

NUCLEOPHILIC SUBSTITUTION

MIDTERM MONDAY

① ELECTROPHILE

A-J CS76

② NUCLEOPHILE

K-Z CS50

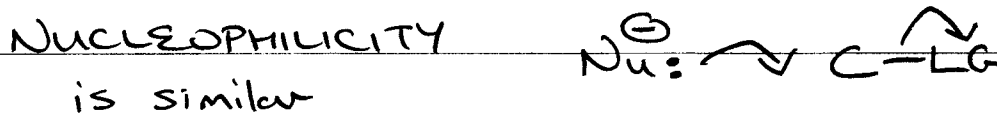
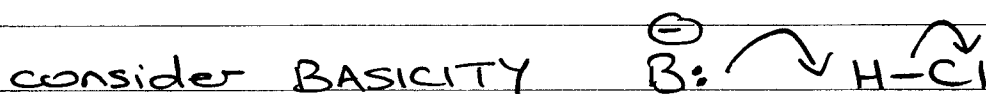
③ LEAVING-GROUP

④ SOLVENT

① ELECTROPHILE

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② NUCLEOPHILE



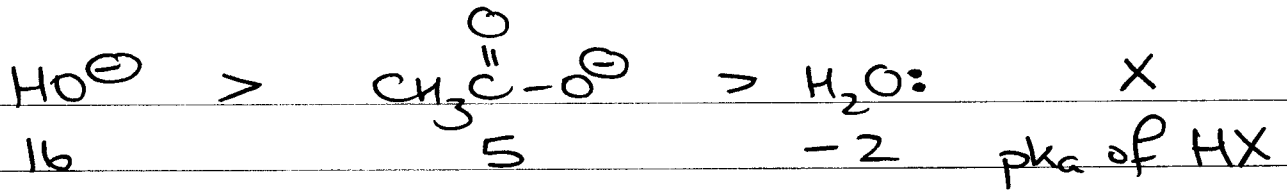
- affinity for a CARBON atom
- KINETIC rather than THERMODYNAMIC effect

IMPRECISE QUANTITY - for any given species can vary depending upon other factors (SOLVENT/ELECTROPHILE)

- General trends

- (i) same nucleophilic atom PARALLELS BASICITY

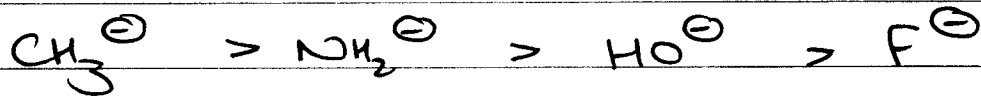
(2)



consider CHARGE/RESONANCE

(ii) nucleophiles in same row

PARALLELS BASICITY

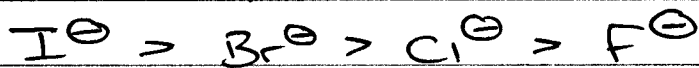
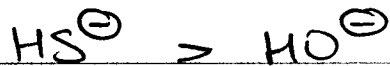


consider ELECTRONEGATIVITY

(iii) nucleophiles in the same group
(COMPLICATED)

SIZE MATTERS

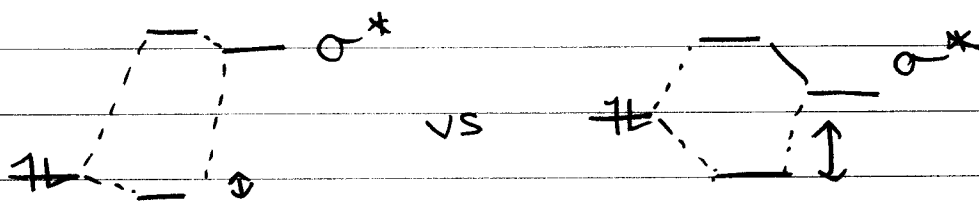
In general nucleophilicity increases going down a group...



