

CHEM 109A

Organic Chemistry

<https://labs.chem.ucsb.edu/zakarian/armen/courses.html>

Chapter 9

Substitution Reactions: S_N2 and S_N1

Elimination Reactions: E2 and E1

Final exam is cumulative

Chapter 1: 1.1 – 1.16	bonding
Chapter 2: 2.1 – 2.10, <u>2.12</u> (Lewis acids)	acids/bases
Chapter 3: 3.1 – 3.15	nomenclature, ph. pr.
Chapter 4: 4.1 – 4.15 (4.16 – 4.17)	stereochemistry
Chapter 5: 5.1 – 5.12 (5.13 , 5.14)	thermodyn./kinetics
Chapter 6: 6.1 – 6.13, 6.16 (6.14 , 6.15)	alkene reactions
Chapter 7: 7.1 – 7.12	alkyne reactions, synthesis
Chapter 8: 8.1 – 8.7, 8.9, 8.11, 8.16 – 8.18	(resonance effect, on pKa, carbocations, intro to aromaticity)
Chapter 9: 9.1 – <u>9.5</u>	S_N1 and S_N2 reactions and mechanisms

- ◆ about ¾ of material from midterms 1-3, about ¼ from 7.6 – 9.5
- ◆ midterms available to pick (CHEM 2138) until Monday 7 pm

Wednesday, March 21, 4:00 – 7 pm, room BUCHN 1910 (last name A – S);
Phelps 1508 (last name T – Z)

Midterm 3 information

Average: 59.5

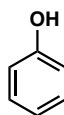
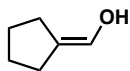
Standard deviation: 16.1

Max 95

Min 18.5

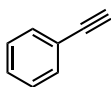
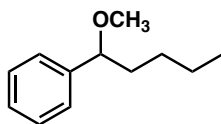
Practice Questions

Draw the keto tautomer of:



Practice Questions

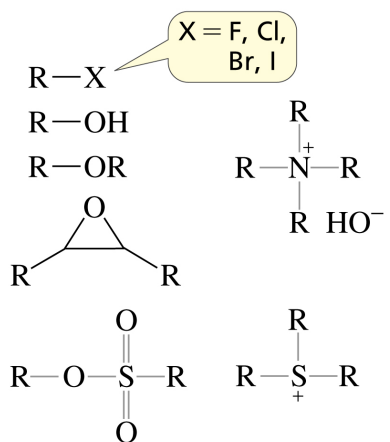
Propose a synthesis of the following molecule from phenylacetylene and any *n*-alkyl halide:



phenylacetylene

The Families of Group II

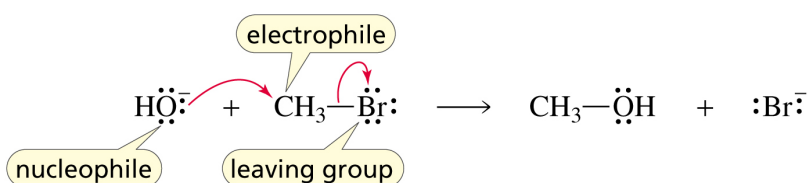
Group II



Summary of the Experimental Evidence for the Mechanism of an S_N2 Reaction

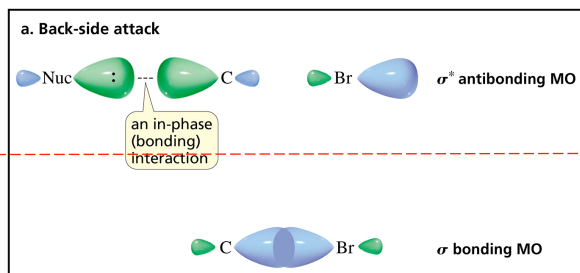
1. Both the **alkyl halide** and the **nucleophile** are in the **transition state** of the rate-limiting step.
2. The relative rate:
primary alkyl halide > **secondary alkyl halide** > **tertiary alkyl halide**
3. The **configuration of the product** is **inverted** compared to the configuration of the reacting chiral alkyl halide.

The Mechanism

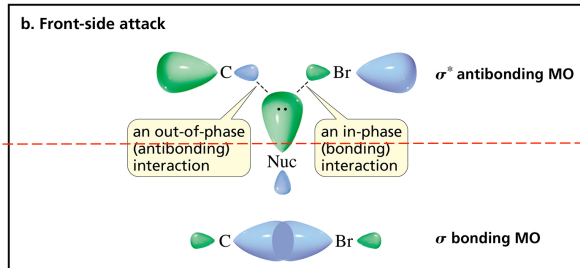
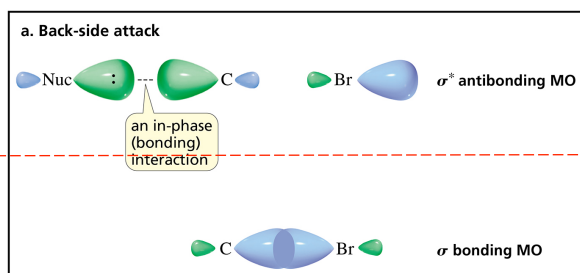


