

LEC (19)

Chem 30A

Nov 18th

(1)

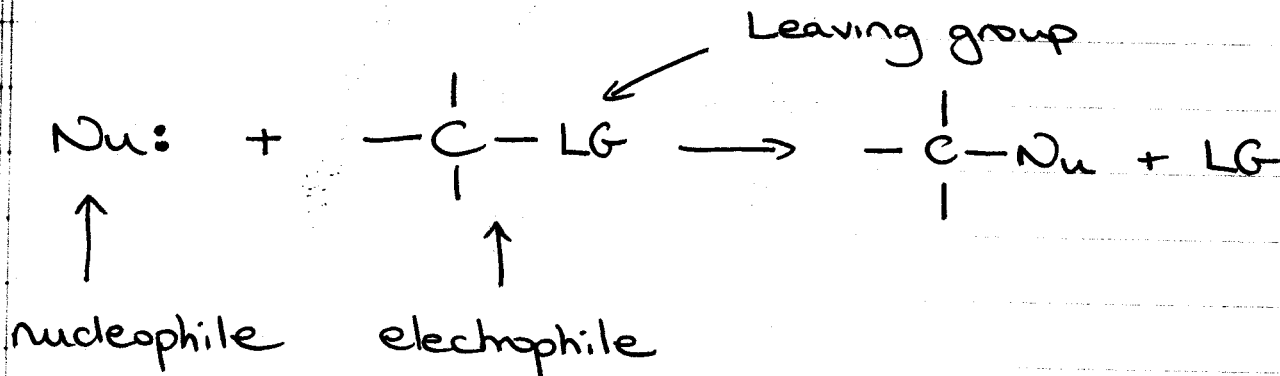
- NUCLEOPHILIC SUBSTITUTION

- (1) INTRODUCTION
- (2) MECHANISMS
- (3) ELECTROPHILE
- (4) NUCLEOPHILE

READ 8.1-8.6  
 PROBLEMS 8.1, 8.2, 8.3, 8.9-8.13

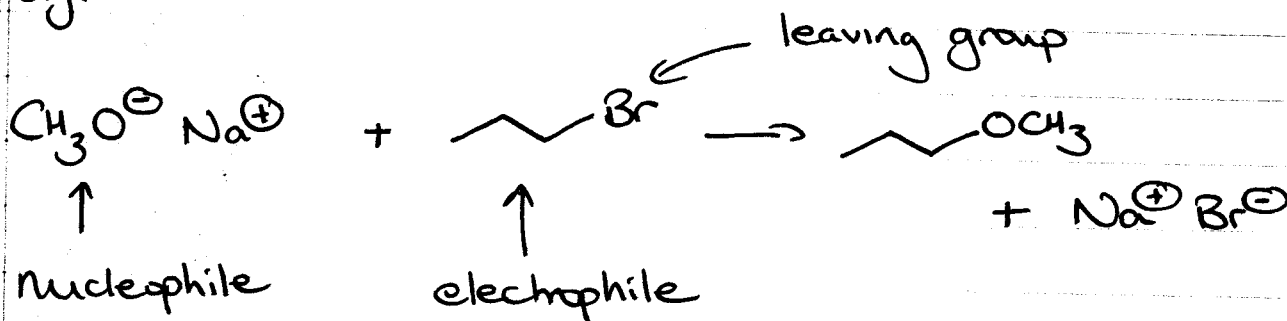
NOTHING ON  
 MIDTERM  
 FROM THIS  
 WEEKS  
LECTURES

