

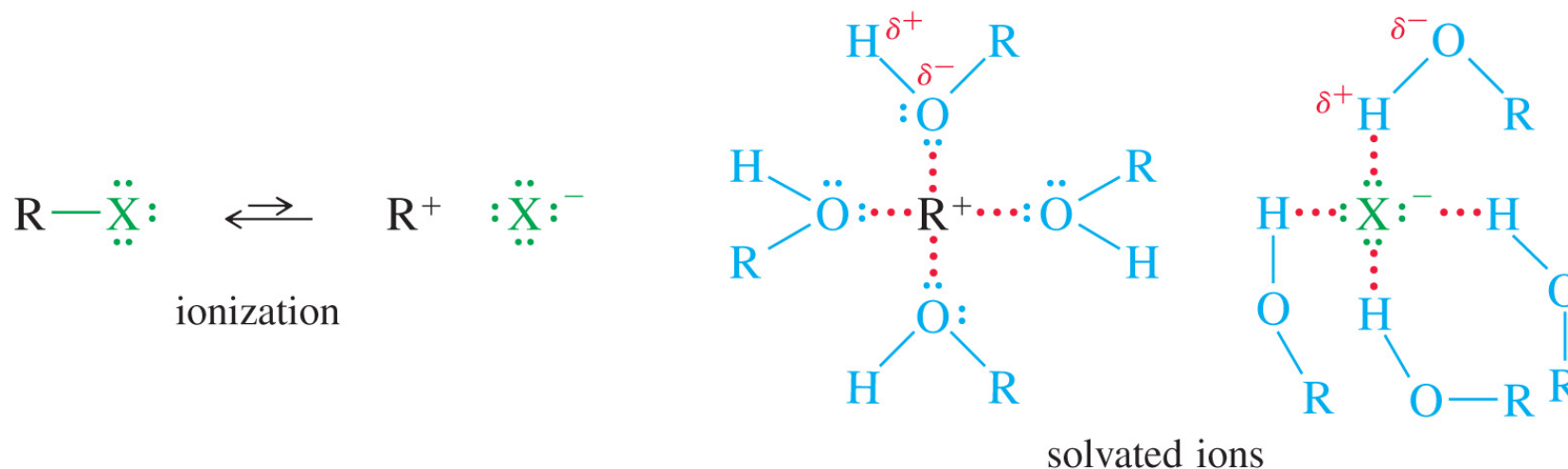
The Effect of Solvent on Nucleophilicity

A **protic solvent** contains a hydrogen bonded to an oxygen or a nitrogen; it is a hydrogen bond donor.

Aprotic polar solvents such as DMSO and DMF facilitate the reaction of ionic compounds because they **solvate cations**.

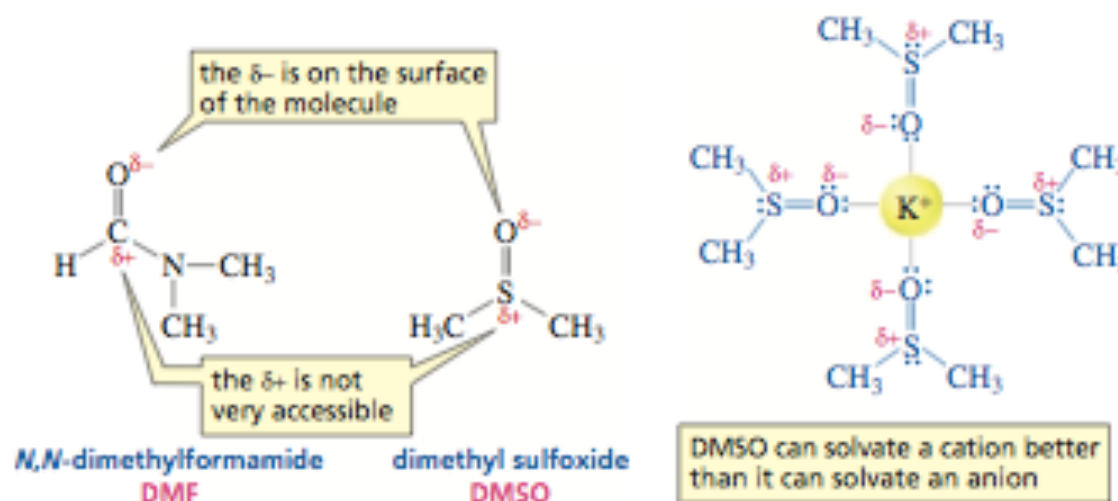
Solvation Effect

- Polar protic solvent best because it can solvate both cations and anions.



