

8.8

Unimolecular Nucleophilic Substitution

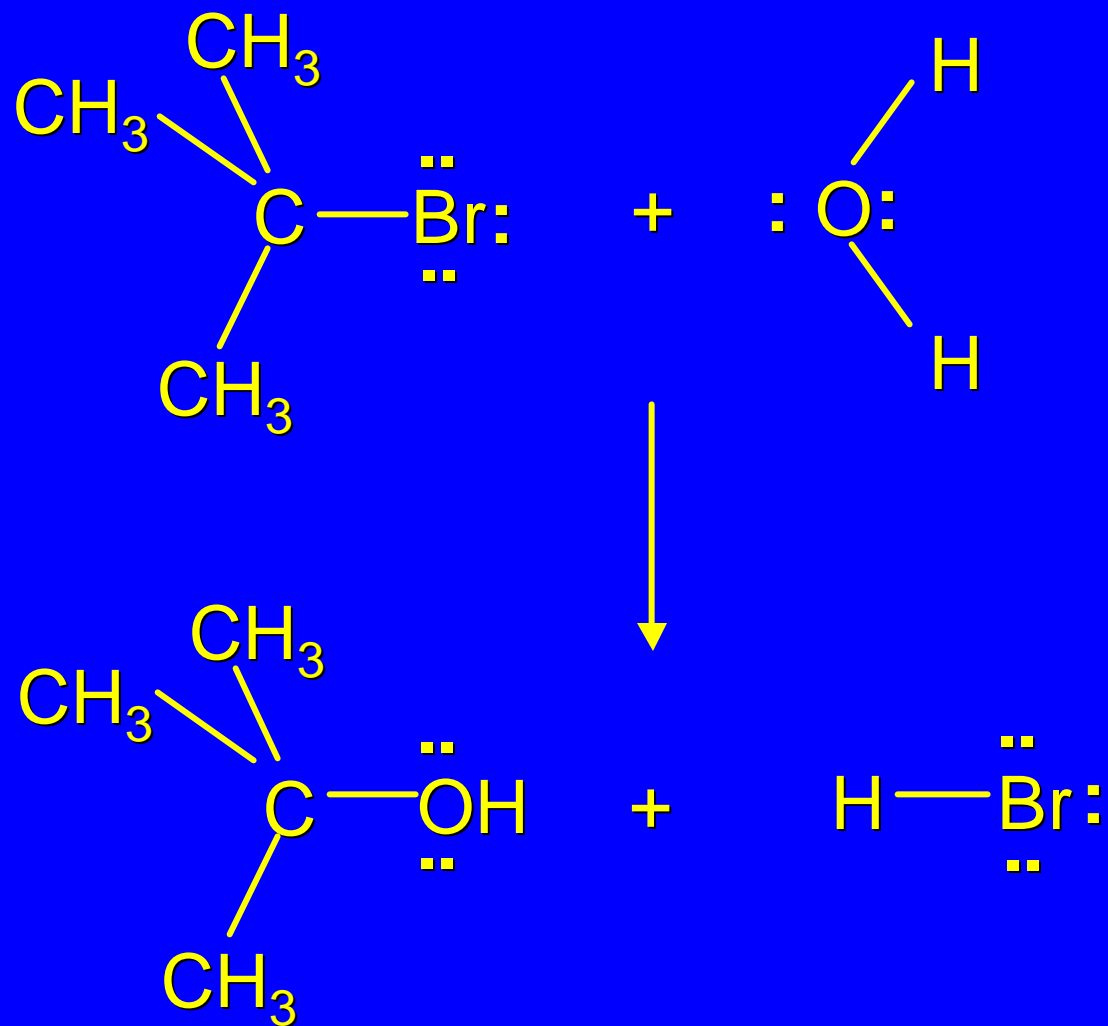
S_N1

A question...

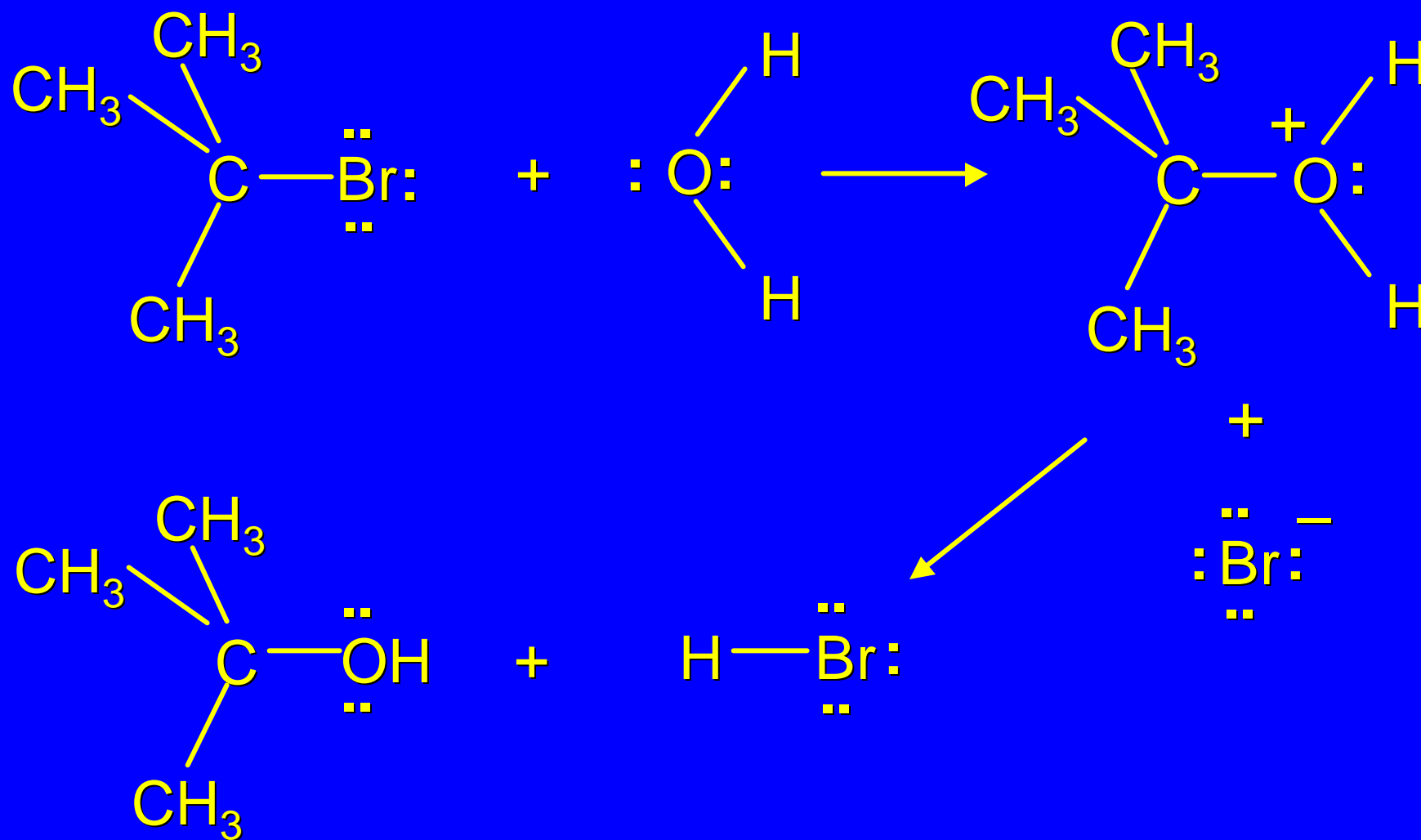
Tertiary alkyl halides are very unreactive in substitutions that proceed by the S_N2 mechanism. Do they undergo nucleophilic substitution at all?

