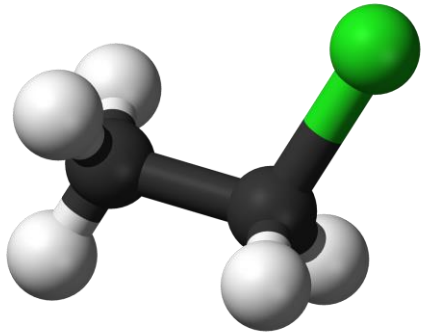
2302263 – Organic Chemistry I – Part III

Lecture 1-3

Alkyl Halides – S_N1 Reaction



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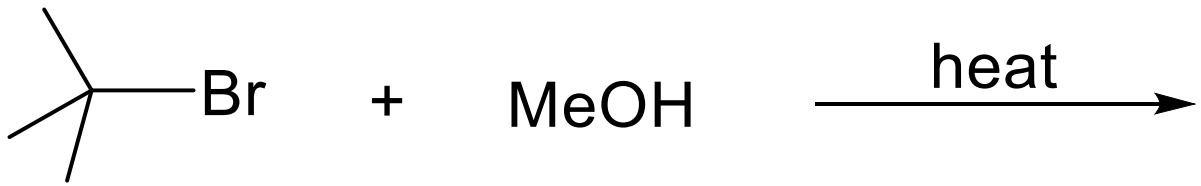
Recommended Textbook:

Chapter 6 in *Organic Chemistry*, 8th Edition, L. G. Wade, Jr., **2010**, Prentice Hall (Pearson Education)

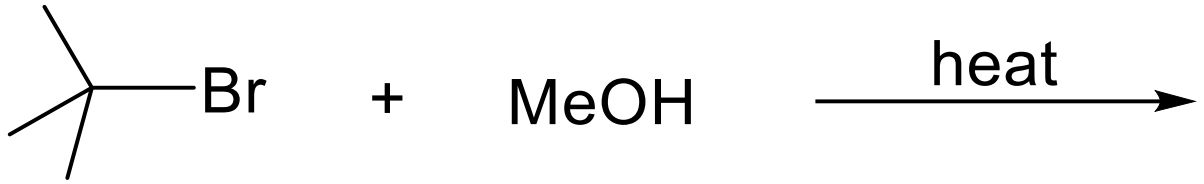
First-Order Nucleophilic Substitution (S_N1)

solvolysis



Rate =

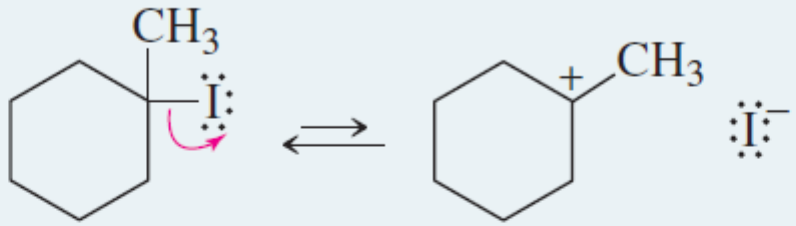
S_N1 - Mechanism



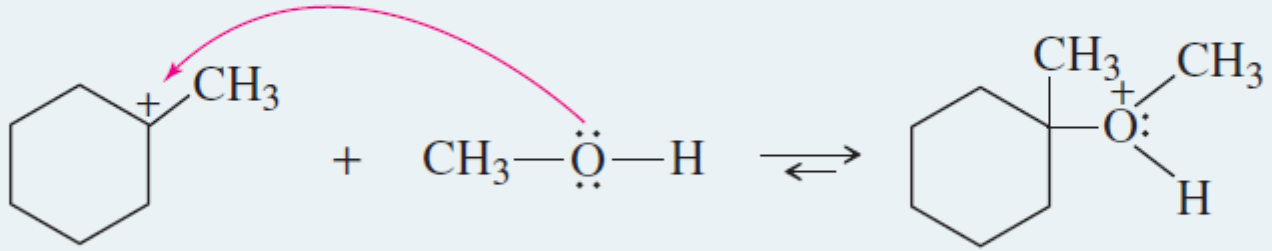
S_N1 - Mechanism

EXAMPLE: Solvolysis of 1-iodo-1-methylcyclohexane in methanol.

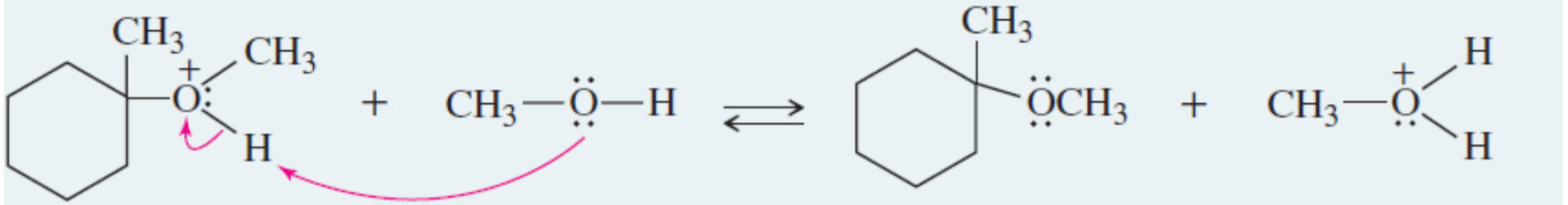
Step 1: Formation of a carbocation (rate-limiting).



Step 2: Nucleophilic attack by the solvent (methanol).