(1) INTRODUCTION



SUBSTITUTION REACTION of Nu Br LG

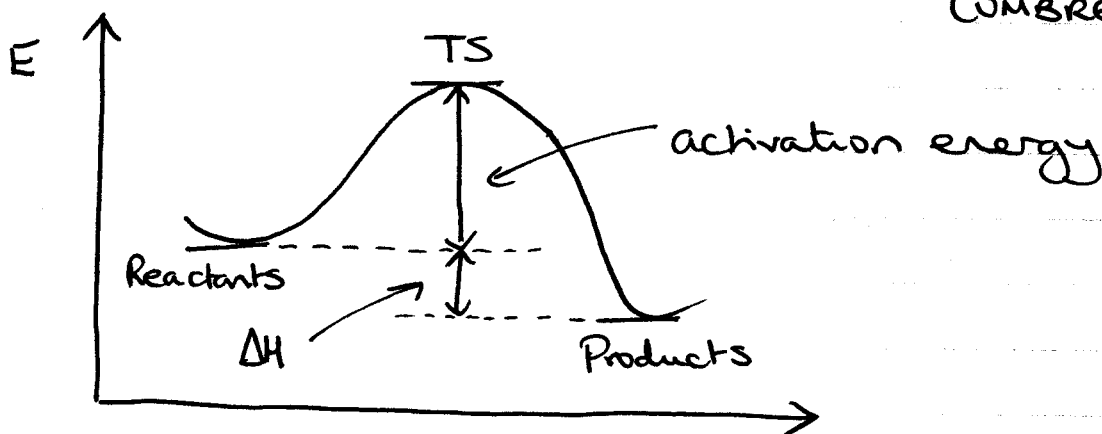
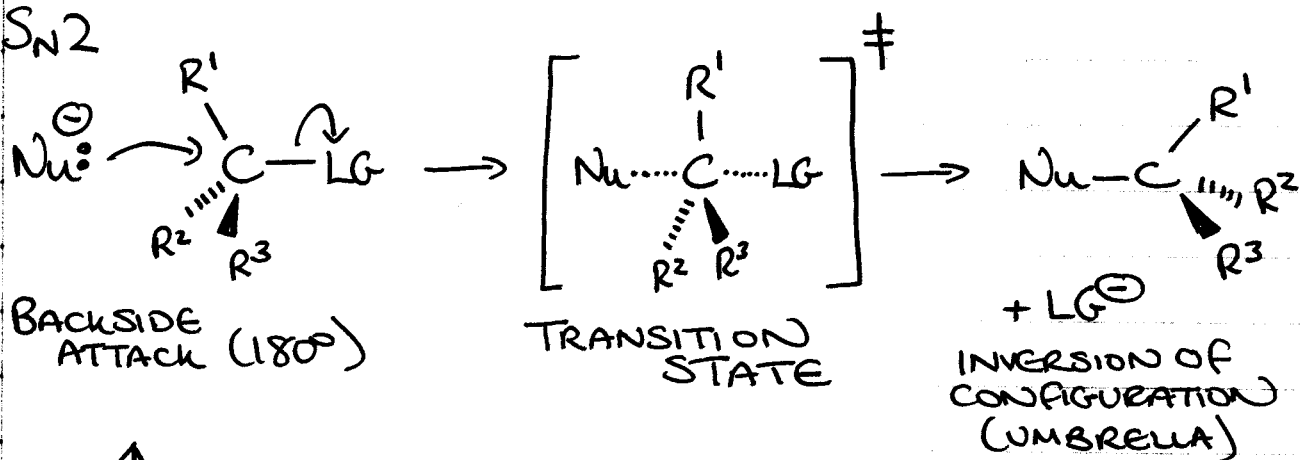
e.g.