Yes. But by a mechanism different from S_N2 . The most common examples are seen in solvolysis reactions.

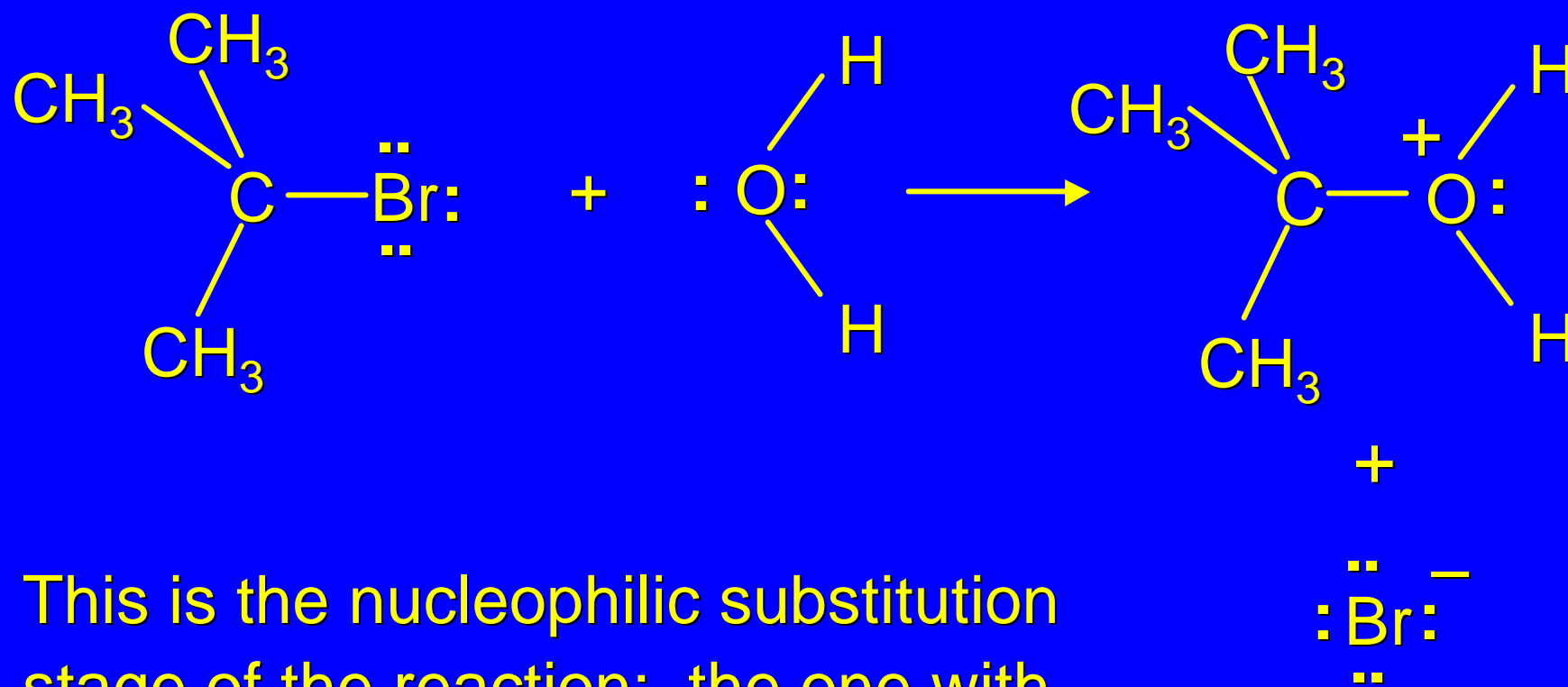
Example of a solvolysis. Hydrolysis of tert-butyl bromide.



Example of a solvolysis. Hydrolysis of tert-butyl bromide.

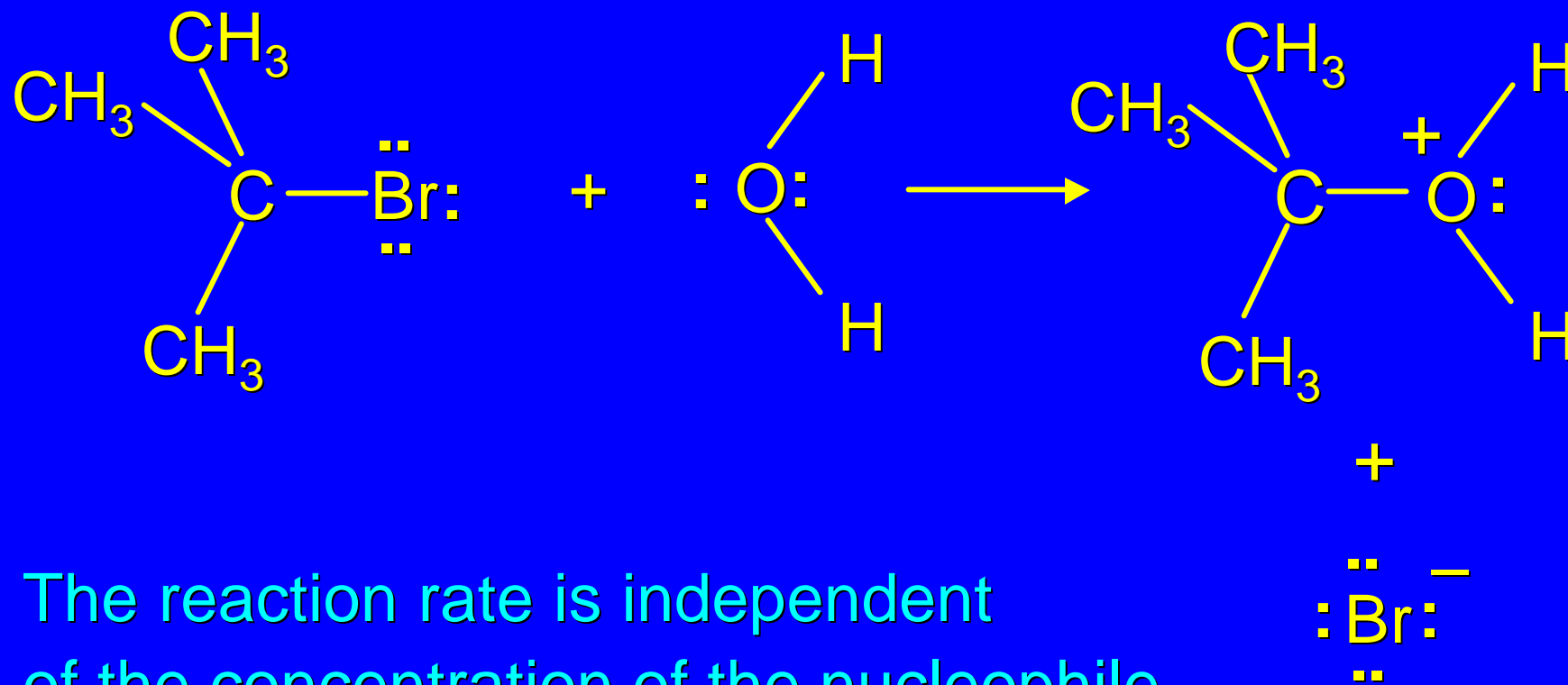


Example of a solvolysis. Hydrolysis of tert-butyl bromide.



