Mechanism of Organic Reactions

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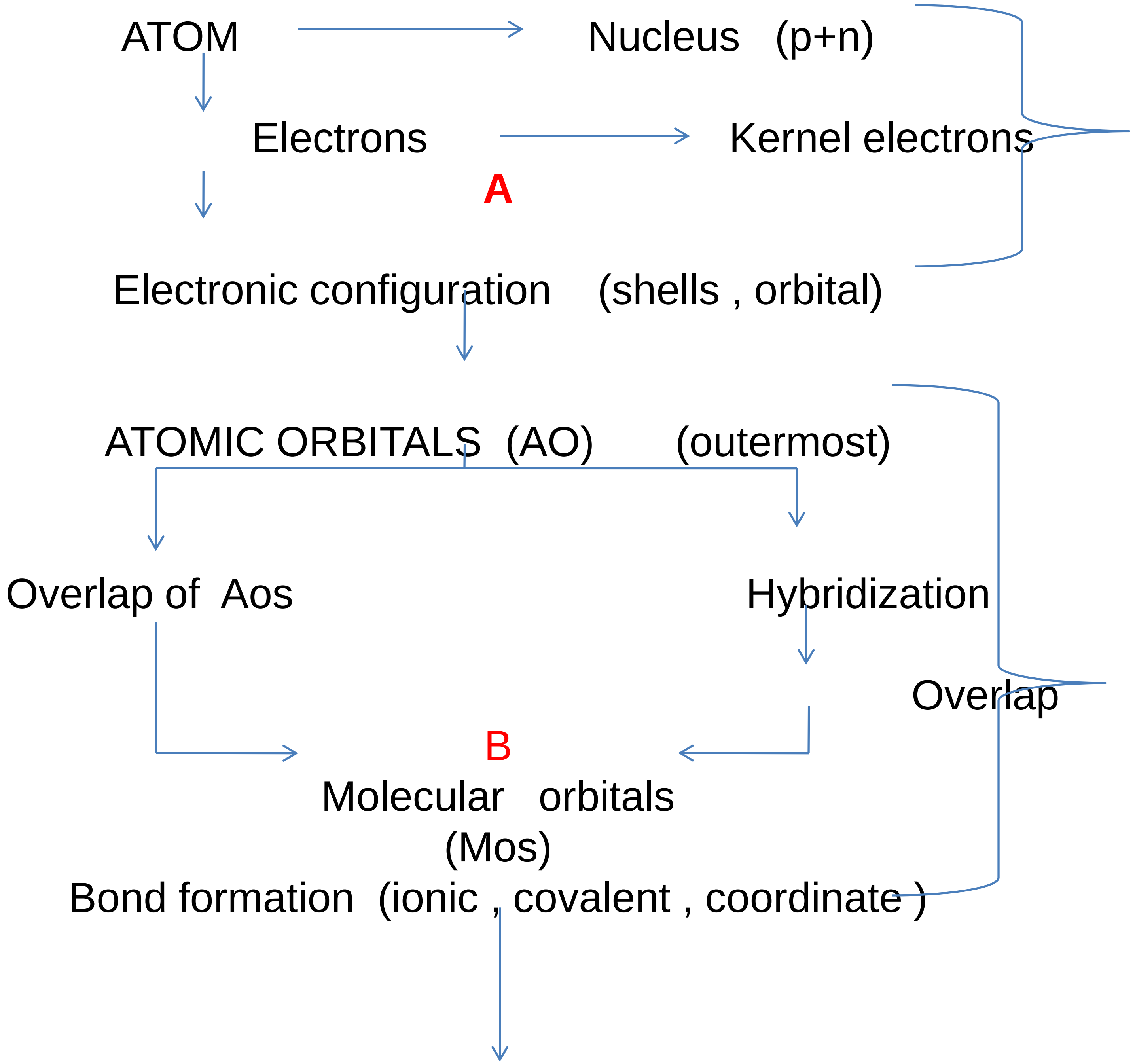
To understand organic chemistry it is necessary to know:

- What occurs in a reaction?
- Why and how chemical reaction takes place?
- How a reaction can be described?

Formation of molecule


ATOM
Nucleus (p+n)
Electrons
Kernel electrons
A
Electronic configuration (shells , orbital)
ATOMIC ORBITALS (AO) (outermost)
Overlap of Aos
Hybridization
Overlap
B
Molecular orbitals
(Mos)
Bond formation (ionic , covalent , coordinate)

MOLECULE

- 3D structure stereochemistry
- Electronic structures
  - (i) Polarization effect –I (inductive effect)
  - (ii) polarizability effect (electromeric effect)
  - (iii) Resonance

C

MOLECULE + MOLECULE

- Bond breaking
  - Homolytic
    - Radicals
  - Heterolytic
    - Cations
    - Anions
- Concentrated reactions (pericyclic reactions)

other species

D

REACTION MECHANISM

Atoms → Molecule

Nuclei → Framework

Electrons → Orbitals

3D Structure → Configurations, conformations, isomerism .....

Prerequisite: Electronic configuration

MOLECULE

3D Structure → Reactivity ← Electronic structure

Reactivity

↓

Reaction

Atomic structure
versus
Molecular structure

AO vs MO

n A.O.s → n M.O.s

(s,p,d,f)

Approximations

Linear combination of atomic orbitals

Consider only the valence orbitals

Consider only that part of your interest

Electronic Structure

Qualitative description of M. O. s of simple acyclic and monoclinic system

(a) Molecular Orbital Energy Diagrams (MOED)

- Explanation of reactivity

(b) Molecular Orbital energies

(c) Orbital overlap

(d) Coefficient of A.O.s in M.Os

(e) Frontier Molecular Orbitals (FMOs)

How is a CHEMICAL BOND formed?

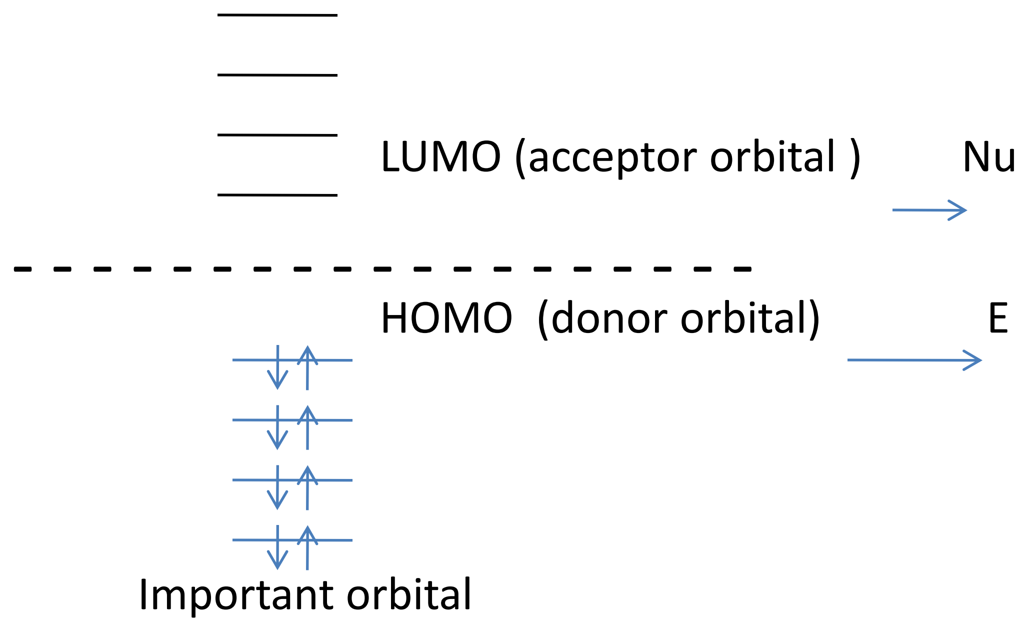
Ionic bond

Covalent bond

Coordinate bond

Hybridization

FMO



Electrophile	LUMO	Nucleophile	HOMO
Acid (lewis)	LUMO	Base (lewis)	HOMO

FMOs in :

Electrophilicity & Basicity

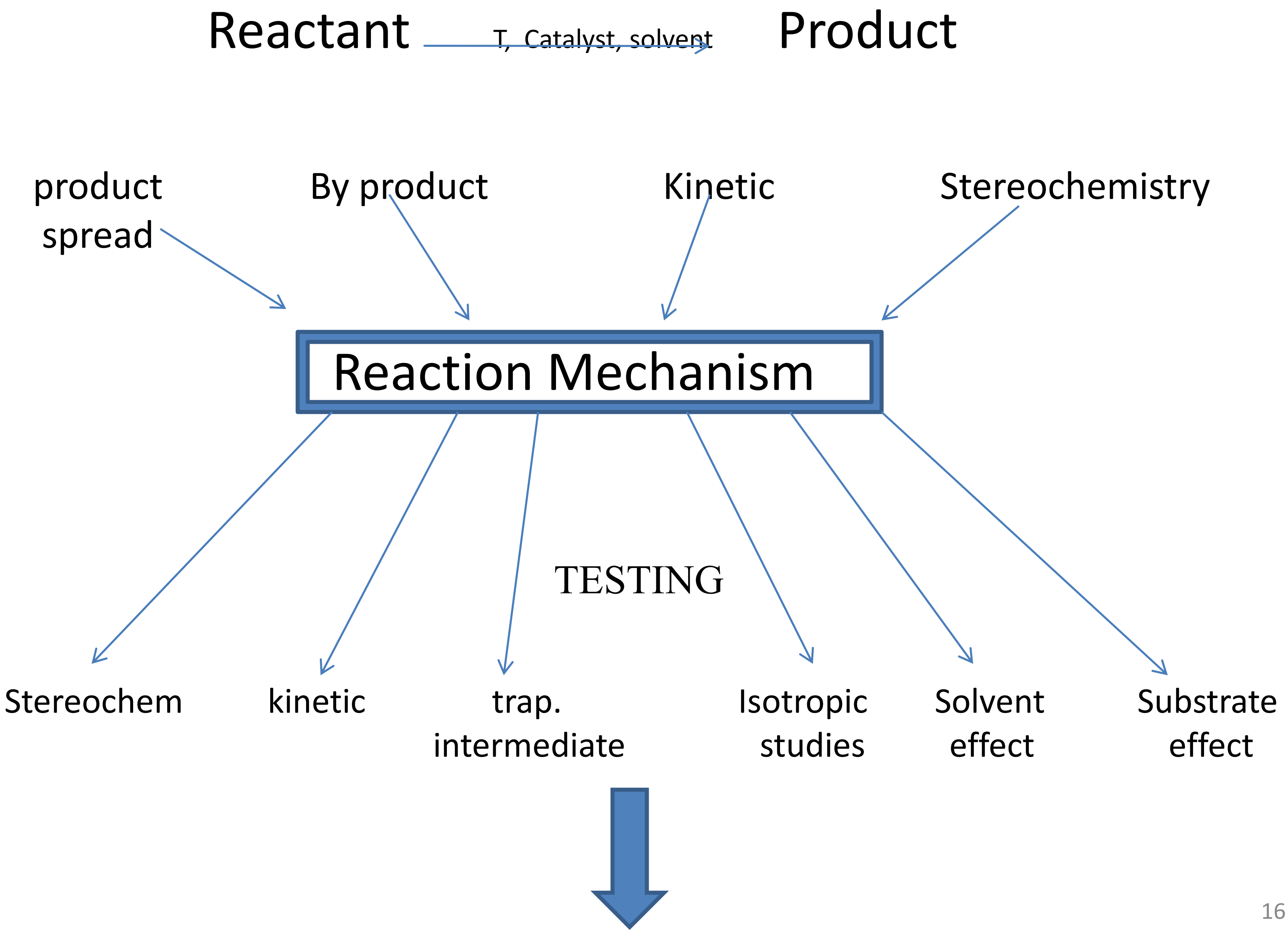
Acidity & Basicity (HSAB)

Simple reactions

Pericyclic reactions

ORGANIC REACTION MECHANISM

Desired reaction :



Mechanism

confirmed

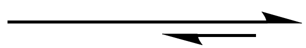
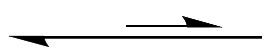
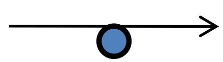
↓

1) explanation of other reaction

2) further development

3) predictions

Important Symbols describing Reaction Mechnaism

$\longrightarrow$	Irreversible reaction to product
$\not\longrightarrow$	Reaction which does not processd
$\rightleftarrows$	Forward & Backward reaction
$\rightarrow \; \rightarrow$	Reaction with more than one step
$\rightleftharpoons$	Reversible reaction
	Reversible reaction ; Equilibrium favours products
	Reversible reaction ; Equilibrium favours reactant
	Reaction with inversion of cofiguration
$\longleftrightarrow$	Indication of resonance

Direction of migration

Migration origin

shift of $2e^-$

Migration terminus

Half headed arrow

1 e^- shift

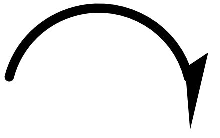
Curly Arrow

Use appropriate symbols

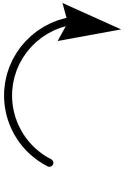
Indicating Steps in Mechanisms

- Curved arrows indicate breaking and forming of bonds

- Arrowhead with a "half" head ("fish-hook") indicates homolytic and homogenic steps (called 'radical processes')

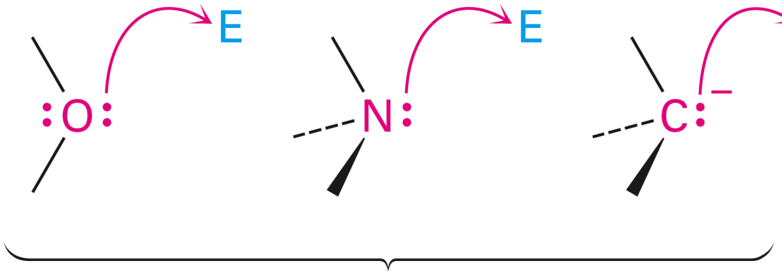


- Arrowhead with a complete head indicates heterolytic and heterogenic steps (called 'polar processes')



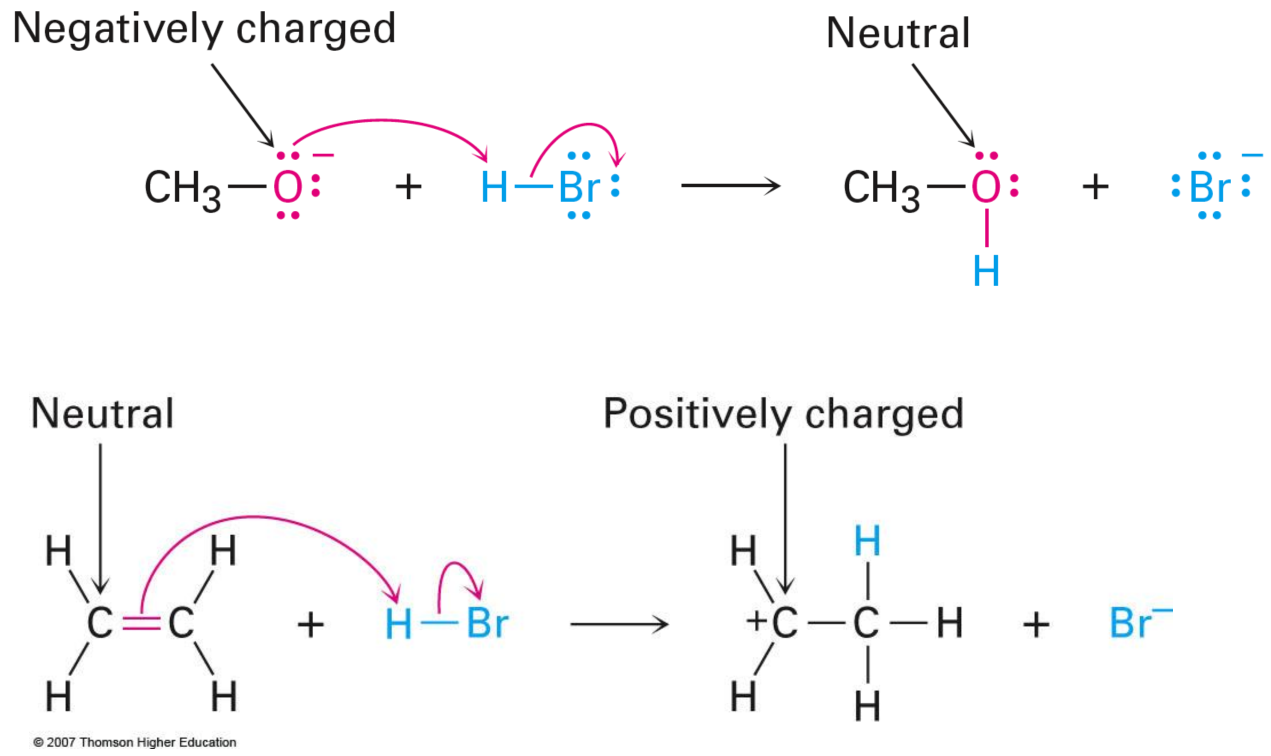
Using Curved Arrows in Polar Reaction Mechanisms

