4.8
Preparation of Alkyl Halides from Alcohols and Hydrogen Halides

$$ROH \quad + \quad HX \quad \rightarrow \quad RX \quad + \quad H_2O$$

Reaction of Alcohols with Hydrogen Halides

$$ROH \; + \; HX \; \rightarrow \; RX \; + \; HOH$$

Hydrogen halide reactivity

HI   HBr   HCl   HF

most reactive   least reactive
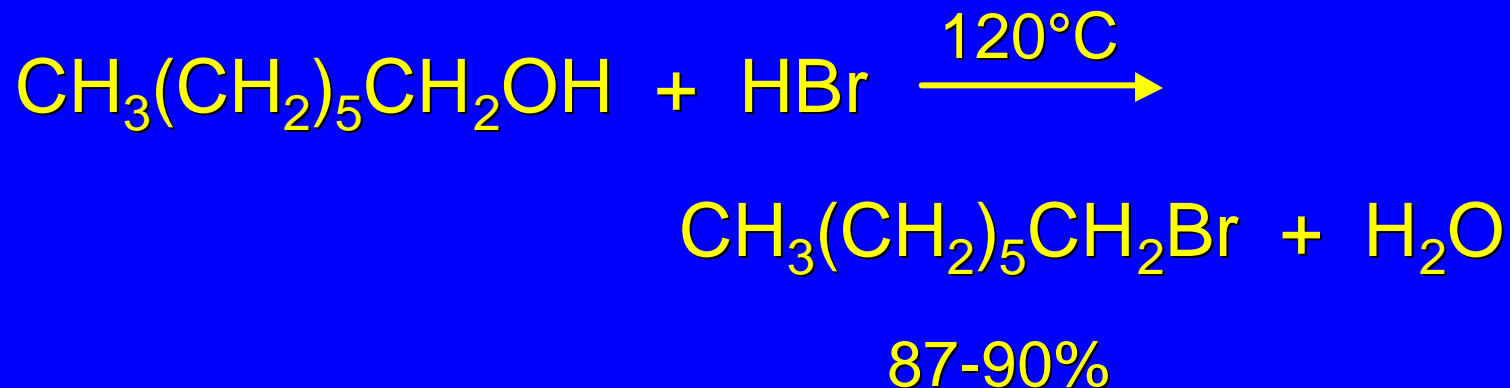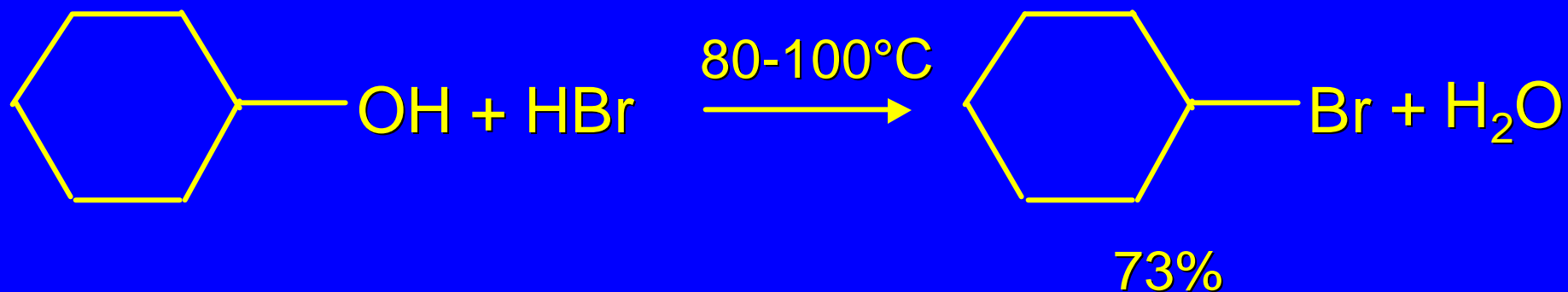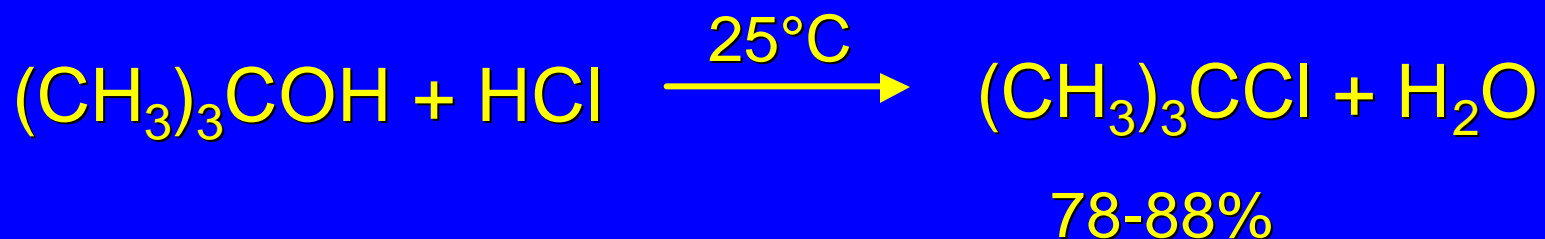
Reaction of Alcohols with Hydrogen Halides

$$ROH \ + \ HX \ \rightarrow \ RX \ + \ HOH$$

Alcohol reactivity

R_3COH	R_2CHOH	RCH_2OH	CH_3OH
Tertiary	Secondary	Primary	Methanol

most reactive   least reactive

Preparation of Alkyl Halides

$$(CH_3)_3COH + HCl \xrightarrow{25°C} (CH_3)_3CCl + H_2O$$

78-88%

$$80\text{-}100°C$$

73%

$$CH_3(CH_2)_5CH_2OH + HBr \xrightarrow{120°C}$$

$$CH_3(CH_2)_5CH_2Br + H_2O$$

87-90%

Preparation of Alkyl Halides

A mixture of sodium bromide and sulfuric acid may be used in place of HBr.

$$CH_3CH_2CH_2CH_2OH \xrightarrow[\text{heat}]{\substack{\text{NaBr}\\ \text{H}_2\text{SO}_4}} CH_3CH_2CH_2CH_2Br$$

70-83%
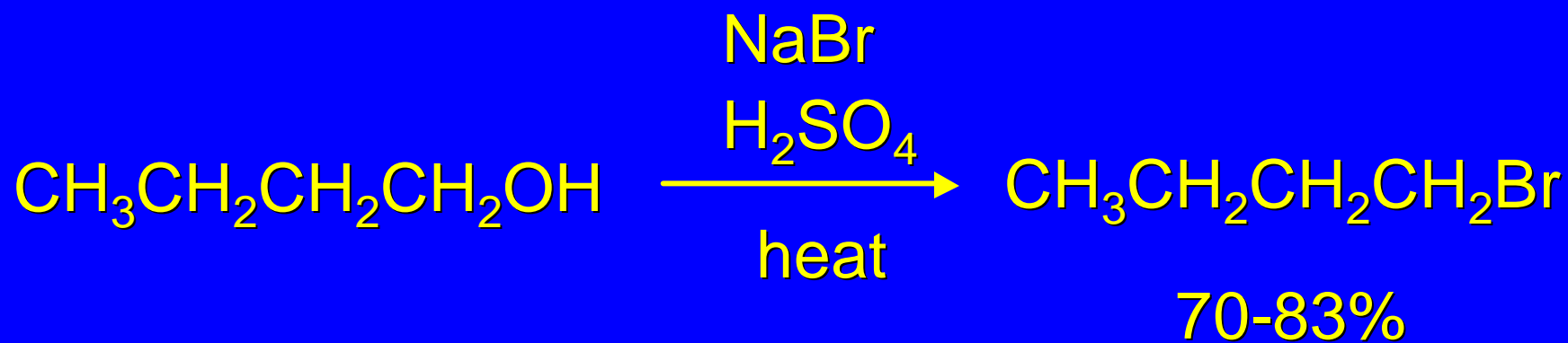
4.9
Mechanism of the Reaction of Alcohols with Hydrogen Halides

Carbocation
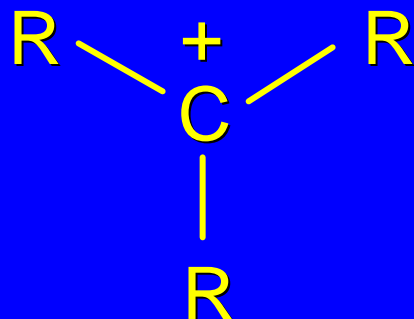
$$
\begin{array}{ccc}
R & + & R \\
 & \diagdown\ \diagup & \\
 & C & \\
 & | & \\
 & R &
\end{array}
$$

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
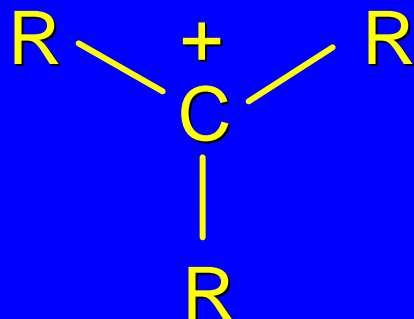
$$R \diagdown \overset{+}{\underset{\underset{R}{|}}{C}} \diagup R$$

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.

$$(CH_3)_3COH + HCl \xrightarrow{25°C} (CH_3)_3CCl + H_2O$$

tert-Butyl alcohol   *tert*-Butyl chloride

Carbocation intermediate is:

$$H_3C \diagdown \overset{+}{\underset{|}{C}} \diagup CH_3$$
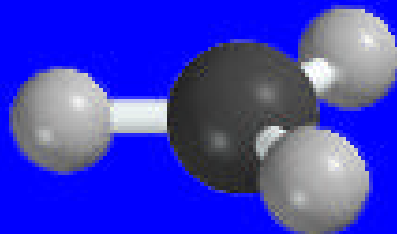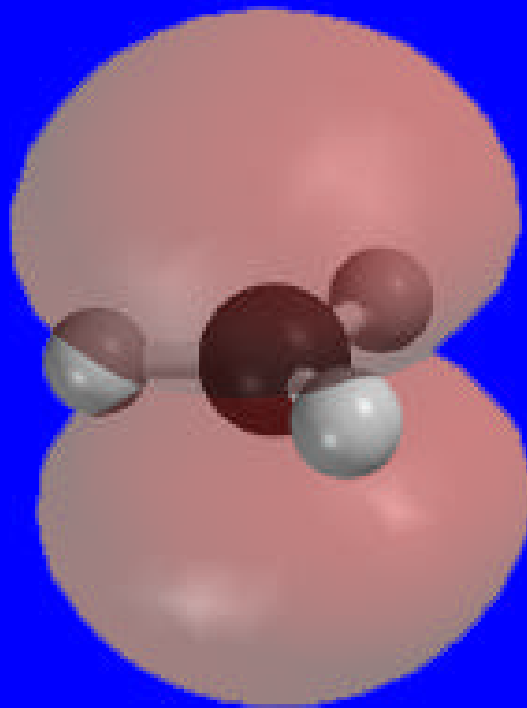$$CH_3$$
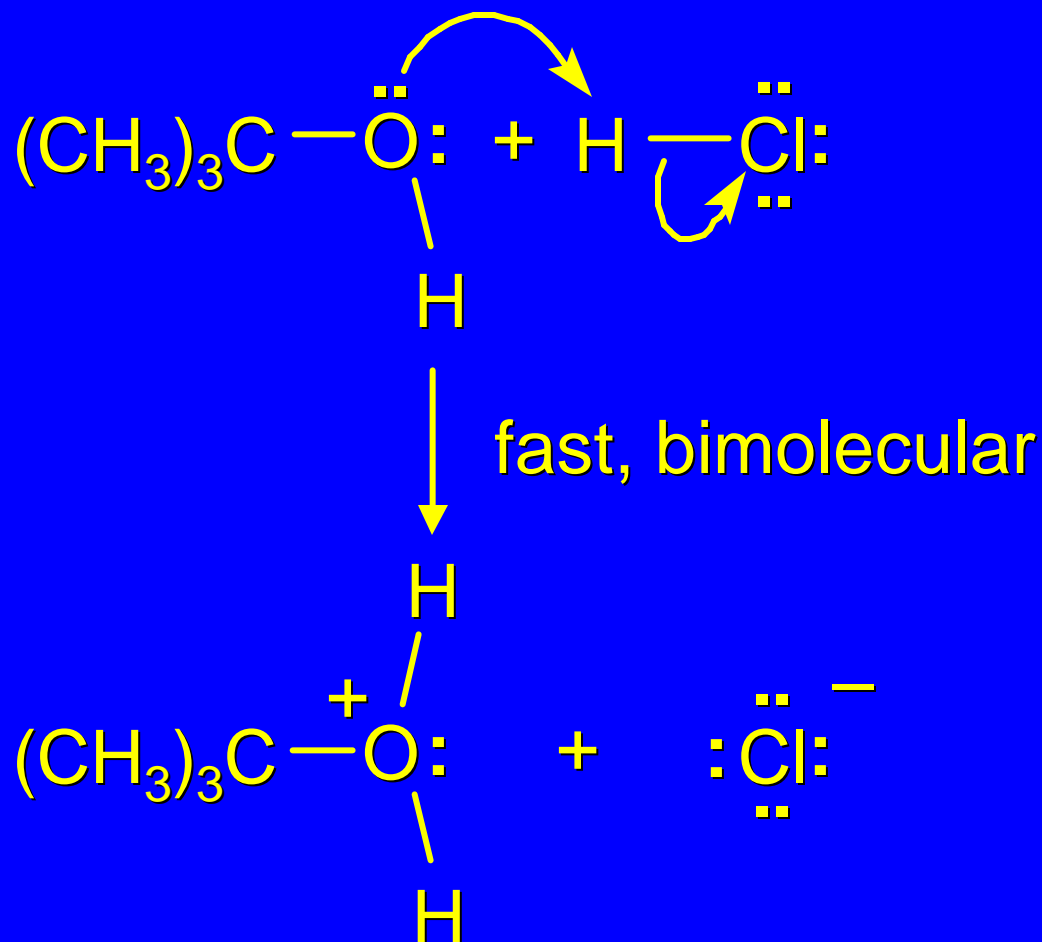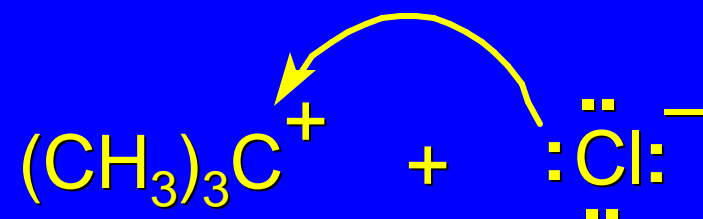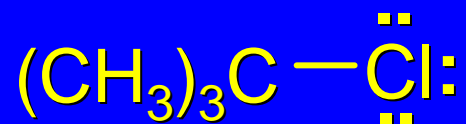
tert-Butyl cation

4.10
Structure, Bonding, and Stability of Carbocations

Figure 4.8 Structure of methyl cation.

Carbon is *sp²* hybridized.
All four atoms lie in same plane.
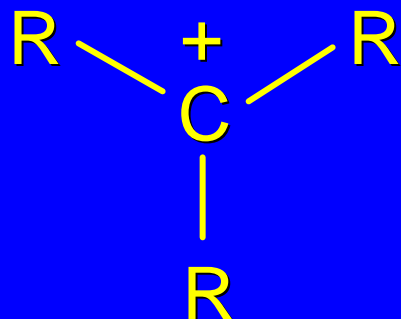
Figure 4.8 Structure of methyl cation.

Empty 2*p* orbital.

Axis of 2*p* orbital is perpendicular to plane of atoms.
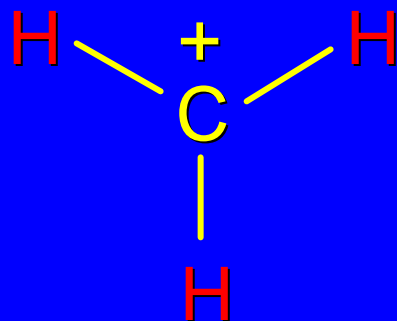
Carbocations

$$R \diagdown \overset{\textstyle +}{\underset{\textstyle |}{C}} \diagup R$$

$$R$$

Most carbocations are too unstable to be isolated.

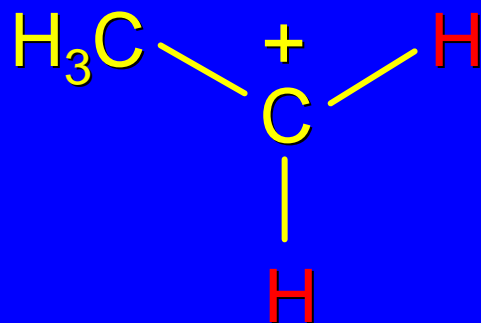When R is an alkyl group, the carbocation is stabilized compared to R = H.
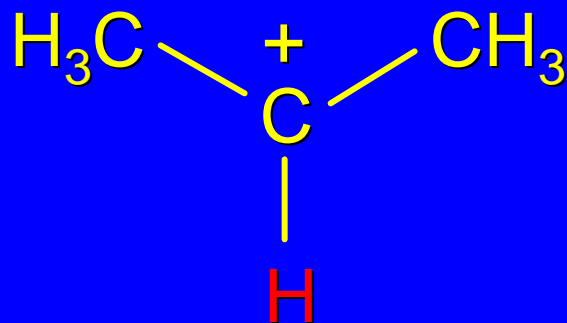
Carbocations

Methyl cation
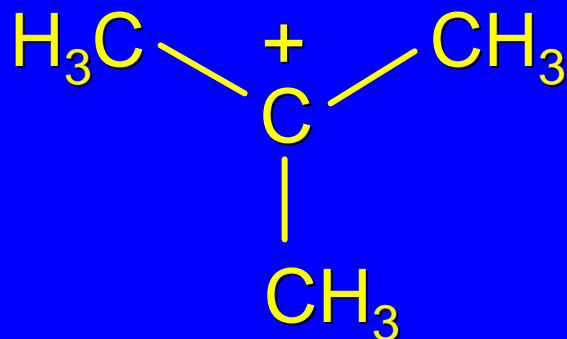
least stable

Carbocations

$$H_3C \diagdown \overset{+}{\underset{|}{C}} \diagup H$$

H

Ethyl cation
(a primary carbocation)
is more stable than CH_3^+

Carbocations

$$H_3C \diagdown \quad \overset{+}{\underset{\displaystyle C}{}} \quad \diagup CH_3$$

$$\underset{\displaystyle H}{\big|}$$

Isopropyl cation
(a secondary carbocation)
is more stable than $CH_3CH_2^+$

Carbocations
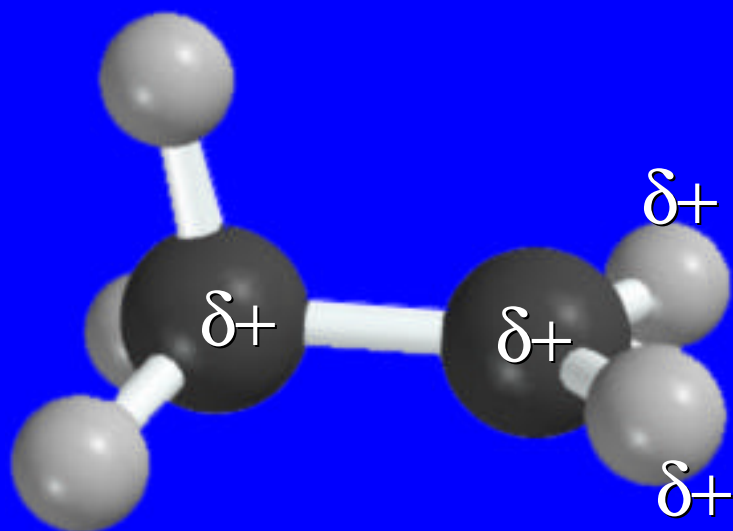
$$H_3C \diagdown \overset{+}{\underset{|}{C}} \diagup CH_3$$
$$CH_3$$

tert-Butyl cation
(a tertiary carbocation)
is more stable than $(CH_3)_2CH^+$

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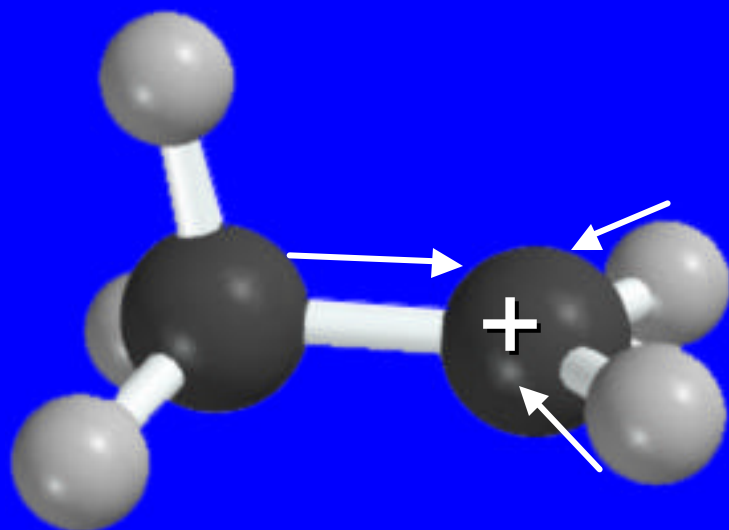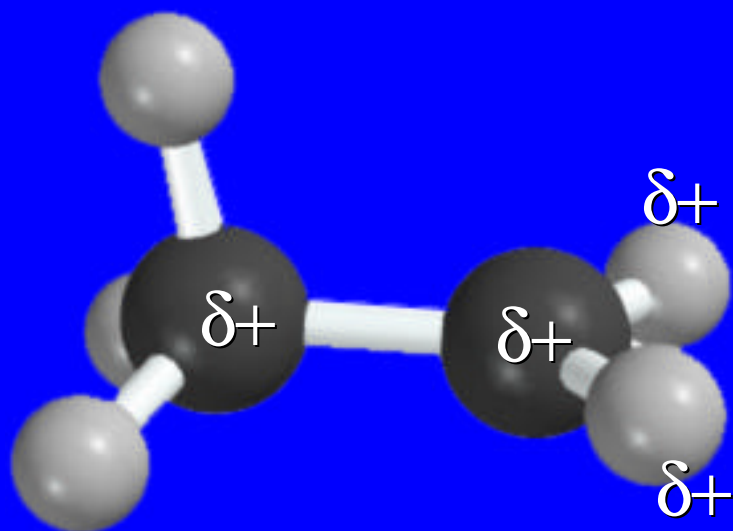
positively charged carbon pulls electrons in σ bonds closer to itself

Figure 4.9 Stabilization of carbocations via the inductive effect

$\delta+$

$\delta+$

$\delta+$

$\delta+$

$\delta+$

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.