back-side attack

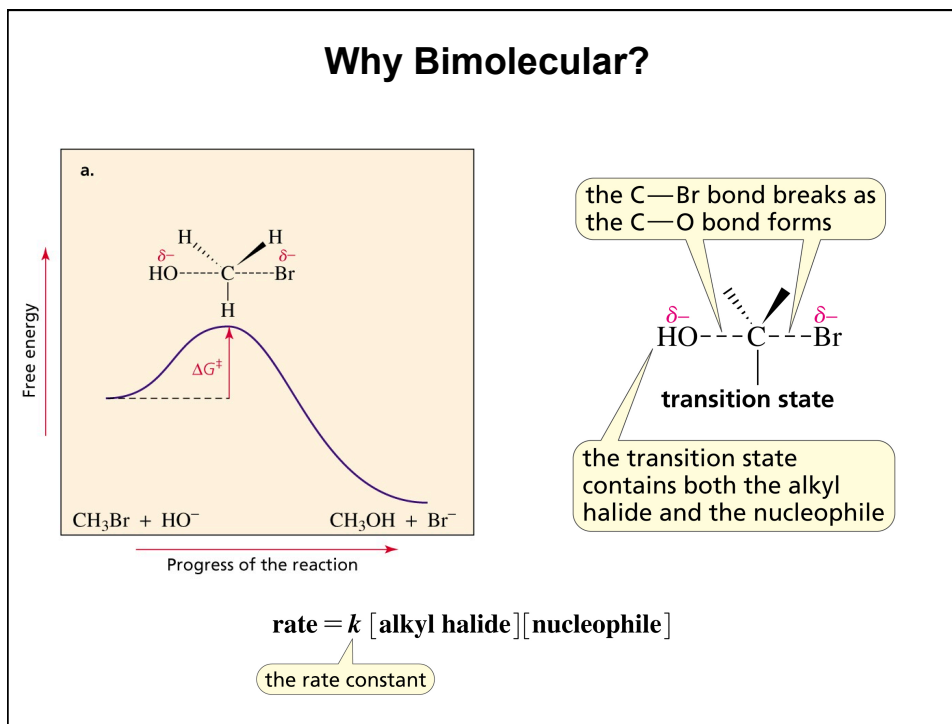
Why Back-Side Attack?



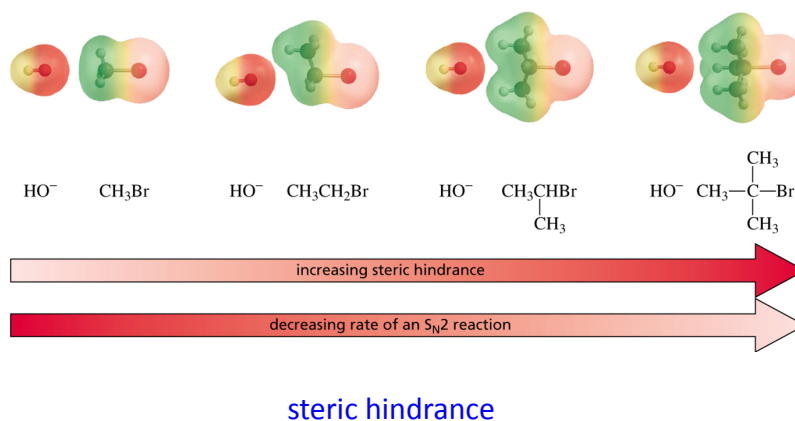
Why Back-Side Attack?



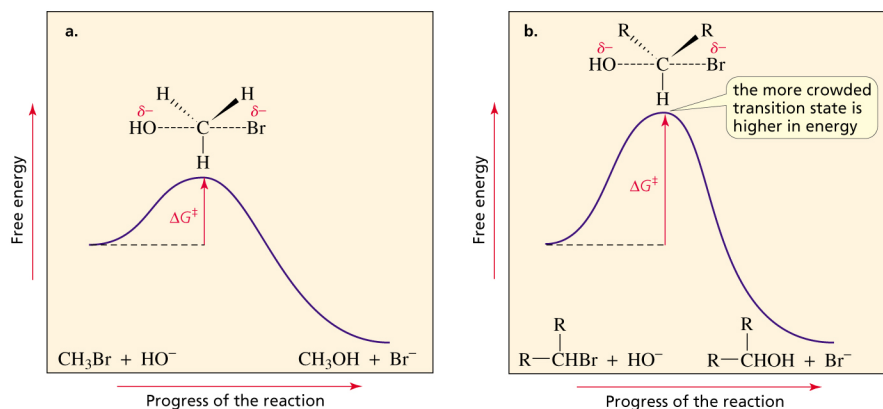
Why Bimolecular?



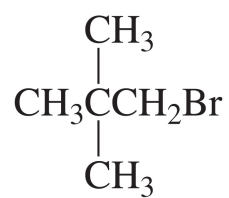
Why Do Methyl Halides React the Fastest and Tertiary the Slowest?



