

- NUCLEOPHILIC SUBSTITUTION

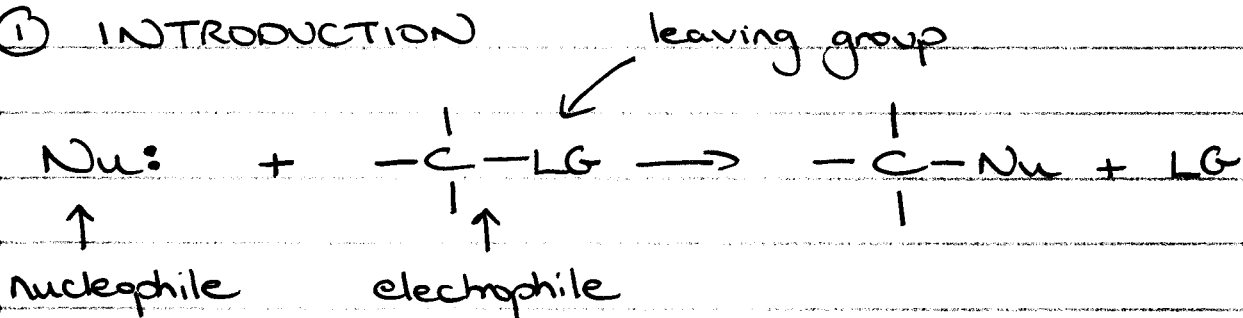
- ① INTRODUCTION
- ② MECHANISMS
- ③ ELECTROPHILE
- ④ NUCLEOPHILE