## ② MECHANISMS

- TWO LIMITING MECHANISMS

(i) S<sub>N</sub>2



S<sub>N</sub>2 = SUBSTITUTION, NUCLEOPHILIC, BIMOLECULAR

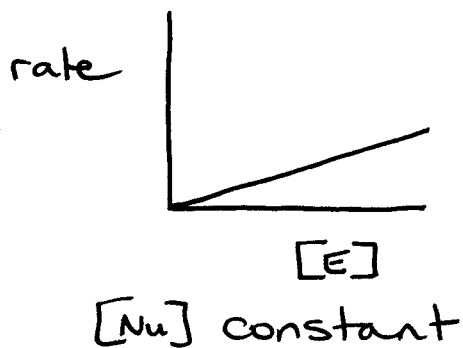
BIMOLECULAR REACTION

— RATE OF REACTION IS DEPENDANT UPON THE CONCENTRATIONS OF BOTH THE NUCLEOPHILE AND THE ELECTROPHILE

$$\text{rate} = k_2 [\text{Nu}] [\text{E}]$$

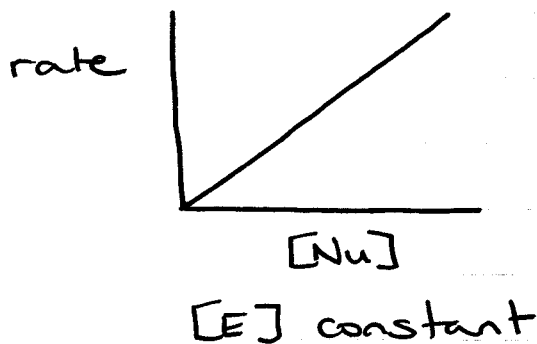
↑  
2nd order rate constant

TWO DIFFERENT EXPERIMENTS



$$\text{rate} = k_a [E]$$

$$k_a = k_2 [Nu]$$

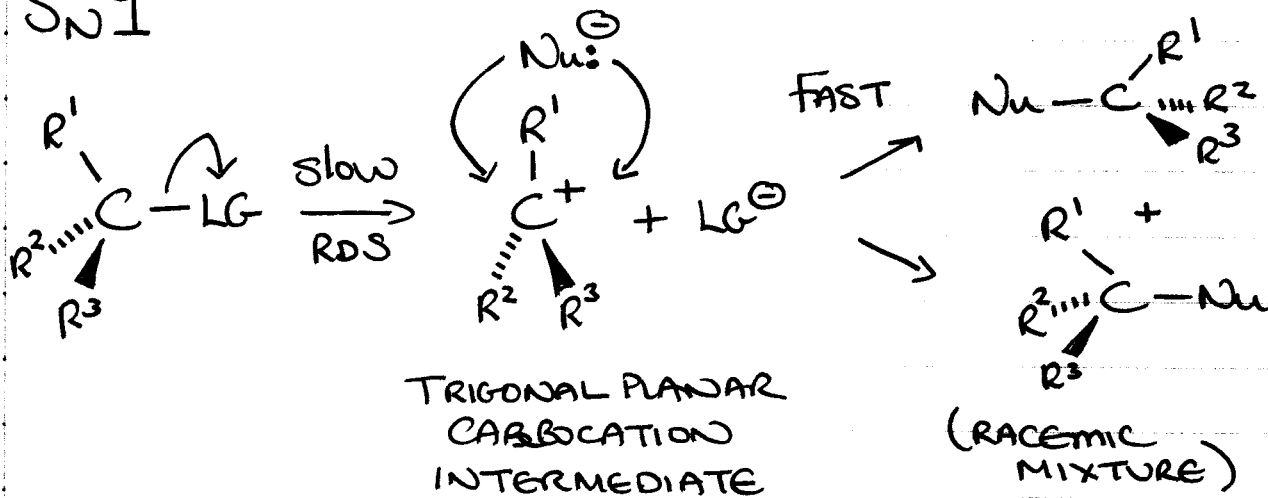


$$\text{rate} = k_b [Nu]$$

$$k_b = k_2 [E]$$

same value

(ii) S<sub>N</sub>1

