Ch9 Haloalkanes and Halorrenes

Ch 9 Haloalkanes and Haloarenes

Contents

9.1 Properties and nomenclature of organohalogen compounds
   (a) Alkyl halides
      (1) Types and names of alkyl halides
      (2) Nomenclature of alkyl halides
   (b) Aryl halide
      (1) Types and names of aryl halides
      (2) Nomenclature of aryl halides

9.2 Structure of organic halides

9.3 Reaction of alkyl halides
   (a) Nucleophilic substitution reaction
      (1) Williamson’s ether synthesis
      (2) Reaction with cyanides
      (3) Esterification
   (b) Stereochemistry of nucleophilic substitution reaction
      (1) Stereochemistry of S_N1 reactions
      (2) Stereochemistry of S_N2 reactions
      (3) Example of inversion
      (4) Simultaneous progress of S_N1 and S_N2.
   (c) Elimination reaction
      (1) Driving force of elimination reaction
      (2) Unimolecular elimination (E1)
      (3) Bimolecular elimination (E2)
      (4) Orientation of elimination reaction
      (5) Competition between substitution reaction and elimination reaction
   (d) Stereochemistry of elimination reaction

9.4 Reactions of aryl halides
   (a) Nucleophilic substitution
   (b) Electrophilic substitution reaction
      (1) Halogens as substituents
      (2) Electronic effect and steric effect
      (3) Grignard reagent

Problems

Organohalogen compounds, in which halogen atoms are substituted on carbon atoms of organic compounds, scarcely exist as such in nature, and many of them are synthetic materials. These are relatively easily synthesized in quantity. Because of their high reactivity, they are widely used as reaction intermediates.

Among halogenated aliphatic compounds, especially haloalkanes of low molecular weight play an important role as organic solvents. These exhibit solubility to many organic compounds higher than corresponding hydrocarbons. Haloarenes, in which halogen atoms are bonded directly to benzene ring are also very useful materials.

When the kind of halogen atoms are changed in organohalogen compounds, their properties are accordingly varied. This fact provides good materials for theoretical study.

Many kinds of organohalogen compounds are produced in industrial scale, and are used as agricultural chemicals, solvents, and for other purposes. Recently, however, there arises a major problem with their residual, stability, and toxicity. Today, there is a
9.1 Properties and nomenclature of organohalogen compounds
(a) Alkyl halides

(1) Types and names of alkyl halides

Organic compounds containing halogens are roughly classified into two groups: one in which halogen atoms are directly bonded to carbon atoms, and the other, acid halides in which the OH group in the carboxy group is substituted by a halogen atom. The latter will be treated in Chapter 12, carboxylic acids and their derivatives.

Organohalogen compounds are roughly classified into two groups: one, alkyl halides or haloalkanes, in which hydrogen atoms of alkanes are replaced with halogen atoms, and the other, haloarenes or aryl halides, in which hydrogen atoms of arenes are replaced with halogen atoms. In addition, there are halogenated alkenes and alkynes.

<table>
<thead>
<tr>
<th>Point:</th>
<th>Classification of organohalogen compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aliphatic halogenated compounds: alkyl halides, etc</td>
<td></td>
</tr>
<tr>
<td>Aromatic halogenated compounds: aryl halides, etc</td>
<td></td>
</tr>
</tbody>
</table>

If hydrogen atoms of alkanes are substituted by chlorine, bromine, or iodine atoms, their melting and boiling points increase in this order. The melting and boiling points of the fluorinated compound change very little. The density of haloalkanes increase due to the introduced halogen atoms.

The volatility of alkyl fluorides is high and their surface tension is small. Alkyl fluorides with a small number of fluorine atoms (including those which contain chlorine in addition to fluorine) are called “flon”, and once widely used as coolants, cleaning solvents, and propellants. It has been pointed out that these compounds are responsible for the destruction of the ozone layer, and now the use of some flons are regulated. Some of chlorinated alkanes are also under regulation.

(2) Nomenclature of alkyl halides

Generally, alkyl halides are named based on both the substitutive nomenclature and radicofunctional nomenclature. Common names are already introduced.

- haloalkane, haloarene (substitutive nomenclature)
- alkyl halide, aryl halide (radicofunctional nomenclature)

In substitutive nomenclature, “halogen” is to be used exclusively as a prefix. Mixed use of two methods of nomenclatures should be avoided.

[Example] \( \text{CH}_3\text{CH}_2\text{CH}_2\text{Cl} \)
- 1-chloropropane (substitutive)
  - propyl chloride (radicofunctional)
- chloropropene (error; mixed use)

[Example] \( \text{CH}_3\text{CHClCH}_3 \)
- 2-chloropropane (substitutive)
  - isopropyl chloride (radicofunctional)

[Example] \( \text{BrCH}_2\text{CH}_2\text{Br} \)
- 1,2-dibromoethane (substitutive)
  - ethylene dibromide (radicofunctional)
  - ethane dibromide (error; mixed use)

[Example] \( \text{CH}_2\equiv\text{CHCl} \)
- chloroethylene (substitutive)
vinyl chloride (radicofunctional)

**Exercise 9.1 Naming of alkyl halides**

(1) Name the following compounds.
   - (a) CH₃CH₂CH₂CH₂Cl
   - (b) (CH₃)₂CHCH₂I
   - (c) BrC≡CC₂H₂Br

(2) Draw the (simplified) structures of the following compounds.
   - (d) 3-chloro-2-methylpentane
   - (e) 3-chloro-1-propene (allyl chloride)

**Answer**

(1)
   - (a) 1-chlorobutane (butyl chloride)
   - (b) 1-iodo-2-methylpropane (isobutyl iodide)
   - (c) 1,3-dibromo-1-propyne

(2)
   - (d) (CH₃)₂CHCHClCH₂CH₃
   - (e) CH₂=CHCH₂Cl

In Table 9.1, examples of haloalkanes (alkyl halides) are listed.