READ 8.1-8.6

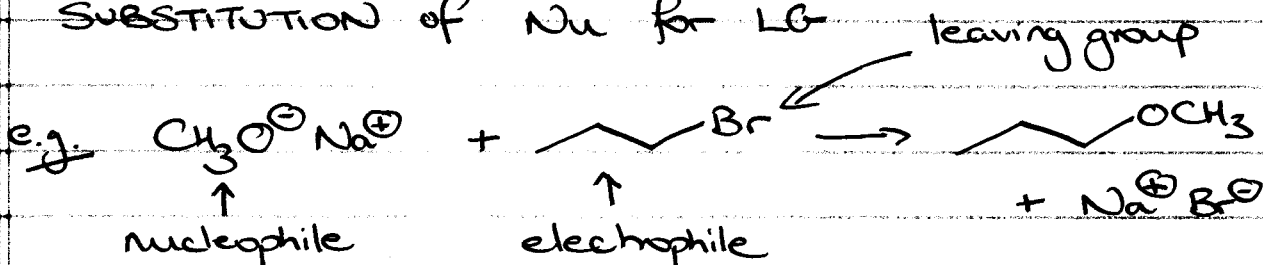
PROBLEMS:
8.1-8.3, 8.9-8.13

- MIDTERM ON WEDS - usual rules
- NOTHING FROM TODAY'S CLASS ON MIDTERM

① INTRODUCTION

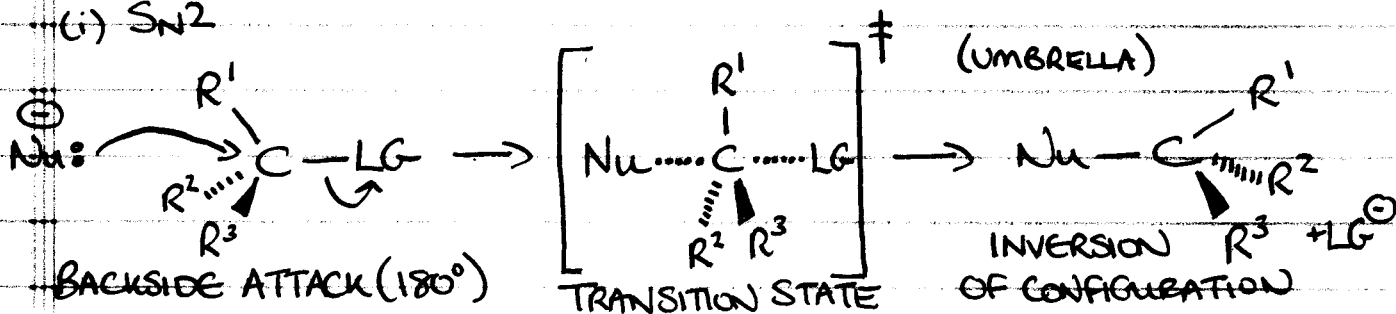


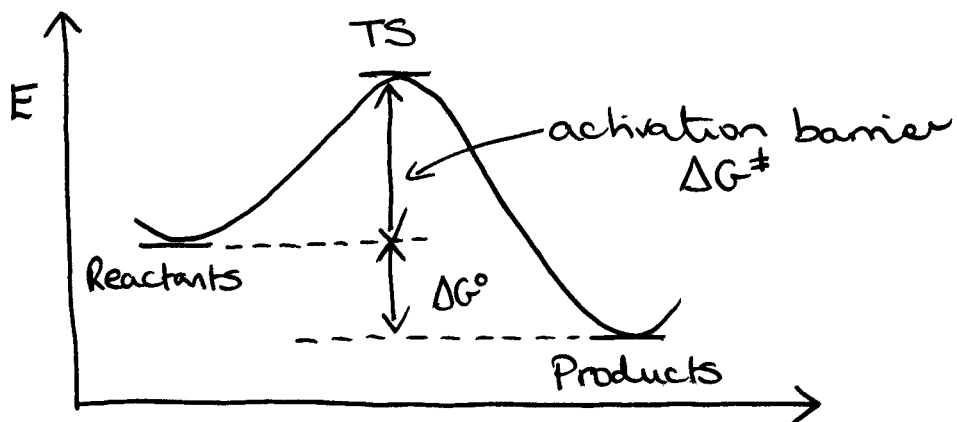
SUBSTITUTION of Nu for LG



② MECHANISMS (2 LIMITING MECHANISMS)

(i) S_N2





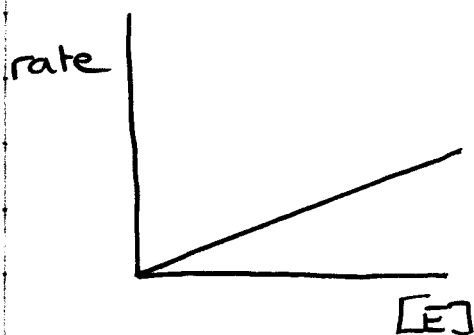
S_N2 = SUBSTITUTION, NUCLEOPHILIC, BIMOLECULAR

