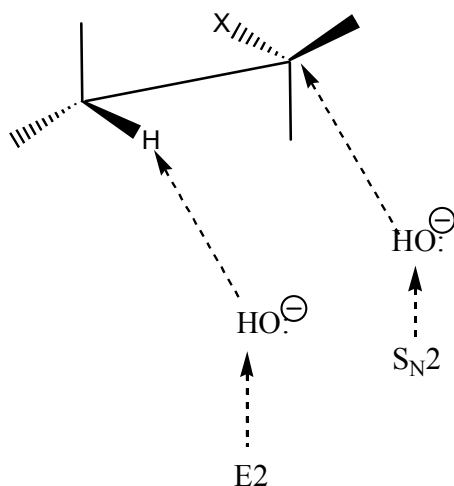# Fundamentals of Theoretical Organic Chemistry

# Lecture 2.

## 1.1.4  Geometrical and Energetic Bases of Reaction Mechanisms

Two types of second order reactions may be distinguished in the case of alkyl halides. The reagent may be HO:⁻ in both cases but the direction of attack and therefore the geometry of the transition state are different.
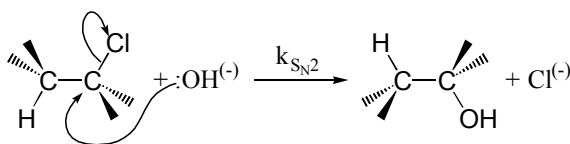


<div align="right">1.1.4—1 eq.</div>

The energetics of the reaction, which may be measured by reaction kinetics will determine which one of two mechanism will dominate the reaction.
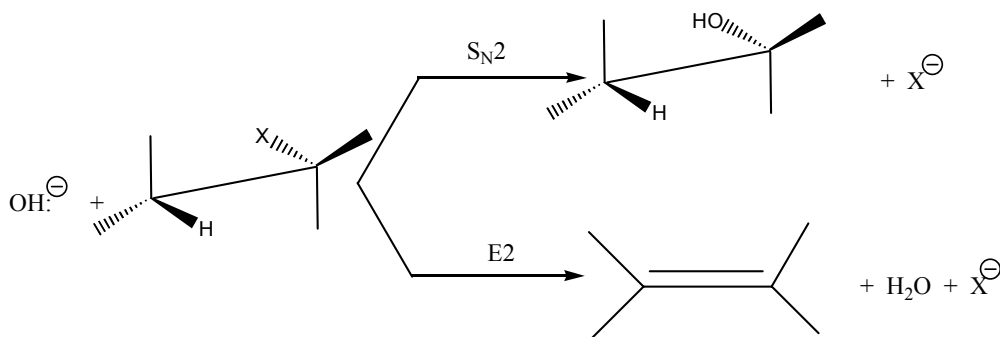


<div align="right">1.1.4—2 eq.</div>
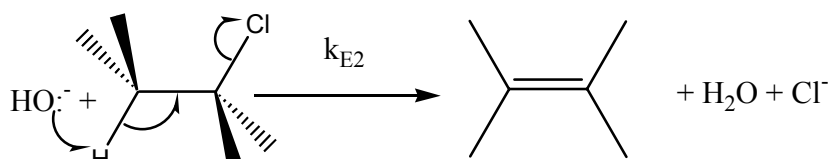
We can now recognize that $S_N2$ and E2 reactions follow second order kinetics, as shown in and 1.1.4—4. eq.



<div align="right">1.1.4—3. eq.</div>

$$v_{S_N2} = k_{S_N2}[\text{R-Cl}][\text{OH}^-]$$

<div align="right">1.1.4—4. eq.</div>

$$1.1.4\text{—}5.\ eq.$$

$$v_{E2} = k_{E2}[\text{R-Cl}][\text{OH}^-]$$

$$1.1.4\text{—}6.\ eq.$$

Note that the $S_N2$ mechanism occurs with an inversion of configuration at the carbon carrying the chlorine. This only occurs if and only if the carbon is a stereo centre and we start with an optically pure enantiomer.

From these relationships, one can see that $S_N2$ and E2 mechanisms are competing or parallel reactions, as emphasized in 1.1.4—7. eq.
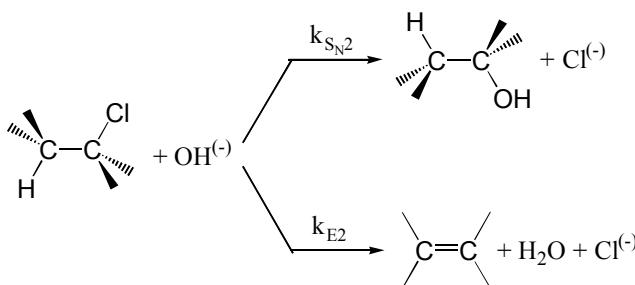


$$1.1.4\text{—}7.\ eq.$$

You will see in the next section that, for parallel or competing mechanisms, the product ratio in the reaction mixture, at any time during the reaction, is equal to the rate constant ratio eq. 1.1.4—8

$$\frac{[\text{H-C-C-OH}]}{[\text{C=C}]} = \frac{k_{S_N2}}{k_{E2}}$$

$$eq.\ 1.1.4\text{—}8$$

**Kinetics of Parallel and Multi-step reactions**

At the end of the previous section we saw that $S_N2$ and E2 mechanisms and $S_N1$ and E1 mechanisms occur in a parallel fashion and are, therefore, competing with each other. Let us examine the situation for the $S_N2$ and E2 mechanisms. The parallel nature of these two reactions was specified in 1.1.4—7. eq.By using a high concentration of the nucleophile (OH⁻ in this case) we can execute the reaction under pseudo-first-order conditions. Thus, 1.1.4—7. eq. can be written as(See appendix 1)

+ NaCl

NaOH

+ NaCl + H$_2$O

1.1.4—9. eq.
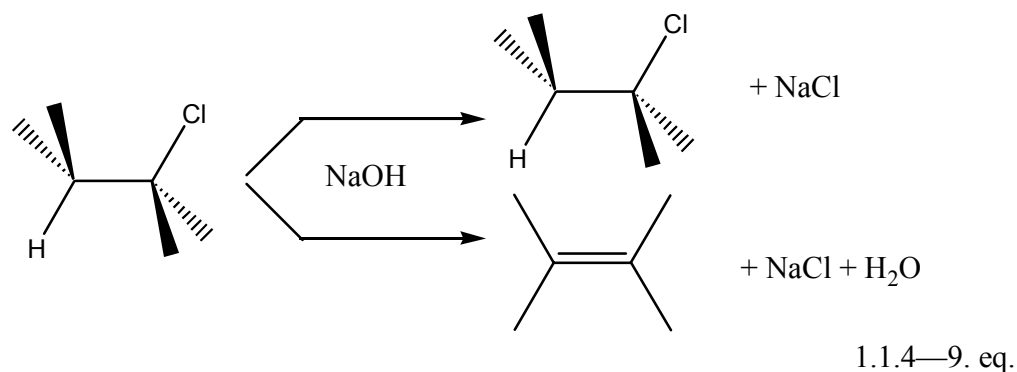
where $k'_{S_N2} = k_{S_N2}[OH^{(-)}]$ and $k'_{E2} = k_{E2}[OH^{(-)}]$

1.1.4—10. eq.

This mechanism can be written in a simplified fashion as:
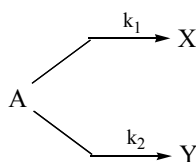


1.1.4—11. eq.

Figure 1.1.4—1shows in a schematic fashion the concentration profiles for these parallel reactions.
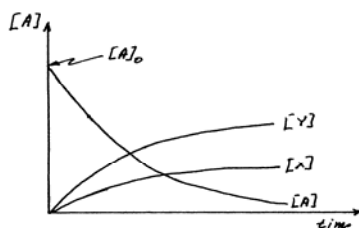


**Figure 1.1.4—1. Concentration profiles for parallel first order reactions.**

The rates of consumption of A to form both X and Y can be characterized by the following differential 1.1.4—12. eq. and integrated eq. 1.1.4—13 rate equations:

$$- \frac{d[A]}{dt} = k_1[A] + k_2[A] = (k_1 + k_2)[A] = k[A]$$

1.1.4—12. eq.

$$[A] = [A]_0\, e^{-kt}$$

eq. 1.1.4—13

Equation 1.1.4—14. eq. and 1.1.4—15. eq. give the individual rates of product formation.

$$\frac{d[X]}{dt} = k_1[A] = [A]_0 k_1 e^{-kt}$$

<div align="right">1.1.4—14. eq.</div>

$$\frac{d[Y]}{dt} = k_2[A] = [A]_0 k_2 e^{-kt}$$

<div align="right">1.1.4—15. eq.</div>

Taking the initial conditions to be

$$[X]_0 = [Y]_0 = 0$$

<div align="right">1.1.4—16. eq.</div>

one may obtain the following integrated rate equations:

$$[X] = \frac{k_1}{k}[A]_0(1 - e^{-kt})$$

<div align="right">1.1.4—17. eq.</div>

$$[Y] = \frac{k_2}{k}[A]_0(1 - e^{-kt})$$

<div align="right">1.1.4—18. eq.</div>

From these two equations we may calculate the product ratio:

$$\frac{[X]}{[Y]} = \frac{k_1}{k_2}$$

<div align="right">1.1.4—19. eq.</div>

Of course, both $k_1$ and $k_2$ are pseudo-first-order rate constants and they incorporate the nucleophile concentration, which cancels in 1.1.4—19. eq. demonstrates the relative importance of $S_N2$/E2 mechanisms, which we stated in eq. 1.1.4—8.

## 1.1.5  Typical reaction mechanisms

We may distinguish three types of reaction mechanisms and each:
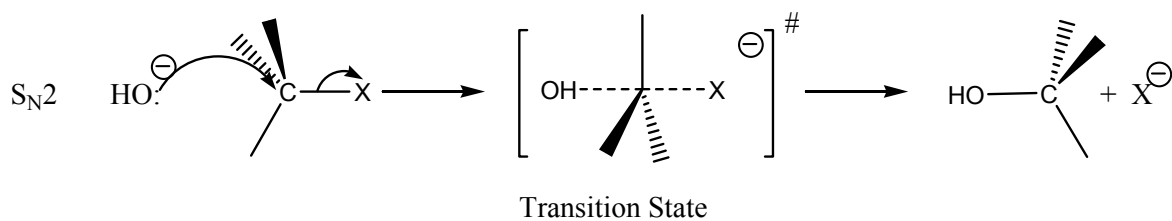
**Table 1.1.5-1 Mechanism types**

| Rection types | Reagent types | | |
|---|---|---|---|
| | Nucleophil(N) Electron rich | Electrophil(E) Electron deficient | Radical(R) |
| Substitution(S) | $S_N$ | $S_E$ | $S_R$ |
| Addition(A) | $A_N$ | $A_E$ | $A_R$ |
| Elmination(E) | $E_N$ | $E_E$ | $E_R$ |

In addition reactions always two molecules are reacting therefore they are bimolecular and second order. They are symbolized: $A_N2$, $A_E2$, $A_R2$. The substitution may be bimolecular and unimolecular. Consequently they are symbolized as: $S_E1$, $S_N1$, $S_R1$ or $S_E2$, $S_N2$, $S_R2$.
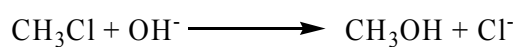
In the case of elimination reactions it could be base induced bimolecular (E2), or it could be acid induced unimolecular (E1).

## Examples for various mechanisms:

**Nucleophil Substitution**

On saturated carbon:

$S_N2$



Transition State

1.1.5-1. eq

$$CH_3Cl + OH^- \longrightarrow CH_3OH + Cl^-$$

1.1.5-2. eq

$S_N1$



Reaction Intermediate

1.1.5-3. eq

$$tBuCl + OH^- \longrightarrow tBuOH + Cl^-$$

1.1.5-4. eq

On aromatic carbon:



2-Methoxy-1,3,5-trinitro
-benzene

2-Ethoxy-1,3,5-trinitro
-benzene
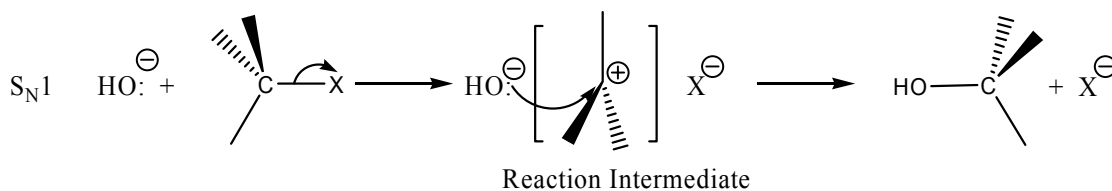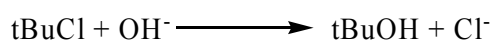
1.1.5-5. eq

**Electrophilic substitution:**

On saturated carbon:

$$S_E2: \quad Y-R \; + \; E^{\oplus} \longrightarrow Y^{\oplus} \; + \; R-E$$

1.1.5-6. eq

$S_E1$:   Y-R   +   $E^{\oplus}$     $\longrightarrow$   $Y^{\oplus}$  +  $R^{\ominus}$ + $E^{\oplus}$   $\longrightarrow$   $Y^{\oplus}$  +  R-E

1.1.5-7. eq

BrMg-R  +  Br-Br     $\longrightarrow$    R-Br   +  $MgBr_2$
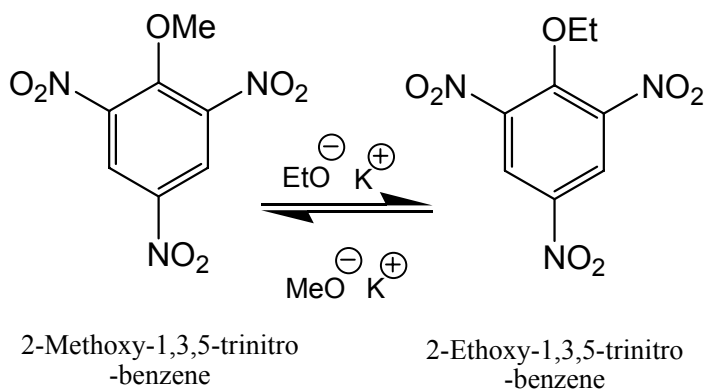
1.1.5-8. eq



1.1.5-9. eq

On aromatic carbon:



1.1.5-10. eq



Benzene                         Nitro-benzene

1.1.5-11. eq
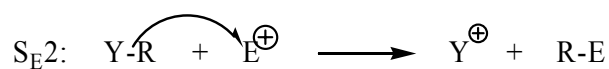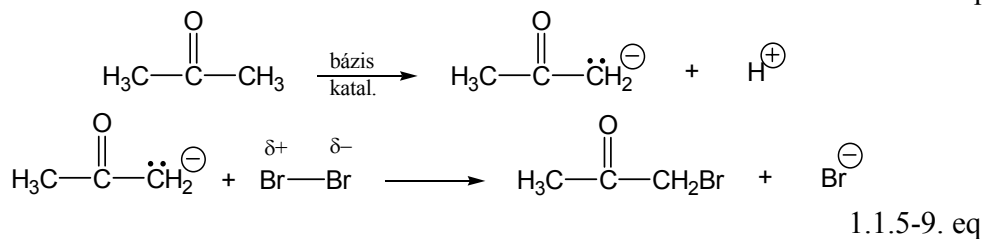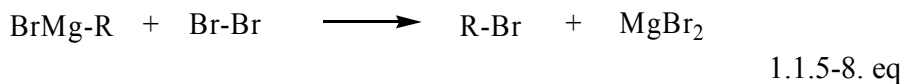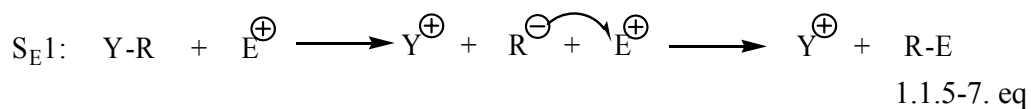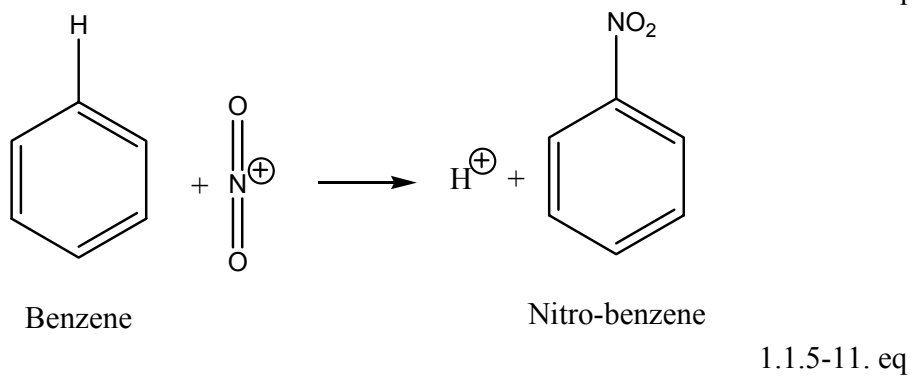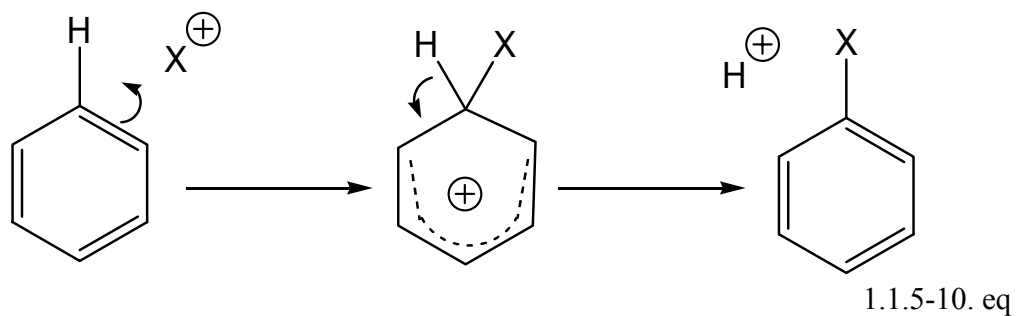
**Radical substitution:**