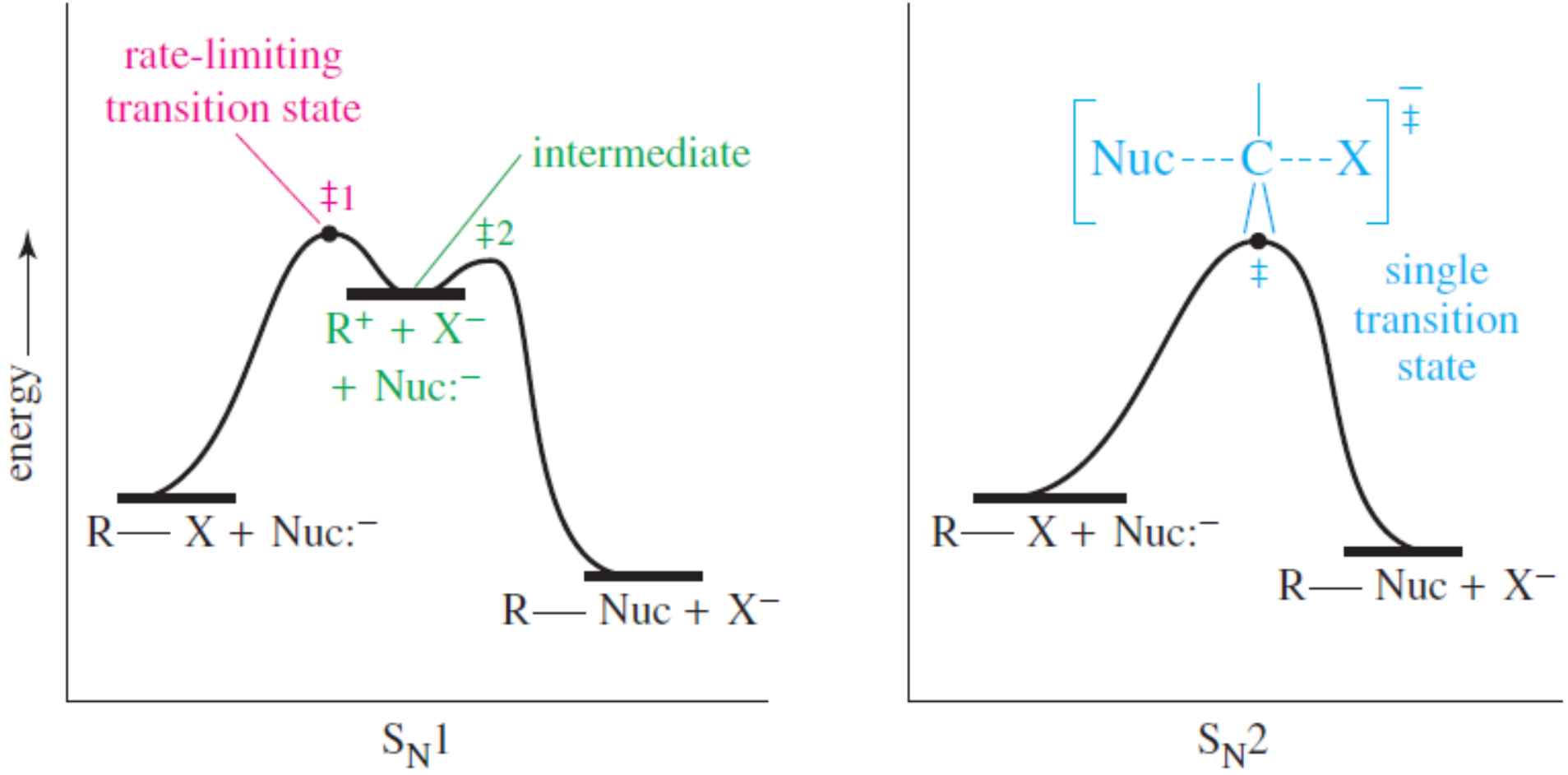


Step 3: Deprotonation to form the product.



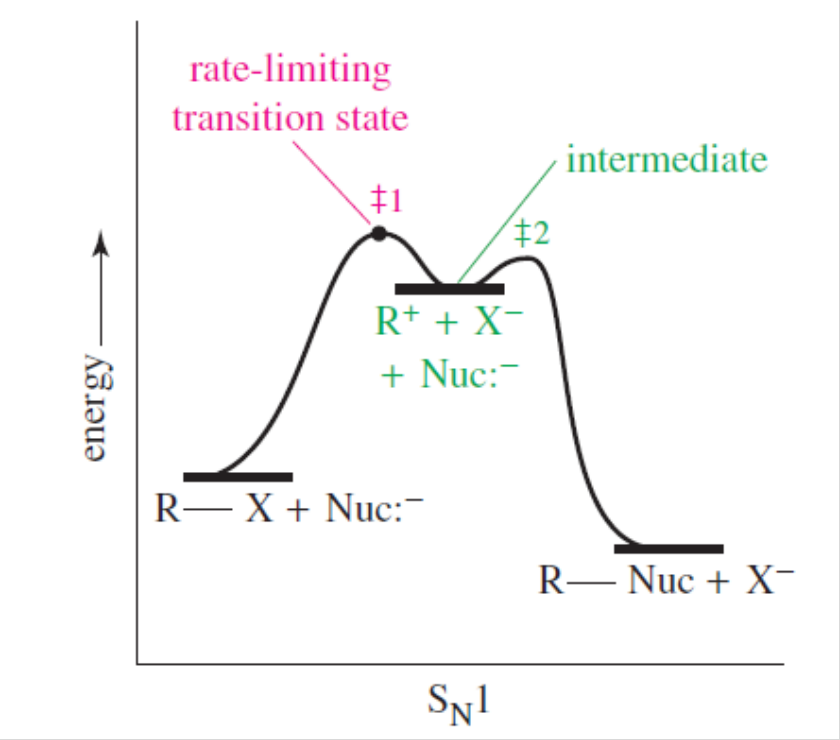
S_N1 - Mechanism

Reaction-energy diagram of S_N1 vs. S_N2 reaction



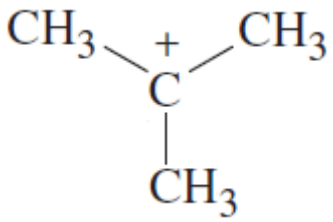
Factors Affecting S_N1 Reactions:

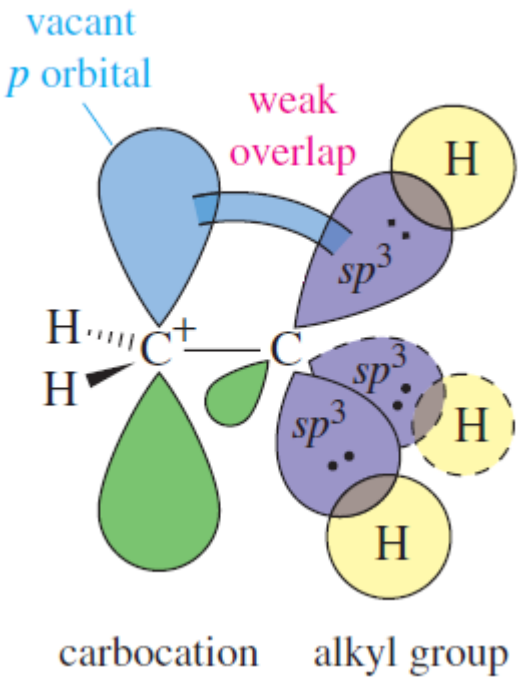
Stability of the Carbocation Intermediate



1) Stabilization from Substituents

- **Alkyl groups** stabilize carbocations by donating electrons through sigma bonds (the _____ effect) and through overlap of filled orbitals with the empty p orbital of the carbocation (_____).