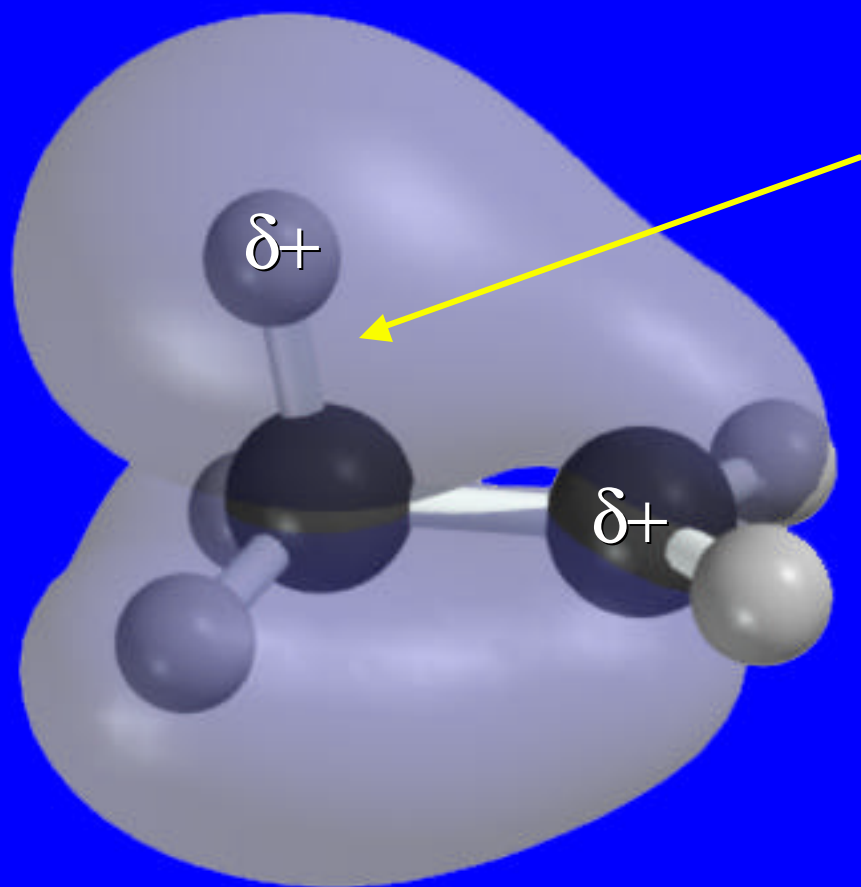Electronic effects transmitted through σ bonds are called "inductive effects."

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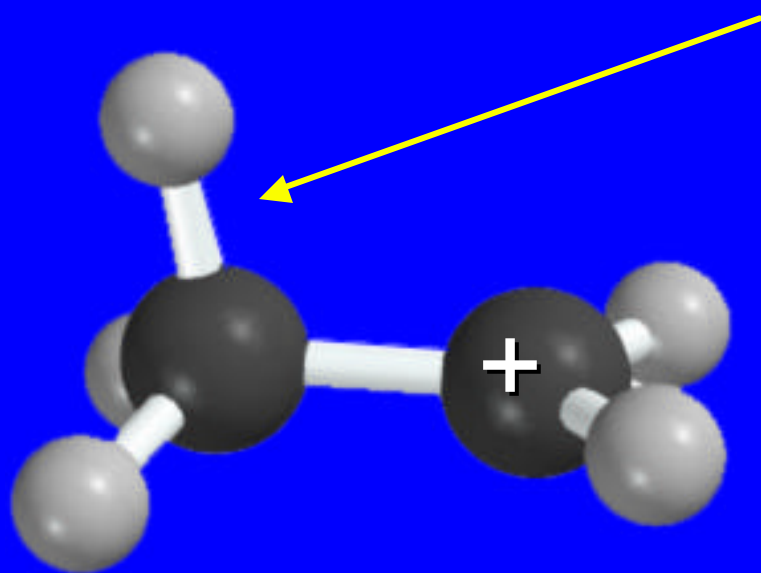
electrons in this σ bond can be shared by positively charged carbon because the s orbital can overlap with the empty 2p orbital of positively charged carbon

Figure 4.10 Stabilization of carbocations via hyperconjugation

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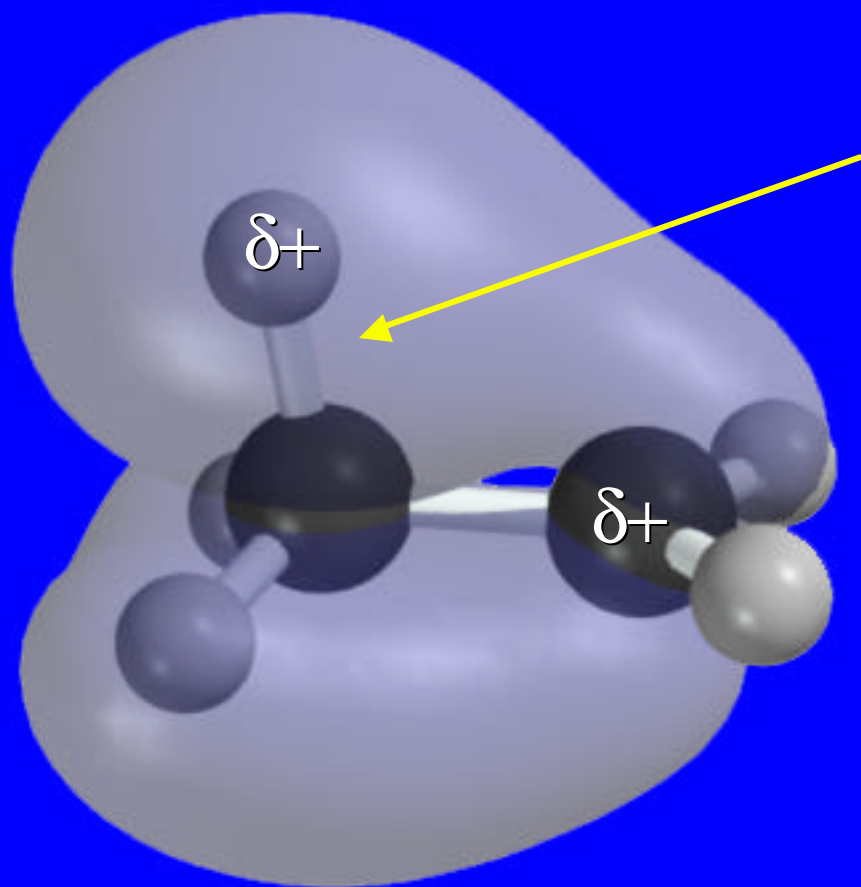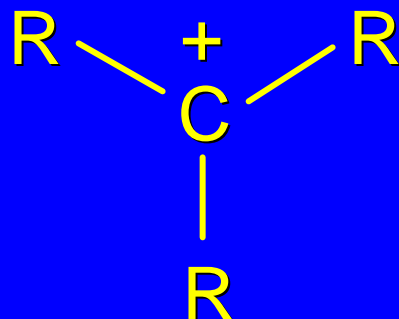
Figure 4.10 Stabilization of carbocations via hyperconjugation

δ+

δ+

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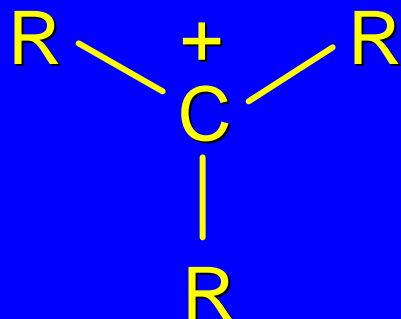
Carbocations

$$R - \overset{\displaystyle +}{\underset{\displaystyle |}{C}} - R$$
$$R$$

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 CH_3^+ are rare.
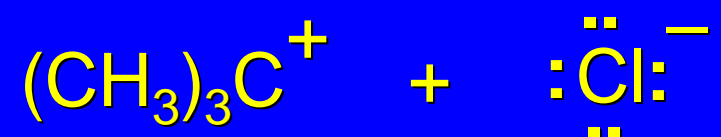
Carbocations

$$R \diagdown \overset{+}{\underset{\displaystyle R}{C}} \diagup R$$

Carbocations are <u>Lewis acids</u> (electron-pair acceptors).

Carbocations are <u>electrophiles</u> (electron-seekers).

<u>Lewis bases</u> (electron-pair donors) exhibit just the opposite behavior. Lewis bases are <u>nucleophiles</u> (nucleus-seekers).

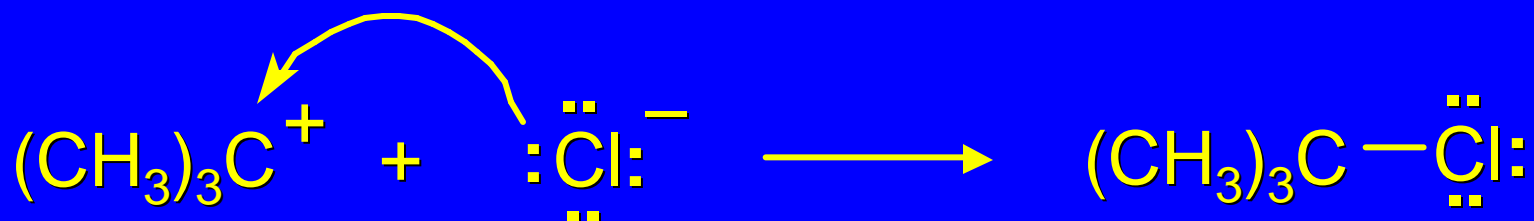**Step 3:** Capture of *tert*-butyl cation by chloride ion.

$$(CH_3)_3C^+ \quad + \quad :\overset{..}{\underset{..}{Cl}}:^-$$

fast, bimolecular

$$(CH_3)_3C \!-\! \overset{..}{\underset{..}{Cl}}:$$
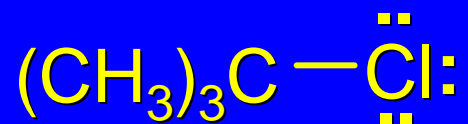
tert-Butyl chloride

Carbocations

$$(CH_3)_3C^+ \quad + \quad :\overset{..}{\underset{..}{Cl}}:^- \quad \longrightarrow \quad (CH_3)_3C-\overset{..}{\underset{..}{Cl}}:$$

