

LEC (21)

CHEM 30A

May 23rd (1)

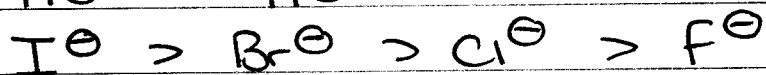
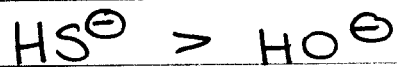
- NUCLEOPHILIC SUBSTITUTION

- (1) NUCLEOPHILE
- (2) LEAVING GROUP
- (3) SOLVENT

MIDTERM (weds) LAST NAME A-O (CSSP)  
P-Z (Royce 19P)

(1) NUCLEOPHILES  
(same group)

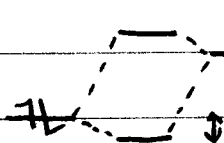
GENERAL TREND: increases down a group



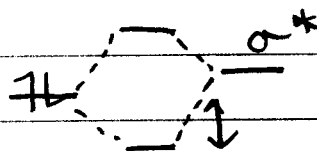
opposite to BASICITY - why?

(i) ENERGY LEVELS

- higher energy of lone pair electrons as you go down the periodic table  $\rightarrow$  better overlap with  $\sigma^*$



vs



(ii) POLARISABILITY

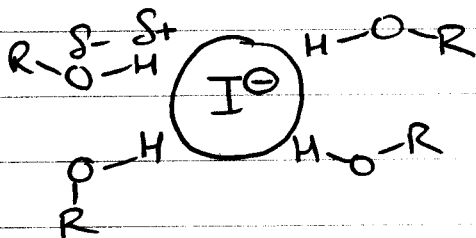
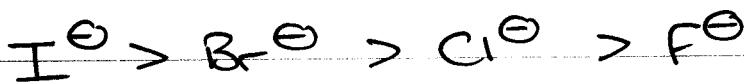
Larger atoms => more diffuse e- clouds  
=> GREATER POLARISABILITY, and BONDS  
can begin to form at greater INTERATOMIC  
DISTANCES.

(iii) SOLVENT (large effect - more later)

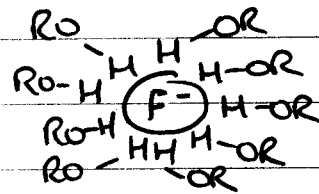
- POLAR PROTIC (H<sub>2</sub>O, MeOH, EtOH, H<sup>+</sup>-OH)

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

POLAR PROTIC SOLVENTS

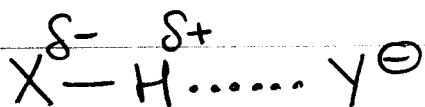


LOW CHARGE DENSITY  
(weak solvent cage)



HIGH CHARGE DENSITY  
(strong solvent cage)

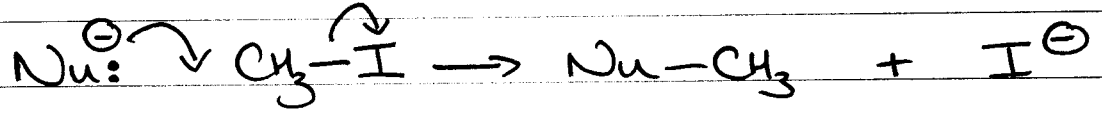
HYDROGEN BONDING - noncovalent interaction