<table>
<thead>
<tr>
<th>name*</th>
<th>structural formula</th>
<th>melting point (°C)</th>
<th>boiling point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>methyl chloride (chloromethane)</td>
<td>CH₃Cl</td>
<td>-97.72</td>
<td>-23.76</td>
</tr>
<tr>
<td>methyl bromide (bromomethane)</td>
<td>CH₃Br</td>
<td>-93.66</td>
<td>3.56</td>
</tr>
<tr>
<td>methyl iodide (iodomethane)</td>
<td>CH₃I</td>
<td>-66.45</td>
<td>42.8</td>
</tr>
<tr>
<td>methylene chloride (dichloromethane)</td>
<td>CH₂Cl₂</td>
<td>-96.8</td>
<td>40.21</td>
</tr>
<tr>
<td>chloroform** (trichloromethane)</td>
<td>CHCl₃</td>
<td>-63.5</td>
<td>61.2</td>
</tr>
<tr>
<td>carbon tetrachloride** (tetrachloromethane)</td>
<td>CCl₄</td>
<td>-28.6</td>
<td>76.74</td>
</tr>
<tr>
<td>ethylidene dichloride (1,1-dichloroethane)</td>
<td>CH₃CHCl₂</td>
<td>-96.7</td>
<td>57.3</td>
</tr>
<tr>
<td>1,2-dichloroethane (1,2-dichloroethane)</td>
<td>ClCH₂CH₂Cl</td>
<td>-35.3</td>
<td>83.38</td>
</tr>
<tr>
<td>vinyl chloride (1-chloroethylene)</td>
<td>CH₂=CHCl</td>
<td>-150.7</td>
<td>-13.70</td>
</tr>
<tr>
<td>vinylidene chloride (1,1-dichloroethylene)</td>
<td>CH₂=CCl₂</td>
<td>-122.1</td>
<td>31.7</td>
</tr>
<tr>
<td>benzyl chloride ((chloromethyl)benzene)**</td>
<td>C₆H₅CH₂Cl</td>
<td>-39.2</td>
<td>179.3-179.4</td>
</tr>
</tbody>
</table>

*radicofunctional name (substitutive name) ** common name *** IUPAC name

(b) Aryl halide

(1) Types and names of aryl halides

Aryl halides are very useful compounds as such, and are used as the starting materials for other aromatic compounds. The problem is their stability, and hence their residual components are problematic if these are used in industry in quantity.

Polychlorobiphenyl (PCB), obtained by chlorination of biphenyl, is a mixture of
compounds containing three or four chlorine atoms. These had been used widely because these are relatively cheap, stable to heat, and have excellent electric property. Their use was prohibited because of their strong toxicity and their bad influence on the environment.

One example of PCB; 2,2',4,4'-tetraphenylbiphenyl.

(2) Nomenclature of aryl halides

Aryl halides are generally named by the substitutive method and halogens are used as prefix.

[Example] C₆H₅Br
bromobenzene (substitutive)
phenyl bromide (radicofunctional; seldom used)

Occasionally some aryl halides are named by substitutive method by combining some group (such as aryl, benzyl, etc) with such as chloride and bromide.

[Example] C₆H₅CH₂Cl
chlorophenylmethane (substitutive)
benzyl chloride (radicofunctional; usually used)

In Table 9.2, examples of aryl halides are listed.

9.2 Structure of organic halides

Because halogens are monovalent, there arises little change in the structures of organic compounds when hydrogen atom(s) in them are substituted by halogen atom(s). A fluorine atom is slightly larger than a hydrogen atom, while the size of a chlorine atom is much the same with a methyl group. A bromine atom and an iodine atom are considerably larger than a chlorine atom.

The repulsion with adjacent hydrogen atoms is not as large as that expected from the van der Waals radii because the carbon-halogen bond length is large. In Table 9.3 van der Waals radii of halogen atoms and the carbon-halogen (C-X) bond length are summarized. A large difference is observed between fluorine and the other atoms.

1,2-dichloroethane and other 1,2-dihaloethanes have antiperiplanar conformations (see Table 5.4). In addition to the steric hindrance, an electric repulsion between two halogen atoms plays a role.