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*

nucleophile
(Lewis base)

electrophile
(Lewis acid)
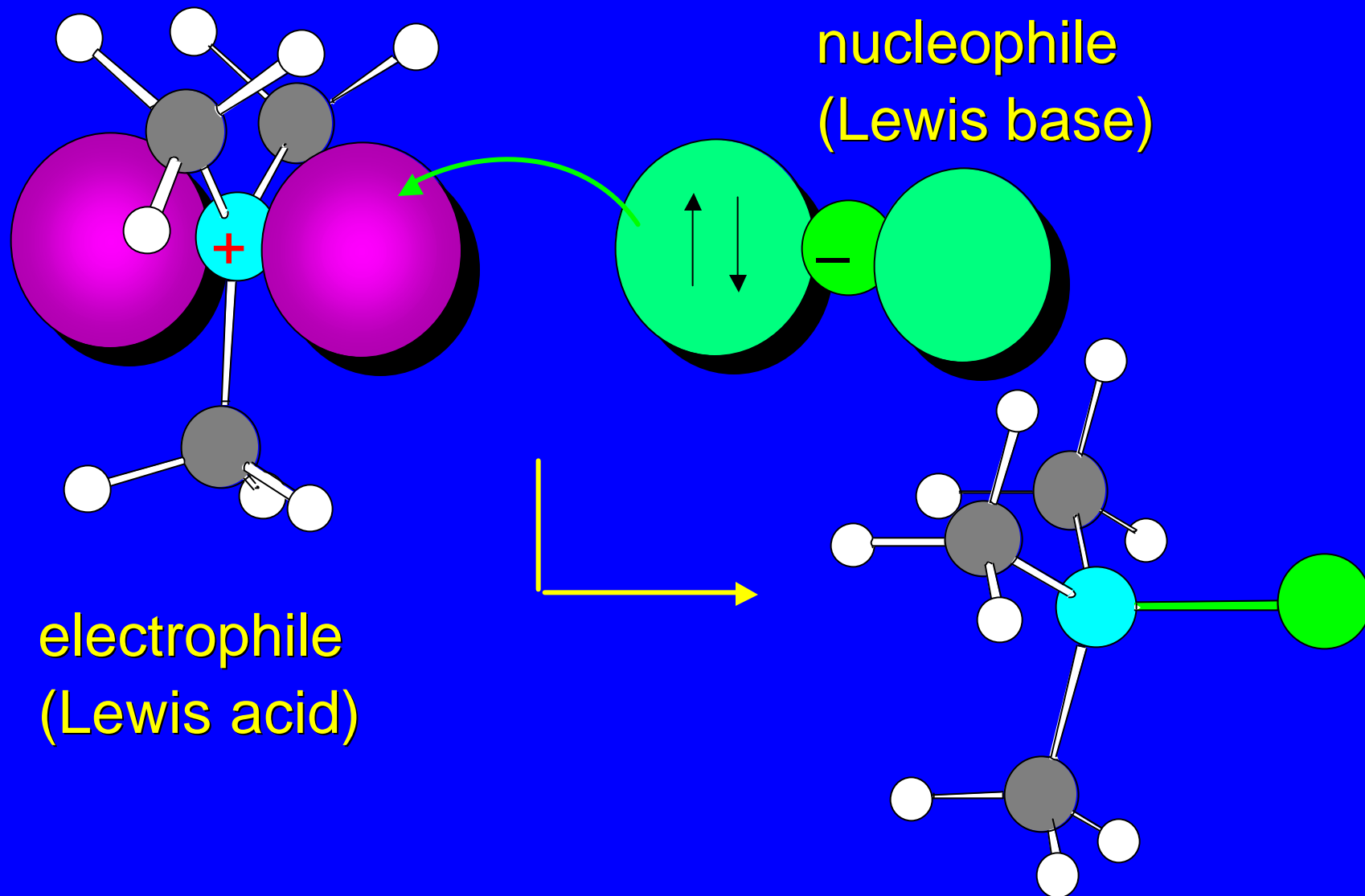
4.11
Potential Energy Diagrams for Multistep Reactions:
The S_N1 Mechanism

The potential energy diagram for a multistep mechanism is simply a collection of the potential energy diagrams for the individual steps.

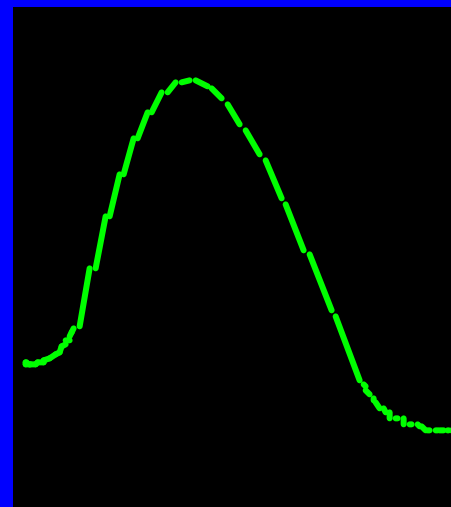Consider the mechanism for the reaction of *tert*-butyl alcohol with HCl.

$$(CH_3)_3COH + HCl \xrightarrow{25°C} (CH_3)_3CCl + H_2O$$

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

$(CH_3)_3C$—$\overset{..}{\underset{|}{O}}:$ + H—$\overset{..}{\underset{..}{Cl}}:$

        |
        H

↓ fast, bimolecular

        H
        |
$(CH_3)_3C$—$\overset{+}{O}:$ + $:\overset{..}{\underset{..}{Cl}}:^{-}$
        |
        H
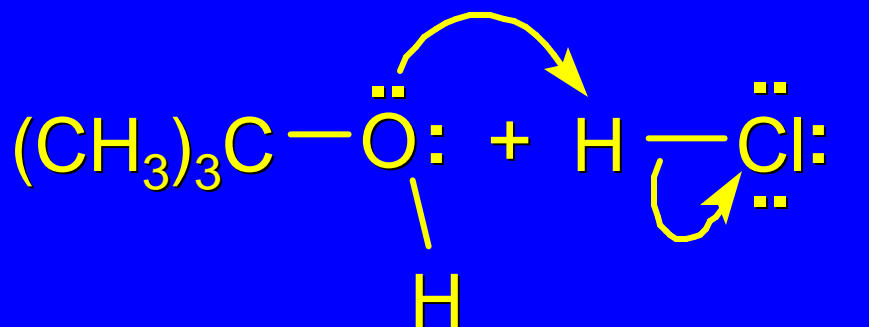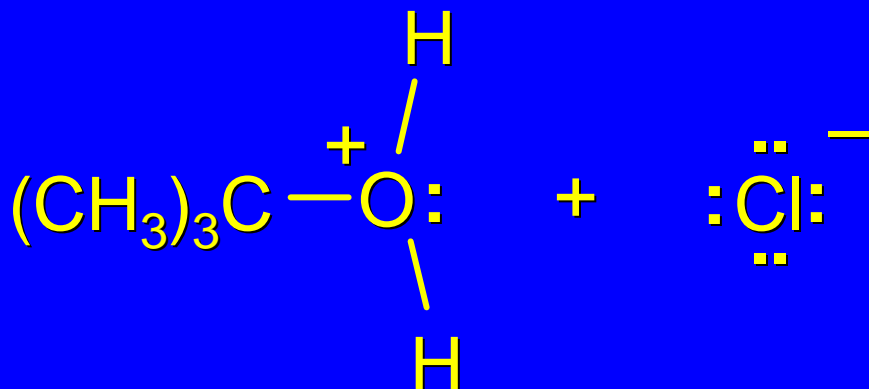
tert-butyloxonium ion

Step 2:   Dissociation of *tert*-butyloxonium ion
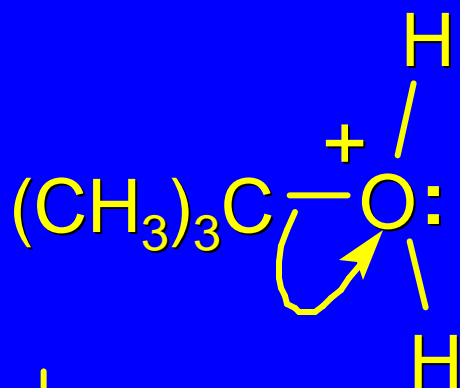
$$\text{(CH}_3)_3\text{C} \overset{+}{-} \text{O} \overset{H}{\underset{H}{:}}$$

↓   slow, unimolecular
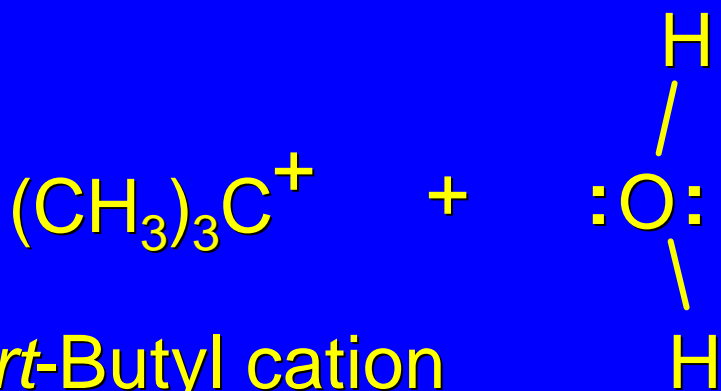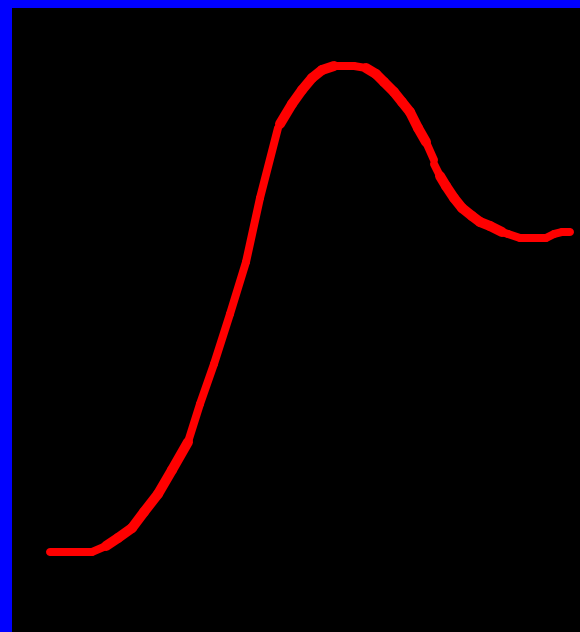
$$\text{(CH}_3)_3\text{C}^+ \quad + \quad :\overset{H}{\underset{H}{\text{O}}}:$$

tert-Butyl cation

Step 3: Capture of *tert*-butyl cation by chloride ion.

