Organic Chemistry I

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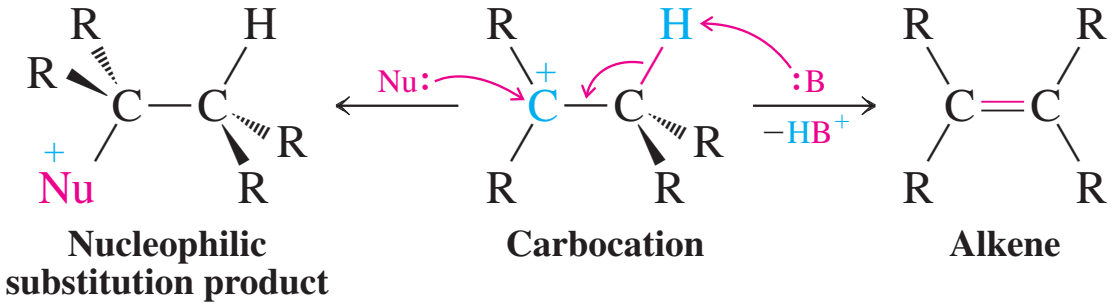
7.6 UNIMOLECULAR ELIMINATION: E1

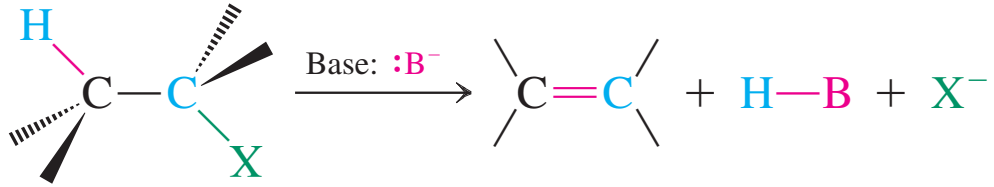
Carbocations are readily attacked by nucleophiles at the positively charged carbon. This is not the only mode of reaction. A competing alternative is **deprotonation** by the nucleophile acting as a **base**, furnishing a new class of compounds, the **alkenes**. This process is possible because the proton neighboring the positive charge is unusually acidic.

Competition Between Nucleophilic and Basic Attack on a Carbocation



Starting from a haloalkane, the overall transformation constitutes the removal of HX with the simultaneous generation of a double bond. The general term for such a process is **elimination,** abbreviated **E.**

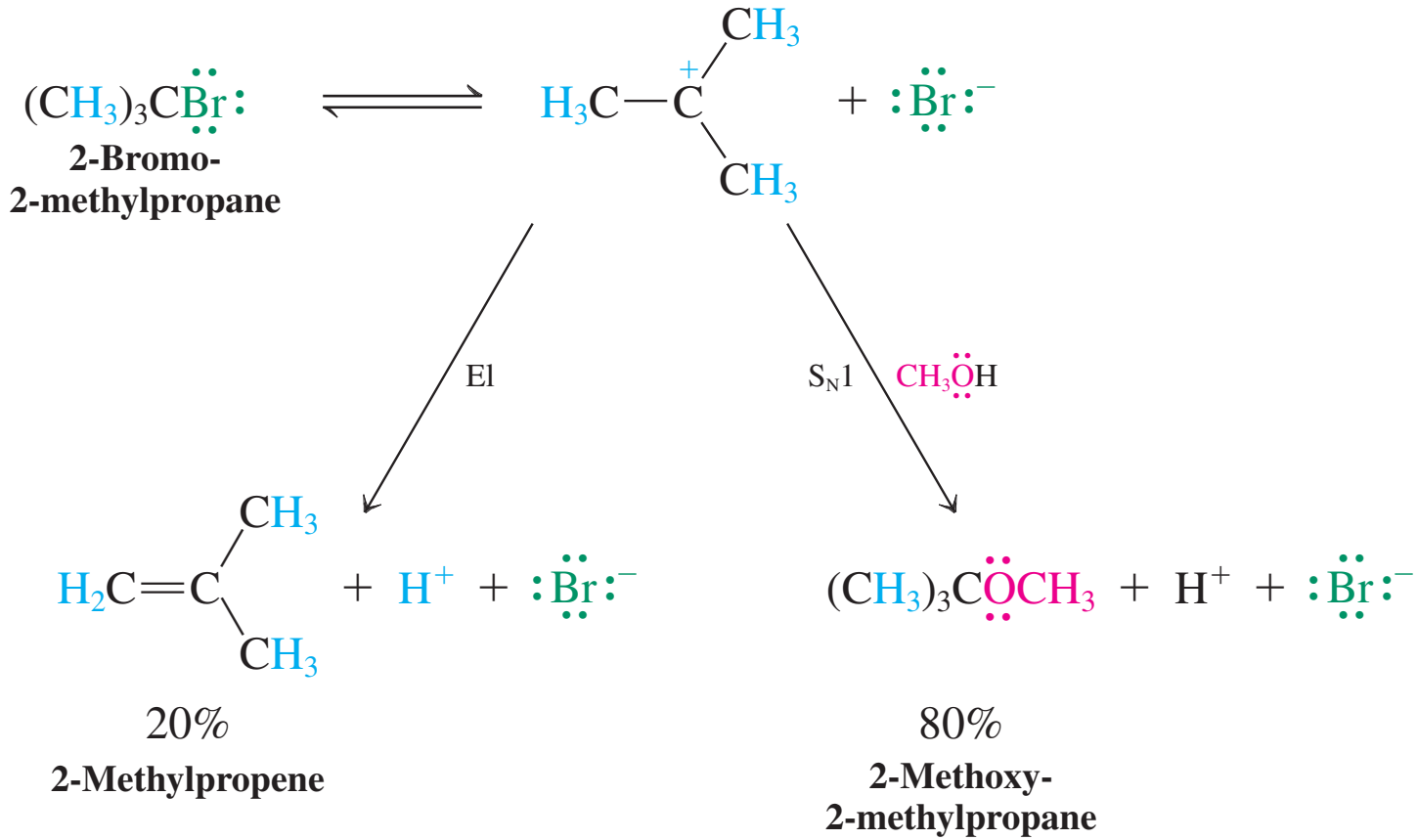
Elimination



When 2-bromo-2-methylpropane is dissolved in methanol, it disappears rapidly, and the major product, 2-methoxy-2-methylpropane, arises by solvolysis.