- Curved arrows are a way to keep track of changes in bonding in polar reaction
- The arrows track "electron movement"
- Electrons always move in pairs
- Charges change during the reaction
- One curved arrow corresponds to one step in a reaction mechanism
- The arrow goes from the nucleophilic reaction site to the electrophilic reaction site

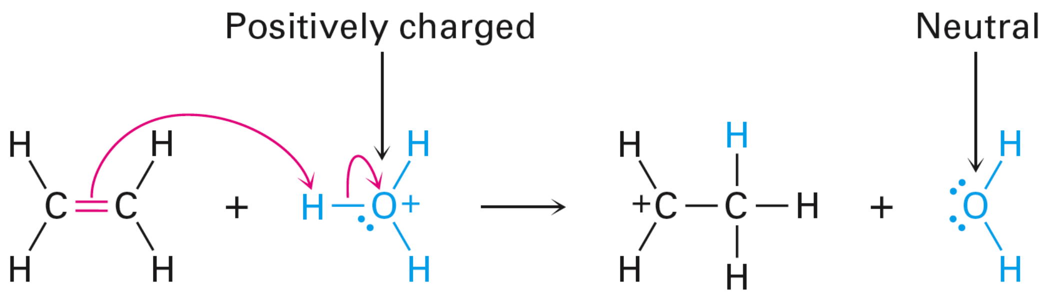


Rules for Using Curved Arrows

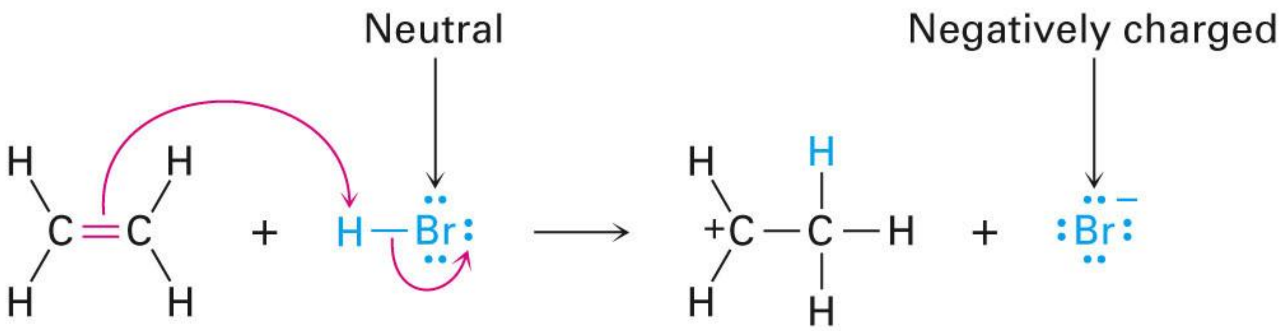
- The nucleophilic site can be neutral or negatively charged

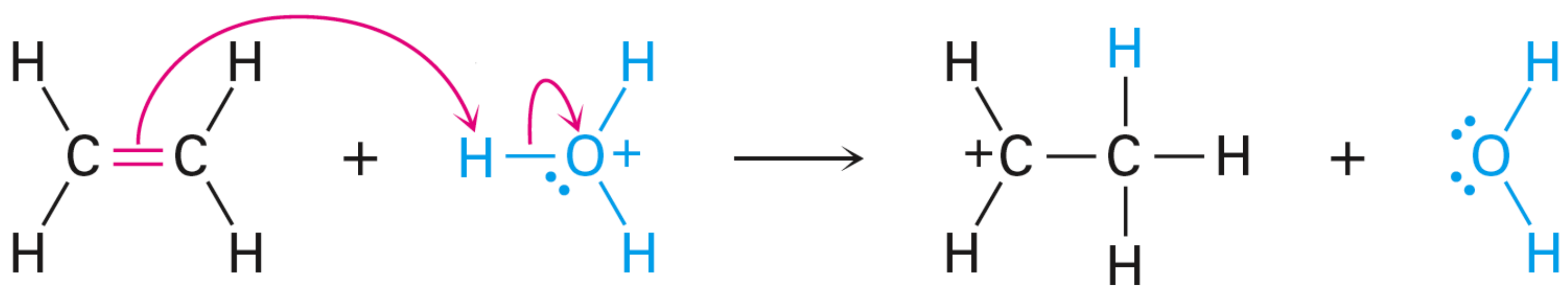


- The electrophilic site can be neutral or positively charged



- Don’t exceed the octet rule (or duet)





Examination of a molecule with respect to its electronic structure

Formal charge

Formal charge =
Valence electrons – (1/2 bonding e^- s + All lone pair e-s)

= Valence e^- s – (lines + dots)

Polarization effect – Inductive effect

Polarizability effect – Electromeric effect

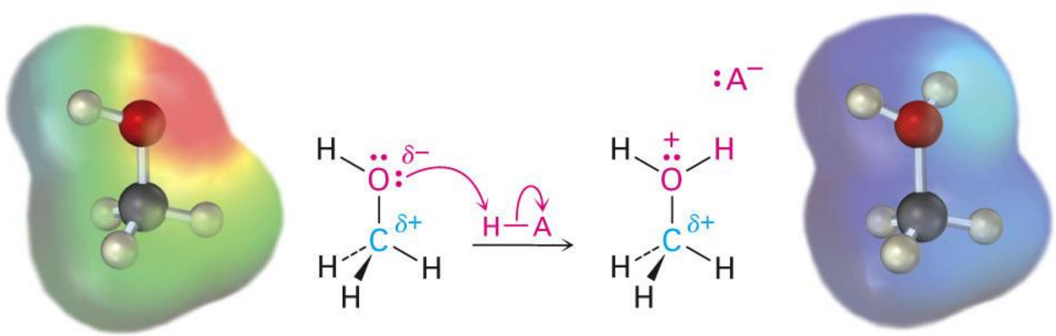
Localized and Delocalized bonds

– Resonance and related phenomena

Polarizability

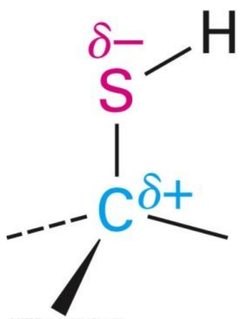
- The ability of the surroundings (solvent or other polar molecules) to make a molecules polar. It is like making something magnetic by pass a magnet over it.
- It starts out neutral but when the right atom or molecule comes close it becomes partial positive or partial negative.

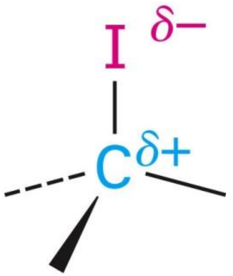
- **Polarization** - change in electron distribution as a response to change in electronic nature of the surroundings
- Polarizability is the tendency to undergo polarization
- Polar reactions occur between regions of high electron density and regions of low electron density



Methanol—weakly electron-poor carbon

Protonated methanol—strongly electron-poor carbon





Resonance

A way to indicate delocalization of electron

Localized vs Delocalized Bonds

Unique Structure vs Resonance structures

Resonance Structures

Hypothetical BUT Useful

Hypothetical means taken to explain REAL object

Drawing of resonance structures

Nuclei do not move – Geometry of the molecule does not change

Electrons move

Follow standard rules of valence

Each resonance structure contributes to some extent to the actual structure of the molecule

Why do Organic Reactions Happen?

Energy change = Coulombic interaction + Orbital interaction

Orbital interaction = FMO interaction + Other interactions

How do the organic reactions occur: Mechanism

- In an organic reaction, we see the transformation that has occurred. The mechanism describes the steps behind the changes that we can observe

- Reactions occur in defined steps that lead from reactant to product

Steps in Mechanisms

- A step involves either the formation or breaking of a covalent bond
- Steps can occur in individually or in combination with other steps
- When several steps occur at the same time they are said to be **concerted**

Understanding unit steps

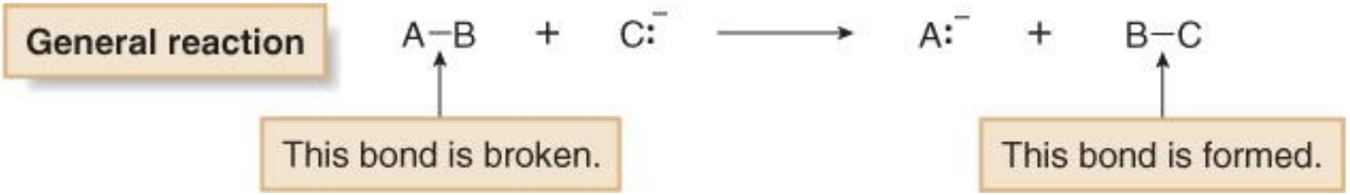
Acid – Base concept

Nucleophile and Electrophile

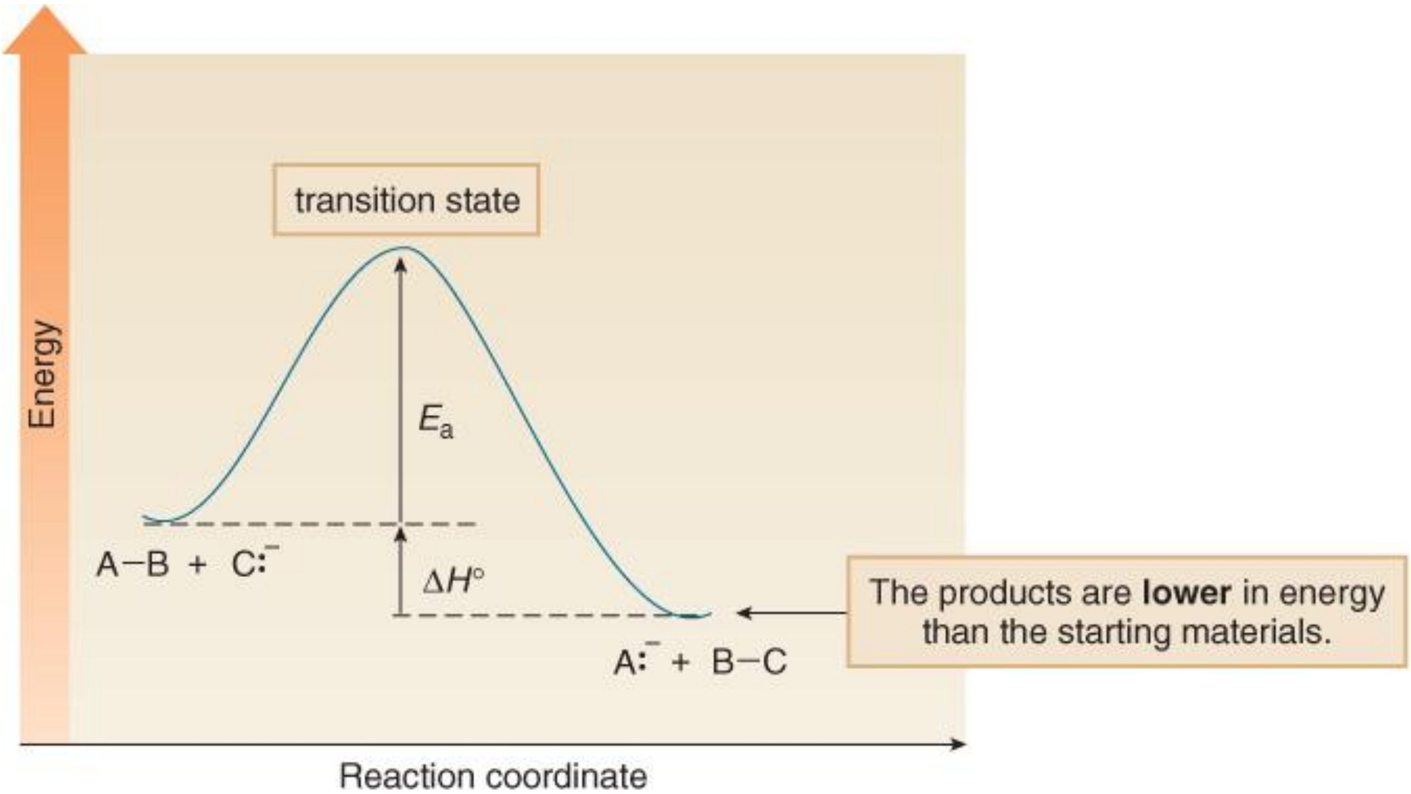
Energy Frofile Diagram

- schematic representation of the energy changes that take place as reactants are converted to products.
- plots the energy on the y axis versus the progress of reaction, often labeled as the reaction coordinate, on the x axis.

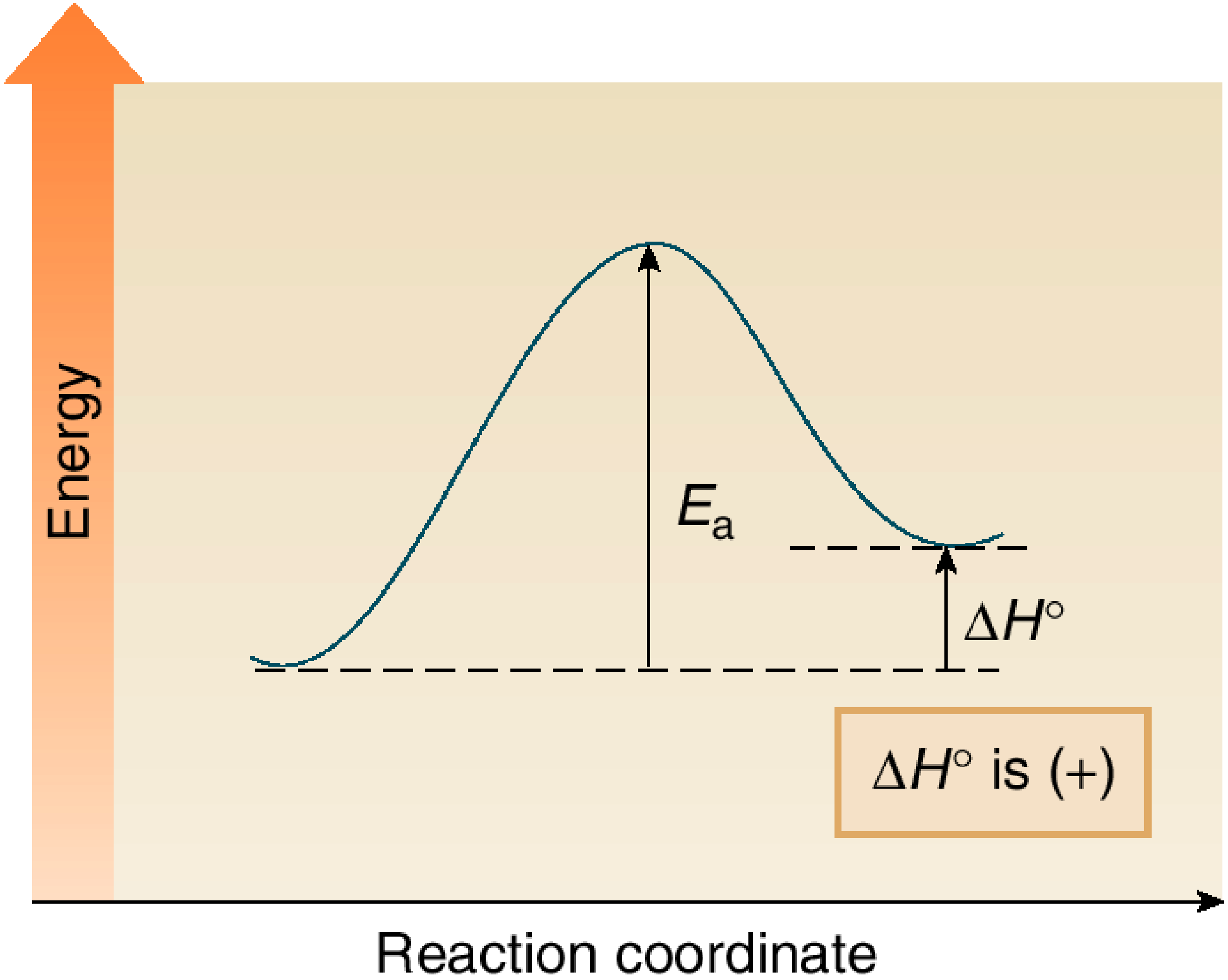
- For the general reaction:



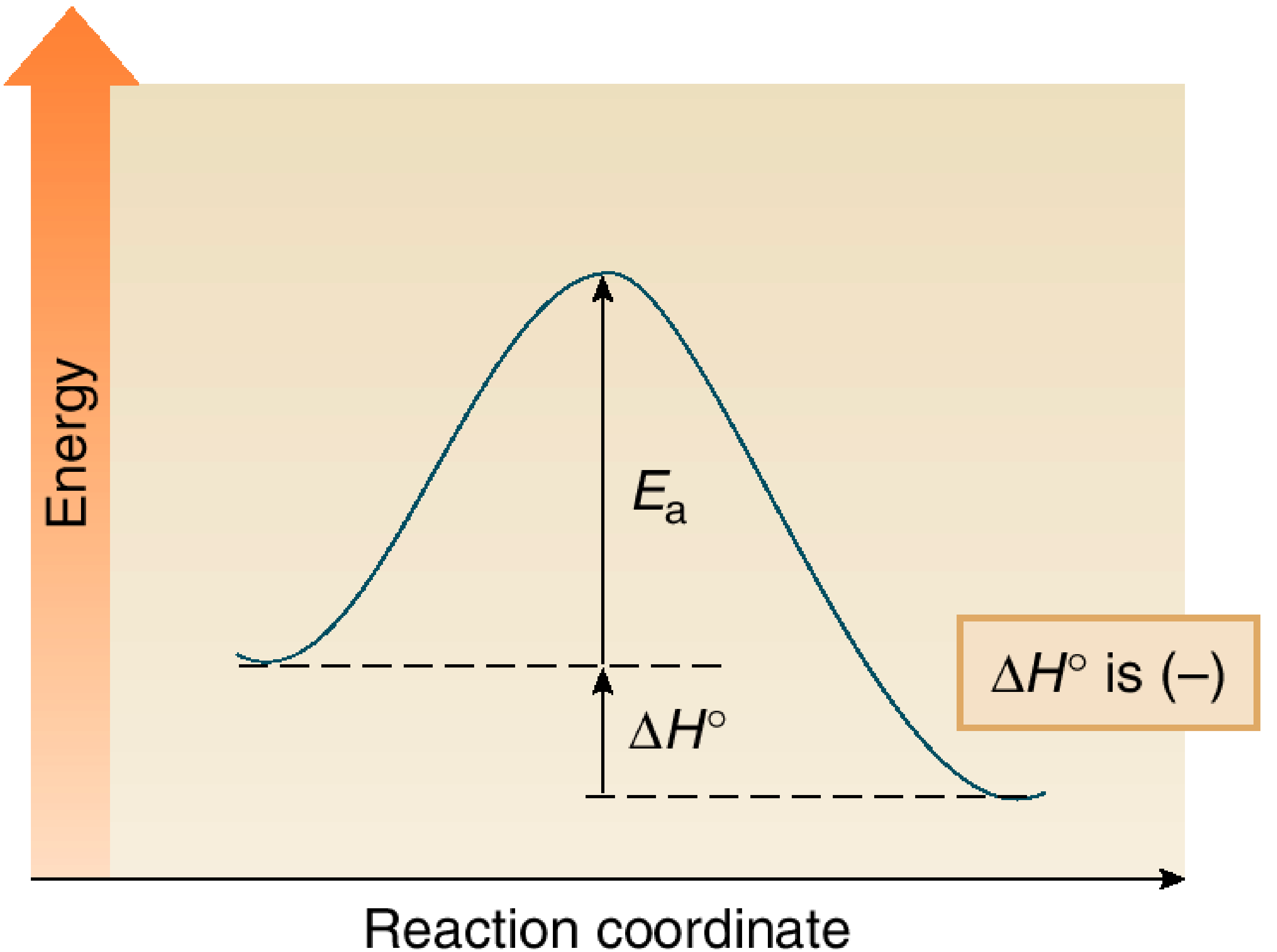
- The energy diagram would be shown as:



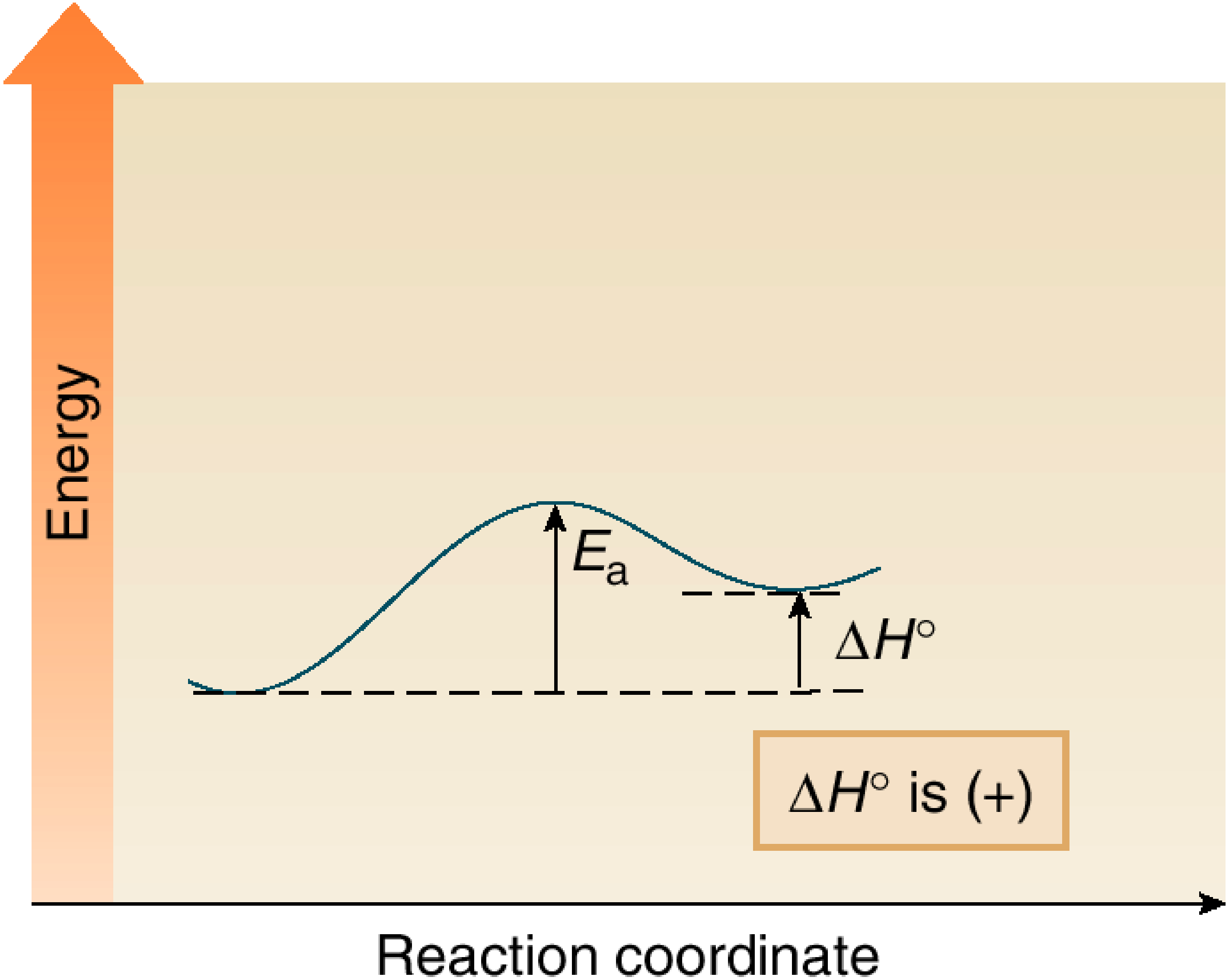
- Large $E_a \longrightarrow$ slow reaction
- (+) $\Delta H^\circ \longrightarrow$ endothermic reaction



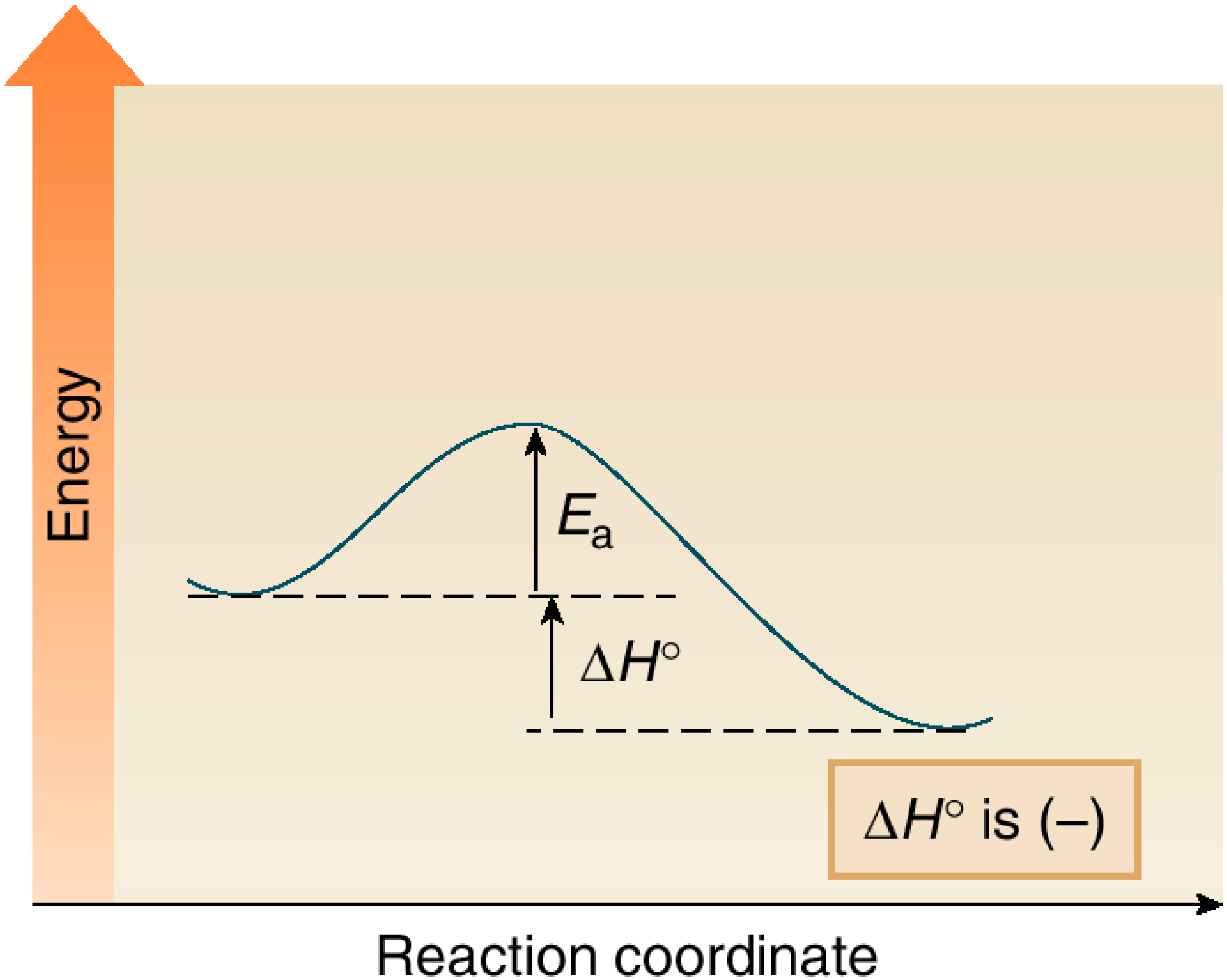
- **Large E_a ⟶ slow reaction**
- **(–) $\Delta H°$ ⟶ exothermic reaction**

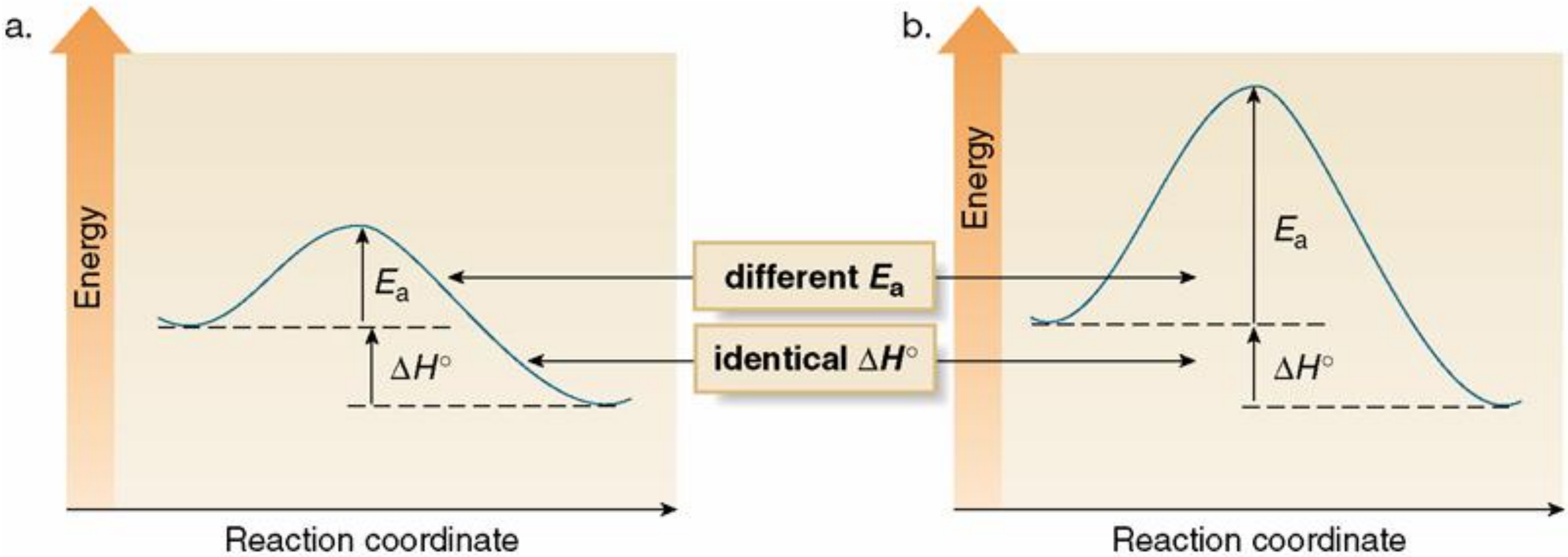


- **Low E_a ⟶ fast reaction**
- **(+) $\Delta H°$ ⟶ endothermic reaction**



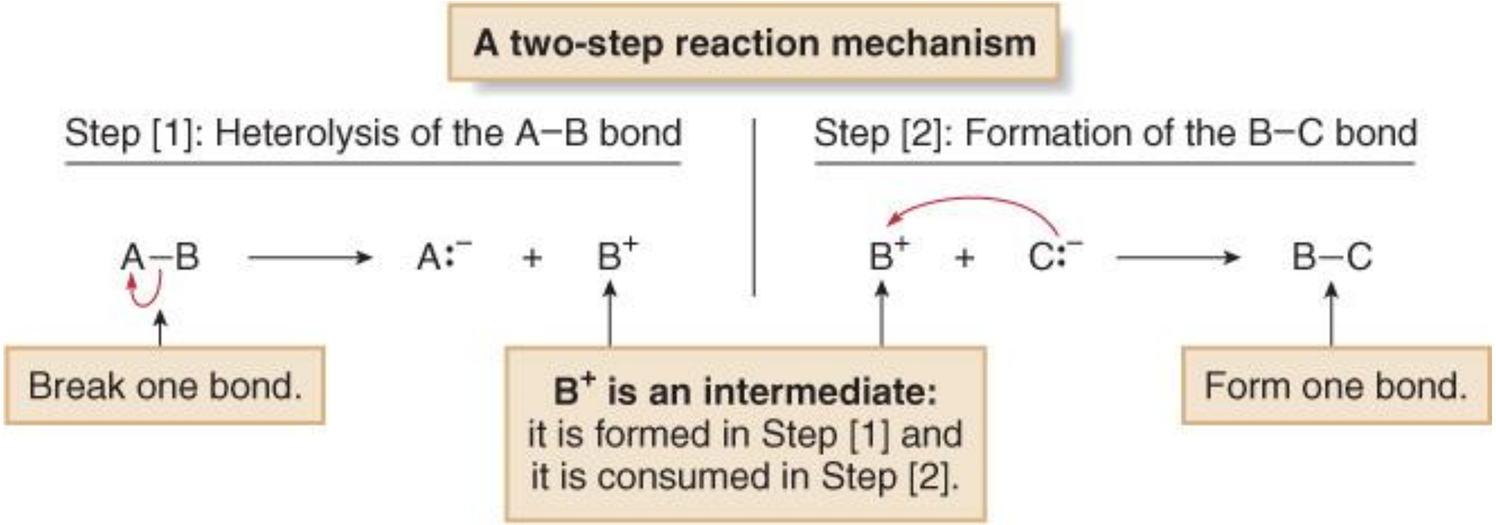
- Low E_a ⟶ fast reaction
- (–) $\Delta H°$ ⟶ exothermic reaction





