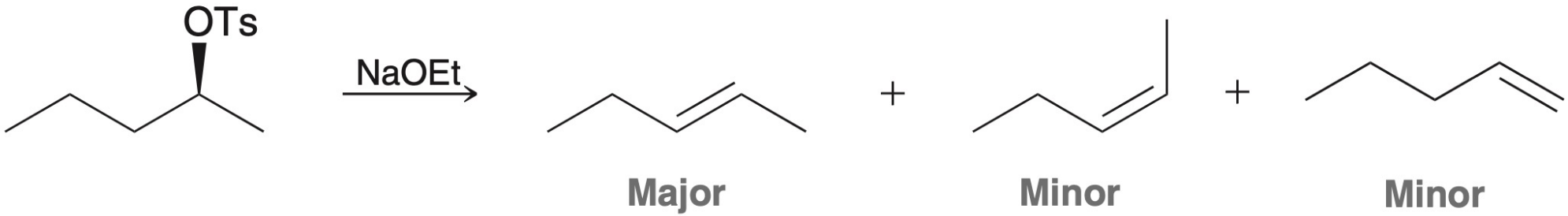
- Practice: predict the product(s) of the following reaction and identify the major and minor products:



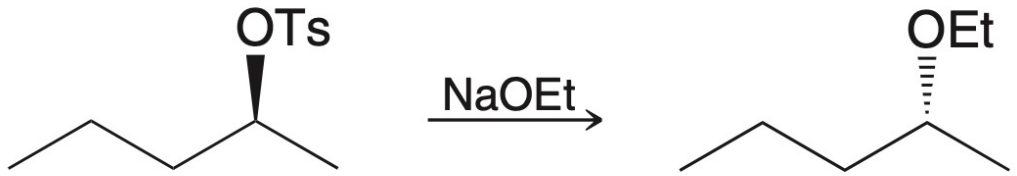
1. Determine the function of the reagent.
2. Analyze the substrate and determine the expected mechanism(s).
3. Consider any relevant regiochemical and stereochemical requirements.