- opposite to BASICITY - why?

a) ENERGY LEVELS

- higher energy of lp electrons as you go down the periodic table → better overlap with σ^*



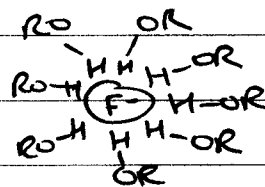
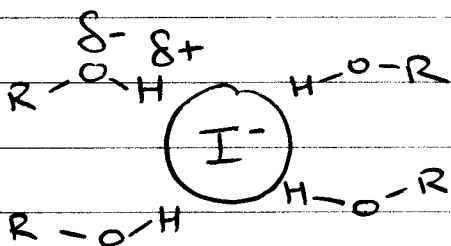
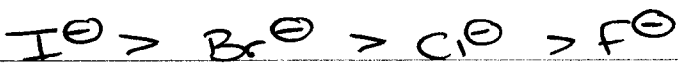
(b) POLARISABILITY

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

(c) SOLVENT (large effect - more later)

- POLAR PROTIC (H₂O, MeOH, EtOH, H-OH⁺)
- POLAR APROTIC (DMSO, DMF, MeCN, Acetone)

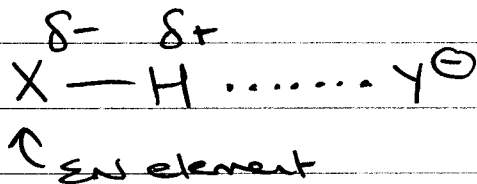
POLAR PROTIC SOLVENTS



LOW CHARGE DENSITY
(weak solvent cage)

HIGH CHARGE DENSITY
(strong solvent cage)

HYDROGEN BONDING



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

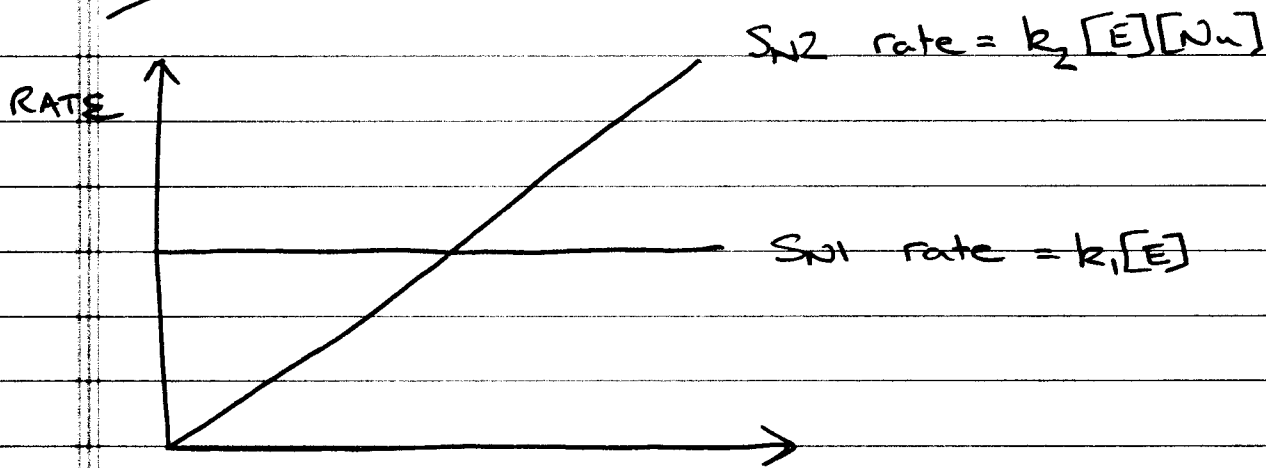
BUT

IN POLAR APROTIC SOLVENTS, anions only weakly solvated & trend is reversed (for halogens) and correlates w/ BASICITY

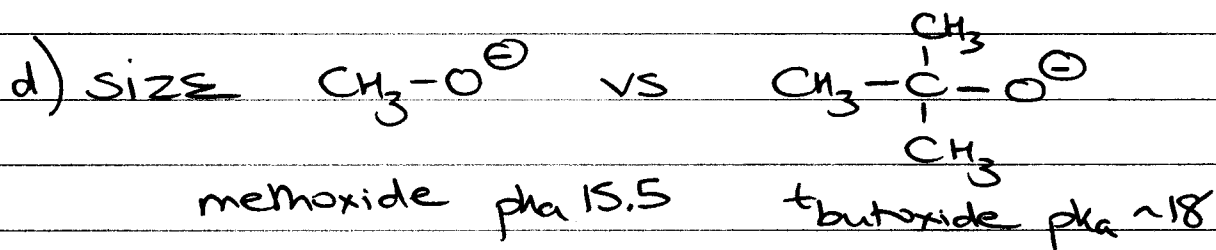


Nu	pKa	MeOH (time to complete RXN)	DMF	equivalent polarities
I ⁻	-10	17 min	8.7s	Overall
Br ⁻	-8	12h	8.7s	message
Cl ⁻	-6	13d	1.4s	POLAR APROTIC
F ⁻	3	2 yrs	<1.2s	SOLVENTS GOOD