On saturated carbon:



eq. 1.1.5—1



eq. 1.1.5—2

On aromatic carbon:



eq. 1.1.5—3



benzoyl peroxide    at relatively low temperature

80°C

2 benzoyloxy radicals

spontaneous decarboxylation



**Ph •** + $O=C=O$



intermediate     **biphenyl**

eq. 1.1.5—4

**Nucleophil addition:**

$A_N2$

eq. 1.1.5—5



Acrylonitrile → 3-Ethoxy-propionitrile

eq. 1.1.5—6



hemiacetal
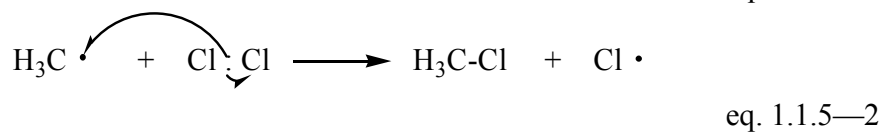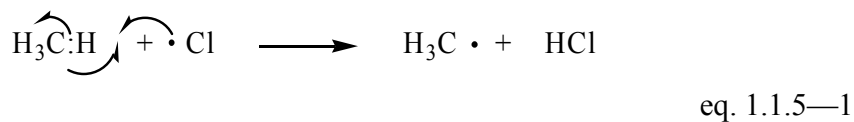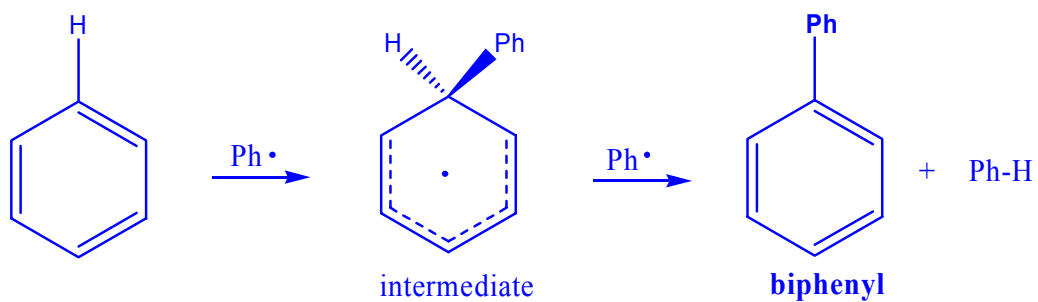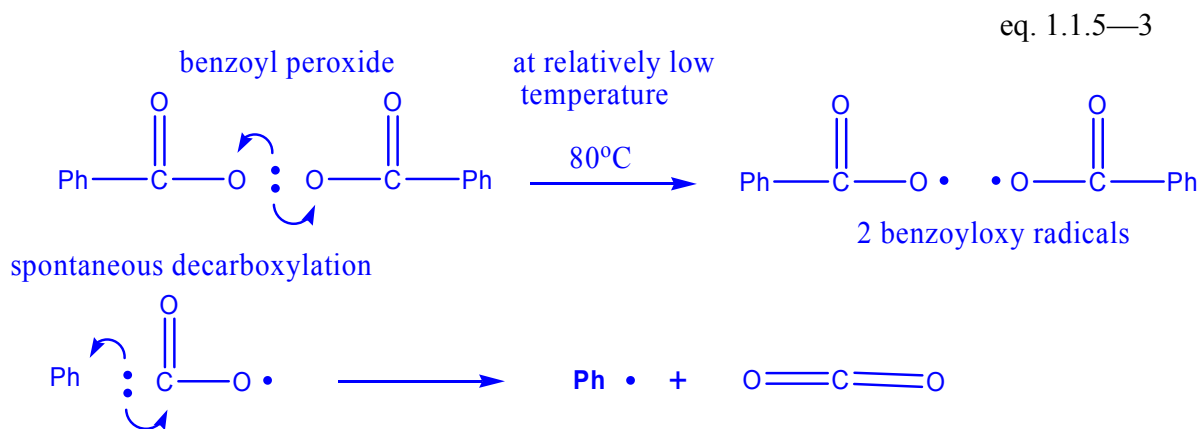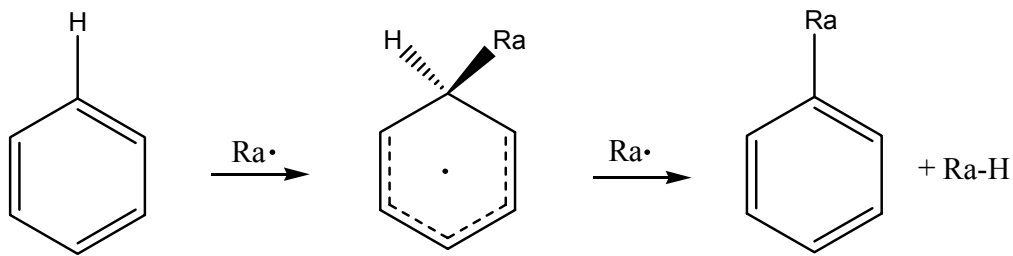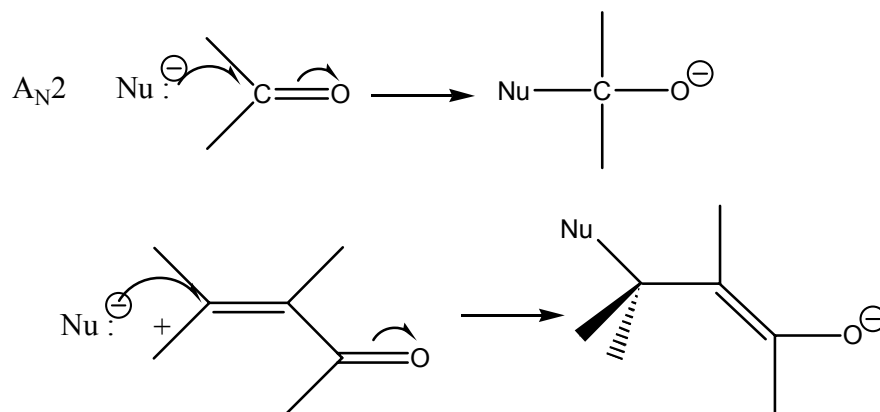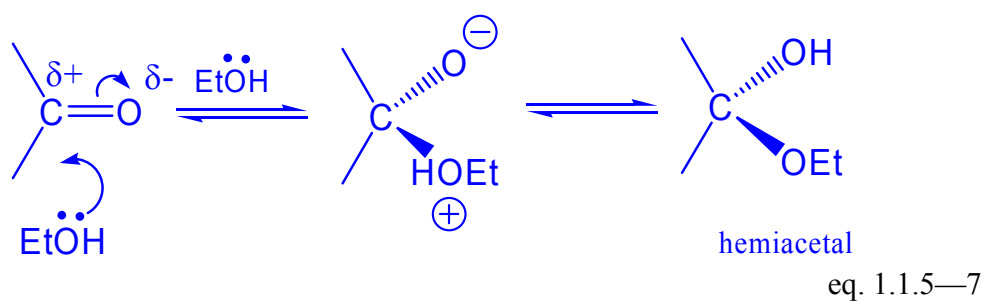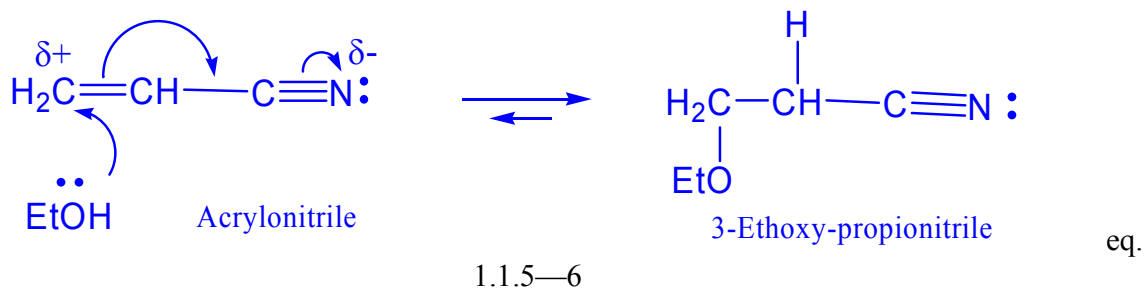
eq. 1.1.5—7

**Electrophilic addition:**
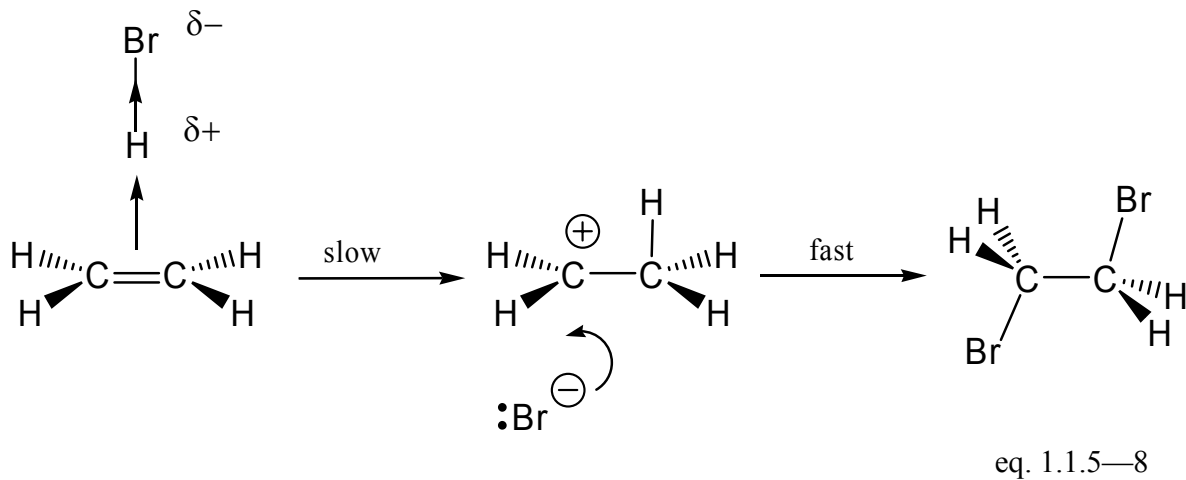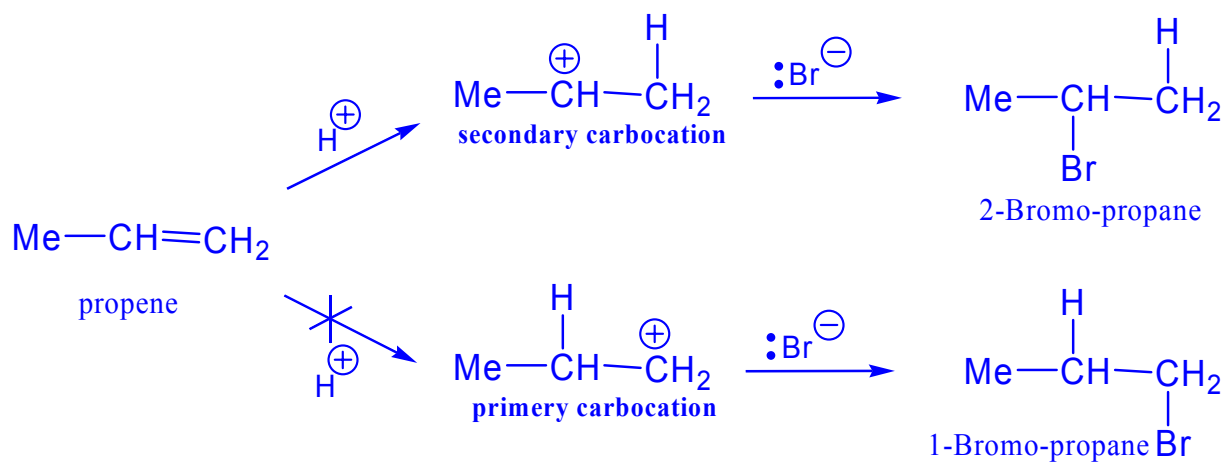


eq. 1.1.5—8

eq. 1.1.5—9

Memo: Markovnikow rule. Which is going to be the major product?

**Radical addition:**

$$HO\cdot \;+\; H\text{-}Br \longrightarrow H_2O \;+\; Br\cdot$$



2,3,4,5-Tetramethyl-hexa-2,4-diene

2-Bromo-2,3,4,5,5-pentamethyl-hex-3-ene
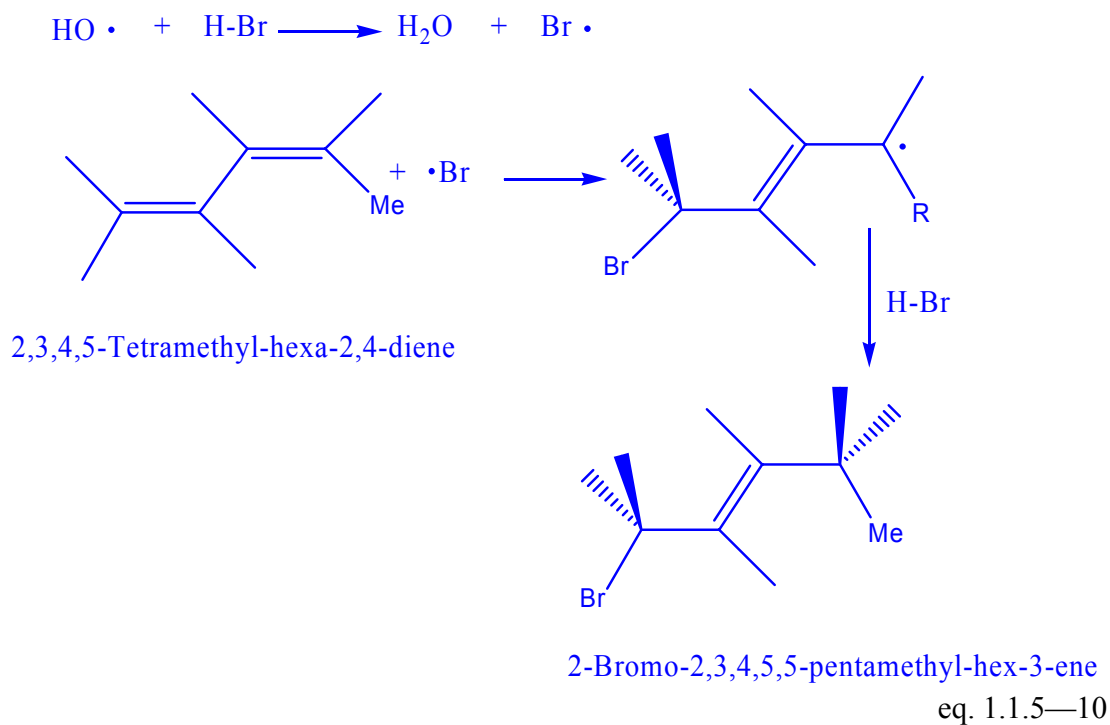
eq. 1.1.5—10

**Nucleophilic (base induced) elimination:**

Bimolecular:

$HO^{\ominus}$ ： 



$$H_2O \ + \ \diagup\!\!=\!\!\diagdown \ + \ Z^{\ominus}$$

eq. 1.1.5—11

HO—H

$H_2C\!=\!CH_2$

$Br^{\ominus}$

**E2**

$\begin{array}{cc} H & OH \\ | & | \\ H_2C\!-\!CH_2 \end{array}$ + $Br^{\ominus}$    $S_N2$
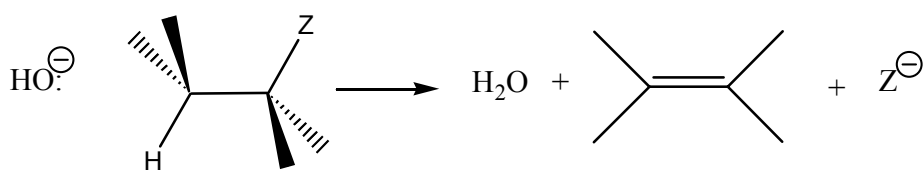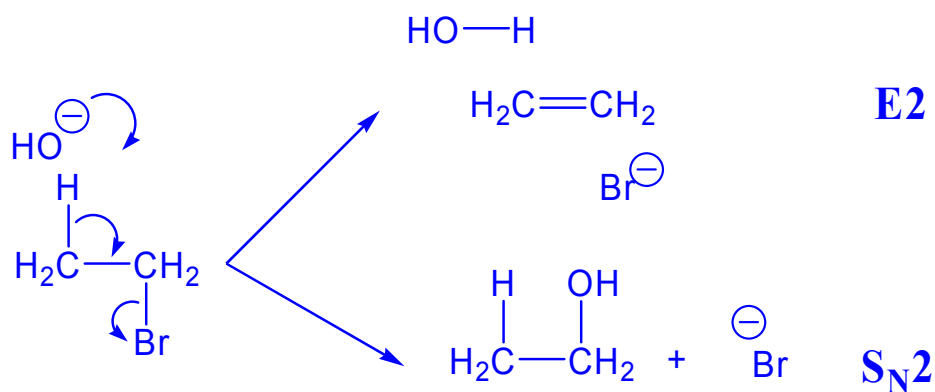
eq. 1.1.5—12

Unimolecular (E1)