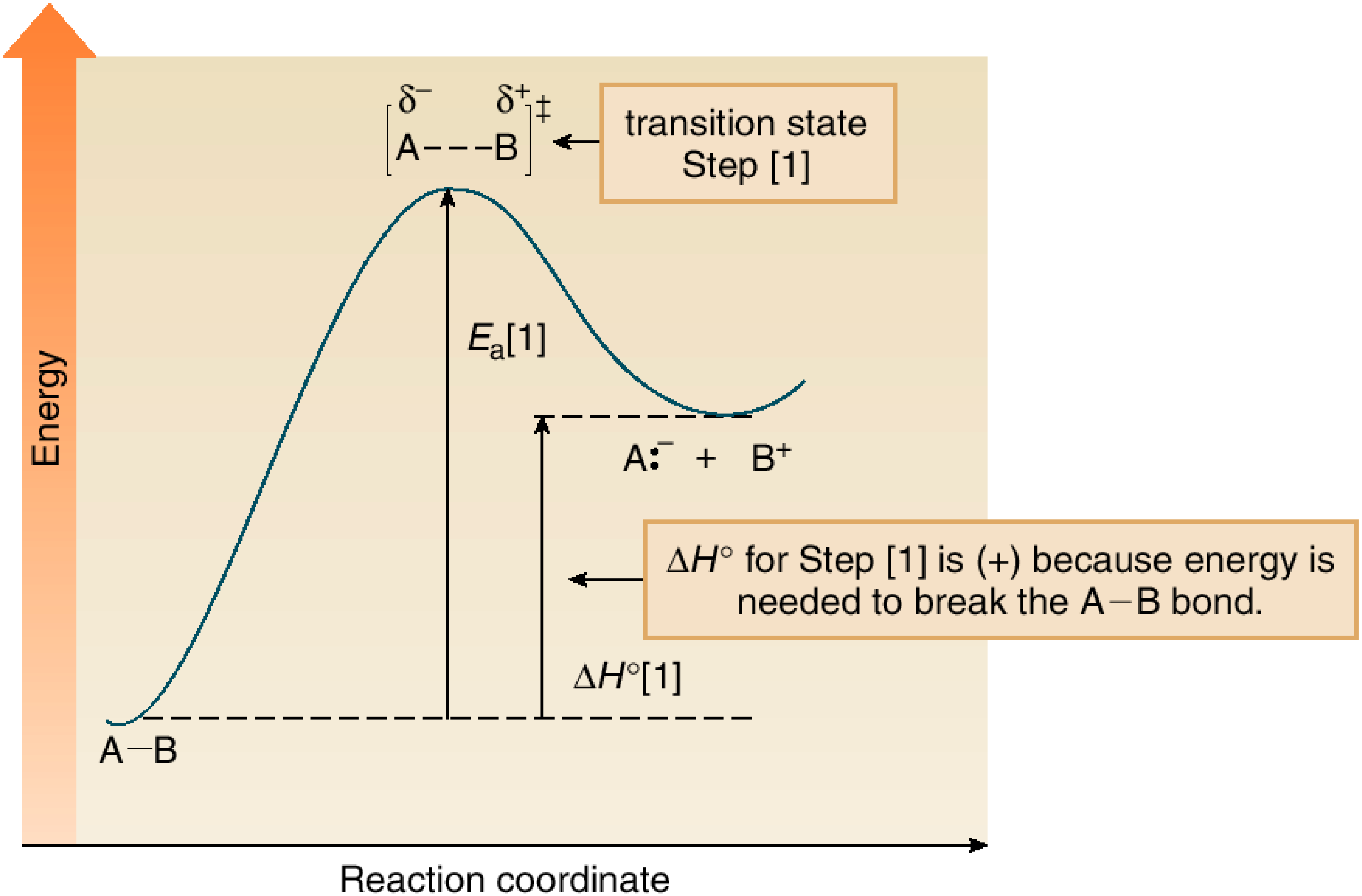
- Energy diagrams in [a] and [b] both depict exothermic reactions with the same negative value of $\Delta H°$.
- E_a in [a] is lower than E_a in [b], so reaction [a] is faster than reaction [b].

- Consider the following two step reaction:

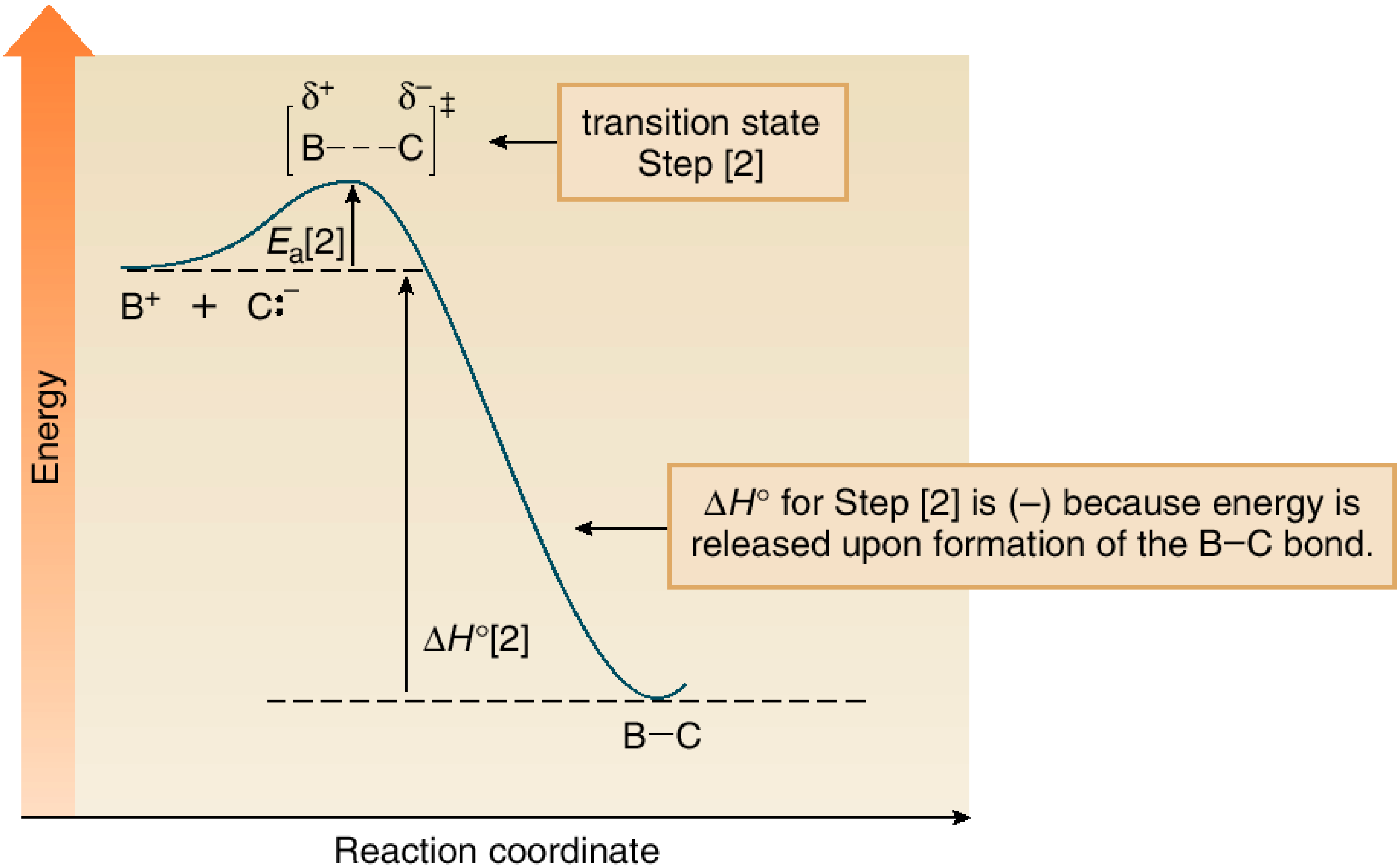


- An energy diagram must be drawn for each step.
- The two energy diagrams must then be combined to form an energy diagram for the overall two-step reaction.
- Each step has its own energy barrier, with a transition state at the energy maximum.

Energy diagram for Step [1]



Energy diagram for Step [2]



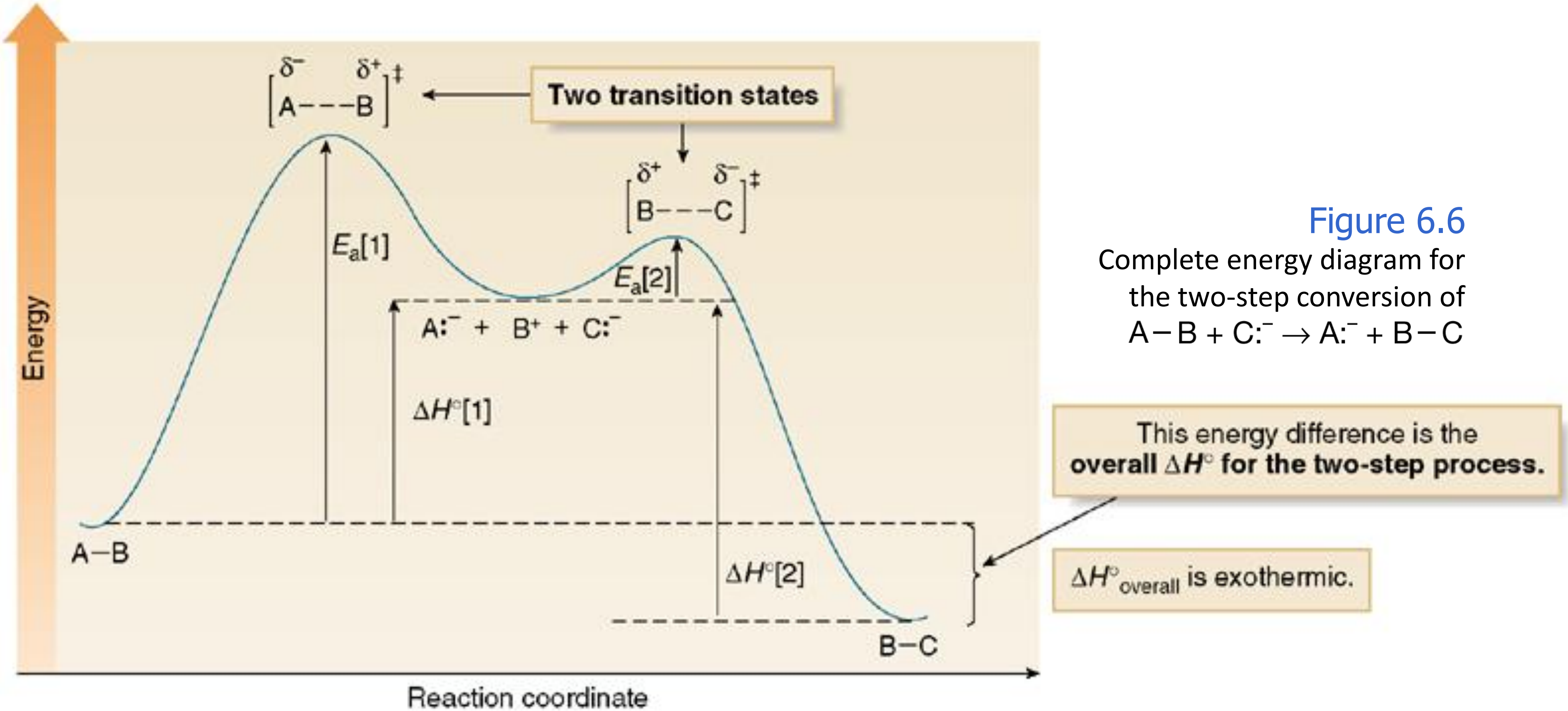
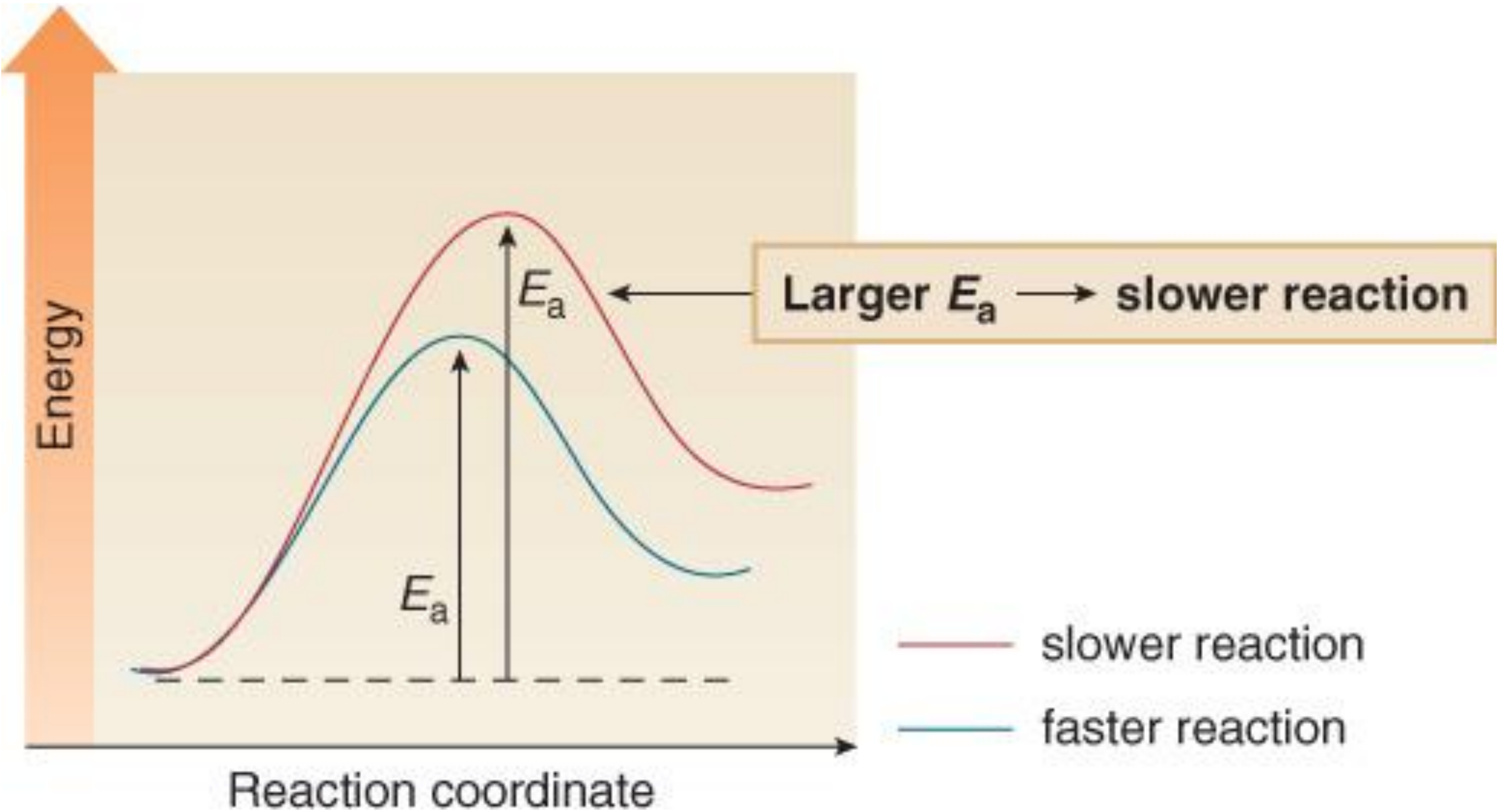
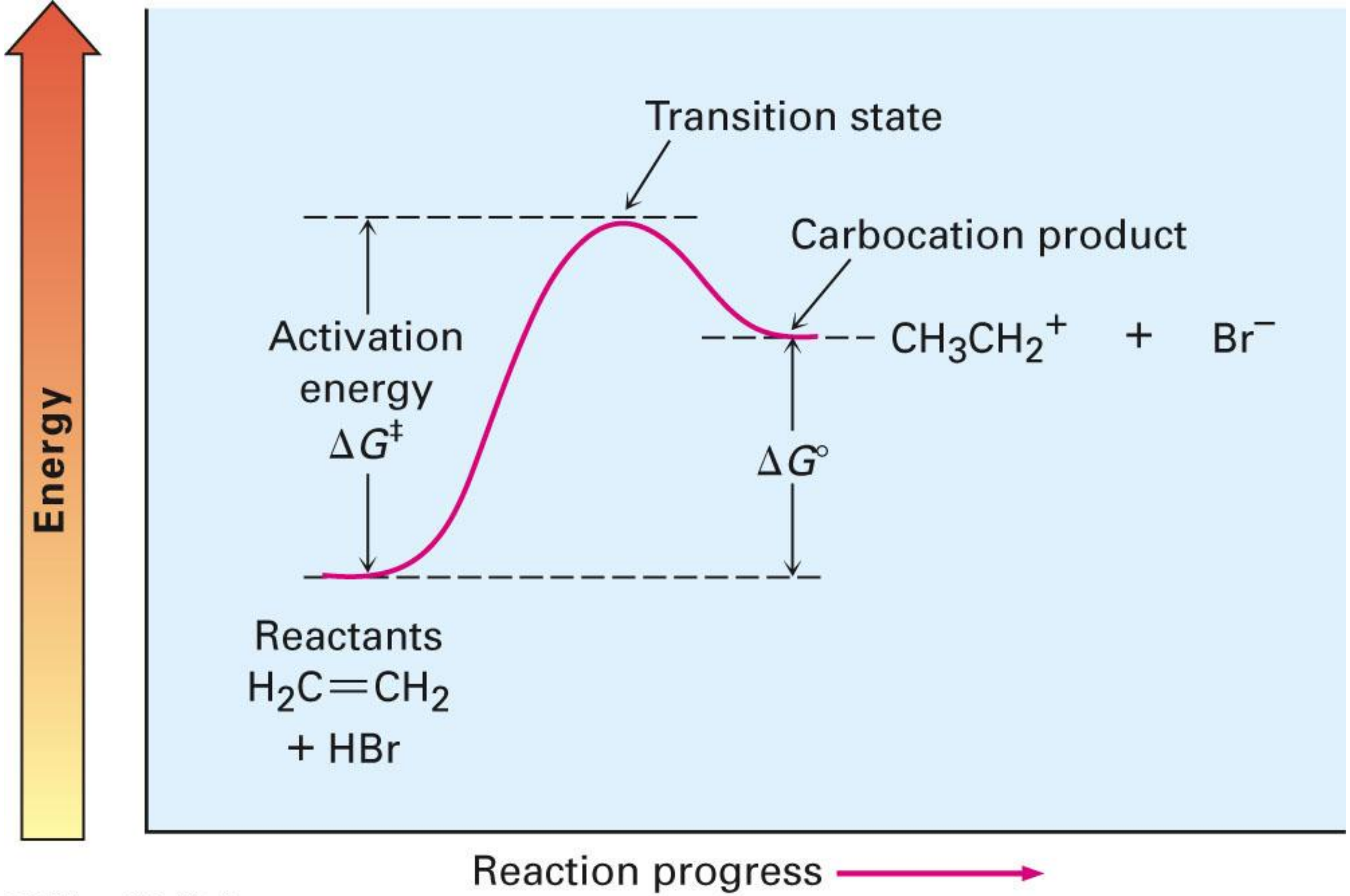