<table>
<thead>
<tr>
<th>Name</th>
<th>Structural Formula</th>
<th>melting point (°C)</th>
<th>boiling point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorobenzene</td>
<td>C₆H₅F</td>
<td>-41.9</td>
<td>82.7</td>
</tr>
<tr>
<td>Chlorobenzene</td>
<td>C₆H₅Cl</td>
<td>-45</td>
<td>132</td>
</tr>
<tr>
<td>Bromobenzene</td>
<td>C₆H₅Br</td>
<td>-30.6</td>
<td>156.15</td>
</tr>
<tr>
<td>Iodobenzene</td>
<td>C₆H₅I</td>
<td>-31.33</td>
<td>188.45</td>
</tr>
<tr>
<td>1,2-dichlorobenzene</td>
<td>1,2-C₆H₄Cl</td>
<td>-17.03</td>
<td>180.48</td>
</tr>
<tr>
<td>(o-dichlorobenzene)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,3-dichlorobenzene</td>
<td>1,3-C₆H₄Cl</td>
<td>-24.76</td>
<td>173.00</td>
</tr>
</tbody>
</table>

Table 9.2 Some alkyl halides
9.3 Reaction of alkyl halides

The most significant feature of chemical properties of organohalogen compounds is the polarization of C-halogen bonds due to the large electronegativities of halogens. In ethyl bromide, for instance, the carbon atom to which the bromine atom is bonded (α-carbon) and the hydrogen atom which is bonded to the adjacent carbon (β-carbon) bear partial positive charge by the effect of bromine atom. As a result, alkyl halides perform elimination reactions in addition to substitution reactions.

(b) Nucleophilic substitution reaction

The nucleophilic substitution reaction is the most important reaction of alkyl halides and this aspect is already discussed in detail in connection with reaction mechanism in ch. 4. A few examples of nucleophilic substitution reactions will be introduced.

(1) Williamson’s ether synthesis

The well-known ether synthesis, that is, heating an alcohol with concentrated sulfuric acid can provide only symmetric ethers such as diethyl ether.

\[
2 \text{C}_2\text{H}_5\text{OH} \longrightarrow \text{C}_2\text{H}_5\text{OC}_2\text{H}_5 + \text{H}_2\text{O}
\]

diethyl ether

To the contrary, Williamson’s ether synthesis, the reaction between alkyl halides and alkoxides (such as methoxide or ethoxide) can provide asymmetric ethers. By changing the combination of starting compounds, any type of ethers can be synthesized.

\[
\text{CH}_3\text{Br} + \text{C}_2\text{H}_5\text{ONa} \longrightarrow \text{CH}_3\text{OC}_2\text{H}_5 + \text{NaBr}
\]

sodium ethoxide

\[
\text{CH}_3\text{Br} + \text{CH}_3\text{ONa} \longrightarrow \text{CH}_3\text{OCH}_3 + \text{NaBr}
\]

sodium methoxide

\[
\text{CH}_3\text{Br} + \text{CH}_3\text{ONa} \longrightarrow \text{CH}_3\text{OC}_2\text{H}_5 + \text{NaBr}
\]

ethyl methyl ether

\[
\text{CH}_3\text{Br} + \text{CH}_3\text{ONa} \longrightarrow \text{CH}_3\text{OCH}_3 + \text{NaBr}
\]
dimethyl ether
(2) **Reaction with cyanides**

The nucleophilic reaction between alkyl halides and cyanide ions produce nitriles which have one more carbon atom than the starting halides. Nitriles are hydrolyzed to carboxylic acids via amides (Ch 12).

This nucleophilic substitution reaction is important as one of the methods to add carbon atoms to organic compounds. In practice, halides and sodium cyanide or potassium cyanide are reacted as shown below.

\[
\text{H}_3\text{C} \quad \text{CH}_2\text{CH}_2\text{Br}^+ + \text{Na}^+ + \text{CN}^- \rightarrow \text{CH}_2\text{CH}_2\text{CN} + \text{NaBr}
\]

(3) **Esterification**

Esters are generally synthesized by the reaction between carboxylic acids and alcohols. However, there are other methods of ester synthesis. One example is the reaction between halides and the salts of carboxylic acids.

\[
\text{CH}_3\text{I} + \text{CH}_3\text{CH}_2\text{COONa} \rightarrow \text{CH}_3\text{CH}_2\text{COOCH}_3 + \text{NaI}
\]

**Exercise 9.2** Analysis of nucleophilic substitution reaction

Analyze the following reaction in a similar manner as the previous example.

\[
\text{CH}_3\text{I} + \text{CH}_3\text{COONa} \rightarrow \text{CH}_3\text{COOCH}_3 + \text{NaI}
\]

**Answer**

The crucial point is that the nucleophilic reagent of this reaction is “carboxylate ion”.

\[
\text{H}_3\text{C}^+ \text{I}^- + \text{Na}^+ + \text{CH}_3\text{COO}^- \rightarrow \text{H}_3\text{C} \quad \text{OCOCH}_3 + \text{NaBr}
\]

(b) **Stereochemistry of nucleophilic substitution reaction**

In Ch 4, the reaction mechanism of the nucleophilic substitution reactions was discussed in detail. The important aspect of stereochemistry of the reaction was not, however, treated.

When the carbon atom of the reaction center is asymmetric, its chirality may be temporarily lost in the intermediate or in the transition state as is suggested from the reaction mechanism discussed in Ch 4.1.

Now we will discuss the stereochemistry of Williamson’s ether synthesis. Firstly, we will consider the case where no asymmetric carbon atom is involved.