$H_2O$

$\xrightarrow{\text{slow}}$

$\begin{array}{c} H \\ | \\ CH_2\!-\!CR_2^{\oplus} \end{array}$

$Br^{\ominus}$

$\xrightarrow{\text{fast}}$

$\begin{array}{c} H \\ | \\ H\!-\!O\!-\!H \\ \oplus \end{array}$

$CH_2\!=\!CR_2$

$Br^{\ominus}$

eq. 1.1.5—13

$\begin{array}{c} H \\ | \\ CH_2\!-\!CMe_2 \end{array}$

Br

$\xrightarrow{\hphantom{xxx}}$

$Br^{\ominus}$

$\begin{array}{c} H \\ | \\ H\!-\!O\!-\!H \\ \oplus \end{array}$

$CH_2\!=\!CMe_2$

2-Bromo-2-methyl-propane                    Isobutene

eq. 1.1.5—14

$$HO^{\ominus} \quad \overset{H}{\underset{Y}{\overset{|}{\underset{|}{X_2C-CH_2}}}} \longrightarrow \quad HO{-}H \quad \overset{\ominus}{\underset{Y}{\overset{}{X_2C-CH_2}}} \longrightarrow \quad HO{-}H \quad \overset{}{X_2C=CH_2} \quad Y^{\ominus}$$

conjugated base
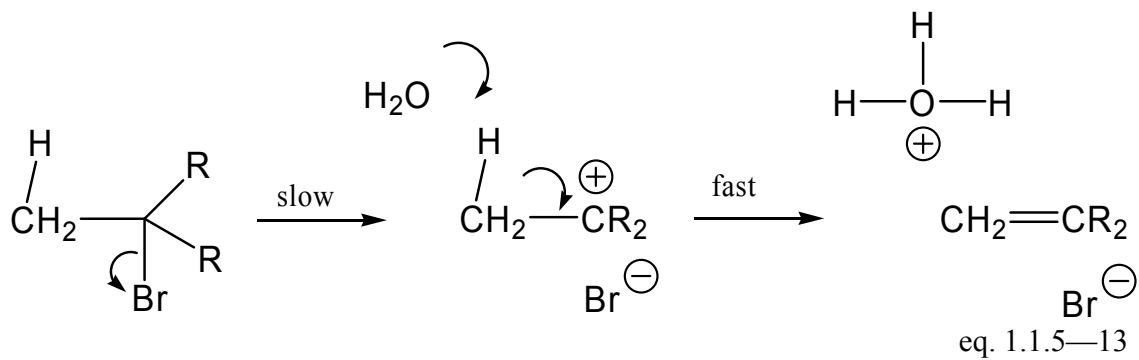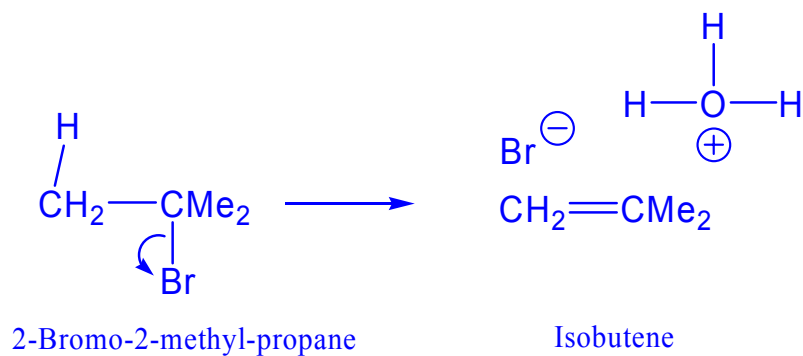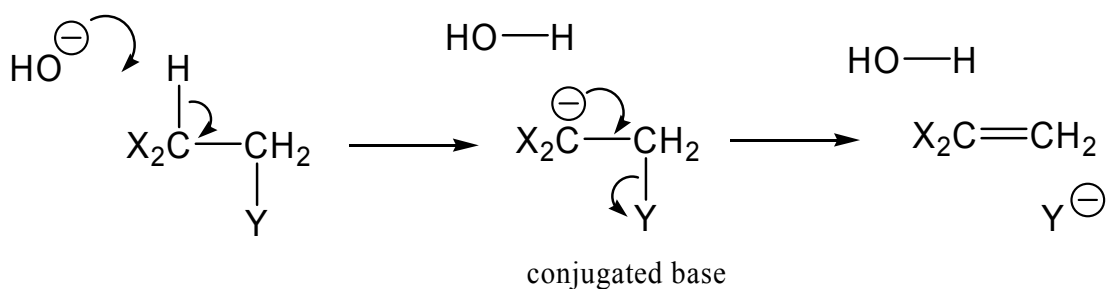
eq. 1.1.5—15

**Electrophilic (acid induced) elimination:**

Unimolecular:

$$\overset{H}{\underset{H^{\oplus} \quad :OH}{\overset{|}{H_2C-CR_2}}} \quad \underset{H_2SO_4}{\rightleftharpoons} \quad \overset{H}{\underset{\underset{\oplus}{HOH}}{\overset{|}{H_2C-CR_2}}} \quad \underset{- H_2O}{\rightleftharpoons}$$

$$\underset{- H_2O}{\rightleftharpoons} \quad \overset{H}{\underset{H_2O:}{\overset{|}{H_2C-CR_2^{\oplus}}}} \quad \underset{- H^{\oplus}}{\rightleftharpoons} \quad \overset{H^{\oplus}}{H_2C=CR_2}$$

eq. 1.1.5—16

$$\overset{H}{\underset{H^{\oplus} \quad :OH}{\overset{|}{H_2C-CMe_2}}} \quad \underset{H_2SO_4}{\rightleftharpoons} \quad \overset{H^{\oplus} \quad H{-}OH}{H_2C=CMe_2}$$

2-Methyl-propan-2-ol                              Isobutene
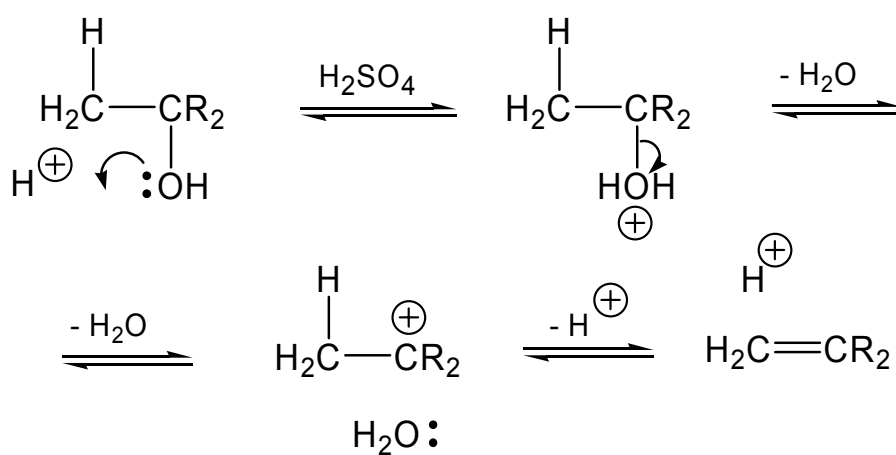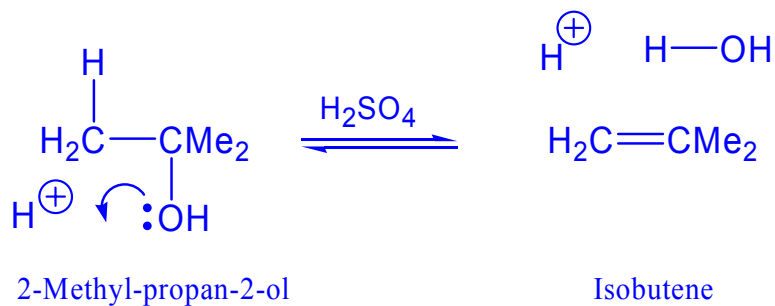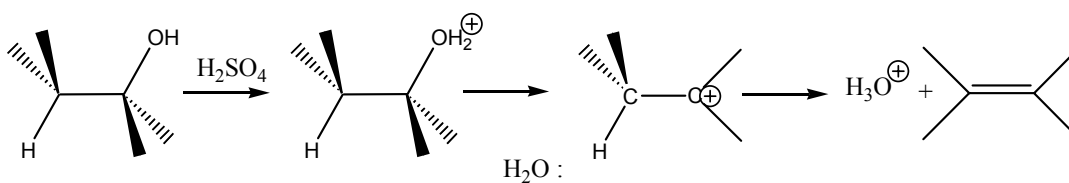
eq. 1.1.5—17



eq. 1.1.5—18

**Radical elimination:**

Not a well established process. Analogously to previous mechanisms it might occur as shown:

$$Ra \cdot \quad H$$
$$\underset{\underset{Y}{|}}{H_2C} - CH_2 \longrightarrow$$

$$Ra - H$$
$$H_2C = CH_2$$
$$Y \cdot$$

eq. 1.1.5—19

$$PhH \quad + \quad \cdot SMe$$

Ph$\cdot$  ...SMe (2,3-Dimethyl-2-methylsulfanyl-butane) $\longrightarrow$ 2,3-Dimethyl-but-2-ene

2,3-Dimethyl-
2-methylsulfanyl-butane
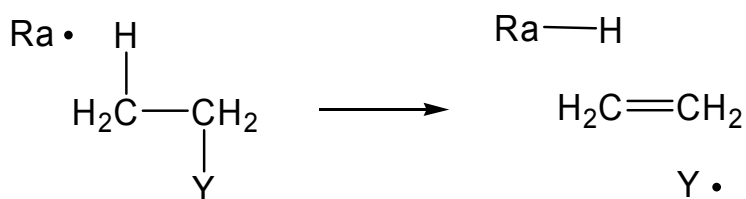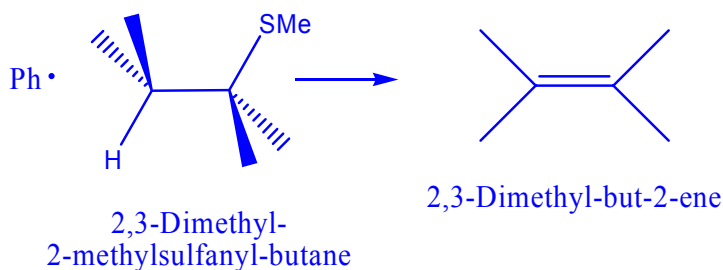
eq. 1.1.5—20

This reaction however could occur in a stepwise fashion.

A great deal of information, on originating from well designed experiment has been accumulated during the 20th century. Before we turn to the discussion of the theoretical background some selected illustration will be given below.

We will cover in the rest of this chapter some special features of reaction mechanism:

## 1.1.5.1 Free radical halogenations of methane and other saturated hydrocarbon.

Homolytic and Heterolytic Bond Dissociation Energies

The endo- and exothermicity of a reaction may be determined from the corresponding bond dissociation energies (BDE). Consider the following example:

$$\mathbf{H - H \quad + \quad Cl - Cl \quad \rightarrow \quad 2\ H - Cl}$$

BDE(kcal/mol):     104     +     58     +     +(-103 x 2)     = 162+(- 206)
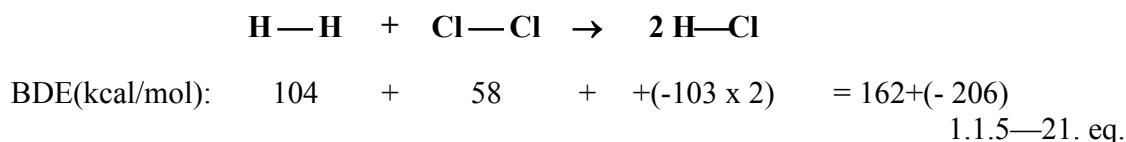
1.1.5—21. eq.

$$\Delta H \text{ of reaction} = -206 - ( -162 ) = -44 \text{ kcal/mol}$$

1.1.5—22. eq.

The process is also illustrated in Figure 1.1.5—1.

$$H\bullet \ + \ \bullet H \quad + \quad Cl \bullet + \ \bullet Cl$$

$$+162 \qquad\qquad -206$$

$$H_2 + Cl_2 \qquad -44$$
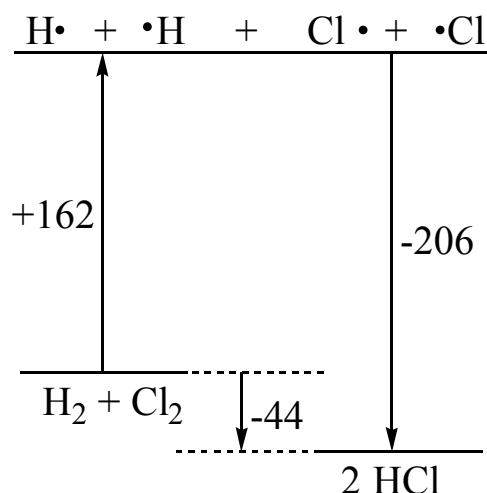
$$2 \ HCl$$

**Figure 1.1.5—1. A schematic illustration of how bond dissociation energies (BDE in kcal/mol) may be used to determine the enthalpy of a reaction ( $\Delta H_{reaction}$). In this example  $H_2 + Cl_2 \rightarrow$ 2HCl is used to illustrate the energetics of the reaction. Enthalpy differences are given in kcal/mol units. (See appendix 1.)**

The Morse potential, that shows the change of energy with increasing bond length, leads to bond dissociation when the internuclear separation, r, is increased to infinity. The depth of the potential curve is a good measure of the BDE if we disregard the zero point vibration (to be discussed later). Figure 1.1.5—2 illustrates the situation for the case of HCl. This figure also shows that heterolytic dissociation is energetically less favourable than homolytic dissociation:

$$H\text{:}Cl \quad \begin{array}{c} \xrightarrow[\text{or ionic}]{\text{heterolytic}} H^{(+)} + Cl^{(-)} \\ \\ \xrightarrow[\text{or free radical}]{\text{homolytic}} H\bullet \ + \ \bullet Cl \end{array}$$
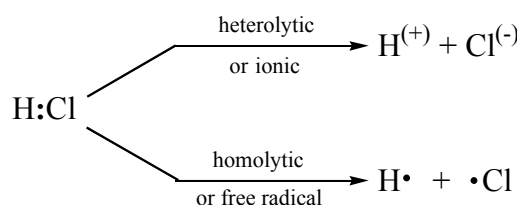
1.1.5—23. eq.

**Figure 1.1.5—2 A schematic illustration of the homolytic (free-radical) and heterolytic (ionic) dissociation potentials of HCl. Energy differences are given in units of kcal/mol. The solid curve is frequently referred to as a "Morse potential".**

     In fact, the heterolytic (ionic) dissociation requires an amount of energy of (103 + 230.4 = 333.4 kcal/mol), which is more than three times that of the homolytic (free-radical) dissociation (103 kcal/mol).

     This observation is not limited to inorganic diatomic molecules. The situation is analogous, for example, to the cleavage of a carbon - chlorine bond. Take, for the sake of simplicity, $H_3C$—Cl. The BDE for C—Cl is 83.5 kcal/mol. As illustrated in Figure 1.1.5—3, the energy gap between $H_3C\bullet + \bullet Cl$ and $H_3C^{(+)} + Cl^{(-)}$ is 176 kcal (i.e., 259.4 - 83.4 = 176.0).[1]
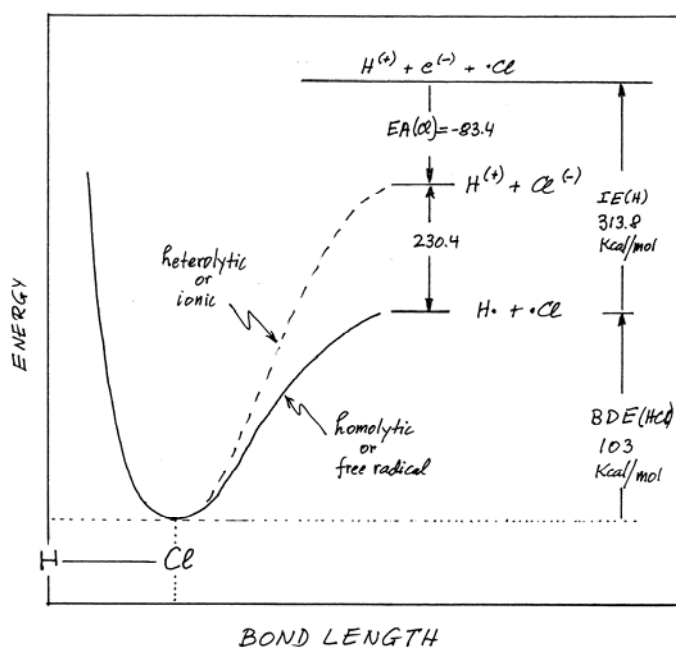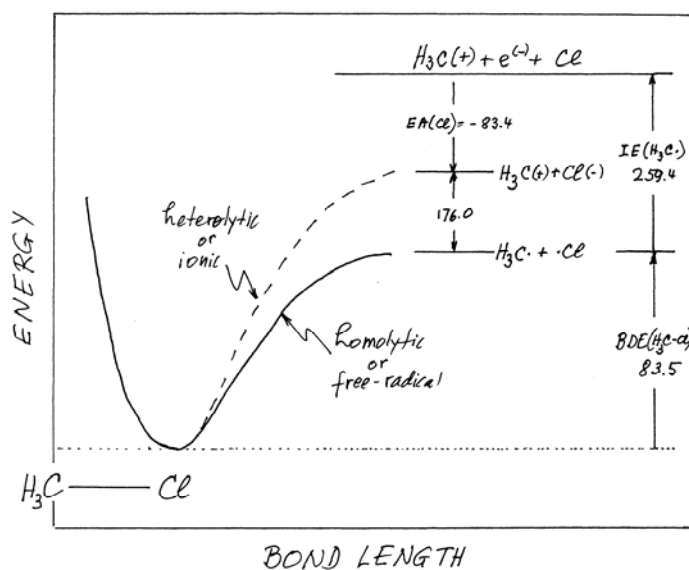
**Figure 1.1.5—3 A schematic illustration of the homolytic (free-radical) and heterolytic (ionic) dissociation potentials of H$_3$C—Cl. Energy differences are given in units of kcal/mol. The solid curve is frequently referred to as a "Morse potential".**

Although the numbers given in Figure 1.1.5—3are different from those of Figure 1.1.5—2the qualitative picture is the same. Heterolytic (ionic) dissociation requires more than three times as much energy as homolytic (free-radical) dissociation. This appears to be in direct contrast with the experience we have accumulated so far. We do know that HCl will dissociate in an ionic fashion in water (like1.1.5—24. eq.) and we have discussed in previous chapter that a C—Cl bond will undergo a heterolytic cleavage in an S$_N$1 reaction mechanism rather than a homolytic cleavage 1.1.5—24. eq. Type of the dissociation
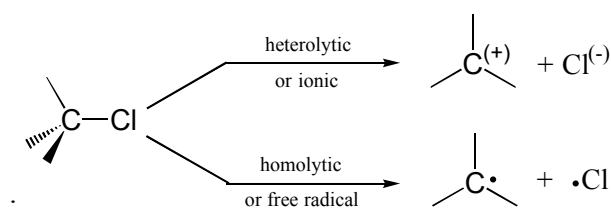


1.1.5—24. eq.

Clearly, there must be an explanation for this apparent discrepancy, the answer lies in the effect of the solvent. Both reactions, i.e., 1.1.5—22. eq. and 1.1.5—21. eq.can occur in aqueous or highly polar solvents. Both the cation and the anion are strongly solvated by polar solvents such as H$_2$O. In any polar solvent, the solvation will stabilize the ion pair with respect to the radical pair. Consequently, ionic reactions will be energetically more favourable. In the gas phase or in a non-polar solvents such stabilization is not possible, therefore free-radical reactions will be energetically more favourable. Most of the concepts reviewed here, in association with the phenomenon of solvation, have been presented.

