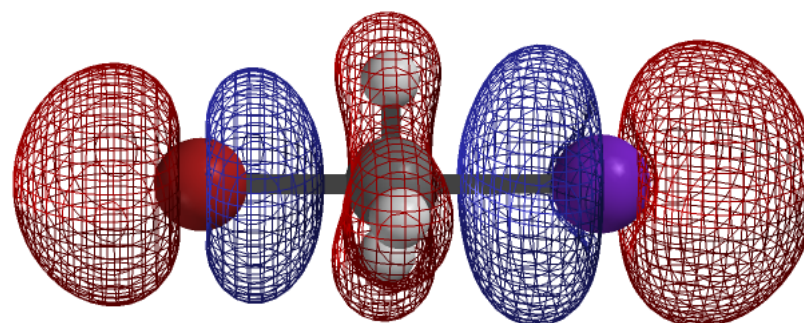


# 10

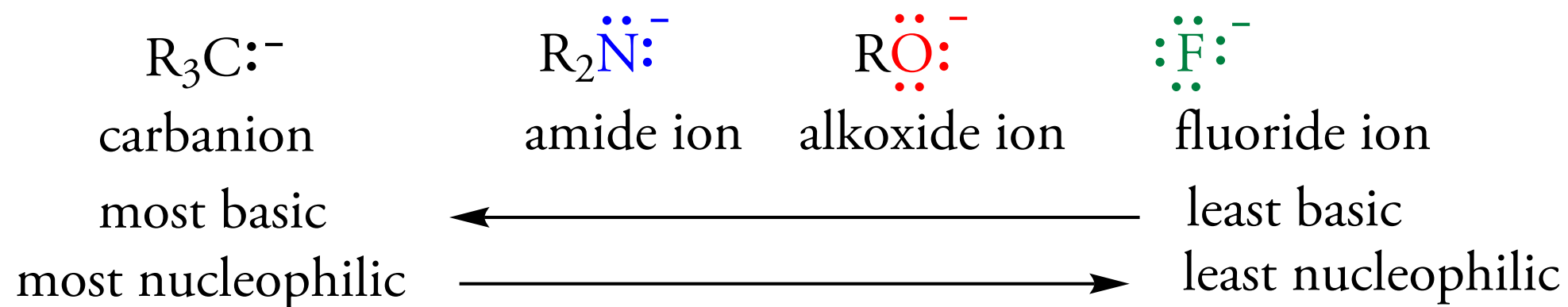
## NUCLEOPHILIC SUBSTITUTION AND ELIMINATION REACTIONS



Transition state for an  $S_N2$  reaction

## 10.1 PROPERTIES OF NUCLEOPHILES

### Trends in Nucleophilicity Within a Period

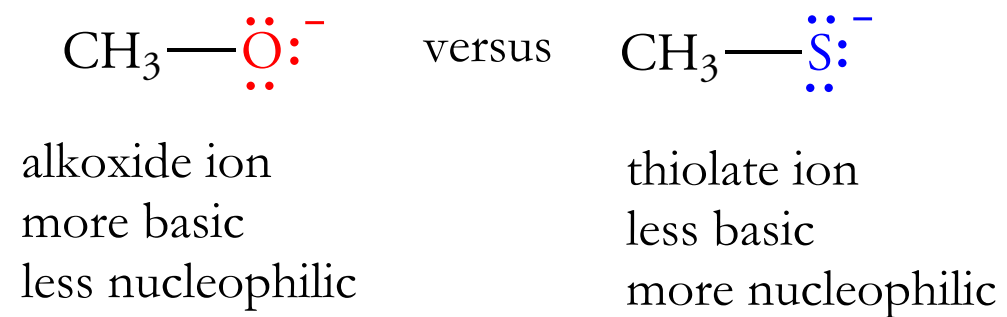
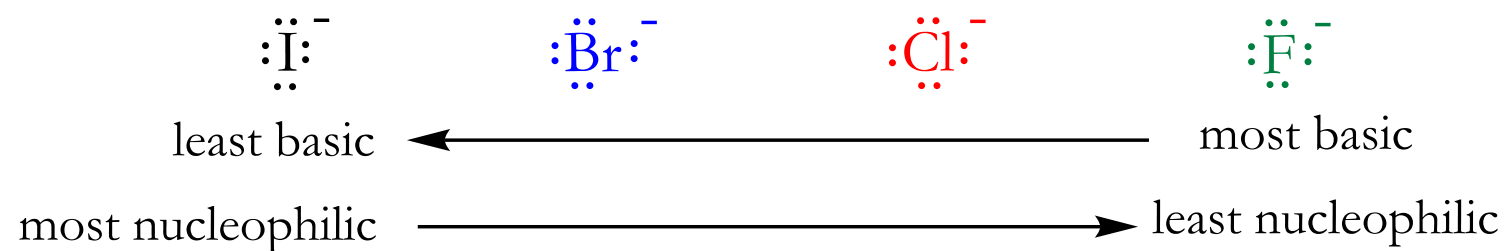