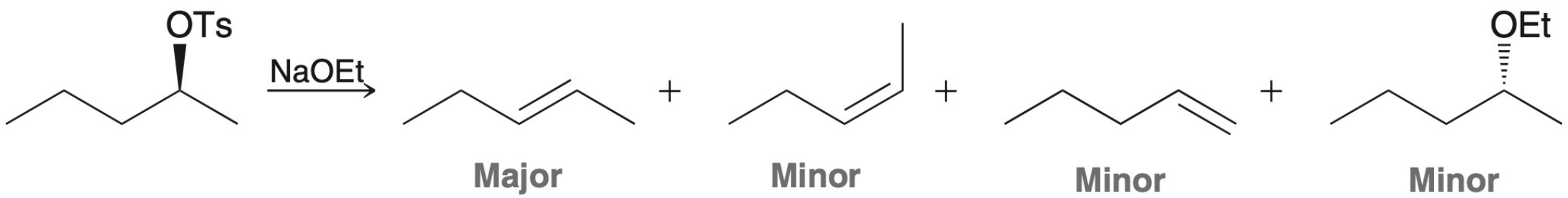
E2



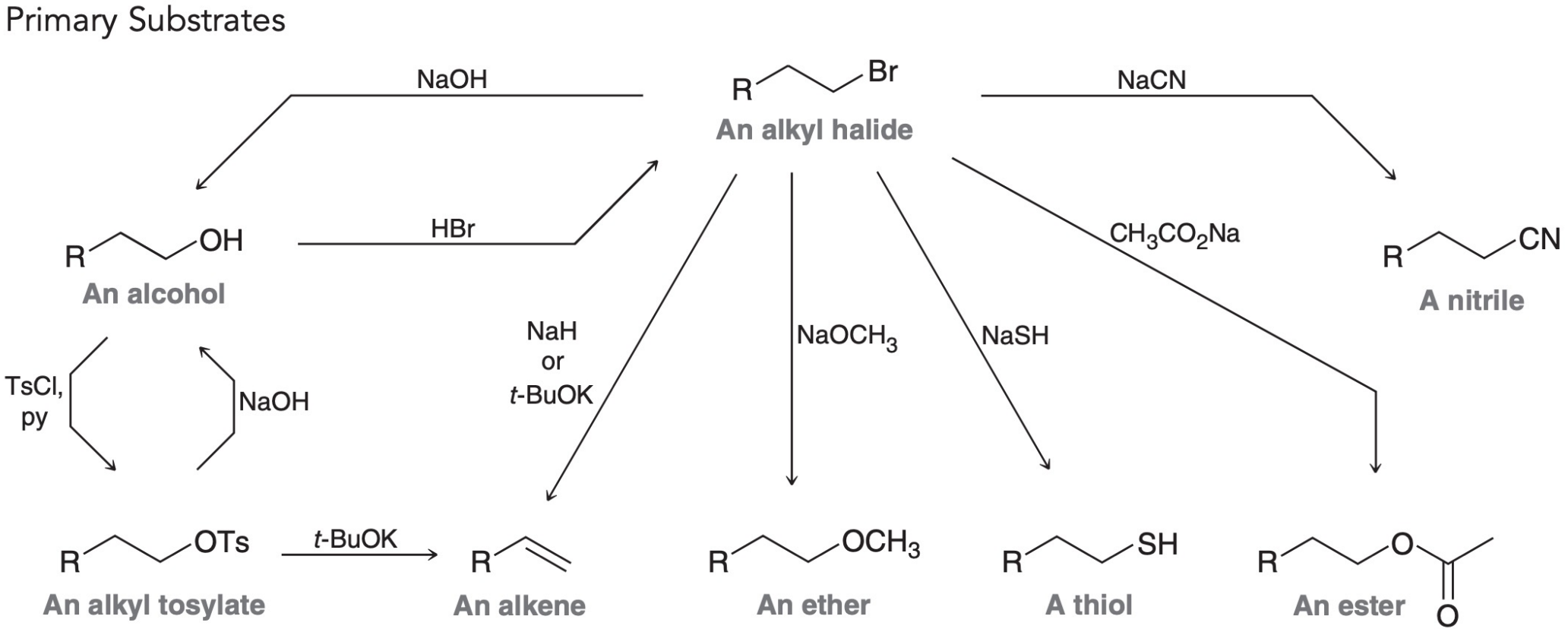
S_N2



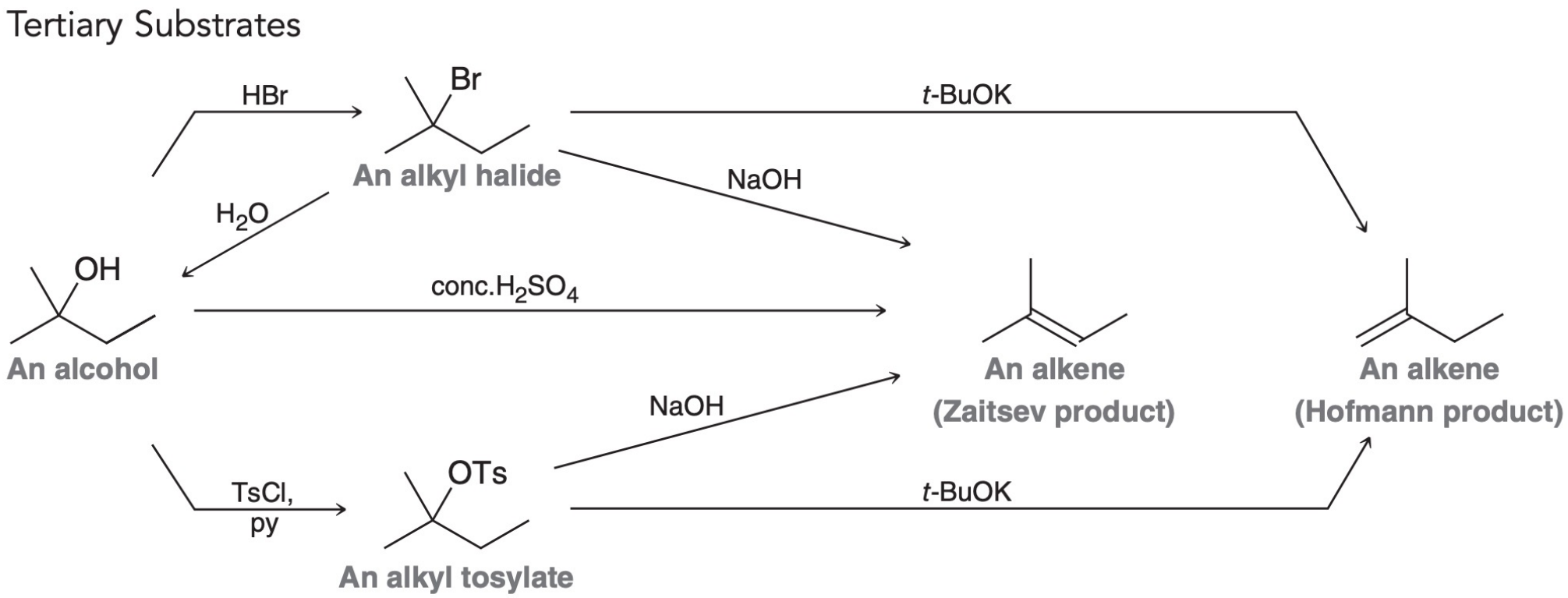
Predict the Product