In most organic textbooks there is a table containing a variety of BDE values. The following values, in kcal/mol units, are given here in table 1.1.5-1 for illustrative purposes only and this list is not meant to be complete

**1.1.5-2. Table Bond dissociation energies[2]**

| Bond type | BDE kcal/mol | Bond type | BDE kcal/mol | Bond type | BDE kcal/mol | Bond type | BDE kcal/mol |
|-----------|--------------|-----------|--------------|-----------|--------------|-----------|--------------|
| $H_3C$-H  | 104          | F-F       | 38           | H-F       | 136          | $H_3C$-F  | 108          |
| $1^0$ C-H | 98           | Cl-Cl     | 58           | H-Cl      | 103          | $H_3C$-Cl | 83.5         |
| $2^0$ C-H | 94.5         | Br-Br     | 46           | H-Br      | 87.5         | $H_3C$-Br | 70           |
| $3^0$ C-H | 91           | I-I       | 36           | H-I       | 71           | $H_3C$-I  | 56           |
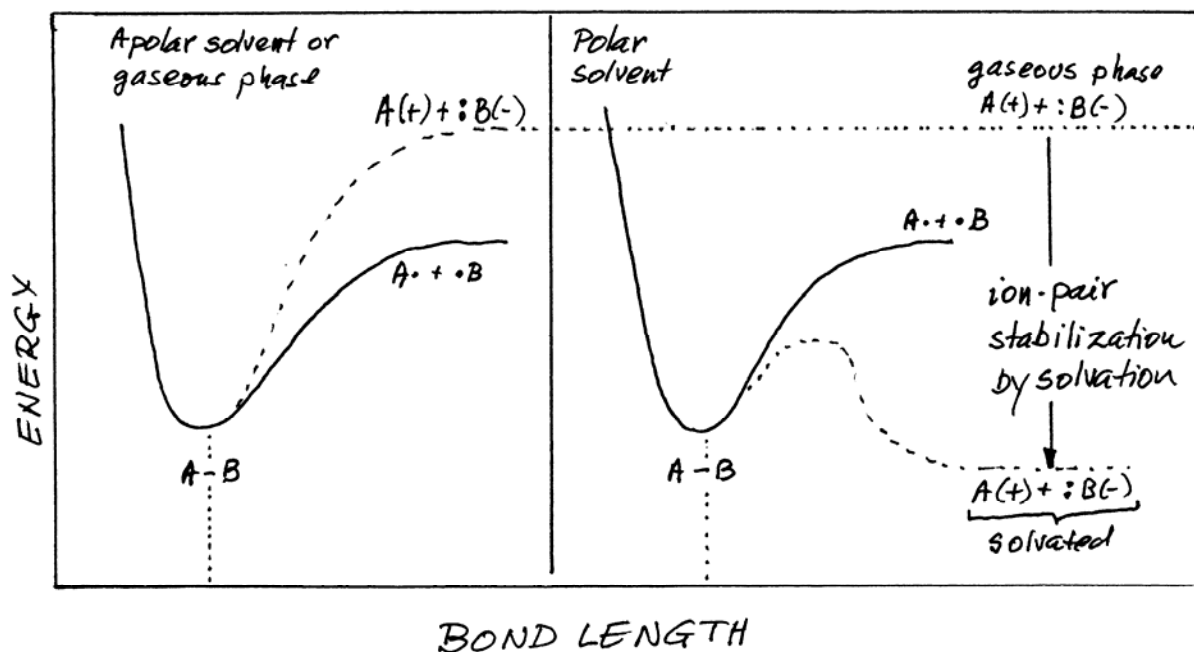


**Figure 1.1.5—4A schematic illustration of ion-pair stabilization by solvation in a polar solvent (dotted line at the right hand side of the figure) compared to the energy level of ion pairs in an apolar solvent or the gaseous phase.**

## Free-Radical Reactions; Halogenation of Hydrocarbons

In most of the reactions we have discussed so far, electrons moved in pairs. This is true for all ionic reactions. In other words, in ionic reactions, two electrons move in a given step. In contrast to the above, in free-radical reactions, one electron moves in a given step. However, electrons are always paired up in organic molecules. For this reason, a free-radical needs to be generated to initiate a radical mechanism. If the free-radical is generated thermally, the BDE is the energy requirement. Sometimes, when a low lying electronic excited state is dissociative, as illustrated Figure 1.1.5—5, free radicals can also be generated photochemically.

**Figure 1.1.5—5 A schematic illustration for the thermal and photochemical generation of radicals (A:A → 2A•) Both way results the same radical. (See appendix 4)**

Consider the chlorination of methane. The following chain mechanism is operative:

$$Cl:Cl \longrightarrow 2\ Cl\bullet \qquad \text{chain initiation}$$

1.1.5—25. eq.

$$\left.\begin{array}{l} H_3C:H + \bullet Cl \longrightarrow H_3C\bullet + HCl \\ H_3C\bullet + Cl:Cl \longrightarrow H_3C\text{–}Cl + \bullet Cl \end{array}\right\} \text{chain propagation}$$
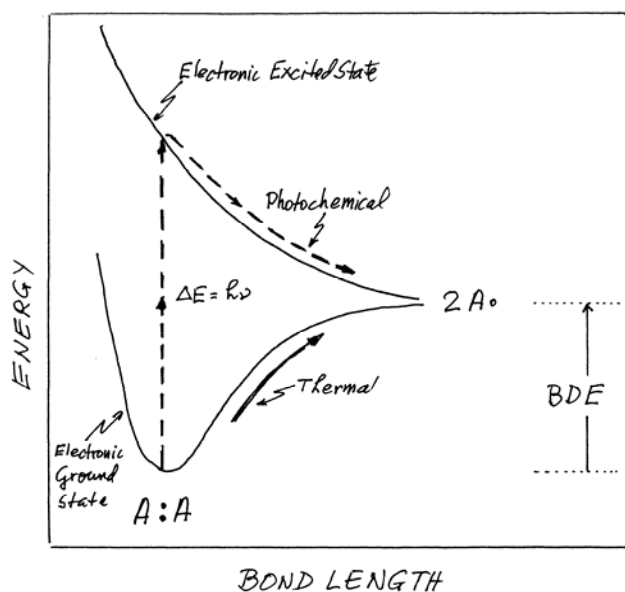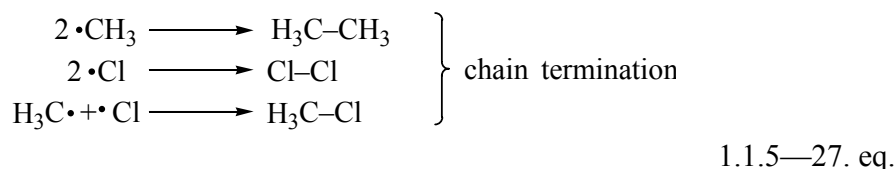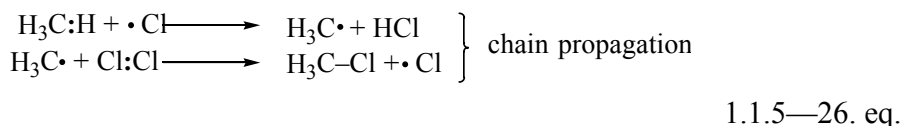
1.1.5—26. eq.

$$\left.\begin{array}{l} 2\ \bullet CH_3 \longrightarrow H_3C\text{–}CH_3 \\ 2\ \bullet Cl \longrightarrow Cl\text{–}Cl \\ H_3C\bullet + \bullet Cl \longrightarrow H_3C\text{–}Cl \end{array}\right\} \text{chain termination}$$

1.1.5—27. eq.
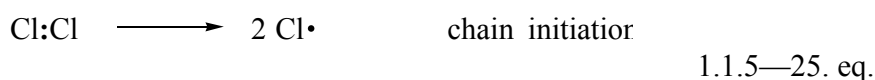
The first step is the initiation 1.1.5—25. eq. of the chain reaction. The energy requirement for this step is the BDE of the halogen molecule. For $Cl_2$, this value is +58 kcal/mol. This is to be supplied by heat or light. Once the chain is initiated, the most important steps are the chain propagations. Both of these steps involve a homolytic bond-breaking and a bond-making. Both the bond-breaking and the bond-making can be represented by a Morse-type of potential. The shapes of the Morse-type potentials are depicted as solid curves in Figure 1.1.5—2 and Figure 1.1.5—3. For the bond- breaking, we go from the minimum to the dissociation limit (from left to right) while for the bond-making, we go from the dissociation limit to the minimum (from right to left). It is practical, therefore, to turn the bond-making curve around, so that the reaction coordinate for the whole process might go from left to right. These pairs of Morse potentials for 1.1.5—26. eq. and 1.1.5—27. eq. are shown in Figure 1.1.5—6.
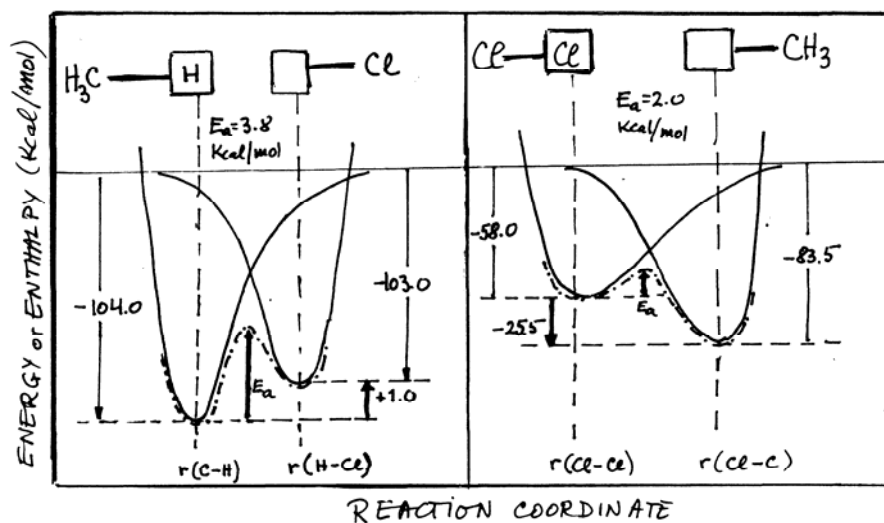
**Figure 1.1.5—6  A schematic illustration showing that an energy profile (— • — • —) for a reaction can be imagined to originate from two Morse Potentials (solid curves).  The left hand side shows H-atom abstraction from $CH_4$ by a Cl-atom ($H_3C$—H + •Cl → $H_3C$• + HCl).  The right hand side shows Cl-atom abstraction from $Cl_2$ by a $CH_3$ radical (Cl—Cl + •$CH_3$ → Cl• + Cl—$CH_3$).  The abstracted atoms simply hop over, along the reaction coordinate, from the left hand side box to the right hand side box shown on the top of the figure.**

The thermochemistry of these abstraction reactions can be calculated from the BDE values:

$$\Delta H_{reaction} \approx \Delta E_{reaction} = BDE_{(product)} - [-BDE_{(reactant)}]$$

1.1.5—28. eq.

However, the activation energy (Ea) values cannot be inferred from the BDE values. They are shown in Figure 1.1.5—6 for the sake of illustration only.

The situation is qualitatively analogous for the other halogens even though they are quantitatively quite different. The BDE of the various halogens are varied, as shown below:

$$F–F → 2\ F•$$
$$BDE\ =\ +38\ kcal/mol$$

eq. 1.1.5—29

$$Cl–Cl → 2\ Cl•$$
$$BDE\ =\ +58\ kcal/mol$$

eq. 1.1.5—30

$$Br–Br → 2\ Br•$$
$$BDE\ =\ +46\ kcal/mol$$

eq. 1.1.5—31

$$I–I → 2\ I•$$
$$BDE\ =\ +36\ kcal/mol$$

1.1.5—32. eq.

(For data derived from theorthical methods see in appendix 5)

Clearly $F_2$ is out of the progression shown by $Cl_2$, $Br_2$ and $I_2$. One may speculate that the six lone pairs (lp) of electrons (three lp are associated with each of the F atoms) destabilize $F_2$ because of its relatively short bond lengths. For the others the bond lengths are longer and the six l ps do not disturb each other so much.

The energetics of the two consecutive chain propagation steps are shown for the four halogens in next picture
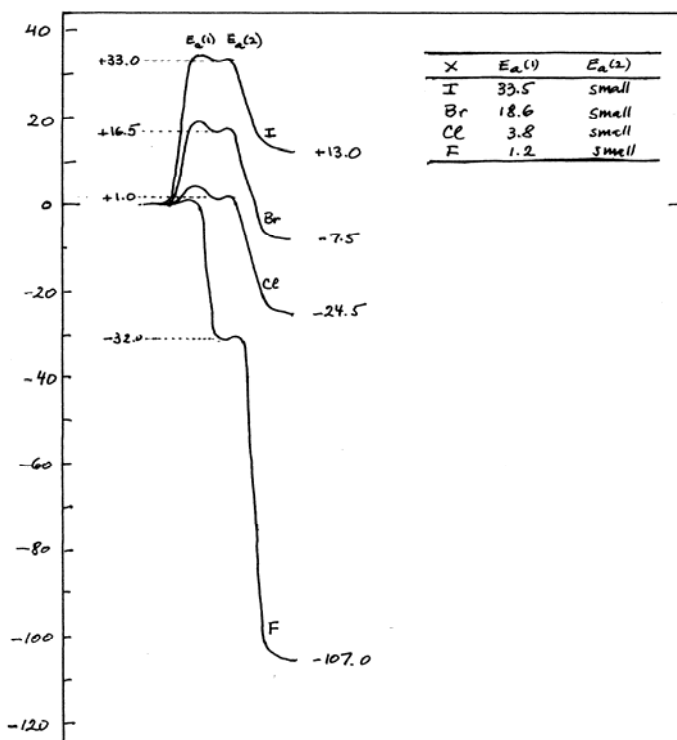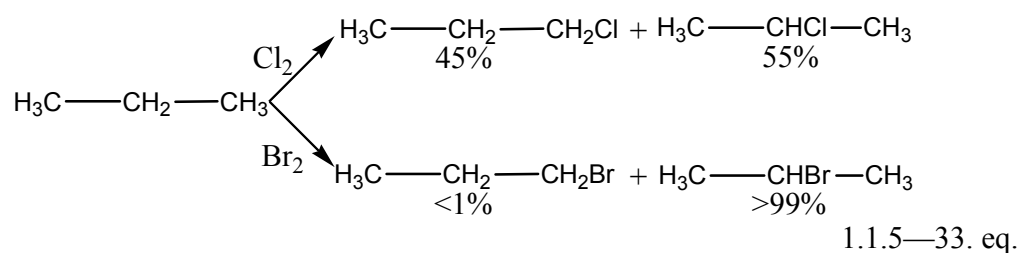


| $X$ | $E_a (1)$ | $E_a (2)$ |
|-----|-----------|-----------|
| I | 33.5 | small |
| Br | 18.6 | small |
| Cl | 3.8 | small |
| F | 1.2 | small |

**Figure 1.1.5—7. Energy profile for the methane halogenation chain propagation steps ($H_3C$—H + •X → $H_3C$• + HX and X—X + •$CH_3$ → X• + X—$CH_3$) for X = F, Cl, Br and I.**

It is clear from Figure 1.1.5—7 that the reaction with fluorine is very exothermic and that can lead to an explosion. In contrast, the reaction with iodine is endothermic and therefore, it does not occur. Consequently, only $Cl_2$ and $Br_2$ come into the picture as halogenating agents. Of these two, $Cl_2$ is more exothermic than $Br_2$. This means that chlorine is a very ferocious reagent, and due to this, it is not very selective. For example, it bites off almost any hydrogen atom it can find in hydrocarbons. On the other hand, bromine is very sluggish and it selectively breaks the weak C—H bonds. Consider, for example, propane ($H_3C$—$CH_2$—$CH_3$). There are six H atoms attached to 1° carbon and two H atoms attached to 2° carbon. Their ratio is 75% : 25%, yet neither chlorination nor bromination yields this statistical ratio (75 : 25 = 3.0). Chlorination does not deviate so much from the statistical ratio as bromination does.[3]

$$H_3C\!\!-\!\!CH_2\!\!-\!\!CH_2Cl + H_3C\!\!-\!\!CHCl\!\!-\!\!CH_3$$
$$45\% \qquad\qquad\qquad 55\%$$

$$\overset{Cl_2}{\nearrow}$$

$$H_3C\!\!-\!\!CH_2\!\!-\!\!CH_3$$

$$\overset{Br_2}{\searrow}$$

$$H_3C\!\!-\!\!CH_2\!\!-\!\!CH_2Br + H_3C\!\!-\!\!CHBr\!\!-\!\!CH_3$$
$$<\!1\% \qquad\qquad\qquad >\!99\%$$

1.1.5—33. eq.

The difference lies in the variation of the C — H BDE. We may utilize the BDE values given in 1.1.5—23. eq.to estimate, according to 1.1.5—24. eq., the enthalpy of the first chain propagating step of the chain reaction.
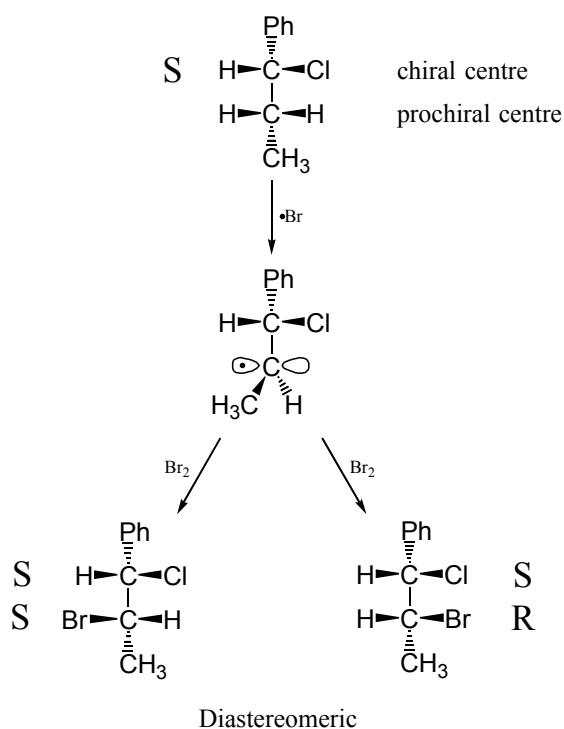
$$\overset{|}{\underset{|}{C}}\!\!-\!\!H + \cdot X \longrightarrow \overset{|}{\underset{|}{C}}\cdot \quad + H\!-\!X$$
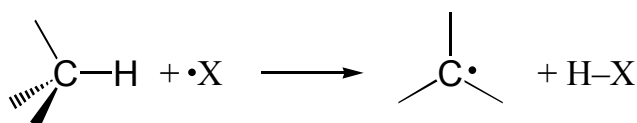
1.1.5—34. eq.