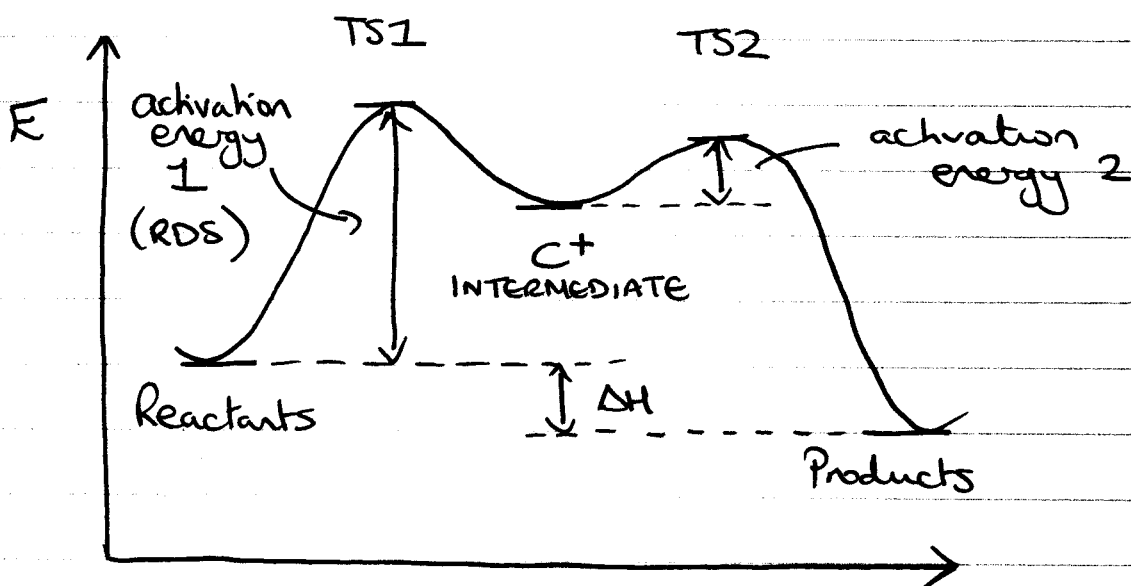


— ANY STEREOCHEMICAL INFORMATION IN THE STARTING MATERIAL IS LOST

S<sub>N</sub>1 — SUBSTITUTION, NUCLEOPHILIC, UNIMOLECULAR

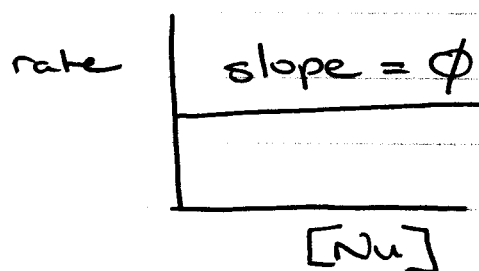
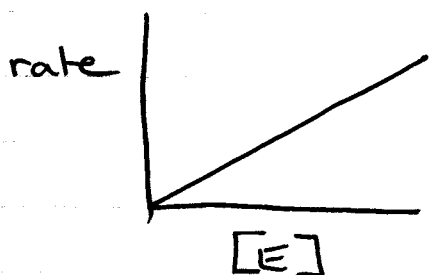
RATE ONLY DEPENDS ON [E]

4



$$\text{rate} = k_1 [E]$$

↑  
first order rate constant

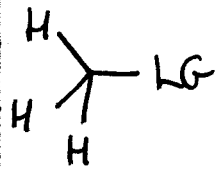


Rate determining step does not involve the NUCLEOPHILE, so adding more of it to the reaction DOES NOT affect the reaction rate.

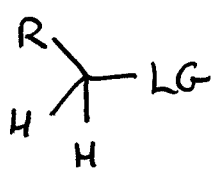
Also, nucleophilicity of the NUCLEOPHILE does not matter.

WHAT DECIDES SN1 VS SN2?