**Table 10.1**

**Relative Rates of Reaction of  
Nucleophiles with Iodomethane**

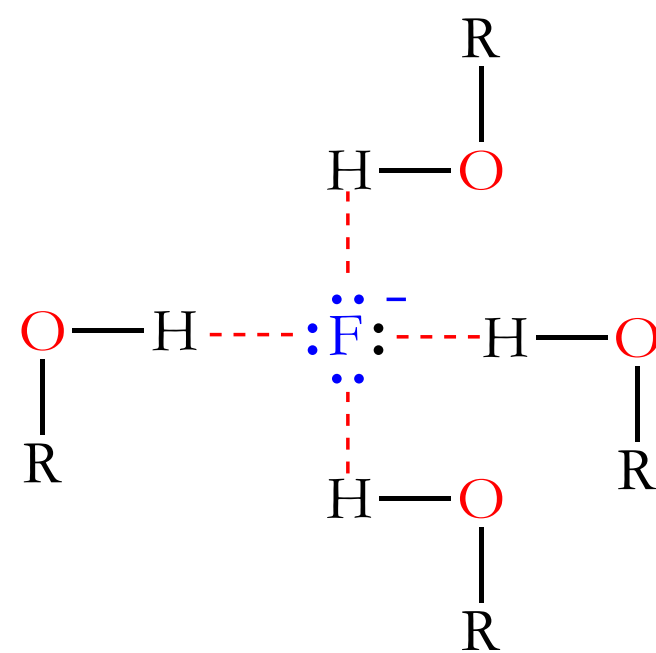
<b>Nucleophile</b>	<b>Relative Rate</b>
CH <sub>3</sub> OH	1
NO <sub>3</sub> <sup>-</sup>	30
F <sup>-</sup>	5 x 10 <sup>2</sup>
SO <sub>4</sub> <sup>-2</sup>	3 x 10 <sup>3</sup>
CH <sub>3</sub> CO <sub>2</sub> <sup>-</sup>	2 x 10 <sup>4</sup>
Cl <sup>-</sup>	2.5 x 10 <sup>4</sup>
NH <sub>3</sub>	3.2 x 10 <sup>5</sup>
N <sub>3</sub> <sup>-</sup>	6 x 10 <sup>5</sup>
Br <sup>-</sup>	6 x 10 <sup>5</sup>
CH <sub>3</sub> O <sup>-</sup>	2 x 10 <sup>6</sup>
I <sup>-</sup>	2.5 x 10 <sup>7</sup>
CH <sub>3</sub> S <sup>-</sup>	1 x 10 <sup>9</sup>

# Trends in Nucleophilicity Within a Group



## Figure 10.1 Solvation of Ions by Protolytic Solvent

The nucleophilicity of anions in a protic solvent such as an alcohol is diminished because of hydrogen bonding between the anion and the solvent.