**Table 1.1.5-3. Calculation of $\Delta H_{reaction}$ for 1.1.5-26 using the thermochemical equation 1.1.5-21**

| Bond | $\Delta H_{reaction}$ (kcal/mol) | |
|---|---|---|
| | X = Cl | X = Br |
| $H_3C$ — H | -103.0 - (-104.0) = + 1.0 | -87.5 - (-104.0) = + 16.5 |
| 1° C — H | -103.0 - (- 98.0) = - 5.0 | -87.5 - (- 98.0) = + 10.5 |
| 2° C — H | -103.0 - (- 94.5) = - 8.5 | -87.5 - (- 94.5) = + 7.0 |
| 3° C — H | -103.0 - (- 91.0) = -12.0 | -87.5 - (- 91.0) = + 3.5 |

In view of such energetics, it is easy to see why chlorine bites off the H atom from almost any C—H bond and why bromine starts with 3°, then 2°, and tries to avoid 1° if possible. Of course the overall bromination reaction is exothermic, but the first chain propagating step is endothermic, and therefore it becomes rate determining.
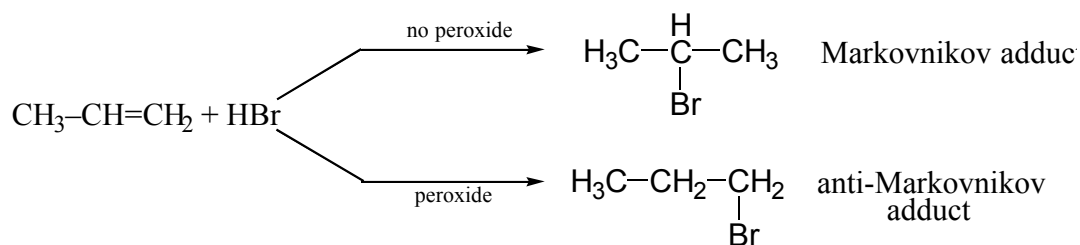
As far as the stereochemistry of the reaction is concerned, if a chiral centre is formed during halogenation the reaction will yield a racemic mixture, due to the planar structure of the carbon radical intermediate. However, if we already have an optically active compound, the resulting compound will be diastereomeric.
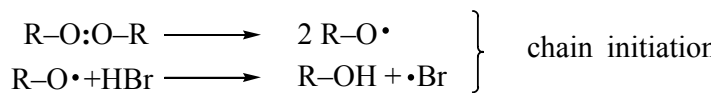
$$
\begin{array}{ll}
\text{S} \quad H\!-\!\overset{Ph}{\underset{|}{C}}\!-\!Cl & \text{chiral centre} \\
\quad\quad H\!-\!\overset{|}{\underset{|}{C}}\!-\!H & \text{prochiral centre} \\
\quad\quad CH_3 &
\end{array}
$$

$\downarrow$ •Br

$$
H\!-\!\overset{Ph}{\underset{|}{C}}\!-\!Cl \\
\quad \odot C \bigcirc \\
H_3C \quad H
$$

Br₂ ↙          ↘ Br₂

$$
\begin{array}{ll}
\text{S} \quad H\!-\!\overset{Ph}{\underset{|}{C}}\!-\!Cl & \\
\text{S} \quad Br\!-\!\overset{|}{\underset{|}{C}}\!-\!H & \\
\quad\quad CH_3 &
\end{array}
\qquad
\begin{array}{ll}
H\!-\!\overset{Ph}{\underset{|}{C}}\!-\!Cl \quad \text{S} & \\
H\!-\!\overset{|}{\underset{|}{C}}\!-\!Br \quad \text{R} & \\
\quad\quad CH_3 &
\end{array}
$$

Diastereomeric

1.1.5—35. eq.

## The anti-Markovnikov addition of HBr to alkenes.

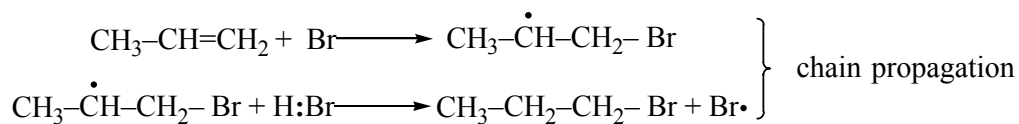In the presence of peroxides, HBr adds anti-Markovnikov to olefinic double bonds.[4]

$CH_3$–$CH$=$CH_2$ + HBr

no peroxide → $H_3C\!-\!\overset{H}{\underset{Br}{C}}\!-\!CH_3$   Markovnikov adduct

peroxide → $H_3C\!-\!CH_2\!-\!\underset{Br}{CH_2}$   anti-Markovnikov adduct

1.1.5—36. eq.

This phenomenon can be understood in terms of the following mechanism:

$$
\left.
\begin{array}{l}
R\!-\!O\textbf{:}O\!-\!R \longrightarrow 2\ R\!-\!O\bullet \\
R\!-\!O\bullet + HBr \longrightarrow R\!-\!OH + \bullet Br
\end{array}
\right\} \quad \text{chain initiation}
$$

1.1.5—37. eq.

$$
\left.
\begin{array}{l}
CH_3\!-\!CH\!=\!CH_2 + \ Br \longrightarrow CH_3\!-\!\overset{\bullet}{C}H\!-\!CH_2\!-\!Br \\
CH_3\!-\!\overset{\bullet}{C}H\!-\!CH_2\!-\!Br + H\textbf{:}Br \longrightarrow CH_3\!-\!CH_2\!-\!CH_2\!-\!Br + Br\bullet
\end{array}
\right\} \quad \text{chain propagation}
$$

1.1.5—38. eq

Because the 2° carbon radical is more stable than the 1° carbon radical, therefore the reaction proceeds as shown above, leading to the anti-Markovnikov adduct.

## Reactivity and Selectivity

The halogenation of propane 1.1.5—33. eq. serves as an excellent example for the illustration of reactivity and selectivity. The hydrogen abstraction by the halogen atom 1.1.5—34. eq. can be written, in details as shown by 1.1.5—39. eq
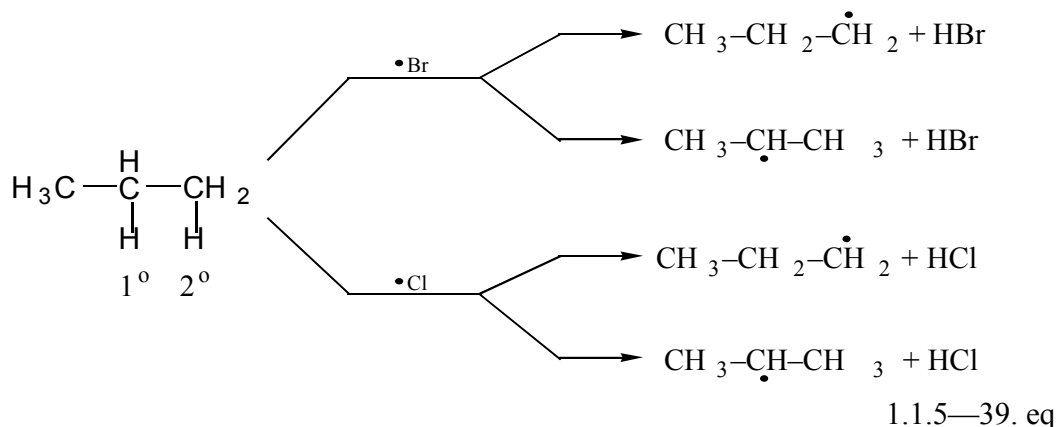


$$1.1.5—39.\ eq$$

The carbon radicals formed in 1.1.5—39. eq first and third part are identical but the energy values of these two product states are different because one has HBr and the other has HCl (The BDE for HCl and HBr are given in 1.1.5—24. eq. as 103.0 and 87.5 kcal/mol respectively). The energies in the thermodynamic sense, for 1.1.5—39. eq are given in Table 1.1.5-3. Figure 1.1.5—8 shows schematically the energy profiles for the four reactions summarized in 1.1.5—39. eq. Note that

$$E_a(Cl) < E_a(Br)$$

$$1.1.5—40.\ eq.$$

for both $1^o$ and $2^o$ C–H. Thus we say Cl is more reactive than Br. Note also that

$$\Delta E_a(Cl)^{1^o\text{-}2^o} < \Delta E_a(Br)^{1^o\text{-}2^o}$$

$$1.1.5—41.\ eq$$

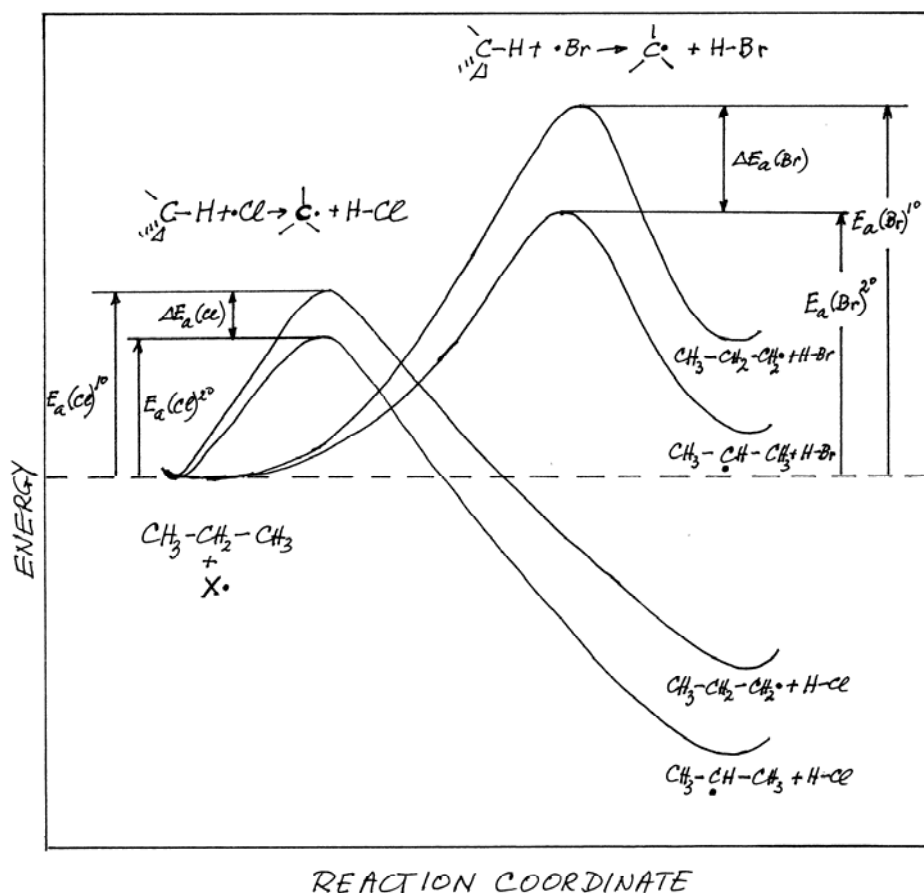which implies that Cl is less selective than Br.

**Figure 1.1.5—8 A schematic illustration of reactivity and selectivity using the reaction of hydrogen abstraction by halogens as an example. A highly reactive reagent (e.g. Cl•) gives early (reactant like) transition state while a less reactive reagent (e.g. Br•) gives a late (product like) transition state. The energetic differences manifested in the activation energies . Using this different substrate (in this case two different C−H bonds of the same substrate) one finds more differentiation in the case of the less reactive reagent (Br• in this case) as specified by 1.1.5—41. eq.**

## 1.1.5.2 Conditions for competing reactions such as Substitution and Elimination

In principle, all four mechanisms ($S_N2$ and E2, as well as $S_N1$ and E1) may occur in competition with one another under certain reaction conditions. However, with carefully selected reaction conditions some mechanisms may be eliminated.

The structure of the substrate influences whether the $S_N2$ or the $S_N1$ mechanism will be predominant. In particular, the 1°, 2° and 3° nature of the carbon of the C-X bond is of primary importance.

$$\begin{array}{ccc}
\overline{\phantom{xxx}} & S_N1 \longrightarrow & \\
1° & 2° & 3° \\
\longleftarrow & S_N2 & \overline{\phantom{xxx}}
\end{array}$$
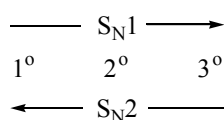
1.1.5—42. eq

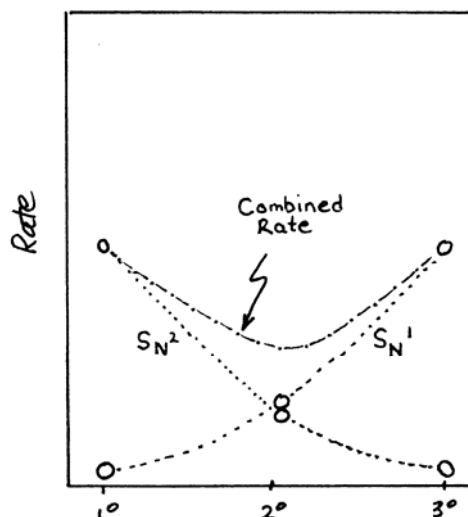Figure 1.1.5—9 illustrates the information given in 1.1.5—42. eq
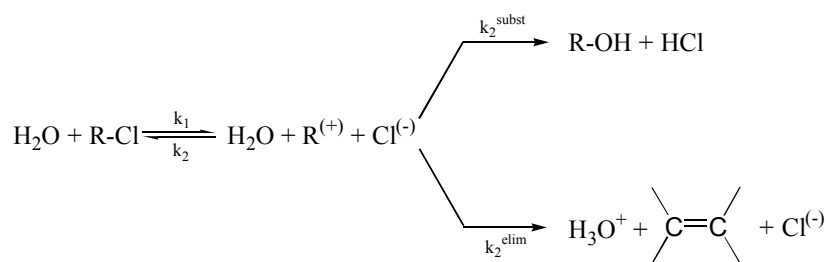


**Figure 1.1.5—9 Variation of substitution rates with degree of substitution at carbon of the C - Halogen bond.**

So for a 3° carbon atom, $S_N1$ dominates over $S_N2$, and the formation of the carbocation opens the door for both $S_N$ and E1. Increasing the polarity of the solvent also enhances the formation of the carbocation. Ionizing solvents that can stabilize both carbocations and halide ions through hydrogen bonding will enhance carbocation formation, and therefore give an equal chance to both $S_N1$ and E1.[5]

$$H_2O + R\text{-}Cl \underset{k_2}{\overset{k_1}{\rightleftharpoons}} H_2O + R^{(+)} + Cl^{(-)} \begin{cases} \overset{k_2^{subst}}{\longrightarrow} R\text{-}OH + HCl \\ \\ \underset{k_2^{elim}}{\longrightarrow} H_3O^+ + \diagup C = C \diagdown + Cl^{(-)} \end{cases}$$
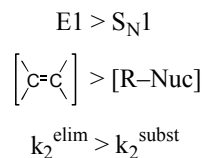
1.1.5—43. eq

However, the relative dominance of $S_N1$ and E1 will be determined by the product ratios and therefore by the rate constant ratios of the steps leading to the product.

$$\frac{S_N1}{E1} = \frac{[ROH]}{\left[ \diagup C = C \diagdown \right]} = \frac{k_2^{subst}}{k_2^{elim}}$$
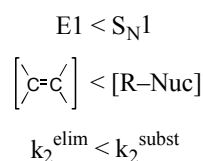
1.1.5—44. eq

The validity of equation 1.1.5—44. eq has already been proven.

The relative magnitude of the rate constants is determined by the basicity of the nucleophile used. Strong Bronsted bases will be more effective in removing a proton from the intermediate carbocation than weak ones. This follows from the definition of Bronsted acid/base strength. Consequently, for strong bases:
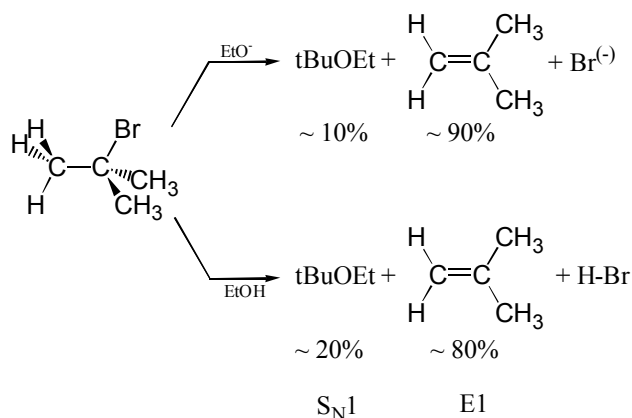
$$E1 > S_N1$$

$$\left[ \begin{array}{c} \diagdown \\ C=C \\ \diagup \end{array} \right] > [R\text{--}Nuc]$$

$$k_2^{elim} > k_2^{subst}$$

1.1.5—45. eq

and for weak bases:

$$E1 < S_N1$$

$$\left[ \begin{array}{c} \diagdown \\ C=C \\ \diagup \end{array} \right] < [R\text{--}Nuc]$$

$$k_2^{elim} < k_2^{subst}$$

1.1.5—46. eq
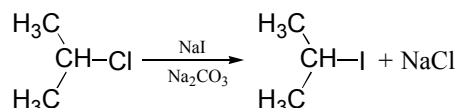
where $\diagup C=C \diagdown$ denotes an alkene.

To assess the situation, consider the following simple example. (The percentage values are only approximate and given here for illustrative purposes).