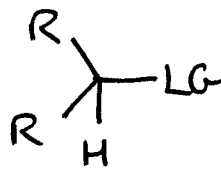
### ③ ELECTROPHILE



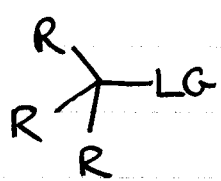
methyl



primary



secondary



tertiary

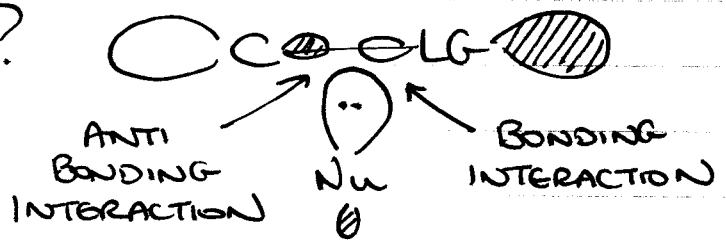
### $S_N2$ Backside attack



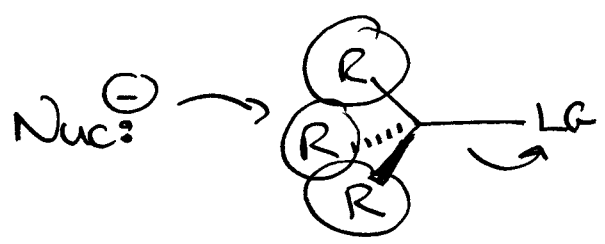
↑  
filled orbital  
in Nucleophile

↑  
 $\sigma^*$  - empty antibonding  
orbital