So, SMALLER Nu = higher charge DENSITY  
=> more SOLVATED, LESS nucleophilic

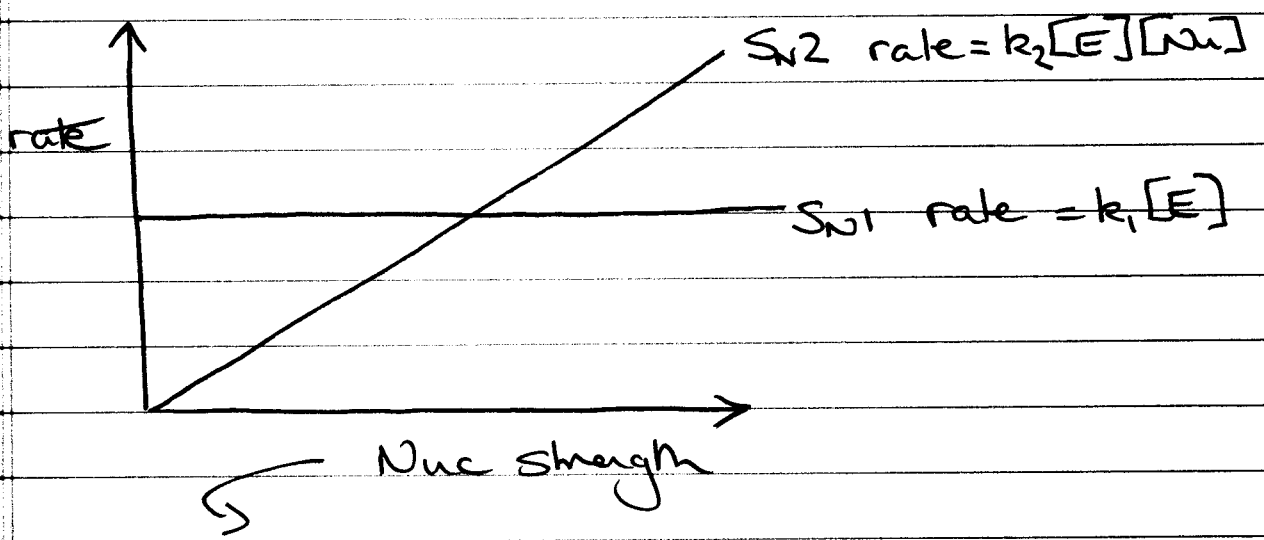
BUT

IN POLAR APROTIC SOLVENTS, ANIONS are weakly solvated, trend is reversed (for halogens) and correlates w/ BASICITY

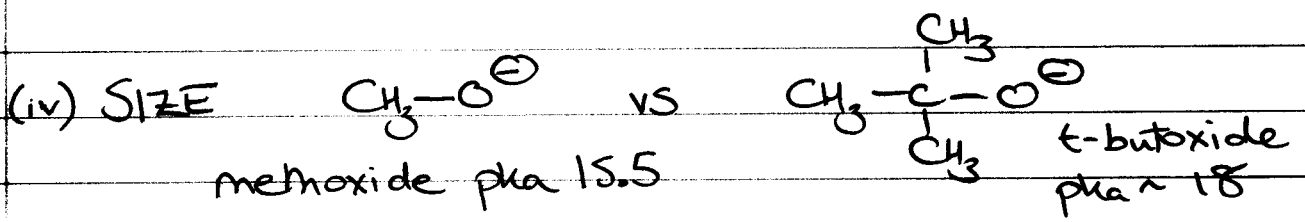


Nu	pKa	MeOH (time to complete rxn)	DMF	equiv polarities
I <sup>-</sup>	-10	17 min	8.7s	Overall message POLAR APROTIC SOLVENTS (GOOD)
Br <sup>-</sup>	-8	12h	8.7s	
Cl <sup>-</sup>	-6	13d	1.4s	
F <sup>-</sup>	3	> 2yrs	< 1.2s	

So S<sub>N</sub>1 vs S<sub>N</sub>2



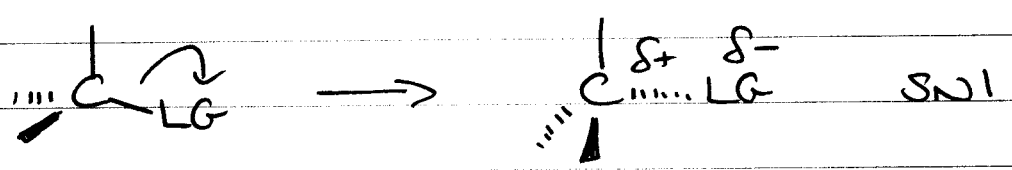
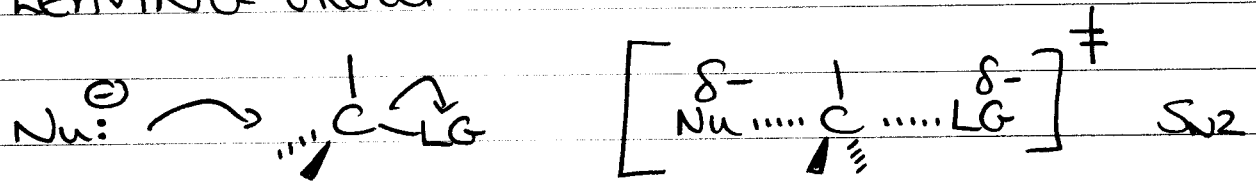
NO EFFECT on S<sub>N</sub>1, but Stronger Nuc favors S<sub>N</sub>2 reactions