$(CH_3)_3C^+$ + $:\ddot{C}l:^-$

↓ fast, bimolecular

$(CH_3)_3C-\ddot{C}l:$
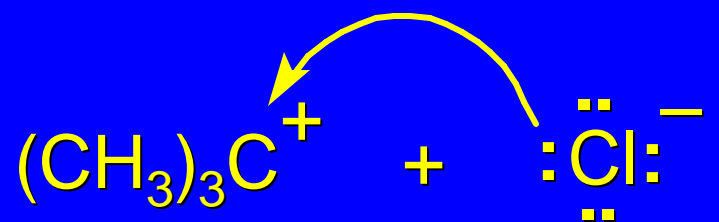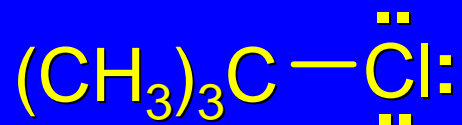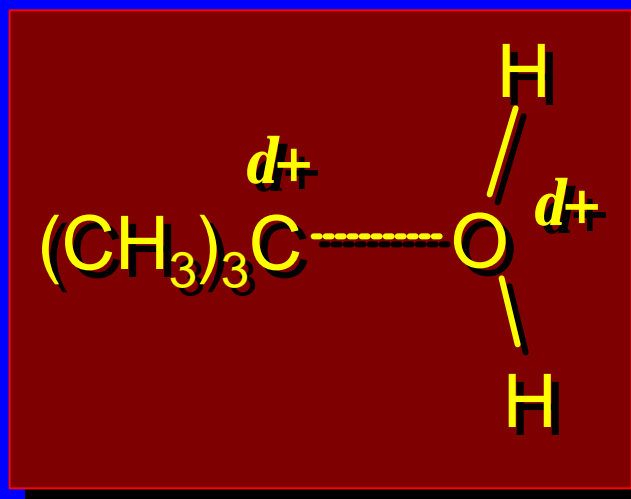
tert-Butyl chloride
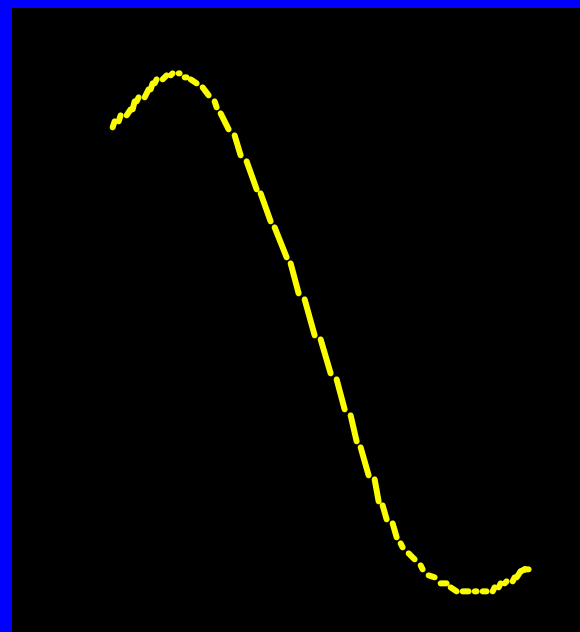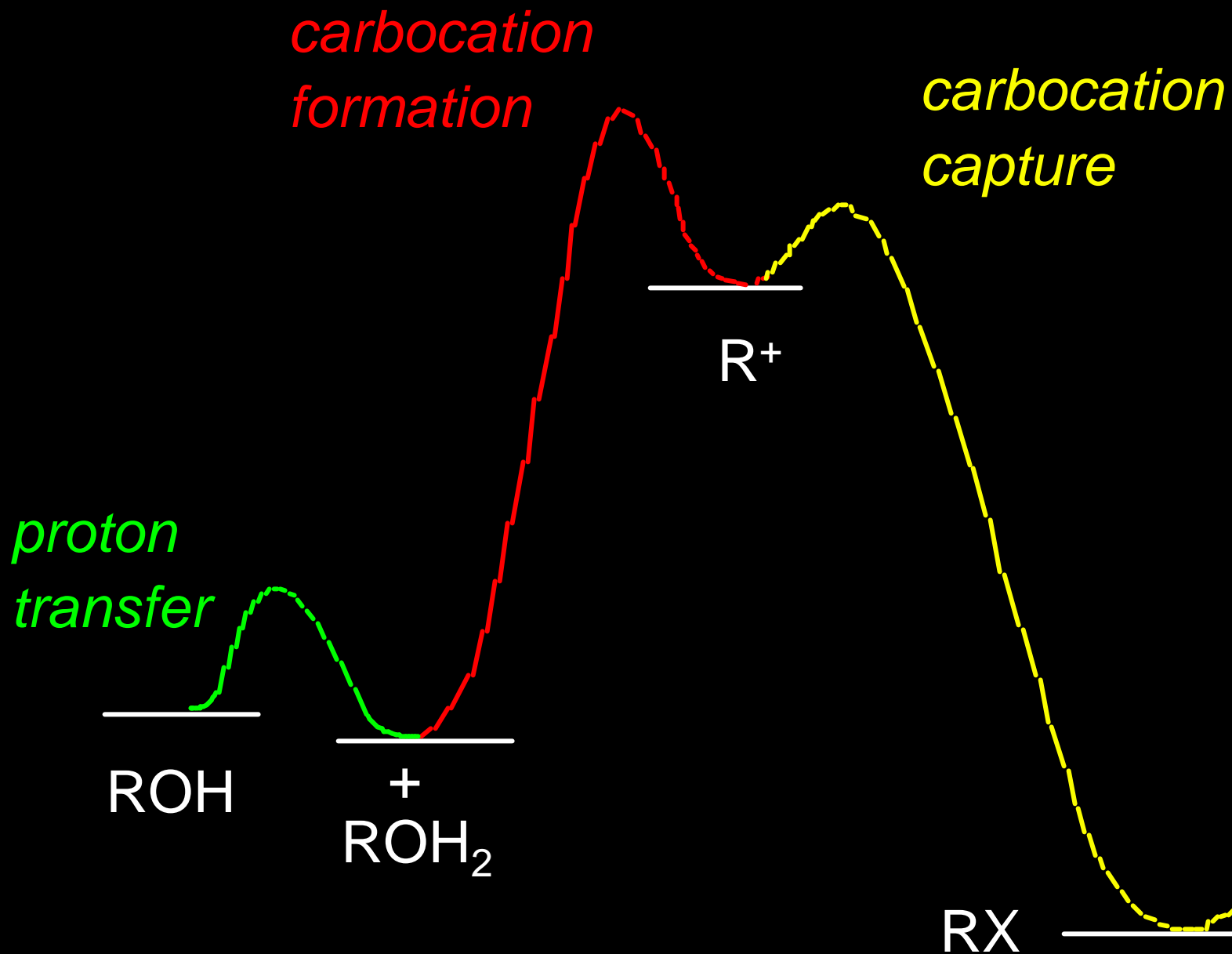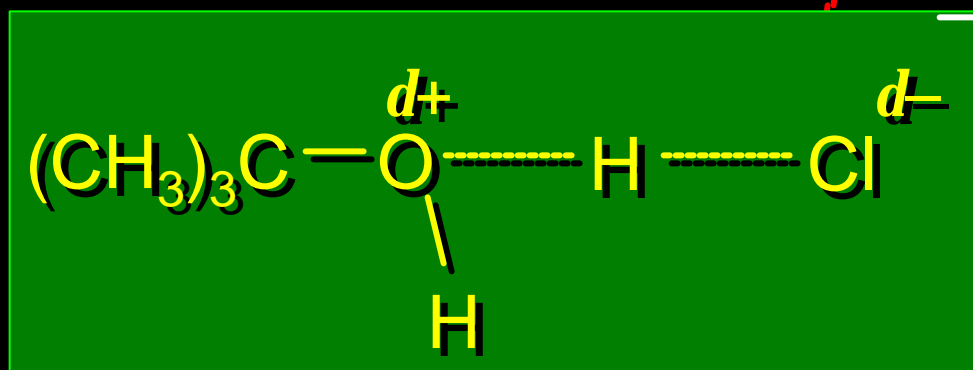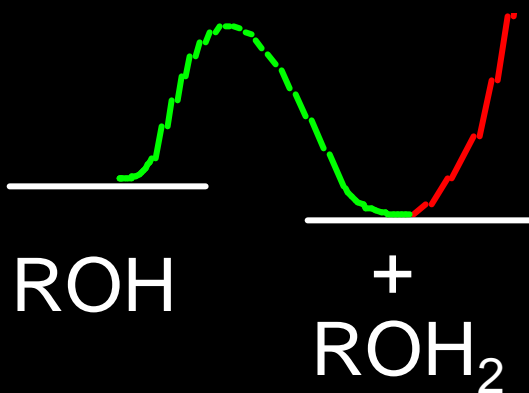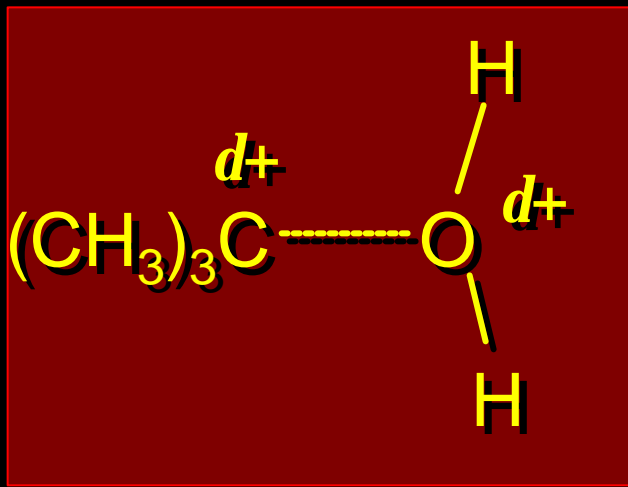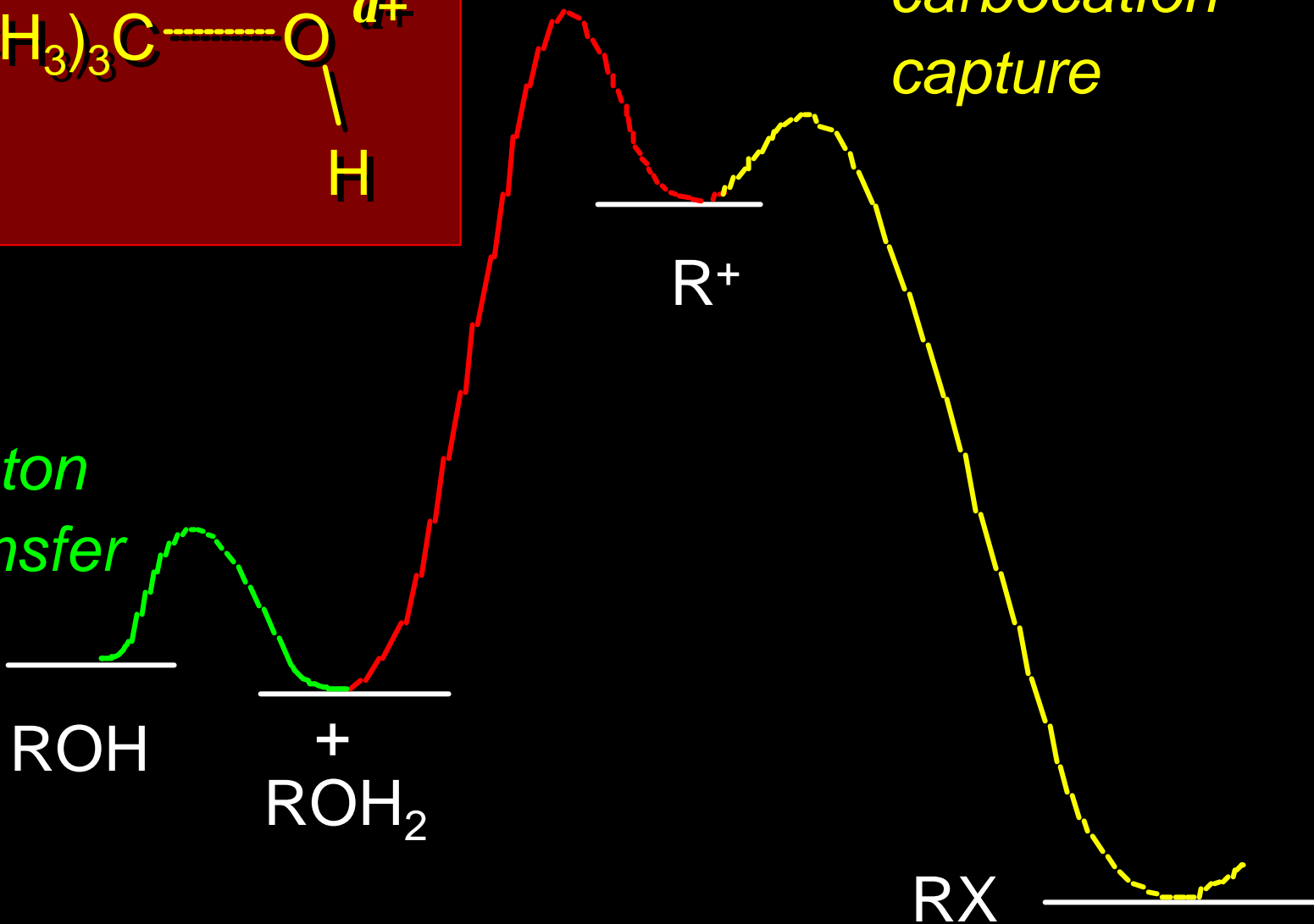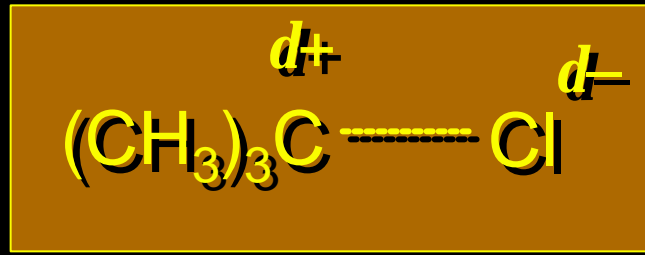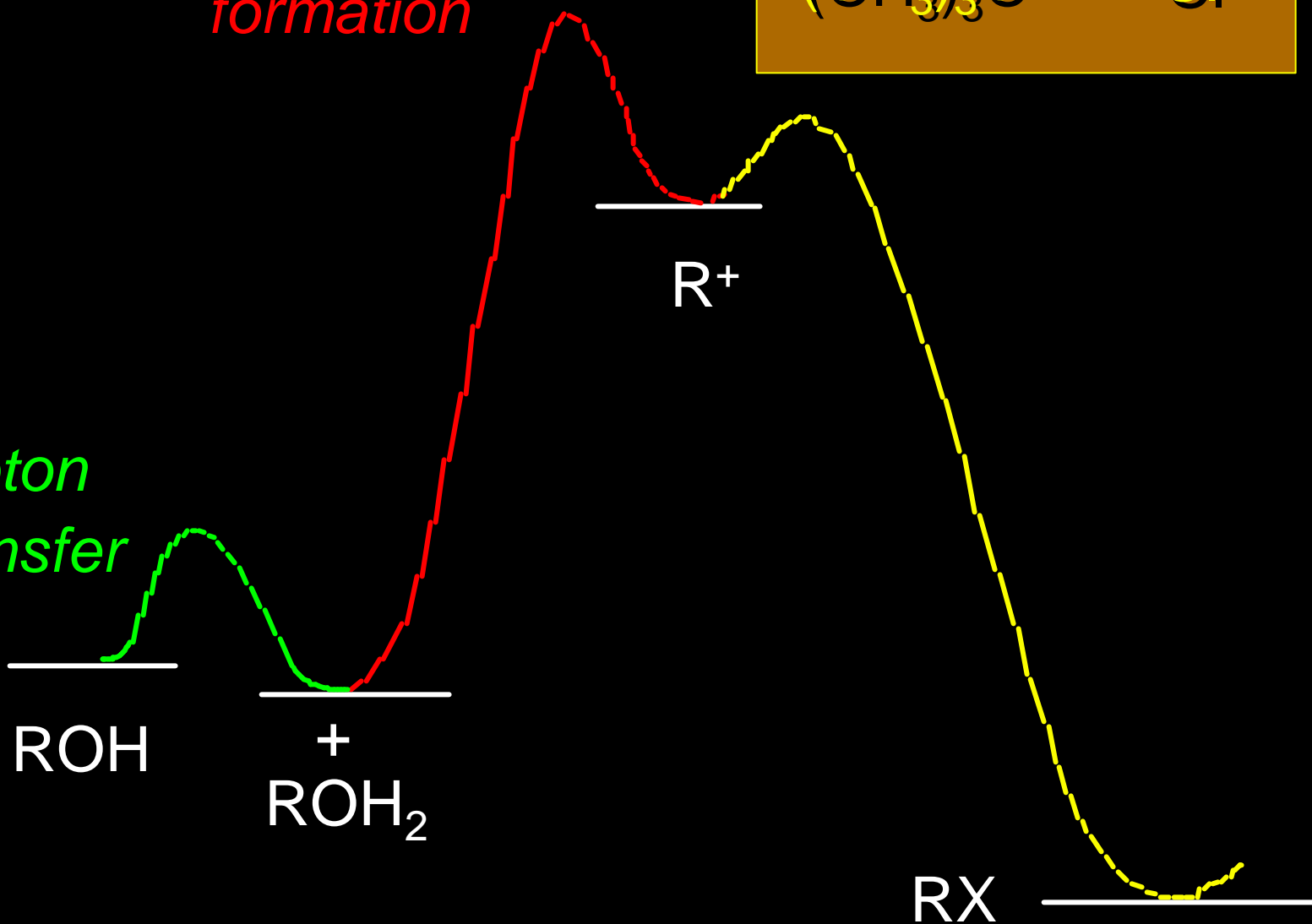
The mechanism just described is an example of an S_N1 process.