1.1.5—47. eq

While $S_N1$ and E1 proceed in ionizing solvents, $S_N2$ and E2 may occur in non-ionizing polar solvents such as acetone:



1.1.5—48. eq

A 1° alkyl halide almost always reacts $S_N2$, and a 3° halide reacts almost exclusively via the E2 mechanism. For 2° halides the system has a choice between $S_N2$ and E2. Again the basicity of the nucleophile will determine the product ratio for 2° alkyl halides. The two second-order rate constant

$k_{SN2}$ and $k_{E2}$ will reflect the difference in basicity of the nucleophile used. Consider the following simple example to assess the situation:
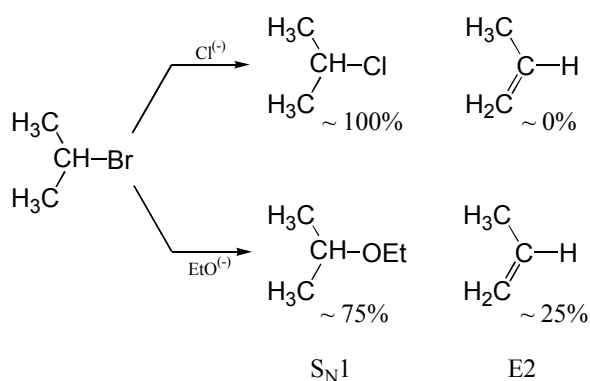


$$1.1.5—49. \ eq$$

The elimination reaction can sometimes lead to cis and trans geometrical isomers. Usually the more stable trans product dominates the product mixture. Constitutional isomers may also be formed in certain cases.
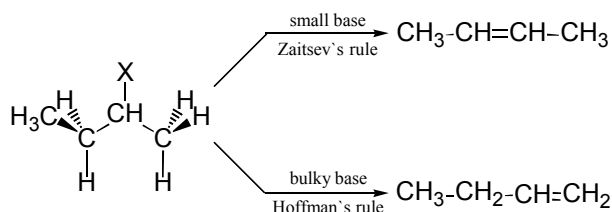


$$1.1.5—50. \ eq$$

## 1.1.5.3 Spatial arrangement of molecular orbitals and reaction stereochemistry

### The frontier orbital (HOMO/LUMO) approach.

The spatial arrangements of molecular orbitals are fundamentally responsible for the stereochemistry of reactions. Consider for example the $S_N2$ mechanism. The backside attack on the C - Cl bond is due to the orientation of the LUMO along the C - Cl axis, pointing away from the carbon (c.f. Figure 1.1.5—10). The HOMO of the nucleophile and the LUMO of the substrate interact to form a new bond and the HOMO of the substrate breaks up during the reaction:
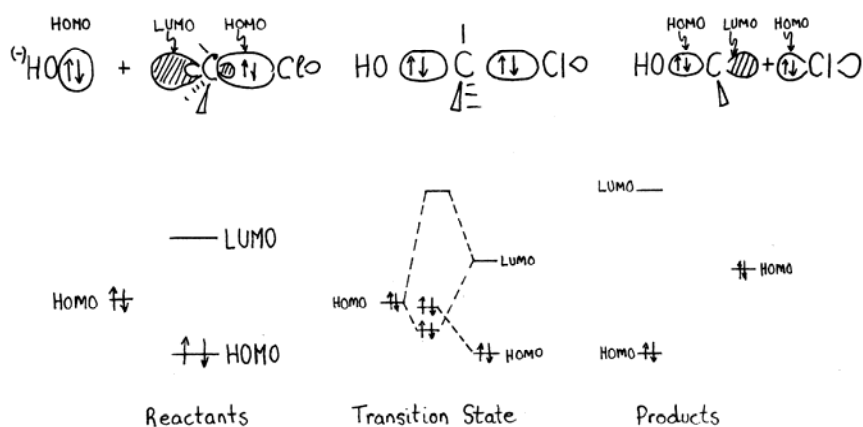
**Figure 1.1.5—10. Interpretation of S$_N$2 stereochemistry in terms of Molecular Orbitals.**

Similarly, in the E2 mechanism, the HOMO and LUMO (frontier orbitals) of the reagent and reactant play a significant role in forming the new bond. Subsequently, the C - H bonding σ-electron pair becomes a π-bond and the leaving group takes the bonding electron pair away (c.f.Figure 1.1.5—11).
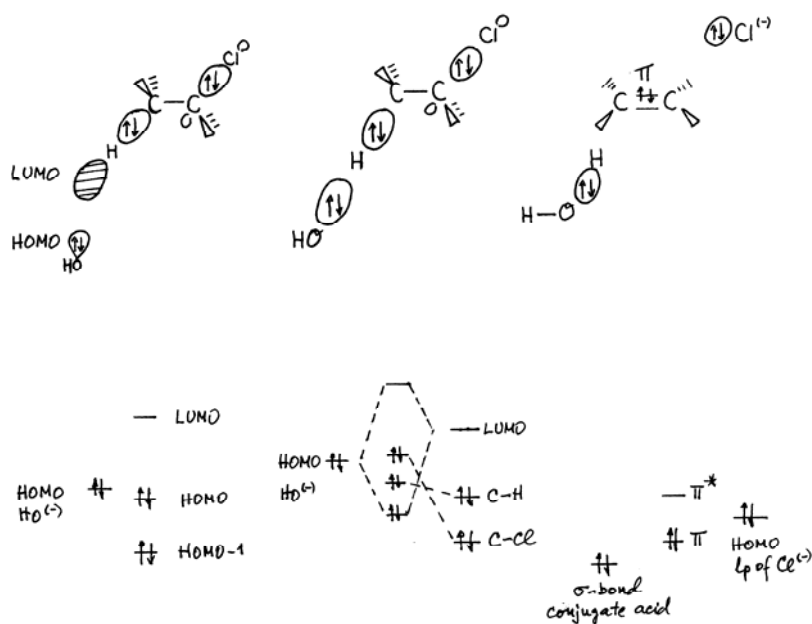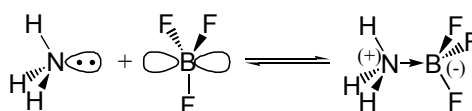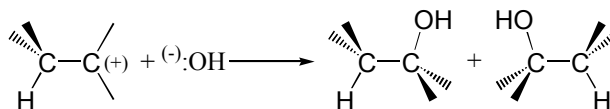


**Figure 1.1.5—11 Interpretation of E2 stereochemistry in terms of molecular orbitals.**

The first step for the S$_N$1 and E1 mechanisms is common. It is the reverse Lewis acid-base reaction:
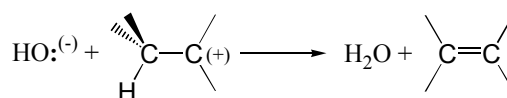
$$1.1.5—51. \text{ eq}$$

In the $S_N1$ mechanism, we see a simple Lewis acid-base reaction such as the collapse of the carbocation and hydroxide ion:
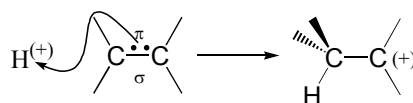
$$1.1.5—52. \text{ eq}$$

without stereochemical control (i.e., chiral alkyl halides yield racemic alcohols).

In the E1 mechanism, the carbocation behaves as a Bronsted acid and a proton is transferred from carbon to the base, such as $^{(-)}:OH$

$$1.1.5—53. \text{ eq}$$

It should not be surprising that the carbocation can act as a proton donor since it may be regarded as a $\pi$-protonated carbon-carbon double bond:

$$1.1.5—54. \text{ eq}$$

The HOMO/LUMO involvement is a general principle of organic reactions. For example, look at the addition reaction to a carbon-oxygen double bond (carbonyl compound):

Lewis base          Lewis or
                    Bronsted acid
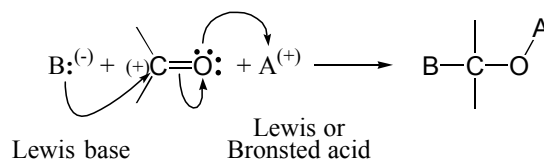
$$1.1.5—55. \text{ eq}$$

The acid, $A^{(+)}$, attaches the HOMO and the base, $:B^{(-)}$, attaches the LUMO of the carbonyl compound. The orbital level diagram of $H_2C = O$, presented here in Figure 1.1.5—12, illustrates this point:

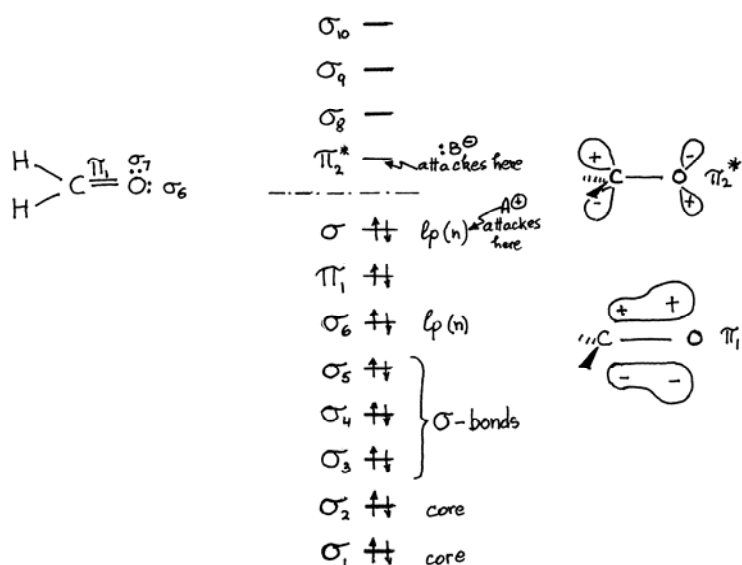**Figure 1.1.5—12 Orbital level diagram of formaldehyde indicating the level attacked by an acid, A(+), and a base :B$^{(-)}$.  The $\pi$-MO, as well as the $\pi^*$-MO are shown at the right hand side.  The two lone pair (lp) CMO's of oxygen are like those shown in Figure 1.30 for H$_2$O.**


## 1.1.5.4 Hard and soft acids and bases (HSAB); Nucleophilicity and electrophilicity; Electron Supply and Demand


<u>Hard and Soft acids and bases (HSAB)</u>

It is relatively straightforward to define Bronsted acidity. It is the proton donating ability in aqueous solution. The pK$_a$ value of an acid is related to the pH value of the aqueous solution:

$$H_2O + HA \rightleftharpoons H_3O^{(+)} + A^{(-)}$$

1.1.5—56. eq
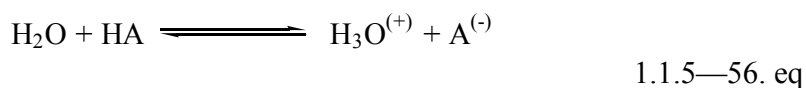
$$pK_a = pH - \log\frac{[A^{(-)}]}{[HA]}$$

1.1.5—57. eq

(Remember that the concentration of H$_2$O is omitted from the definition of K$_a$ and pK$_a$.) All of these have been discussed in earlier section

The important point here is that while it is relatively easy to define acid/base strength for Bronsted acids and bases, because in all cases what actually happens is a proton transfer, the same type of simplicity is not present for Lewis acidity and basicity.

In a Lewis acid/base reaction, a Lewis complex is formed as illustrated in 1.1.5—58. eq
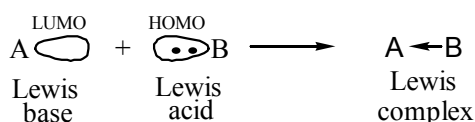
$$1.1.5\text{—}58.\ eq$$

The electron pair of the bond formation between B and A originates from the base, therefore it is called a "dative bond" and it is denoted by an arrow in 1.1.5—58. eq. The classic example usually used in first year chemistry is the $NH_3$ plus $BF_3$ reaction:
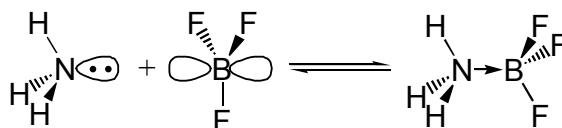


$$1.1.5\text{—}59.\ eq$$

Just in passing, we might mention that, as has been pointed out, practically all organic reactions may be regarded as acid/base reactions either in the Brönsten sense or in the Lewis sense. The last time this point has been emphasized in this chapter was in connection with the second step of the $S_N1$ mechanism (Lewis) and the second step of the E1 mechanism (Bronsted), 1.1.5—52. eq and 1.1.5—53. eq respectively.

Returning to the main theme, the strengths of Lewis acids depend on the structure of the bases employed. Consequently, the strength of a Lewis acid cannot be tabulated as was possible in the case of Bronsted acids. Note that while in a Bronsted acid-base reaction the important step is proton transfer, in the Lewis acid-base reaction no such common factor is possible. Only a few measurements of Lewis acidity have been made. The relative strength of some selected Lewis acids (where X - Halogen) is given below[6]

$$BX_3 > AlX_3 > FeX_3 > GaX_3 > SbX_5 > SnX_4 > AsX_5 > ZnX_2 > HgX_2$$
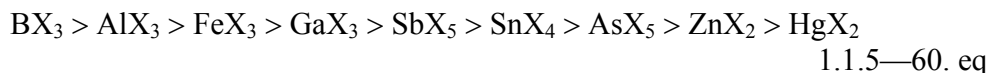
$$1.1.5\text{—}60.\ eq$$

The reactivity of Lewis acids and bases depends not only on their strengths but also on the polarizability of the acceptor and donor atoms. On this basis we can subdivide them into so-called hard and soft acids and hard and soft bases.

**Hard Lewis acids** are electron acceptors which, in general, are small in size and possess a positive charge. Their electronegativity is high and their polarizability low. They have no lone electron pairs.

**Soft Lewis acids** are also electron acceptors, but, in general are relatively large in size, and therefore their positive charge density is relatively small. Their electronegativity is low and their polarizability is high. They very often have lone electron pairs.

**Hard Lewis bases** have strongly bound valence electrons. Their electronegativity is high and their polarizability low. They are hard to oxidize.

**Soft Lewis bases** have loosely bound valence electrons. Their electronegativity is low and their polarizability high. They are easy to oxidize.

The above points are summarized in Table 1.1.5-4.

The softness of bases varies according to rows and columns of the periodic table as illustrated below:[7]

$$CH_3^- > NH_2^- > OH^- > F^-$$

$$1.1.5\text{—}61.\ eq$$

$$I^- > Br^- > Cl^- > F^-$$

<div align="right">
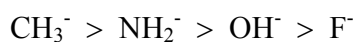
1.1.5—62. eq
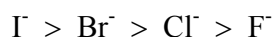</div>

Selected hard and soft acids and bases as well as some borderline cases are listed in Table 1.1.5-5

Accumulated experience has led to the principle of hard and soft acids and bases (HSAB): hard acids react favorably with hard bases and soft acids react favorably with soft bases. In other words, the Lewis complex to be formed is always more stable if both the acid and

**Table 1.1.5-4 Some characteristics of Lewis acids and bases**

| Lewis | Characteristics | Hard | Soft |
|-------|-----------------|------|------|
|       | size | small | large |
|       | (+) charge density | high | low |
| Acid  | electronegativity | high | low |
|       | polarizability | low | high |
|       | lone pair | no | yes |
|       | valence electrons bonded | strongly | loosely |
|       | (-) charge density | high | low |
| Base  | electronegativity | high | low |
|       | polarizability | low | high |
|       | oxidation | hard | easy |

**Table 1.1.5-5 Selected hard and soft acids and bases.**

| Hard bases | Borderline bases | Soft bases |
|------------|------------------|------------|
| $NH_3, RNH_2, H_2O, OH$ $R2O, ROH, RO^-, F^-, AcO^-$ $PO_4^{3-}, SO_4^{2-}, Cl^-, CO_3^{2-}$ $ClO_4^-, NO_3^-$ | $C_6H_5NH_2, C_5H_5N, N_3^-$ $Br^-, NO_2^-, SO_3^{2-}$ | $R_2S, RSH, RS^-, R_3P,$ $(RO)_3P, RNC, CO, C_2H_4,$ $C_6H_6, I^-, SCN^-, S_2O_3^{2-}, CN^-$ $H^-, R^-$ |
| **Hard acids** | **Borderline acids** | **Soft acids** |
| $H^+, Li^+, Na^+, K^+,$ $Mg^{2+}, Ca^{2+}, Mn^{2+},$ $Al^{3+}, Cr^{3+}, Co^{3+}, Fe^{3+},$ $RCO^+, BF_3, B(OR)_3, Al$ $Me_3,$ $AlCl_3, AlH_3, SO_3,$ $CO_2, HX$ (hydrogen-bonded molecules) | $Fe^{2+}, Co^{2+}, Ni^{2+} Cu^{2+}$ $Zn^{2+}, Sn^{2+}, Sb^{3+}, Pb^{2+},$ $Bi^{3+}, NO^+, R_3C^+, C_6H_5^+,$ $BMe_3, SO_2, GaH_3$ | $Cu^+, Ag^+, Hg^+, Pd^{2+}$ $Pt^{2+}, Hg^{2+}, RS^+, I^+, Br^+,$ $HO^+, RO^+, I_2, Br_2, BH_3, GaCl_3,$ $1,3,5-(NO_2)_3C_6H_3,$ quinones, $(NC)_2C=C(CN)_2$ $CH_2,$ carbenes |

base components are of the same hardness. This principle can be illustrated by the following examples. In the case of halide ions $F^-$ is a stronger base with respect to $H^+$ and $I^-$ is a stronger base with respect to $Ag^+$. Also, a proton is a stronger acid with respect to amines and a silver cation is a stronger acid with respect to phosphines, and not the other way around (c.f. Table 1.1.5-5).

The interaction between Lewis acids and Lewis bases may be rationalized in terms of frontier orbitals. In general, hard acids have a high-energy LUMO, while hard bases have a low-energy

HOMO, and the energy difference between the two orbitals is relatively large. For this reason, in the reaction of a hard acid with a hard base no strong covalent bond formation will occur. The bonding will be ionic in type. Nevertheless, the complex is still quite stable, due to the electrostatic interaction existing between the positively charged acid and the negatively charged base. On the other hand, for soft acids and soft bases the energy difference between HOMO and LUMO is relatively small, and a strong covalent bond can be formed (Figure 1.1.5—13). Beyond these two cases, there are two mismatches: the reactions between hard acids and soft bases, and soft acids and hard bases. In the case of these two mismatches, the stability of the complexes is low because neither strong covalent bonds nor strong electrostatic interactions result.
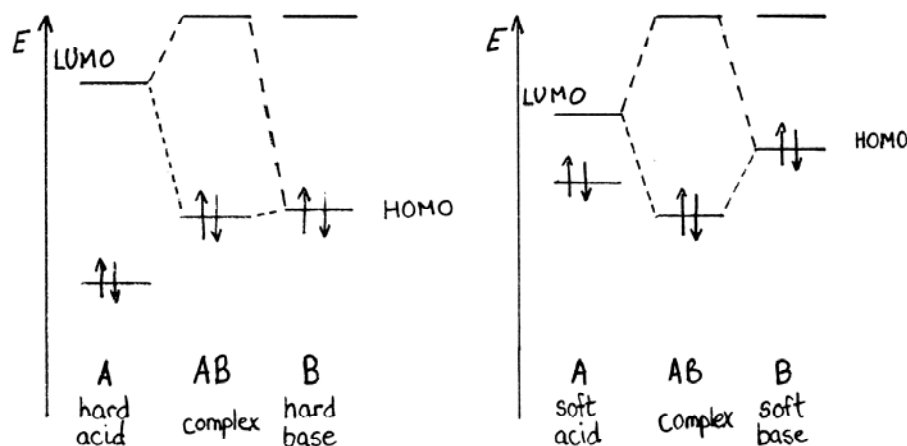


**Figure 1.1.5—13  Interaction of HOMO and LUMO in the case of a hard acid with a hard base and a soft acid with a soft base.**

## Nucleophiles and electrophiles

Neutral and negatively charged compounds, containing lone electron pairs, are Lewis bases as well as nucleophilic reagents. Similarly, electron pair-accepting-Lewis acids may be regarded as electrophiles.  Base strength is usually measured by the protonation equilibrium, and nucleophilicity by the rate of nucleophilic reaction. Consequently, basicity is a thermodynamic property and nucleophilicity is a kinetic property. Parallelism between basicity and nucleophilicity exists only between molecules of similar architecture. Such a closely related family of compounds usually contains identical nucleophilic heteroatoms. If the nucleophilic centers are different in two compounds (e.g. $:NH_3$ and $:PH_3$) or two groups of compounds, then one may not expect a very good correlation between basicity and nucleophilicity.