This is the nucleophilic substitution stage of the reaction; the one with which we are concerned.

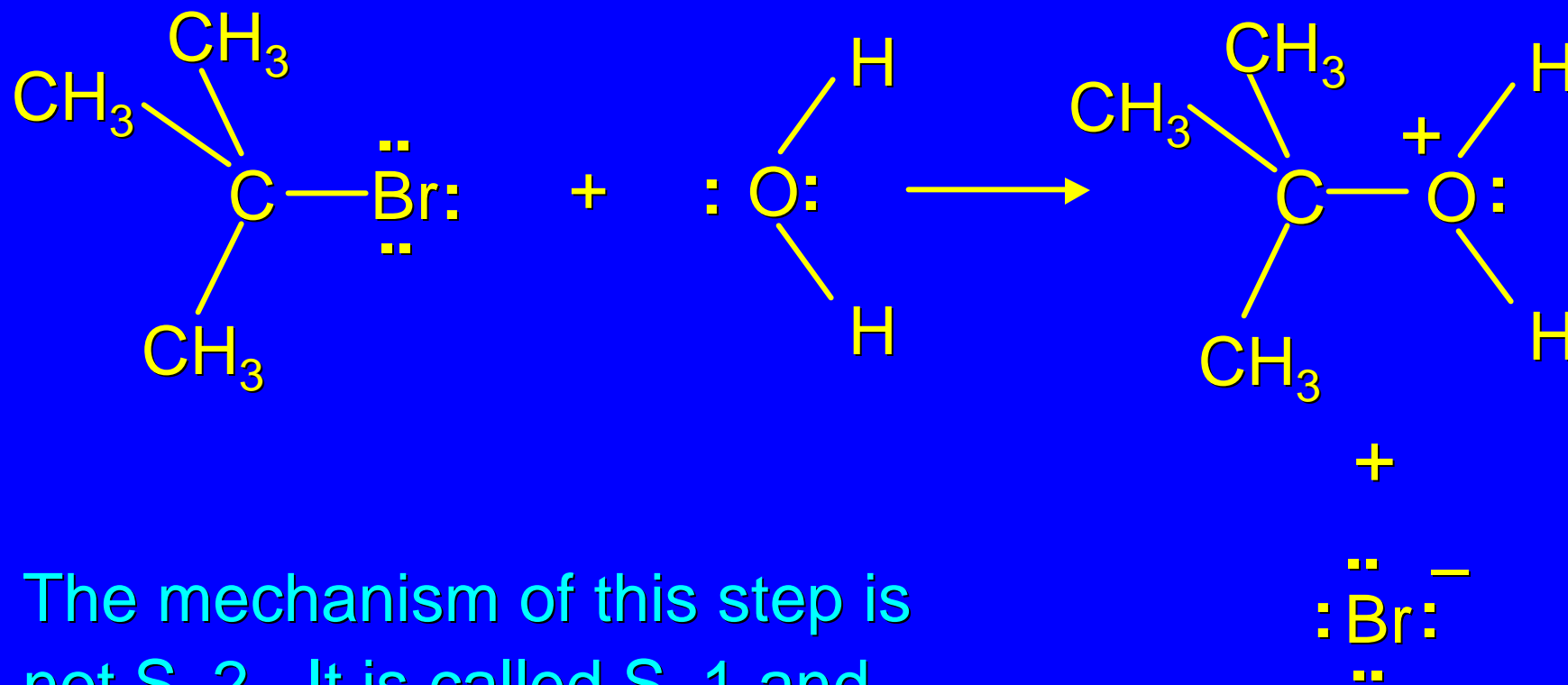
Example of a solvolysis. Hydrolysis of tert-butyl bromide.



The reaction rate is independent of the concentration of the nucleophile and follows a first-order rate law.

$$\text{rate} = k[(\text{CH}_3)_3\text{CBr}]$$

Example of a solvolysis. Hydrolysis of tert-butyl bromide.



The mechanism of this step is not S_N2. It is called S_N1 and begins with ionization of (CH₃)₃CBr.

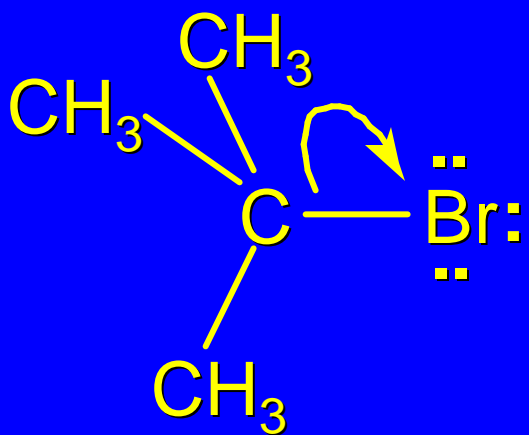
Kinetics and Mechanism

$$\text{rate} = k[\text{alkyl halide}]$$

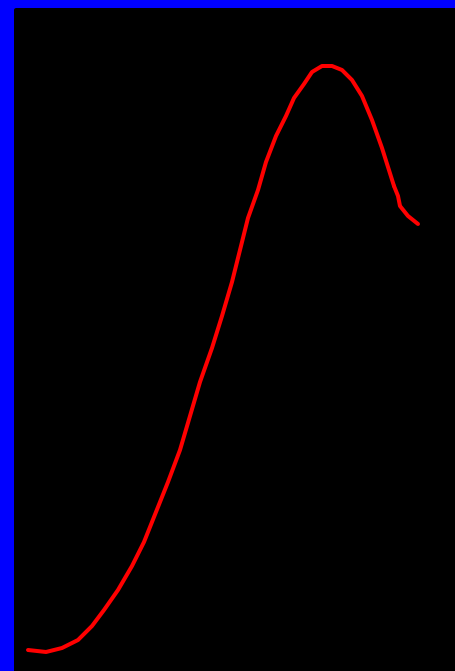
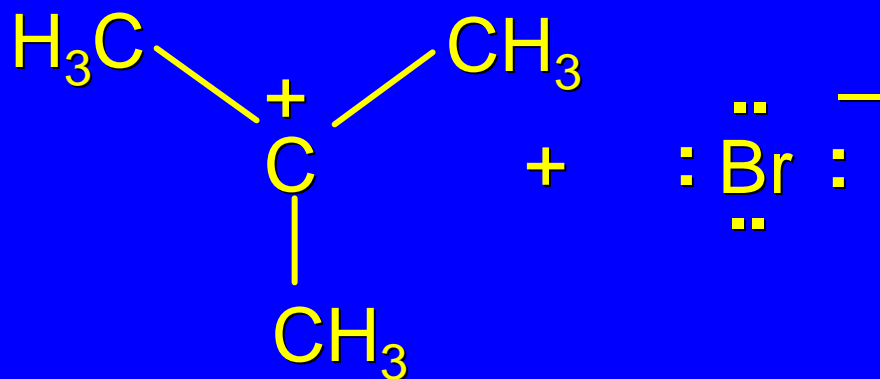
First-order kinetics implies a unimolecular rate-determining step.