BIMOLECULAR - 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

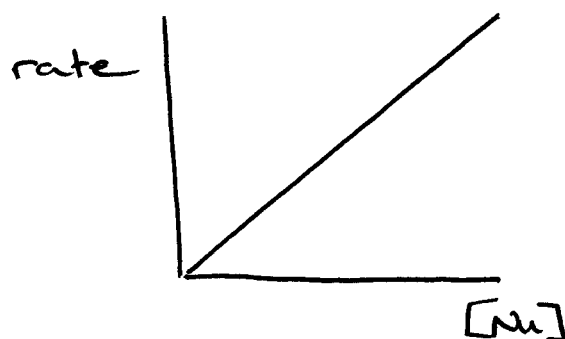
TWO DIFFERENT EXPERIMENTS



$[\text{Nu}]$ CONSTANT

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

$$k_a = k_2 [\text{Nu}]$$



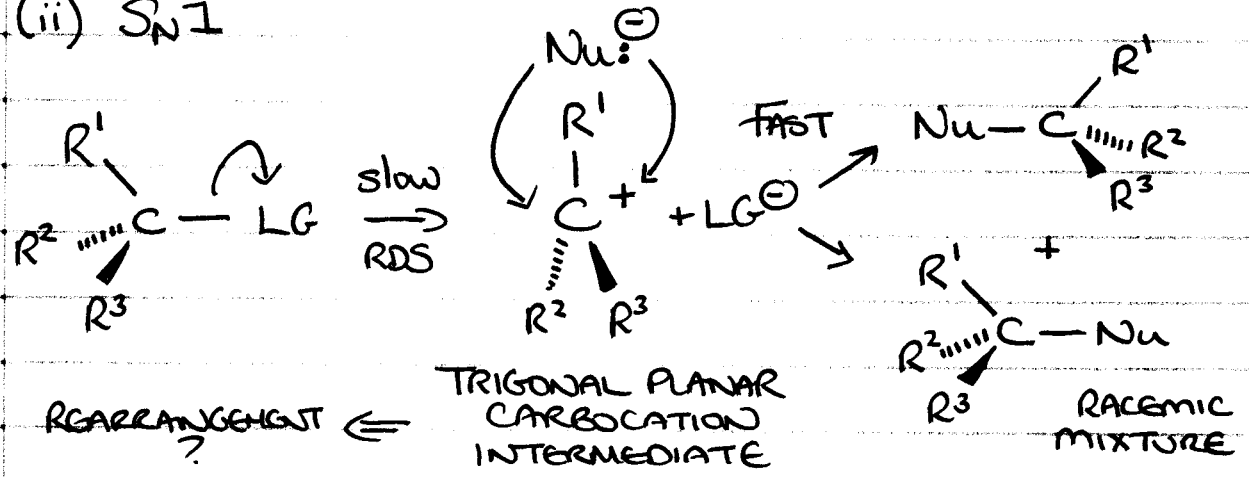