Hydrogen-bonded anion

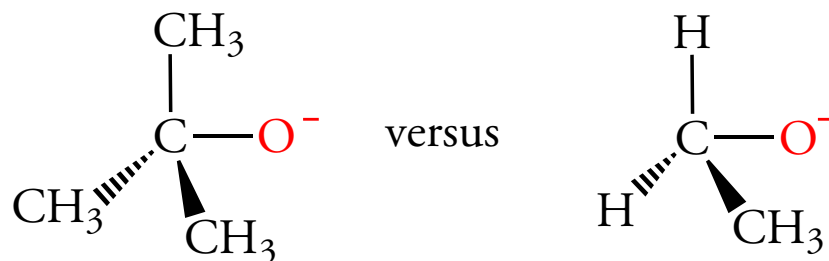
## Effects of Charge on Nucleophilicity



alkoxide ion  
more basic  
more nucleophilic

alcohol  
less basic  
less nucleophilic

## Steric Effects on Nucleophilicity



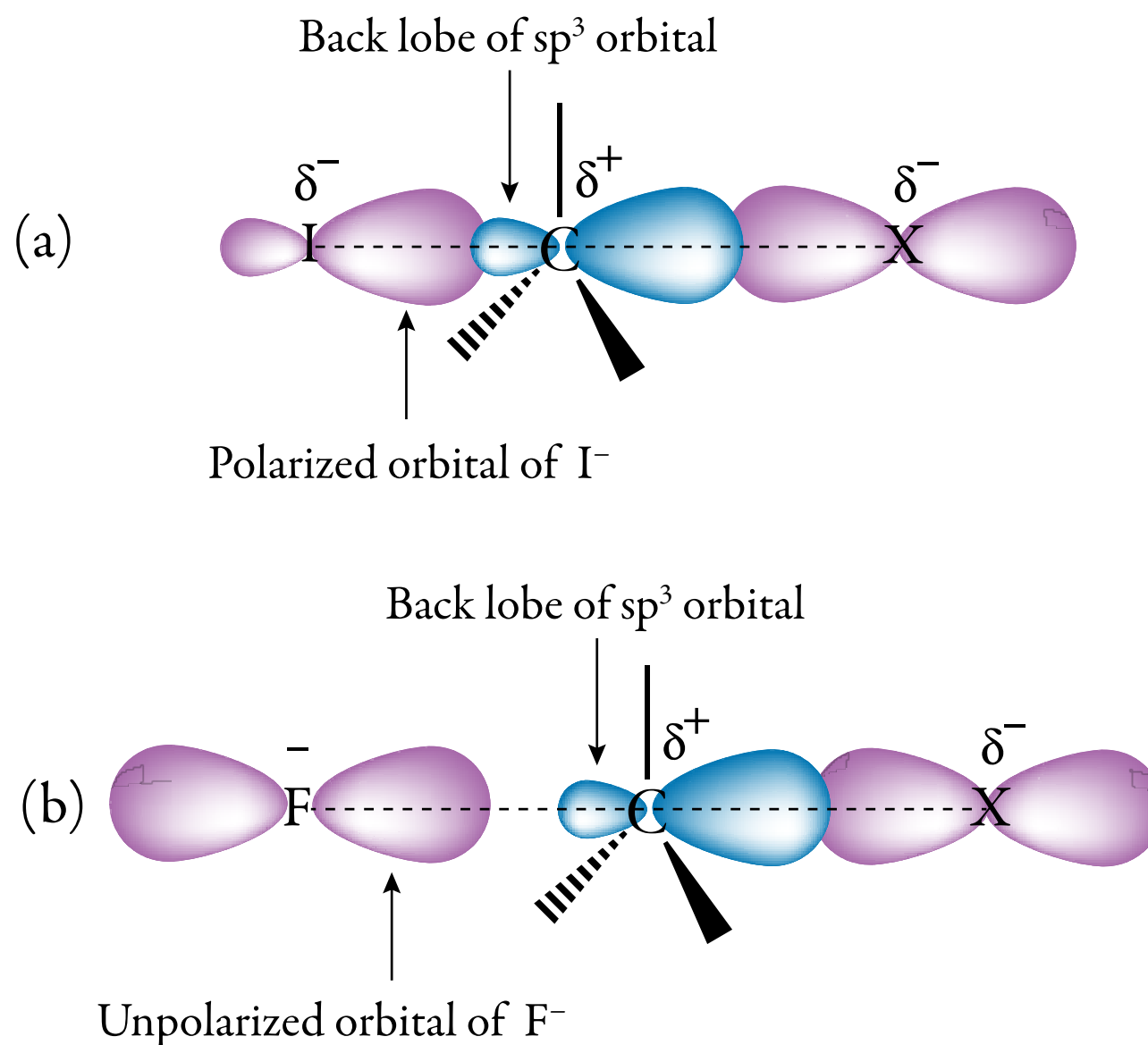
*tert*-Butoxide  
Sterically hindered  
Poor nucleophile.

Ethoxide  
Not sterically hindered  
Better nucleophile.

## Figure 10.2 Polarizability and Nucleophilicity

(a) The nonbonded electrons of iodide are highly polarizable. One of the nonbonding electron pairs can overlap effectively with the back lobe of the  $sp^3$ -hybridized carbon atom in a nucleophilic substitution reaction. Therefore, iodide is an excellent nucleophile, even though it is not very basic.

(b) The valence electrons of fluoride, in contrast, are not very polarizable, and do not effectively overlap the back lobe of the  $sp^3$ -hybridized carbon atom in a nucleophilic substitution reaction. Therefore, fluoride is a poor nucleophile, even though it is much more basic than iodide.