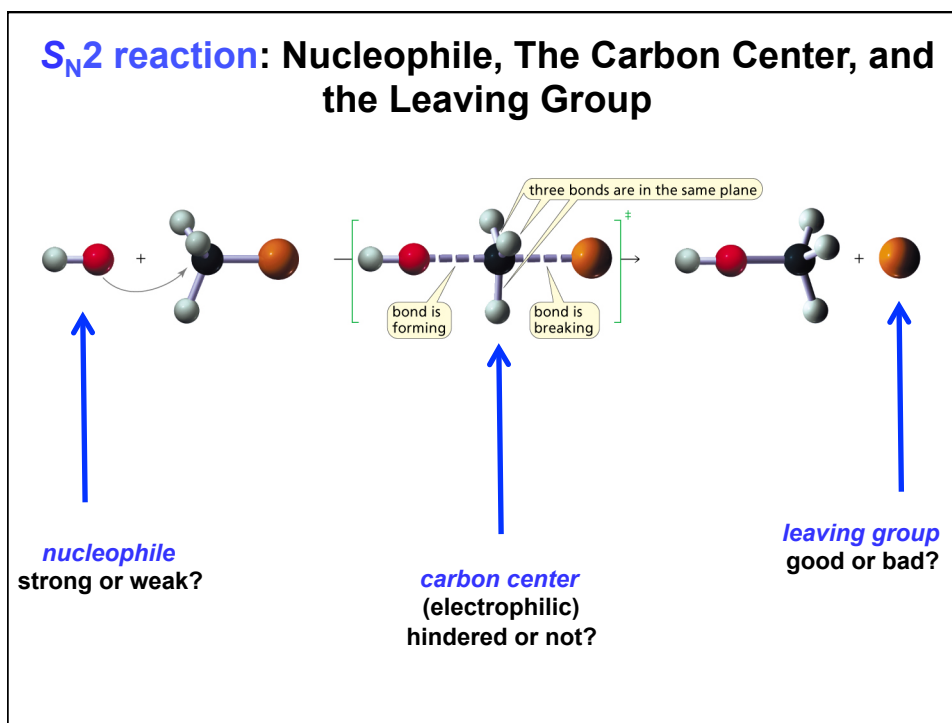
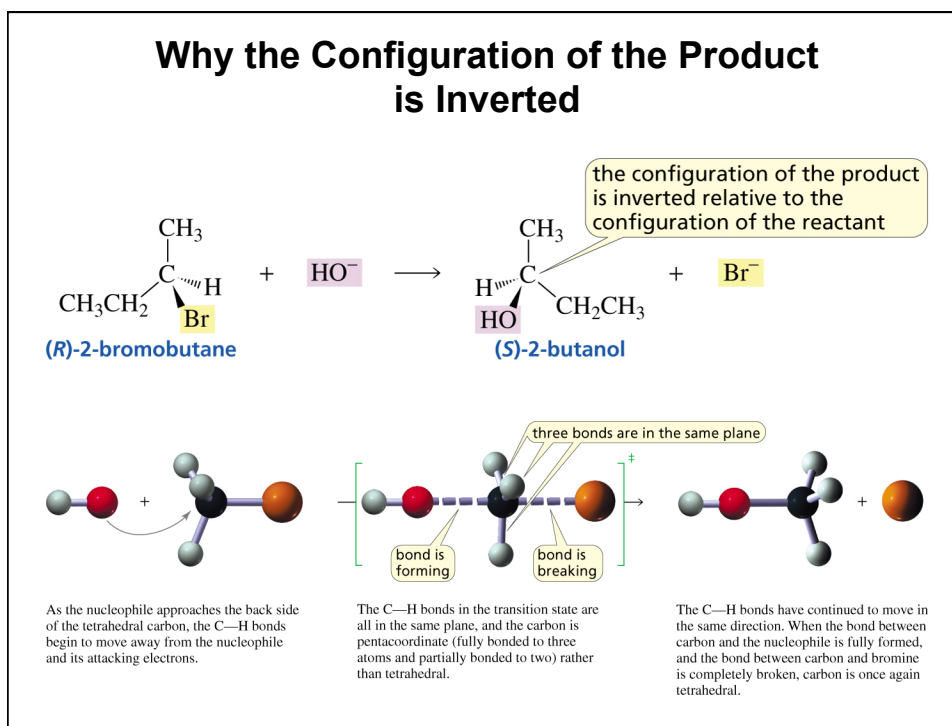
Steric Hindrance Decreases the Rate