$[\text{E}]$ CONSTANT

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

$$k_b = k_2 [\text{E}]$$

← Same value →

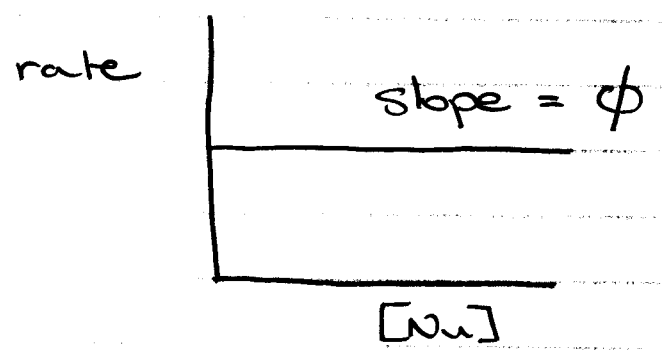
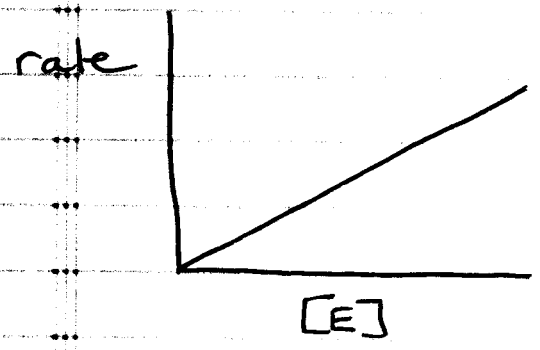
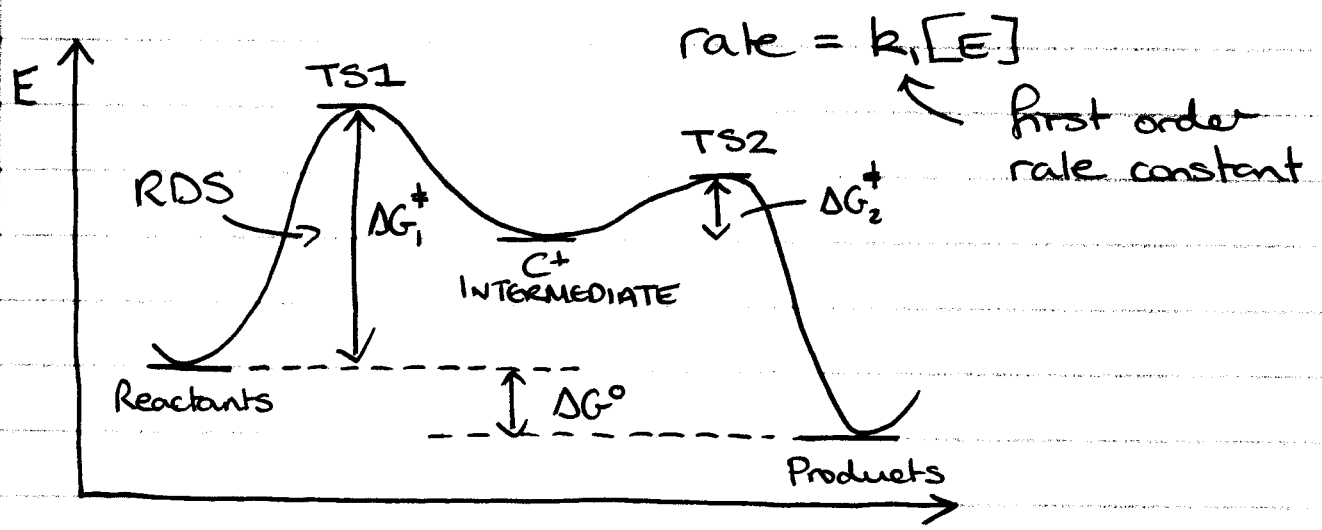
(ii) S_N1