(1) **Stereochemistry of S_N1 reactions**

We will examine the process of the reaction between ethyl bromide and sodium methoxide

\[
\text{C}_2\text{H}_5\text{Br} + \text{CH}_3\text{ONa} \rightarrow \text{CH}_3\text{OC}_2\text{H}_5 + \text{NaBr}
\]
in a three-dimensional manner.

If the reaction proceeds via S_N1, bromide ion leaves first, and a three (or tri) coordinate and sp² hybridized carbocation intermediate is formed (Fig 9.1). Methoxide ion, the nucleophile, will approach to the carbocation from the right side and from the left side with equal probability. As a result, the product will be a mixture of equal amount of the one with the configuration same to the starting molecule and the other with the reverse configuration to the starting molecule.

In this case, however, the one with the original configuration and the other with
inverse configuration are identical. Hence only one product will be obtained.

**Figure 9.1** Stereochemistry of $S_N$1 reaction of ethyl bromide

What will happen if the reactant is $s$-butyl bromide (2-bromobutane; in this example $R$-configuration) which has an asymmetric carbon atom? The nucleophilic reagent approaches to the generated carbocation from both sides with equal probability (Figure 9.2).

The product, 2-methoxybutane, is a 1:1 racemic mixture of the one with the original configuration and the other with inverted configuration. Thus, $S_N$1 reaction of optically active ($R$)-$s$-butyl bromide yields the product, an optically inactive racemic mixture of 2-methoxybutane. If the starting molecule is optically active, and the product is a racemic mixture, you can say that the reaction proceeded via $S_N$1.

**Figure 9.2** Stereochemistry of $S_N$1 reaction of $s$-butyl bromide

(2) Stereochemistry of $S_N$2 reactions

Suppose the reaction between ethyl bromide and sodium methoxide proceeds via $S_N$2. First, methoxide ion will approach to the carbon atom from the opposite side of bromine to form penta-coordinated transition state (Figure 9.3). Then, the bromine atom is removed as a bromide ion. During this process, the hybridization state of the carbon atom returns to sp3 the position of bromine atom and that of methoxide ion is exchanged. Hence the configuration of the product is inversed.

The product, ethyl methyl ether has no asymmetric carbon atom and optically inactive. This means that the inversion is not proved in this case.
What will happen if the reactant is (R)-s-butyl bromide (2-bromobutane) which has an asymmetric carbon atom? First, methoxide ion will approach to the carbon atom from the opposite side of bromine to form penta-coordinated transition state (Figure 9.4). Then, the bromide ion is removed and the inversion of configuration takes place. The result is different from the case of ethyl bromide since in this case both the reactant and the product are optically active, and the inversion can be proved from the change of specific rotation.

In practice, if the specific rotations of (R)- and (S)-s-butyl bromide and (R)- and (S)-methoxybutane are known, the stereochemical process of the reaction can be traced by measuring the specific rotation. In fact, the stereochemistry of S_N1 and S_N2 reactions has been proved by many experiments involving measurements of specific rotation.

You must notice that there is no relation between the configuration and the sign of specific rotation, as was mentioned before (p. 159). Even if (R)-reactant is inverted to become (S)-product, sometimes the sign does not change (the value itself may, however, change).

(3) Example of inversion
An example which proves the inversion does in fact take place by measuring the specific rotation. The starting compound is optically active 1-phenyl-2-propanol, and its dextrorotatory, i.e., (+)-isomer. Fig. 9.5 shows the course of the reaction.

The ethyl ether of 1-phenyl-2-propanol is synthesized via two different procedures. The absolute value of specific rotation of the product via reactions A and B, and that of the product via reactions C and D are relatively close. The signs are, however, opposite, indicating that the two are enantiomers each other. This means that an inversion in fact takes place at one of the reactions A, B, C, and D. What happens in each reaction is summarized below.
Nucleophilic substitution of optically active 1-phenyl-2-propanol ($\alpha = [\alpha_D]$)

**Reaction A:** bond cleaved; O-H. bond formed O-S
**Formation of an ether by the reaction between acid chloride and ethanol**

**Reaction B:** bond cleaved; C-O. bond formed C-O
**Formation of an alkoxide by the reaction between acid bromide and ethanol**

**Reaction C:** bond cleaved; O-H. bond formed O-C (Williamson’s ether synthesis)
**Formation of an alkoxide by the reaction between acid chloride and ethanol**

Notice that the asymmetric carbon atom is not the reaction center.

Except reaction B, no reaction takes place at the asymmetric carbon atom. Hence, if an inversion takes place, this should occur in reaction B.

In this way, the fact that an inversion really takes place and that the reaction B proceeds via $S_N2$ is experimentally proved.

**Point:** Stereochemistry of nucleophilic substitution ($S_N$) reactions

- $S_N1$ is related to racemization
- $S_N2$ is related to inversion

These relations can only be proved by experiments with the one enantiomer of optically active pair.

**Exercise 9.3** Experimental proof of inversion

Following the method of Figure 9.5, analyze each step of the reaction below. Guess the conclusion which can be obtained from the measurements of specific rotation.

**Answer**

The reactant and the product are both 1-phenyl-2-propanol. The magnitude of their specific rotation is much the same but the sign is different. This indicates that at some stage an inversion occurred. What happens in the reactant in each reaction is summarized below.

