4.8
Preparation of Alkyl Halides from Alcohols and Hydrogen Halides

$$\text{ROH} + \text{HX} \rightarrow \text{RX} + \text{H}_2\text{O}$$
Reaction of Alcohols with Hydrogen Halides

ROH + HX → RX + HOH

Hydrogen halide reactivity

HI  HBr  HCl  HF

most reactive  least reactive
**Reaction of Alcohols with Hydrogen Halides**

$$\text{ROH} + \text{HX} \rightarrow \text{RX} + \text{HOH}$$

**Alcohol Reactivity**

- $R_3\text{COH}$ (Tertiary)
- $R_2\text{CHOH}$ (Secondary)
- $R\text{CH}_2\text{OH}$ (Primary)
- $\text{CH}_3\text{OH}$ (Methanol)

*most reactive*  
*least reactive*
Preparation of Alkyl Halides

\[
\text{(CH}_3\text{)}_3\text{COH} + \text{HCl} \xrightarrow{25^\circ C} \text{(CH}_3\text{)}_3\text{CCl} + \text{H}_2\text{O} \quad 78\text{-}88\%
\]

\[
\text{CH}_3\text{(CH}_2\text{)}_5\text{CH}_2\text{OH} + \text{HBr} \xrightarrow{120^\circ C} \text{CH}_3\text{(CH}_2\text{)}_5\text{CH}_2\text{Br} + \text{H}_2\text{O} \quad 87\text{-}90\%
\]

\[
\text{CH}_3\text{(CH}_2\text{)}_5\text{CH}_2\text{OH} + \text{HBr} \xrightarrow{80\text{-}100^\circ C} \text{CH}_3\text{(CH}_2\text{)}_5\text{CH}_2\text{Br} + \text{H}_2\text{O} \quad 73\%
\]
A mixture of sodium bromide and sulfuric acid may be used in place of HBr.

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH} \xrightarrow{\text{H}_2\text{SO}_4, \text{heat}} \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} \quad 70-83\% 
\]

Preparation of Alkyl Halides
4.9 Mechanism of the Reaction of Alcohols with Hydrogen Halides
The key intermediate in reaction of secondary and tertiary alcohols with hydrogen halides is a carbocation.

A carbocation is a cation in which carbon has 6 valence electrons and a positive charge.
Carbocation

The key intermediate in reaction of secondary and tertiary alcohols with hydrogen halides is a carbocation.

The overall reaction mechanism involves three elementary steps; the first two steps lead to the carbocation intermediate, the third step is the conversion of this carbocation to the alkyl halide.
Example

\[
(\text{CH}_3)_3\text{COH} + \text{HCl} \quad \xrightarrow{25^\circ C} \quad (\text{CH}_3)_3\text{CCl} + \text{H}_2\text{O}
\]

*tert*-Butyl alcohol

*tert*-Butyl chloride

**Carbocation intermediate is:**

\[
\begin{array}{c}
\text{H}_3\text{C} \\
\text{C} \\
\text{CH}_3 \\
\text{CH}_3
\end{array}
\]

*tert*-Butyl cation
Step 1: Proton transfer from HCl to tert-butyl alcohol

\[
(CH_3)_3C\overset{\ddot{\text{O}}:}{\text{O}} + H\overset{\ddot{\text{Cl}}:}{\text{Cl}} \rightarrow \text{fast, bimolecular}
\]

\[
(CH_3)_3C\overset{\ddot{\text{O}}:}{\text{O}} + :\overset{\ddot{\text{Cl}}:}{\text{Cl}} \rightarrow \text{tert-Butyloxoonium ion}
\]
Step 2: Dissociation of tert-butyloxonium ion

\[
\text{H} \quad \quad \quad + \quad \quad \quad \text{O}: \\
\quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \ quad
Step 3: Capture of tert-butyl cation by chloride ion.

\[(\text{CH}_3)_3\text{C}^+ + \text{Cl}^- \rightarrow (\text{CH}_3)_3\text{C}^\text{Cl}\]\n
fast, bimolecular

\[\text{tert-Butyl chloride}\]
4.10
Structure, Bonding, and Stability of Carbocations
Carbon is $sp^2$ hybridized.
All four atoms lie in same plane.
Figure 4.8  Structure of methyl cation.

Empty 2p orbital.
Axis of 2p orbital is perpendicular to plane of atoms.
Most carbocations are too unstable to be isolated.