Proposed mechanism is called S_N1 , which stands for
substitution nucleophilic unimolecular

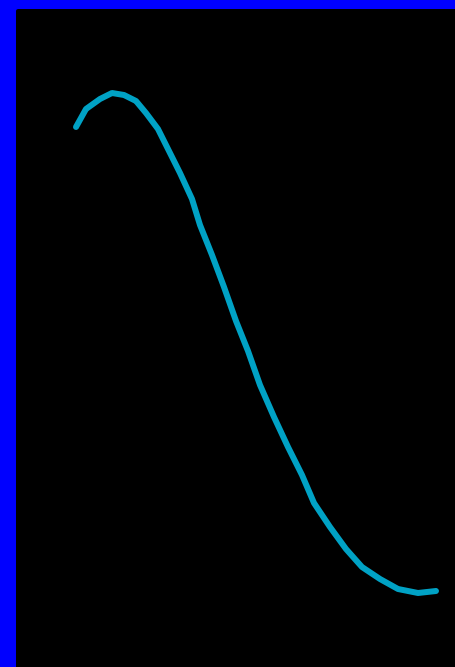
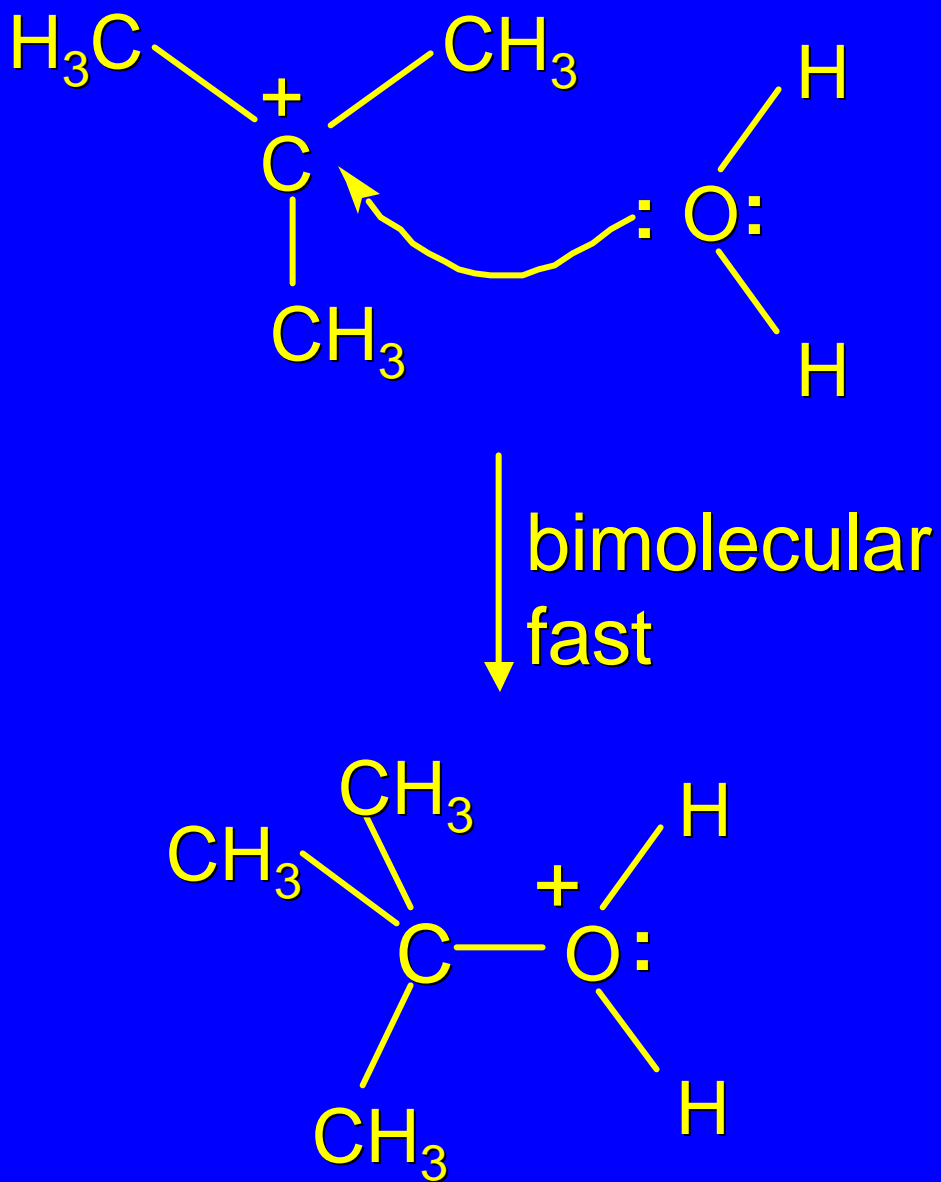
Mechanism