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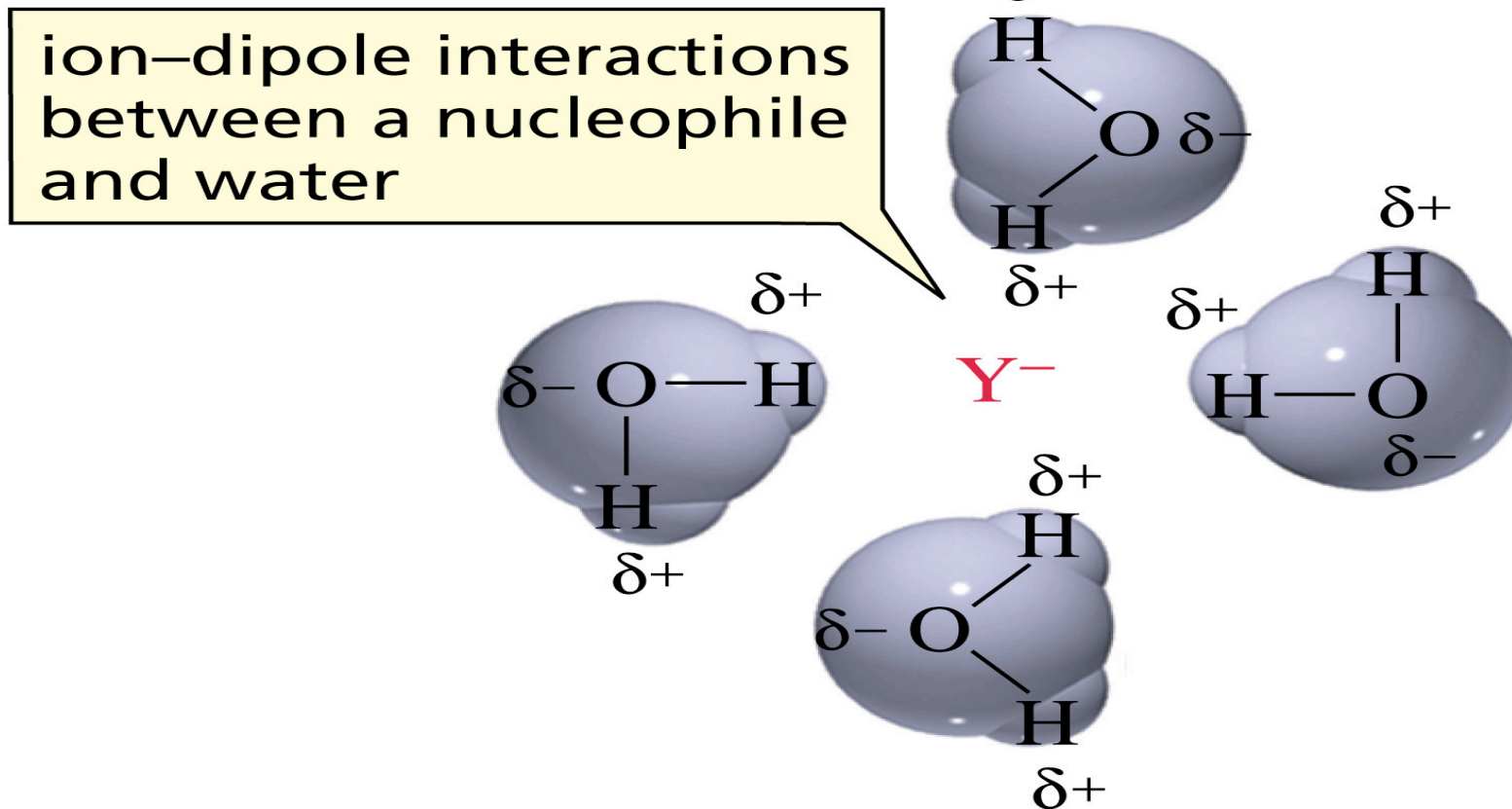
An **aprotic polar solvent is not a hydrogen bond donor** because it does not have a hydrogen attached to an oxygen or to a nitrogen, so there are no positively charged hydrogens to form ion–dipole interactions. The molecules of an **aprotic polar solvent have a partial negative charge on their surface that can solvate cations**, but the **partial positive charge is on the inside of the molecule, which makes it less accessible**. The relatively “*naked*” anion can be a powerful nucleophile in an aprotic polar solvent. **Fluoride ion, therefore, is a better nucleophile in DMSO than it is in water.**