- ANY STEREOCHEMICAL INFORMATION IN THE STARTING MATERIAL IS LOST

S_N1 - SUBSTITUTION, NUCLEOPHILIC, UNIMOLECULAR

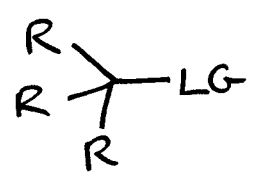
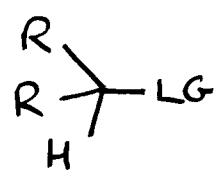
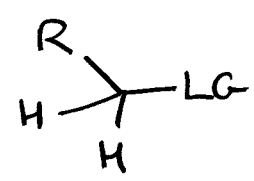
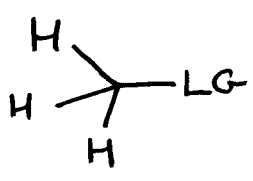
RATE ONLY DEPENDS ON [E]



RDS does not involve the nucleophile, so adding more of it to the reaction does not affect the rate => ALSO, reactivity of nucleophile does not matter.

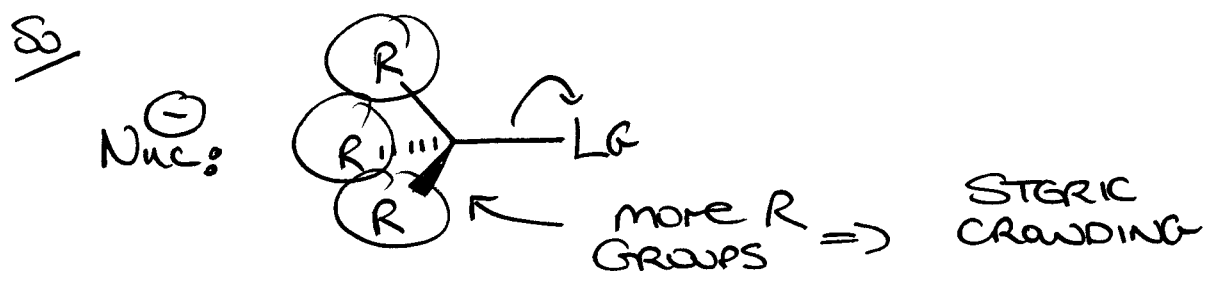
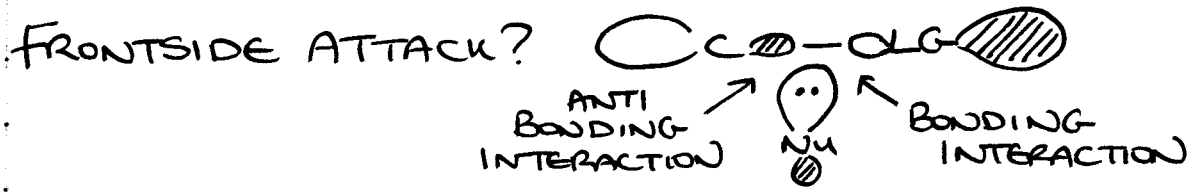
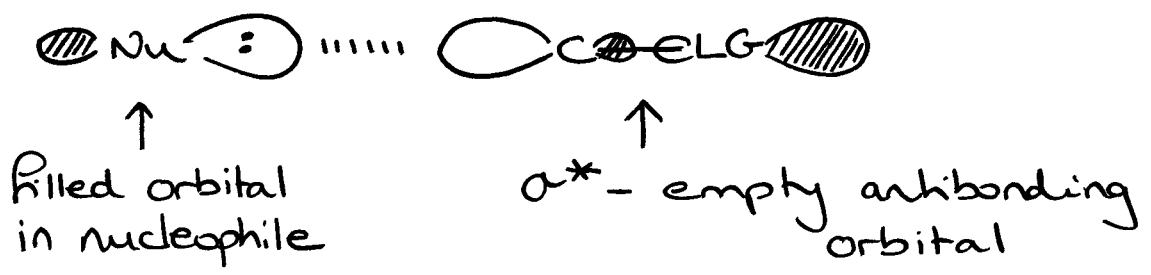
WHAT DECIDES S_N1 vs S_N2 ?