There is also a significant amount of another compound, 2-methylpropene, the product of *elimination* of HBr from the original substrate.

Competition Between E1 and S_N1 in the Methanolysis of 2-Bromo-2-methylpropane



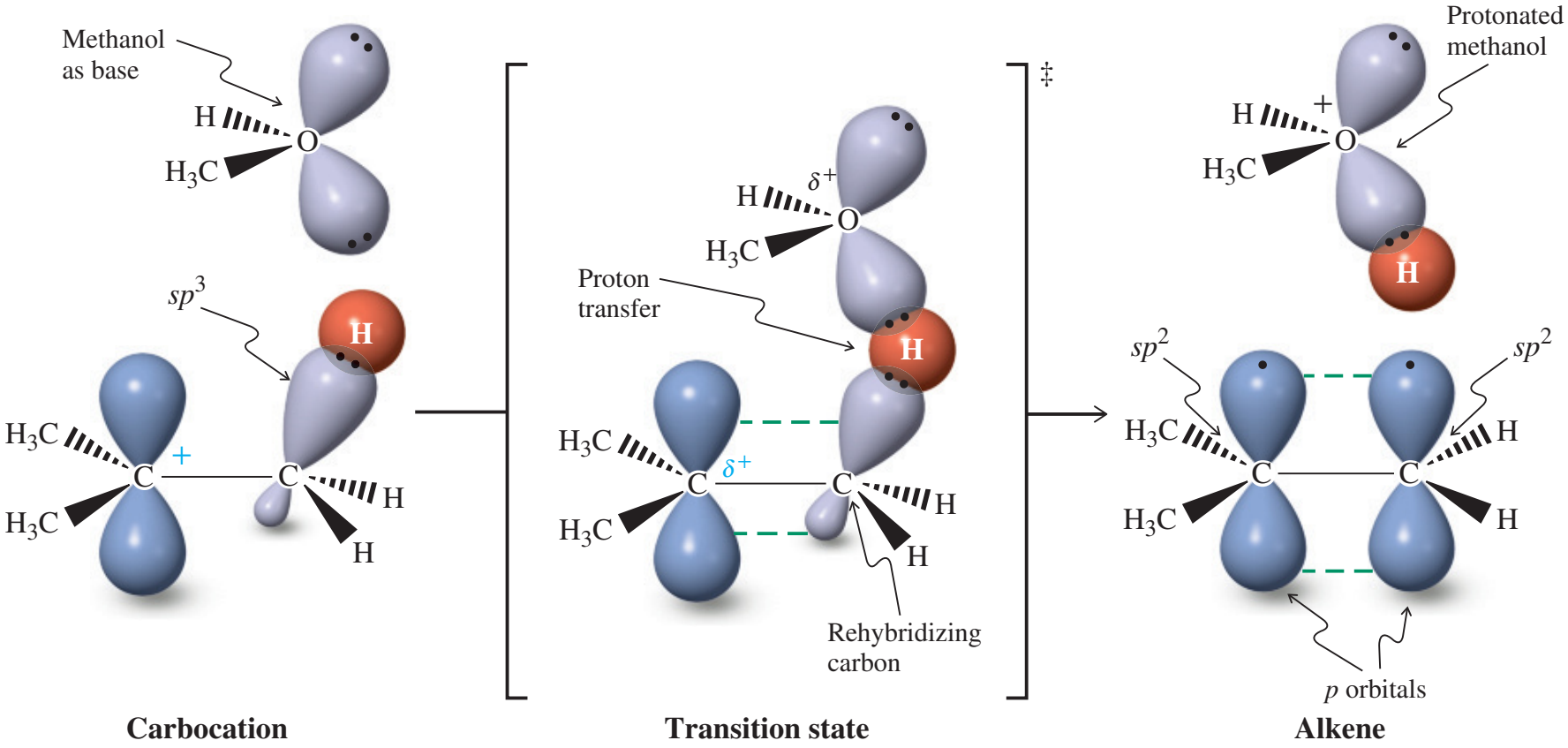
The rate of alkene formation depends on the concentration of *only* the starting halide; the reaction is first order. Because they are unimolecular, eliminations of this type are labeled **E1.**

The rate-determining step in the E1 process is the same as that in S_N1 reactions: dissociation to a carbocation. This intermediate then has a second pathway at its disposal along with nucleophilic trapping: loss of a proton from a carbon adjacent to the one bearing the positive charge.