Although it is Primary, it Reacts Very Slowly



1-bromo-2,2-dimethylpropane

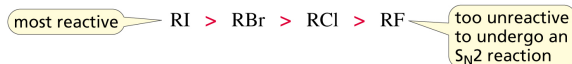


Leaving Group Effect: The Weakest Base is the Best

The Rate of an S_N2 Reaction is Affected by the Leaving Group

	relative rates of reaction	pK_a values of HX
$HO^- + RCH_2I \longrightarrow RCH_2OH + I^-$	30,000	-10
$HO^- + RCH_2Br \longrightarrow RCH_2OH + Br^-$	10,000	-9
$HO^- + RCH_2Cl \longrightarrow RCH_2OH + Cl^-$	200	-7
$HO^- + RCH_2F \longrightarrow RCH_2OH + F^-$	1	3.2

relative reactivities of alkyl halides in an S_N2 reaction



Nucleophile effect: Bases and Nucleophiles

Table 9.1 Common Nucleophiles/Bases

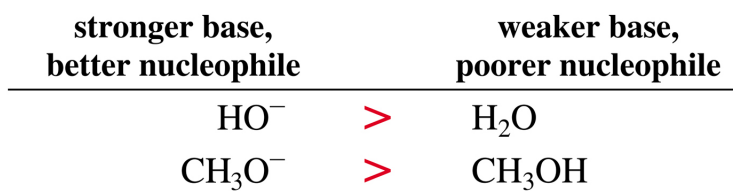
HO^-	RO^-	H_2O	ROH	$RCOO^-$
HS^-	RS^-	H_2S	RSH	
$\bar{N}H_2$	RNH^-	NH_3	RNH_2	
$\bar{C}\equiv N$	$RC\equiv C^-$			
Cl^-	Br^-	I^-		

A **base** shares its lone pair with a **proton**.

A **nucleophile** shares its lone pair with an atom **other than a proton**.

1. Nucleophile Strength: stronger base, better Nu

A negatively charged atom is a stronger base and a better nucleophile than the same atom that is neutral.

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stronger base, better nucleophile		weaker base, poorer nucleophile
HO^-	>	H_2O
CH_3O^-	>	CH_3OH
$^- \text{NH}_2$	>	NH_3

A negatively charged atom is a stronger base and a better nucleophile than the same atom that is neutral.

1. Nucleophile Strength: stronger base, better Nu

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HO^-	>	H_2O
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$^- \text{NH}_2$	>	NH_3
$\text{CH}_3\text{CH}_2\text{NH}^-$	>	$\text{CH}_3\text{CH}_2\text{NH}_2$

A negatively charged atom is a stronger base and a better nucleophile than the same atom that is neutral.

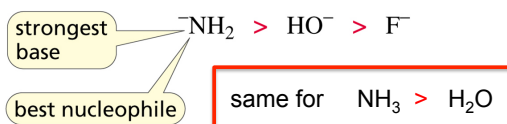
2. Nucleophile Strength: same row elements

nucleophilicity goes up



5	6	7	8	9	10
B	C	N	O	F	Ne
boron	carbon	nitrogen	oxygen	fluorine	neon
10.81	12.011	14.007	15.999	18.998	20.180
[10.806, 10.821]	[12.009, 12.012]	[14.006, 14.008]	[15.999, 16.000]		
13	14	15	16	17	18

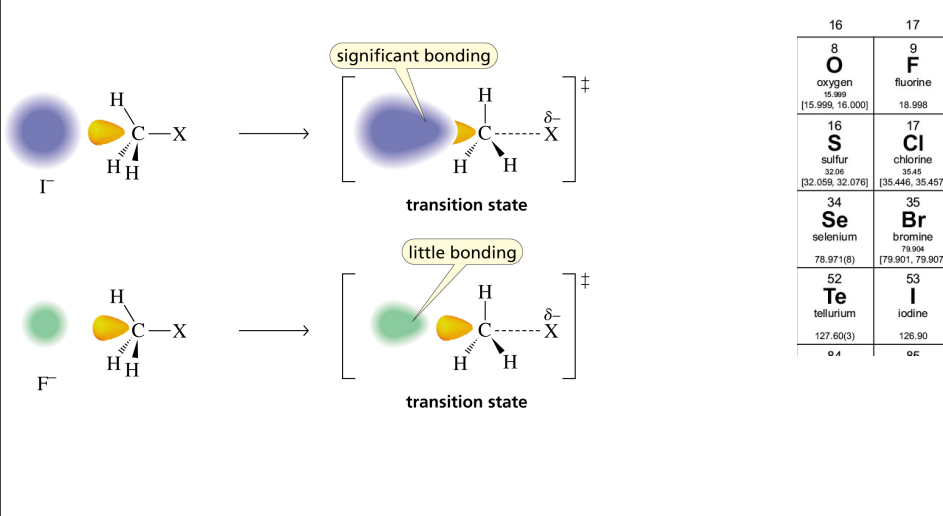
relative base strengths and relative nucleophilicities



If atoms are in the same row,
the **strongest base** is the **best nucleophile**.