unimolecular
slow



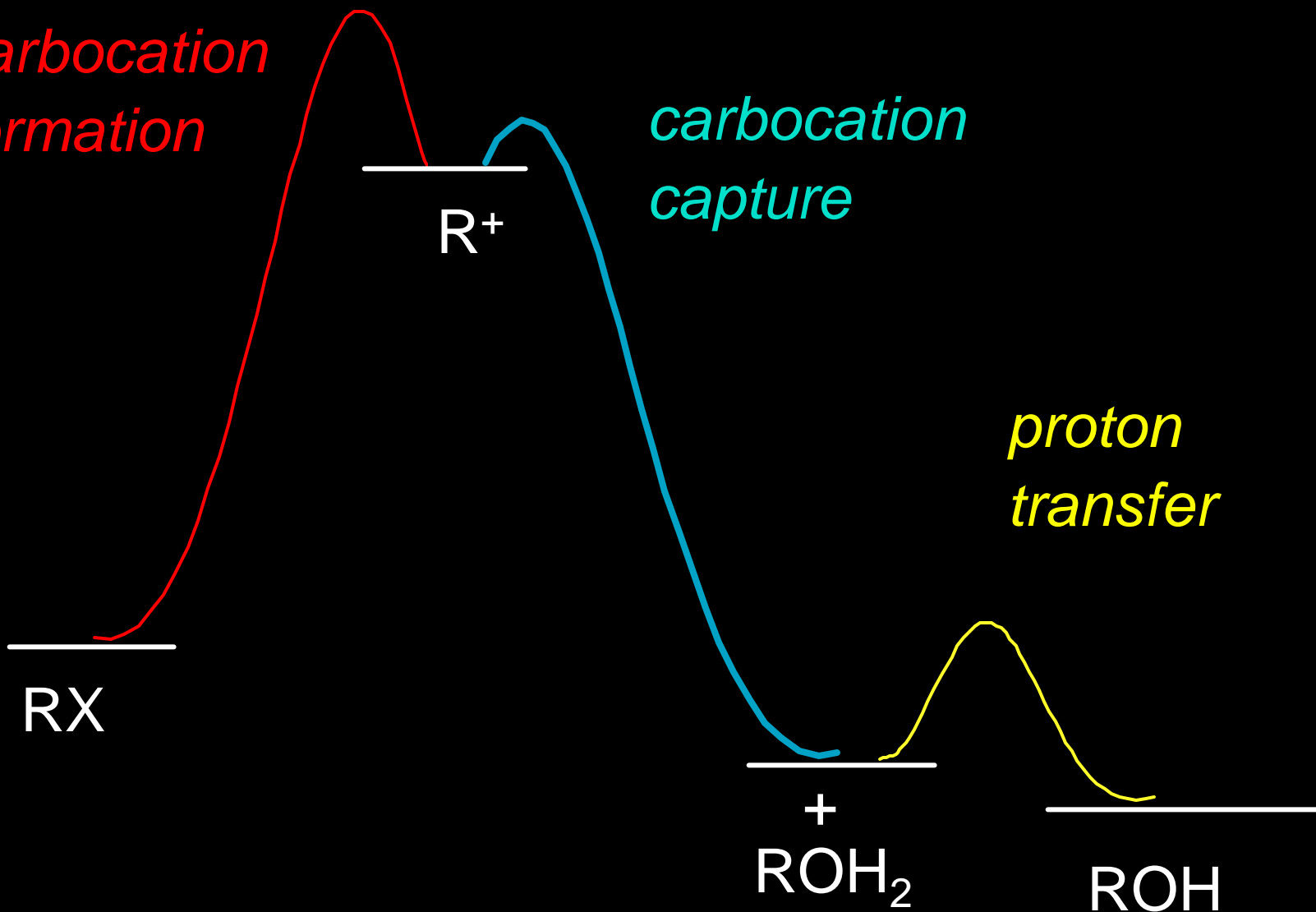
Mechanism



*carbocation
formation*

*carbocation
capture*

*proton
transfer*



Characteristics of the S_N1 mechanism

first order kinetics: rate = $k[RX]$

unimolecular rate-determining step

carbocation intermediate

rate follows carbocation stability

rearrangements sometimes observed

reaction is not stereospecific

much racemization in reactions of
optically active alkyl halides

8.9
Carbocation Stability and S_N1 Reaction
Rates

Electronic Effects Govern S_N1 Rates

The rate of nucleophilic substitution by the S_N1 mechanism is governed by electronic effects.

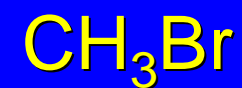
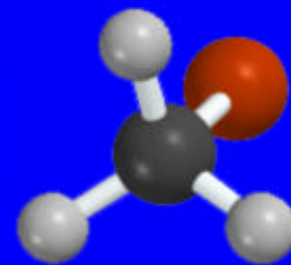
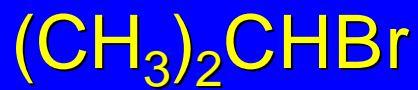
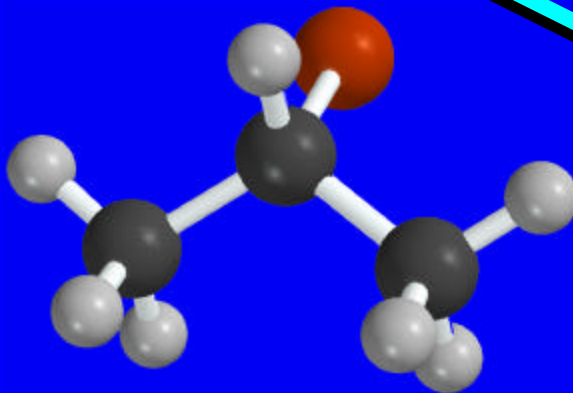
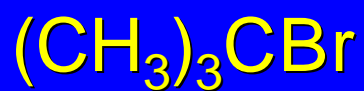
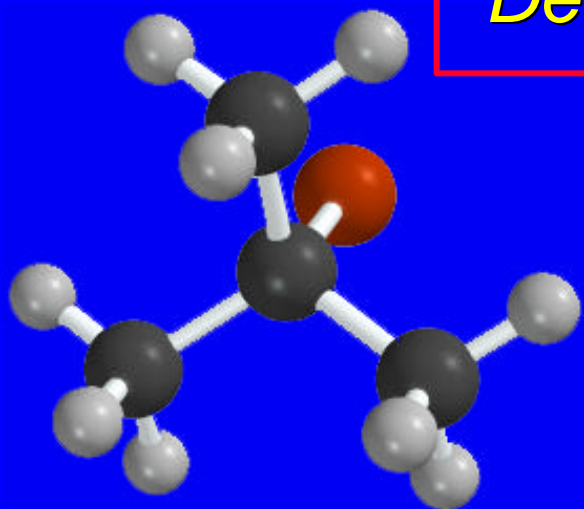
Carbocation formation is rate-determining. The more stable the carbocation, the faster its rate of formation, and the greater the rate of unimolecular nucleophilic substitution.

Table 8.5 Reactivity toward substitution by the S_N1 mechanism

RBr solvolysis in aqueous formic acid

Alkyl bromide	Class	Relative rate
CH_3Br	Methyl	1
$\text{CH}_3\text{CH}_2\text{Br}$	Primary	2
$(\text{CH}_3)_2\text{CHBr}$	Secondary	43
$(\text{CH}_3)_3\text{CBr}$	Tertiary	100,000,000

Decreasing S_N1 Reactivity



8.10
Stereochemistry of S_N1 Reactions

Generalization

Nucleophilic substitutions that exhibit first-order kinetic behavior are not stereospecific.

Stereochemistry of an S_N1 Reaction

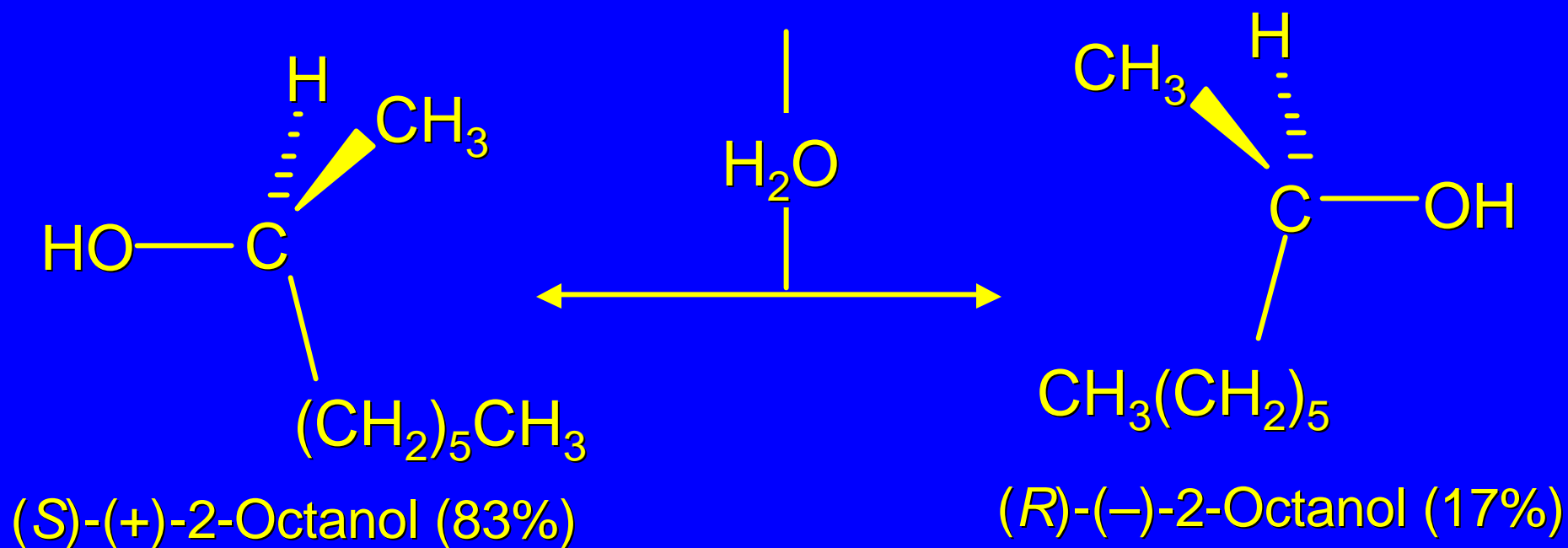
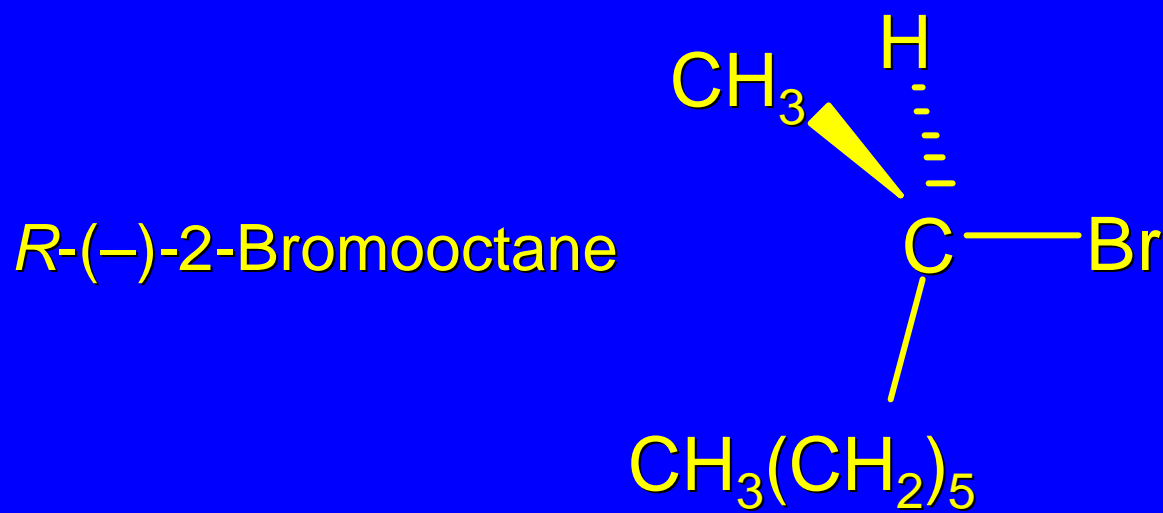
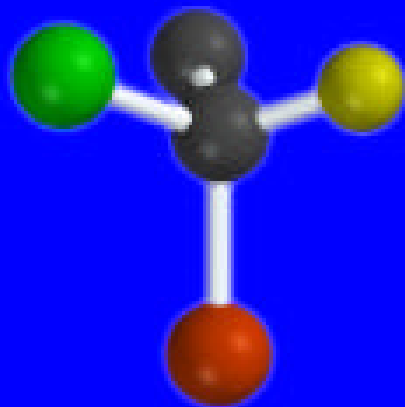