$t\text{BuO}^\ominus$  more BASIC than  $\text{MeO}^\ominus$ , but LESS nucleophilic, due to BAD STERICS

② LEAVING GROUP



LG develops -ve charge in TS, so better charge stabilization, lower energy TS, faster rxn.

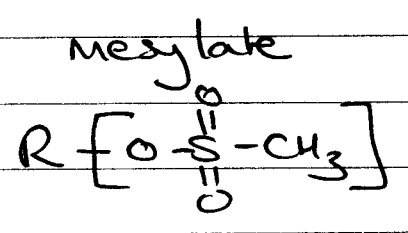
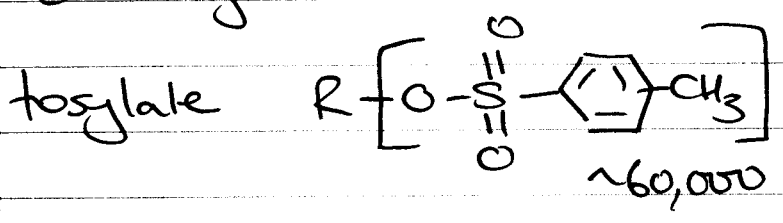
Thus MORE ACIDIC H-LG, more stable  $\text{LG}^\ominus$

GOOD/BAD LEAVING GROUPS

- relative reactivity

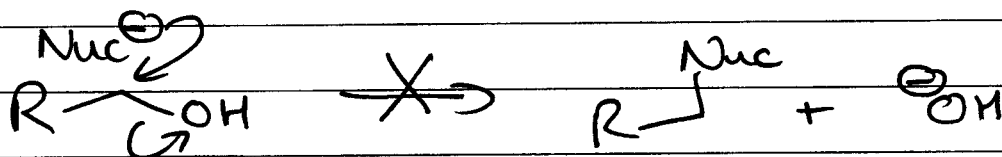
$\text{NH}_2^\ominus$	$\text{OH}^\ominus$	$\text{OR}^\ominus$	$\text{F}^\ominus$	$\text{Cl}^\ominus$	$\text{Br}^\ominus$	$\text{I}^\ominus$
~~~~~						
<< 1			1	200	10000	30000

other good LG

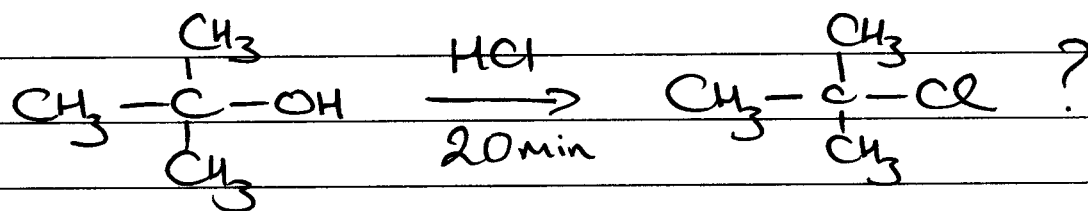


So  $R-F$ ,  $R-OH$ ,  $R-OR'$ ,  $R-NH_2$