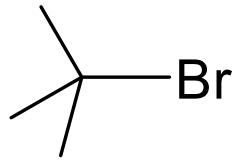


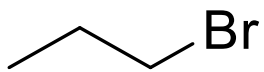
S_N1 reactivity:	**3º**	**2º**	**1º**	**CH_3X**
S_N2 reactivity:	**3º**	**2º**	**1º**	**CH_3X**

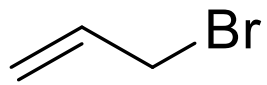
Factors Affecting S_N1 Reactions:

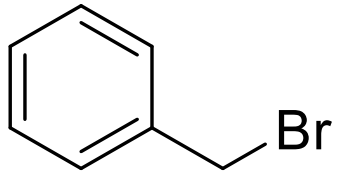
1) Stabilization from Substituents

- **Allyl halides** and **Benzyl halides: Resonance stabilization**





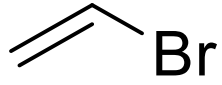


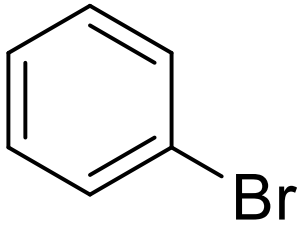


Factors Affecting S_N1 Reactions:

1) Stabilization from Substituents

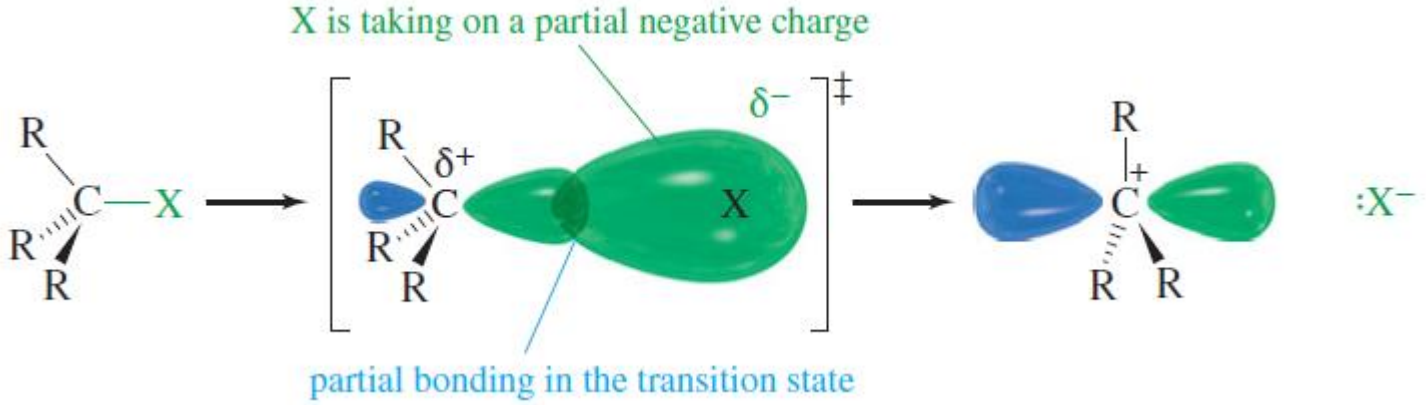
- **Vinyl halides** and **Aryl halides**





Factors Affecting S_N1 Reactions:

2) Leaving-Group Effects



For good leaving group:

1. **polarizable**

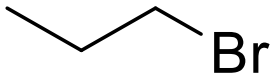
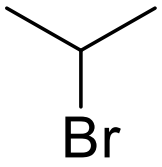
2. **stable once it has left**

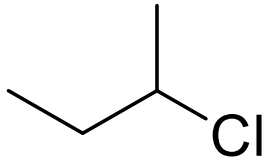
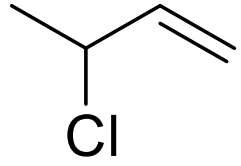
TABLE 6-4 Weak Bases That Are Common Leaving Groups

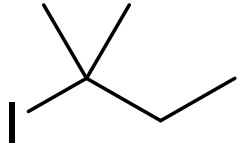
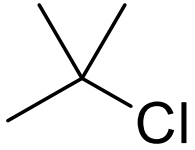
Ions:	$^-:\ddot{Cl}:$	$^-:\ddot{Br}:$	$^-:\ddot{I}:$	$^-:\ddot{O}-\overset{\overset{\ddot{O}}{\|}}{\underset{\underset{\ddot{O}}{\|}}{S}}-R$	$^-:\ddot{O}-\overset{\overset{\ddot{O}}{\|}}{\underset{\underset{\ddot{O}}{\|}}{S}}-\ddot{O}R$	$^-:\ddot{O}-\overset{\overset{:O:}{\|}}{\underset{\underset{\ddot{O}}{\|}}{P}}-\ddot{O}R$
	halides			sulfonate	sulfate	phosphate
Neutral molecules:	$:\ddot{O}(H)-H$	$:\ddot{O}(H)-R$	$:\ddot{N}(R)-R$	$:\ddot{S}-R$	$:\ddot{P}(R)-R$	
	water	alcohols	amines	sulfides	phosphines	

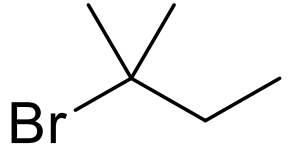
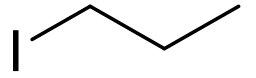
Factors Affecting S_N1 Reactions:

Example 1 Which substrate will react faster by the S_N1 mechanism.

(a)  vs 

(b)  vs 

(c)  vs 

(d)  vs 

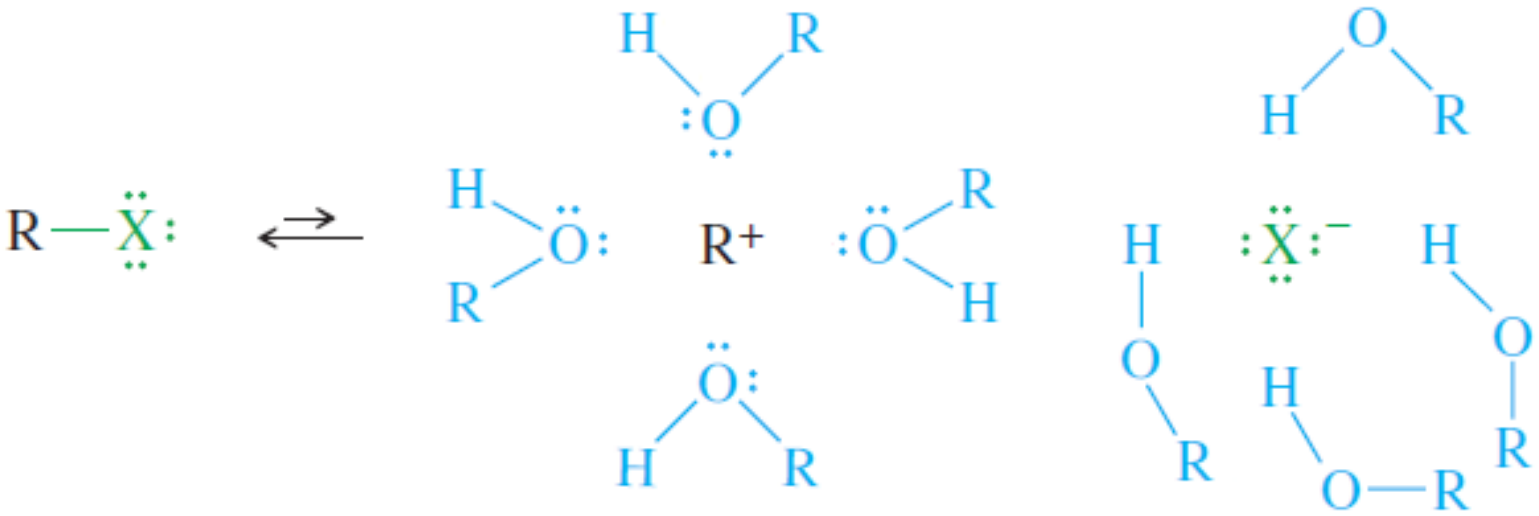
Factors Affecting S_N1 Reactions:

3) Solvent Effects

The S_N1 reaction goes much more readily in **polar solvents** that stabilize ions.