Polar aprotic solvents solvate **cations only**.

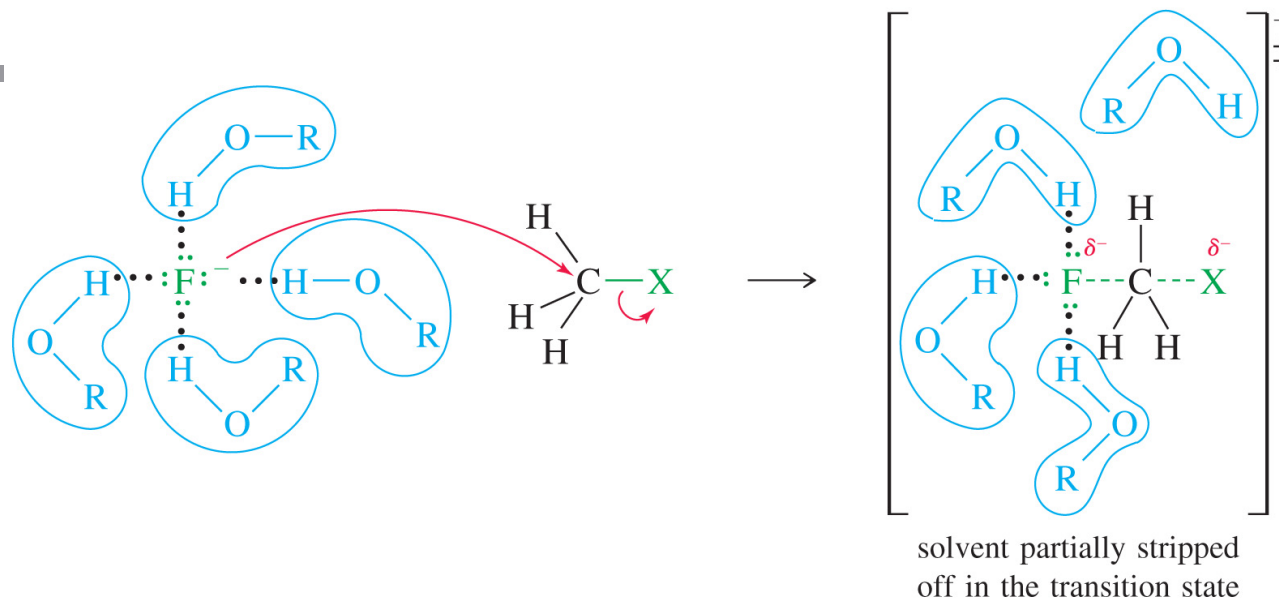
The Effect of Solvent on Nucleophilicity

Consider the ion–dipole interaction



The solvent **shields the nucleophile**, therefore, at least one of the ion–dipole interactions must be broken before the nucleophile can participate in an S_N2 reaction.

Solvent Effects: Protic Solvents



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- Polar protic solvents have acidic hydrogens (O—H or N—H) which can solvate the nucleophile reducing their nucleophilicity.
- Nucleophilicity in protic solvents **increases as the size** of the atom increases.

