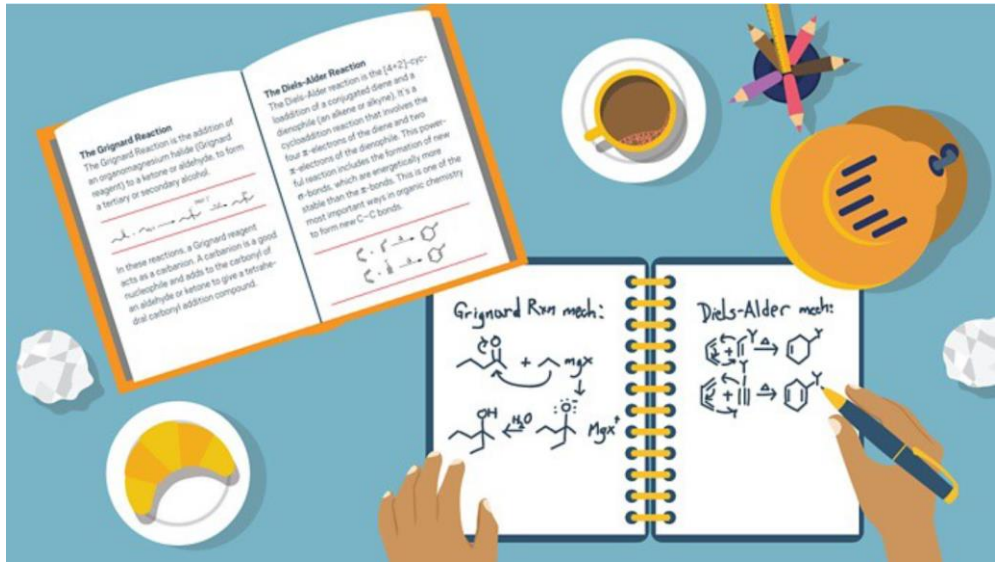
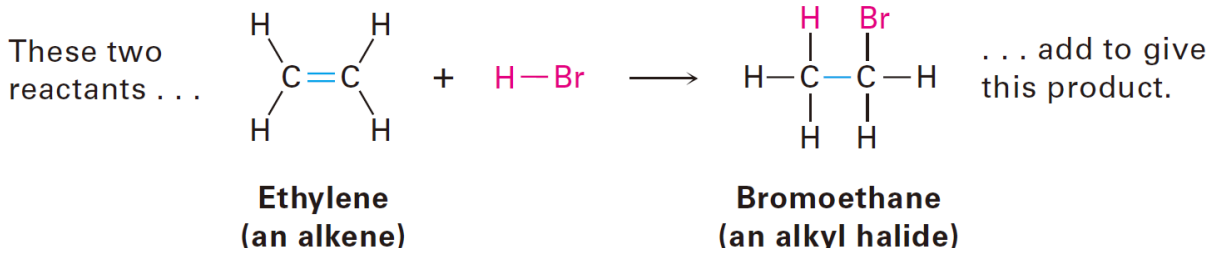

The Grignard Reaction
The Diels-Alder Reaction
Grignard Rxn mech:
Diels-Alder mech:

6
有机化学的反应类型

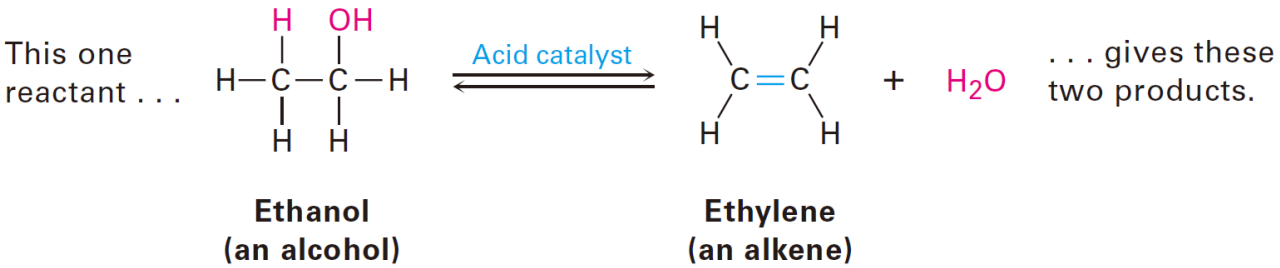
6.1 四种主要的反应类型

- 加成反应，消除反应，取代反应和重排反应。

* **Addition reactions** occur when two reactants add together to form a single product with no atoms "left over." An example that we'll be studying soon is the reaction of an alkene, such as ethylene, with HBr to yield an alkyl bromide.



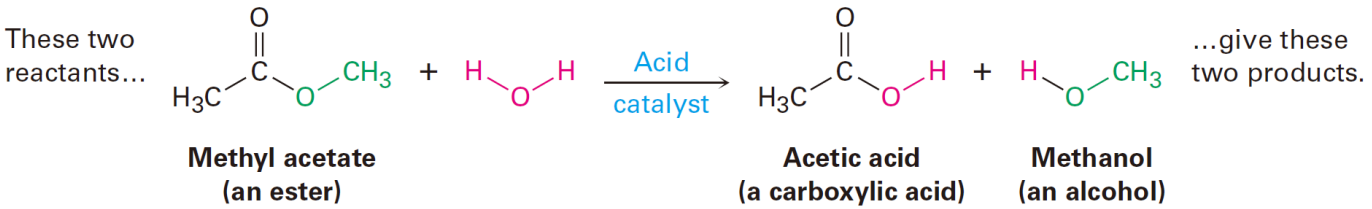
* **Elimination reactions** are, in a sense, the opposite of addition reactions. They occur when a single reactant splits into two products, often with formation of a small molecule such as water or HBr. An example is the acid-catalyzed reaction of an alcohol to yield water and an alkene.



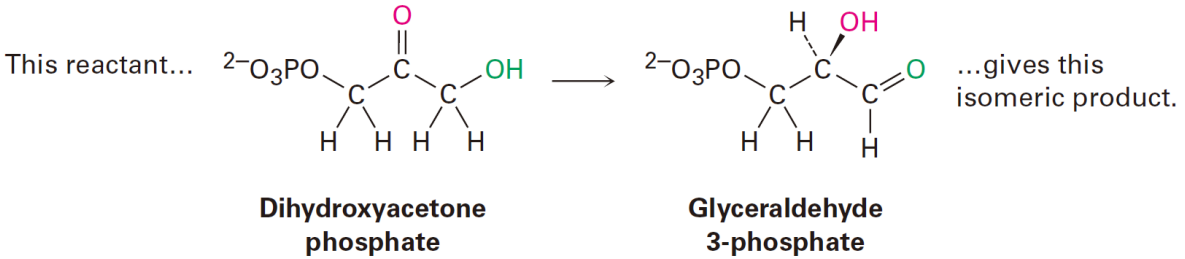
6.1 四种主要的反应类型

- 加成反应，消除反应，取代反应和重排反应。

* **Substitution reactions** occur when two reactants exchange parts to give two new products. An example is the reaction of an ester such as methyl acetate with water to yield a carboxylic acid plus an alcohol. Similar reactions occur in many biological pathways, including the metabolism of dietary fats.



* **Rearrangement reactions** occur when a single reactant undergoes a reorganization of bonds and atoms to yield an isomeric product. An example is the conversion of dihydroxyacetone phosphate into its constitutional isomer glyceraldehyde 3-phosphate, a step in the glycolysis pathway by which carbohydrates are metabolized.



6.1 四种主要的反应类型

- 课堂练习

Problem 6.1

Classify each of the following reactions as an addition, elimination, substitution, or rearrangement:

(a) $CH_3Br + KOH \rightarrow CH_3OH + KBr$

(b) $CH_3CH_2Br \rightarrow H_2C{=}CH_2 + HBr$

(c) $H_2C{=}CH_2 + H_2 \rightarrow CH_3CH_3$

6.2 反应机理

- 化学中，反应机理用来描述某一化学变化所经由的全部基元反应。虽然整个化学变化所发生的物质转变可能很明显，但为了探明这一过程的反应机理，常常需要实验来验证。 机理详细描述了每一步转化的过程，包括过渡态的形成，键的断裂和生成，以及各步的相对速率大小，等等
- 键的均裂和异裂；成键的两种方式。

键的断裂

Symmetrical bond-breaking (radical):
one bonding electron stays with each product.

Unsymmetrical bond-breaking (polar):
two bonding electrons stay with one product.

键的形成

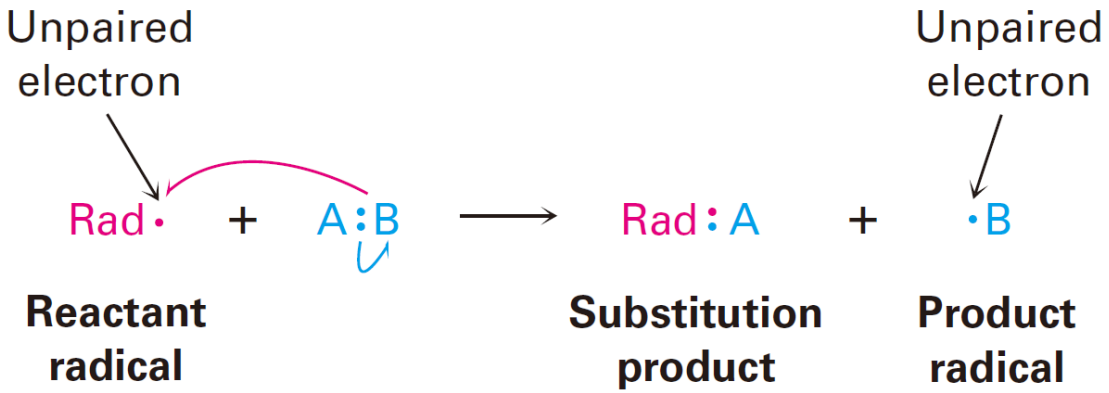
Symmetrical bond-making (radical):
one bonding electron is donated by each reactant.