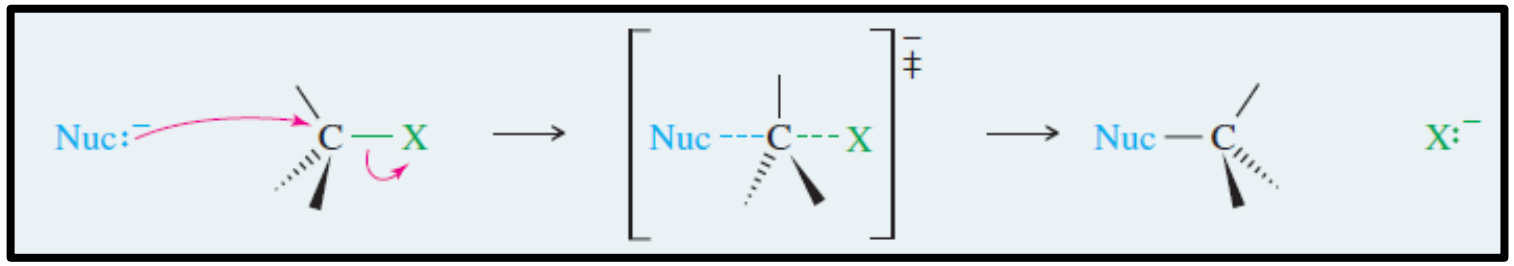
Dielectric Constants (ϵ) and Ionization Rates of *tert*-Butyl Chloride in Common Solvents

Solvent	ϵ	Relative Rate
water	78	8000
methanol	33	1000
ethanol	24	200
acetone	21	1
diethyl ether	4.3	0.001
hexane	2.0	<0.0001



Stereochemistry of the S_N1 Reactions

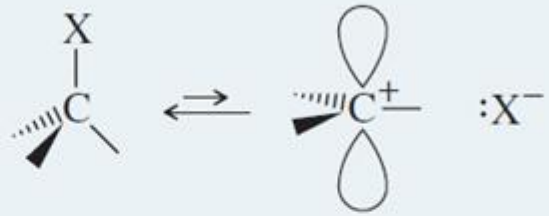
S_N2: _____



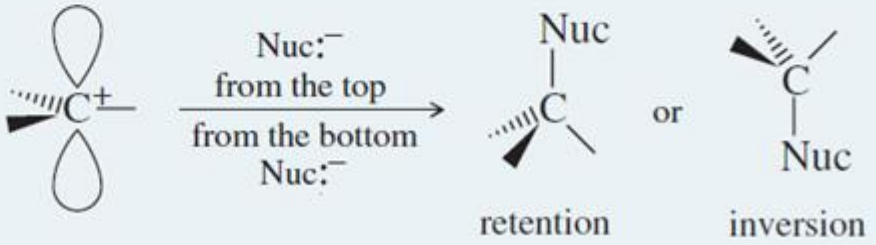
S_N1: _____

The S_N1 reaction involves ionization to a flat carbocation, which can be attacked from either side.

Step 1: Ionization of a tetrahedral carbon gives a flat carbocation.

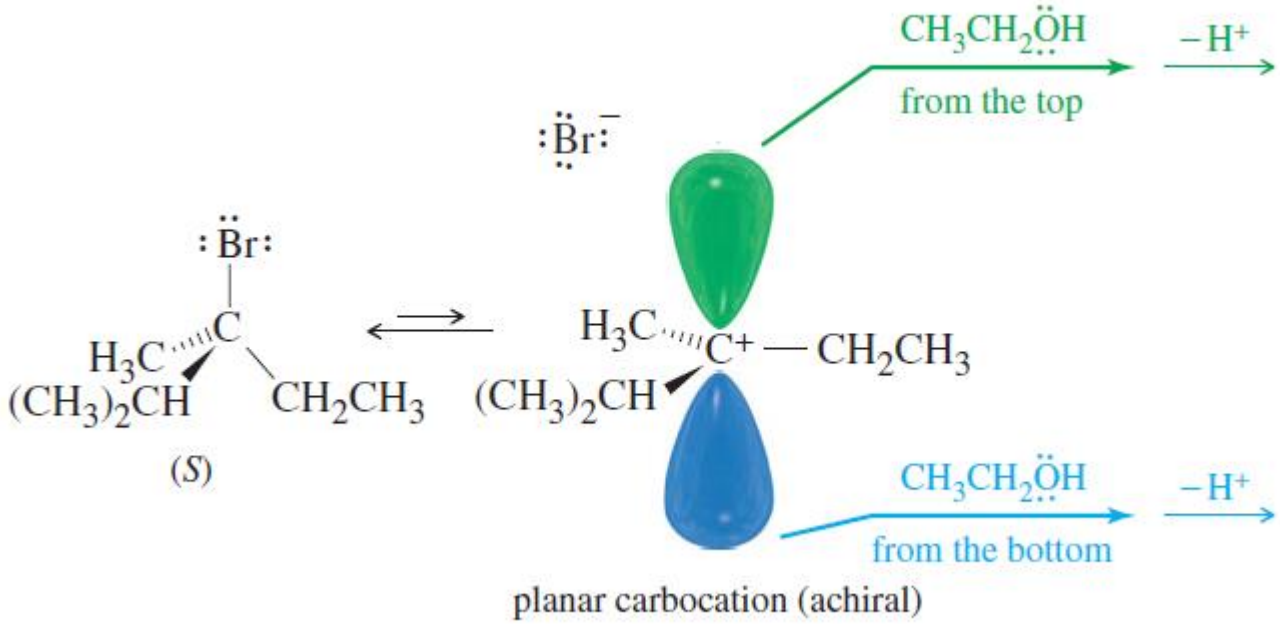


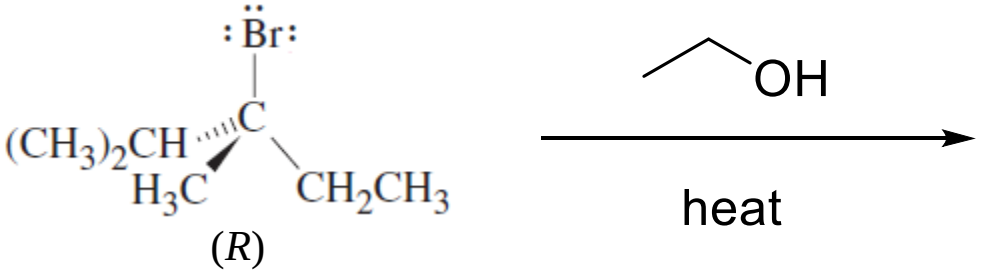
Step 2: A nucleophile may attack either side of the carbocation.