It is **easier to break the ion-dipole interactions** between a weak base and the solvent than between a strong base and the solvent

Aprotic polar solvents such as DMSO and DMF facilitate the reaction of ionic compounds because they solvate cations.

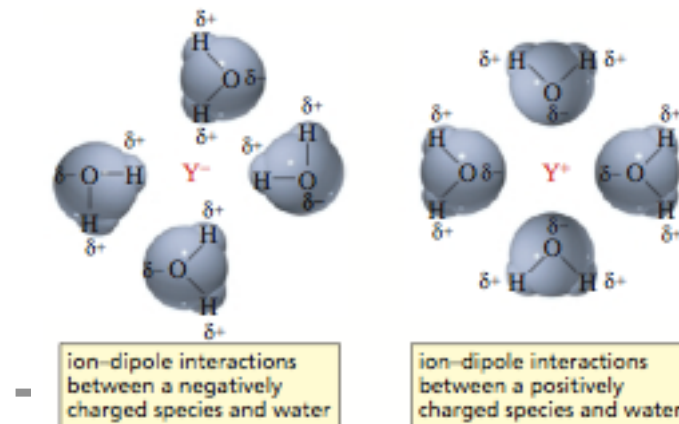
The Role of the Solvent in S_N2 and S_N1 Reactions

The **dielectric constant** of a solvent is a measure of how well the solvent can insulate (solvate) opposite charges from one another.

Solvent molecules insulate charges by clustering around a charge, so that the positive poles of the solvent molecules surround negative charges while the negative poles of the solvent molecules surround positive charges.



The interaction between a solvent and an ion or a molecule dissolved in that solvent is called *solvation*.

When an ion interacts with a polar solvent, the charge is **no longer localized** solely on the ion, **but is spread out to the surrounding solvent molecules**. **Spreading out the charge stabilizes the charged species**.



Polar solvents have **high dielectric constants** and thus **are very good at insulating (solvating) charges**. Nonpolar solvents have **low dielectric constants** and **are poor insulators**. The dielectric constants of some common solvents are listed in Table 10.7. In this table, solvents are divided into two groups: **protic solvents and aprotic solvents**.

Table 10.7 The Dielectric Constants of Some Common Solvents

Solvent	Structure	Abbreviation	Dielectric constant (ϵ , at 25 °C)	Boiling point (°C)
<i>Protic solvents</i>				
Water	H ₂ O	—	79	100
Formic acid	HCOOH	—	59	100.6
Methanol	CH ₃ OH	MeOH	33	64.7
Ethanol	CH ₃ CH ₂ OH	EtOH	25	78.3
<i>tert</i> -Butyl alcohol	(CH ₃) ₃ COH	<i>tert</i> -BuOH	11	82.3
Acetic acid	CH ₃ COOH	HOAc	6	117.9
<i>Aprotic solvents</i>				
Dimethyl sulfoxide	(CH ₃) ₂ SO	DMSO	47	189
Acetonitrile	CH ₃ CN	MeCN	38	81.6
Dimethylformamide	(CH ₃) ₂ NCHO	DMF	37	153
Hexamethylphosphoric acid triamide	[(CH ₃) ₂ N] ₃ PO	HMPA	30	233
Acetone	(CH ₃) ₂ CO	Me ₂ CO	21	56.3
Dichloromethane	CH ₂ Cl ₂	—	9.1	40
Tetrahydrofuran		THF	7.6	66
Ethyl acetate	CH ₃ COOCH ₂ CH ₃	EtOAc	6	77.1
Diethyl ether	CH ₃ CH ₂ OCH ₂ CH ₃	Et ₂ O	4.3	34.6
Benzene		—	2.3	80.1
Hexane	CH ₃ (CH ₂) ₄ CH ₃	—	1.9	68.7

The Effect of the Solvent on the Rate of a Reaction

One simple rule describes how a change in solvent will affect the rate of most chemical reactions: *Increasing the polarity of the solvent will decrease the rate of the reaction if one or more reactants in the rate-determining step are charged and will increase the rate of the reaction if none of the reactants in the rate-determining step is charged.*

The **rate of a reaction** depends on **the difference between the free energy** of the reactants and the free energy of the transition state in the rate-determining step of the reaction.