### Frontside attack?



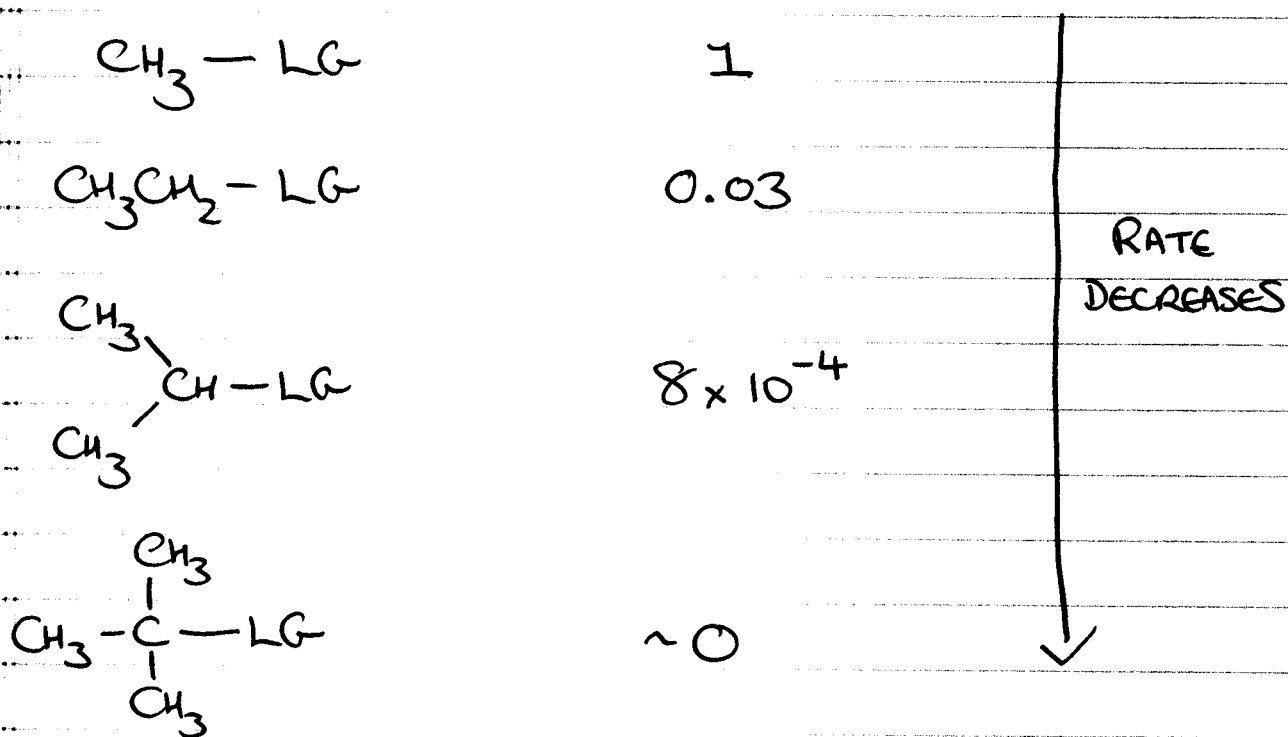
So/



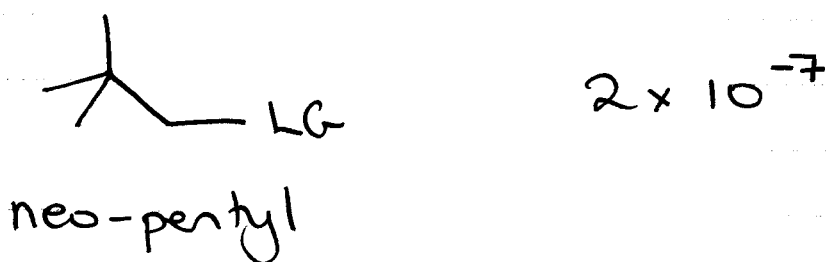
↑ more R groups  
⇒ STERIC CROWDING

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## Relative rates of $S_N2$ rxns



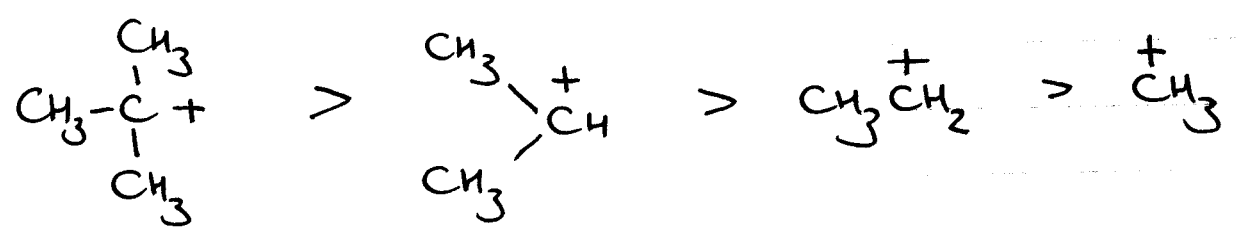
- Some  $1^\circ$  groups can also drastically alter reaction rate