So SN1 vs SN2

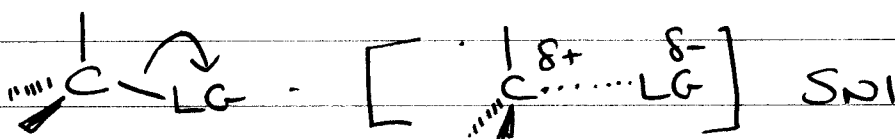
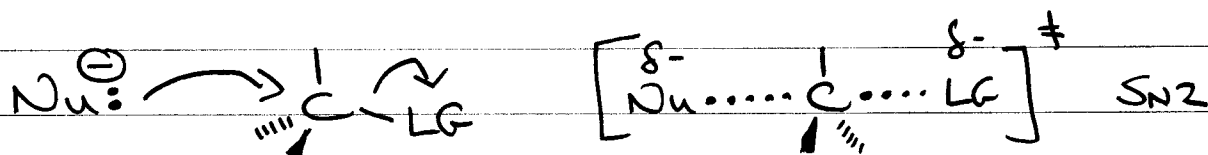


no effect on SN1, but stronger Nuc favors SN2



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

③ LEAVING GROUP

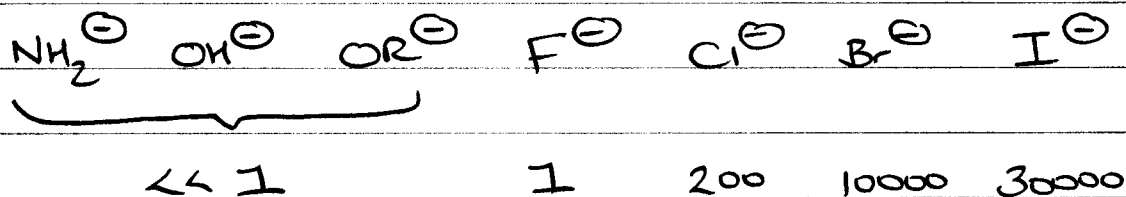


LG develops -ve CHARGE in TS, so better charge stabilization, lower energy TS, faster RXN.

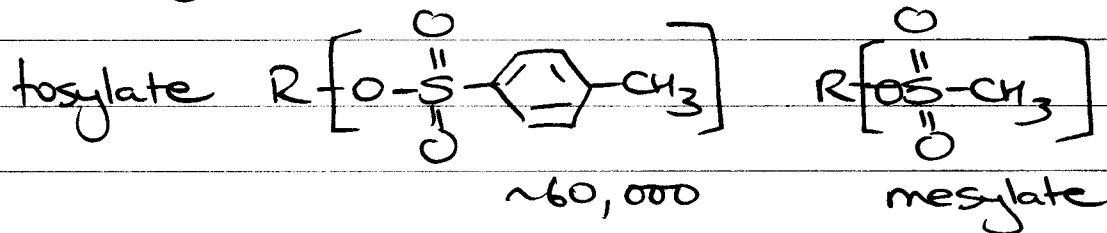
Thus more ACIDIC H-LG, more stable LG^\ominus