The greater the charge on the solvated molecule, **the stronger the interaction** with a polar solvent and **the more the charge will be stabilized.**

The Effect of the Solvent on the Rate of an S_N1 Reaction

The alkyl halide is the only reactant in the rate-determining step of an S_N1 reaction. It is a neutral molecule with a small dipole moment. The rate-determining transition state has a greater charge because as the carbon–halogen bond breaks, the carbon becomes more positive and the halogen becomes more negative. **Since the charge on the transition state is greater than the charge on the reactant, increasing the polarity of the solvent will increase the rate of the S_N1 reaction** (Figure 10.8).

If, however, the compound undergoing an S_N1 reaction is charged, increasing the polarity of the solvent will *decrease the rate of the reaction* because the more polar solvent will stabilize the full charge on the reactant to a greater extent than it will stabilize the dispersed charge on the transition state (Figure 10.7).

rate-determining step of an S_N1 reaction

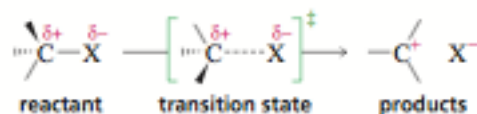


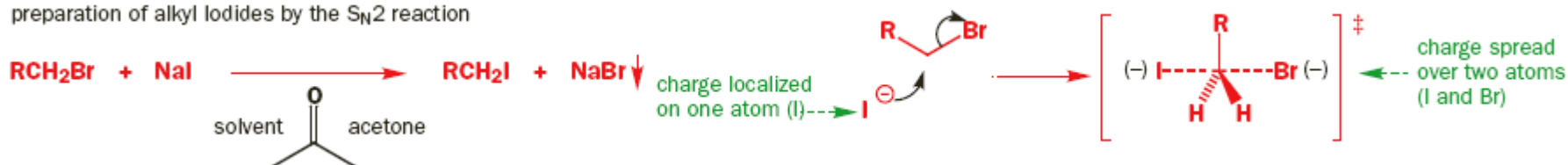
Table 10.8 The Effect of the Polarity of the Solvent on the Rate of Reaction of *tert*-Butyl Bromide in an S_N1 Reaction

Solvent	Relative rate
100% water	1200
80% water / 20% ethanol	400
50% water / 50% ethanol	60
20% water / 80% ethanol	10
100% ethanol	1

The Effect of the Solvent on the Rate of an S_N2 Reaction

Most S_N2 reactions of alkyl halides involve a **neutral alkyl halide and a charged nucleophile**. Increasing the polarity of a solvent will have a strong stabilizing effect on the negatively charged nucleophile. The transition state also has a negative charge, but the charge is **dispersed over two atoms**. Consequently, the interactions between the solvent and the transition state are not as strong as the interactions between the solvent and the fully charged nucleophile. Therefore, a polar solvent stabilizes the nucleophile more than it stabilizes the transition state, so *increasing the polarity of the solvent will decrease the rate of the reaction* (Figure 10.7).

preparation of alkyl iodides by the S_N2 reaction



If, however, the S_N2 reaction involves an **alkyl halide and a neutral nucleophile**, the charge on the transition state will be larger than the charge on the neutral reactants, so **increasing the polarity of the solvent will increase the rate of the substitution reaction** (Figure 10.8).

The Effect of the Solvent on the Rate of an S_N2 Reaction

Aprotic polar solvents solvate negative charges particularly poorly (Section 10.3). Thus, the rate of an S_N2 reaction involving a negatively charged nucleophile will be greater in an aprotic polar solvent than in a protic polar solvent. Consequently, **an aprotic polar solvent is the solvent of choice for an S_N2 reaction in which the nucleophile is negatively charged, whereas a protic polar solvent is used if the nucleophile is a neutral molecule.**

When an alkyl halide can undergo either S_N1 or S_N2 ,

➤ the concentration of the nucleophile,

➤ the reactivity of the nucleophile,

➤ and the solvent of the reaction

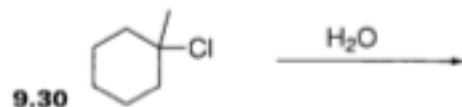
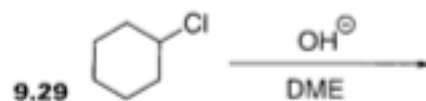
will determine which reaction will predominate

An S_N2 reaction of an alkyl halide is favored by a high concentration of a good (*negatively charged*) nucleophile in an aprotic polar solvent.