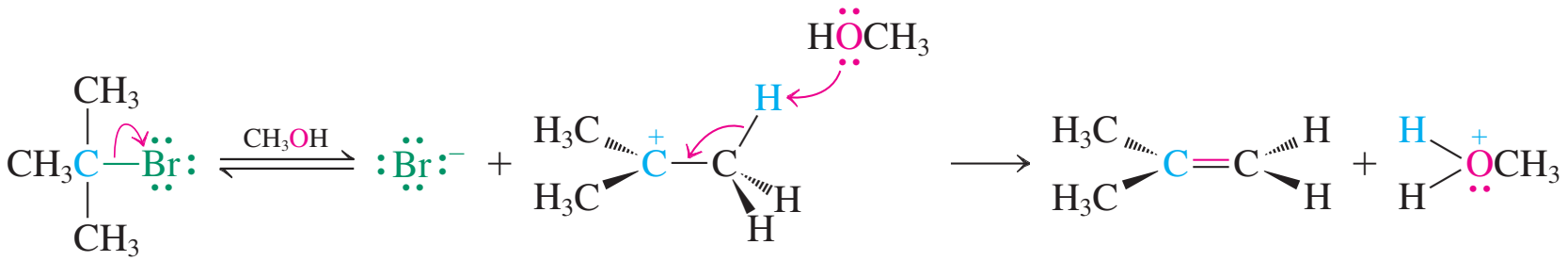
A Lewis base typically removes the proton. In aqueous solution, water plays this role, giving H_3O^+; here, the proton is carried off by CH_3OH as $CH_3OH_2^+$, an alkyloxonium ion.

The carbon left behind rehybridizes from sp^3 to sp^2.

As the C–H bond breaks, its electrons shift to overlap in a π fashion with the vacant *p* orbital at the neighboring cationic center. The result is a hydrocarbon containing a double bond: an alkene.



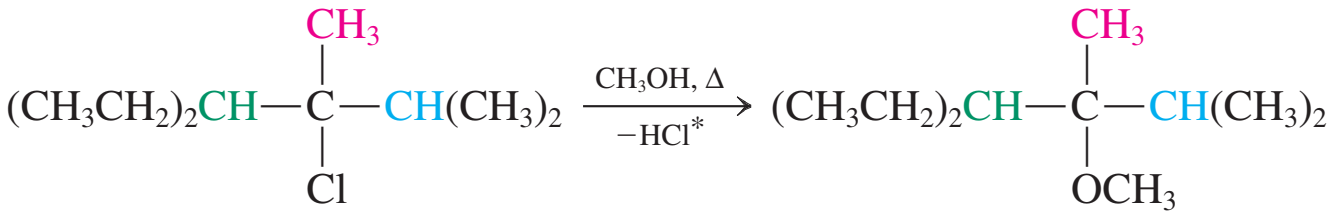
The E1 Reaction Mechanism



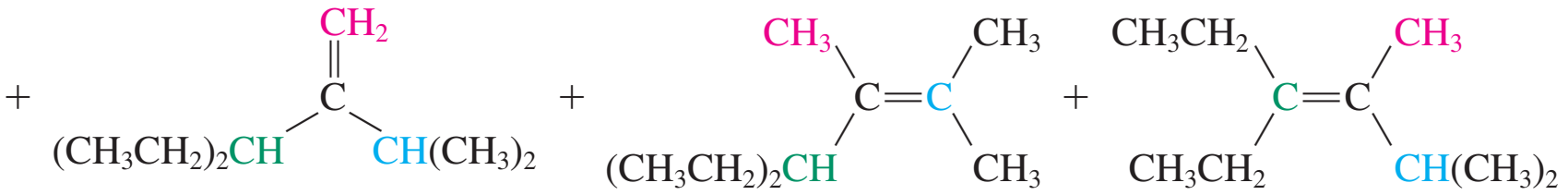
Any hydrogen positioned on *any carbon next to the center bearing the leaving group* can participate in the E1 reaction. The *tert*-butyl cation has nine such hydrogens, each of which is equally reactive. In this case, the product is the same regardless of the identity of the proton lost.

In other cases, more than one product may be obtained.

The E1 Reaction Can Give Product Mixtures



S_N1 product



E1 products

The identity of the leaving group should have no effect on the ratio of substitution to elimination, because the carbocation formed is the same in each case.

The product ratio may be affected by the addition of base, but at low base concentration this effect is usually small.

Strong bases are usually strong nucleophiles, addition of a base will not greatly favor deprotonation of the carbocation at the expense of nucleophilic attack, and the ratio of E1 to S_N1 products remains approximately constant.

By using *high* concentrations of strong base, the proportion of elimination rises dramatically.

Table 7-3 Ratio of S_N1 to E1 Products in the Hydrolyses of 2-Halo-2-methyl-propanes at 25°C

X in $(CH_3)_3CX$	Ratio S_N1:E1
Cl	95:5
Br	95:5
I	96:4

7.7 BIMOLECULAR ELIMINATION: E2

In addition to S_N2, S_N1, and E1 reactions, there is a fourth pathway by which haloalkanes may react with nucleophiles *that are also strong bases:* elimination by a *bimolecular* mechanism.

Strong bases effect bimolecular elimination

A dramatic change of the kinetics is observed at higher concentrations of strong base. The rate of alkene formation becomes proportional to the concentrations of both the starting halide *and* the base:

The kinetics of elimination are now second order and the process is called **bimolecular elimination,** abbreviated **E2.**