Unsymmetrical bond-making (polar):
two bonding electrons are donated by one reactant.

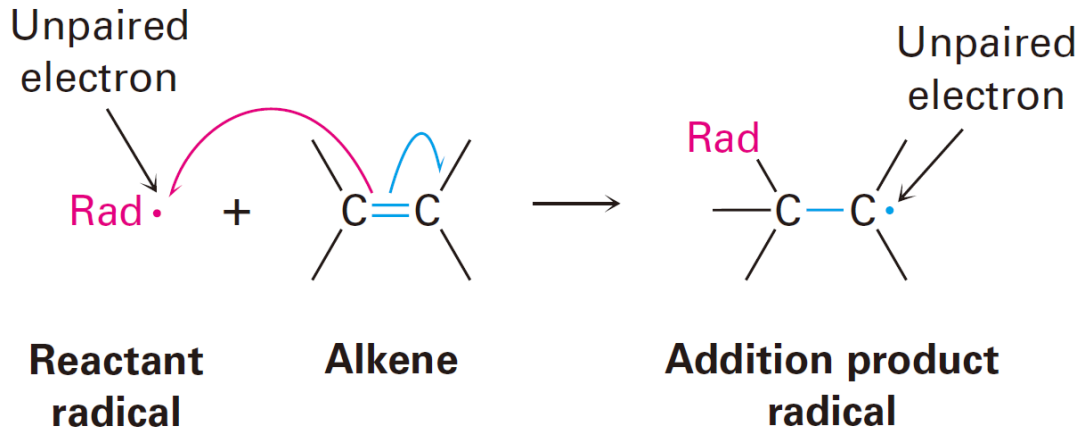
6.3 自由基反应

- 自由基，又称游离基，是指化合物的分子在光热等外界条件下，共价键发生均裂而形成的具有不成对电子的原子或基团。具有很强的反应活性。
- 自由基反应的分类：自由基取代反应和自由基加成反应。

自由基取代反应：

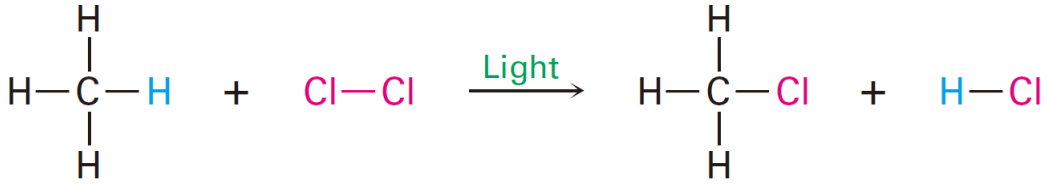


自由基加成反应：



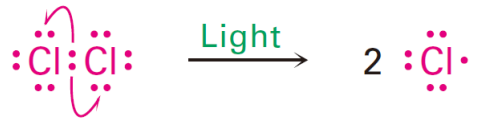
6.3 自由基反应

- 以甲烷的氯化为例

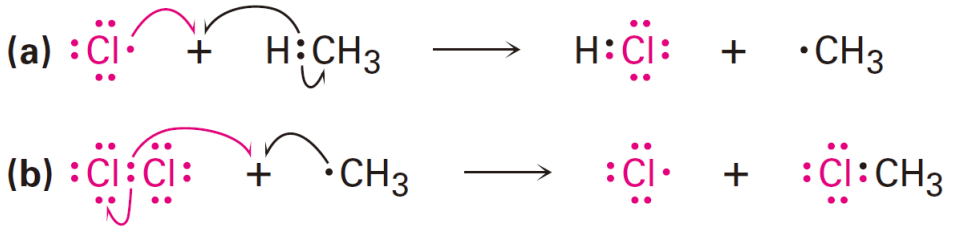


Methane **Chlorine** **Chloromethane**

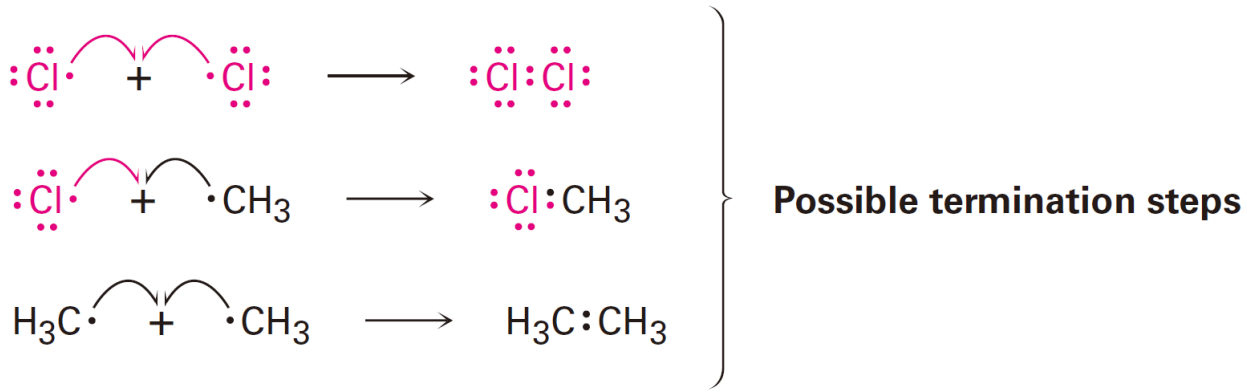
链引发：



链增长：

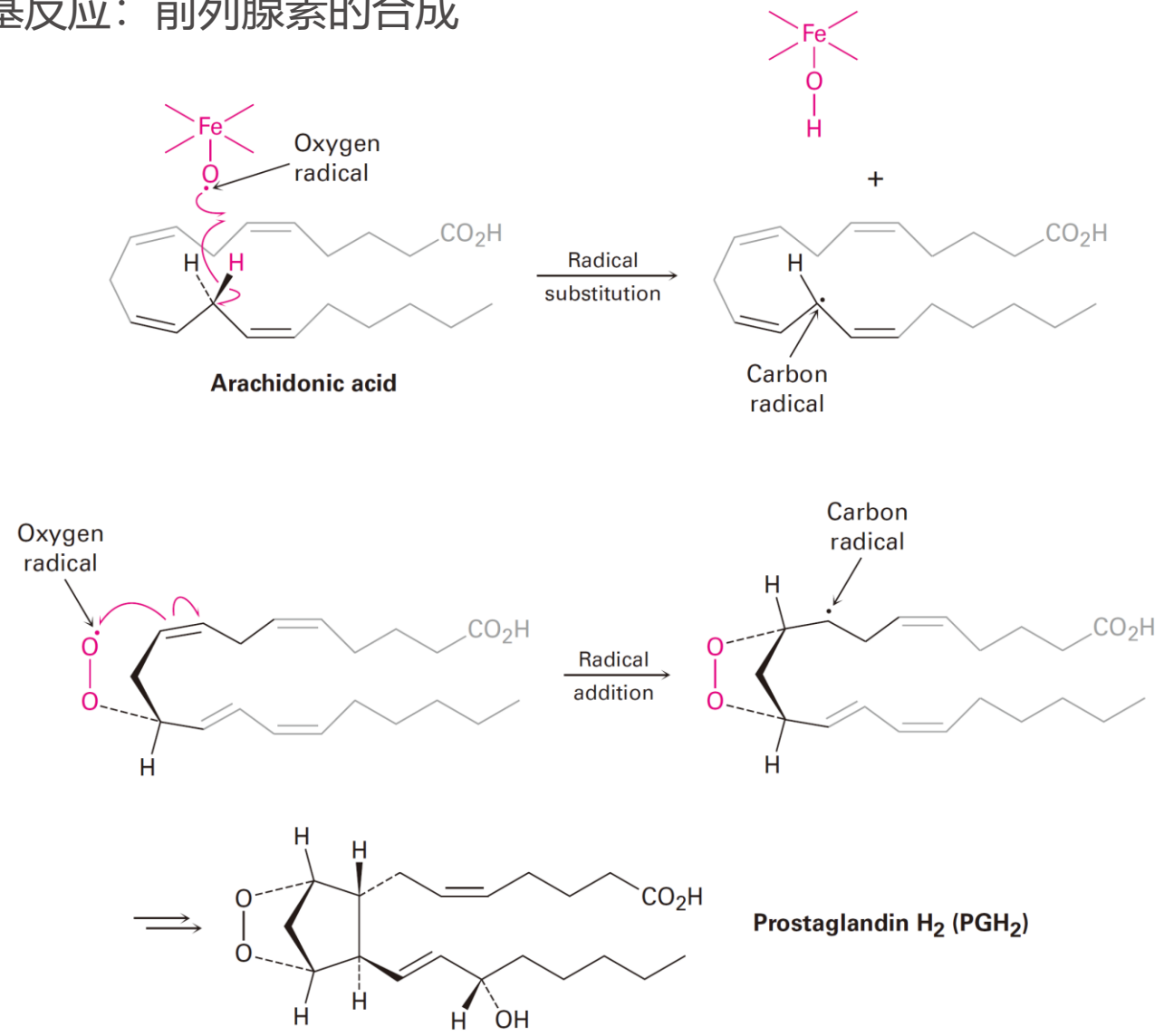


链终止：



6.3 自由基反应

- 生物合成中的自由基反应：前列腺素的合成



6.3 自由基反应

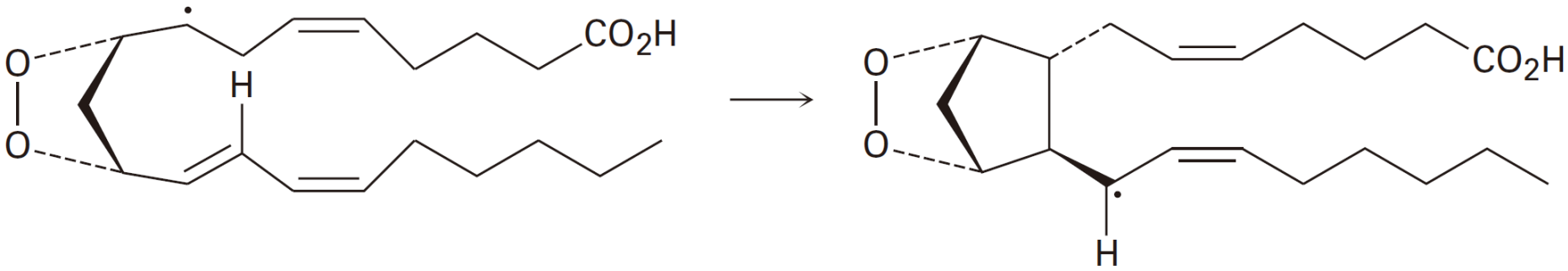
- 课堂练习

Problem 6.2

Radical chlorination of alkanes is not generally useful because mixtures of products often result when more than one kind of C—H bond is present in the substrate. Draw and name all monochloro substitution products $C_6H_{13}Cl$ you might obtain by reaction of 2-methylpentane with Cl_2.