GOOD/BAD LG

- relative reactivity

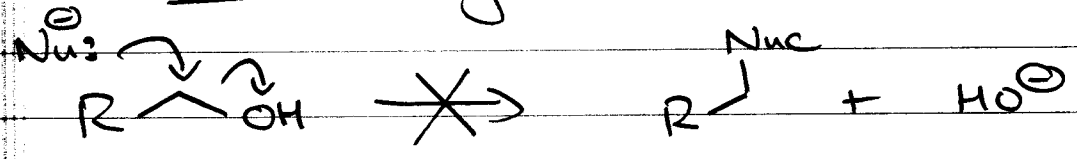


other good LG

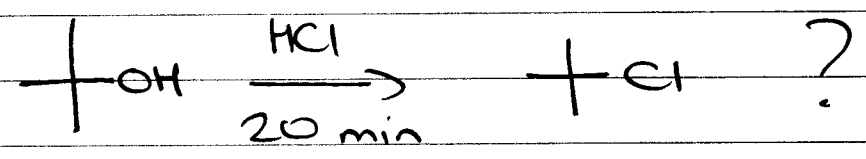


So, R-F, R-OH, R-OR', R-NH₂

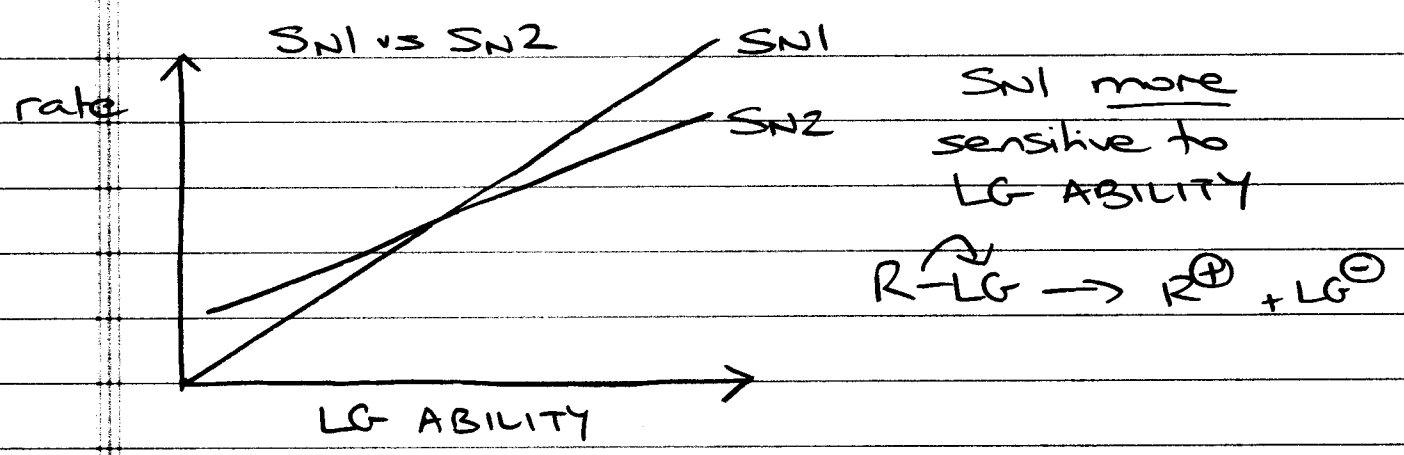
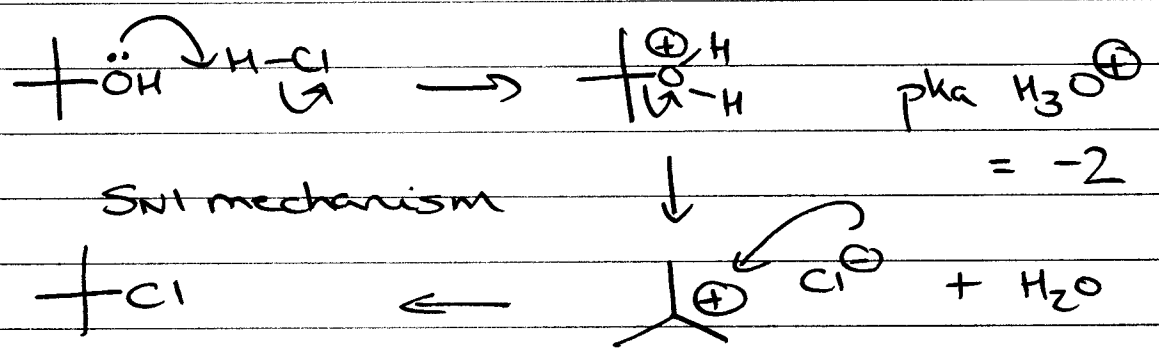
do NOT undergo S_N2 reactions



BUT



-OH converted into good leaving group



In S_N2, as long as LG[⊖] more stable than Nu[⊖], reaction can proceed.

BUT LG ABILITY ALONE cannot determine S_N1 vs S_N2