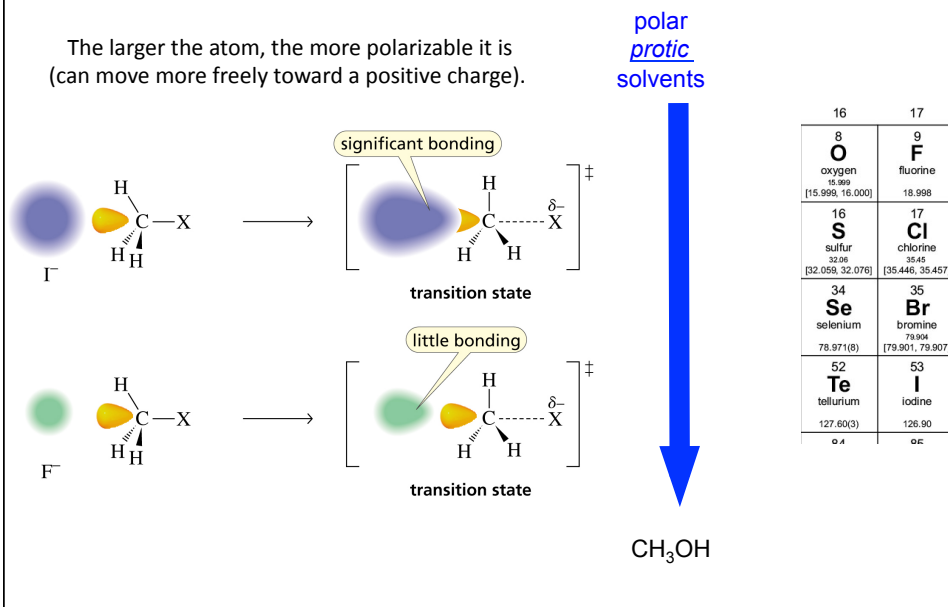
3. Nucleophile Strength: Polarizability

The larger the atom, the more polarizable it is
(can move more freely toward a positive charge).



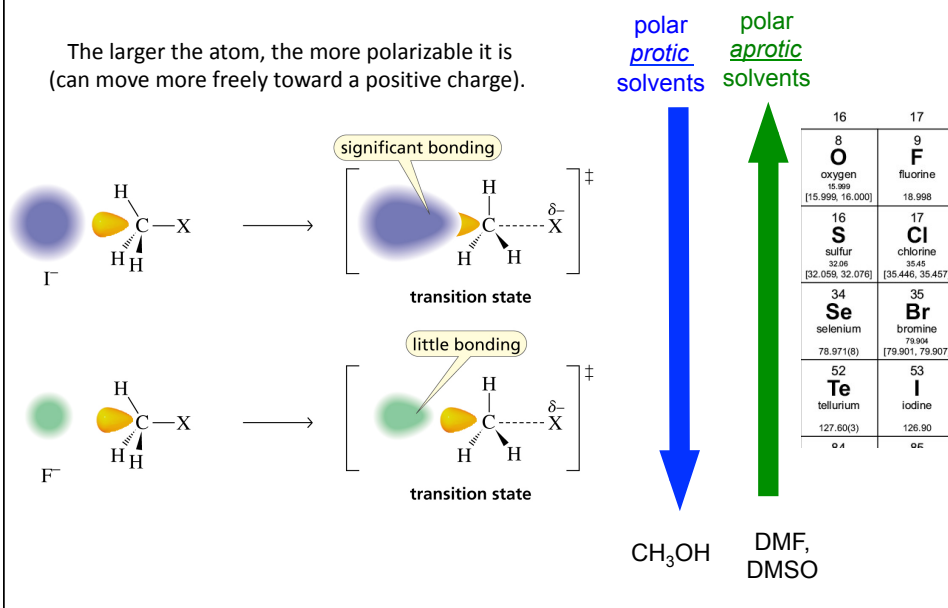
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Solvents

1. nonpolar solvents: hexane, benzene – normally not used in substitution reactions
(Negatively charged species cannot dissolve in nonpolar solvents).

2. protic polar solvents: have an OH group (H_2O , CH_3OH)

3. aprotic polar solvents: polar, but no OH group



DMF

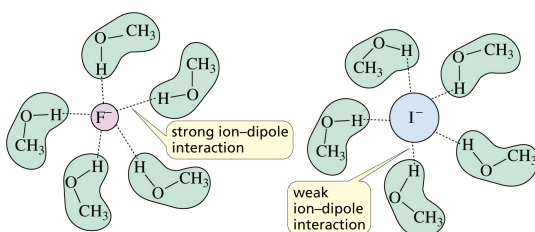


DMSO

Why Do Protic Polar Solvents Make the Strongest Bases the Poorest Nucleophiles?

I^- is the **best nucleophile** in a **protic** polar solvent.

polar
protic
solvents



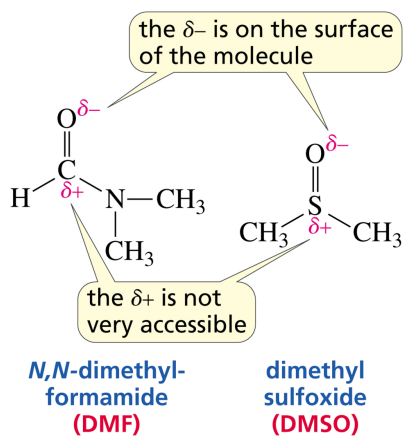
excellent solvation

poor solvation

CH_3OH

16	17
8 O oxygen 15.999 [15.999, 16.000]	9 F fluorine 18.998
16 S sulfur 32.06 [32.059, 32.078]	17 Cl chlorine 35.45 [35.446, 35.457]
34 Se selenium 78.96 [78.971(8)]	35 Br bromine 79.904 [79.901, 79.907]
52 Te tellurium 127.60(3)	53 I iodine 126.90
o4	o4