Consider  $S_N1$  REACTIONS: opposite effect



### C<sup>+</sup> STABILITY

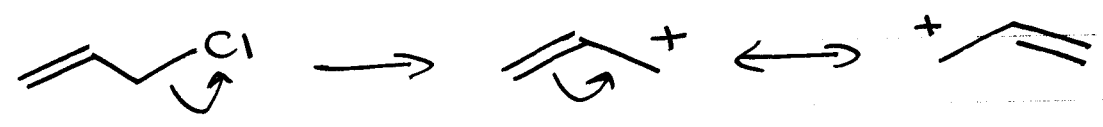


So, 1° and CH<sub>3</sub> electrophiles sp<sup>2</sup>

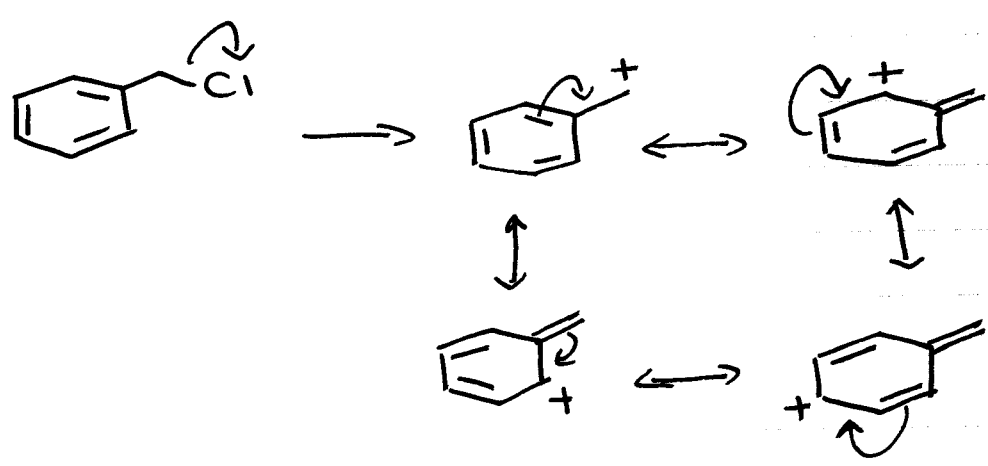
3° electrophiles sp<sup>3</sup>

2° C<sup>+</sup> can react either way, depending on other factors.

Other types of C<sup>+</sup>



RESONANCE STABILIZED  
1° ALLYLIC



RESONANCE STABILIZED BENZYLIC C<sup>+</sup>

1° ALLYLIC/BENZYLIC electrophiles =>  
S<sub>N</sub>1 or S<sub>N</sub>2 (depends on other factors)

STERICS favors S<sub>N</sub>2

ELECTRONICS favors S<sub>N</sub>1

2°/3° ALLYLIC/BENZYLIC electrophiles =>  
ALMOST exclusively S<sub>N</sub>1

#### ④ THE NUCLEOPHILE

consider BASICITY  $B:^{\ominus} \rightarrow H-Cl$

NUCLEOPHILICITY is similar  $Nu:^{\ominus} \rightarrow C-LG$

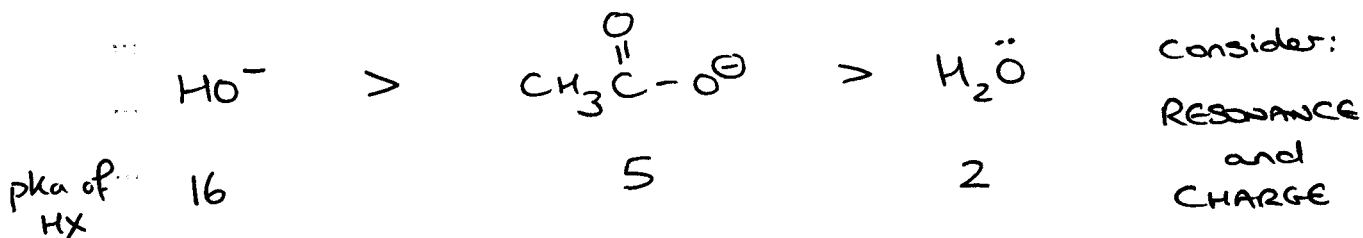
- AFFINITY FOR C atom

- KINETIC rather than THERMODYNAMIC EFFECT

IMPRECISE QUANTITY - for ANY GIVEN SPECIES,  
can vary depending on SOLVENT/ELECTROPHILE

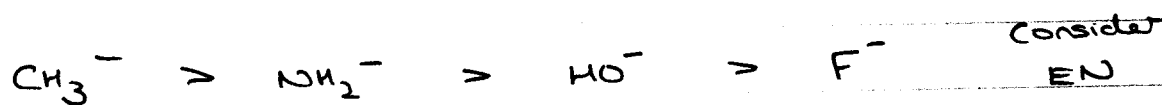
#### GENERAL TRENDS

- SAME NUCLEOPHILIC ATOM (parallels BASICITY)



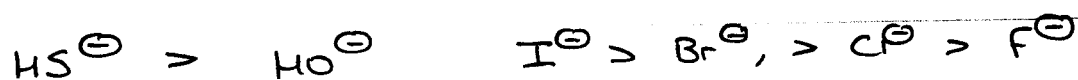


- NUCLEOPHILES in the SAME ROW (parallels BASICITY)



- NUCLEOPHILES in the SAME GROUP

In general, nucleophilicity INCREASES going down a group, i.e.,



OPPOSITE TO BASICITY - why?