Figure 8.8



Ionization step
gives carbocation; three
bonds to stereogenic
center become coplanar

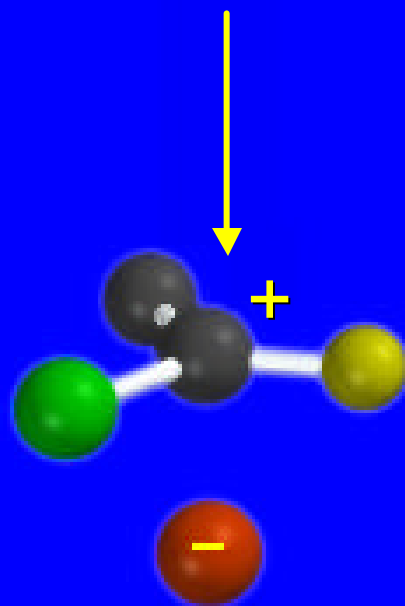
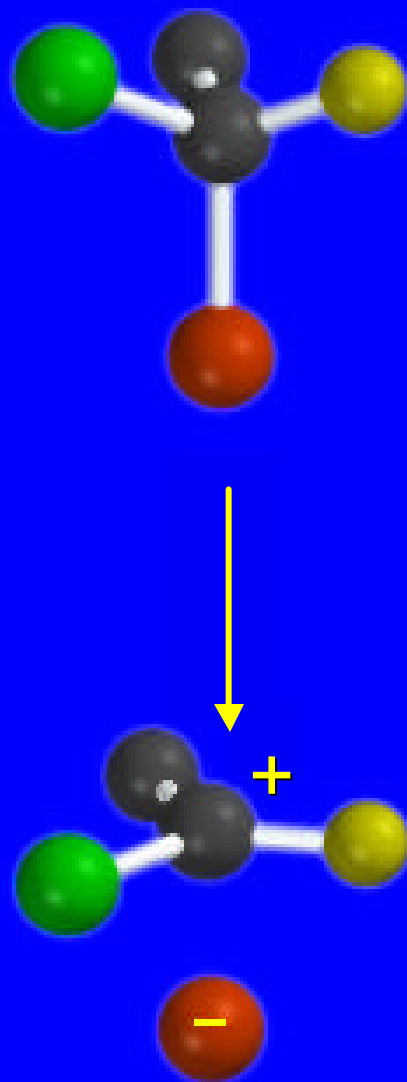
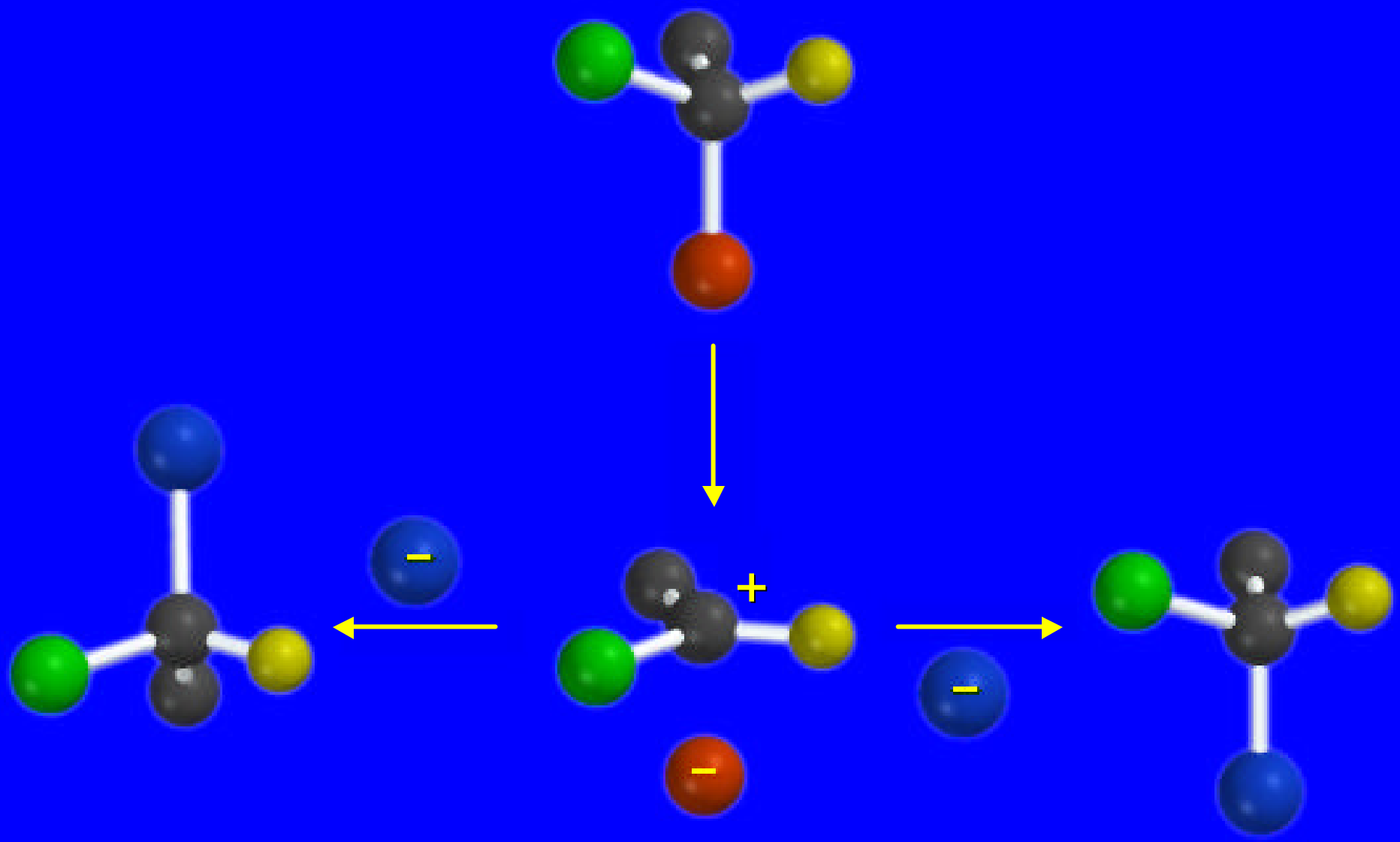