Kinetics of the E2 Reaction of 2-Chloro-2-methylpropane

$$(CH_3)_3CCl + Na^+ {}^-OH \xrightarrow{k} CH_2{=}C(CH_3)_2 + NaCl + H_2O$$

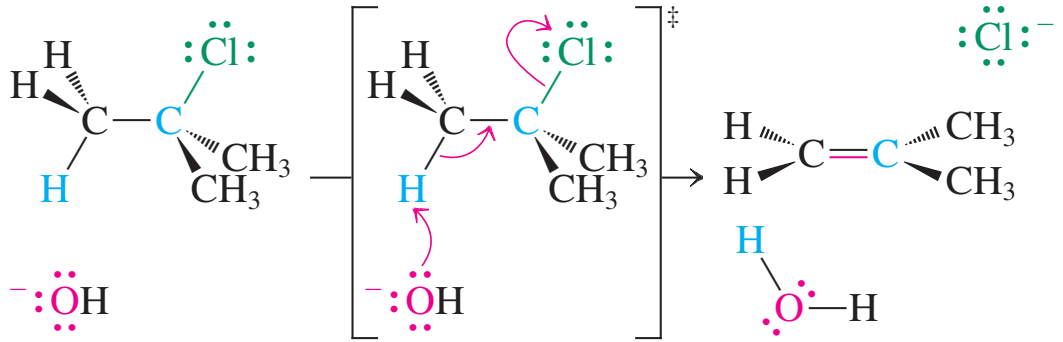
$$\text{Rate} = k[(CH_3)_3CCl][{}^-OH] \text{ mol L}^{-1} \text{ s}^{-1}$$

Strong bases (e.g., hydroxide: HO^-, and alkoxides: RO^-) can attack haloalkanes before carbocation formation. The target is a hydrogen on a carbon atom *next to* the one carrying the leaving group.

This reaction pathway is not restricted to tertiary halides, although in secondary and primary systems it must compete with the S_N2 process.

E2 reactions proceed in one step

The E2 Reaction Mechanism



The bimolecular elimination mechanism consists of a *single step.* The bonding changes occur in its transition state with electron-pushing arrows:

1. Deprotonation by the base
2. Departure of the leaving group
3. Rehybridization of the reacting carbon centers from sp^3 to sp^2 to furnish the two *p* orbitals of the emerging double bond

All three changes take place *simultaneously*: The E2 is a **one-step**, ***concerted*** process.

Notice that the E1 and E2 mechanisms are very similar, differing only in the sequence of events. In the bimolecular reaction, proton abstraction and leaving-group departure are simultaneous. In the E1 process, the halide leaves first, followed by an attack by the base.

A good way of thinking about the difference is to imagine that the strong base participating in the E2 reaction is more aggressive. It does not wait for the tertiary or secondary halide to dissociate but attacks the substrate directly.

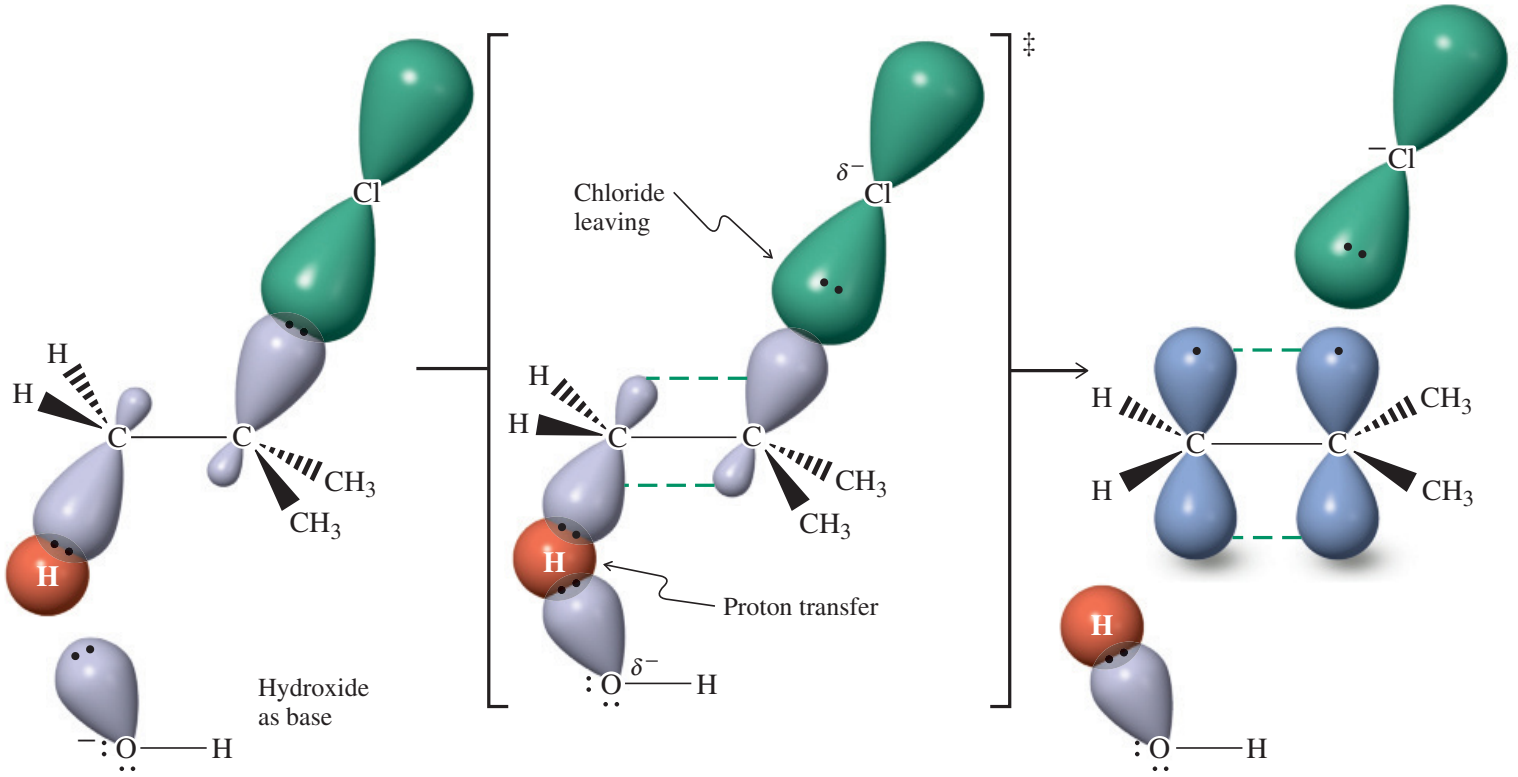
Experiments elucidate the detailed structure of the E2 transition state

The second-order rate law requires that both the haloalkane and the base take part in the rate-determining step.