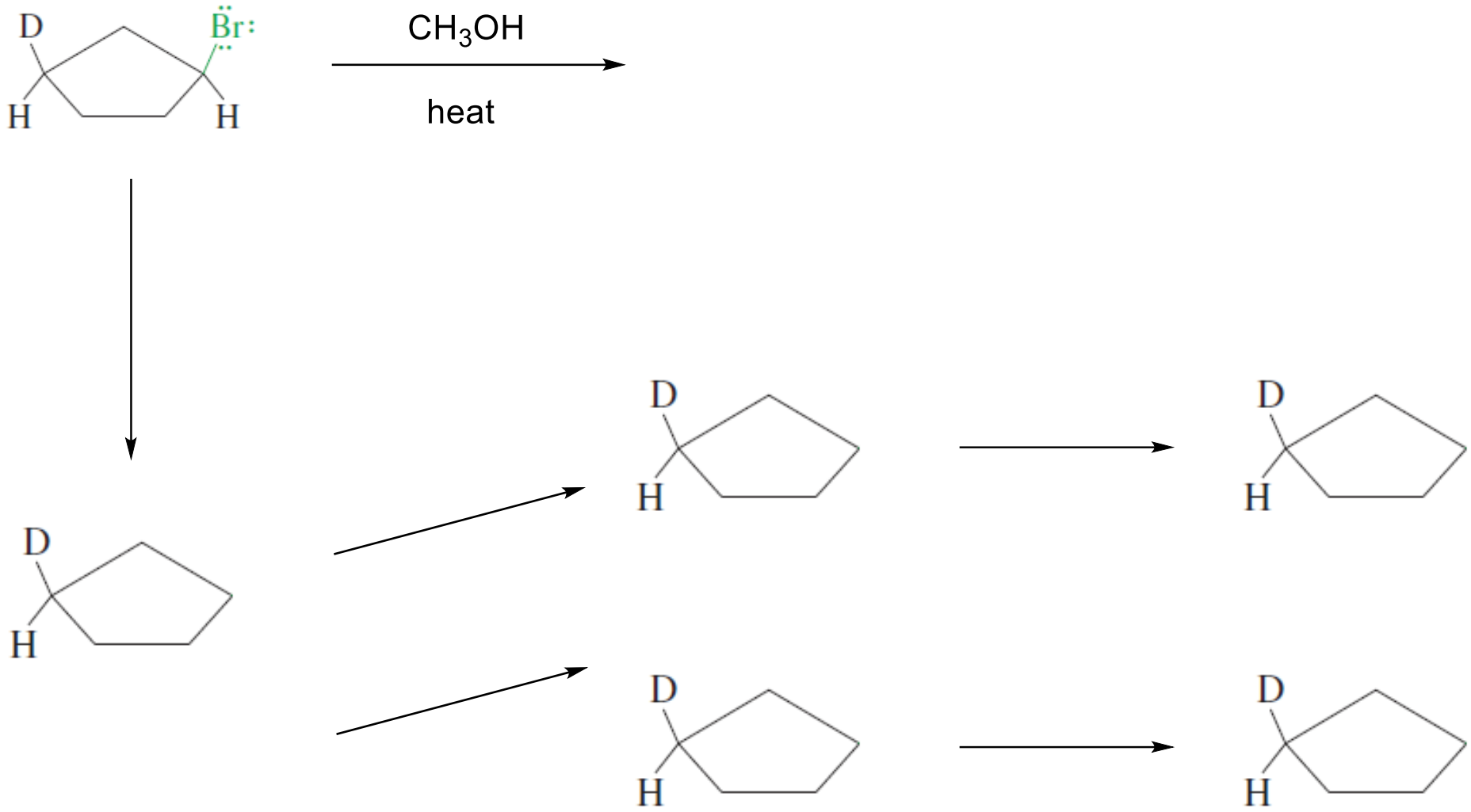
These two products may be different if the carbon atom is stereogenic.

Stereochemistry of the S_N1 Reactions



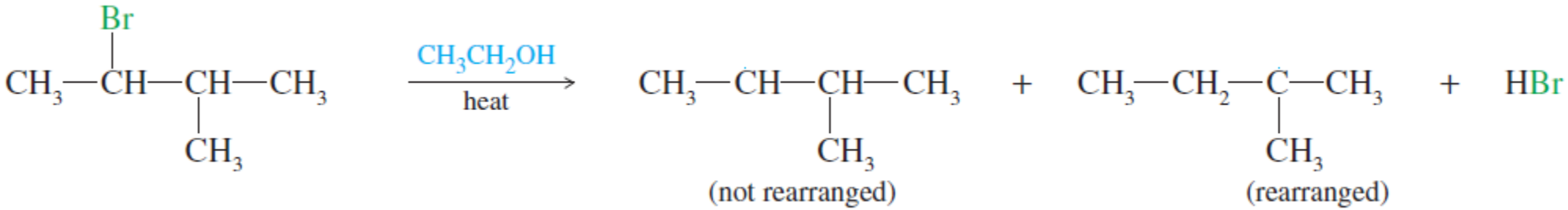


Stereochemistry of the S_N1 Reactions



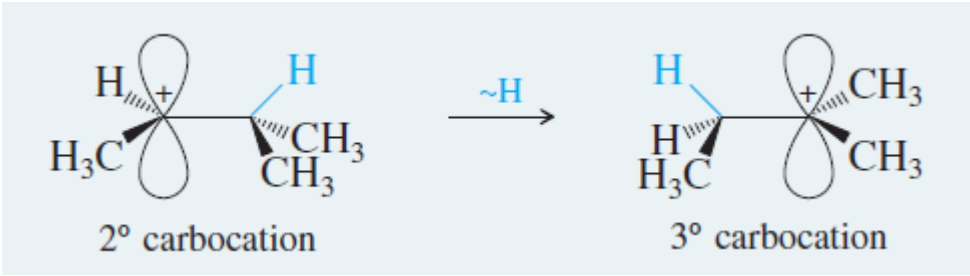
Rearrangements in the S_N1 Reactions

- **Carbocations** frequently undergo structural changes, called **rearrangements**, to form **more stable ions**.
- Rearrangements are **not seen in S_N2** reactions, where no carbocation is formed.