- MANY FACTORS

(i) ENERGY LEVELS

Higher energy of lone pair electrons as you go down the table, better overlap with  $\sigma^*$

(ii) POLARISABILITY

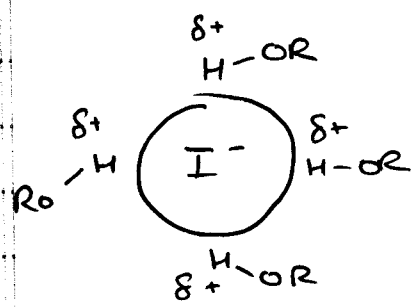
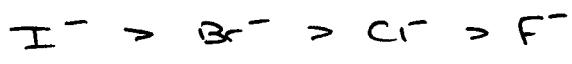
Larger atoms  $\Rightarrow$  more diffuse electron clouds, greater POLARISABILITY  $\rightarrow$  BONDS can begin to form at greater INTERATOMIC DISTANCES.

SOLVENT HAS LARGEST EFFECT

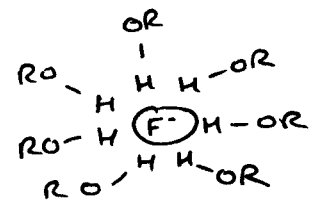
- POLAR PROTIC ( $\text{H}_2\text{O}$ ,  $\text{MeOH}$ ,  $\text{EtOH}$ )

- POLAR APROTIC ( $\text{DMSO}$ ,  $\text{DMF}$ ,  $\text{MeCN}$ , Acetone)

- POLAR PROTIC SOLVENTS

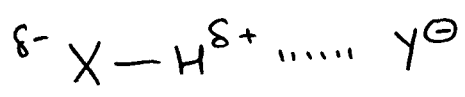


LOW CHARGE DENSITY  
(weak solvent cage)



HIGH CHARGE DENSITY  
(strong solvent cage)

HYDROGEN BONDING - noncovalent interaction



So, smaller Nu = higher charge density  
→ more solvated, less nucleophilic

- BUT/ IN POLAR APROTIC SOLVENTS

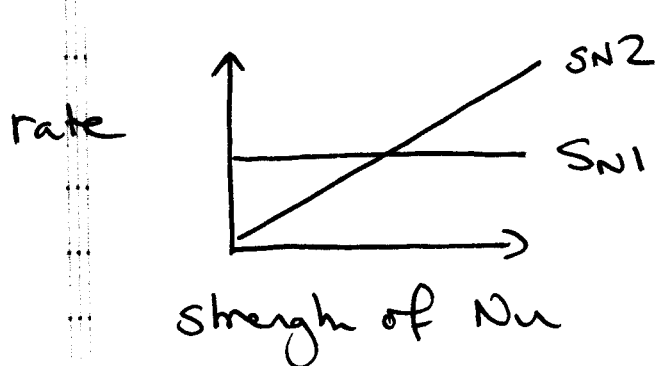
ANIONS WEAKLY SOLVATED, TREND REVERSED,  
& CORRELATES w/ BASICITY



Nuc <sup>-</sup>	pKa	MeOH (Time to complete reaction)	DMF	
I <sup>-</sup>	-10	17 min	8.7 s	Overall message → POLAR APROTIC SOLVENTS <u>GOOD</u>
Br <sup>-</sup>	-8	12h	8.7 s	
Cl <sup>-</sup>	-6	13d	1.4 s	
F <sup>-</sup>	3	> 2 yrs	< 1.2 s	

DMF / MeOH → equivalent polarities

## $S_N1$ vs $S_N2$



$$\text{rate} = k_2 [E] [Nu]$$

$$\text{rate} = k_1 [E]$$

Has no effect on  $S_N1$ , but stronger nucleophiles tend to favor  $S_N2$  reactions