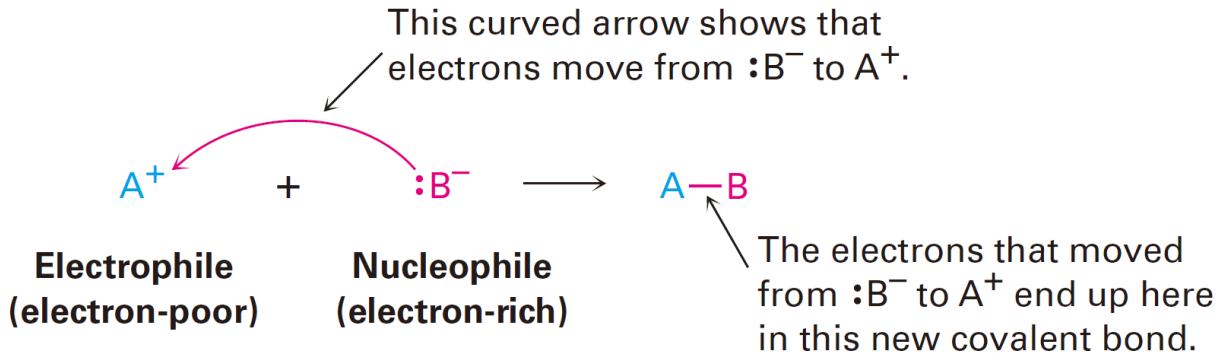
Problem 6.3

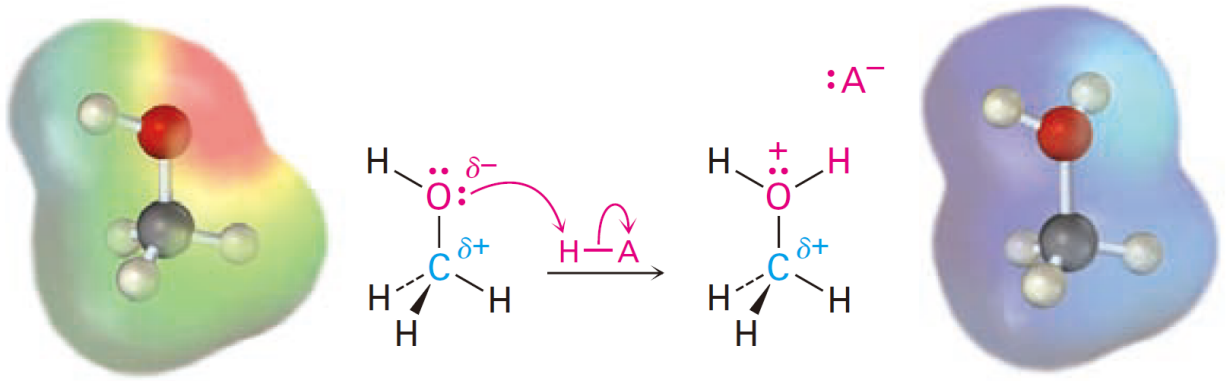
Using a curved fishhook arrow, propose a mechanism for formation of the cyclopentane ring of prostaglandin H_2.



6.4 极性反应

- 极性反应是分子中官能团的正极化中心和负极化中心之间的电吸引而形成一个新的化学键。



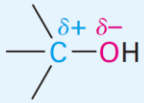
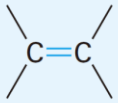
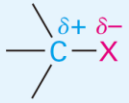
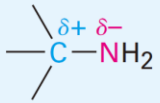
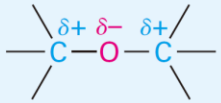
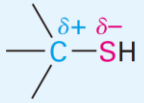
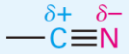
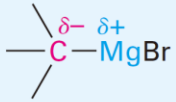
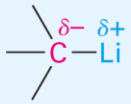


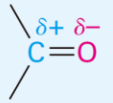
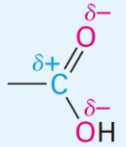
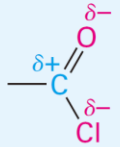
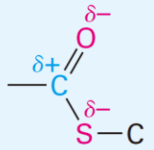
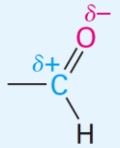
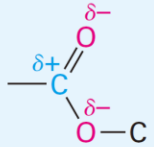
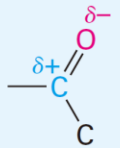
Methanol—weakly electron-poor carbon

Protonated methanol—strongly electron-poor carbon

6.4 极性反应

Table 6.1 Polarity Patterns in Some Common Functional Groups

Compound type	Functional group structure
Alcohol	
Alkene	
	Symmetrical, nonpolar
Alkyl halide	
Amine	
Ether	
Thiol	
Nitrile	
Grignard reagent	
Alkyllithium	

Compound type	Functional group structure
Carbonyl	
Carboxylic acid	
Carboxylic acid chloride	
Thioester	
Aldehyde	
Ester	
Ketone	

6.4 极性反应

- 一些亲核试剂和亲电试剂

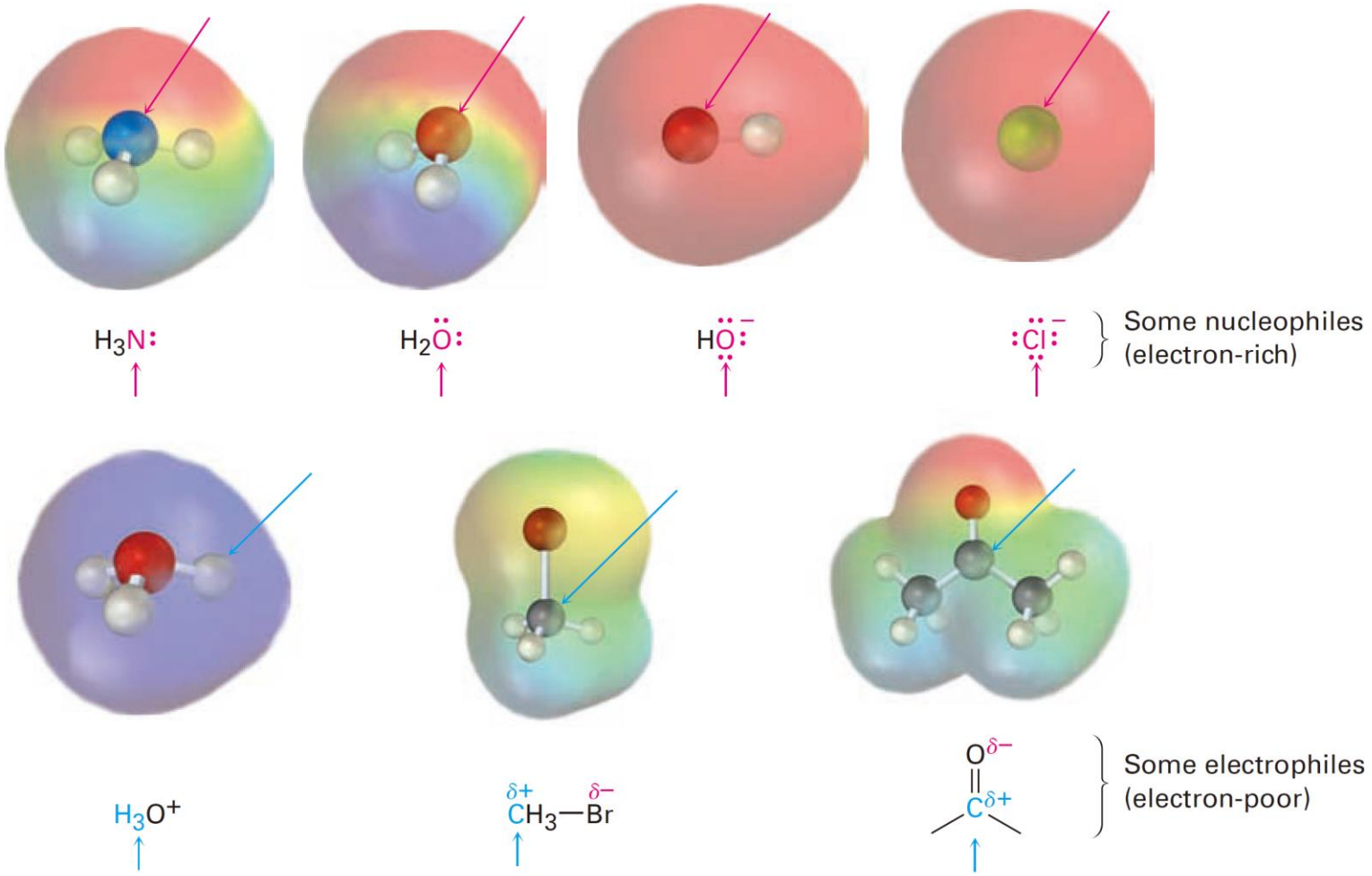


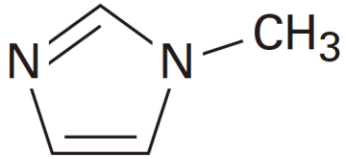
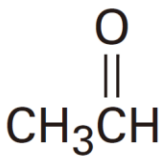
Figure 6.1 Some nucleophiles and electrophiles. Electrostatic potential maps identify the nucleophilic **(negative)** and electrophilic **(positive)** atoms.