Aprotic Polar Solvents



They can solvate a cation (+) better than they can solvate an anion (-).

polar
aprotic
solvents

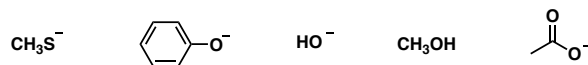


16	17
8 O oxygen 15.999 (15.999, 16.000)	9 F fluorine 18.998
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34 Se selenium 78.96 (78.971(8))	35 Br bromine 79.904 (79.901, 79.907)
52 Te tellurium 127.60(3)	53 I iodine 126.90
o.4	o.6

DMF,
DMSO

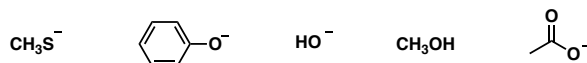
Aprotic Polar Solvents

Rank the following from best to poorest nucleophile in an aqueous solution:



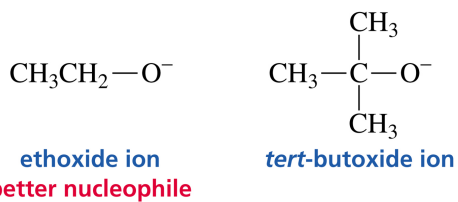
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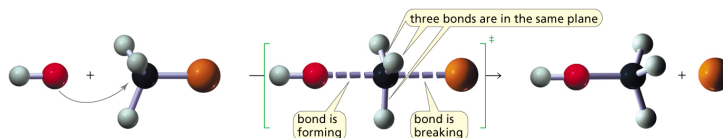


how about in DMF?

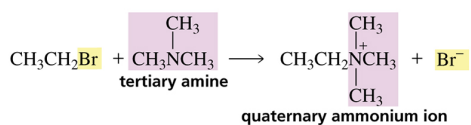
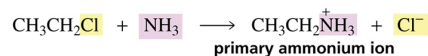
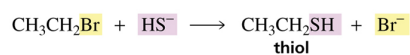
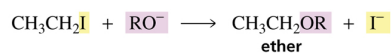
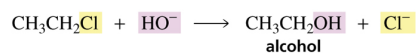
4. Steric Hindrance Decreases Nucleophilicity



mostly when comparing same-class nucleophiles – here, alkoxides

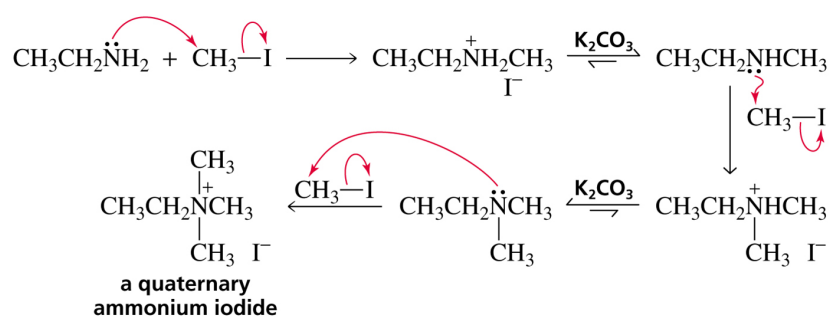


S_N2 Reactions Can Be Used to Make a Variety of Compounds



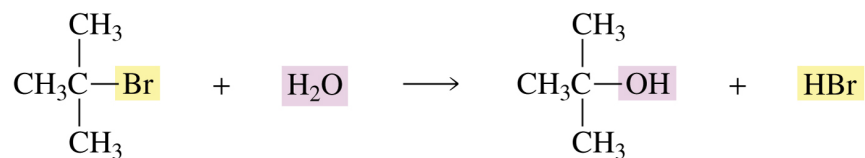
The reactions are **irreversible** because a weak base cannot displace a strong base.

Synthesizing an Amine



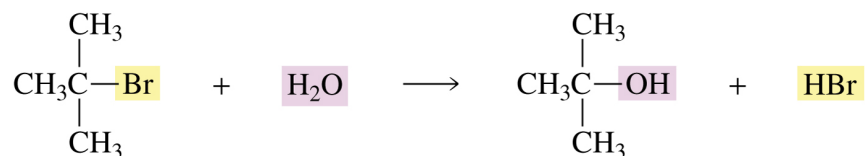
K_2CO_3 makes the solution **basic** so that the amine will exist in its **basic form**.

Another Substitution Reaction: S_N1



The reaction is surprisingly fast,
so it must be taking place by a **different mechanism**.