**Reaction A:** bond cleaved; O-H. bond formed O-S (the same with Fig. 9.5)
**Reaction B:** bond cleaved; C-O. bond formed C-O.

- Nucleophilic substitution between an ester and acetoxide ion $\text{AcO}^-$
- Reaction C: bond cleaved; O-C. bond formed O-H
  - (Hydrolysis of an ester)

The bond cleavage or bond formation at the asymmetric carbon atom takes place only in reaction B. It can be concluded that the inversion takes place in this reaction.
(4) Simultaneous progress of S_N1 and S_N2

This problem was already discussed in Ch 4.4. This can be proved by using optically active reactants. Simultaneous progress of S_N1 and S_N2 tends to occur when the reactant is a secondly compound (Figure 9.6). Experiments, that is, incomplete racemization or incomplete inversion, prove this fact.

![Figure 9.6 An example of simultaneous progress of S_N1 and S_N2](image)

Exercise 9.4 Simultaneous progress of S_N1 and S_N2

Estimate the proportion of inversion (S_N2) to (racemization) S_N1 based on the distribution of stereochemistry of the products.

**Answer**

Make the ratio of inversion as x. By inversion, x of S isomer will be formed while by racemization each (1 - x)/2 of S isomer and R isomer will be formed.

For S, x + (1 - x)/2 = 0.64. For R, (1 - x)/2 = 0.36. Then x = 0.28. Racemization is 28%.

(c) Elimination reaction

(1) Driving force of elimination reaction

So far, we do not consider the possibility of simultaneous progress of two reactions. Though S_N1 and S_N2 do progress simultaneously, these are expressed by the same reaction formula. In this sense these two reactions may be regarded as the same reaction. In the world of organic chemistry, rather frequently, two, or more than two reactions progress simultaneously. For example, the reaction between ethyl bromide and sodium hydroxide proceeds via S_N2 mechanism because the halide is a primary compound devoid of steric hindrance.

\[
\text{C}_2\text{H}_5\text{Br} + \text{NaOH} \rightarrow \text{C}_2\text{H}_5\text{OH} + \text{NaBr}
\]

Generally, however, in the substitution reaction in which a halide ion is replaced by a hydroxide ion, an elimination reaction in which a hydrogen halide is removed accompanies.

\[
\text{C}_2\text{H}_5\text{Br} + \text{NaOH} \rightarrow \text{H}_2\text{C}=\text{CH}_2 + \text{NaBr} + \text{H}_2\text{O}
\]

The driving force of this reaction is also the polarization of C-halogen bond due to the large electronegativity of halogen.

In Ch 9.3, it was shown that the hydrogen atom H_β bonded to C_β bears some positive charge because positively charged C_α draws electron from neighboring atoms including C_β. The nucleophile, hydroxide ion in this case, attacks H_β rather than C_α and withdraw H^+ from ethyl bromide (to form H_2O) competitively. By the following processes, hydrogen bromide is eliminated from ethyl bromide to form ethylene.

(2) Unimolecular elimination (E1)

If the rate of elimination reaction is determined, and examined the dependency of the concentration of the reactant, it is possible to differentiate the unimolecular reaction and the bimolecular reaction. The situation is the same with substitution reactions. For the reaction...
Ch9 Haloalkanes and Halorrenes

\[ \text{RCH}_2\text{CH}_2\text{Br} + \text{NaOH} \rightarrow \text{RCH}==\text{CH}_2 + \text{NaBr} + \text{H}_2\text{O} \]

The rate equation will be one out of the two.
\[ v = k[\text{RCH}_2\text{CH}_2\text{Br}] \] (unimolecular reaction, E1)
\[ v = k[\text{RCH}_2\text{CH}_2\text{Br}][\text{OH}^-] \] (bimolecular reaction, E2)

Each type of the reaction is designated as E1 or E2 (E stands for elimination).

Following the example of S_N1, the rate-determining step of E1 should be removal of bromide ion from alkyl bromide (i.e., formation of carbocation). In this case also tertiary alkyl halide is more reactive for E1 than primary halide. The process up to this stage is the same if the reaction proceeds via S_N1 mechanism. If the electrophilic part of nucleophile (i.e., hydroxide ion) will attack C_α, the mechanism will be S_N1. If, however, the hydroxide ion attacks H_α to pull it up as a proton, a double bond is formed between C_α and C_β. Thus, the elimination reaction E1 is complete.

The flow of the elimination reaction with t-butyl bromide as the reactant is shown in Figure 9.7. Three stages of the reaction should clearly be recognized.

**Figure 9.7 Unimolecular elimination (E1) of t-butyl bromide**

**Point**: The three stages of unimolecular elimination (E1)
1) Elimination of bromide ion and formation of carbocation
2) Pulling out of H_β by a base (arrow 1 in Figure 9.7)
3) Removal of hydrogen (as water). The shared electron pair of C-H bond is used to form a double bond (arrow 2 in Figure 9.7).
(1) and (2) occurs simultaneously.

**3) Bimolecular elimination (E2)**

Bimolecular eliminations (E2) tend to occur, as is the case with nucleophilic substitution, when the reactants are primary alkyl halides. Fig. 9.8 shows the flow of the reaction. Three stages of the reaction should clearly be recognized.