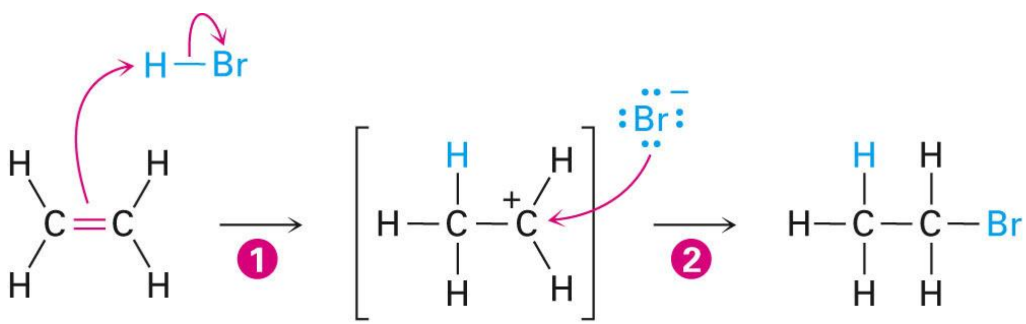
Figure 6.6
Complete energy diagram for the two-step conversion of $A-B + C:^- \rightarrow A:^- + B-C$

- **The transition states are located at energy maxima, while the reactive intermediate B^+ is located at an energy minimum.**
- Each step is characterized by its own value of ΔH° and E_a.
- The overall energy difference between starting material and products is labeled as $\Delta H^\circ_{overall}$. In this example, the products of the two-step sequence are at lower energy than the starting materials.
- Since Step [1] has the higher energy transition state, it is the **rate-determining step.**

E_a is the energy barrier that must be exceeded for reactants to be converted to products.



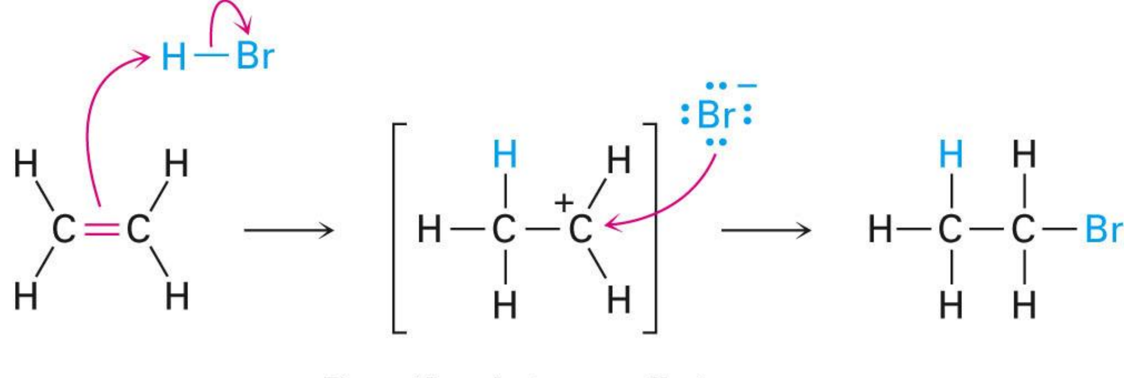


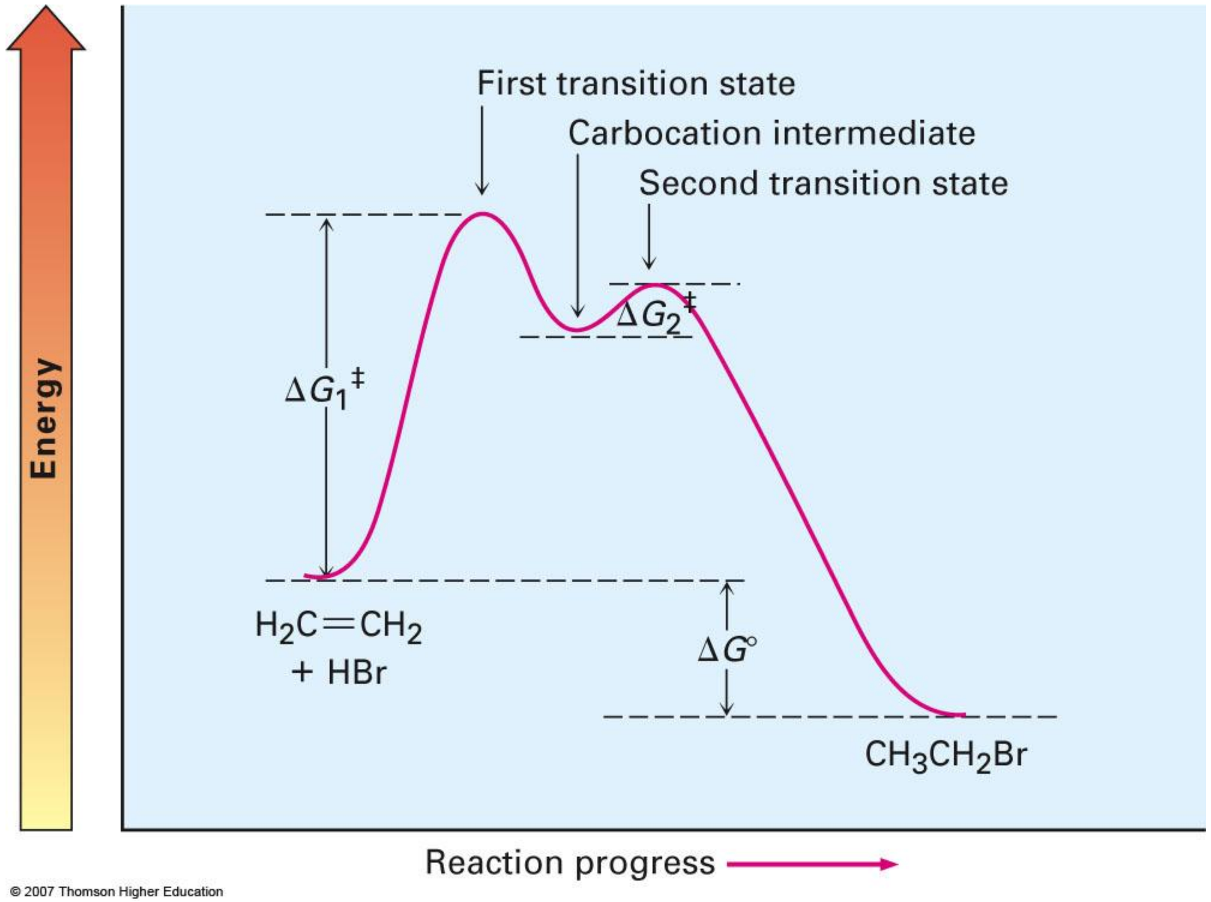


Carbocation

Describing a Reaction: Intermediates

- If a reaction occurs in more than one step, it must involve species that are neither the reactant nor the final product
- These are called **reaction intermediates** or simply “intermediates”
- Each step has its own free energy of activation

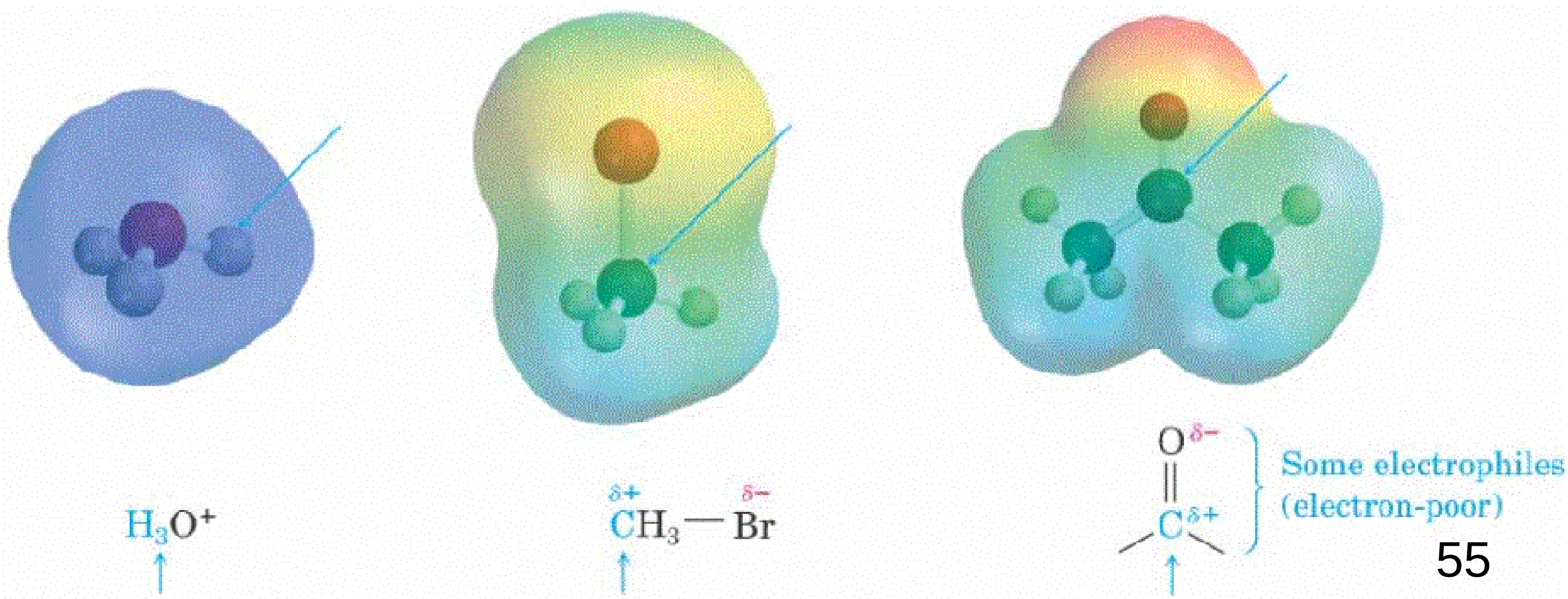

H—Br
:Br:⁻
Reaction intermediate


Energy
First transition state
Carbocation intermediate
Second transition state
ΔG₂‡
ΔG₁‡
H₂C=CH₂
+ HBr
ΔG°
CH₃CH₂Br
Reaction progress

Acids and Bases

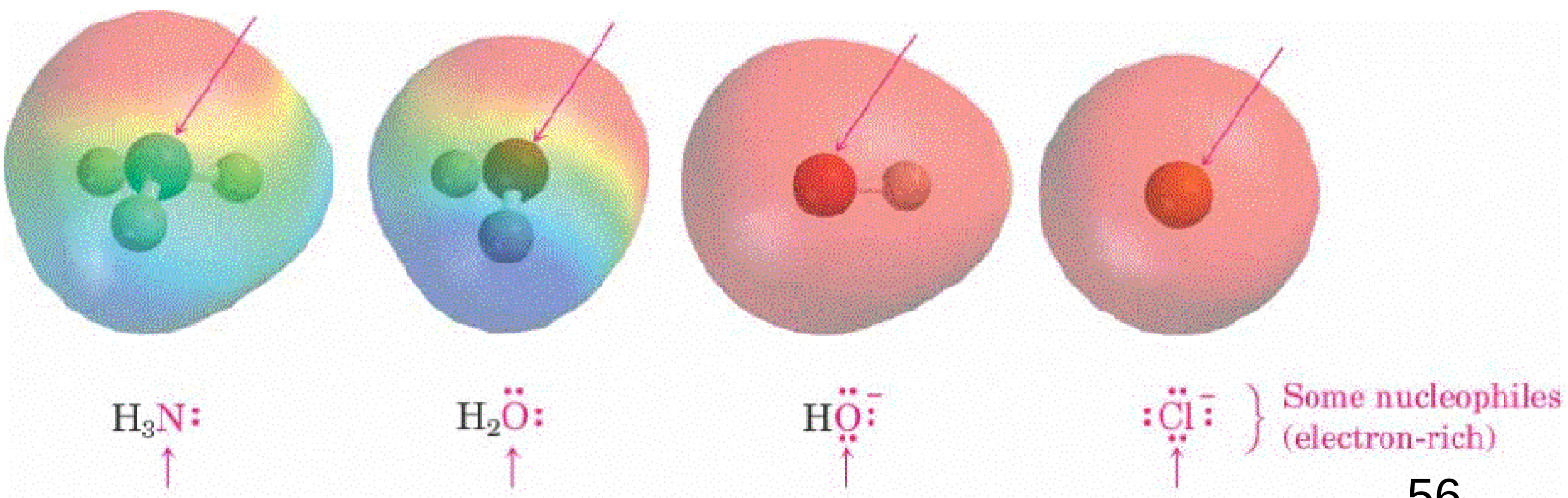
An electrophile

- is “electron-loving”
- is an electron-poor species
- can form a bond by accepting a pair of electrons
- may be either neutral or positively charged
- is a Lewis acid



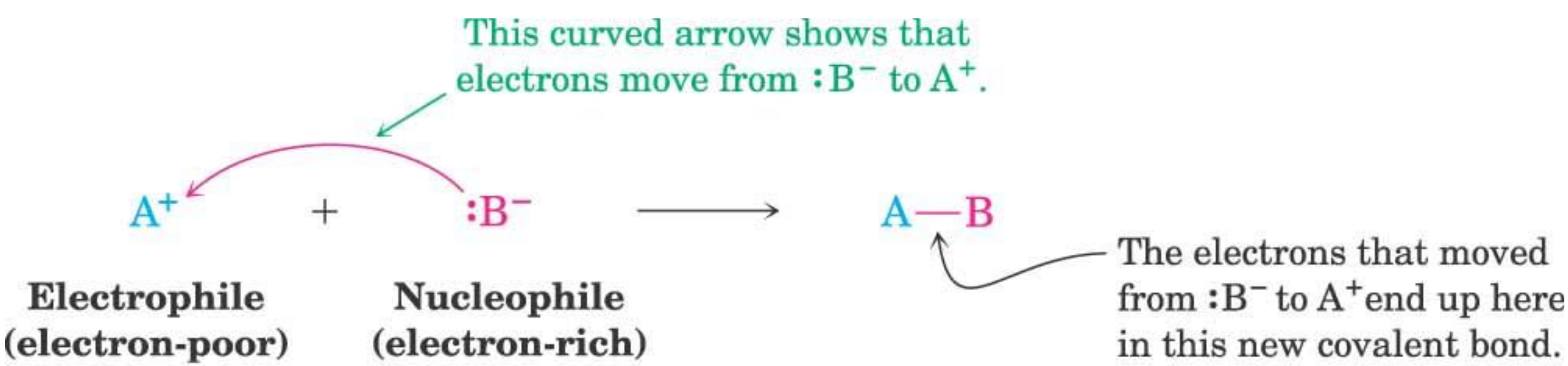
A nucleophile

- is “nucleus-loving”
- is an electron-rich species
- can form a bond by donating a pair of electrons
- may be either neutral or negatively charged
- is a Lewis base