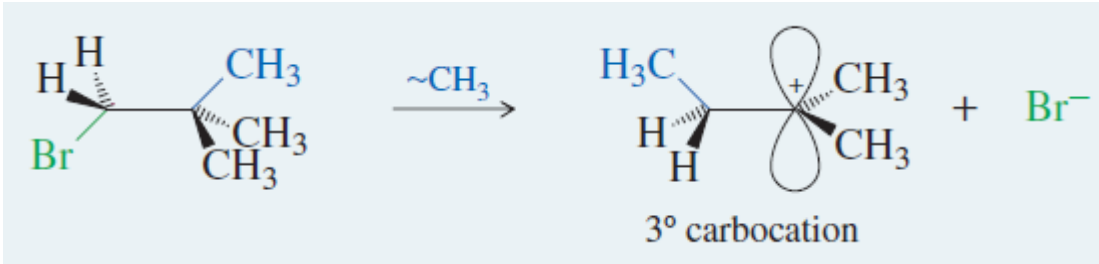


There are 2 main types of rearrangements

- **Hydride shift**

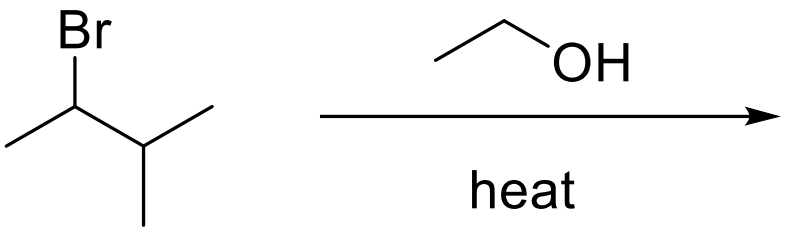


- **Alkyl shift**



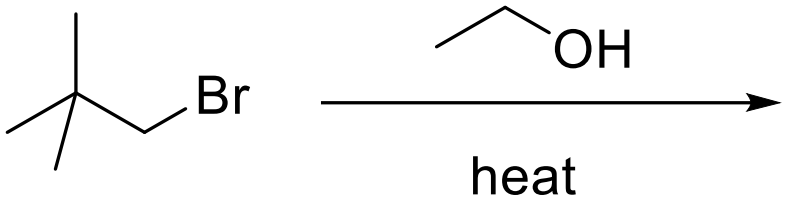
Rearrangements in the S_N1 Reactions

- **Hydride shift**



Rearrangements in the S_N1 Reactions

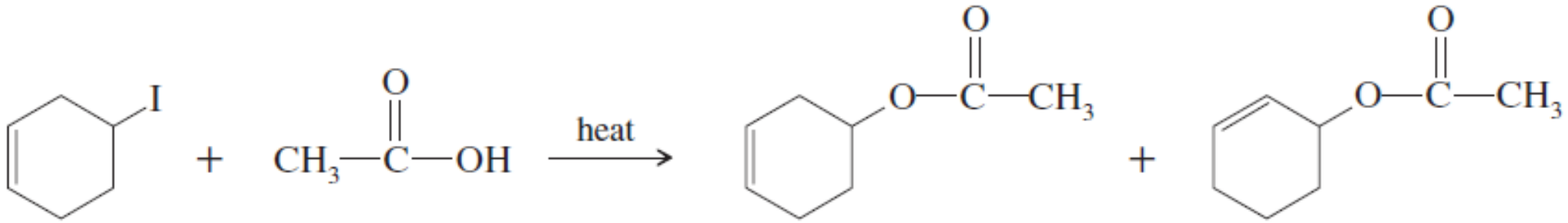
- **Alkyl shift**



Rearrangements in the S_N1 Reactions

Example 2 Propose a mechanism involving a hydride shift or an alkyl shift for each solvolysis reaction.

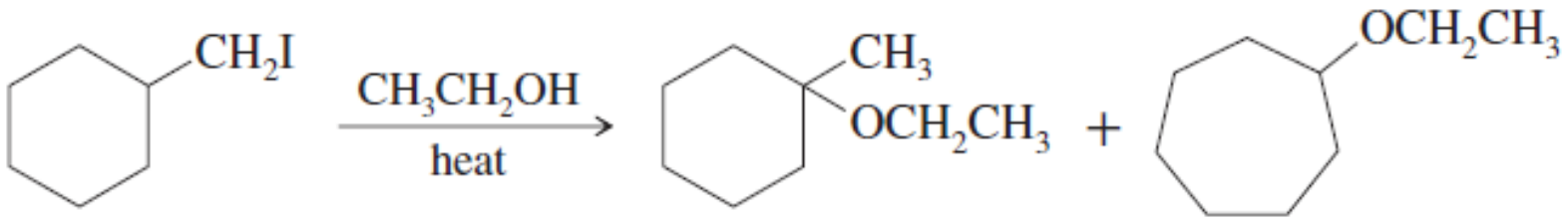
(a)



Rearrangements in the S_N1 Reactions

Example 2 Propose a mechanism involving a hydride shift or an alkyl shift for each solvolysis reaction.

(b)