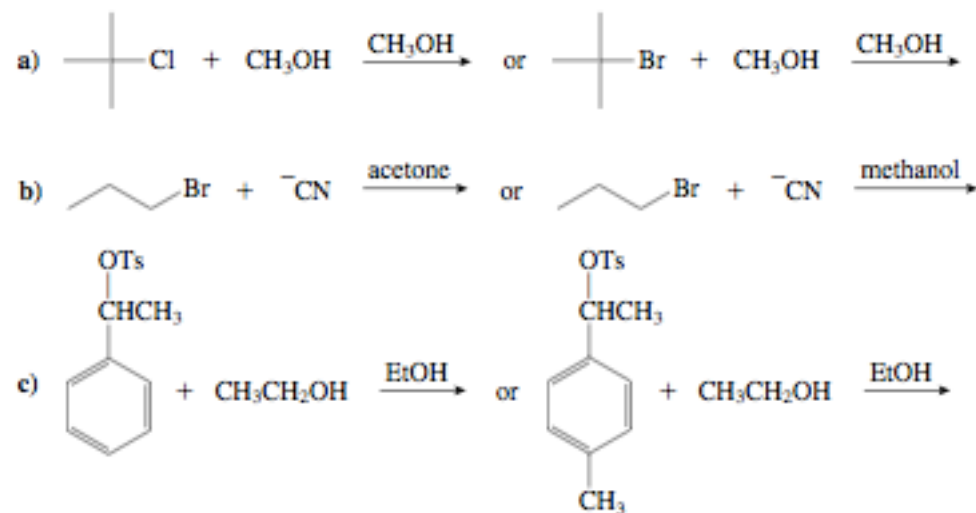
An S_N1 reaction of an alkyl halide is favored by a low concentration of a poor (*neutral*) nucleophile in a protic polar solvent.

For each reaction below, look at all of the reagents and conditions, and determine if the reaction will proceed via an S_N2 or an S_N1 , or both or neither.

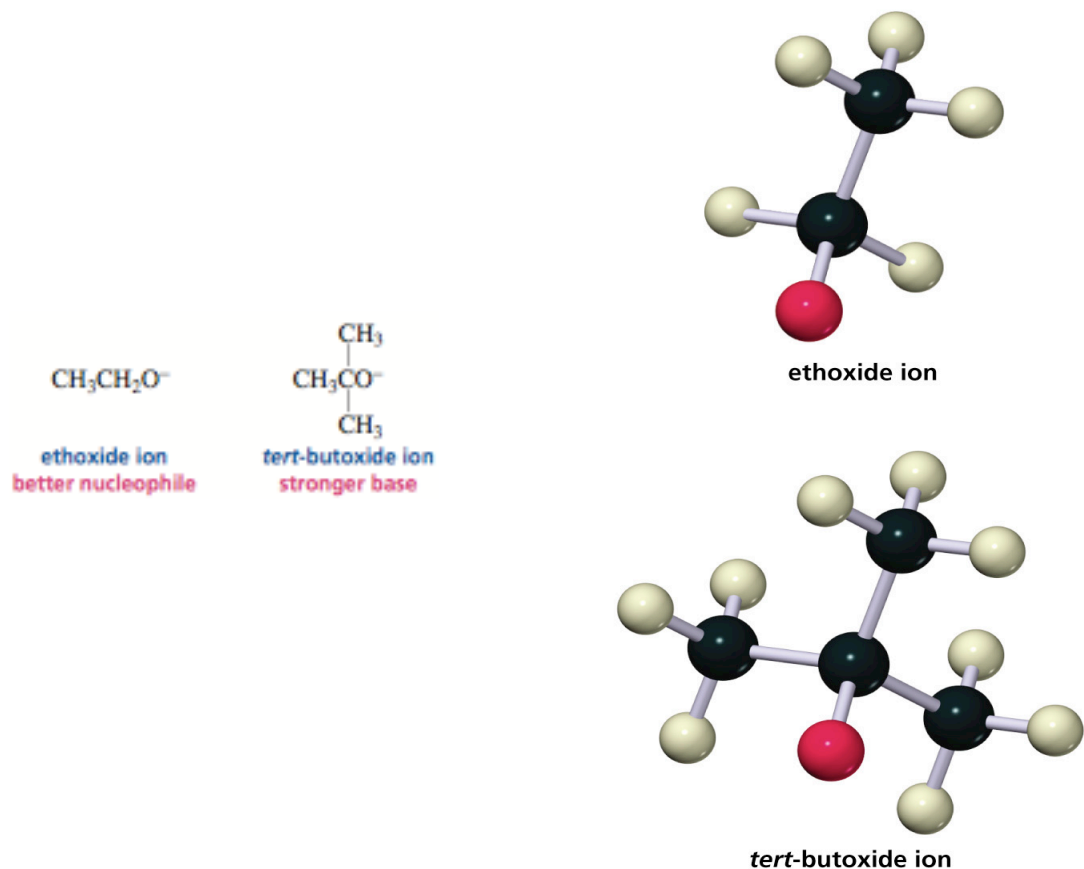
PROBLEMS For each reaction below, look at all of the reagents and conditions, and determine if the reaction will proceed via an S_N2 or an S_N1 , or both or neither.