6.4 极性反应

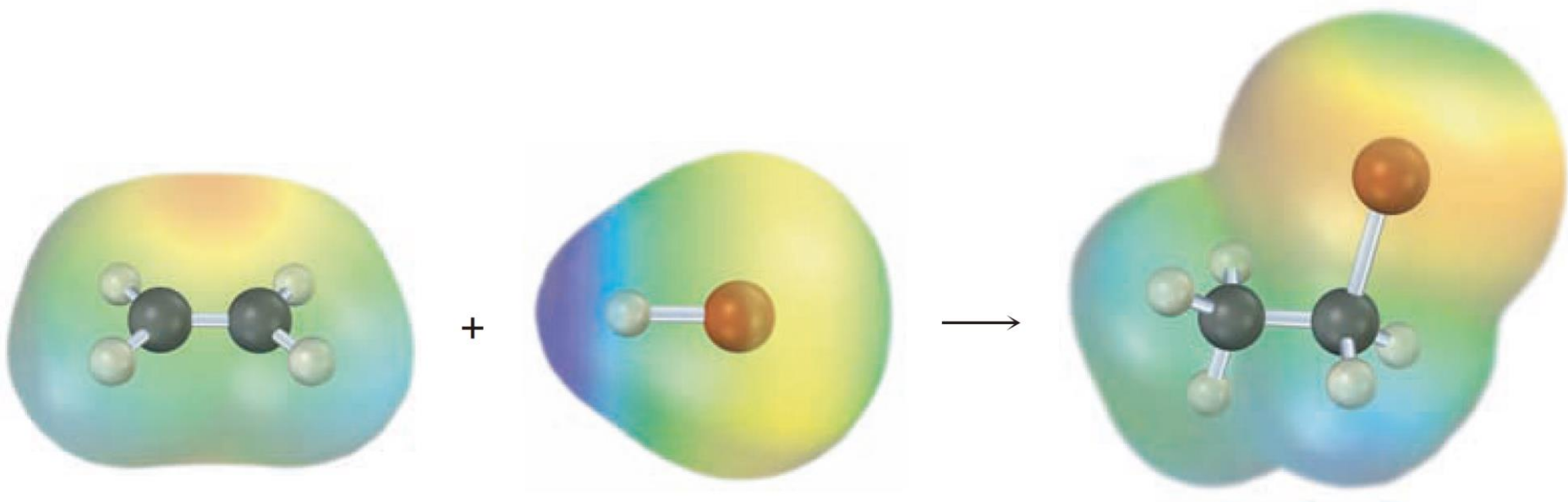
- 课堂练习

Problem 6.4

Which of the following species are likely to be nucleophiles and which electrophiles? Which might be both?

(a) CH_3Cl **(b)** CH_3S^- **(c)**  **(d)** 

6.5 溴化氢对乙烯的加成反应



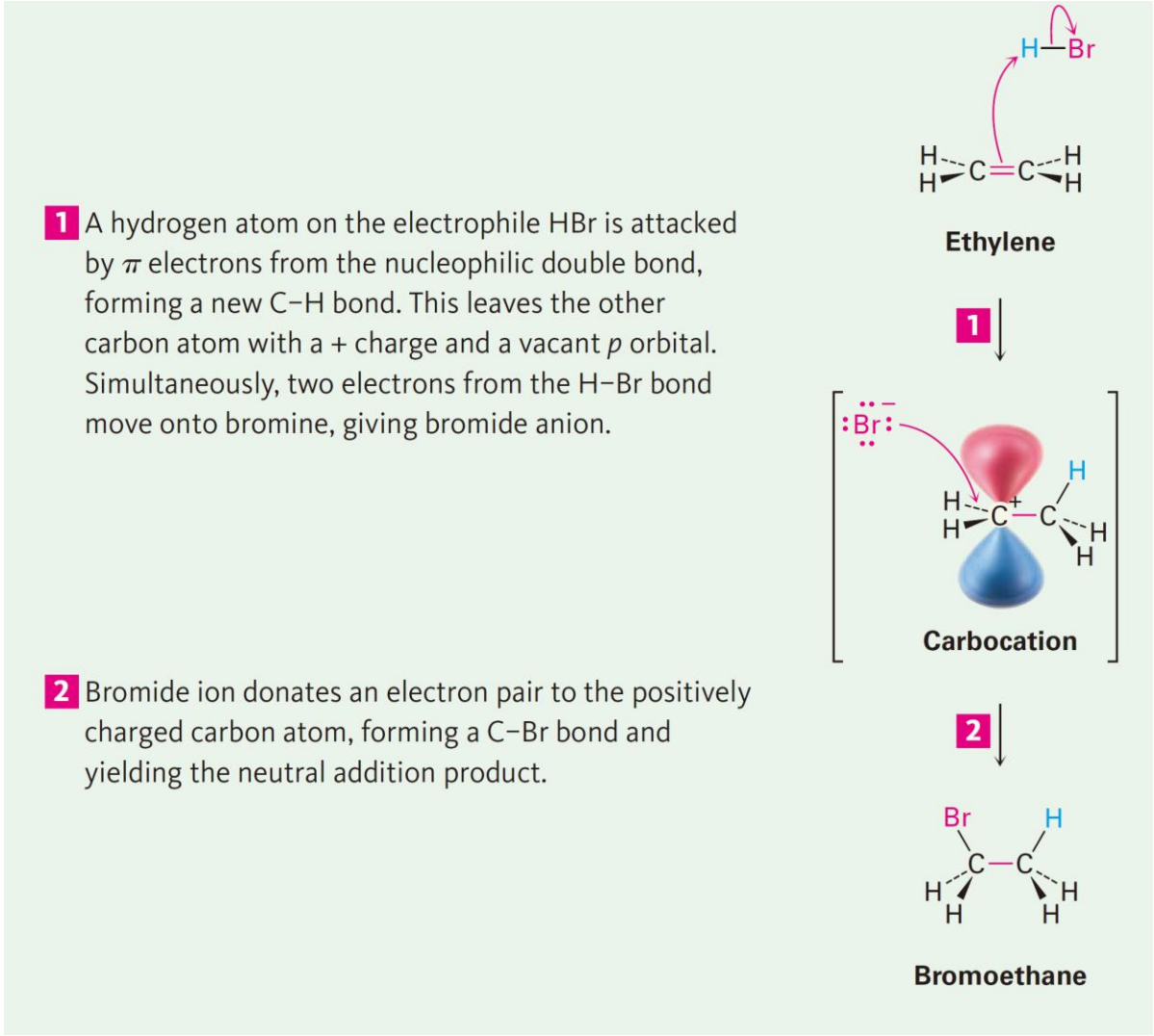
Ethylene
(nucleophile)

Hydrogen bromide
(electrophile)

Bromoethane

6.5 溴化氢对乙烯的加成反应

- 碳正离子(Carbenium ion)是一种带正电的不稳定的有机物。与自由基一样，是一个活泼的中间体，有一个正电荷，最外层有6个电子。经典的碳正离子是平面结构。



1 A hydrogen atom on the electrophile HBr is attacked by π electrons from the nucleophilic double bond, forming a new C–H bond. This leaves the other carbon atom with a + charge and a vacant *p* orbital. Simultaneously, two electrons from the H–Br bond move onto bromine, giving bromide anion.

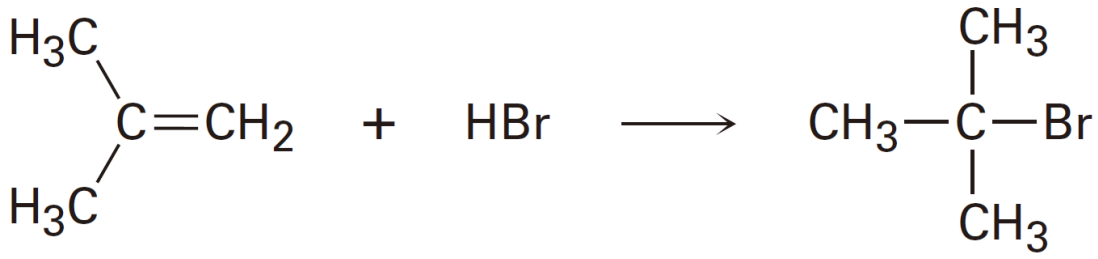
2 Bromide ion donates an electron pair to the positively charged carbon atom, forming a C–Br bond and yielding the neutral addition product.

6.5 溴化氢对乙烯的加成反应

- 课堂练习

Problem 6.7

Reaction of HBr with 2-methylpropene yields 2-bromo-2-methylpropane. What is the structure of the carbocation formed during the reaction? Show the mechanism of the reaction.