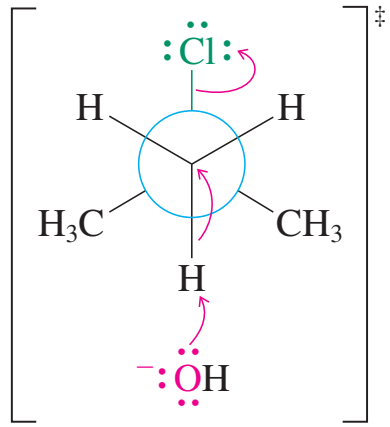
Better leaving groups result in faster eliminations.

Both the C–H and the C–X bonds, are broken in the transition state, describes their relative orientation in space when this event takes place (**stereochemistry**).

The substrate in an ***anti*** conformation provides the conditions for the breaking C–H and C–X bonds simultaneously.



Newman Projection of E2 Transition State



Relative Reactivity in the E2 Reaction

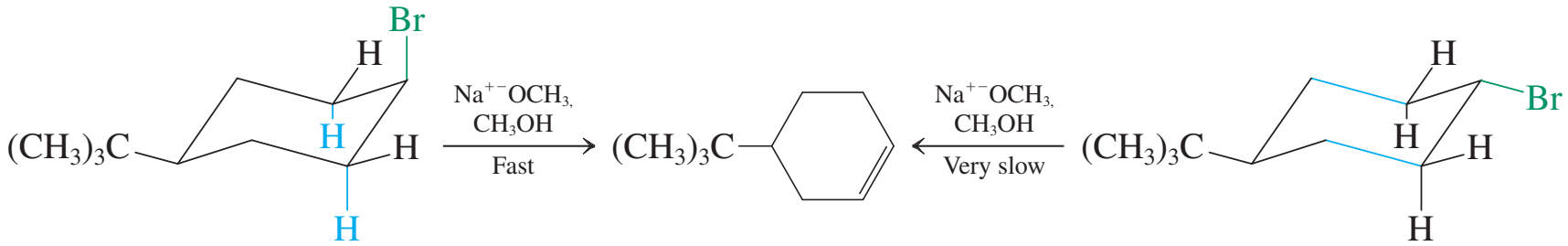
RI > RBr > RCl > RF

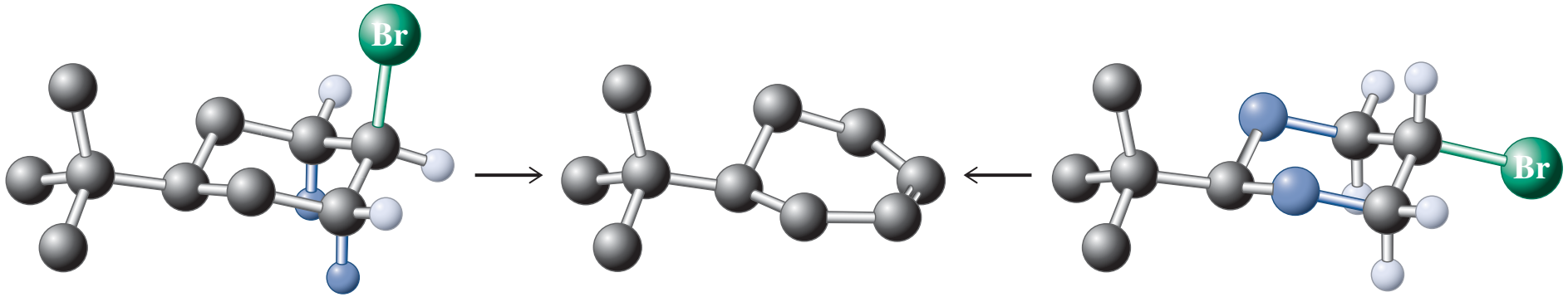
Increasing

Treatment of *cis*-1-bromo-4-(1,1-dimethylethyl)cyclohexane with strong base leads to rapid bimolecular elimination to the corresponding alkene.

In contrast, under the same conditions, the trans isomer reacts only very slowly. **Why?**

Anti Elimination Occurs Readily for _cis_- but Not for _trans_-1-Bromo-4-(1,1-dimethylethyl)cyclohexane





***cis*-1-Bromo-4-(1,1-dimethylethyl)cyclohexane**
(Two *anti* hydrogens)

***trans*-1-Bromo-4-(1,1-dimethylethyl)cyclohexane**
(No *anti* hydrogens; only *anti* ring carbons)

When we examine the most stable chair conformation of the cis compound, we find that two hydrogens are located *anti* to the axial bromine substituent.

This geometry is very similar to that required by the E2 transition state, and consequently elimination is easy.

Conversely, the trans system has no C–H bonds aligned *anti* to the equatorial leaving group.

E2 elimination in this case would require either ring-flip to a diaxial conformer or removal of a hydrogen *gauche* to the bromine, both of which are energetically costly.

The latter would be an example of an elimination proceeding through an unfavorable ***syn*** transition state (*syn,* Greek, together).