③ THE ELECTROPHILE



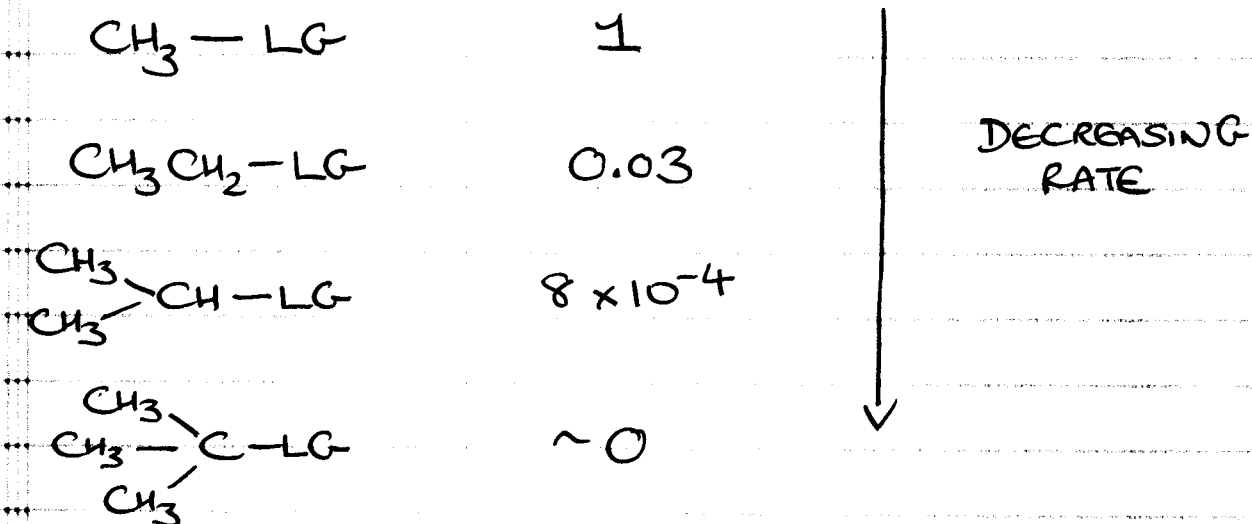
methyl primary secondary tertiary

S_N2 BACKSIDE ATTACK

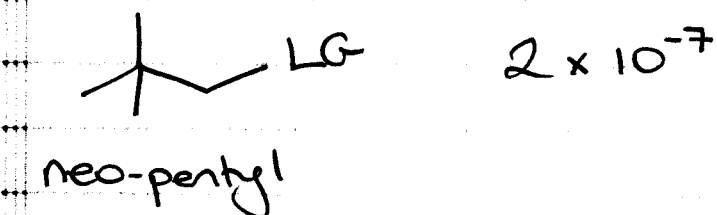


5

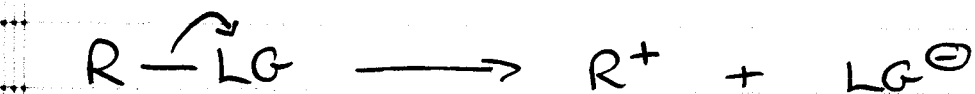
Relative Rates of S_N2 reactions



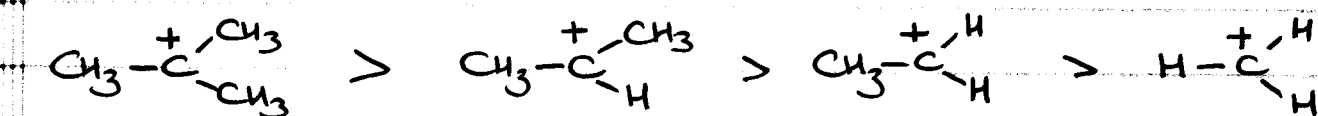
- Some 1° groups also slow things down



CONSIDER S_N1 REACTIONS: OPPOSITE EFFECT



C⁺ STABILITY



So, 1° and CH₃ electrophiles S_N2

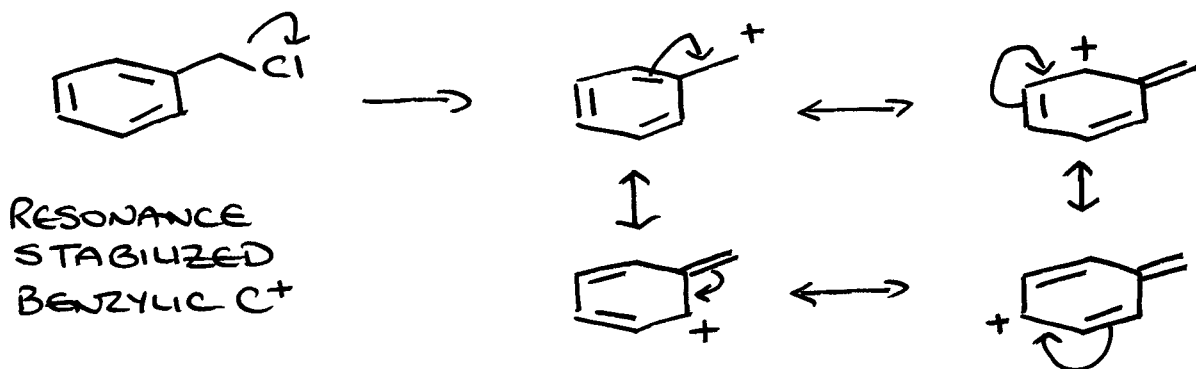
3° electrophiles S_N1

WHAT ABOUT SECONDARY?

6

2°C^+ can react either way - depending on other factors

- other types of C^+

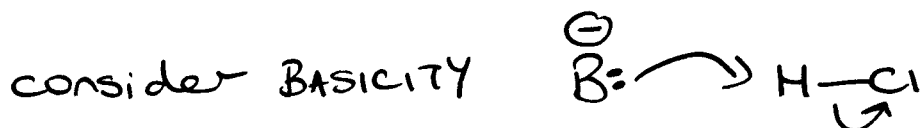


1° ALLYLIC / BENZYLIC electrophiles \Rightarrow
 $\text{S}_\text{N}1$ / $\text{S}_\text{N}2$ depends on other factors

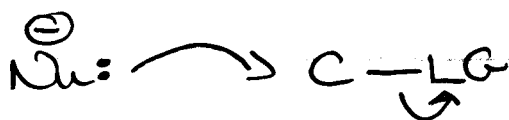
STERICS favors $\text{S}_\text{N}2$ ELECTRONICS favors $\text{S}_\text{N}1$

$2^\circ/3^\circ$ ALLYLIC / BENZYLIC electrophiles \Rightarrow
almost exclusively $\text{S}_\text{N}1$