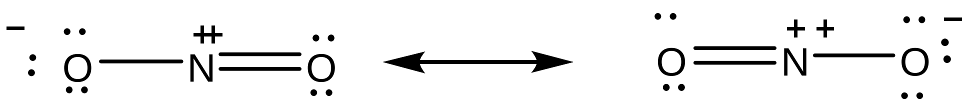
Generalized Polar Reactions

- An electrophile, an electron-poor species, combines with a nucleophile, an electron-rich species

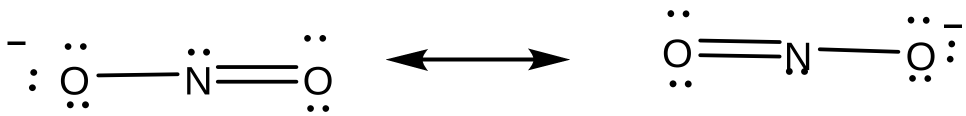


- The combination is indicated with a curved arrow from nucleophile to electrophile

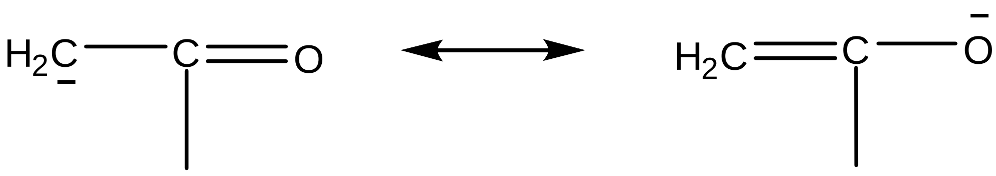
Ambident Nucleophiles



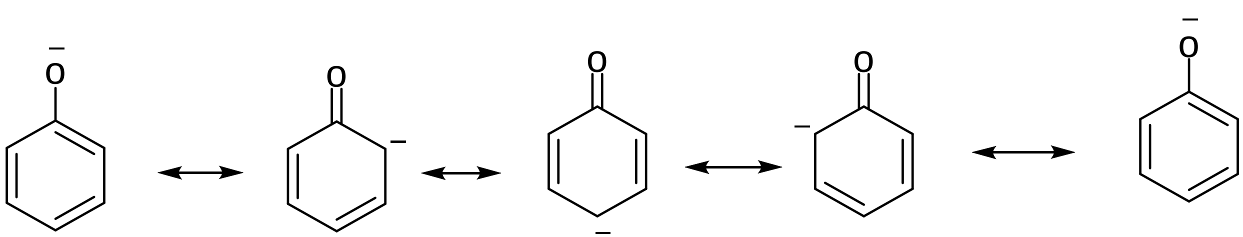
$(NO2)^{+}$



$(NO2)^{-}$



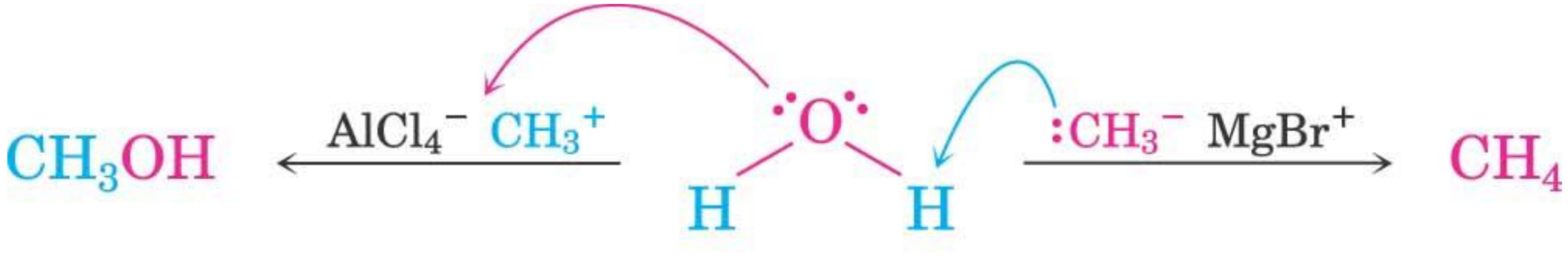
(enolate)



(phenolate ion)

- Some species can act as an electrophile or a nucleophile depending on the circumstances

    - *Example* – Water acts as a nucleophile when it donates a pair of electrons, and acts as an electrophile when it donates H^+

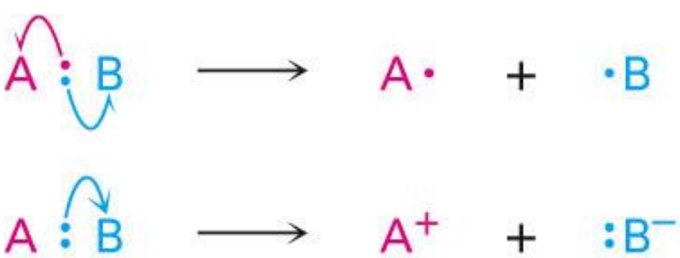


Bond Breaking –
in anticipation of better bonds

HOW and What it Results into

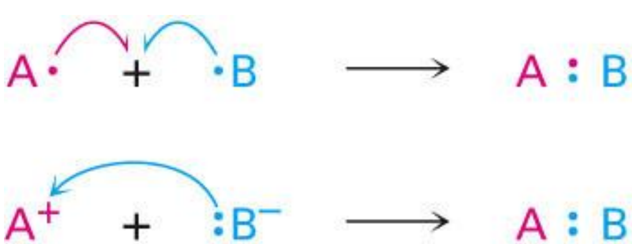
Types of Steps in Reaction Mechanisms

- Bond formation or breakage can be symmetrical or unsymetrical
- **Symmetrical -** homolytic
- **Unsymmetrical -** heterolytic



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

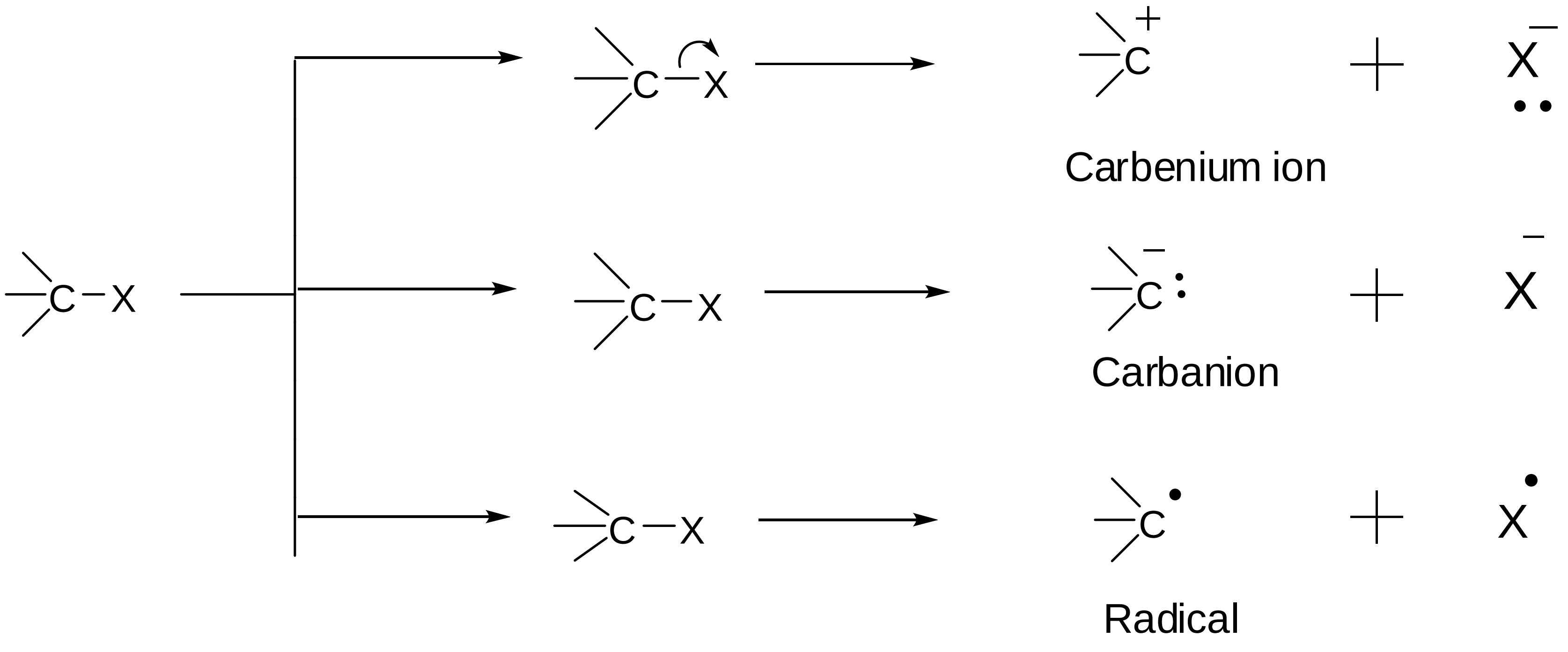
Unsymmetrical bond-breaking (polar):
two bonding electrons stay with one product.

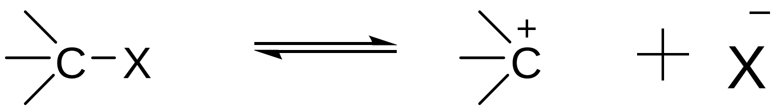


Symmetrical bond-making (radical):
one bonding electron is donated by each reactant.

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

General C-X Bond Breaking processes

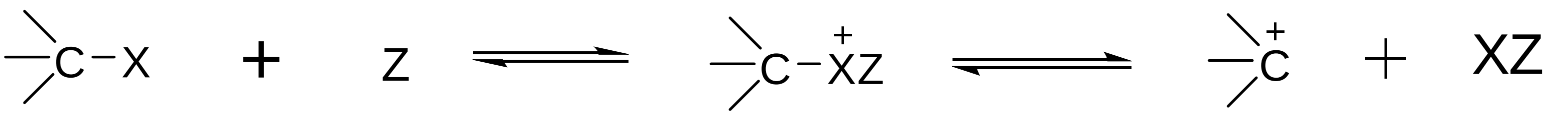




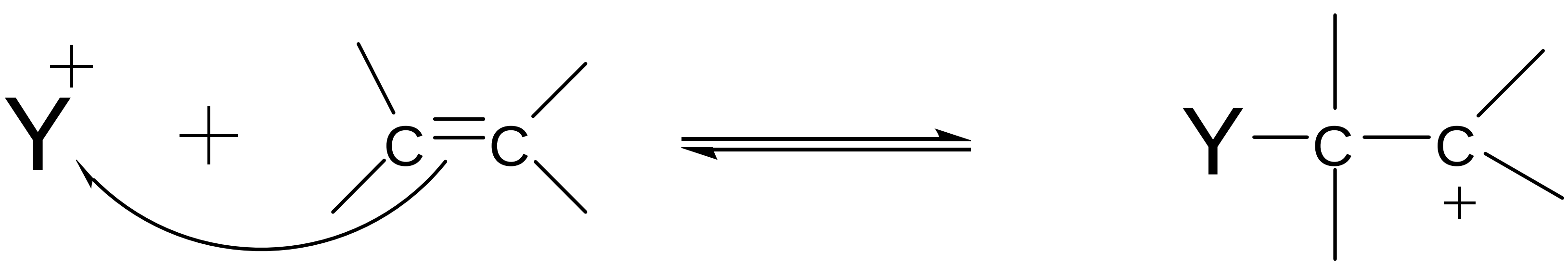
X Leaving group

Self dissociation

OR



assisted dissociation



Addition

Intermediates

What are they?
Transition State and Intermediates
How are they formed?
How do they look like?
Are they stable?
What are their typical reactions?

Structures

Carbocation: Trivalent, Planar, Trigonal

Carbanion: Trivalent, Tetrahedral

Carbon radical: Tetrahedral or Trigonal

General principles of stability:

Increase charge → Unstable

Decrease charge → Stable

Localise charge → Unstable

Disperse, delocalise change → Stable

RADICAL REACTION

A] Propagation processes :

1) Abstraction

$$\dot{R} + H{-}C\equiv \longrightarrow R{-}H + \dot{C}\equiv$$

2) Addition

3) Decompostion

$$R{-}\underset{\dot{O}}{\underset{|}{C}}{=}O \longrightarrow \dot{R} + O{=}C{=}O$$

$$\dot{R} + \text{Mol} \longrightarrow \ddot{R} + \dot{\text{Mol}}$$

$$\dot{R} \longrightarrow \text{Mol} + \ddot{R}$$

B] Termination process :

1) Combination :

$$\dot{R} + \dot{R} \longrightarrow R{-}R$$

2) Disproportion :

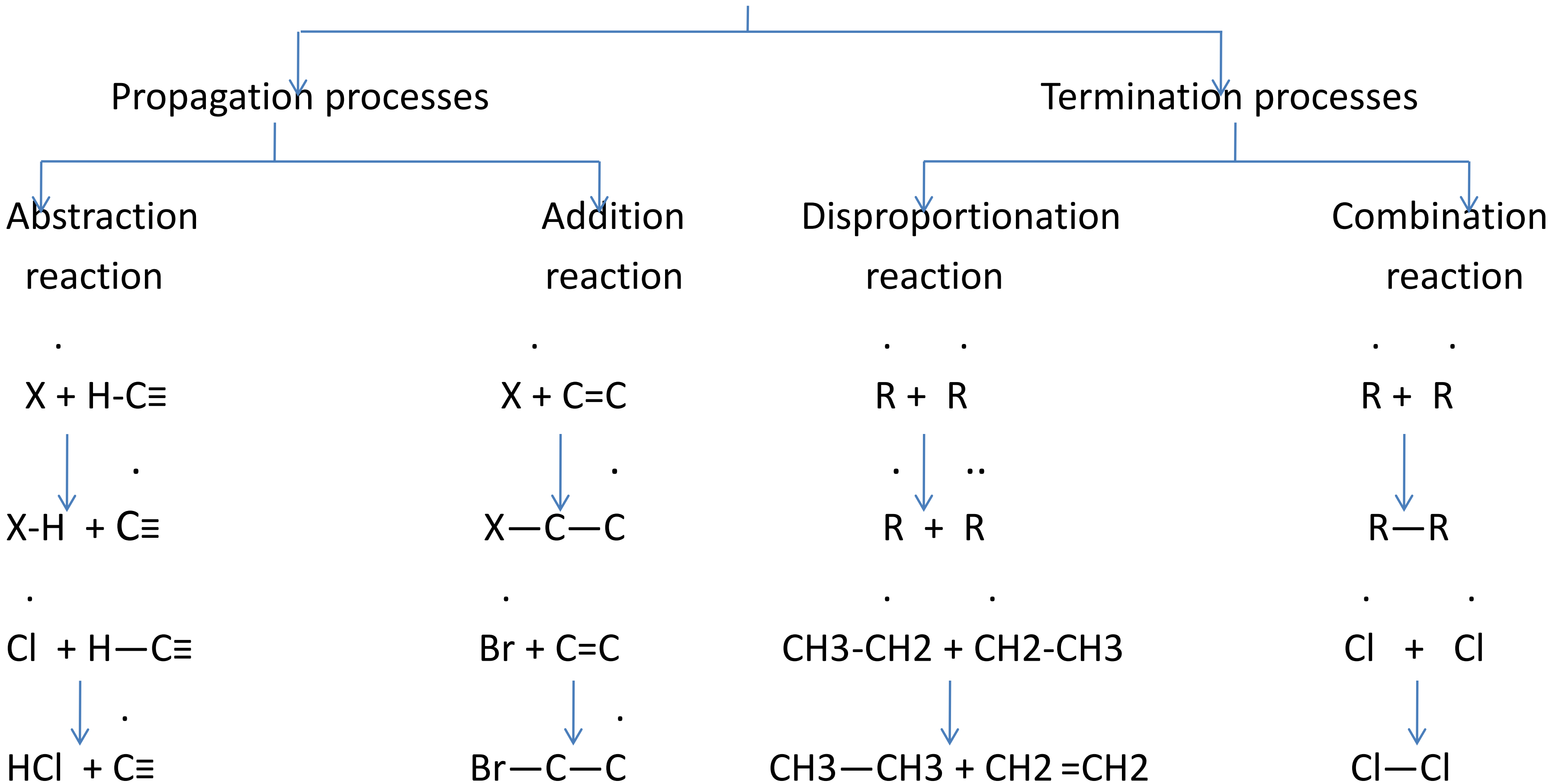
$$\dot{R} \longrightarrow \dot{\text{Mol}} + \ddot{\text{Mol}}$$

C] Rearrangements : Not common

Characteristics

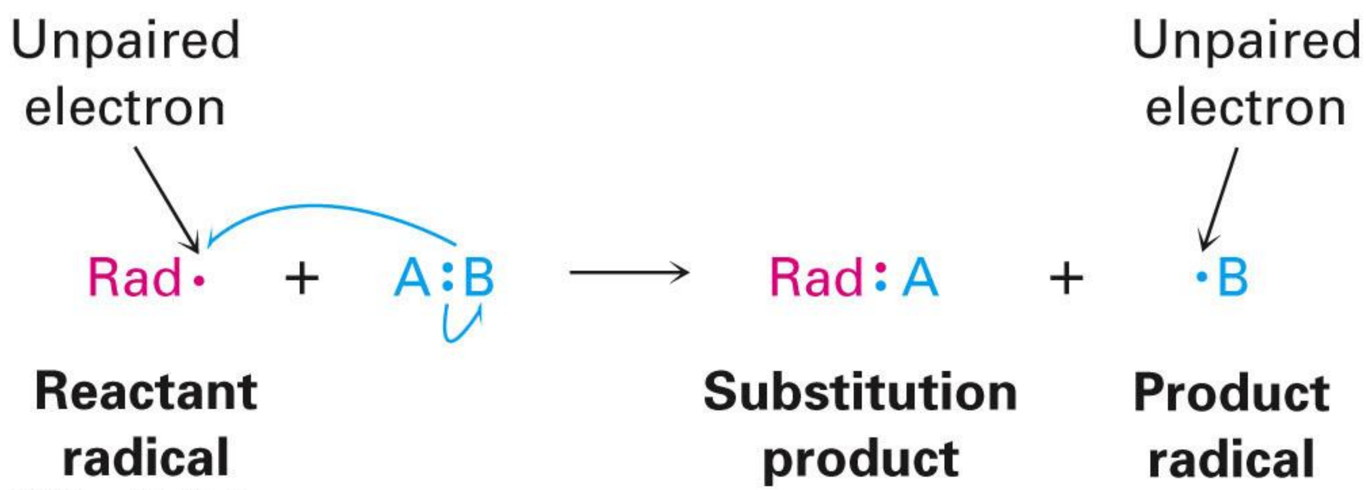
* Susceptible to radicals
* Chain mechanisms
* Conc. Of radicals is low
  - Termination processes less frequent
  - termination process have negligible E act
* Susceptible to inhibitors
* Ionic mechanism may compete.