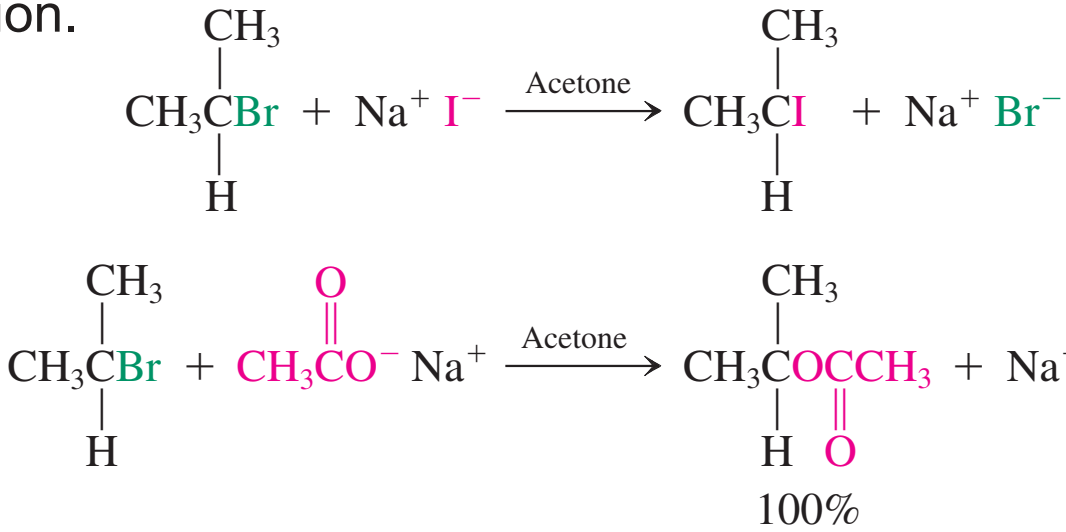
7.8 KEYS TO SUCCESS: SUBSTITUTION VERSUS ELIMINATION—STRUCTURE DETERMINES FUNCTION

This section will explain how consideration of *base strength* and *steric bulk* of the reacting species can help us decide whether substitution or elimination will predominate.

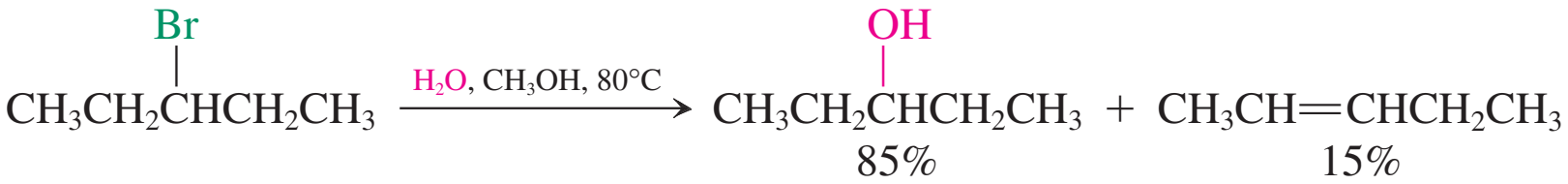
Weakly basic nucleophiles give substitution

Good nucleophiles (e.g., I^-, Br^-, RS^-, N_3^-, $RCOO^-$, and PR_3) that are weaker bases than hydroxide (OH^-) give good yields of S_N2 products with primary and secondary halides and of S_N1 products with tertiary substrates.

2-bromopropane reacts with both iodide and acetate ions cleanly through the S_N2 pathway, with virtually no competing elimination.



Weak nucleophiles such as water and alcohols react at appreciable rates only with secondary and tertiary halides, substrates capable of following the S_N1 pathway. Unimolecular elimination is usually only a minor side reaction.