2-Methylpropene **2-Bromo-2-methylpropane**

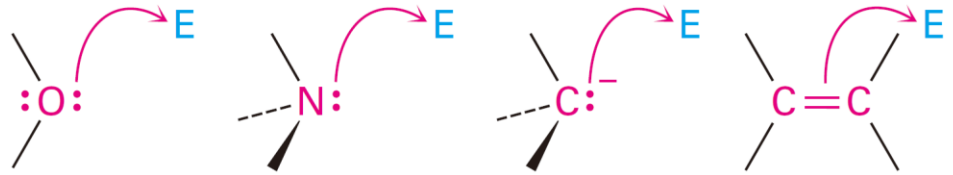
6.6 反应机理的画法

- 规则一：箭头的方向是电子的去向

RULE 1

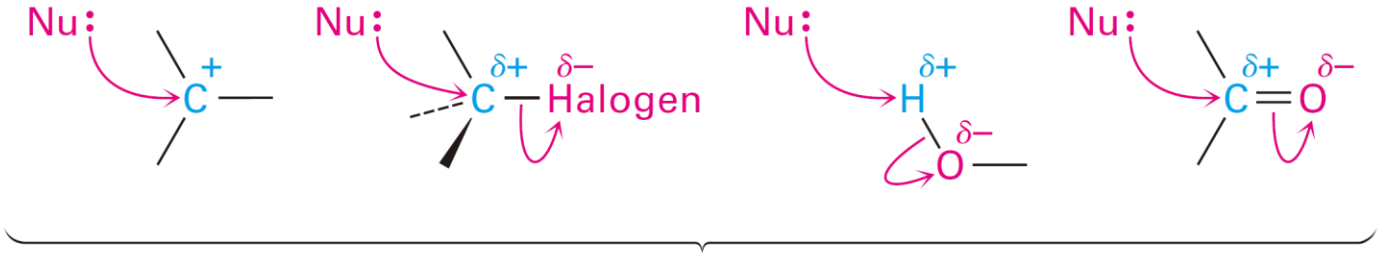
Electrons move *from* a nucleophilic source (Nu: or Nu:$^-$) *to* an electrophilic sink (E or E$^+$). The nucleophilic source must have an electron pair available, usually either as a lone pair or in a multiple bond. For example:

Electrons usually flow *from* one of these nucleophiles.



The electrophilic sink must be able to accept an electron pair, usually because it has either a positively charged atom or a positively polarized atom in a functional group. For example:

Electrons usually flow *to* one of these electrophiles.

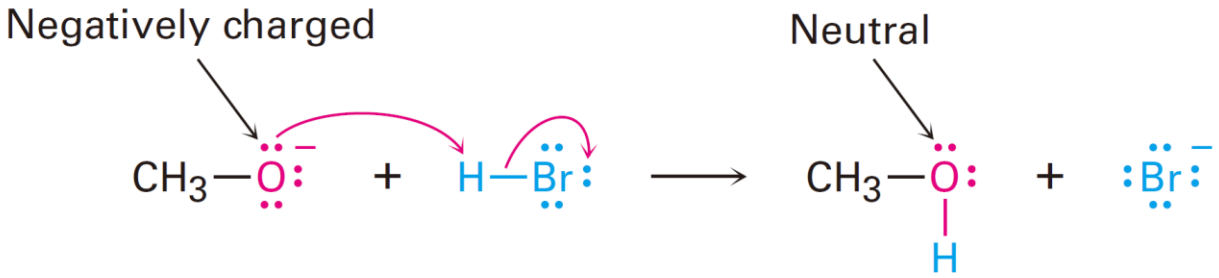


6.6 反应机理的画法

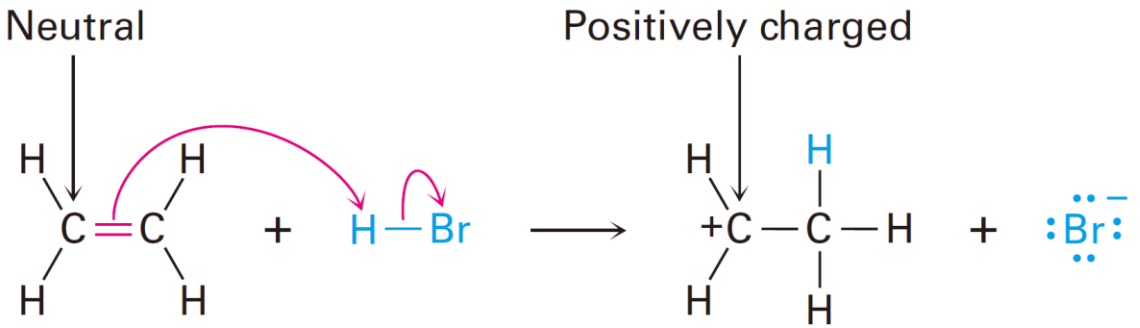
- 规则二：亲核试剂可以是带负电的基团也可以是中性的

RULE 2

The nucleophile can be either negatively charged or neutral. If the nucleophile is negatively charged, the atom that donates an electron pair becomes neutral. For example:



If the nucleophile is neutral, the atom that donates the electron pair acquires a positive charge. For example:

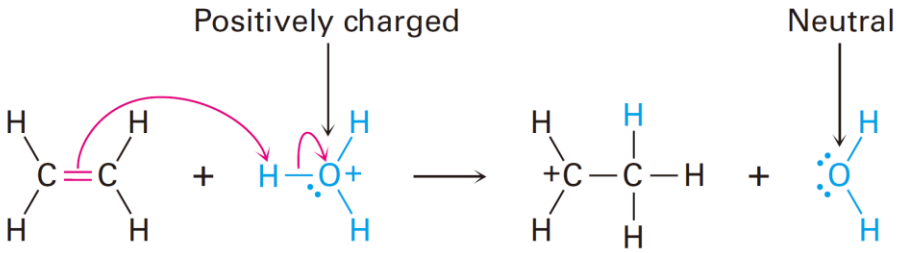


6.6 反应机理的画法

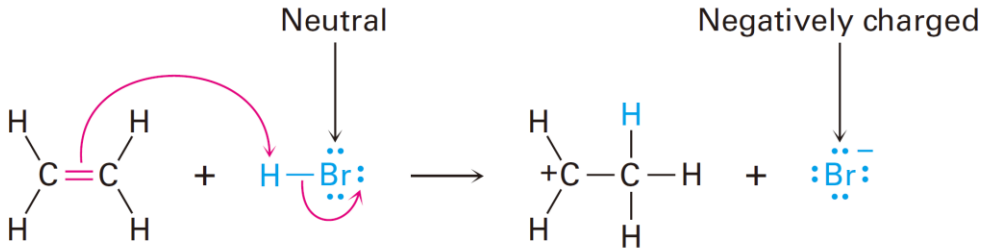
- 规则三：亲电试剂可以是带正电的基团也可以是中性的

RULE 3

The electrophile can be either positively charged or neutral. If the electrophile is positively charged, the atom bearing that charge becomes neutral after accepting an electron pair. For example:



If the electrophile is neutral, the atom that ultimately accepts the electron pair acquires a negative charge. For this to happen, however, the negative charge must be stabilized by being on an electronegative atom such as oxygen, nitrogen, or a halogen. Carbon and hydrogen do not typically stabilize a negative charge. For example:

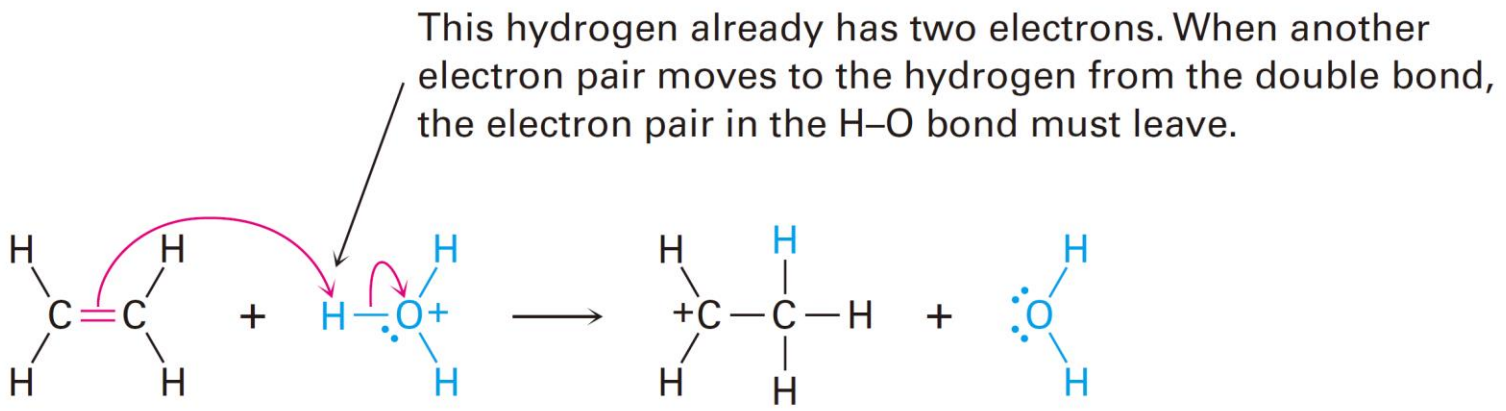


6.6 反应机理的画法

- 规则四：必须符合八隅规则

RULE 4

The octet rule must be followed. That is, no second-row atom can be left with ten electrons (or four for hydrogen). If an electron pair moves *to* an atom that already has an octet (or two for hydrogen), another electron pair must simultaneously move *from* that atom to maintain the octet. When two electrons move from the C=C bond of ethylene to the hydrogen atom of H_3O^+, for instance, two electrons must leave that hydrogen. This means that the H–O bond must break and the electrons must stay with the oxygen, giving neutral water.