S_N1 stands for substitution-nucleophilic-unimolecular.

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

4.12
Effect of Alcohol Structure
on Reaction Rate

slow step is:

$$ROH_2^+ \rightarrow R^+ + H_2O$$

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).
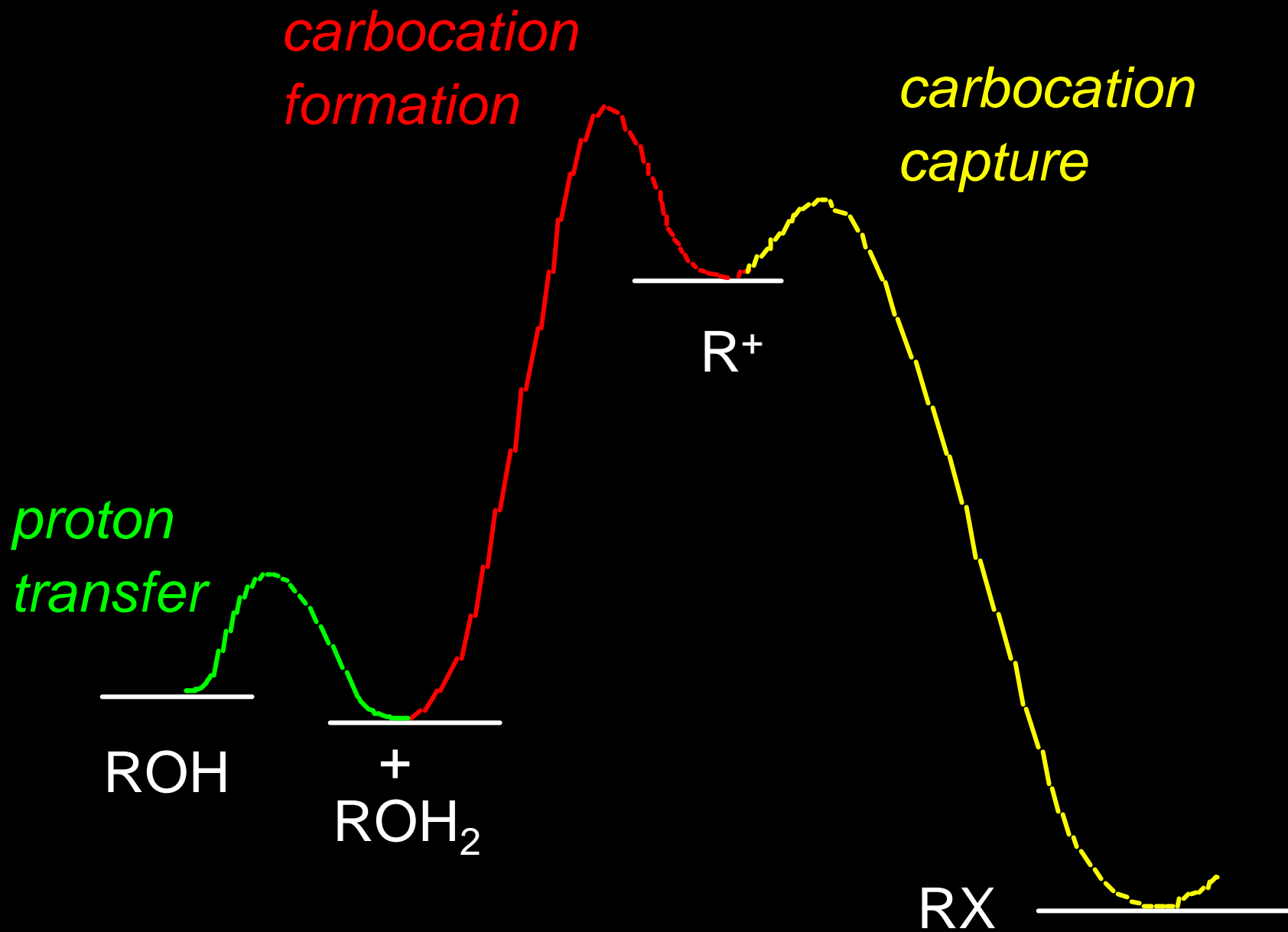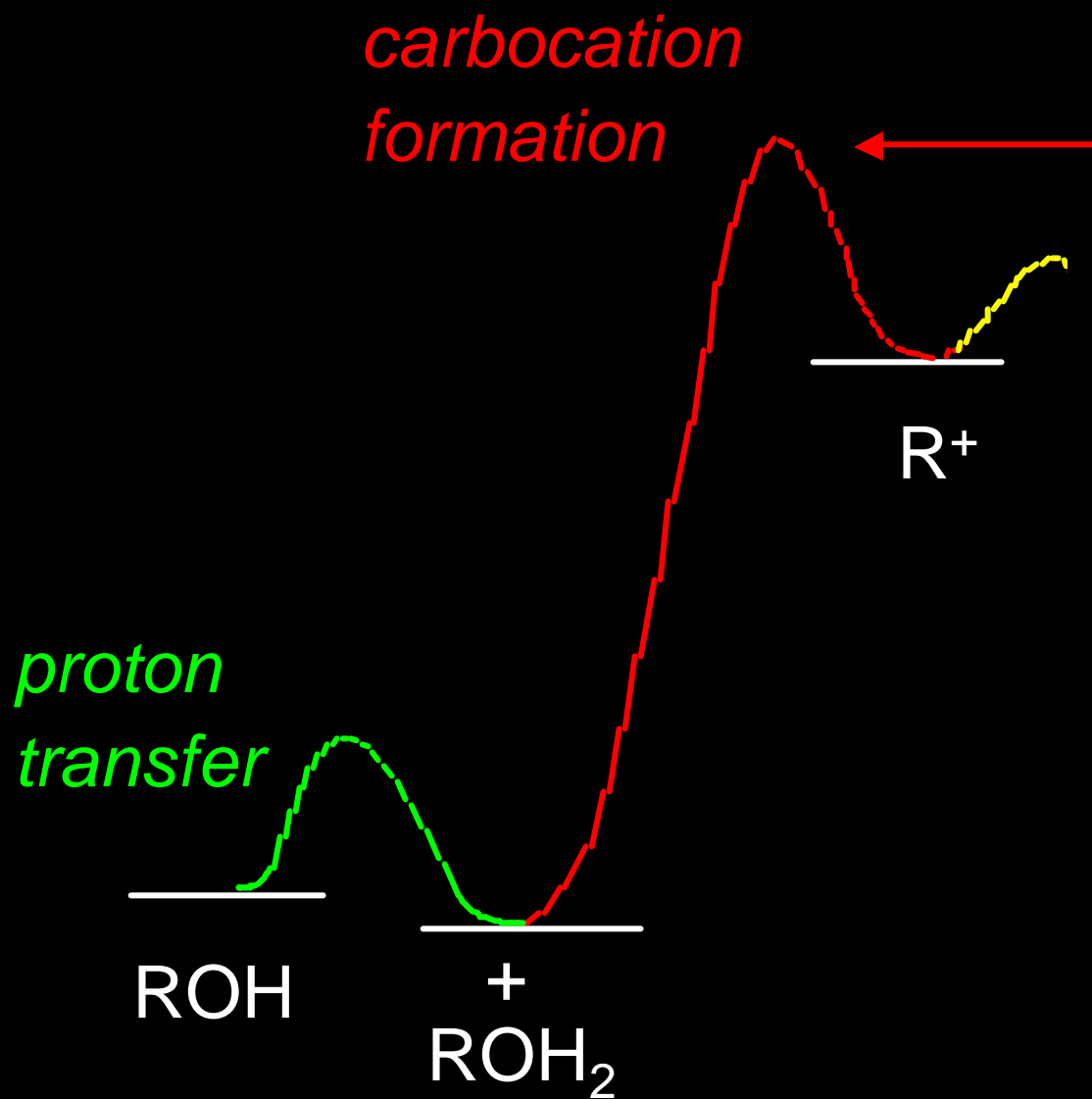
4.13
Reaction of Primary Alcohols with Hydrogen Halides.
The S_N2 Mechanism