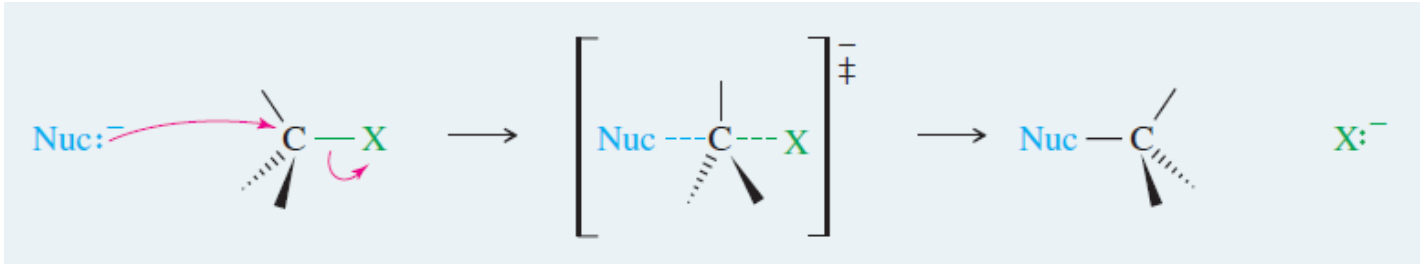


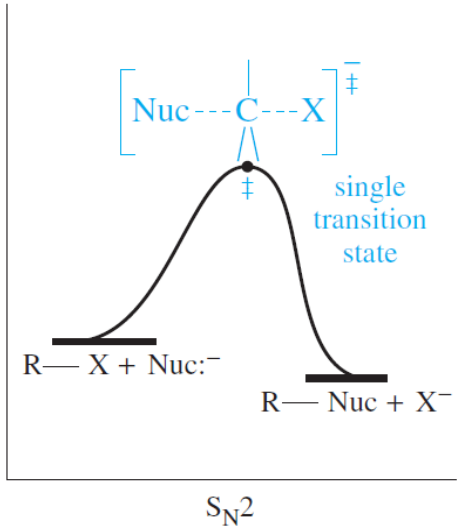
Comparison of S_N2 vs. S_N1 Reactions

1) Kinetic

2) Nucleophile

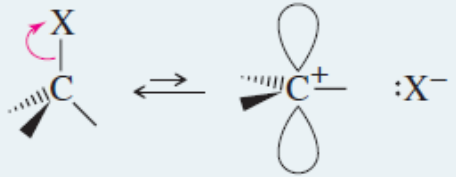
S_N2



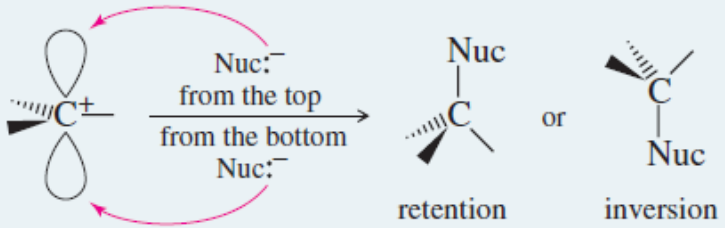


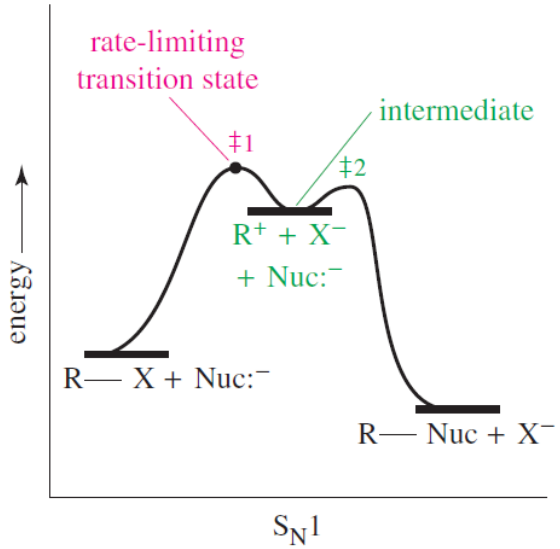
S_N1

Step 1: Ionization of a tetrahedral carbon gives a flat carbocation.



Step 2: A nucleophile may attack either side of the carbocation.



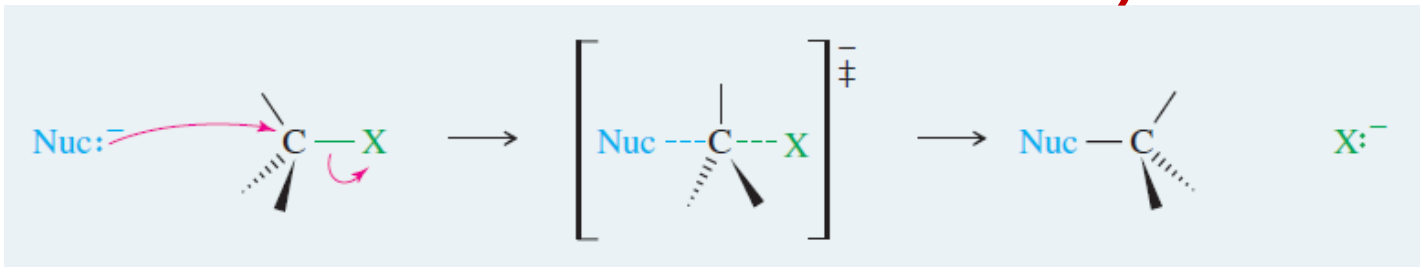


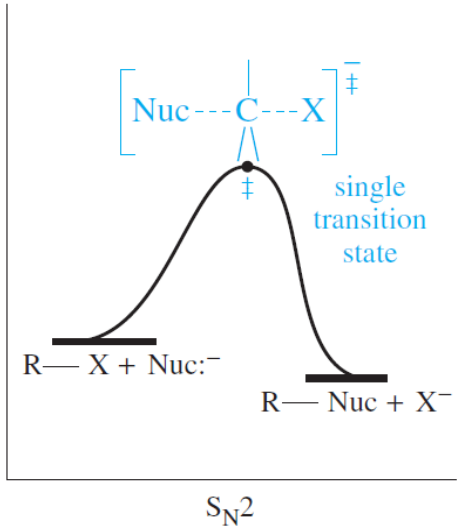
Comparison of S_N2 vs. S_N1 Reactions

3) Substrate

4) Solvent

S_N2





S_N1

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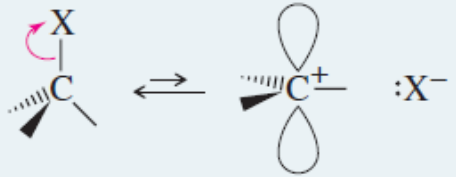

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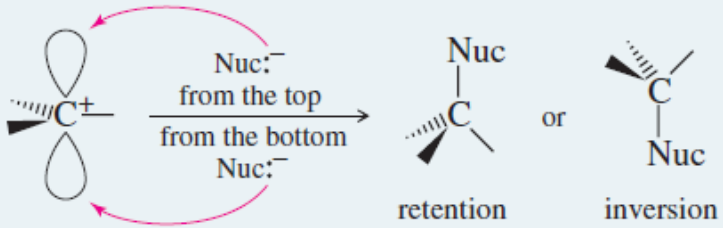
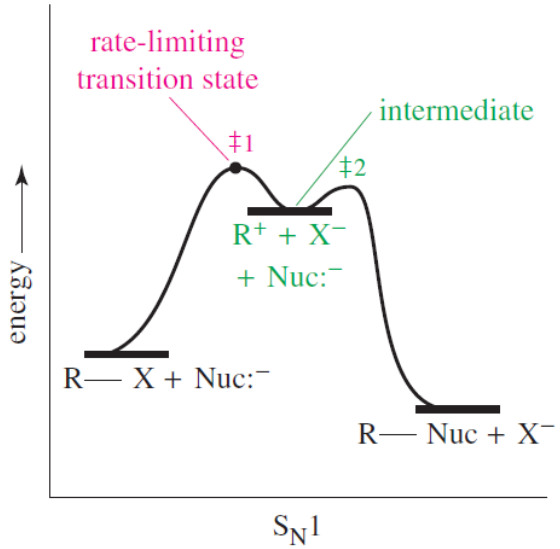