**Figure 9.8 Bimolecular elimination of ethyl bromide**

**Point**: The three stages of bimolecular elimination (E2)
(1) Pulling out of H^+ by a base (arrow 1 in Figure 9.8)
(2) The shared electron pair of C-H bond moved to form a double bond (arrow 2 in Fig
(3) Elimination of bromide ion. The shared electron pair of C-Br bond turns into unshared electron pair of bromide ion. (1), (2), and (3) occurs simultaneously.

(4) Orientation of elimination reaction

Suppose a hydrogen halide is added to an alkene with differently substituted two carbon atoms. The structure of the products may be different depending on the carbon atom firstly attacked by the hydrogen atom. Which one is in fact obtained is the orientation of addition reaction (see Ch. 6.3).

Orientation is also relevant to elimination reaction. If there are two or more than two carbon atoms adjacent to the carbon atom bonded to the halogen atom to be removed and possess removable hydrogen(s), the problem of orientation arises.

An example is given below. When hydrogen bromide is eliminated from 2-bromoethane, two processes (1) and (2) are possible depending on which hydrogen is removed. The products will be either 1-butene or 2-butene depending on the processes (1) or (2) (Fig 9.9). According to the experiment, the product is 2-butene by the process (2).

Russian chemist A. M. Zeitsev summarized the experimental results into an empirical rule, that is, Zeitsev rule.

![Figure 9.9 Orientation of elimination reaction](image)

**Point:** Zeitsev rule

When hydrogen halides are eliminated from alkyl halides, the more substituted alkenes will be formed.

**Exercise 9.5 Zeitsev rule**

Draw the structure of the main product when 1-bromo-1-methylcyclohexane is reacted with a strong base (e.g., KOH).

**Answer**

![Exercise 9.5 Answer](image)

(5) Competition between substitution reaction and elimination reaction

When organohalogen compounds react with nucleophiles, four types of reactions may take place depending on the structure of reactants and reaction condition. Whether reaction conditions are acidic (e.g., in concentrated hydrochloric acid), or basic (e.g., nucleophiles are OH⁻, OCH₃⁻ or OC₂H₅⁻) are very important. In Figure 9.10, a few examples are summarized. In both acidic conditions and basic conditions, S_N1 and E1 do
Ch9 Haloalkanes and Halorrenes

not take place when the substrates are primary. In basic conditions, E2 occur rather easily when the substrates are secondary or tertiary.

### Table 9.4 Competition between substitution reactions and elimination reactions

<table>
<thead>
<tr>
<th>structure of reactant</th>
<th>condition</th>
<th>S_N1</th>
<th>S_N2</th>
<th>E1</th>
<th>E2</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCH₂X(primary)</td>
<td>acidic</td>
<td>x</td>
<td>o</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>RR’CHX(secondary)</td>
<td>basic</td>
<td>x</td>
<td>o</td>
<td>△</td>
<td>△</td>
</tr>
<tr>
<td>RR’R”CX(tertiary)</td>
<td>acidic</td>
<td>△</td>
<td>△</td>
<td>x</td>
<td>O</td>
</tr>
<tr>
<td>RR’R”CX(tertiary)</td>
<td>basic</td>
<td>△</td>
<td>△</td>
<td>x</td>
<td>O</td>
</tr>
</tbody>
</table>

**Figure 9.10** Competition between substitution reactions and elimination reactions

When reactants are primary, S_N2 are main reactions, but E2 are also possible. When reactants are secondary, there are competition between substitution (S_N1 or S_N2) and elimination (E1). Judging from the amount of the products, elimination is more important.

When reactants are tertiary, there are competition between substitution (S_N1) and elimination (E1) in acidic conditions. These points are summarized in Table 9.4. This is a mere guideline, and cases different from this table may take place depending on the structures and properties of reactants or reagents, or on reaction condition.
(d) Stereochemistry of elimination reaction
In the case of nucleophilic substitution reactions, the nucleophile approaches to the carbon atom from the back side of the leaving group. This is to avoid the steric hindrance which is unavoidably involved. This should be the case with elimination reactions, the hydroxide ion approaches to Hβ, it chooses the hydrogen atom which is furthest to bromine atom, that is, trans hydrogen. In other words, the leaving hydrogen atom and bromine atom are trans each other. Hence elimination of this type is named trans elimination, or anti elimination. In Figure 9.11, trans elimination of ethyl bromide is illustrated by two ways, the perspective view and Newman projection.

Fig 9.11 The stereochemistry of the trans elimination of ethyl bromide

The situation is very close to the case of trans addition of bromine or hydrogen bromide to alkenes. Similarly, it is impossible to confirm that this reaction does take place according to this pathway. In Figure 9.11, even if a hydrogen which is not trans to the bromine atom, the product is also ethylene. This is because the reactant, and hence the product is much too simple.