Figure 8.8



Leaving group shields
one face of carbocation;
nucleophile attacks
faster at opposite face.



More than 50%

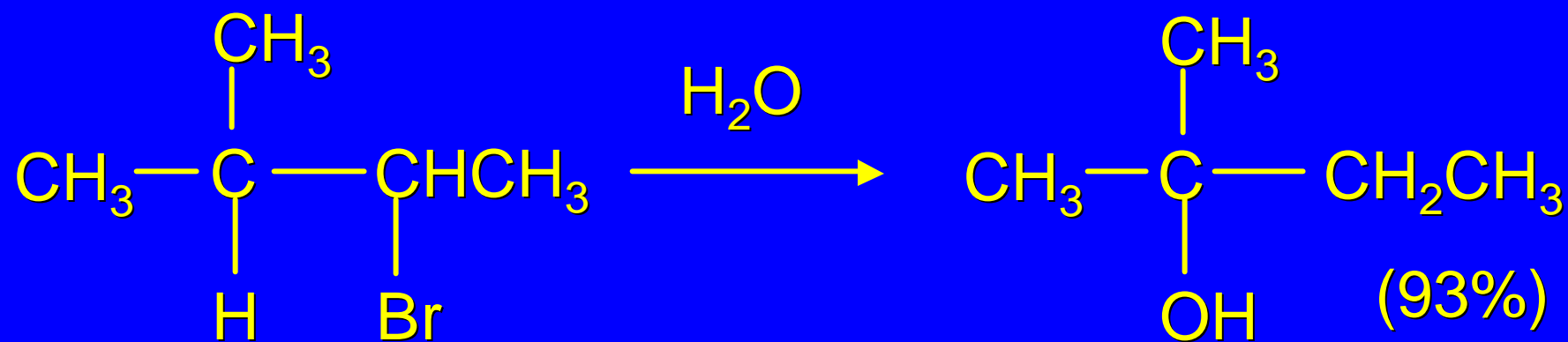
Less than 50%

8.11
Carbocation Rearrangements
in S_N1 Reactions

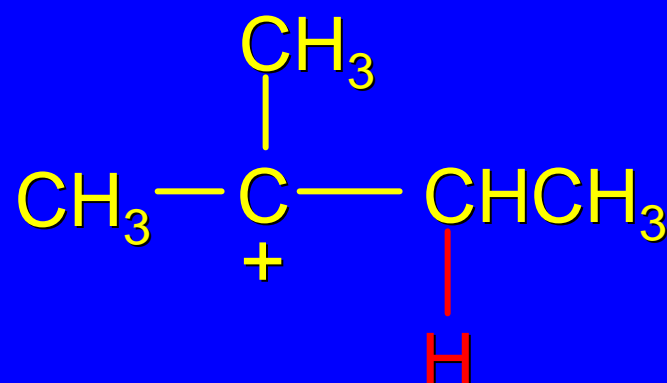
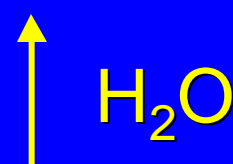
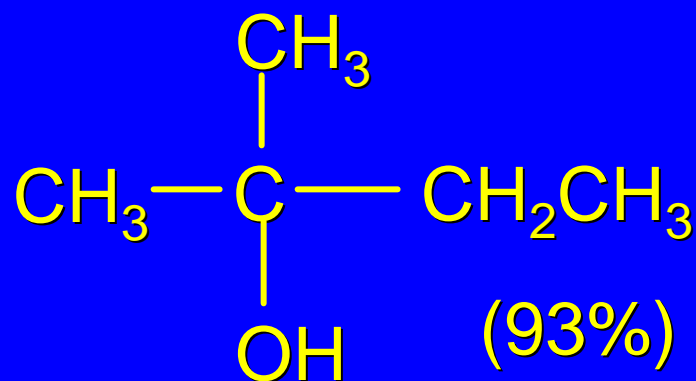
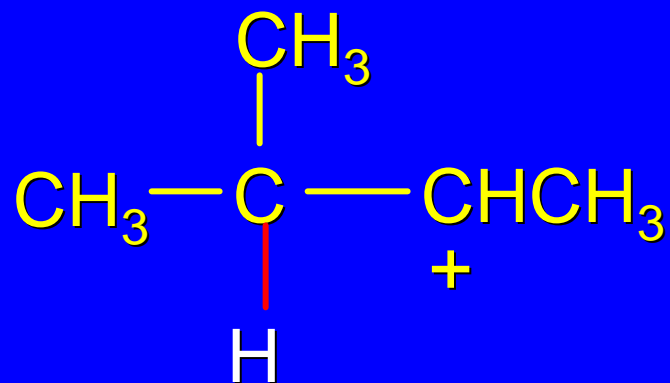
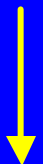
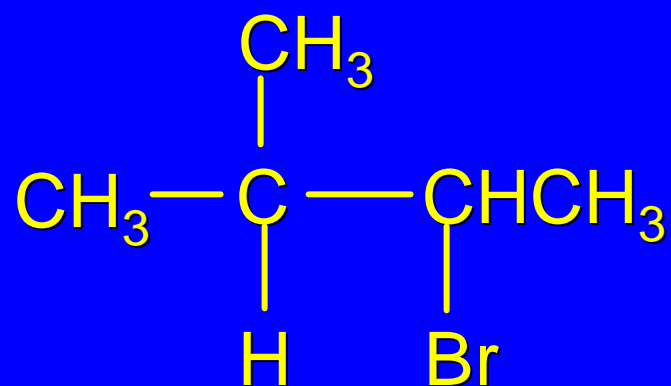
Because...

*carbocations are intermediates
in S_N1 reactions, rearrangements
are possible.*

Example



Example



8.12 Solvent Effects

In general...