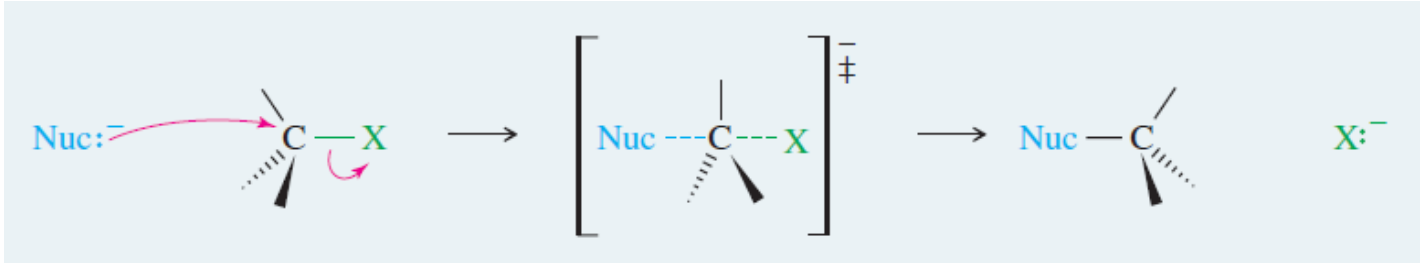


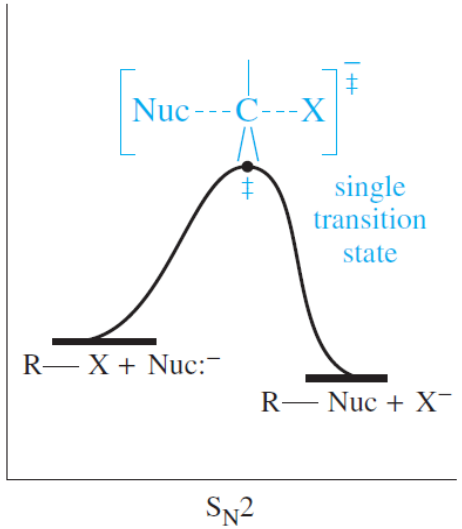
Comparison of S_N2 vs. S_N1 Reactions

5) Stereochemistry of the Product

6) Rearrangements

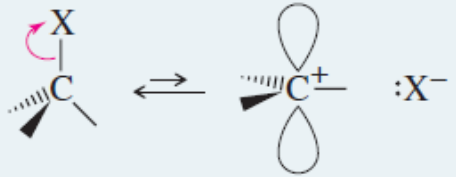
S_N2



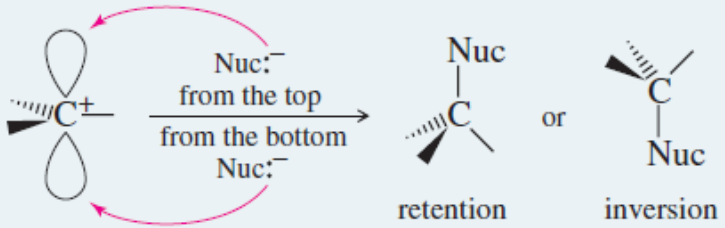


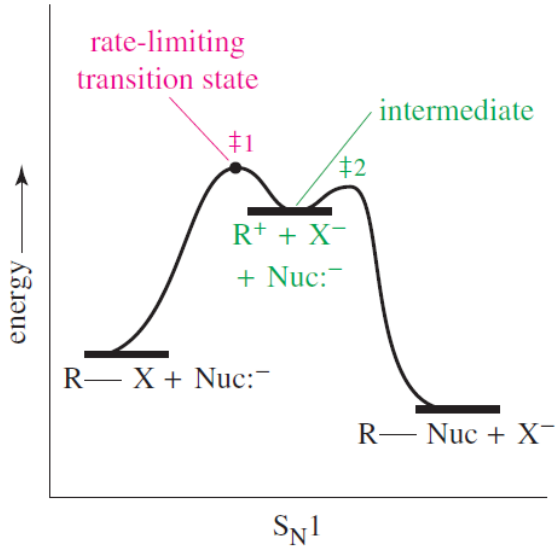
S_N1

Step 1: Ionization of a tetrahedral carbon gives a flat carbocation.



Step 2: A nucleophile may attack either side of the carbocation.





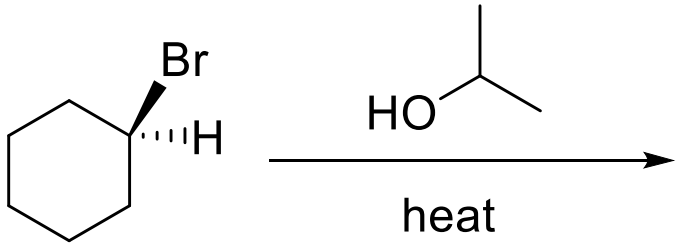
Comparison of S_N2 vs. S_N1 Reactions

	S_N2	S_N1
Promoting factors		
nucleophile	strong nucleophile needed	weak nucleophiles are OK
substrate (RX)	$CH_3X > 1° > 2°$	$3° > 2°$
solvent	wide variety of solvents	good ionizing solvent needed
leaving group	good one required	good one required
other		$AgNO_3$ forces ionization
Characteristics		
kinetics	second order, $k_r[RX][Nuc:^-]$	first order, $k_r[RX]$
stereochemistry	complete inversion	mixture of inversion and retention
rearrangements	impossible	common

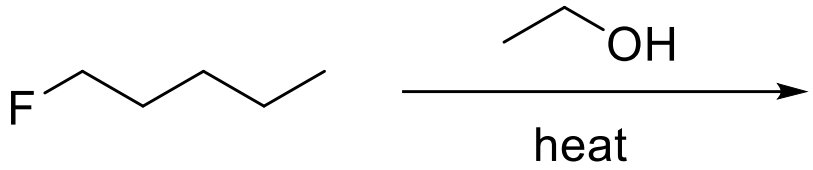
Comparison of S_N2 vs. S_N1 Reactions

Example 3 For each reaction, give the expected substitution product, and predict whether the mechanism will be predominantly S_N2 or S_N1.

(a)



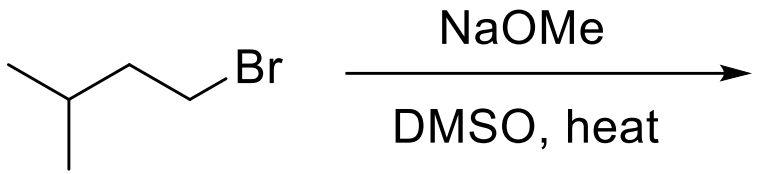
(b)



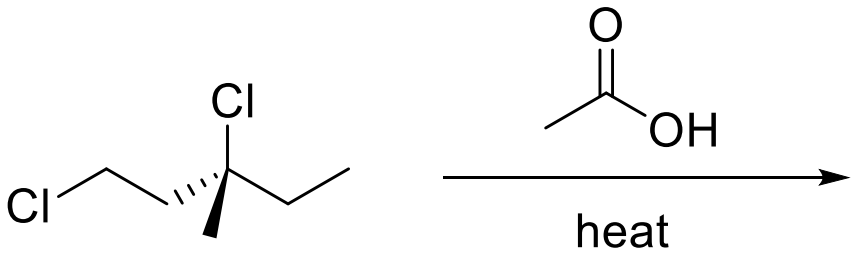
Comparison of S_N2 vs. S_N1 Reactions

Example 3 For each reaction, give the expected substitution product, and predict whether the mechanism will be predominantly S_N2 or S_N1.

(c)



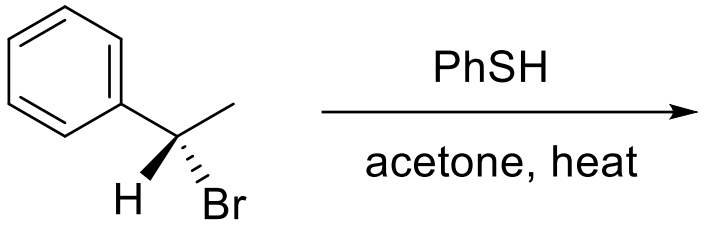
(d)



Comparison of S_N2 vs. S_N1 Reactions

Example 3 For each reaction, give the expected substitution product, and predict whether the mechanism will be predominantly S_N2 or S_N1.

(e)



(f)