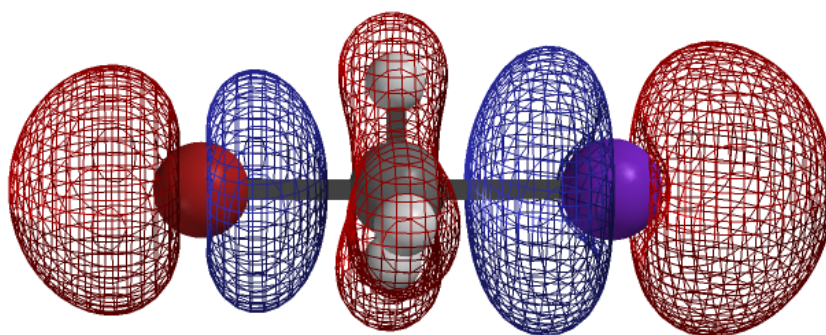
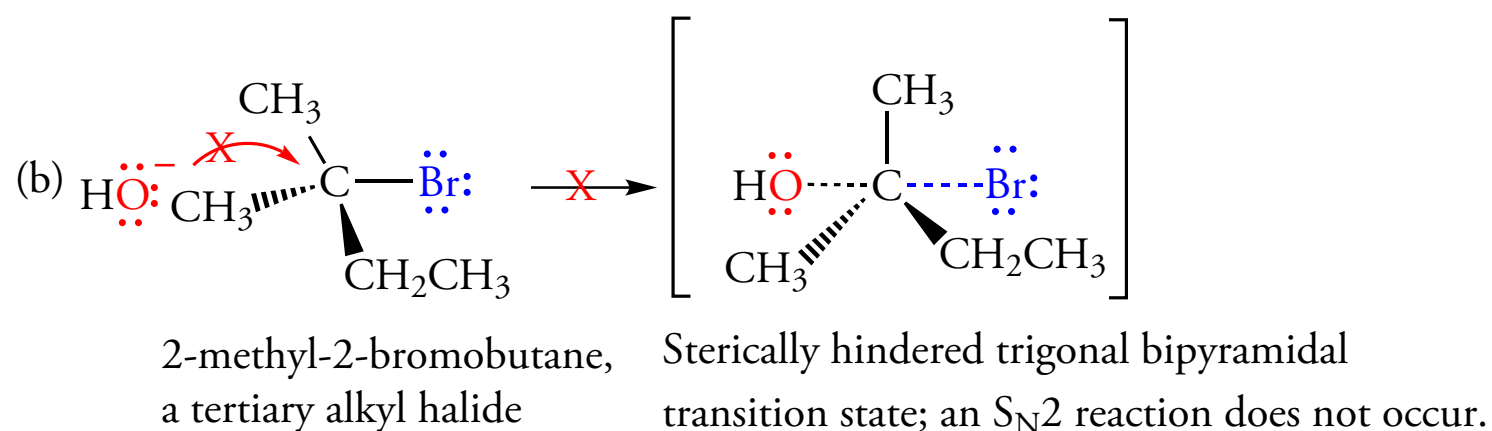
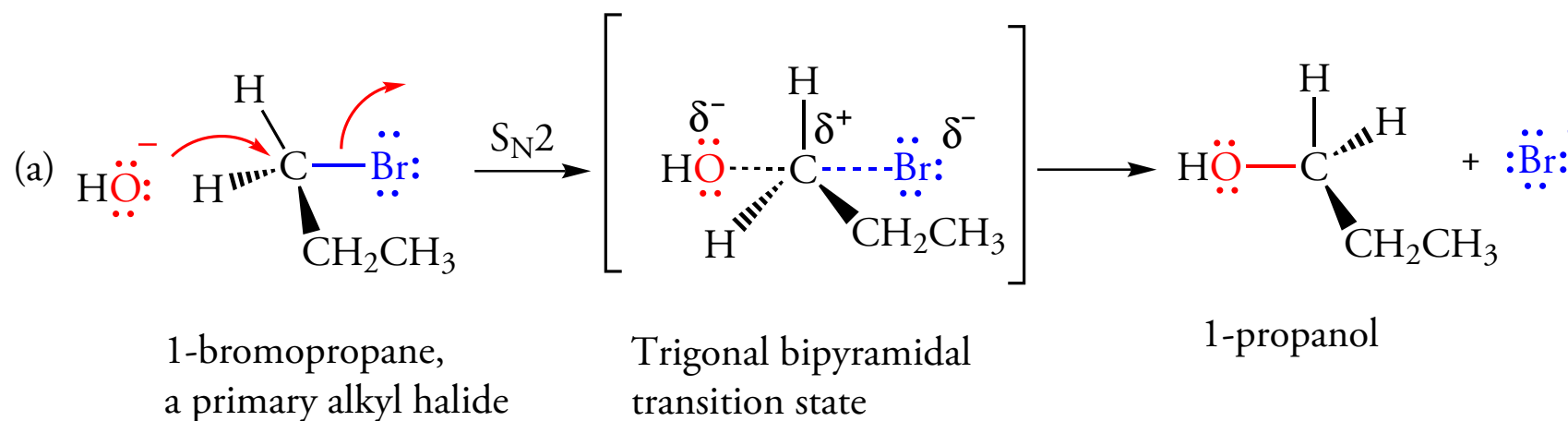