The principle of HSAB theory is applicable for the reactions of nucleophiles and electrophiles. As stated before, hard electrophiles react favorably with hard nucleophiles. Analogously, soft electrophiles react favorably with soft nucleophiles. In order to illustrate this point, let us consider the following example: an alkene is a soft nucleophile and it reacts favorably with bromine, which is a soft electrophile, as compared to the protonation reaction, where the reacting proton is a hard electrophile:
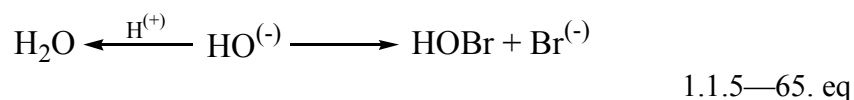
$$\overset{(+)}{R C H}—CH_2R \xleftarrow{H^{(+)}} RCH{=}CHR \xrightarrow{Br^{(-)}} \underset{\underset{Br\ \ Br}{|\ \ \ |}}{RHC—CHR}$$
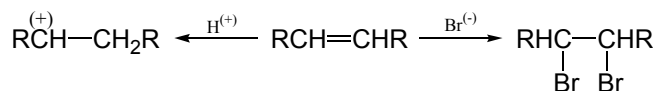
1.1.5—63. eq

It is not surprising therefore, that the following inequality is observed for the above reactions:

$$k_{H^+} < k_{Br_2}$$

1.1.5—64. eq

On the other hand, protonation of the hard OH$^-$ is a faster process than its reaction with bromine, as shown by equation 1.1.5—65. eq
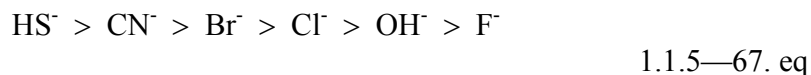
$$H_2O \xleftarrow{\quad H^{(+)} \quad} HO^{(-)} \xrightarrow{\quad\quad} HOBr + Br^{(-)}$$
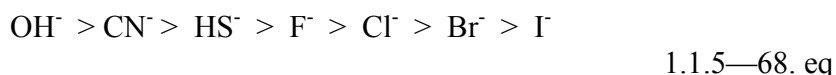
1.1.5—65. eq

Thus, the inequality of the rate constants is:

$$k_{H^+} > k_{Br_2}$$

1.1.5—66. eq

The reactivity of nucleophiles with soft electrophiles can be ordered as follows[8]:

$$HS^- > CN^- > Br^- > Cl^- > OH^- > F^-$$

1.1.5—67. eq

The order, however, is different when the same nucleophiles are reacting with hard electrophiles:

$$OH^- > CN^- > HS^- > F^- > Cl^- > Br^- > I^-$$

1.1.5—68. eq

The sequence in 1.1.5—68. eq is analogous to the order of basicity.

In reactions between soft nucleophiles and soft electrophiles, HOMO-LUMO interaction is the driving force for the formation of the covalent bond. On the other hand, in the case of reactions between hard nucleophiles and hard electrophiles the attraction of opposite charges plays a major role and the reaction may be regarded as having ionic character. Thus, the former reaction may be referred to as an orbital-controlled reaction and the latter one as a charge-controlled reaction.

Consider the $S_N1$ reaction. The formation of the carbocation is rate-determining, and this intermediate will react very rapidly with the nucleophile. Thus, the $S_N1$ reaction is charge-controlled. In contrast to this, in $S_N2$ reactions the electrophilic center is attacked by a reagent of high nucleophilicity in the rate-determining step. The HOMO-LUMO overlaps play an important role in this reaction. Thus, the $S_N2$ reaction is orbital-controlled. Since the fluoride ion is a hard nucleophile, it is practical to prepare fluoro compounds via $S_N1$ reactions. In such cases the reactions may be enhanced by choosing a good leaving group such as tosylate. The departure of the leaving group, my be further enhanced by the use of ionizing solvents.

Needless to say, nucleophilicity depends on the nature of the solvent as well. Small sized, hard bases with a large negative charge density (F$^-$, Cl$^-$, RO$^-$ etc.) form hydrogen bonds in protic solvents, so their solvation is rather extensive and therefore their reactivity is decreased. Large-sized, soft nucleophiles, with a small negative charge density (I$^-$, SCN$^-$, etc.), especially those in which negative charge is delocalized, are only very weakly involved in hydrogen bonding, so their reactivity is usually enhanced by protic solvents. In dipolar aprotic solvents, hard bases are solvated less extensively, and therefore become more reactive, as compared with polarizable soft bases which are usually solvated much better. Taking one electrophile: methyl iodide, the order of nucleophilicity in protic solvents is given below[9]:

$$I^- > SCN^- \approx CN^- > N_3^- \approx Br^- > Cl^- > AcO^-$$
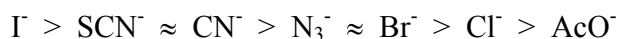
<div align="right">1.1.5—69. eq</div>

and the order is different in dipolar aprotic solvents:

$$CN^- \approx AcO^- \approx Cl^- \approx Br^- \approx N_3^- > I^- > SCN^-$$

<div align="right">1.1.5—70. eq</div>

Clearly the order of reactivity is almost reversed with the change of the nature of the solvent.

## Electron supply and demand

The electronic effects of substituents are of great importance in organic chemistry. Electron withdrawing groups (EWG) make a molecule less basic or more acidic while electron donating groups (EDG) make a molecule more basic or less acidic. Such substitutions, of course, will alter the balance of electron supply and electron demand. The underlying principle for the change of such a balance is due to the lowering or rising of the HOMO and LUMO levels. This is illustrated for two extreme cases with respect to the standard situation in the following figure:
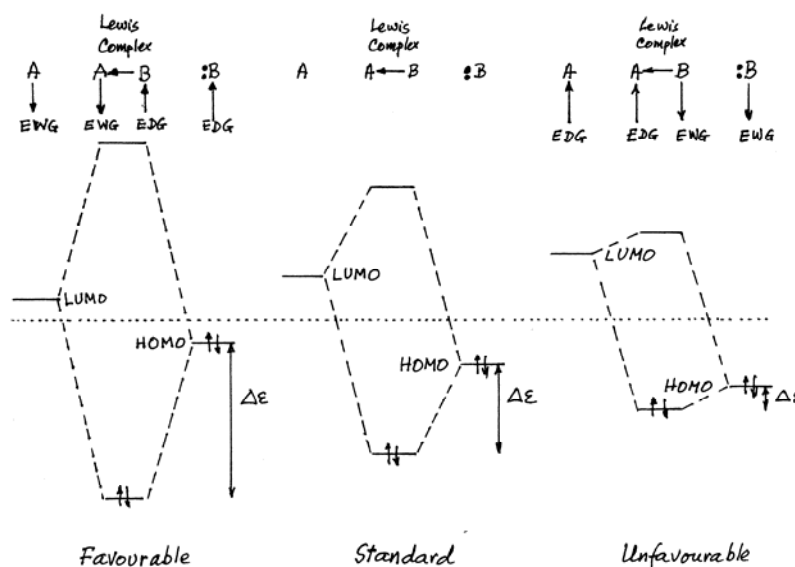


**Figure 1.1.5—14 The effect of substituents on the frontier orbital energies of Lewis acids and Lewis bases and their effect on the subsequent Lewis Complex Stability.**

## 1.1.5.5 Thermodynamic and Kinetic control of competing mechanism.

In most cases of parallel reactions the thermodynamic stability of the products formed and the kinetic stability of the transition states leading to product formation are parallel (c.f. Figure 1.1.5—15 A). In contrast to this, the potential energy surfaces may cross, leading to transition state stabilities which are different from product stabilities (c.f. Figure 1.1.5—15 B).
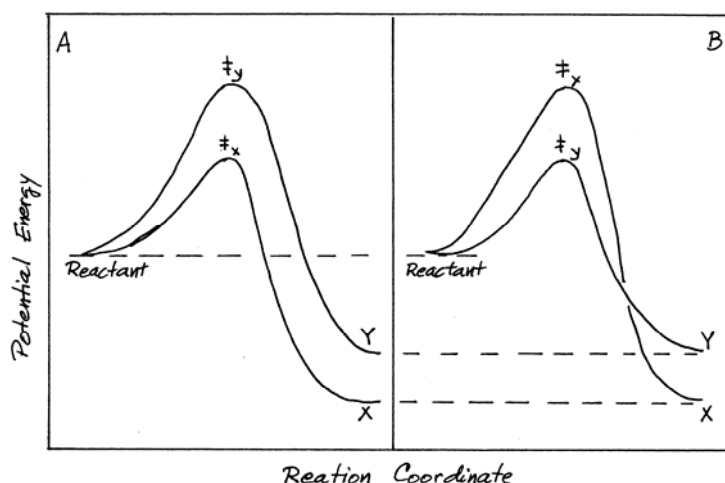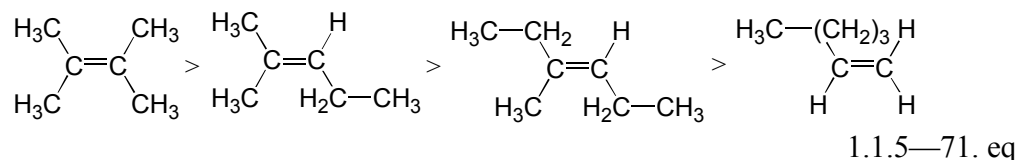
**Figure 1.1.5—15 A schematic illustration of nearly parallel (A) and crossing (B) (PES) for competing reaction mechanism.**
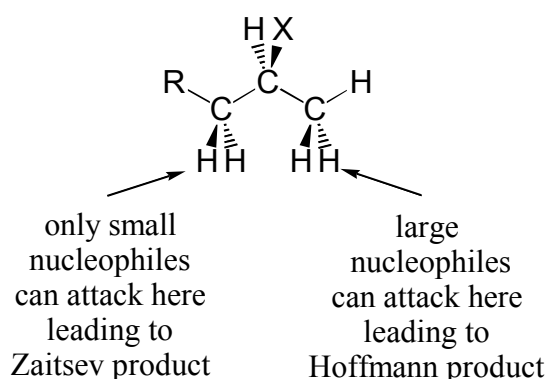
In the case shown in Figure 1.1.5—15 A both product stability and transition state stability would predetermine compound X to be the major product. However, the case shown in Figure 1.1.5—15 B is not all that clear. A lower barrier implies a larger rate constant and therefore a faster rate. If the rate is faster, more products is formed per unit time; thus, the relative rates would predetermine the product ratio. The situation presented in Figure 1.1.5—15 B is such that the thermodynamically least stable Y will be the major product.

The more heavily an olefin is substituted, the greater its stability[10]:

$$\underset{H_3C}{\overset{H_3C}{>}}C=C\underset{CH_3}{\overset{CH_3}{}} \; > \; \underset{H_3C}{\overset{H_3C}{>}}C=C\underset{H_2C-CH_3}{\overset{H}{}} \; > \; \underset{H_3C}{\overset{H_3C-CH_2}{>}}C=C\underset{H_2C-CH_3}{\overset{H}{}} \; > \; \underset{H}{\overset{H_3C-(CH_2)_3}{>}}C=C\underset{H}{\overset{H}{}}$$

$$1.1.5\text{—}71. \text{ eq}$$

Thus it is easy to predict which isomer is to be formed in parallel elimination reactions. The Zaitsev rule presented in upper reaction in 1.1.5—50. eq corresponds to the situation of Figure 1.1.5—15A, while the Hofmann rule down in 1.1.5—50. eq represents the case shown in Figure 1.1.5—15 B. We may say therefore, that the Hofmann product is under kinetic control while the Zaitsev product follows the thermodynamic stability of the product.

The size of the nucleophile plays a dominant role in determining whether the Zaitsev or the Hofmann product is formed:

only small
nucleophiles
can attack here
leading to
Zaitsev product

large
nucleophiles
can attack here
leading to
Hoffmann product

1.1.5—72. eq

In these cases there is no return from the product state. However, various other reactions that do go from kinetic control to thermodynamic control with changing reaction conditions (like a temperature change) will be discussed later.

## 1.1.5.6 Potential Energy Surface (PES) representation of Chemical Reaction

For an n-atomic molecule 3n coordinates (i.e., x, y, and z for every atom) are needed to describe the whereabouts of the n atoms. If 3 coordinates are reserved for the translational mode (i.e. the x, y and z are coordinates for the center of mass, CM) and 3 coordinates are used to describe the rotation of the molecule in space about its three principal axis of inertia, then 3n - 6 internal coordinates need to be used to define the structure and distortion of the molecule in question (Figure 1.1.5—16).
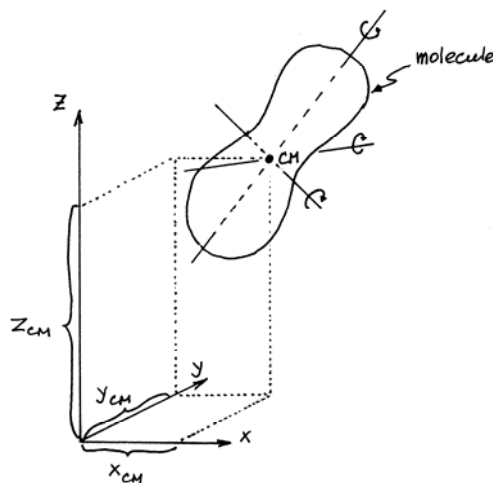


**Figure 1.1.5—16  Three translational coordinates and 3 rotational coordinates of a general n-atomic molecule leave 3n - 6 internal coordinates.**

During a chemical reaction all 3n - 6 internal coordinates change. Thus, the potential energy hypersurface may be regarded as a multivariable function:

$$E = f(x_1, x_2, x_3, \ldots\ldots, x_{3n-6})$$

<div align="right">1.1.5—73. eq</div>

However, if we are lucky, we can single out 2 of the 3n - 6 coordinates that change more drastically than the others during the chemical reaction. Let us consider nucleophilic substitution, both $S_N2$ and $S_N1$.
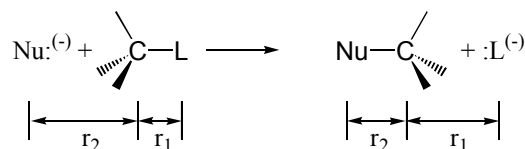


<div align="right">1.1.5—74. eq</div>

Initially, $r_1$ is short and $r_2$ is long and at the completion of the reaction $r_2$ becomes short and $r_1$ stretches out to be long. The change of potential energy with the variation of $r_1$ and $r_2$ is shown:
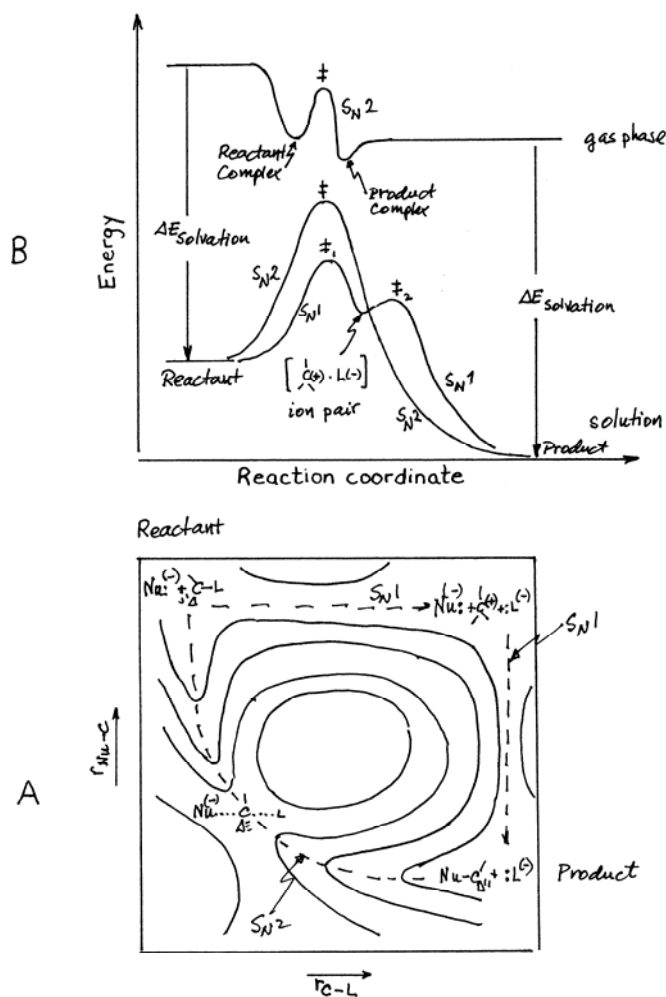


**Figure 1.1.5—17 Energies of $S_N1$ and $S_N2$ reactions: (A) schematic energy contours; reaction coordinates are shown as broken lines; (B) schematic potential energy profiles along the reaction coordinates.**

The one-dimensional crossection (Figure 1.1.5—17 B) is neither along $r_{C-L}$ nor along $r_{Nu-C}$, but along a combination of these two internal coordinates. Such combinations of internal coordinates are called reaction coordinates if the energy along such lines represent the shallowest ascent. Two distinct reaction paths are seen on Figure 1.1.5—17 A, one corresponding to the $S_N1$ and the other to the $S_N2$ route. The changes of energy along these two paths are the energy profiles of the two mechanisms. These are shown in Figure 1.1.5—17 B. The relative heights of the barriers depend on the structure of the alkyl group.