If a little more complex reactant is employed, the product via trans elimination and the product via another route will be different. In Fig 9.12, both C1 and C2 of 1-bromo-1,2-diphenylpropane are asymmetric carbon atom. Hence, if the leaving bromine atom and hydrogen atom take trans position, the positions of remaining atoms and groups of atoms are fixed, and cis-1,2-1,2-diphenyl-1-propene is necessarily formed.
Exercise 9.6 Trans elimination
(1) Determine the configuration of 1-bromo-1,2-diphenylpropane given in Fig 9.12 in terms of \((R, S)\) convention.
(2) Draw the process, like Fig 9.11, of the trans elimination of hydrogen bromide from 1-bromo-1,2-diphenylpropane which has the reverse configuration at C\(^2\).

Answer
(1) The priority is as follows.
C\(^1\): Br > C\(_6\)H\(_5\) > the half of the molecule > H \((R\) configuration\)
C\(^2\): the half of the molecule > C\(_6\)H\(_5\) > CH\(_3\) > H \((S\) configuration\)
The configuration is \((1R, 2R)\)
(2) The trans elimination of \((1S, 2R)\)-1-bromo-1,2-diphenylpropane is explained by Fig 9.13. The product is trans-1,2-diphenyl-1-propene.

Figure 9.12 The stereochemistry of trans elimination of 1-bromo-1,2-diphenylpropane

Figure 9.13 trans-elimination of \((1S, 2R)\)-1-bromo-1,2-diphenylpropane
9.4 Reactions of aryl halides

(a) Nucleophilic substitution

Will nucleophilic substitution reactions, most popular for alkyl halides, also take place for aryl halides? Differences in the reactivity of aromatic and aliphatic compounds also exist among organohalogen compounds. Under the condition in which ethyl bromide reacts with sodium hydroxide to form ethanol, bromobenzene does not react with sodium hydroxide to form phenol.

\[
\text{C}_2\text{H}_5\text{Br} + \text{NaOH} \rightarrow \text{C}_2\text{H}_5\text{OH} + \text{NaBr}
\]

The difference of reactivity of alkyl halides and that of aryl halides is due to the presence of aromatic ring. Because of the large electronegativity of halogens the C-X bond is polarized and the carbon atom to which the halogen atom is bonded bears a partial positive charge (I effect). The situation is much the same with alkyl halides.

\[
\begin{align*}
\text{Cl} & \quad \text{Cl}^+ \\
\text{δ-} & \quad \text{δ+}
\end{align*}
\]

The unshared electron pair of halogen atom flows into the benzene ring (delocalization), and the ring as a whole (including the carbon atom to which the halogen atom is bonded) bears partial negative charge (R effect). Hence, the situation is different from alkyl halides (Figure 9.14). For this reason nucleophilic substitution reactions do not easily occur.

\[
\begin{align*}
\text{(A)} & \quad \text{(B)} & \quad \text{(C)} & \quad \text{(D)}
\end{align*}
\]

**Figure 9.14** Resonance structure of chlorobenzene

When two or more than two strong electron withdrawing groups (such as NO\(_2\) group) are introduced into the benzene ring, electrophilic substitution reactions also occur with aryl halides. Under high pressure high temperature condition, the reaction between aryl halides and sodium hydroxide afford phenol via phenoxides. This reaction is employed for industrial purpose (Figure 9.15).

2,4,6-trinitrochlorobenzene turns into 2,4,6-trinitrophenol (picric acid) when water is added and warmed.

(b) Electrophilic substitution reaction

(1) Halogens as substituents

Typical reactions of aromatic halides are aromatic electrophilic substitution. When compared with aromatic electrophilic substitution of benzene, as is the case with toluene,
the following two points are to be discussed.

(i) Are aryl halides more reactive than benzene?
(ii) In which position will the second substituent be introduced?

The answer to question (i) may be obtained from the result of toluene. Halogens have +R and −I effects to benzene. If the latter is superior, the electron density of benzene ring is as a whole increased, aryl halides are more susceptible to electrophilic substitution.

Since nitration of chlorobenzene requires a little more severe reaction condition as compared with that of benzene, the reactivity of aryl halides is lower than that of benzene. Since the effect of deceasing electron density due to the electron withdrawing effect of halogens, the reactivity is decreased. Such substituents like halogens are called inactive substituents.

The answer to question (ii) is more easily predictable. When resonance effect is in action, the electron density of o- and p-positions are increased (but not for m-position), it is expected that the second substituent selectively enters into o- and p-positions. As the experimental results indicate (Figure 9.16), the prediction is confirmed.

### Figure 9.15 Nucleophilic substitution reaction of chlorobenzene

![Nucleophilic substitution reaction of chlorobenzene](image)

### Figure 9.16 Nitration of chlorobenzene

![Nitration of chlorobenzene](image)

### Point
Substituent effect of aromatic electrophilic substitution

Go in and out of electrons occur at o- or p-position.

- If the substituents are electron-donating, electron density increases.
- If the substituents are electron-withdrawing, electron density decreases.

I-effect: Depends on the type on substituents. The effect is larger if the substituents are closer.

R-effect: Effective only at o- or p-position. No direct effect at m-position.

The decreasing order of electron density

- Electron donating substituents: ortho, para > meta
(2) **Electronic effect and steric effect**

In case of nitration of chlorobenzene, suppose the reactivity of o- and p-positions are completely equal, statistically o-isomer is expected to be formed twice as much as that of p-isomer. The reverse is, however, the case.