④ NUCLEOPHILE



Nucleophilicity
is similar

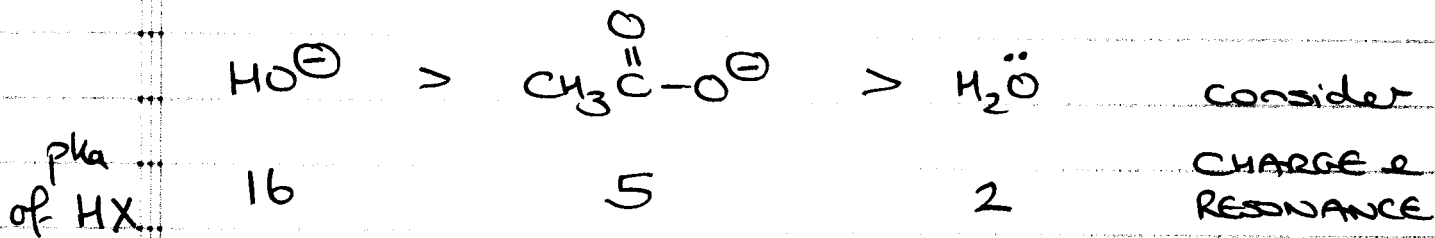


- AFFINITY for C atom
- KINETIC rather than THERMODYNAMIC effect

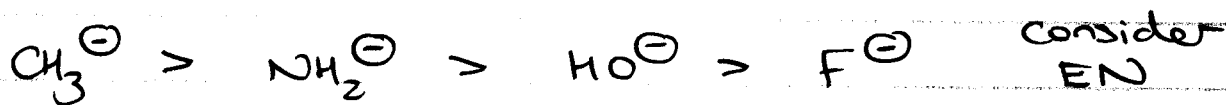
IMPRECISE QUANTITY - for any given species
can vary depending upon other factors
(solvent, electrophile)

- General trends

(i) SAME NUCLEOPHILIC ATOM (parallels BASICITY)



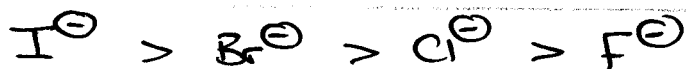
(ii) NUCLEOPHILES IN THE SAME ROW (parallels BASICITY)



(iii) NUCLEOPHILES IN THE SAME GROUP (COMPLICATED)

ALL COMES DOWN TO SIZE

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 periodic table \Rightarrow better overlap w/ o^*

(ii) POLARISABILITY

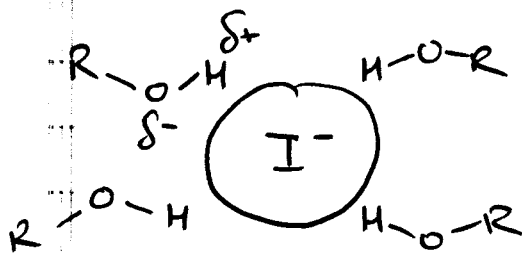
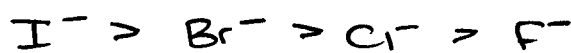
Larger atoms, more diffuse electron clouds \Rightarrow greater POLARISABILITY \rightarrow BONDS can begin to form at greater INTERATOMIC DISTANCES

(iii) SOLVENT (largest effect)

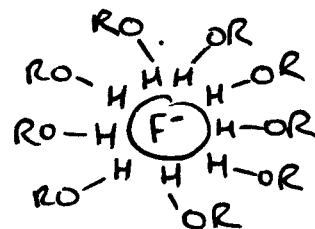
- POLAR PROTIC (H_2O , MeOH, EtOH)

- POLAR APROTIC (DMSO, DMF, MeCN, Acetone)

- POLAR PROTIC SOLVENTS

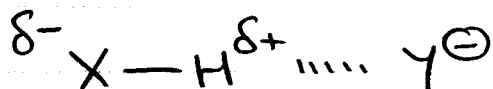


LOW CHARGE DENSITY
(weak solvent cage)



HIGH CHARGE DENSITY
(strong solvent cage)

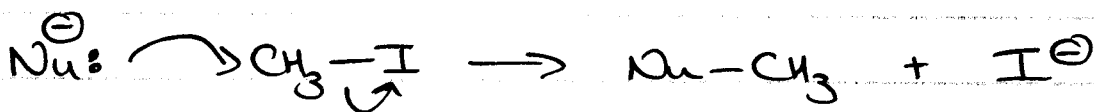
HYDROGEN BONDING - noncovalent interaction



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

BUT IN POLAR APROTIC SOLVENTS

\Rightarrow ANIONS WEAKLY SOLVATED, TREND IS REVERSED & CORRELATES w/ BASICITY



Nu	pKa	MeOH (Time to complete rxn)	DMF	
I ⁻	-10	17min	8.7s	Overall message \rightarrow
Br ⁻	-8	12h	8.7s	
Cl ⁻	-6	13d	1.4s	POLAR APROTIC SOLVENTS ARE <u>GOOD</u>
F ⁻	3	>2yrs	<1.2s	

DMF/meOH \rightarrow equivalent polarities

S_N1 vs S_N2