Let us consider the elimination reaction; both E2 and E1. In fact there is a third mechanism labeled as $E1_{cb}$ (elimination first order conjugate base). In the E1 mechanism the leaving group (L) leaves first followed by a proton loss, while in the $E1_{cb}$ the proton is transferred first to the base (Bronsted acid base reaction), followed by the loss of the leaving group, taking its bonding electron pair with it.
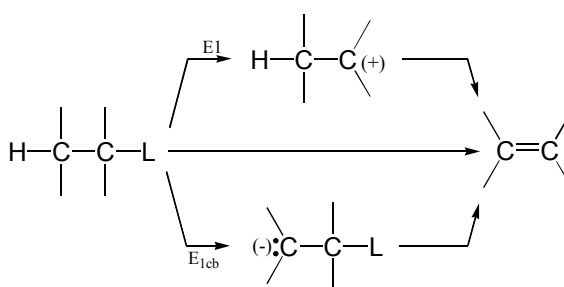


$$1.1.5—75. \text{ eq}$$

For all three mechanisms the following pair of bond lengths may be singled out as those internal coordinates that change the most during the elimination reaction.
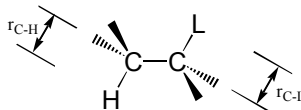


$$1.1.5—76. \text{ eq}$$

A schematic (PES) for the elimination reaction is shown in Figure 1.1.5—18

The three reaction mechanisms correspond to three routes on the (PES). Of course the molecular structure, the nature of the leaving group, the basicity and concentration of the nucleophile as well as the polarity of the solvent will influence which route will be the most favorable energetically.
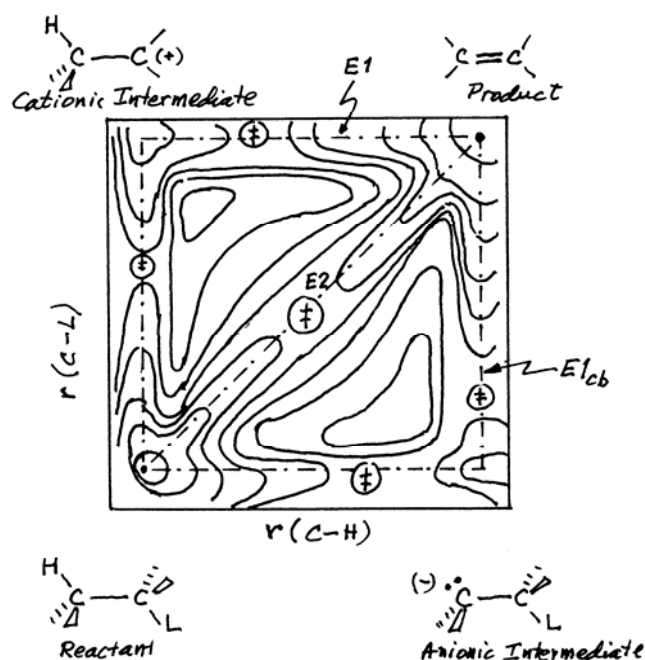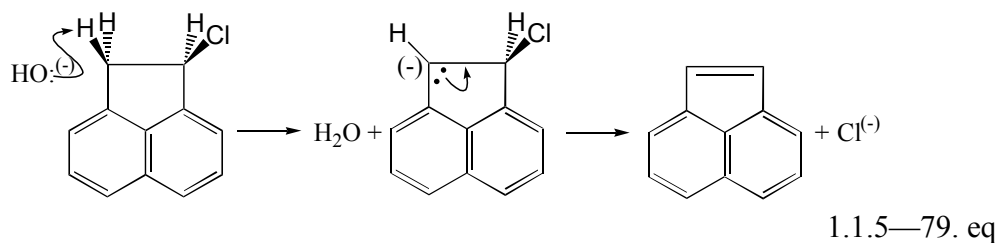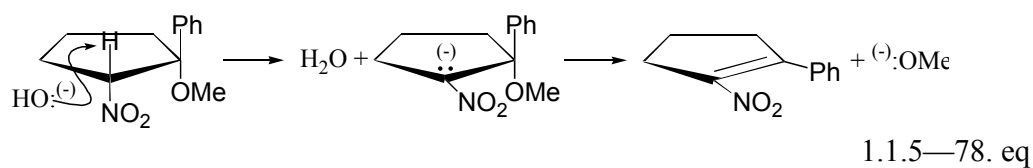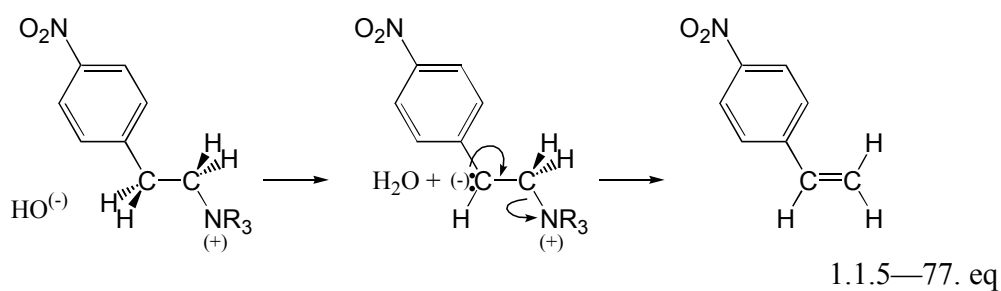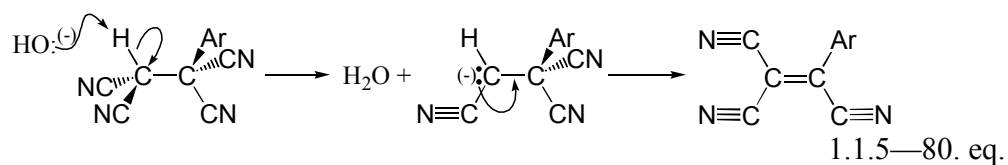
**Figure 1.1.5—18 A schematic (PES) of a 1, 2 - elimination reaction.**

There are rare molecular structures that favor $E1_{cb}$ mechanisms and some of examples are shown below:



1.1.5—77. eq



1.1.5—78. eq



1.1.5—79. eq

1.1.5—80. eq.

However, in most cases either the E2 or the E1 mechanisms represent the lowest energy path. These two alternatives are illustrated schematically in Figure 1.1.5—19 It is assumed here that under these rather ordinary conditions the $E1_{cb}$ mechanism is the least favored one.
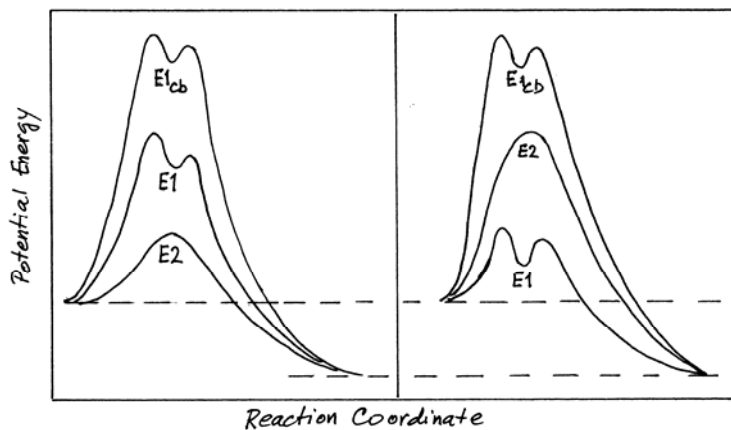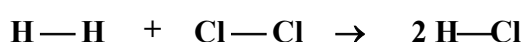


**Figure 1.1.5—19 A schematic illustration of two extreme cases: E2 is favored over E1 (left hand side) and E1 is favored over E2 (right hand side). It is assumed that under ordinary circumstances $E1_{cb}$ is the least favored mechanism.**

# Appendix

## Appendix 1

**Problem**: Compute the BDE and any other energy of the following process at different basis sets:

$$H\!-\!H \quad + \quad Cl\!-\!Cl \quad \rightarrow \quad 2\ H\!-\!Cl$$
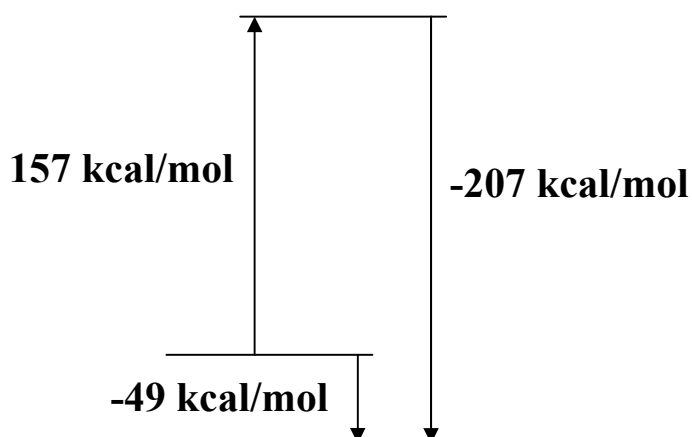
**Solution:**

In the table below you can see the results at different basis. (to get the energy in kcal/mol from hartree you have to multiply the values in hartree with 627.51)

no vibration correction

RHF/6-31Gd

| | E(Hartree) | | E(Hartree) | | kcal/mol | | kcal/mol |
|---|---|---|---|---|---|---|---|
| H2 | -1.1268278 | Hdoublet | -0.4982329 | BDE of H2 | 81.80346 | H2+Cl2->2H.+2Cl. | 92.4016 |
| Cl2 | -918.9128170 | Cldoublet | -459.4479639 | BDE of Cl2 | 10.59814 | 2H.+2Cl.-> 2HCl | -142.795 |
| HCL | -460.0599763 | | | energy of HCl form | 50.39386 | H2+Cl2->2HCl | -50.3939 |

B3LYP/6-311++G(d,p)

| | E(Hartree) | | E(Hartree) | | kcal/mol | | kcal/mol |
|---|---|---|---|---|---|---|---|
| H2 | -1.1795715 | Hdoublet | -0.5022570 | BDE of H2 | 109.8504 | H2+Cl2->2H.+2Cl. | 157.4305 |
| Cl2 | -920.4095888 | Cldoublet | -460.1668825 | BDE of Cl2 | 47.58014 | 2H.+2Cl.-> 2HCl | -206.927 |
| HCL | -460.8340192 | | | energy of HCl form | 49.49676 | H2+Cl2->2HCl | -49.4968 |

MP2/6-311++G(d,p)

| | E(Hartree) | | E(Hartree) | | kcal/mol | | kcal/mol |
|---|---|---|---|---|---|---|---|
| H2 | -1.1325014 | Hdoublet | -0.4998179 | BDE of H2 | 83.37444 | H2+Cl2->2H.+2Cl. | 95.24172 |
| Cl2 | -918.9673750 | Cldoublet | -459.4742316 | BDE of Cl2 | 11.86728 | 2H.+2Cl.-> 2HCl | -152.394 |
| HCL | -460.0954774 | | | energy of HCl form | 57.15264 | H2+Cl2->2HCl | -57.1526 |

# at B3LYP/6-311++G(d,p)
*no vibrational corr.*

**157 kcal/mol**          **-207 kcal/mol**

**-49 kcal/mol**

**Appendix 2**

**Problem:** Compute the homolytic and heterolytic dissociation potencial of HCl

**Solution:** Input file for Homolytic dissociation:

```
%chk=hcl_hom_dis
%mem=100MB
%nproc=1
#p opt=modredundant hf/3-21g

hcl homolytic cleavage

0 3
 Cl
 H                     1                     B1

   B1                1.00000000

B 2 1 S 20 0.050000 1.000000 2.000000
```

Input file for heterolytic dissociation:

```
%chk=hcl_het_dis
%mem=100MB
%nproc=1
#p opt=modredundant hf/3-21g

hcl heterolitikus hasitas

0 1
 Cl
 H                     1                     B1

   B1                1.00000000
```
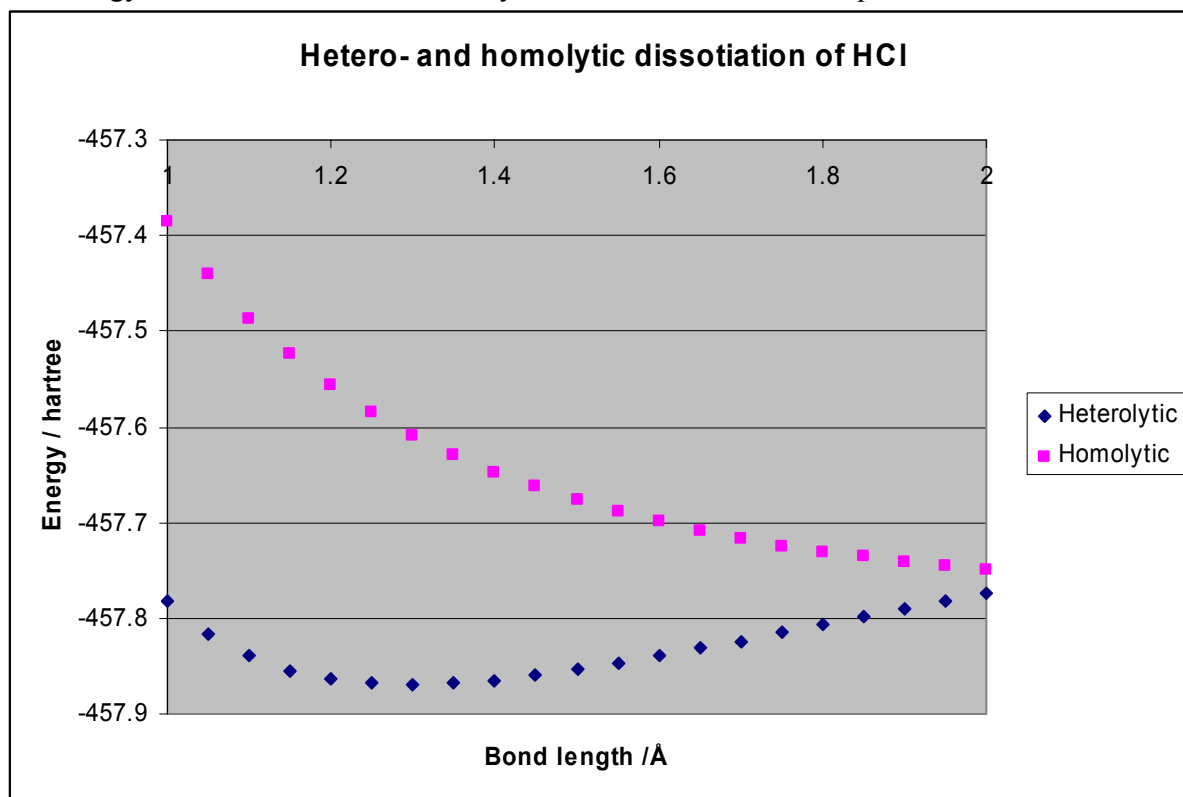
```
B 2 1 S 20 0.050000 1.000000 2.000000
```

The energy curves of homo- and heterolytic dissociation of HCl computed at HF- 3-21G basis set.



## Appendix 3

**Problem:** Compute the homolytic and heterolytic dissociation potencial of MeCl.

**Solution:** The calculation of homolytic reaction path at HF-3-21G basis set did not give useful results.

Input file for heterolytic dissociation:

```
%chk=mecl_het_dis
%mem=100MB
%nproc=1
#p opt=modredundant hf/3-21g

MeCl heterolytic cleavage

0 1
 C
 H                 1         B1
 H                 1         B2   2          A1
 H                 1         B3   3          A2   2          D1
 Cl                1         B4   4          A3   3          D2

   B1              1.07000000
```
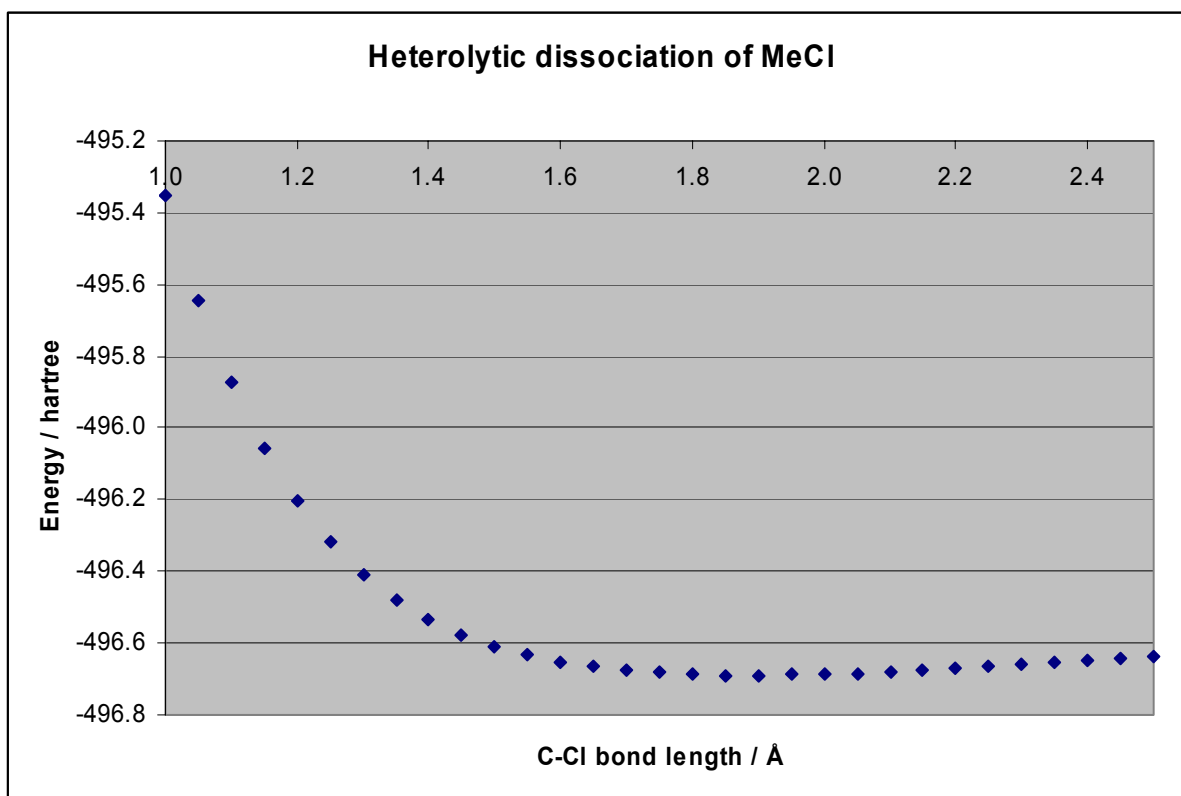
```
   B2              1.07000000
   B3              1.07000000
   B4              1.00000000
   A1            109.47120255
   A2            109.47121829
   A3            109.47121829
   D1            120.00000060
   D2           -120.00003407

B 5 1 S 30 0.050000 1.000000 2.500000
```



**Appendix 4**

**Problem:** calculate excitation energy of hydrogen molecule in singlet and triplet state.

**Solution:** Optimize the $H_2$ molecule in singlet state and calculate the energy of the triplet state with same geometry.

Energy of singlet state: - 1.17548238 au Hartree
Energy of triplet state: - 0.76796621 au Hartree

# References

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