## Figure 10.3 Steric Effects in $S_N2$ Reactions

(a) Primary alkyl halides react with nucleophiles by an  $S_N2$  mechanism that proceeds through a trigonal bipyramidal transition state.

(b) Tertiary alkyl halides do not react by an  $S_N2$  mechanism because the substrate blocks the approach of the nucleophile. The trigonal bipyramidal transition state cannot form because it is too sterically crowded.

(c) The linear arrangement of the nucleophile and the leaving group in the transition state for an  $S_N2$  reaction requires a primary or secondary center on carbon because a tertiary center blocks the approach of the nucleophile.

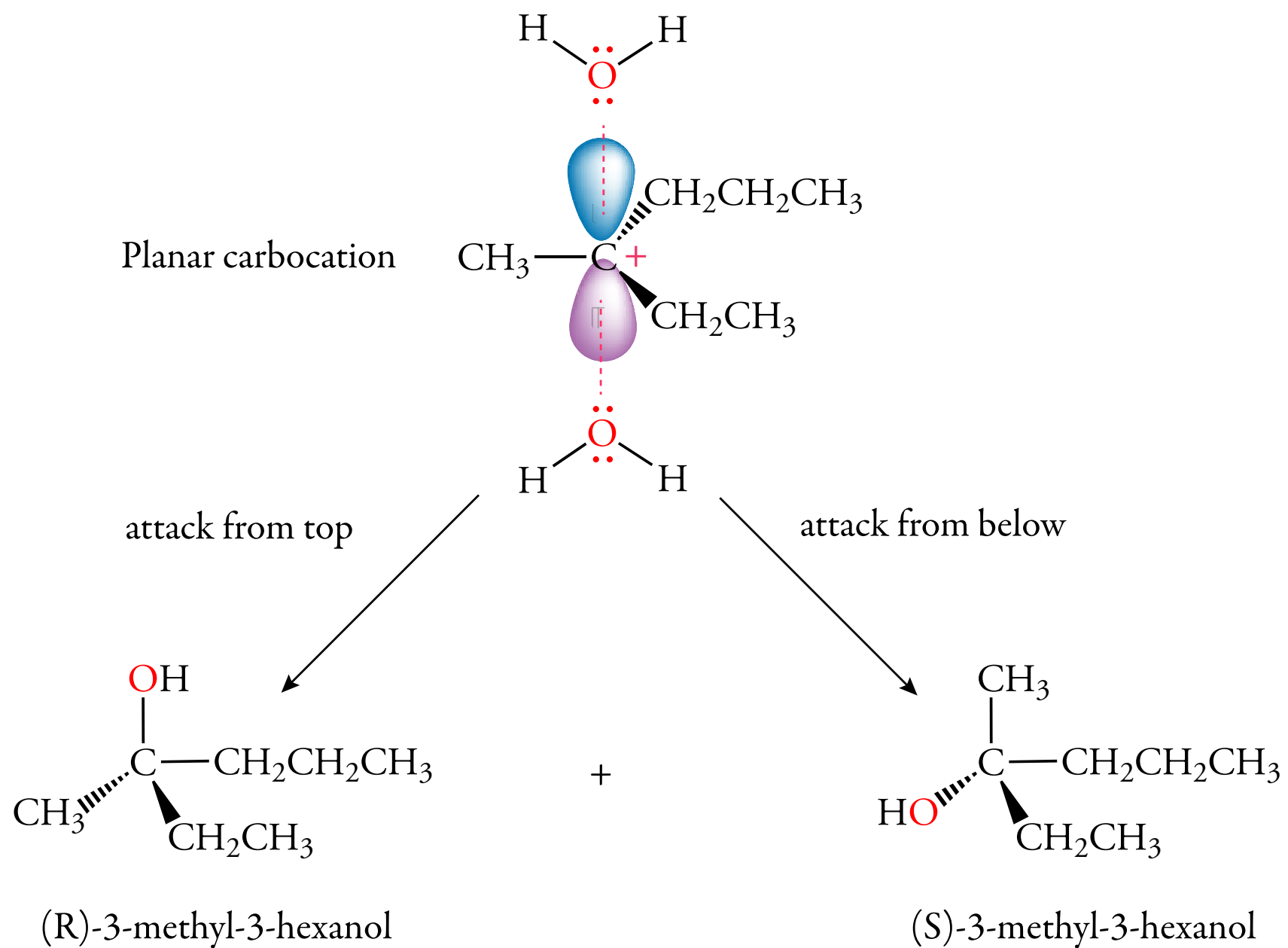


(c) Molecular orbitals in the transition state of an  $S_N2$  reaction.



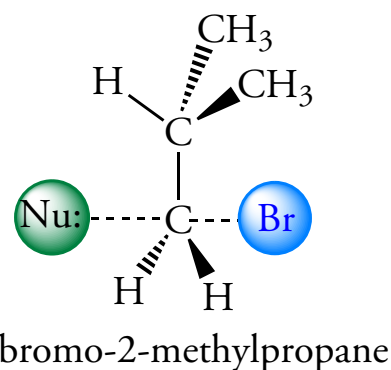
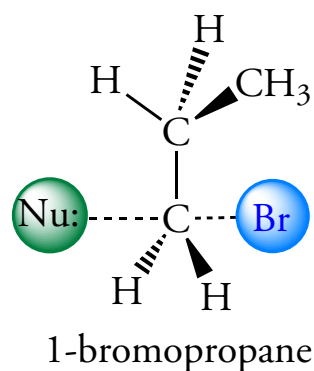