*S_N1 Reaction Rates Increase
in Polar Solvents*

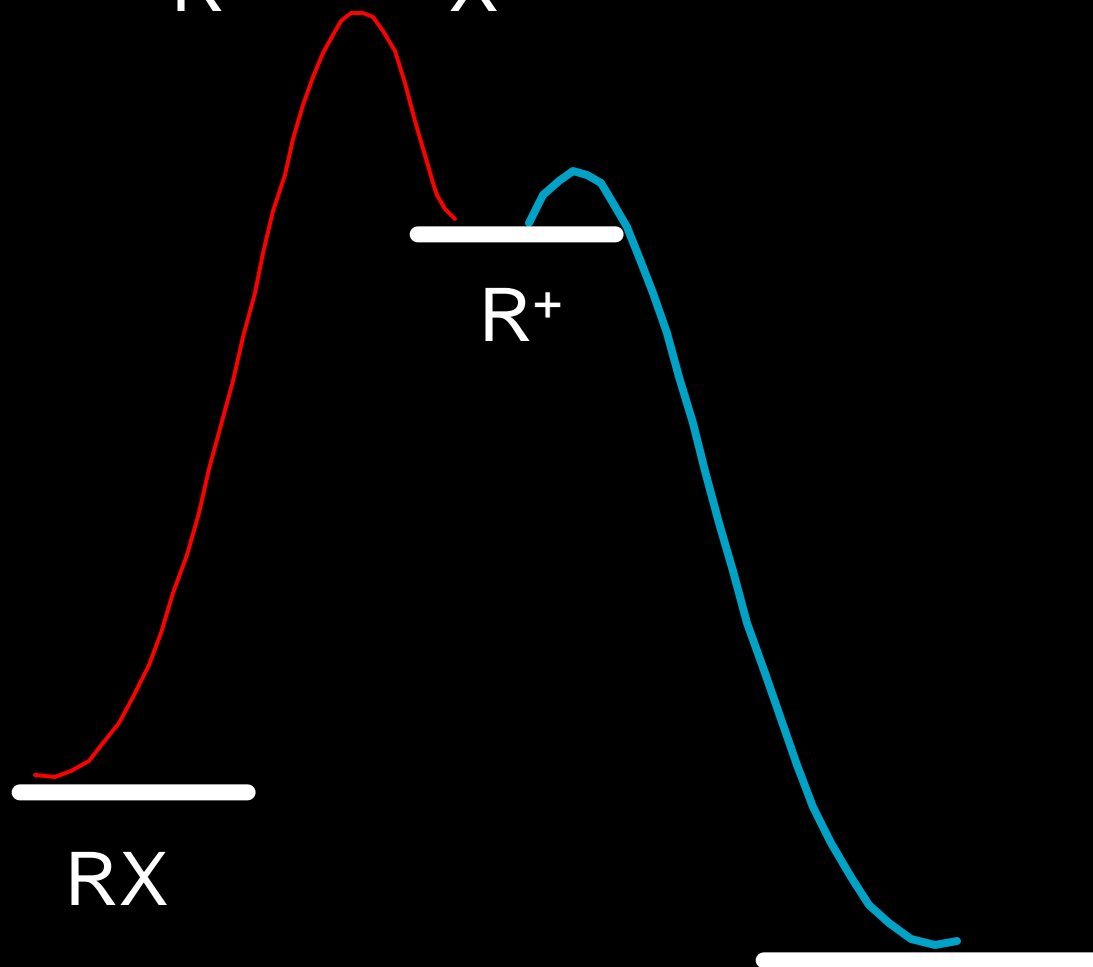
Table 8.6
S_N1 Reactivity versus Solvent Polarity

Solvent	Dielectric constant	Relative rate
acetic acid	6	1
methanol	33	4
formic acid	58	5,000
water	78	150,000

transition state
stabilized by
polar solvent



energy of RX
not much
affected by
polarity of
solvent

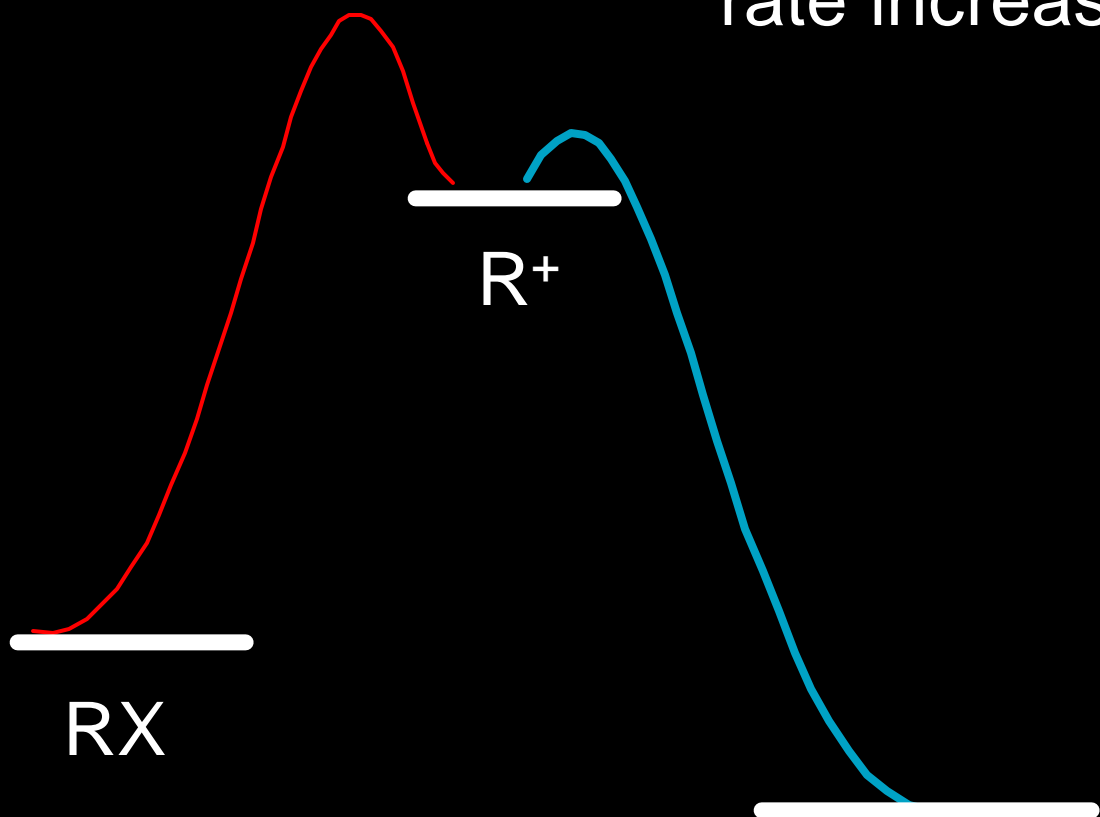


transition state stabilized by polar solvent

activation energy decreases; rate increases



energy of RX not much affected by polarity of solvent



In general...

*S_N2 Reaction Rates Increase in
Polar Aprotic Solvents*

An aprotic solvent is one that does not have an —OH group.

Table 8.7
S_N2 Reactivity versus Type of Solvent



Solvent	Type	Relative rate
CH ₃ OH	polar protic	1
H ₂ O	polar protic	7
DMSO	polar aprotic	1300
DMF	polar aprotic	2800
Acetonitrile	polar aprotic	5000

Mechanism Summary
S_N1 and S_N2

When...

primary alkyl halides undergo nucleophilic substitution, they always react by the S_N2 mechanism

tertiary alkyl halides undergo nucleophilic substitution, they always react by the S_N1 mechanism

secondary alkyl halides undergo nucleophilic substitution, they react by the

S_N1 mechanism in the presence of a weak nucleophile (solvolysis)

S_N2 mechanism in the presence of a good nucleophile