8.28 Explain whether each pair of reactions should follow an S_N1 or an S_N2 mechanism. Then explain which member of the pair should proceed at a faster rate.



Nucleophilicity Is Affected by Steric Effects



Steric effects affect nucleophilicity, but not basicity

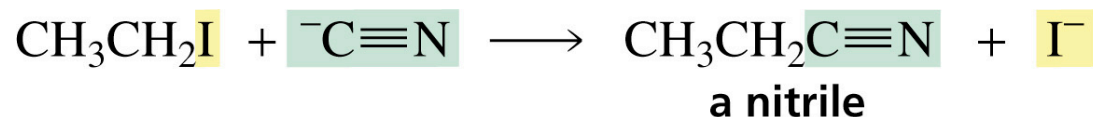
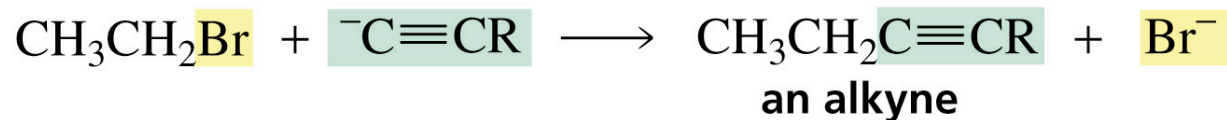
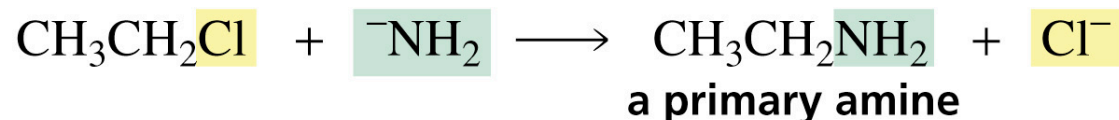
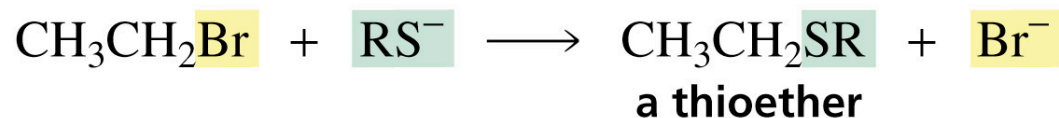
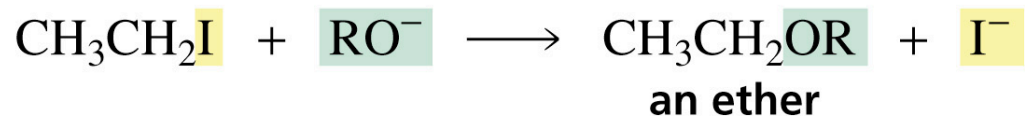
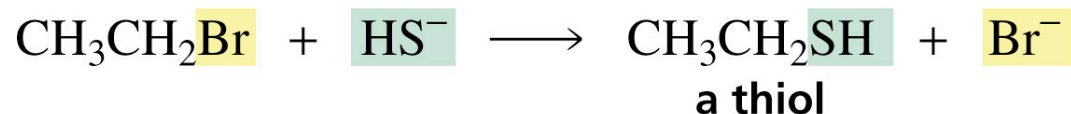
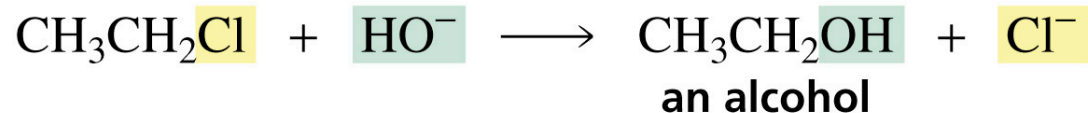
Nucleophilicity Is Affected by Steric Effects