Preparation of Alkyl Halides

$(CH_3)_3COH + HCl \xrightarrow{25°C} (CH_3)_3CCl + H_2O$

78-88%

 $OH + HBr \xrightarrow{80\text{-}100°C}$ $Br + H_2O$

73%

$CH_3(CH_2)_5CH_2OH + HBr \xrightarrow{120°C}$

$CH_3(CH_2)_5CH_2Br + H_2O$

87-90%
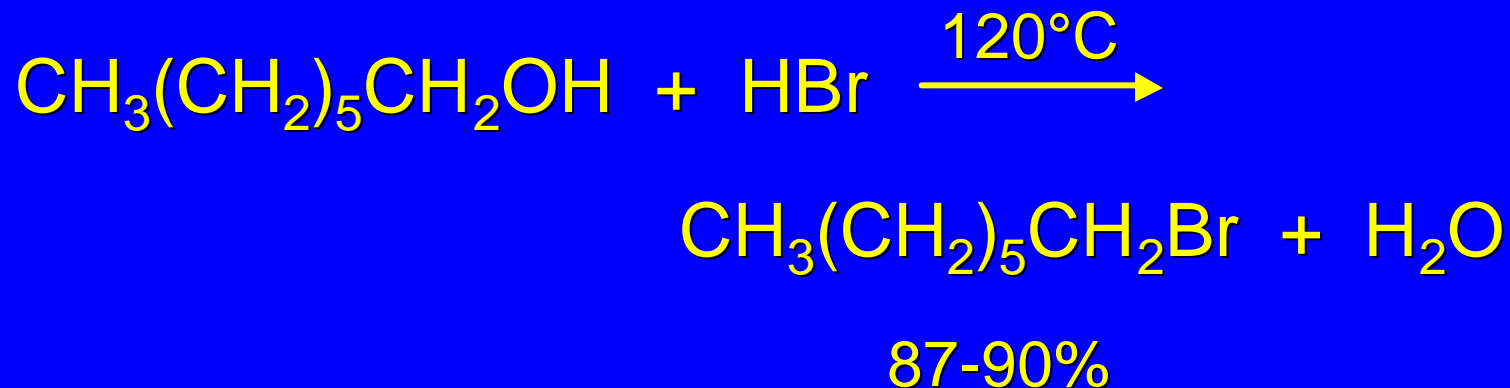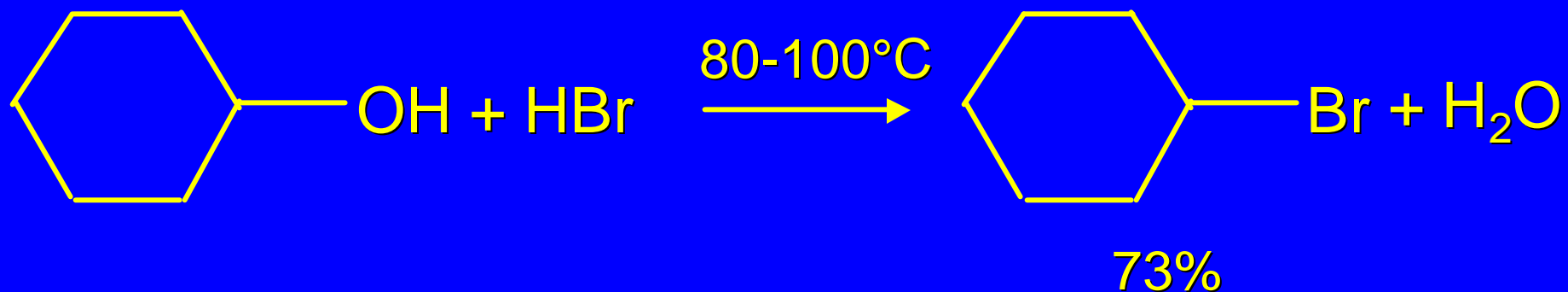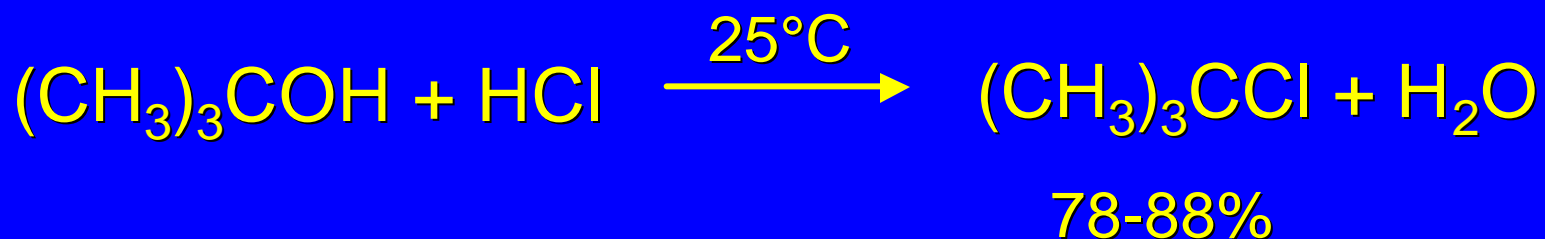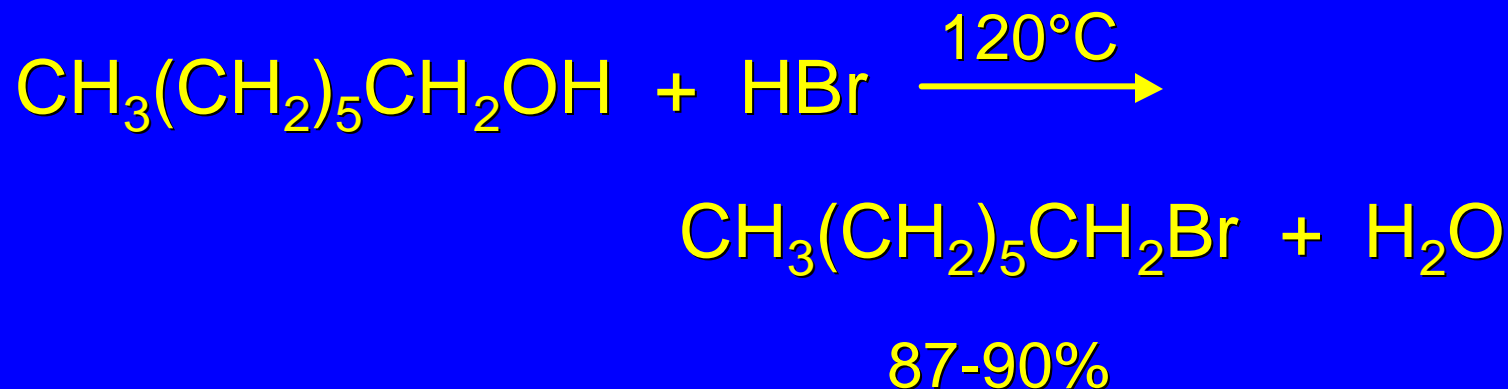
Preparation of Alkyl Halides

Primary carbocations are too high in energy to allow S_N1 mechanism. Yet, primary alcohols are converted to alkyl halides.

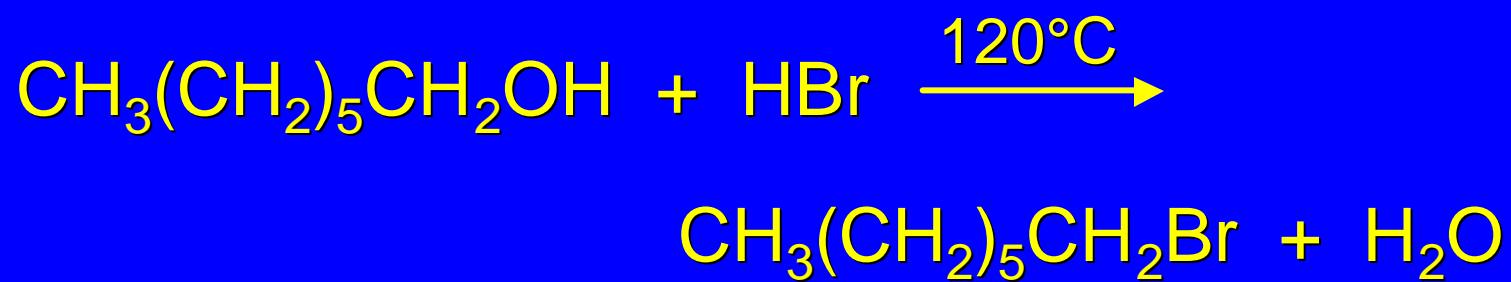Primary alcohols react by a mechanism called S_N2 (substitution-nucleophilic-bimolecular).

$$CH_3(CH_2)_5CH_2OH \ + \ HBr \ \xrightarrow{\ 120°C\ }$$

$$CH_3(CH_2)_5CH_2Br \ + \ H_2O$$

87-90%

The S_N2 Mechanism

Two-step mechanism for conversion
of alcohols to alkyl halides:
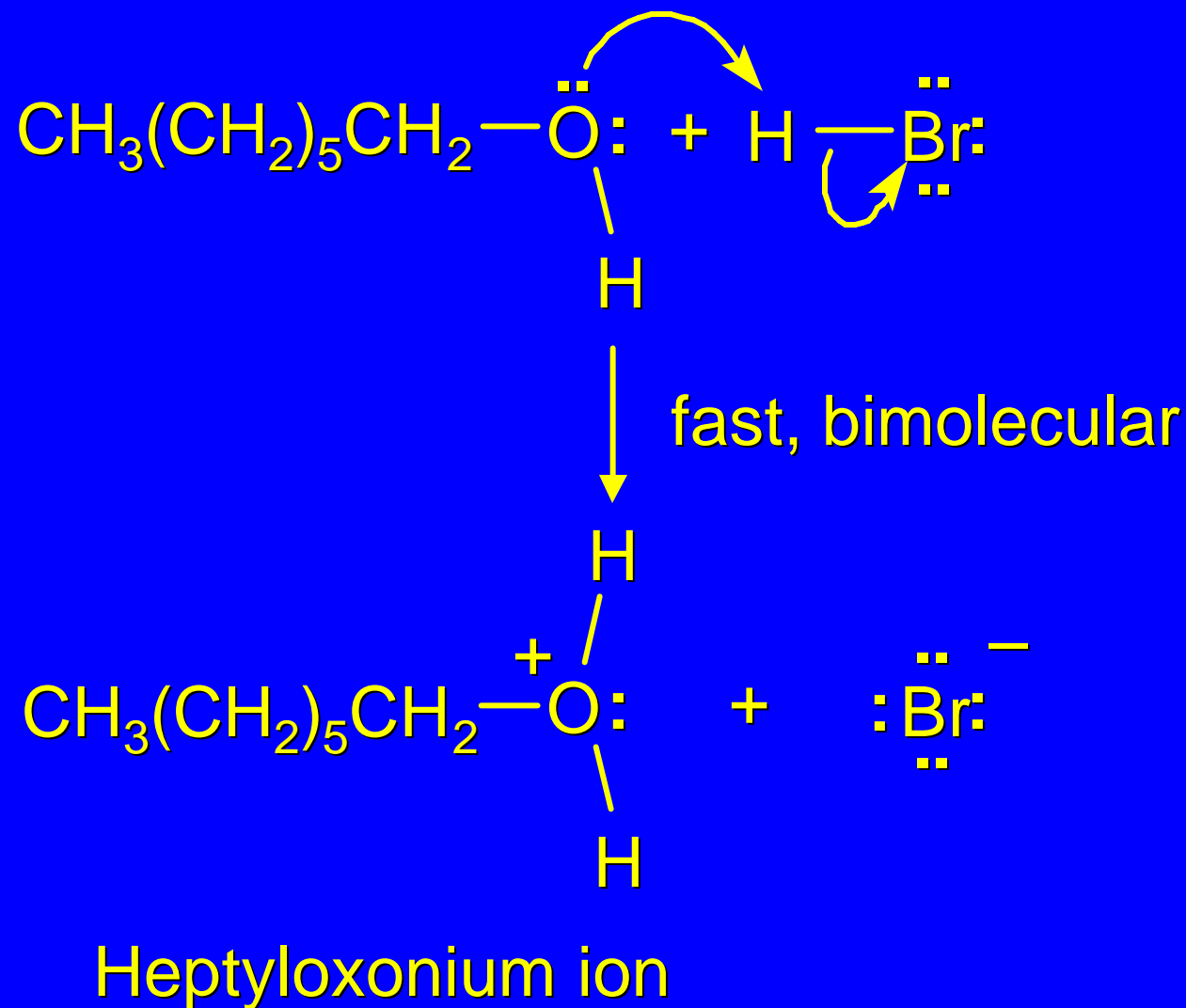
(1) proton transfer to alcohol to form
alkyloxonium ion