When R is an alkyl group, the carbocation is stabilized compared to R = H.
**Carbocations**

\[
\begin{array}{c}
\text{H} \\
\text{C} \\
\text{H} \\
\end{array}
\]

Methyl cation

least stable
Carbocations

Ethyl cation
(a primary carbocation)
is more stable than $\text{CH}_3^+$
Isopropyl cation
(a secondary carbocation)
is more stable than CH$_3$CH$_2^+$
Carbocations

tert-Butyl cation
(a tertiary carbocation)
is more stable than \((\text{CH}_3)_2\text{CH}^+\)
Figure 4.9 Stabilization of carbocations via the inductive effect

positively charged carbon pulls electrons in σ bonds closer to itself
Figure 4.9 Stabilization of carbocations via the inductive effect

positive charge is "dispersed", i.e., shared by carbon and the three atoms attached to it.
Figure 4.9 Stabilization of carbocations via the inductive effect

Electrons in C—C bonds are more polarizable than those in C—H bonds; therefore, alkyl groups stabilize carbocations better than H.

Electronic effects transmitted through σ bonds are called "inductive effects."
Figure 4.10 Stabilization of carbocations via hyperconjugation

Electrons in this $\sigma$ bond can be shared by positively charged carbon because the $s$ orbital can overlap with the empty $2p$ orbital of positively charged carbon.
electrons in this $\sigma$ bond can be shared by positively charged carbon because the $s$ orbital can overlap with the empty $2p$ orbital of positively charged carbon.
Figure 4.10 Stabilization of carbocations via hyperconjugation

Notice that an occupied orbital of this type is available when sp$^3$ hybridized carbon is attached to C$^+$, but is not available when H is attached to C$^+$. Therefore, alkyl groups stabilize carbocations better than H does.
Carbocations

The more stable a carbocation is, the faster it is formed.

Reactions involving tertiary carbocations occur at faster rates than those proceeding via secondary carbocations. Reactions involving primary carbocations or $\text{CH}_3^+$ are rare.
Carbocations are **Lewis acids** (electron-pair acceptors).

Carbocations are **electrophiles** (electron-seekers).

**Lewis bases** (electron-pair donors) exhibit just the opposite behavior. **Lewis bases** are **nucleophiles** (nucleus-seekers).
Step 3: Capture of tert-butyl cation by chloride ion.

\[(\text{CH}_3)_3\text{C}^+ + \cdot\cdot\cdot\text{Cl}^- \rightarrow (\text{CH}_3)_3\text{C}^-\cdot\cdot\cdot\text{Cl}^:\]

fast, bimolecular

*tert*-Butyl chloride
The last step in the mechanism of the reaction of tert-butyl alcohol with hydrogen chloride is the reaction between an electrophile and a nucleophile. 

*tert*-Butyl cation is the electrophile. Chloride ion is the nucleophile.
**Fig. 4.11** Combination of tert-butyl cation and chloride ion to give tert-butyl chloride.
4.11
Potential Energy Diagrams for Multistep Reactions:
The S_N1 Mechanism
Recall...

the potential energy diagram for proton transfer from HBr to water

Potential energy

Reaction coordinate

\[ \text{H}_2\text{O} + \text{H–Br} \rightarrow \text{H}_2\text{O–H} + \text{Br}^- \]
The potential energy diagram for a multistep mechanism is simply a collection of the potential energy diagrams for the individual steps.

Consider the mechanism for the reaction of \( \text{tert}-\text{butyl alcohol with HCl} \).

\[
(CH_3)_3COH + HCl \xrightarrow{25^\circ C} (CH_3)_3CCl + H_2O
\]
Mechanism

Step 1: Proton transfer from HCl to tert-butyloxonium ion

\[
(CH_3)_3C\overset{\ddots}{O}^- + H\overset{\ddots}{Cl}^-
\]

\[
\downarrow\text{fast, bimolecular}
\]

\[
(CH_3)_3C\overset{\ddots}{O}^- + :\overset{\ddots}{Cl}^-
\]

tert-butyloxonium ion
Step 2: Dissociation of \textit{tert}-butyloxoionium ion

\[
\begin{align*}
\text{(CH}_3\text{)}_3\text{C}^+ + \text{O}: &\quad \rightarrow \quad \text{(CH}_3\text{)}_3\text{C}^+ + \text{H} + \text{H} \\
\text{slow, unimolecular} &\quad \rightarrow \quad \text{tert-Butyl cation} + \text{H} + \text{H}
\end{align*}
\]
Step 3: Capture of *tert*-butyl cation by chloride ion.

\[(\text{CH}_3)_3\text{C}^+ + \text{Cl}^- \rightarrow (\text{CH}_3)_3\text{C}^-\text{Cl}^-\]

*tert*-Butyl chloride
proton transfer

carbocation formation

+ carbocation capture

ROH

ROH

ROH$_2$

R$^+$

RX
carbocation formation

\[
\text{(CH}_3\text{)}_3\text{C}^\delta+\text{O}^\delta-\text{H}^\delta+\text{Cl}^\delta-
\]

\begin{align*}
\text{ROH} + \text{ROH}_2 & \rightarrow \text{RX} \\
\end{align*}
proton transfer

(carbocation capture)

(proton transfer)

ROH

+ ROH$_2$

R$^+$

RX
proton transfer

carbocation formation

ROH

+ ROH₂

R⁺

RX

(CH₃)₃C

Cl

δ⁺

δ⁻
The mechanism just described is an example of an $S_{N1}$ process.