General Reaction of Free Radicals



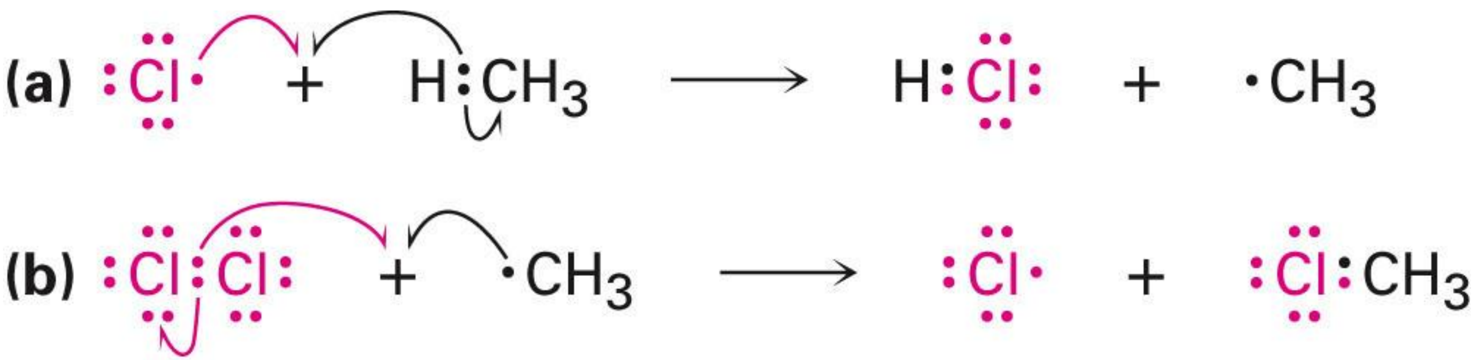
Radical Reactions

- Not as common as polar reactions
- **Radicals** react to complete electron octet of valence shell
  - A radical can break a bond in another molecule and abstract a partner with an electron, giving substitution in the original molecule
  - A radical can *add* to an alkene to give a new radical, causing an addition reaction



Steps in Radical Substitution

- Three types of steps
  - **Initiation** – homolytic formation of two reactive species with unpaired electrons
    - Example – formation of Cl atoms form Cl_2 and light
  - **Propagation** – reaction with molecule to generate radical
    - Example - reaction of chlorine atom with methane to give HCl and $CH_3\cdot$



  - **Termination** – combination of two radicals to form a stable product: $CH_3\cdot + CH_3\cdot \rightarrow CH_3CH_3$

Photohalogenation of alkanes (ΔH in kJ/mol))

Steps	F	Cl	Br	I
$X{-}X \longrightarrow \dot{X} + \dot{X}$	+150.6	+242.7	+188.3	+150.6
$\dot{X} + CH_4 \longrightarrow \dot{C}H_3 + HX$	-146.4	-12.55	+50.21	+117.2
$\dot{C}H_3 + X_2 \longrightarrow H_3C{-}X + \dot{X}$	-334.7	-83.68	-96.23	-62.76
Overall	-481.1	-96.23	-46.23	+54.44

Act. E :

$\dot{Cl} + CH_4 \longrightarrow \dot{CH_3} + HCl$ 16.11 Kj

$\dot{CH_3} + Cl_2 \longrightarrow CH_3Cl + \dot{Cl}$ < 21 kj

Alternative mechanism :

$\dot{Cl} + CH_4 \longrightarrow H_3C\text{--}Cl + \dot{H}$

$\dot{H} + Cl_2 \longrightarrow HCl + \dot{Cl}$

Both steps endothermic (only at High T)

Act . E :

$\dot{Br} + CH_4 \longrightarrow \dot{CH_3} + HBr$ (∽74.48 kj)

	H—CH_3	H—CH_2—CH_3	$HCHMe_2$	$HCMe_3$
C—H Bond E (kcal/mol)	102	96	92	89

(∽77)

Radical addition to (C=C)

$$R + HX \longrightarrow R{-}H$$

Radicals always attack less substituted (terminal) carbon atom of a double bond

X in HX	F	Cl	Br	I (Kcal/mol)
	-45	-26	-5	+7
	+37	+5	-11	-27

Radical mechanism effectively competes with ionic mechanism in the case of HBr

General Reaction of Carbenion Ion

Nucleophilic attack

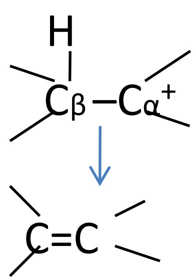
$\equiv C^+ + :Nu \rightarrow \equiv C-Nu$

S_N1 (II)

A_E1 (II)

(A)

Elimination of H^+ from β –position



olefins

E_1

(B)

Rearrangement (common)

less stable (C^+) → more stable (C^+)

Wagner – Meerwein

(C) → A or B

Additon to C=C

$\equiv C^+ + C=C \rightarrow \equiv C-C-C^+$

(D) → A or B; D (polym^n)

CARBOCATION

Carbonium ion

C^+, C - pentavalent

CH_5^+

Carbenium ion

C^+, C - trivalent ,

CH_3^+

Carbonium ion (onium)

Carb-enium ion (enium)

Carbanion

Self Dissociation:

$$R\text{-}Cl \overset{K_1}{\rightleftharpoons} R^+Cl^-$$ ionizat

Tight ion pair

$$R^+Cl^- \overset{\text{Solvent, } K_2}{\rightleftharpoons} R^+ \vdots\vdots Cl^-$$

Solvent separated ion pa

$$R^+ \vdots\vdots Cl^- \overset{K_3}{\rightleftharpoons} R^+ + Cl^-$$ dissoc

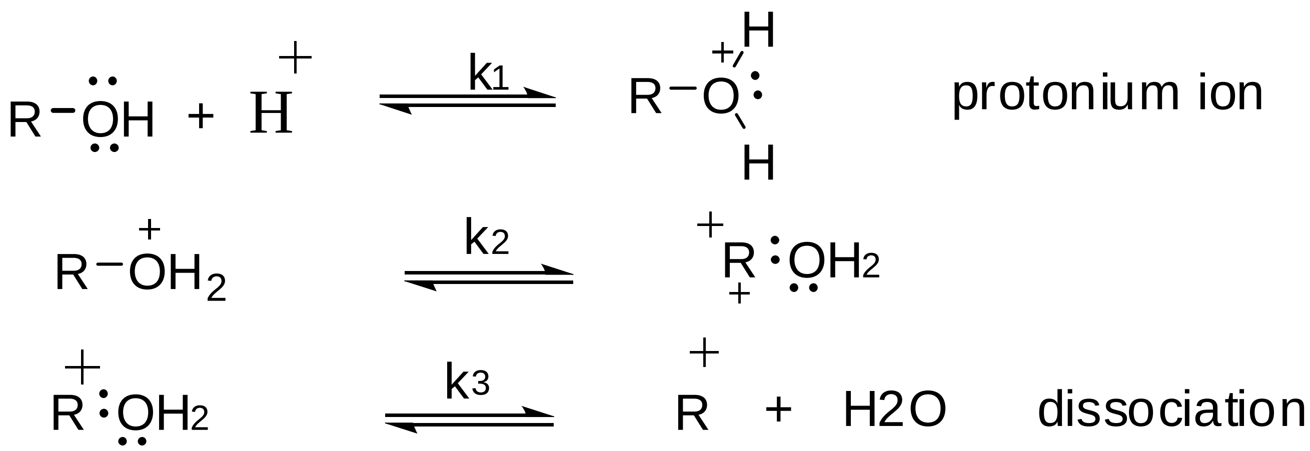
ions

* Stereochemical outcome:

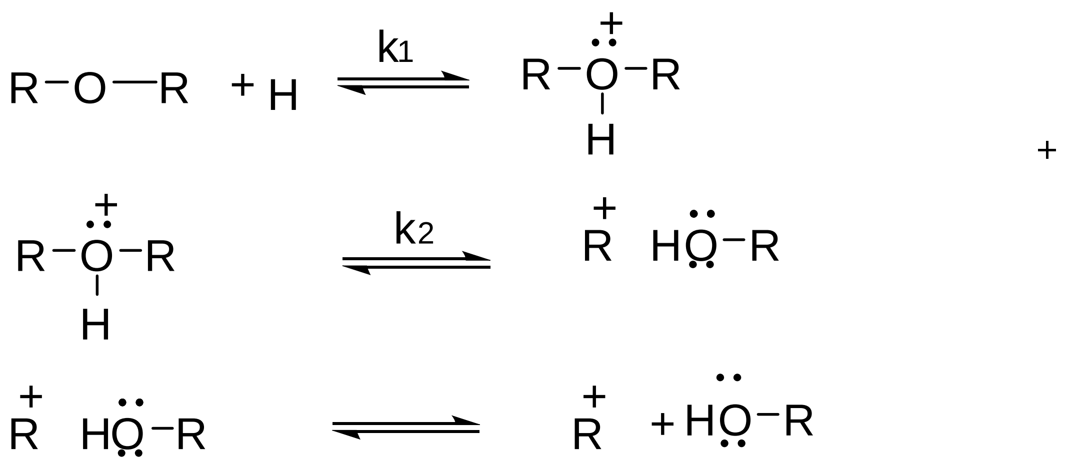
Nu-R Nu R^+ Nu

PROTONATION PROCESSES

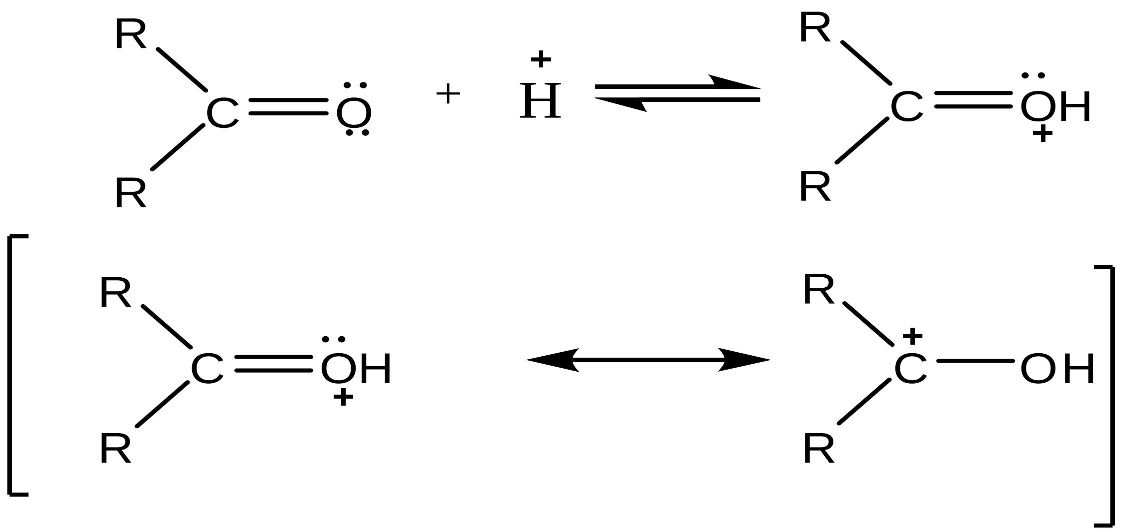
1. Protonation of alchols :



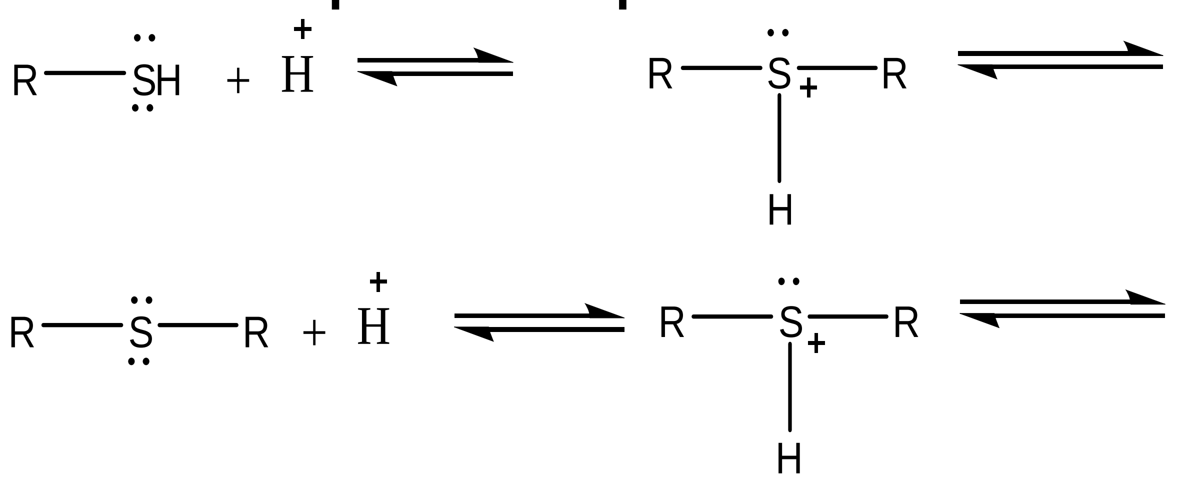
2. Protonation of ethers :



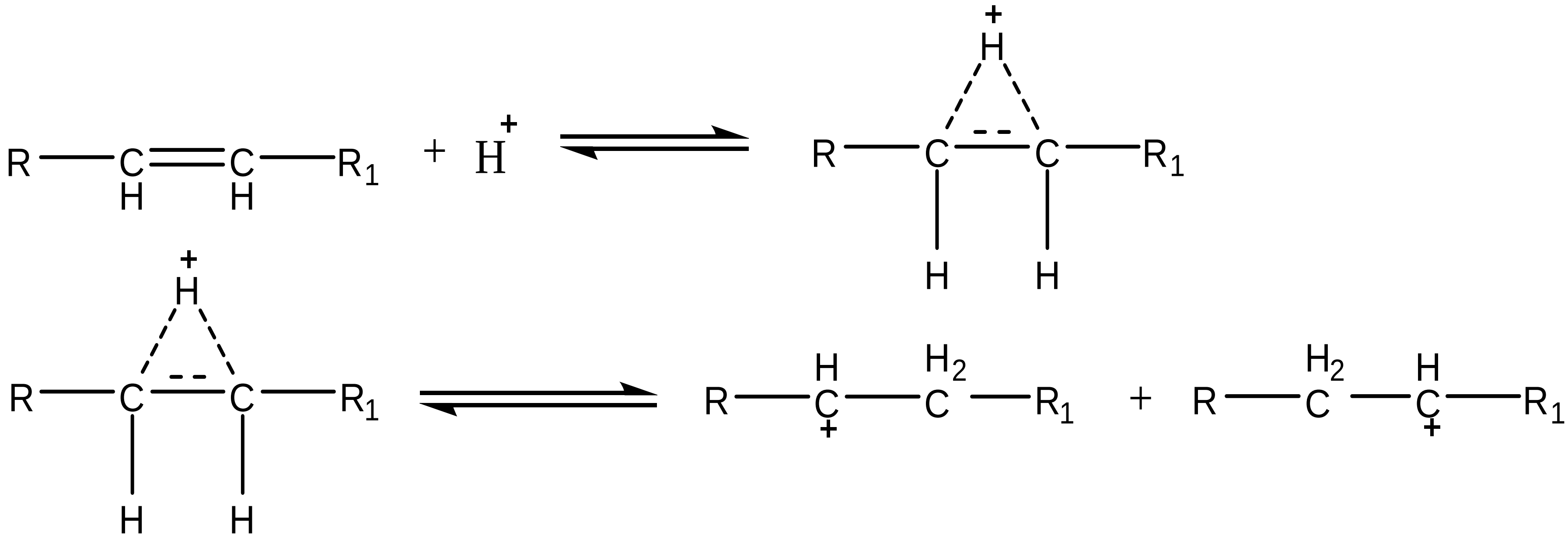
3. Protonation of a carbonyl group :