Another Substitution Reaction: S_N1



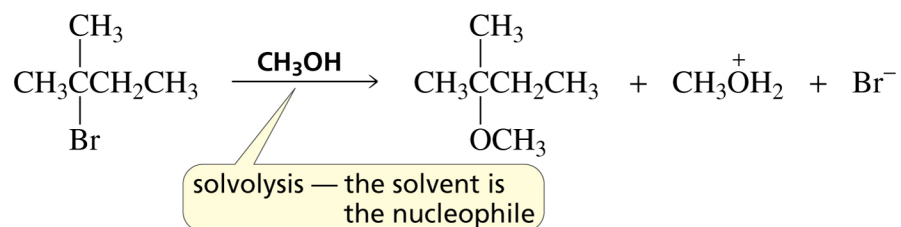
$$\text{rate} = k [\text{alkyl halide}]$$

an S_N1 reaction:

only the **alkyl halide** is in the **transition state** of the rate-limiting step.

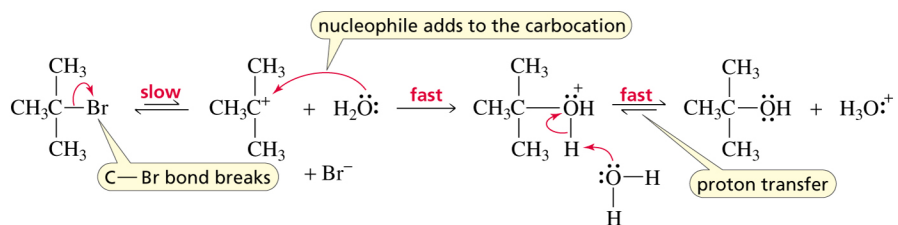
The reaction is surprisingly fast,
so it must be taking place by a **different mechanism**.

Solvolysis Reaction



A lot of S_N1 reactions are solvolysis reactions;
the solvent is the nucleophile.

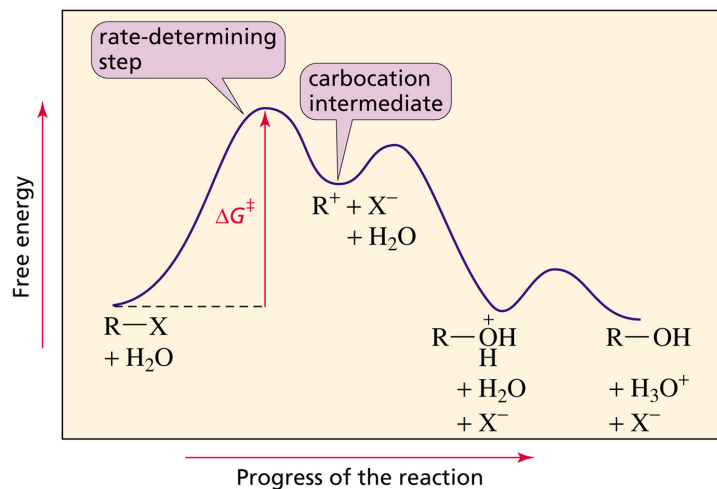
The Mechanism



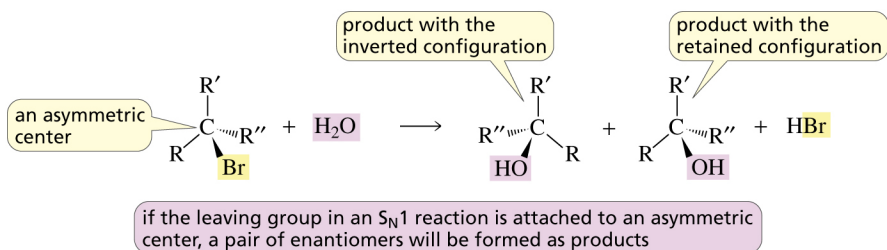
The leaving group departs **before** the nucleophile approaches.

The slow step is **carbocation formation**.