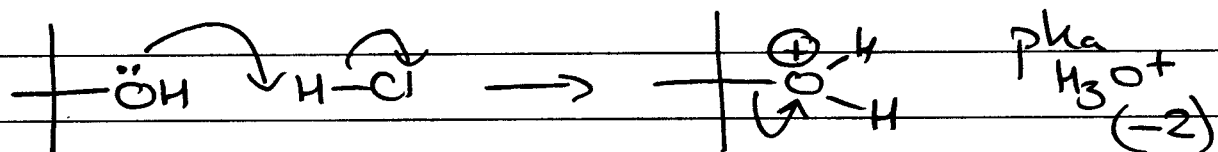
do NOT undergo  $S_N2$  reactions



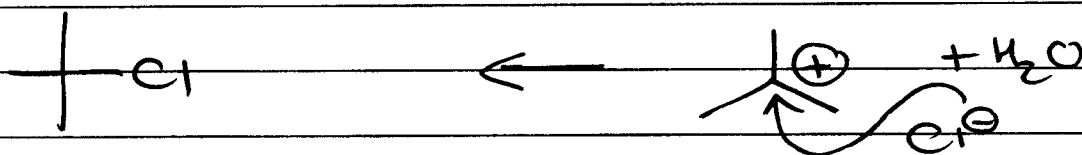
BUT



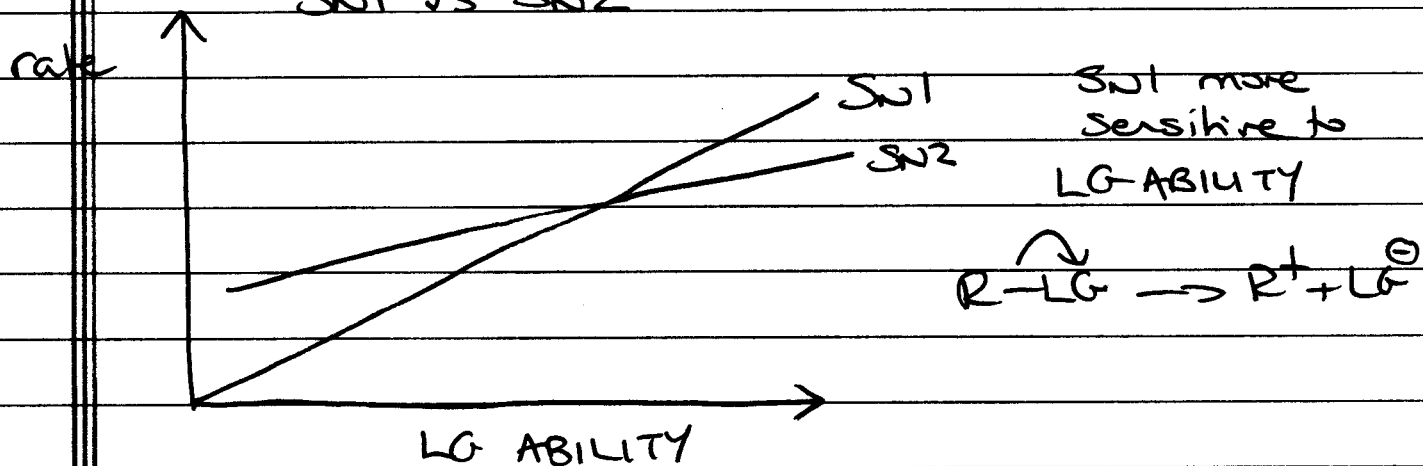
$-OH$  converted into good LG



$S_N1$  MECHANISM



$S_N1$  vs  $S_N2$



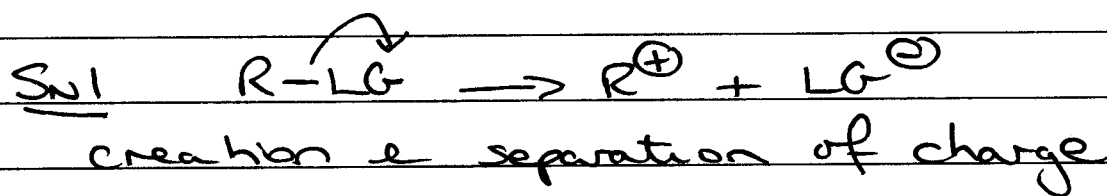
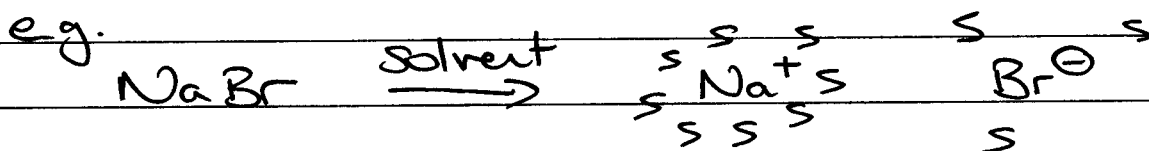
6

In  $S_N2$  reaction, as long as  $LG^-$  is more stable than  $Nuc^-$ , reaction can proceed.

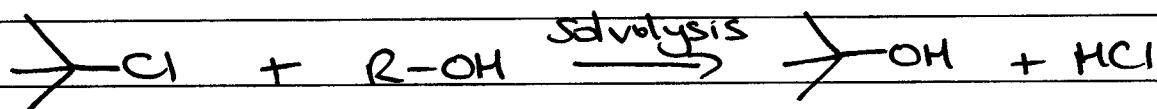
BUT cannot determine  $S_N1$  vs  $S_N2$  on LG ability alone

### ③ SOLVENT

$S_N2$  POLAR APROTIC solvents  
(solvate cations well, but not anions)



$\Rightarrow$  more polar the solvent, the better



Water/EtOH

Relative rate