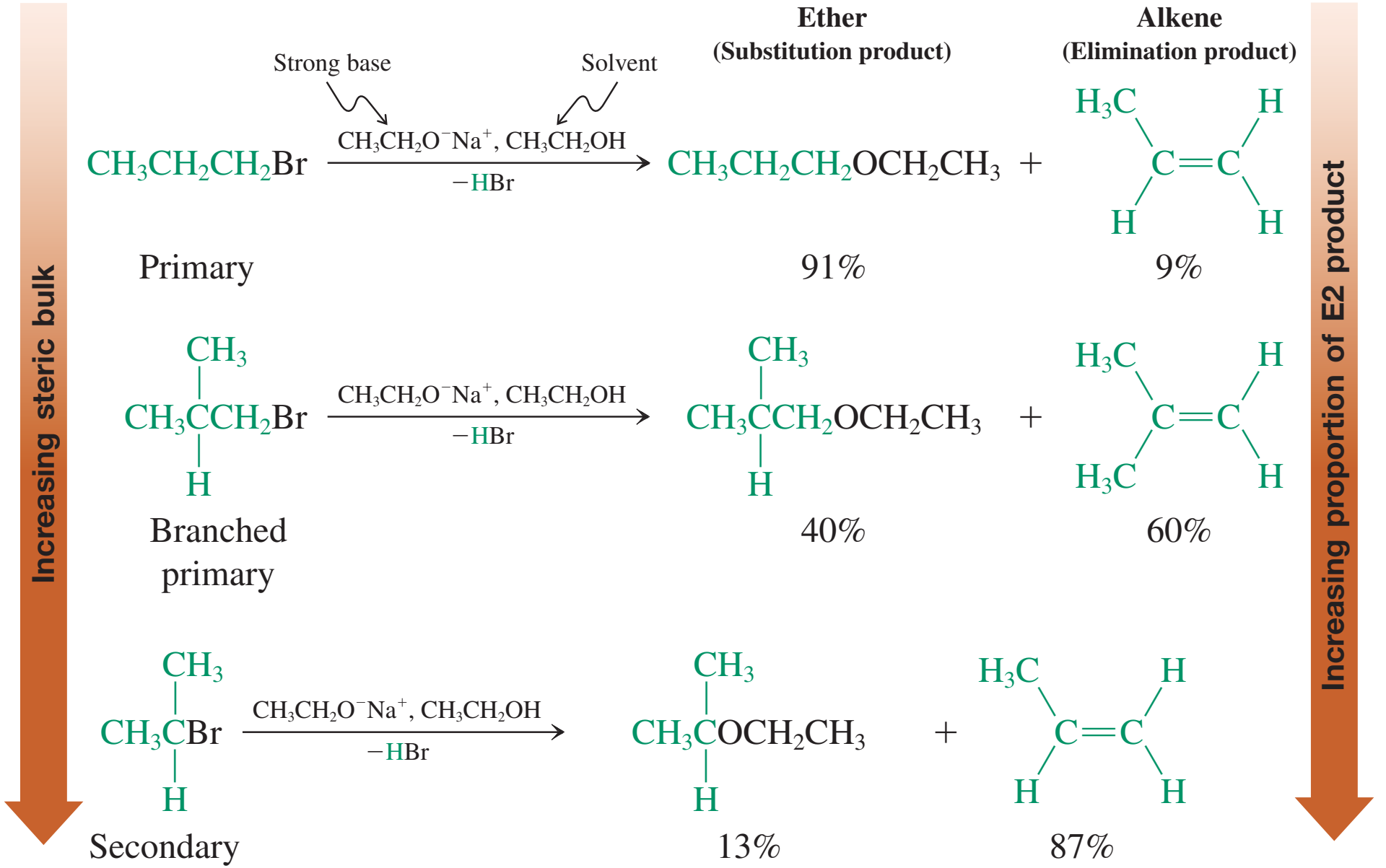


Strongly basic nucleophiles give more elimination as steric bulk increases

Reactions of simple primary halides with strongly basic nucleophiles give mostly S_N2 products.

As steric bulk is increased around the carbon bearing the leaving group, substitution is retarded relative to elimination because an attack at carbon is subject to more steric hindrance than is an attack on hydrogen.

Thus, branched primary substrates give about equal amounts of S_N2 and E2 reaction, whereas E2 is the major outcome with secondary substrates.

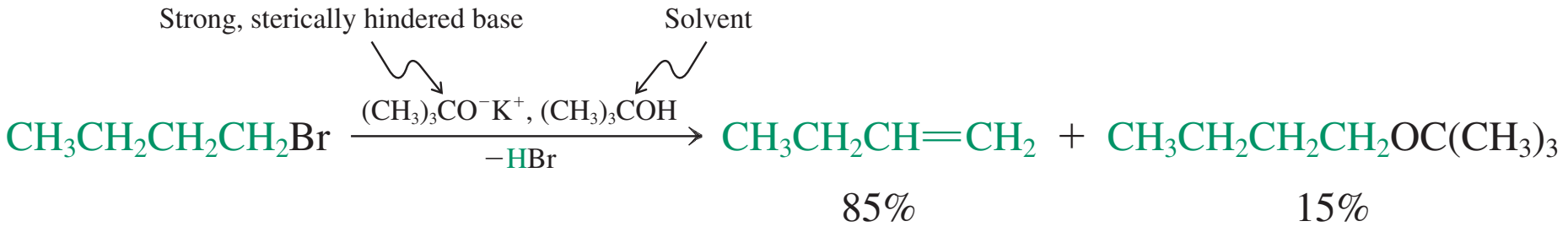

Increasing steric bulk
Strong base
Solvent
Ether
(Substitution product)
Alkene
(Elimination product)
CH3CH2CH2Br
CH3CH2O−Na+, CH3CH2OH
−HBr
CH3CH2CH2OCH2CH3
+
Primary
91%
9%
CH3
CH3CCH2Br
H
CH3CH2O−Na+, CH3CH2OH
−HBr
CH3CCH2OCH2CH3
+
Branched
primary
40%
60%
CH3
CH3CBr
H
CH3CH2O−Na+, CH3CH2OH
−HBr
CH3COCH2CH3
+
Secondary
13%
87%
Increasing proportion of E2 product

The S_N2 mechanism is disfavored for tertiary halides.

S_N1 and E1 pathways compete under neutral or weakly basic conditions. High concentrations of strong base give exclusively E2 reaction.

Sterically hindered basic nucleophiles favor elimination

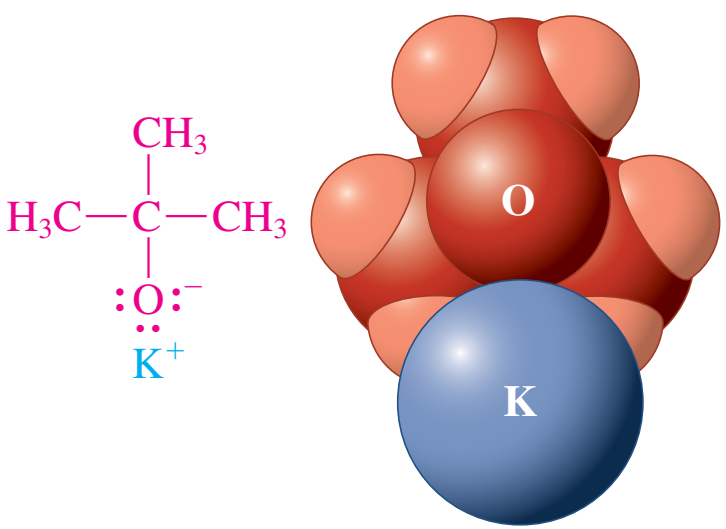
The steric bulk of the nucleophile hinders attack at the electrophilic carbon, thus elimination may predominate, even with primary systems, through deprotonation at the less hindered periphery of the molecule.