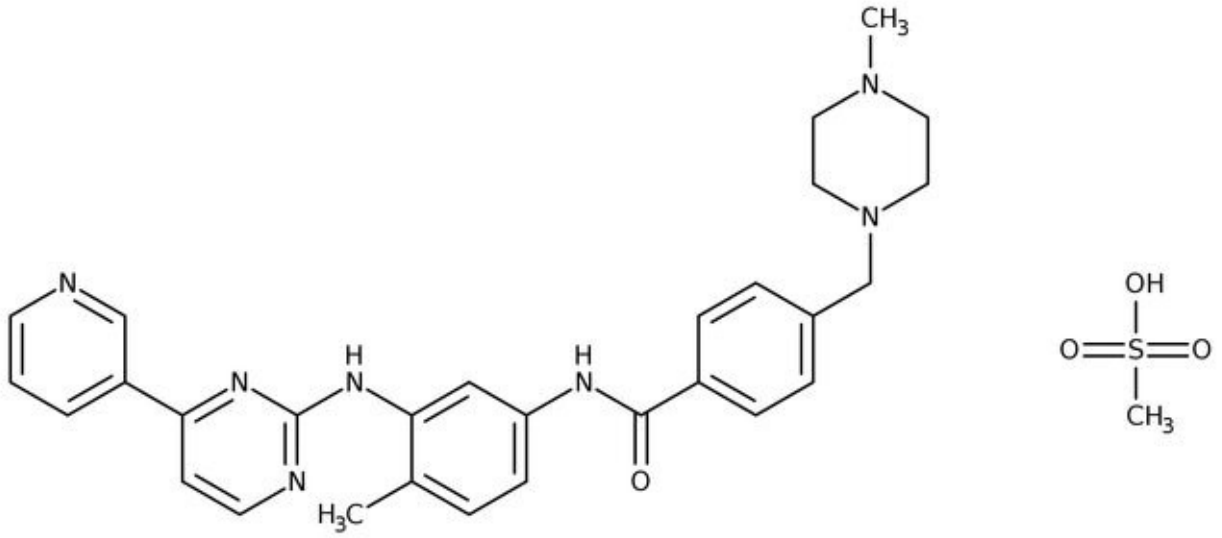
- Review of Reactions



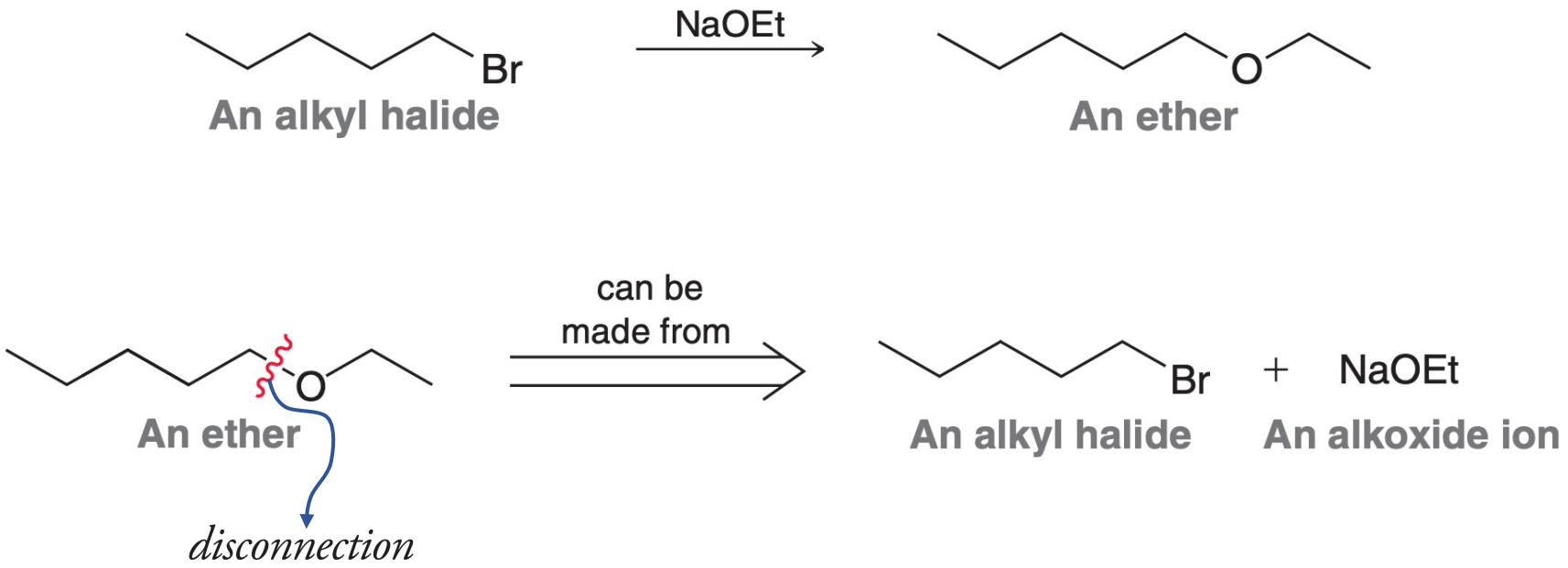
- Review of Reactions



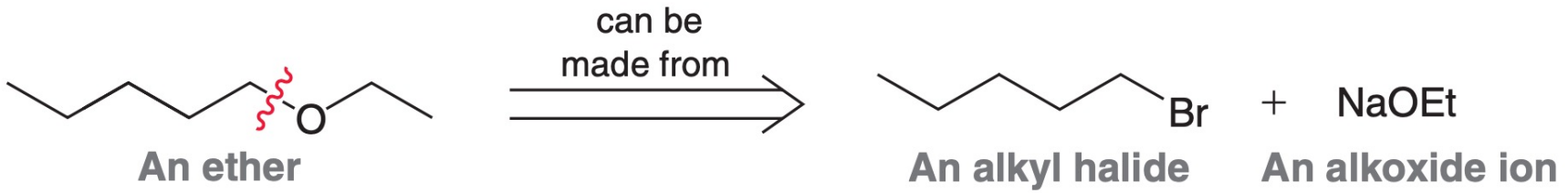
- Organic synthesis – create new things from basic substances
  - Forward synthetic analysis
  - Retrosynthetic analysis