100 / 0	100,000
80 20	14,000
40 60	100
0 100	1

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S<sub>N</sub>2 reactions

DISFAVORED IN PROTIC SOLVENTS

(ground state energy lowered by solvation)

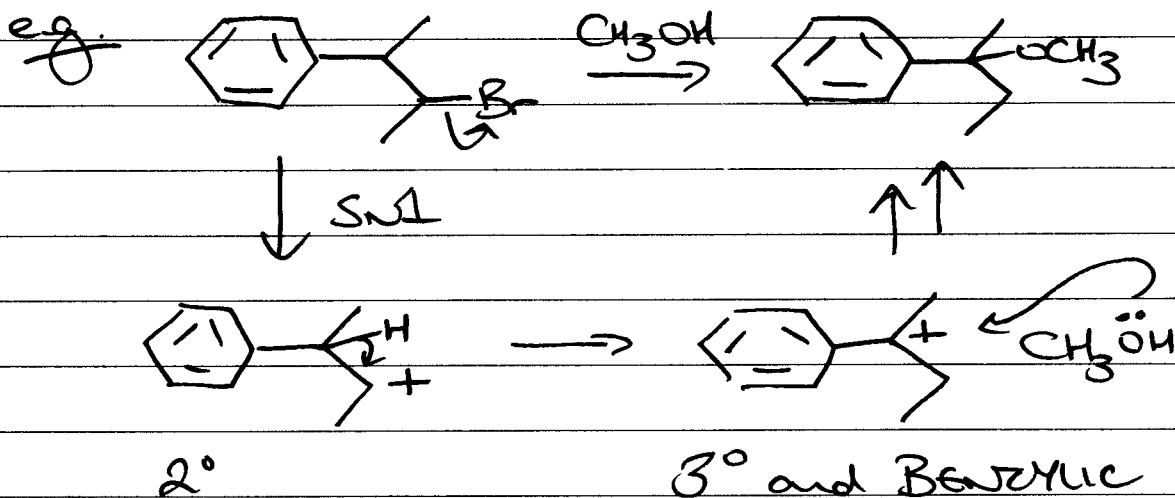
S<sub>N</sub>1 reactions

FAVORED IN PROTIC SOLVENTS

(transition state energy lowered by solvation)

Note about S<sub>N</sub>1

- goes thru C<sup>+</sup>, so look for rearrangement



- SUMMARY of S<sub>N</sub> RXNS

2

ELECTROPHILE

S<sub>N</sub>2

S<sub>N</sub>1

Me/1°

✓

X

2°

FAVORED

FAVORED

GOOD Nuc

POOR Nuc

POLAR APROTIC Solvents

PROTIC Solvents

v. GOOD LG,

BASEYUC/NUYUC

3°

X

✓

— but it gets COMPLICATED

⇒ COMPETING ELIMINATION RXNS...