4. Protonation of mercaptans & sulphides :

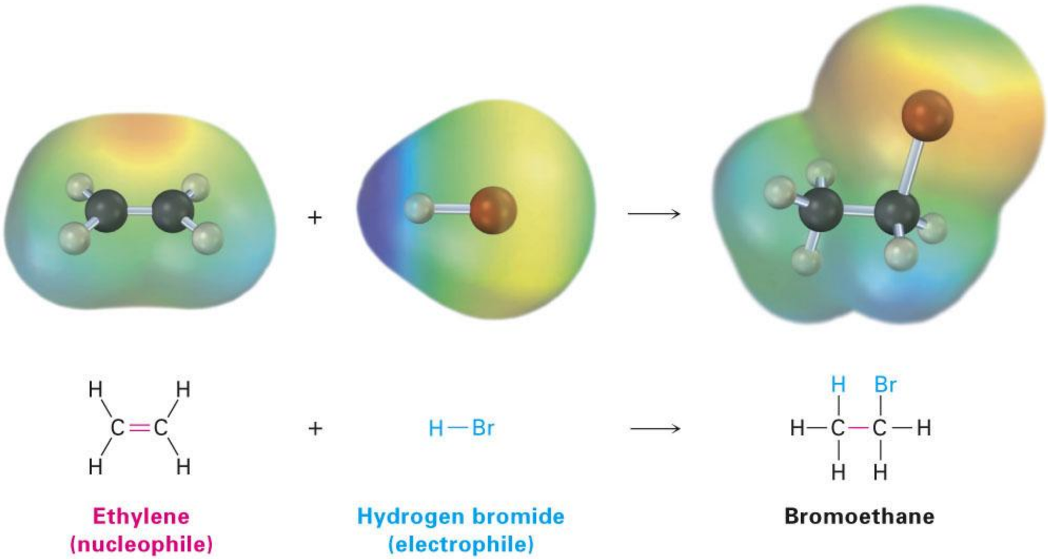


5. Protonation of an olefin :



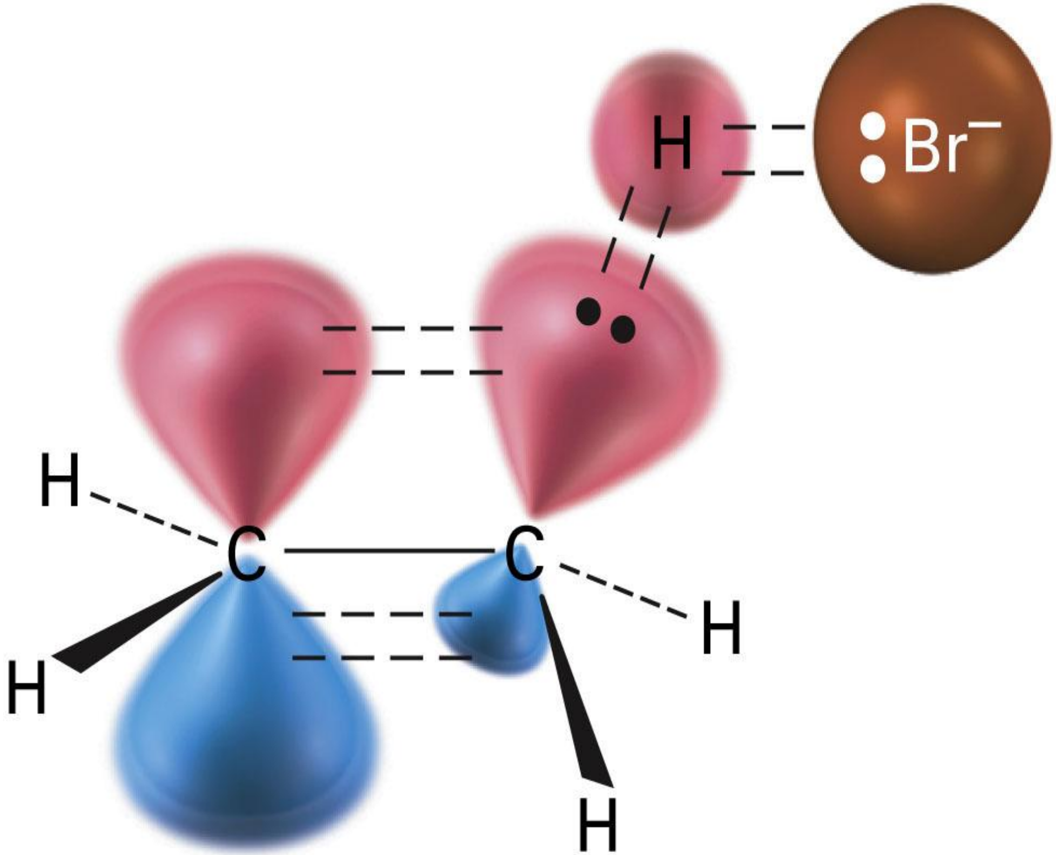
An Example of a Polar Reaction: Addition of HBr to Ethylene

- HBr adds to the π part of C-C double bond
- The π bond is electron-rich, allowing it to function as a nucleophile
- H-Br is electron deficient at the H since Br is much more electronegative, making HBr an electrophile

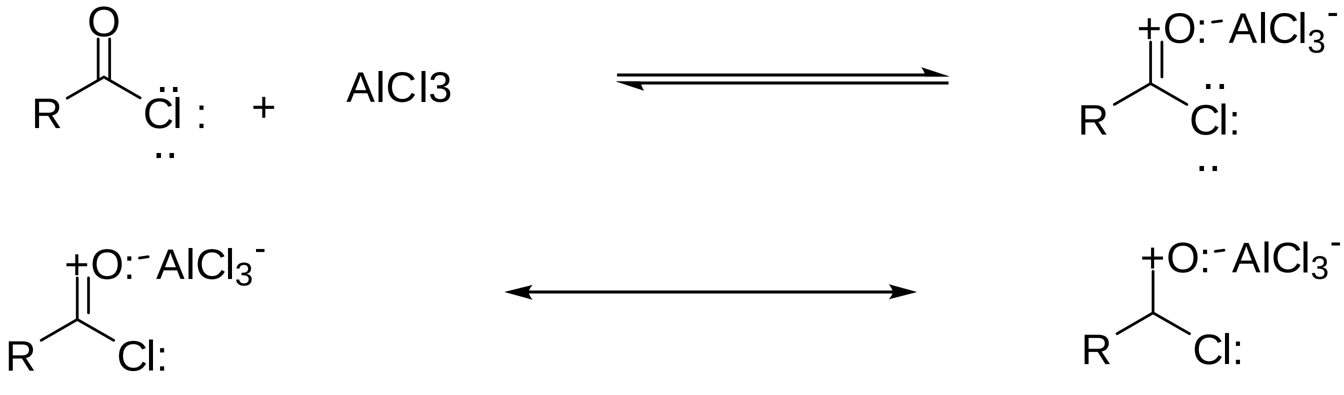


First Step in Addition

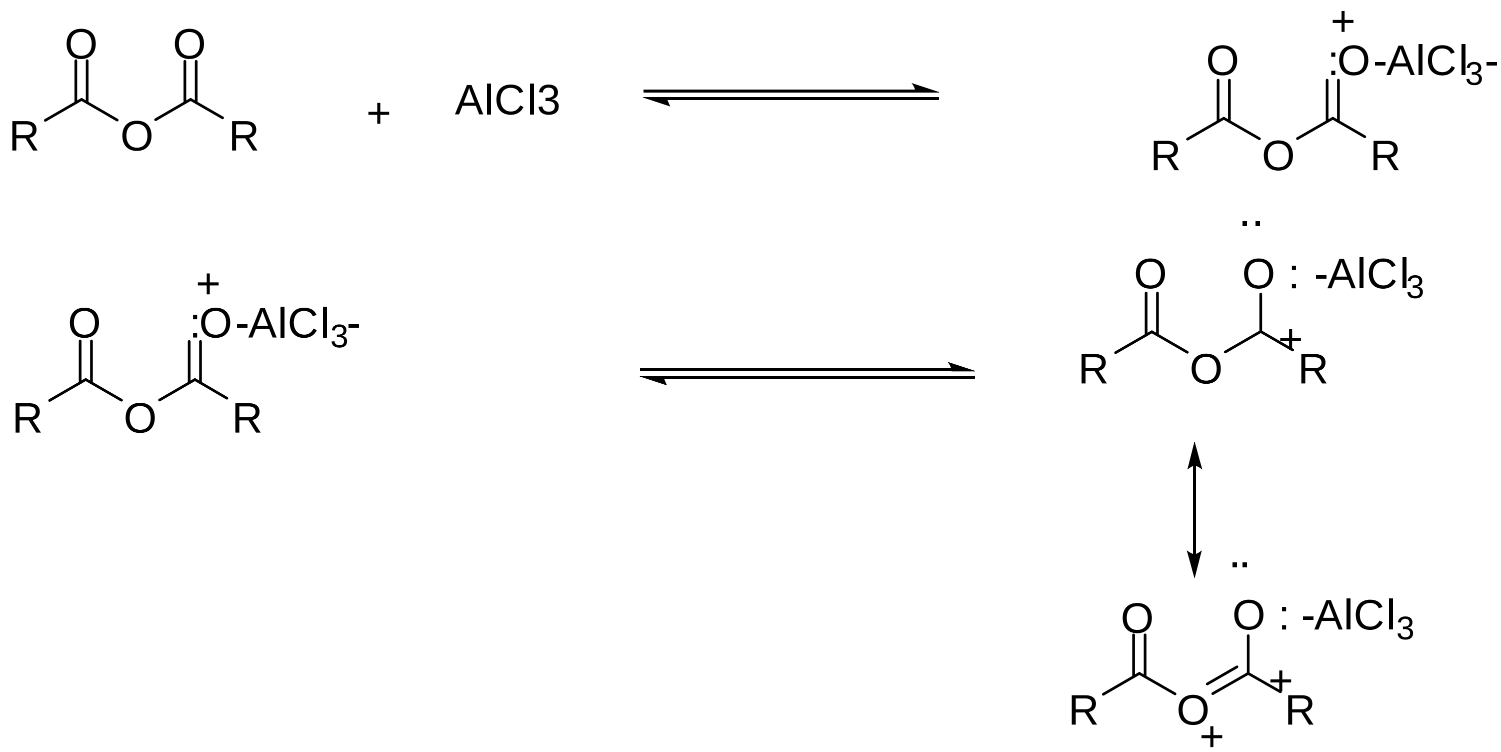
- In the addition of HBr the (conceptual) transition-state structure for the first step
- The π bond between carbons begins to break
  - The C–H bond begins to form
  - The H–Br bond begins to break



* With Acid halide:



* With Acid anhydride:



Complexation of alkyl halide with a Lewis acid

$$R\text{-}Cl: \; + \; AlCl_3 \; \overset{K_1}{\rightleftharpoons} \; \overset{+\quad -}{R\text{-}Cl\text{-}AlCl_3}$$

Complex

$$\overset{+\quad -}{R\text{-}Cl\text{-}AlCl_3} \; \overset{K_2}{\rightleftharpoons} \; R+(AlCl4)^-$$

tight ion pair

$$R+(AlCl4)^- \; \overset{K_3,\ \text{solvent}}{\rightleftharpoons} \; R+ \quad (AlCl4)^-$$

Solvent separted ion pair

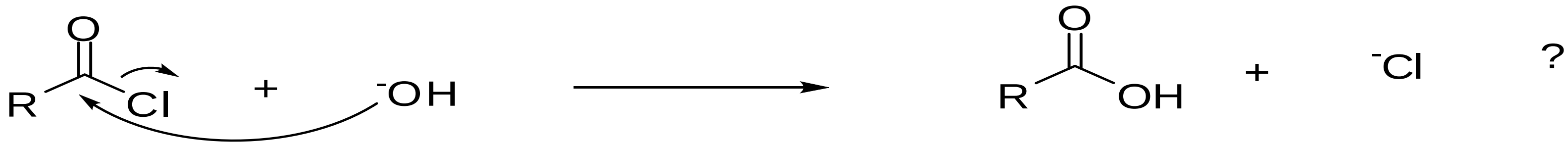
$$R+ \quad (AlCl4)^- \; \overset{K_4}{\rightleftharpoons} \; R+ \; + \; (AlCl4)^-$$

ions (dissociation)

General Raction of Carbanion

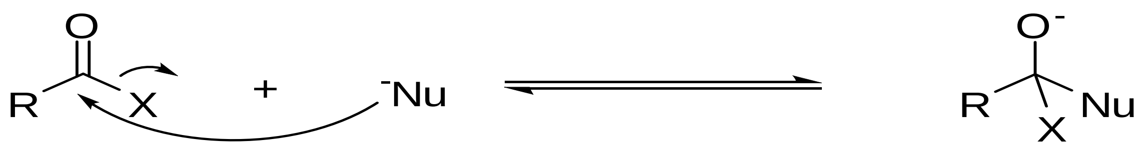
- Protonation
  ≡C: $^-$ + H
  → ≡C—H
- Attack at e – deficient carbon
  - sp^3 carbon
    C- alkylation
  - sp^2 carbon
    - At C=C
      polymerisation
      (Anionic)
    - At C=O
      Tetrahedral mechanism
      (Aldol type reaction)
- Elimination of nucleofuge from β position
- Rearrangement (rare)

Tetrahedral Mechanism:



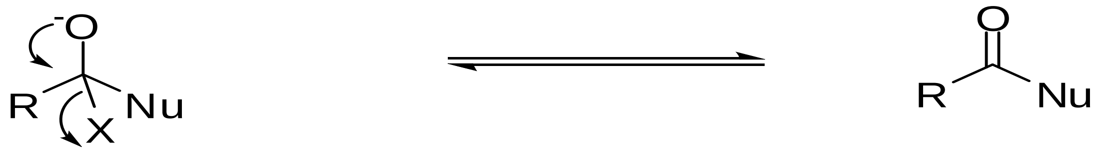
(SN^2 type)

(a)



SP^3

tetrahedral



SP^2

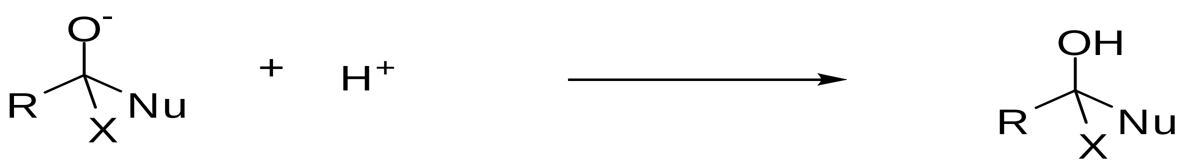
Planar

Substitution

Nu= ^-OH, H_2O, NH_3, $R\text{-}NH_2$

OR

X= Cl, OH, OCOR, NH_2



X= H, akyl , NH_2

Addition

ELECTRON BOOK KEEPING

Homogenic bond formations

(1) $\dot{C}H_3 + \dot{C}H_3 \longrightarrow CH_3\text{-}CH_3$

(2) $CH_3\text{-}\dot{C}H_2 + \cdot\ddot{Cl}: \longrightarrow CH_3\text{-}CH_2\text{-}Cl$

Heterogenic bond formations

(3) $\overset{+}{C}H_3 + {}^{\ominus}:\ddot{O}H \longrightarrow CH_3\text{-}OH$

(4) $(C_2H_5)_3\ddot{N} + H^+ \longrightarrow (C_2H_5)_3\overset{\oplus}{N}H$

(5) $(CH_3)_3\ddot{N} + \ddot{O}: \longrightarrow (CH_3)_3\overset{\oplus}{N}\text{-}O^{\ominus}$

Heterogenic bond formations