The reason is that o-position suffers from the steric hindrance by chlorine atom, and as a result, NO$_2^+$ is difficult to approach to the site.

When organic reactions are discussed, not only electronic effect (R-effect and I-effect) but also steric effect is to be considered simultaneously.

<table>
<thead>
<tr>
<th>Exercise 9.7 Nitration of chlorobenzene</th>
</tr>
</thead>
<tbody>
<tr>
<td>If nitration of chlorobenzene is carried out at higher temperature, it is anticipated that two or more than two nitro groups will be introduced to benzene ring. Predict the structure of the products.</td>
</tr>
</tbody>
</table>

**Answer**

Since chlorine atom is an o,p-directing group, much the same result will be expected as that of toluene.

![Image of nitrobenzene isomers]

(3) **Grignard reagent**

Aryl halides, such as chlorobenzene or bromobenzene, are readily obtainable from benzene, and these can be good starting material of a variety of organic compounds.

When bromobenzene is reacted with magnesium (as powder or flake) in diethyl ether, phenylmanesium bromide, in which magnesium atom inserts between carbon atom and magnesium atom, is obtained (Figure 9.17).

![Image of Grignard reaction]

**Figure 9.17** An example of Grignard reaction

Phenylmagnesium bromide is a kind of organometallic compounds in which carbon-metal bonds are incorporated. This type of organometallic compounds is named Grignard reagent after the name of the inventor, F. V. A. Grignard. Reactions in which Grignard reagents are participating are named **Grignard reactions**, and these are widely used in organic synthesis (details are given in Ch11.4 (h)).

In the above example, Grignard reagent and carbon dioxide reacts to give benzoic acid by the hydrolysis of the product. It is very difficult to introduce directly a carboxy
group into a benzene ring except rather special cases such as Kolbe-Schmitt reaction (Ch 10.3). Thus, this method is now accepted as the standard procedure to obtain aromatic carboxylic acid.

**Problems**

9.1 Give names to the following compounds.

9.2 Draw the structural formulas of the following compounds.

(a) 2,3-dichloro-4-methylhexane
(b) 2-chloro-4-iodoheptanne
(c) chlorocyclohexane
(d) 1-bromo-3,5-dimethylbenzene
(e) 2-fluoronaphthalene

9.3 Complete the following equations.

(a) \((\text{CH}_3)_2\text{CHI} + \text{KCN} \rightarrow ?\)
(b) \((\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{Cl} + \text{CH}_3\text{CH}_2\text{ONa} \rightarrow ?\)
(c) \(\text{CH}_3\text{COONa} + \text{CH}_3\text{CH}_2\text{I} \rightarrow ?\)

9.4 Draw the perceptive view of the following reaction intermediates or transition states. If possible, explain the hybridization states of carbon atoms.

(a) \((\text{CH}_3)_3\text{C}^+\)
(b) \((\text{CH}_3)_2\text{C}^-\)
(c) Transition state of the reaction \(\text{CH}_3\text{CH}_2\text{Br} + \text{KOH} \rightarrow \text{CH}_3\text{CH}_2\text{OH} + \text{KBr}\)

9.5 When each of the following compounds is heated with KOH in ethanol, alkenes are formed.

(a) Give names to each compound.
(b) Draw the structural formulas of all alkenes which may possibly be formed.
(c) Indicate the alkene that is formed in the largest amount. Explain the reason why.

**Answers**

9.1
(a) 3-bromo-3,5-dimethylhexane
(b) 2,4-dichloro-2,4-dimethylpentane
(c) 1-iodopentane (pentyl iodide)
(d) $p$-fluoroethylbenzene
(e) 4-bromo-2-chlorotoluene

9.2
(a) \[
\text{CH}_3\text{CH}_2\text{CH} - \text{CHCHCH}_3
\]
(b) \[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CHCHCH}_3
\]
(c) \[
\text{H}\text{Cl}
\]
(d) \[
\text{Br}
\]
(e) \[
\text{Fl}
\]

9.3
(a) (CH$_3$)$_2$CH + KCN →(CH$_3$)$_2$CN + KI
(b) (CH$_3$)$_2$CHCH$_2$Cl + CH$_3$CH$_2$Oc →(CH$_3$)$_2$CHCH$_2$CH$_2$OCH$_2$CH$_3$ + NaCl
(c) CH$_3$COONa + CH$_3$CH$_2$I → CH$_3$COOCH$_2$CH$_3$ + NaI

9.4
(a) \[
\text{CH}_3\text{CH}_2\text{CH} - \text{CHCHCH}_3
\]
(b) \[
\text{CH}_3\text{CH}_2\text{CH} - \text{CHCHCH}_3
\]
(c) \[
\text{CH}_3\text{OH}^+ + \text{C}_2\text{H}_5^+ \rightarrow \text{CH}_3\text{O}^-
\]

9.5
(1)
(a) 3-bromo-3,5-dimethylhexane
(b) 1-chloro-1,2-dimethylcyclohexane
(2)
(a) \[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + \text{OH}^- \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + \text{H}_2\text{O}
\]
(b) \[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + \text{OH}^- \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 + \text{H}_2\text{O}
\]
(3)
(a3) and (b3). Both do not have hydrogen atoms directly bonded to the double bonds.