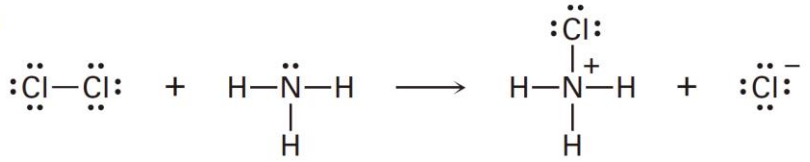
6.6 反应机理的画法

- 课堂练习

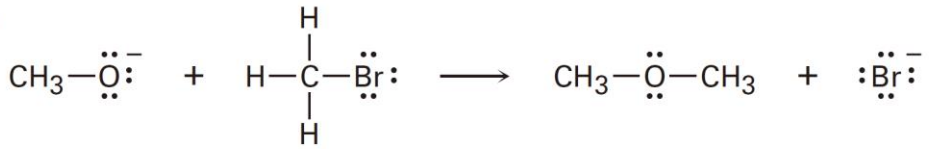
Problem 6.8

Add curved arrows to the following polar reactions to indicate the flow of electrons in each:

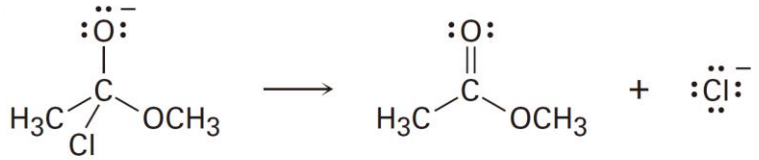
(a)



(b)

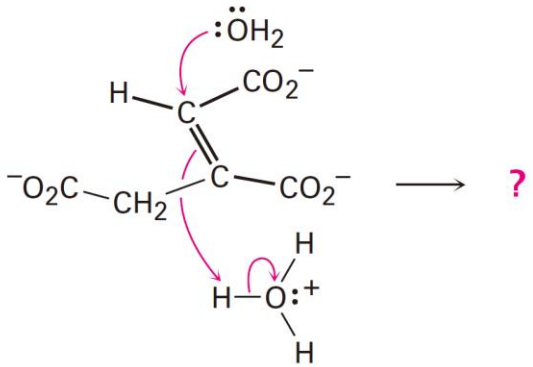


(c)



Problem 6.9

Predict the products of the following polar reaction, a step in the citric acid cycle for food metabolism, by interpreting the flow of electrons indicated by the curved arrows:



6.7 化学反应热力学

- 化学热力学的核心理论有三个：所有的物质都具有能量，能量是守恒的，各种能量可以相互转化；事物总是自发地趋向于平衡态；处于平衡态的物质系统可用几个可观测量描述。

Table 6.2 Explanation of Thermodynamic Quantities: $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

Term	Name	Explanation
ΔG°	Gibbs free-energy change	The energy difference between reactants and products. When ΔG° is negative, the reaction is **exergonic**, has a favorable equilibrium constant, and can occur spontaneously. When ΔG° is positive, the reaction is **endergonic**, has a unfavorable equilibrium constant, and cannot occur spontaneously.
ΔH°	Enthalpy change	The heat of reaction, or difference in strength between the bonds broken in a reaction and the bonds formed. When ΔH° is negative, the reaction releases heat and is **exothermic**. When ΔH° is positive, the reaction absorbs heat and is **endothermic**.
ΔS°	Entropy change	The change in molecular randomness during a reaction. When ΔS° is negative, randomness decreases. When ΔS° is positive, randomness increases.

6.7 化学反应热力学

- 化学平衡是指在宏观条件一定的可逆反应中，化学反应正逆反应速率相等，反应物和生成物各组分浓度不再改变的状态。

定义：

$$aA + bB \rightleftharpoons cC + dD$$

$$K_{eq} = \frac{[C]^c\ [D]^d}{[A]^a\ [B]^b}$$

例如：

$$H_2C{=}CH_2 + HBr \rightleftharpoons CH_3CH_2Br$$

$$K_{eq} = \frac{[CH_3CH_2Br]}{[H_2C{=}CH_2]\,[HBr]} = 7.1 \times 10^7$$

6.7 化学反应热力学

$$\Delta G^\circ = -RT \ln K_{eq} \qquad \text{or} \qquad K_{eq} = e^{-\Delta G^\circ/RT}$$

where $R = 8.314\ \text{J/(K} \cdot \text{mol)} = 1.987\ \text{cal/(K} \cdot \text{mol)}$

T = Kelvin temperature

$e = 2.718$

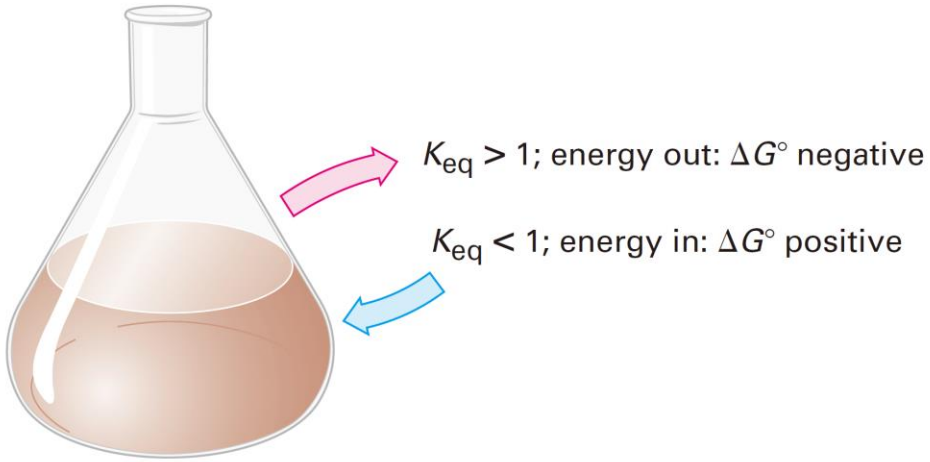
$\ln K_{eq}$ = natural logarithm of K_{eq}

For example, the reaction of ethylene with HBr has $K_{eq} = 7.1 \times 10^7$, so $\Delta G^\circ = -44.8$ kJ/mol (-10.7 kcal/mol) at 298 K:

$$K_{eq} = 7.1 \times 10^7 \qquad \text{and} \qquad \ln K_{eq} = 18.08$$

$$\Delta G^\circ = -RT \ln K_{eq} = -[8.314\ \text{J/(K} \cdot \text{mol)}]\ (298\ \text{K})\ (18.08)$$

$$= -44{,}800\ \text{J/mol} = -44.8\ \text{kJ/mol}$$



6.7 化学反应热力学

- 课堂练习

Problem 6.10

Which reaction is more energetically favored, one with $\Delta G° = -44$ kJ/mol or one with $\Delta G° = +44$ kJ/mol?

Problem 6.11

Which reaction is likely to be more exergonic, one with $K_{eq} = 1000$ or one with $K_{eq} = 0.001$?

6.8 键的解离能

- 键解离能是指断裂或形成分子中某一个键所消耗或放出的能量。键解离能是代表着此共价键牢固程度的一种物理量，键解离能越大，此共价键越稳定。

We've just seen that heat is released (negative ΔH) when a bond is formed because the products are more stable and have stronger bonds than the reactants. Conversely, heat is absorbed (positive ΔH) when a bond is broken because the products are less stable and have weaker bonds than the reactants. The amount of energy needed to break a given bond to produce two radical fragments when the molecule is in the gas phase at 25 °C is a quantity called *bond strength*, or **bond dissociation energy (*D*)**.

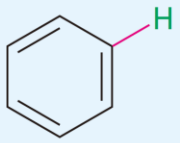
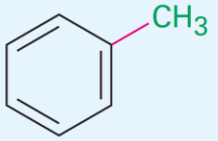
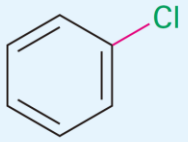
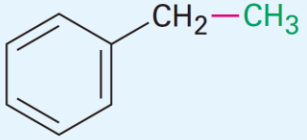
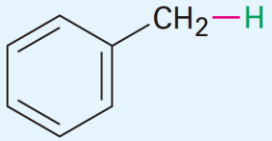
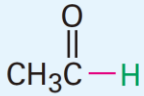
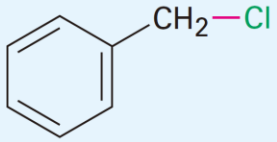
$$A:B \xrightarrow[\text{energy}]{\text{Bond dissociation}} A\cdot + \cdot B$$

Each specific bond has its own characteristic strength, and extensive tables of data are available. For example, a C–H bond in methane has a bond dissociation energy D = 439.3 kJ/mol (105.0 kcal/mol), meaning that 439.3 kJ/mol must be added to break a C–H bond of methane to give the two radical fragments $\cdot CH_3$ and ·H. Conversely, 439.3 kJ/mol of energy is released when a methyl radical and a hydrogen atom combine to form methane. Table 6.3 lists some other bond strengths.

6.8 键的解离能

- 一些化学键的解离能

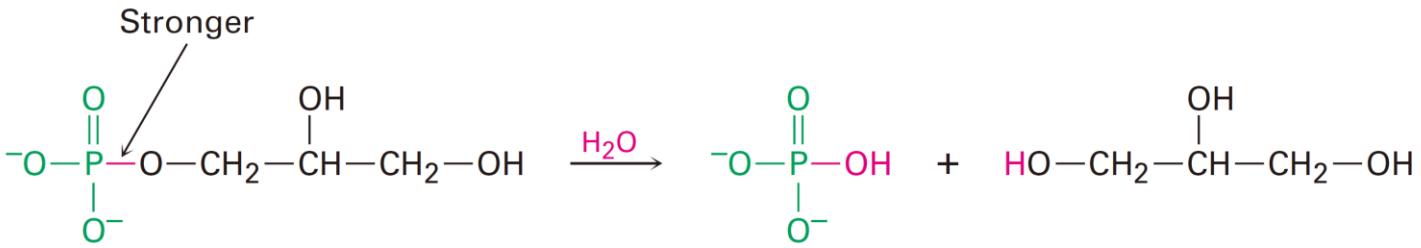
Table 6.3 Some Bond Dissociation Energies, *D*

Bond	*D* (kJ/mol)	Bond	*D* (kJ/mol)	Bond	*D* (kJ/mol)
H—H	436	$(CH_3)_3C$—I	227	$(CH_3)_2CH$—CH_3	369
H—F	570	H_2C=CH—H	464	$(CH_3)_3C$—CH_3	363
H—Cl	431	H_2C=CH—Cl	396	H_2C=CH—CH_3	426
H—Br	366	H_2C=$CHCH_2$—H	369	H_2C=$CHCH_2$—CH_3	318
H—I	298	H_2C=$CHCH_2$—Cl	298	H_2C=CH_2	728
Cl—Cl	242		472		427
Br—Br	194				
I—I	152				
CH_3—H	439		400		325
CH_3—Cl	350				
CH_3—Br	294				
CH_3—I	239		375		374
CH_3—OH	385				
CH_3—NH_2	386				
C_2H_5—H	421		300	HO—H	497
C_2H_5—Cl	352			HO—OH	211