## Figure 10.4 Stereochemical Effects in $S_N1$ Reactions

A chiral starting material, (S)-3-methyl-3-bromohexane, reacts with water to give a tertiary carbocation. This intermediate is planar, and can be attacked by water either from the top or bottom side to give a racemic mixture of products. The reaction proceeds by an  $S_N1$  mechanism.



## Figure 10.5 Steric Effects of $\beta$ -Substituents in $S_N2$ Reactions

$\beta$ -Substituents decrease the rates of  $S_N2$  reactions by interfering with the approach of the nucleophile. Both 1-bromopropane, and 1-bromo-2-methylpropane have conformations in which the methyl groups do not completely hinder the approach of the nucleophile. However, in 1-bromo-2,2-dimethylpropane, no conformation exists that allows the nucleophile to reach the  $\beta$  carbon, so the rate is very slow.



Steric hindrance by methyl group.

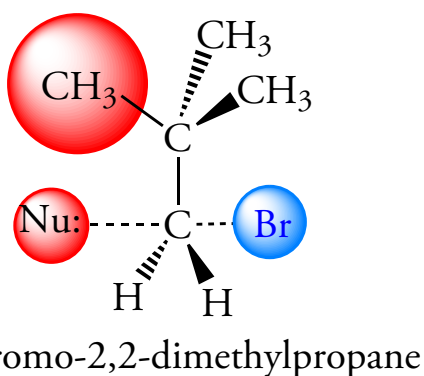
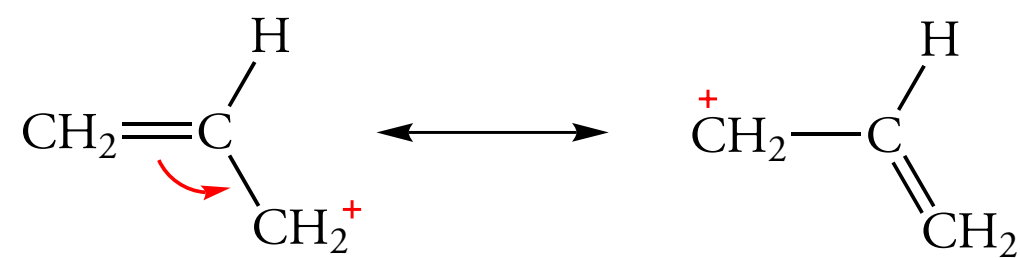