$S_{N1}$ stands for substitution-nucleophilic-unimolecular.

The molecularity of the rate-determining step defines the molecularity of the overall reaction.
The molecularity of the rate-determining step defines the molecularity of the overall reaction.

Mechanistic notation

Rate-determining step is unimolecular dissociation of alkyloxonium ion.
4.12
Effect of Alcohol Structure on Reaction Rate
The more stable the carbocation, the faster it is formed.

Tertiary carbocations are more stable than secondary, which are more stable than primary, which are more stable than methyl.

Tertiary alcohols react faster than secondary, which react faster than primary, which react faster than methanol.
Hammond's Postulate

If two succeeding states (such as a transition state and an unstable intermediate) are similar in energy, they are similar in structure.

Hammond's postulate permits us to infer the structure of something we can't study (transition state) from something we can study (reactive intermediate).
proton transfer

carbocation formation

carbocation capture

ROH

ROH₂

RX
Proton transfer reaction.

Carbocation formation.

Rate is governed by energy of this transition state.

Infer structure of this transition state from structure of state of closest energy; in this case the nearest state is the carbocation.
4.13
Reaction of Primary Alcohols with Hydrogen Halides.
The $S_{N2}$ Mechanism
Preparation of Alkyl Halides

\[ (\text{CH}_3)_3\text{COH} + \text{HCl} \rightarrow (\text{CH}_3)_3\text{CCl} + \text{H}_2\text{O} \]

- 78-88% yield at 25°C

\[ \text{Cyclohexanol} + \text{HBr} \rightarrow \text{Cyclohexyl bromide} + \text{H}_2\text{O} \]

- 73% yield at 80-100°C

\[ \text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{OH} + \text{HBr} \rightarrow \text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{Br} + \text{H}_2\text{O} \]

- 87-90% yield at 120°C
Primary carbocations are too high in energy to allow $S_N1$ mechanism. Yet, primary alcohols are converted to alkyl halides.

Primary alcohols react by a mechanism called $S_N2$ (substitution-nucleophilic-bimolecular).

$$\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{OH} + \text{HBr} \xrightarrow{120^\circ C} \text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{Br} + \text{H}_2\text{O}$$

87-90%
Two-step mechanism for conversion of alcohols to alkyl halides:

1. Proton transfer to alcohol to form alkyloxonium ion
2. Bimolecular displacement of water from alkyloxonium ion by halide
Example

\[
\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{OH} + \text{HBr} \xrightarrow{120^\circ \text{C}} \text{H}_2\text{O} \\
\text{CH}_3(\text{CH}_2)_5\text{CH}_2\text{Br} + \text{H}_2\text{O}
\]
Step 1: Proton transfer from HBr to 1-heptanol

\[
\text{CH}_3(\text{CH}_2)_5\text{CH}_2\overset{\text{O}:}{\sim} + \text{H} \overset{\text{Br}:}{\sim} \rightarrow \text{CH}_3(\text{CH}_2)_5\text{CH}_2\overset{\text{O}:}{\sim} + \text{H} \overset{\text{Br}:}{\sim}
\]

Heptyloxonium ion
Step 2: Reaction of alkyloxonium ion with bromide ion.

\[ \text{H} \quad :\text{Br}^- \quad + \quad \text{CH}_3\text{(CH}_2\text{)}_5\text{CH}_2\text{O}^+ \quad \rightarrow \quad \text{CH}_3\text{(CH}_2\text{)}_5\text{CH}_2\text{Br}^- \quad + \quad :\text{O}^- \]

1-Bromoheptane

slow, bimolecular
proton transfer

ROH

CH$_3$(CH$_2$)$_4$CH$_2$

ROH$_2$

RX
4.14
Other Methods for Converting Alcohols to Alkyl Halides
**Reagents for ROH to RX**

Thionyl chloride

\[
\text{SOCl}_2 + \text{ROH} \rightarrow \text{RCl} + \text{HCl} + \text{SO}_2
\]

Phosphorus tribromide

\[
\text{PBr}_3 + 3\text{ROH} \rightarrow 3\text{RBr} + \text{H}_3\text{PO}_3
\]
Examples

\[
\begin{align*}
\text{CH}_3\text{CH(CH}_2\text{)}_5\text{CH}_3 & \xrightarrow{\text{SOCl}_2} \text{CH}_3\text{CH(CH}_2\text{)}_5\text{CH}_3 \\
& \xrightarrow{\text{K}_2\text{CO}_3} \text{Cl} \\
(\text{pyridine often used instead of } & \text{K}_2\text{CO}_3) \\
(\text{CH}_3)_2\text{CHCH}_2\text{OH} & \xrightarrow{\text{PBr}_3} (\text{CH}_3)_2\text{CHCH}_2\text{Br} \\
& \text{(55-60%)}
\end{align*}
\]