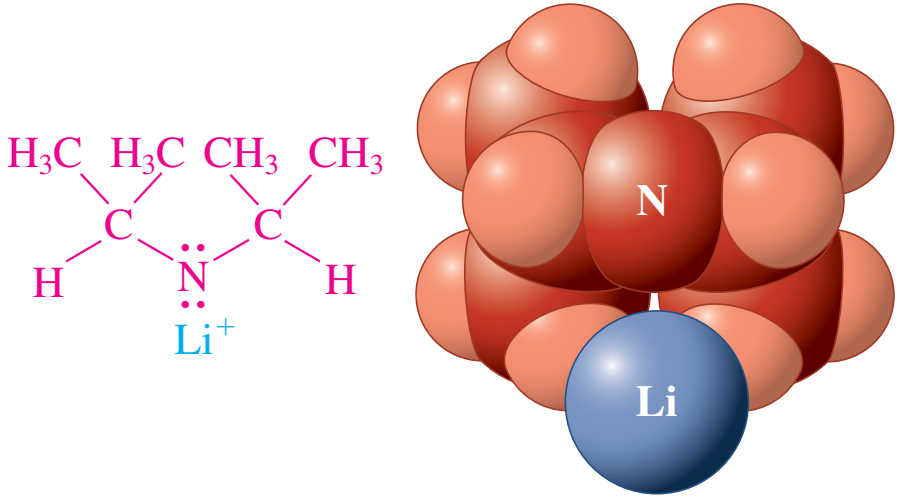
Two examples of sterically hindered bases that are frequently employed in eliminations are potassium *tert*-butoxide and lithium diisopropylamide (LDA).

For use in such reactions, these bases are frequently dissolved in their conjugate acids, 2-methyl-2-propanol (*tert*-butyl alcohol; pK_a = 18) and 1-methyl-*N*-(1-methylethyl)ethanamine (diisopropylamine; pK_a = 36), respectively.

Sterically Hindered Bases



Potassium *tert*-butoxide



Lithium diisopropylamide (LDA)

In Summary three principal factors affect the competition between substitution and elimination: basicity of the nucleophile, steric hindrance in the haloalkane, and steric bulk around the nucleophilic (basic) atom.

Factor 1. Base strength of the nucleophile

Weak Bases	Strong Bases
H_2O,* ROH,* PR_3, halides, RS^-, N_3^-, NC^-, $RCOO^-$	HO^-, RO^-, H_2N^-, R_2N^-
Substitution more likely	**Likelihood of elimination increased**

Factor 2. Steric hindrance around the reacting carbon

Sterically Unhindered	Sterically Hindered
Primary haloalkanes	Branched primary, secondary, tertiary haloalkanes
Substitution more likely	**Likelihood of elimination increased**

Factor 3. Steric hindrance in the nucleophile (strong base)

Sterically Unhindered	Sterically Hindered
HO^-, CH_3O^-, $CH_3CH_2O^-$, H_2N^-	$(CH_3)_3CO^-$, $[(CH_3)_2CH]_2N^-$
Substitution may occur	**Elimination strongly favored**

For simple predictive purposes, we assume that each of these factors is of equal importance in determining the ratio of elimination to substitution.

7.9 SUMMARY OF REACTIVITY OF HALOALKANES

Primary Haloalkanes. Unhindered primary alkyl substrates always react in a bimolecular way and almost always give predominantly substitution products, except when sterically hindered strong bases (e.g., potassium *tert*-butoxide) are employed.

In these cases, the S_N2 pathway is slowed down sufficiently for steric reasons to allow the E2 mechanism to take over. Another way of reducing substitution is to introduce branching.

Good nucleophiles still furnish predominantly substitution products. Only strong bases (e.g., alkoxides: RO^- or amides: R_2N^-) tend to react by elimination.

Primary (and methyl) haloalkanes react so exceedingly slowly with poor nucleophiles that for practical purposes we consider the combination to give “no reaction.”

Secondary Haloalkanes. Secondary alkyl systems undergo (depending on conditions) both eliminations and substitutions by either possible pathway: uni- or bimolecular.

Good nucleophiles favor S_N2, strong bases result in E2, and weakly nucleophilic polar media give mainly S_N1 and E1.

Tertiary Haloalkanes. Tertiary systems eliminate (E2) with concentrated strong base and are substituted in nonbasic media (S_N1).

Bimolecular substitution is almost never observed, but elimination by E1 accompanies S_N1.

Table 7-4 Likely Mechanisms by Which Haloalkanes React with Nucleophiles (Bases)

	Type of nucleophile (base)			
Type of haloalkane	Poor nucleophile (e.g., H_2O)	Weakly basic, good nucleophile (e.g., I^-)	Strongly basic, unhindered nucleophile (e.g., CH_3O^-)	Strongly basic, hindered nucleophile (e.g., $(CH_3)_3CO^-$)
Methyl	No reaction	S_N2	S_N2	S_N2
Primary				
Unhindered	No reaction	S_N2	S_N2	E2
Branched	No reaction	S_N2	E2	E2
Secondary	Slow S_N1, E1	S_N2	E2	E2
Tertiary	S_N1, E1	S_N1, E1	E2	E2