(2) bimolecular displacement of water
from alkyloxonium ion by halide

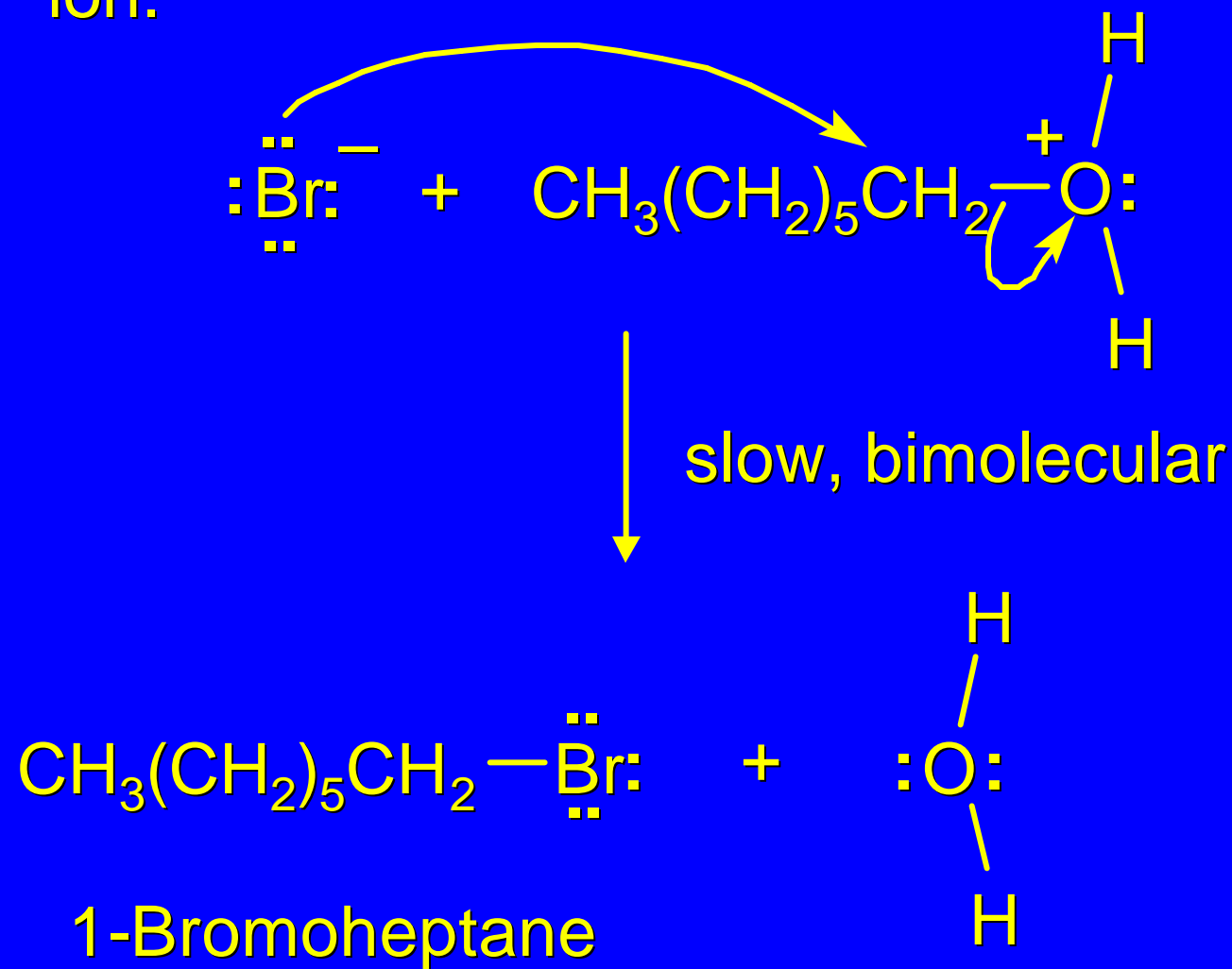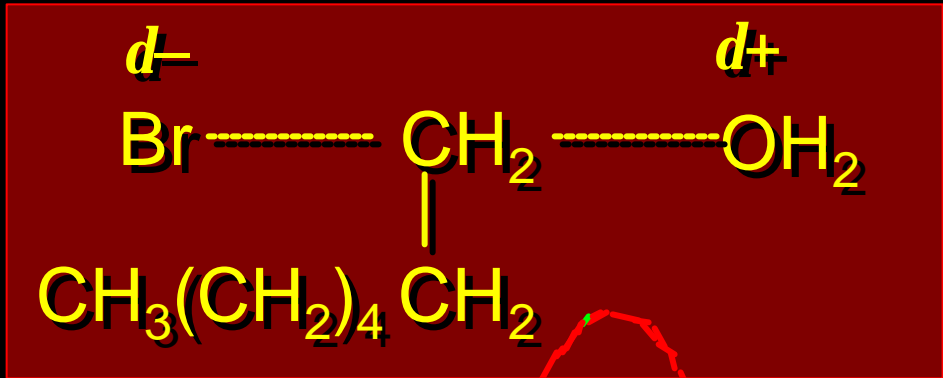$$CH_3(CH_2)_5CH_2OH \ + \ HBr \ \xrightarrow{120°C}$$

$$CH_3(CH_2)_5CH_2Br \ + \ H_2O$$
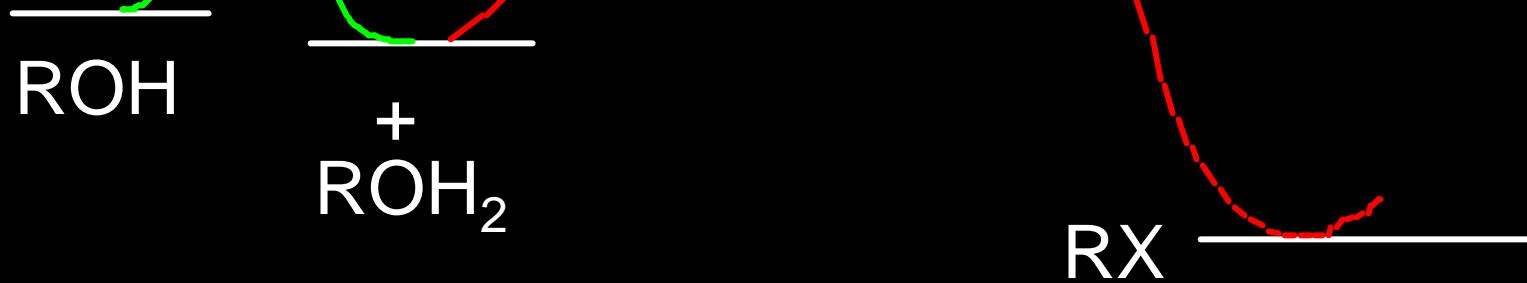
4.14
Other Methods for Converting Alcohols to Alkyl Halides

Reagents for ROH to RX

Thionyl chloride

$$SOCl_2 + ROH \rightarrow RCl + HCl + SO_2$$

Phosphorus tribromide

$$PBr_3 + 3ROH \rightarrow 3RBr + H_3PO_3$$

$$CH_3CH(CH_2)_5CH_3 \xrightarrow[K_2CO_3]{SOCl_2} CH_3CH(CH_2)_5CH_3$$

$$\underset{OH}{|} \qquad\qquad\qquad\qquad\qquad \underset{Cl}{|}$$

(81%)
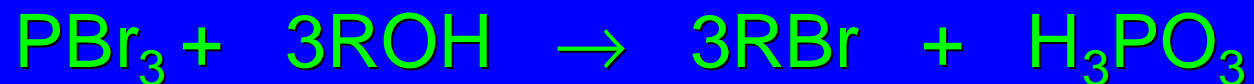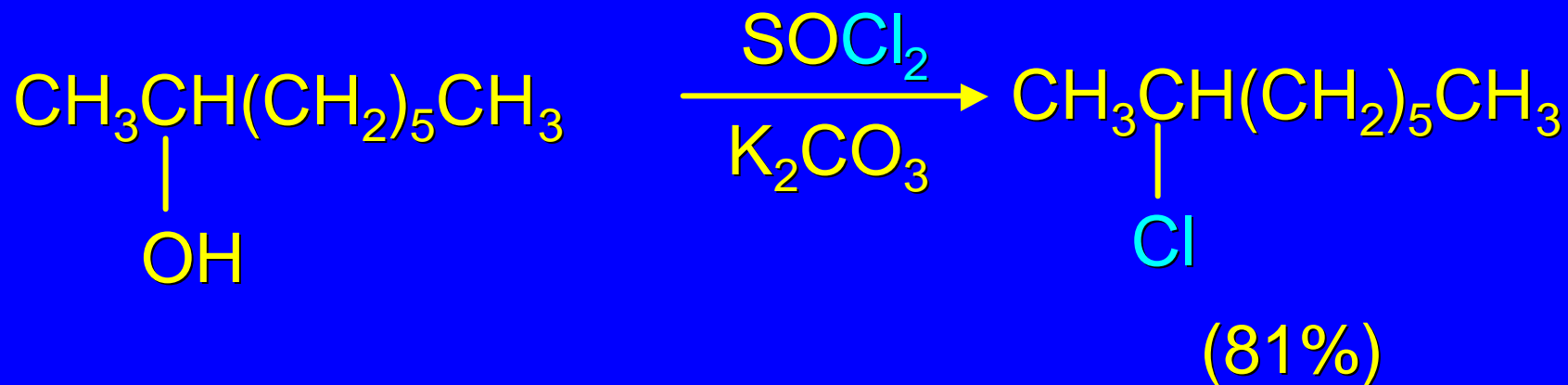
(pyridine often used instead of K_2CO_3)

$$(CH_3)_2CHCH_2OH \xrightarrow{PBr_3} (CH_3)_2CHCH_2Br$$

(55-60%)