The Reaction Coordinate Diagram

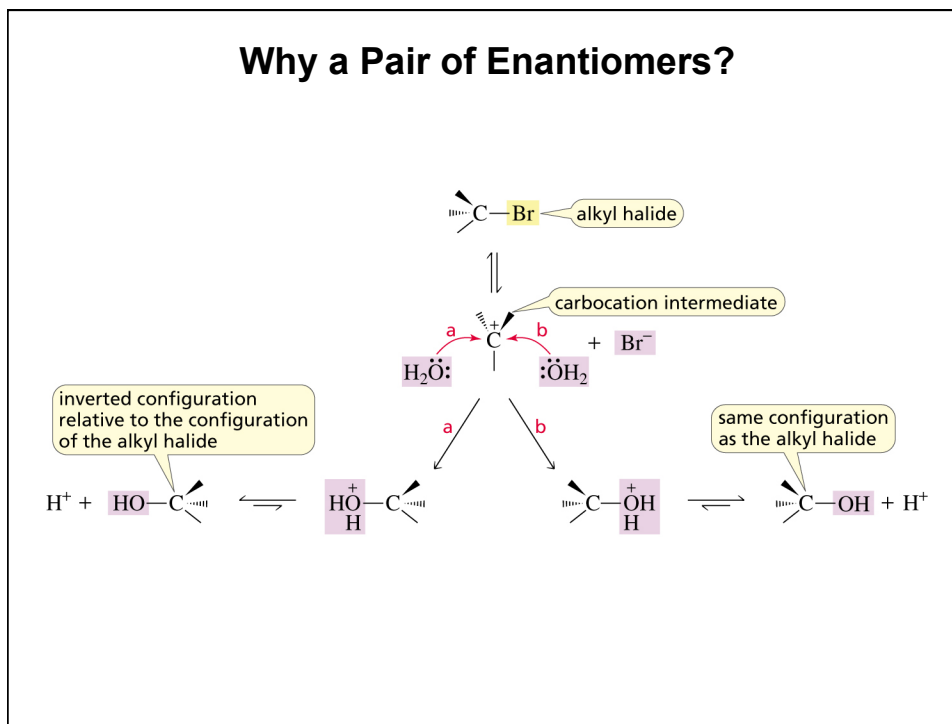


The Product is a Pair of Enantiomers

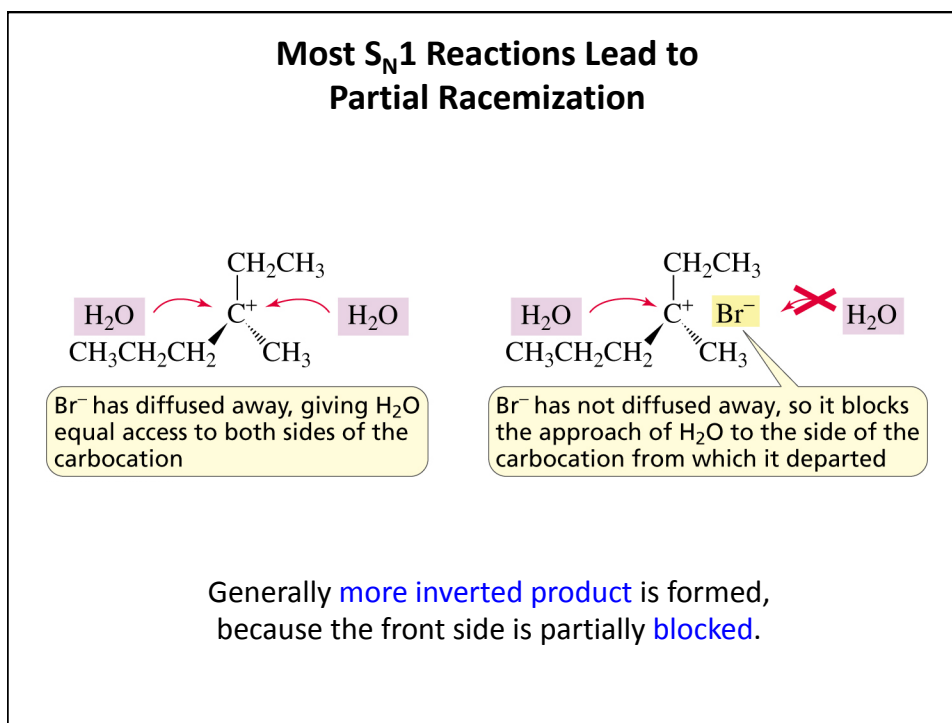


If the halogen is bonded to an asymmetric center, the product will be a **pair of enantiomers**.

Why a Pair of Enantiomers?

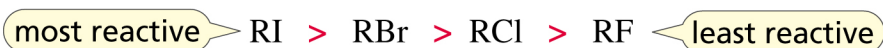


Most S_N1 Reactions Lead to Partial Racemization



Leaving Group Effect on S_N1 reactions: The Weakest Base is the Best Leaving Group

relative reactivities of alkyl halides in an S_N1 reaction



Comparing S_N2 and S_N1 Reactions

Table 9.3 Comparing S_N2 and S_N1 Reactions

S_N2	S_N1
one-step mechanism	two-step mechanism with a carbocation intermediate
bimolecular rate-determining step	unimolecular rate-determining step
rate decreases with increasing steric hindrance	rate decreases with decreasing stability of the carbocation
product has the inverted configuration relative to that of the reactant	products have both the retained and inverted configurations relative to that of the reactant
leaving group: $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$	leaving group: $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$
alkyl halide reactants: methyl, primary, secondary	alkyl halide reactants: tertiary
the better the nucleophile, the faster the rate of the reaction	the strength of the nucleophile does not affect the rate of the reaction

S_N1 and S_N2 reactions: brief summary

$$\text{rate} = k_2 [\text{alkyl halide}][\text{nucleophile}] + k_1 [\text{alkyl halide}]$$

contribution to the rate
by an S_N2 reaction

contribution to the rate
by an S_N1 reaction

primary alkyl halides and methyl halides

only S_N2

They cannot form carbocations.

secondary alkyl halides

only S_N2

Carbocation formation is too slow to make up
for the large concentration of the nucleophile
in a solvolysis reaction.

tertiary alkyl halides

only S_N1

They cannot undergo back-side attack.