6.8 键的解离能

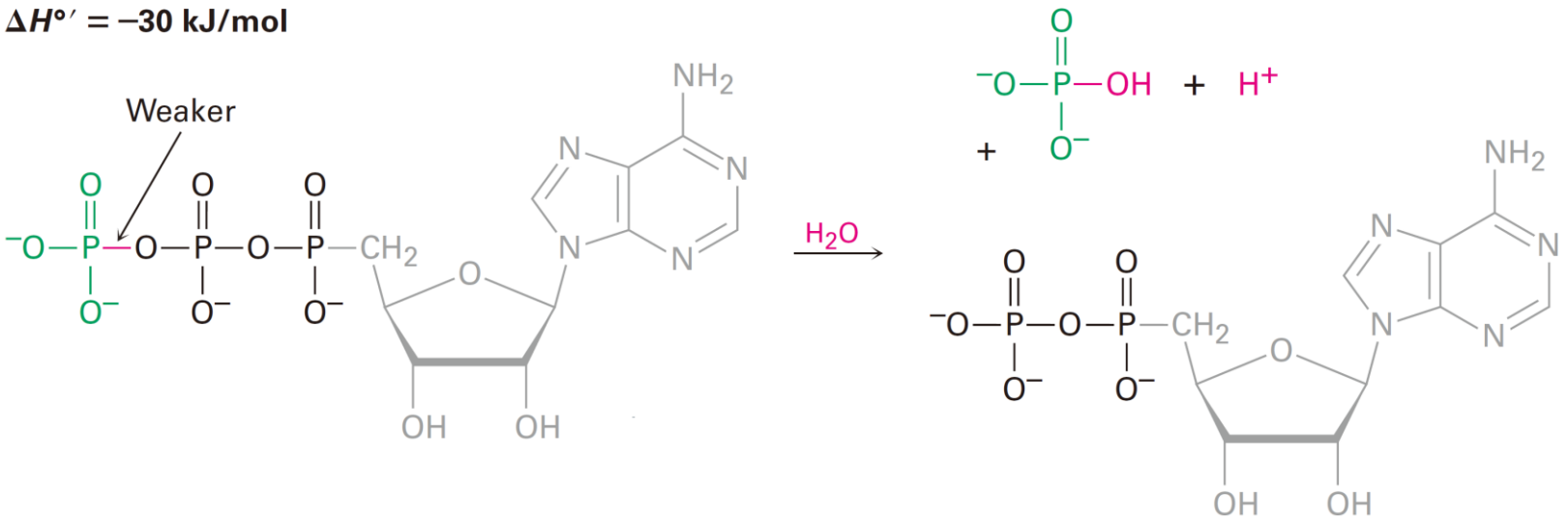
- 键能为生物体系提供能量

$\Delta H^{\circ\prime} = -9$ kJ/mol



Glycerol 3-phosphate **Glycerol**

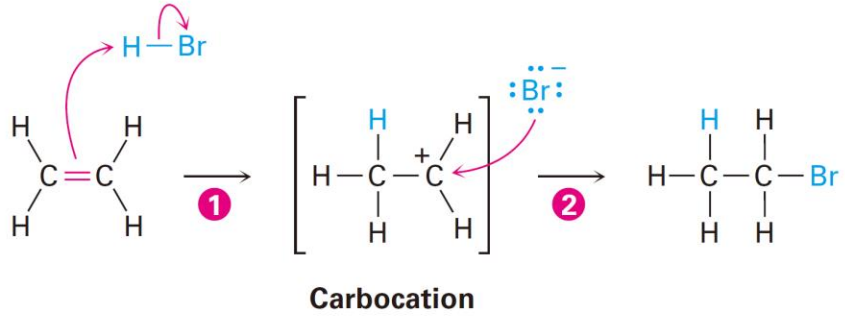
$\Delta H^{\circ\prime} = -30$ kJ/mol

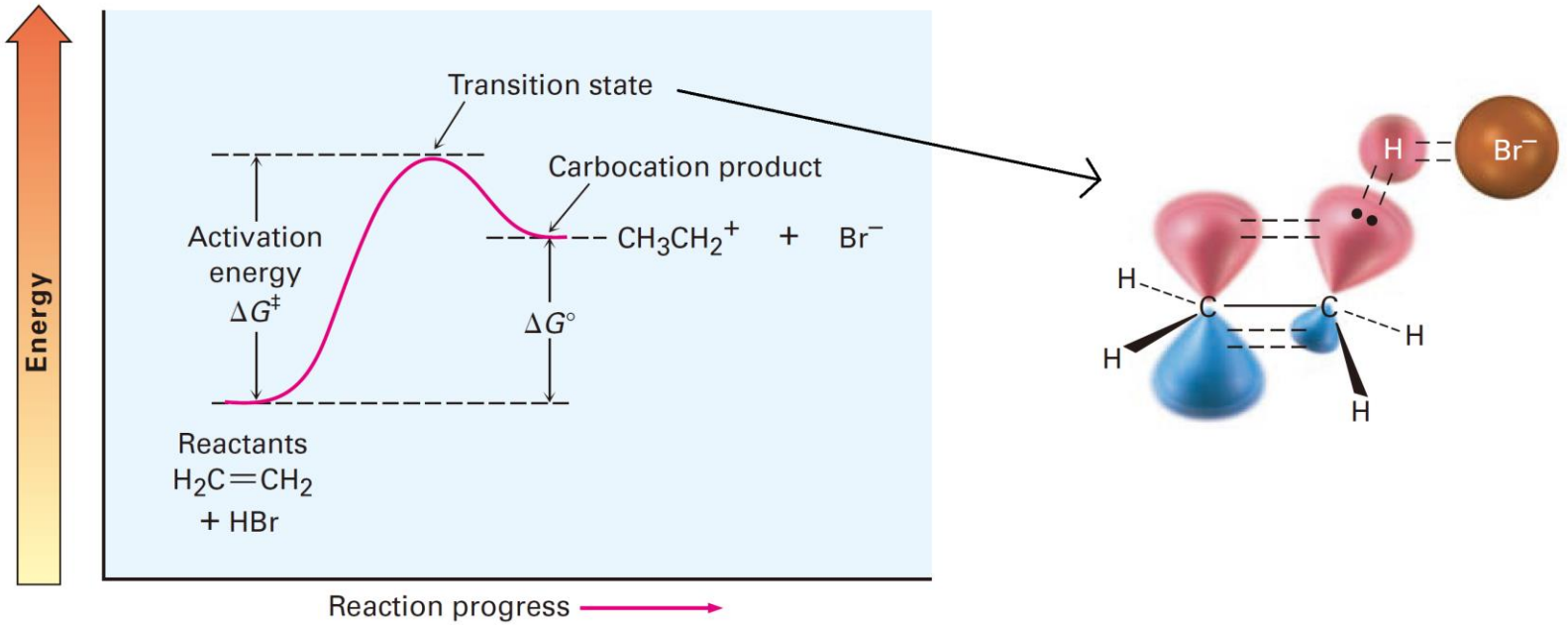


Adenosine triphosphate (ATP) **Adenosine diphosphate (ADP)**

6.9 过渡态理论

- 过渡态理论即活化络合物理论(transition-state theory)。以量子力学对反应过程中的能量变化的研究为依据，认为从反应物到生成物之间形成了势能较高的活化络合物，活化络合物所处的状态叫过渡态。