Base strength is relatively unaffected by steric effects because a base removes a relatively unhindered proton. Thus, *tert-butoxide ion is a stronger base than ethoxide ion since tert-butanol ($pK_a = 18$) is a weaker acid than ethanol ($pK_a = 15.9$).*

Steric effects, on the other hand, do affect nucleophilicity. A bulky nucleophile cannot approach the back side of a carbon as easily as a less sterically hindered nucleophile can. Thus, the bulky *tert-butoxide ion, with its three methyl groups, is a poorer nucleophile than ethoxide ion even though tert-butoxide ion is a stronger base.*

The Reversibility of an S_N2 Reaction

An S_N2 reaction proceeds in the direction that allows the strongest base to displace the weaker base



Various products that can be obtained via substitution reactions.



<i>Nucleophile</i>		\longrightarrow	<i>Product</i>		<i>Class of Product</i>
R—X	+ $\text{:}\ddot{\text{I}}\text{:}$	\longrightarrow	R— $\ddot{\text{I}}\text{:}$		alkyl halide
R—X	+ $\text{:}\ddot{\text{O}}\text{H}$	\longrightarrow	R— $\ddot{\text{O}}\text{H}$		alcohol
R—X	+ $\text{:}\ddot{\text{O}}\text{R}'$	\longrightarrow	R— $\ddot{\text{O}}\text{R}'$		ether
R—X	+ $\text{:}\ddot{\text{S}}\text{H}$	\longrightarrow	R— $\ddot{\text{S}}\text{H}$		thiol (mercaptan)
R—X	+ $\text{:}\ddot{\text{S}}\text{R}'$	\longrightarrow	R— $\ddot{\text{S}}\text{R}'$		thioether (sulfide)
R—X	+ :NH_3	\longrightarrow	R— NH_3^+	X^-	amine salt
R—X	+ $\text{:}\ddot{\text{N}}=\overset{+}{\text{N}}=\ddot{\text{N}}\text{:}^-$	\longrightarrow	R— $\ddot{\text{N}}=\overset{+}{\text{N}}=\ddot{\text{N}}\text{:}^-$		azide
R—X	+ $\text{:C}\equiv\text{C—R}'$	\longrightarrow	R— $\text{C}\equiv\text{C—R}'$		alkyne
R—X	+ $\text{:C}\equiv\text{N:}$	\longrightarrow	R— $\text{C}\equiv\text{N:}$		nitrile
R—X	+ $\text{R}'\text{—CO}\ddot{\text{O}}\text{:}^-$	\longrightarrow	R'— COO—R		ester
R—X	+ :PPh_3	\longrightarrow	$[\text{R—PPh}_3]^+$	X^-	phosponium salt

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