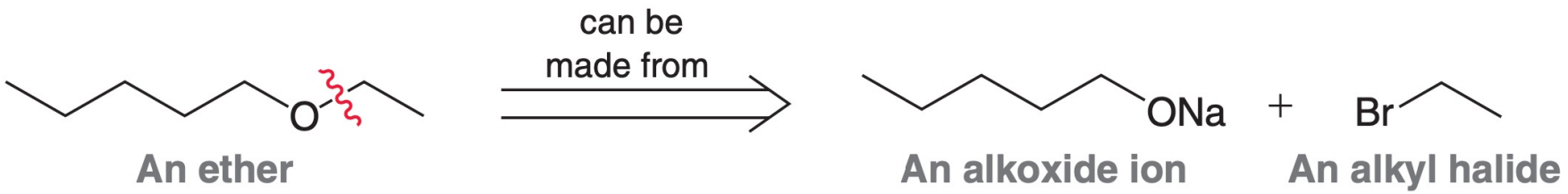


- Retrosynthetic analysis

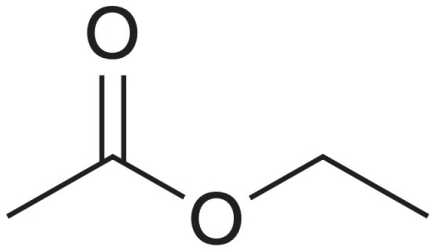


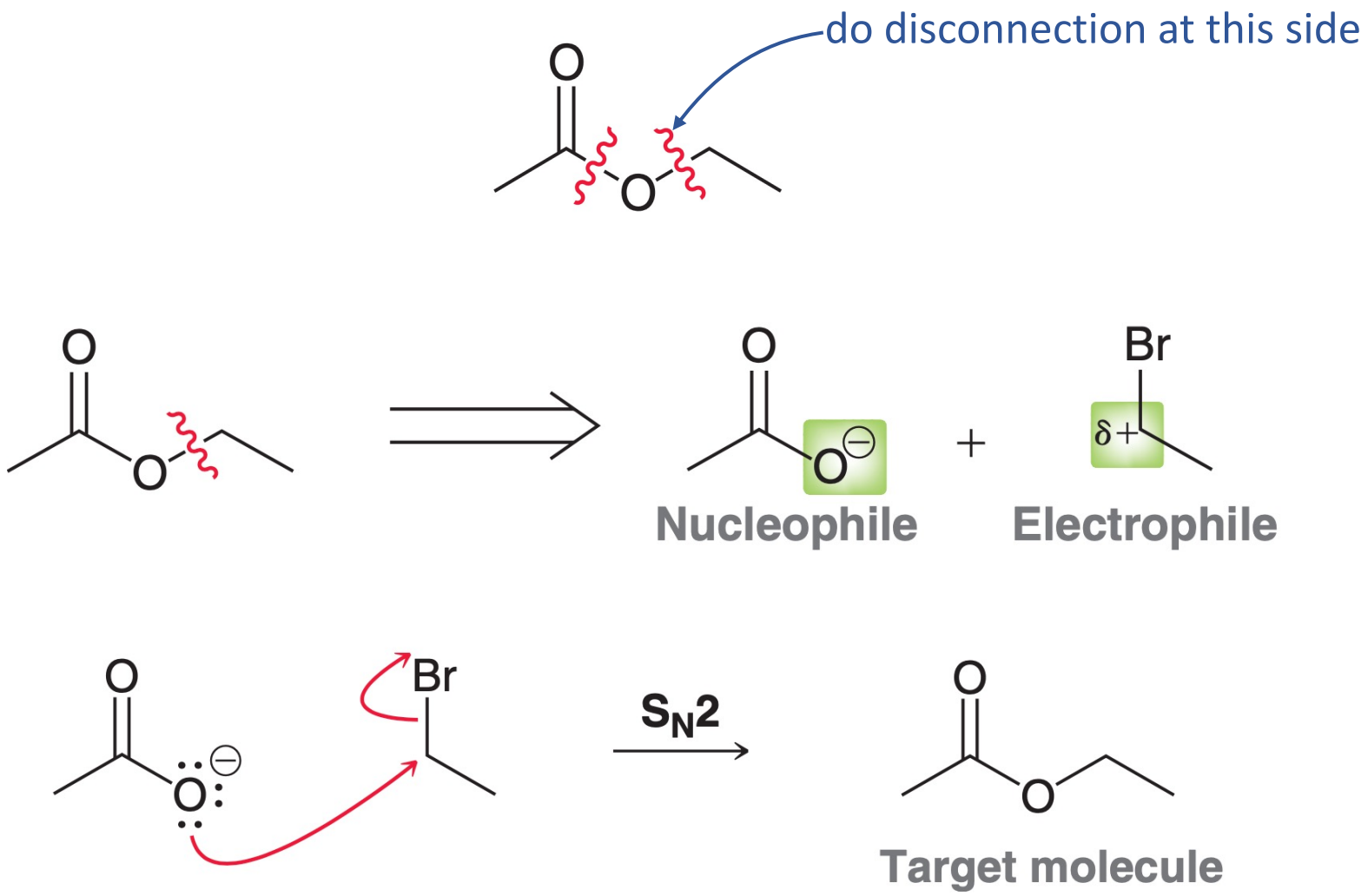
- Two methods

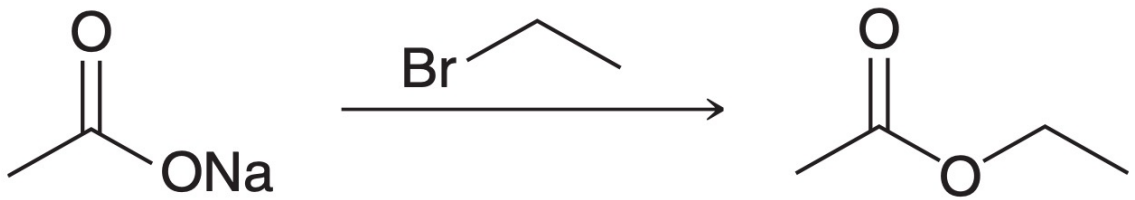

can be
made from
O
Br
+
NaOEt
An ether
An alkyl halide
An alkoxide ion


can be
made from
O
ONa
+
Br
An ether
An alkoxide ion
An alkyl halide

- Practice: provide a synthesis for the target molecule shown below, **starting with O compounds that contain no more than two carbon atoms**. Show your retrosynthetic analysis, and then provide a complete synthesis, showing all necessary reagents.




do disconnection at this side
O
O
O
O
Br
δ+
Nucleophile
Electrophile
O
O
Br
SN2
O
O
Target molecule


O
ONa
Br
O
O