6.9 过渡态理论

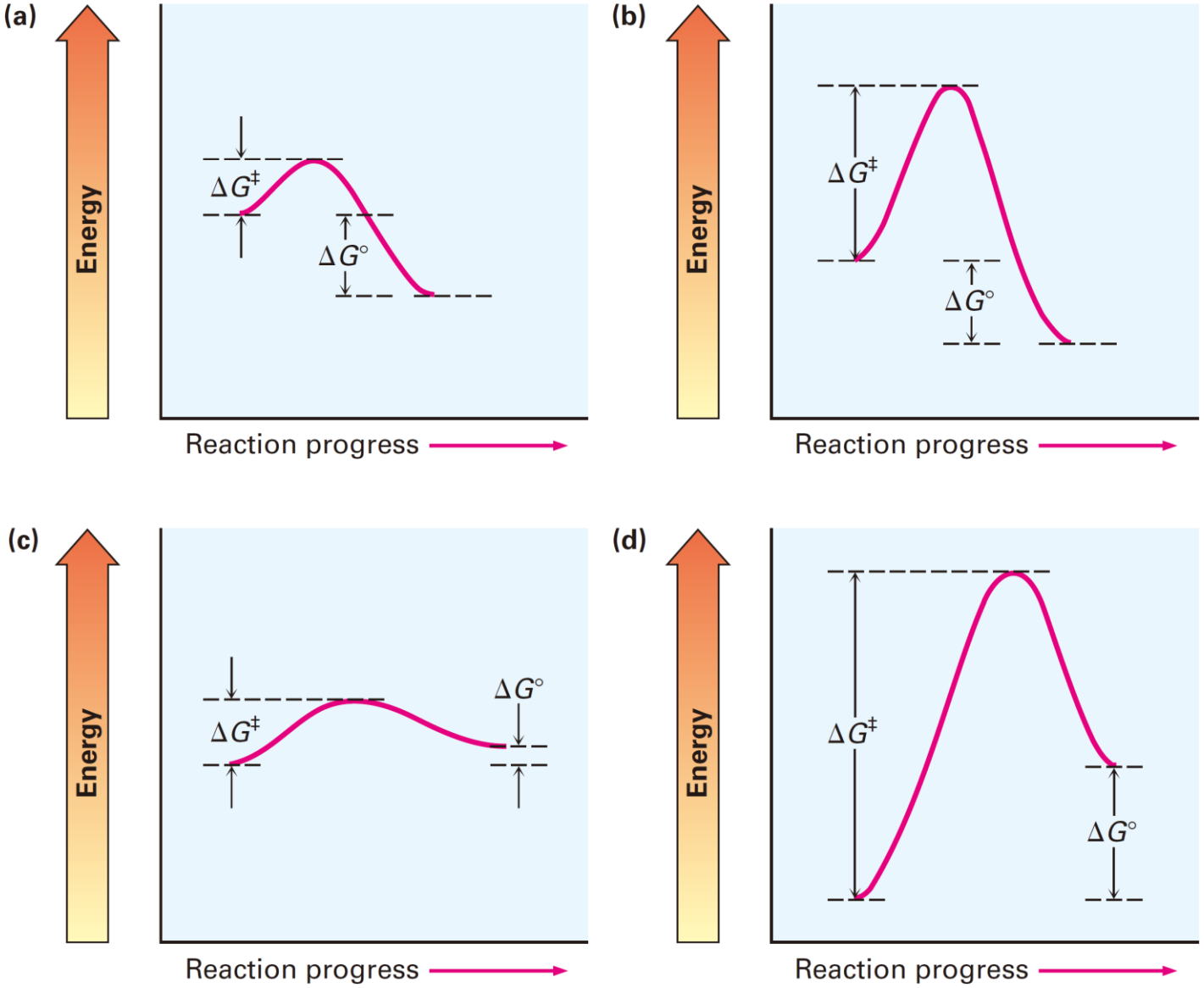
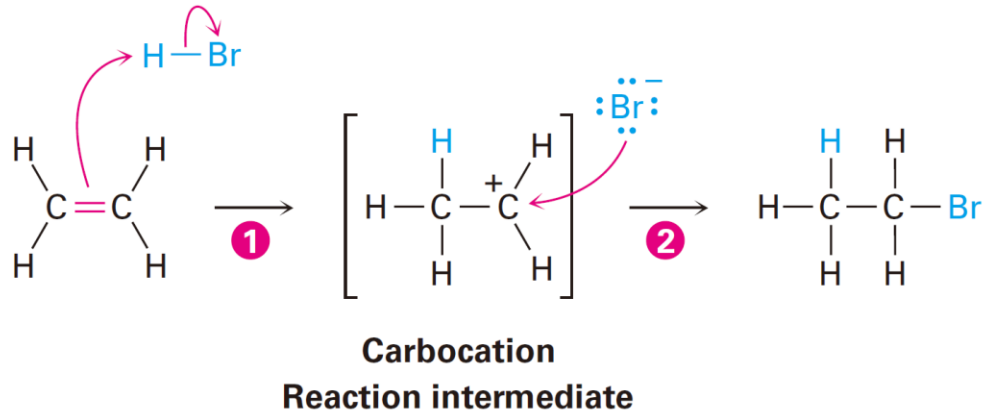
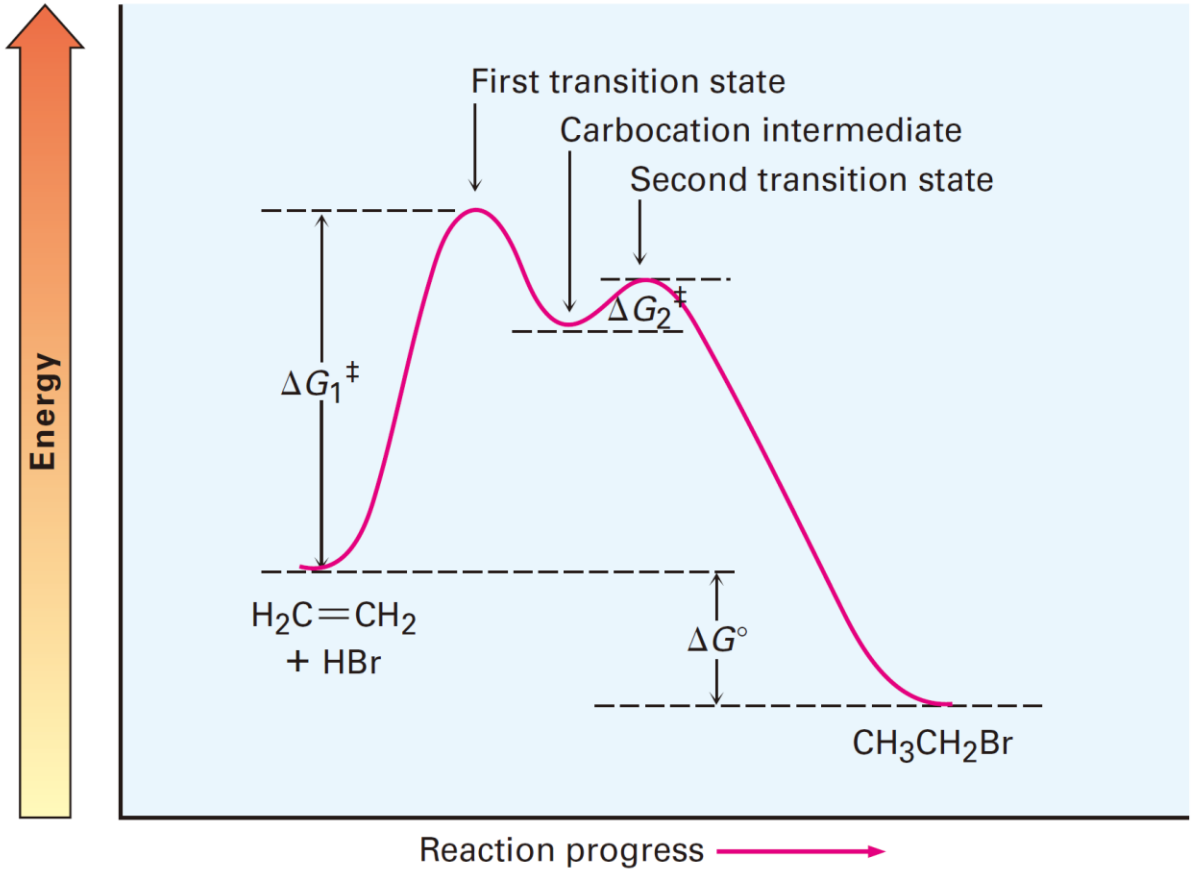


Figure 6.6 Some hypothetical energy diagrams: **(a)** a fast exergonic reaction (small $\Delta G^{\ddagger}$, negative ΔG°); **(b)** a slow exergonic reaction (large $\Delta G^{\ddagger}$, negative ΔG°); **(c)** a fast endergonic reaction (small $\Delta G^{\ddagger}$, small positive ΔG°); **(d)** a slow endergonic reaction (large $\Delta G^{\ddagger}$, positive ΔG°).

6.10 反应中间体

- 化学动力学中，反应中间体指在一个非基元反应中反应物转化为产物过程出现的中间物种。通常，反应中间体的寿命很短，浓度相对反应物和产物也很低，因此不出现在最终产物中。

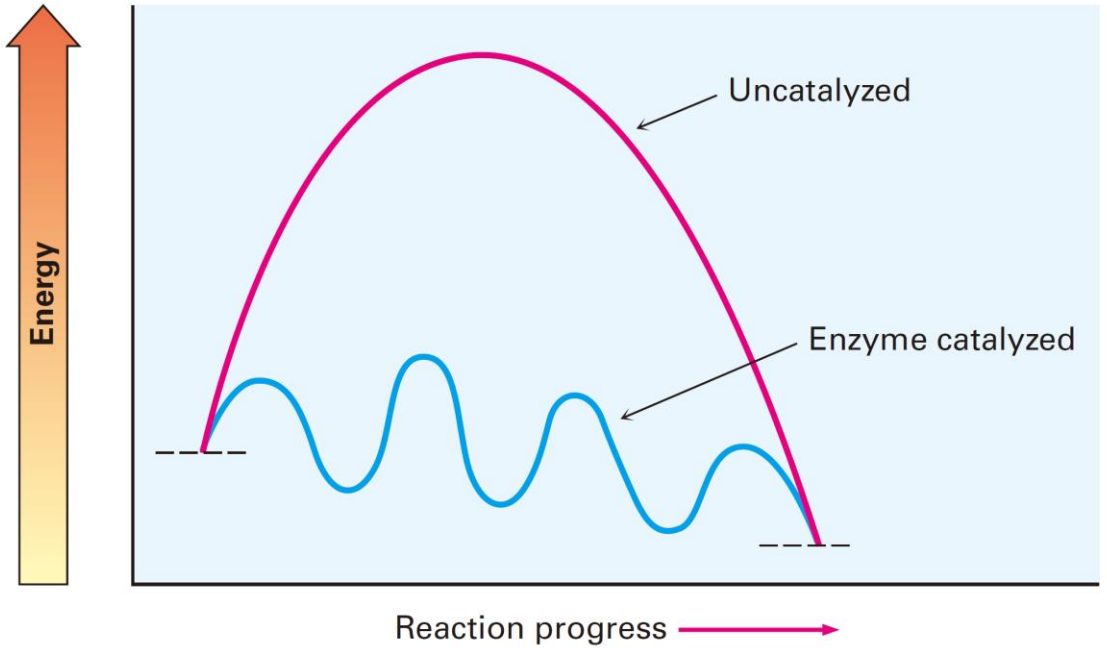




6.10 反应中间体

- 生物体中的酶催化反应

The biological reactions that take place in living organisms have the same energy requirements as reactions that take place in the laboratory and can be described in similar ways. They are, however, constrained by the fact that they must have low enough activation energies to occur at moderate temperatures, and they must release energy in relatively small amounts to avoid overheating the organism. These constraints are generally met through the use of large, structurally complex, enzyme catalysts that change the mechanism of a reaction to an alternative pathway that proceeds through a series of small steps rather than one or two large steps. Thus, a typical energy diagram for a biological reaction might look like that in **Figure 6.8**.



作业

- 6.35-6.43