Table 10.2

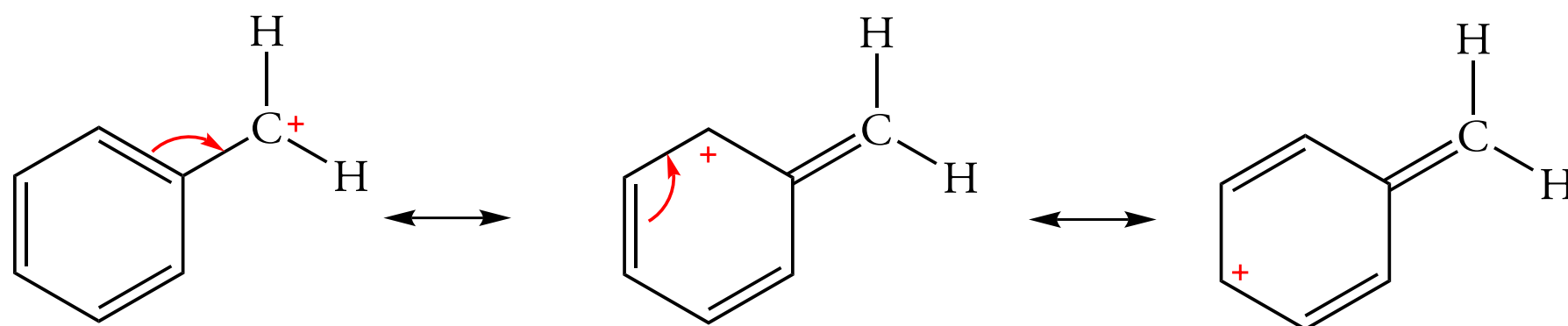
### Relative Rates of $S_N2$ Reactions of Branched Bromoalkanes

Bromoalkane	Relative Rate ( <i>I</i> )	Relative Rate ( $CH_3CH_2O^-$ )
$CH_3-CH_2-Br$	1	1
$CH_3-CH_2-CH_2-Br$	0.8	0.3
$\begin{array}{c} CH_3 \\   \\ CH_3-CH-CH_2-Br \end{array}$	$3.0 \times 10^{-3}$	$3.0 \times 10^{-2}$
$\begin{array}{c} CH_3 \\   \\ CH_3-C-CH_2-Br \\   \\ CH_3 \end{array}$	$1 \times 10^{-5}$	$4 \times 10^{-6}$

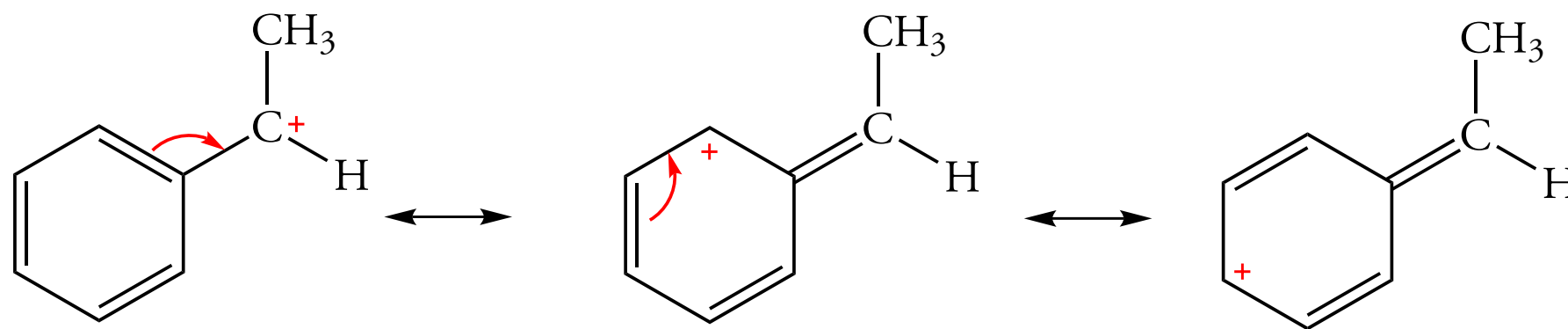
# Figure 10.6 Resonance Structures of Allylic and Benzylic Carbocations



Allyl carbocation ( $1^\circ$ )



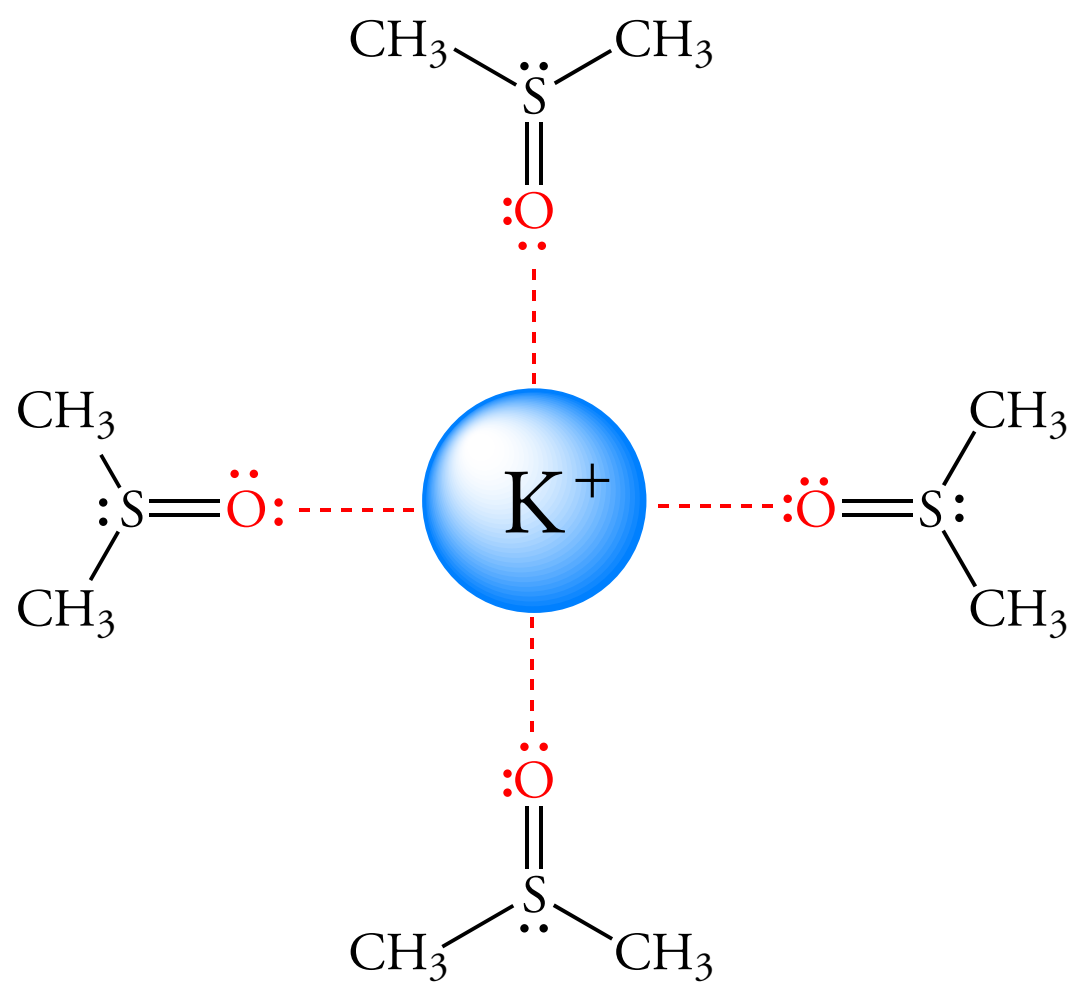
primary benzylic carbocation



secondary benzylic carbocation

## Figure 10.7 Solvation of Cations by Polar Aprotic Solvents

Cations are solvated by polar aprotic solvents. The partner anion (counterion) remains unsolvated, and “naked.” As a result, its nucleophilicity increases.



**Table 10.3**  
Relative Rates of S<sub>N</sub>1 Reactions  
and Solvent Polarity

<i>Solvent</i>	<i>Dielectric Constant</i>	<i>Relative Rate</i>
Acetic acid	6	1
Methanol	33	4
Formic Acid	58	5 x 10 <sup>3</sup>
Water	78	1.5 x 10 <sup>5</sup>

**Table 10.4**  
Relative Rates of S<sub>N</sub>2 Reactions and Solvent  
Polarity  
CH<sub>3</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>Br + N<sub>3</sub><sup>-</sup> → CH<sub>3</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>N<sub>3</sub> + Br<sup>-</sup>

<i>Solvent</i>	<i>Relative Rate</i>
methanol	1
formamide	12
methylformamide	45
dimethylformamide	1.2 x 10 <sup>6</sup>

## Figure 10.8 Stereoelectronic Effects in E2 Reactions

The E2 reaction is most favorable when the hydrogen on the  $\beta$ -carbon and the halogen are in an anti periplanar conformation. This is the case in *cis*-1-bromo-4-*tert*-butyl-cyclohexane. A Newman projection structure shows this favorable conformation.

