

c. Nucleophiles / Nucleophilicity

- looking at how fast a Lewis base displaces a LG. (Kinetics)

Very good: I^- HS^- CN^-

Good: Br^- OH^- OR^- N_3^-

Fair: NH_3 , Cl^- F^- RCO_2^-

Weak: H_2O ROH

V. Weak: RCO_2H

In general, anions are better nucleophiles than neutral molecules

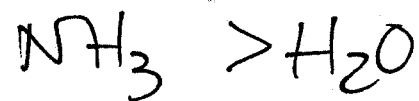
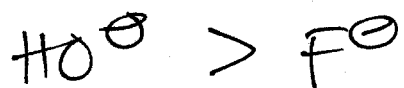
* there is no direct connection between nucleophilicity + basicity.

However:

1. So long as the nucleophilic atom is the same, the more basic one is better (anions > neutral)



2. When going along a row on the periodic table, the more basic one is better.



3. When going down a column on the periodic table, the connection doesn't work.

I^- - least basic
- most nucleophilic

Also: polarizability is important. The more polarizable the e^- cloud, the more the

bond is formed @ long distances +
the faster the rxn.

nucleophilicity: measured by relative rates
of rxn - kinetic

Basicity (think pK_a): measured by the
position of an equilibrium - thermodynamic

d. Solvent effects

polar vs nonpolar
protic vs aprotic

nonpolar: hexane, CCl_4

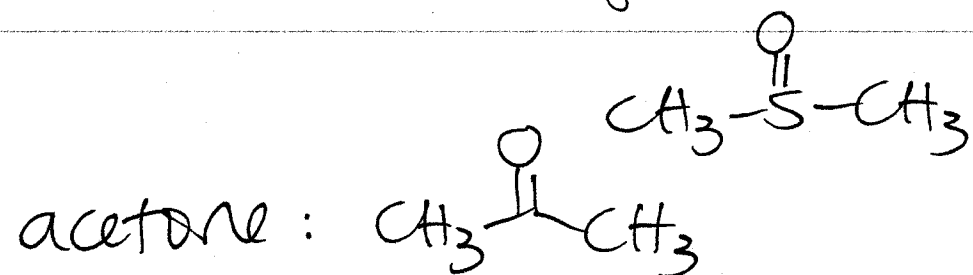
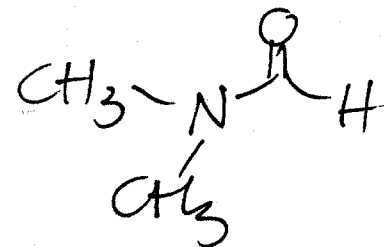
polar protic: H_2O , CH_3OH , CH_3CH_2OH

polar aprotic: acetone, DMF, DMSO

protic - has
a proton on an
e⁻neg atom
(can H-bond
w/ itself)

DMF: dimethylformamide

DMSO: dimethylsulfoxide

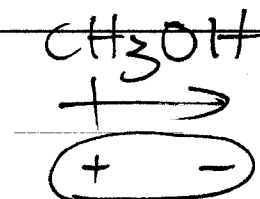
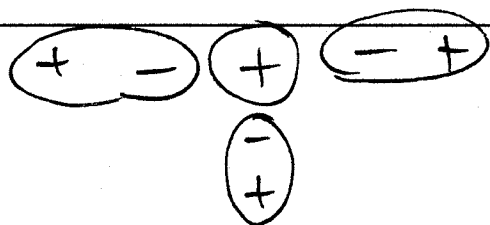


$\text{S}_{\text{N}}1$ rxns go best in polar protic solvents.

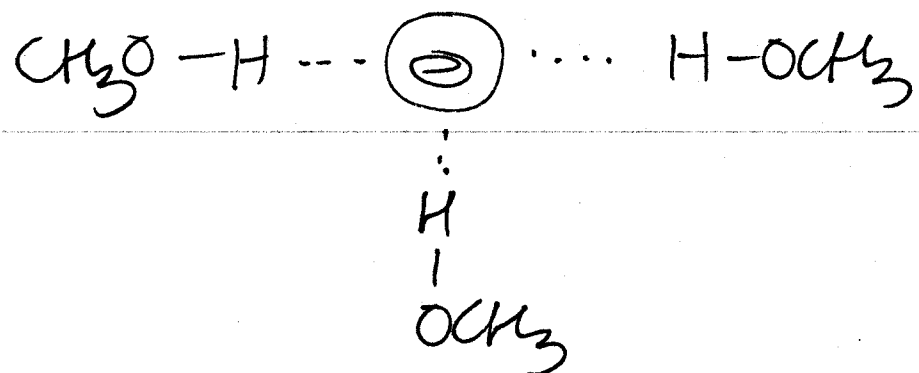
(solvolysis: solvent is the nucleophile)

Polar protic solvents can solvate anions and cations. Sometimes referred to as "ionizing" solvents - encourage ionization because stabilize both products.

cations: dipole-dipole interactions.



anions: H-bonding



$\text{S}_\text{N}2$ rxns go better in polar aprotic solvents.

* Note - that doesn't mean that they don't work in polar protic solvents!

Why? Polar aprotic solvent will solvate the cation but not the anion. (No H-bonding) — whereas a polar protic solvent will effectively "blanket" the anion/nucleophile, a polar aprotic one doesn't \Rightarrow a "naked nucleophile".

Therefore the nucleophile has a much easier time getting at the LG in polar aprotic solvent.

NOTE: nucleophilicity changes in polar aprotic solvents.

In DMSO: $F > Cl > Br > I$

usual combinations:

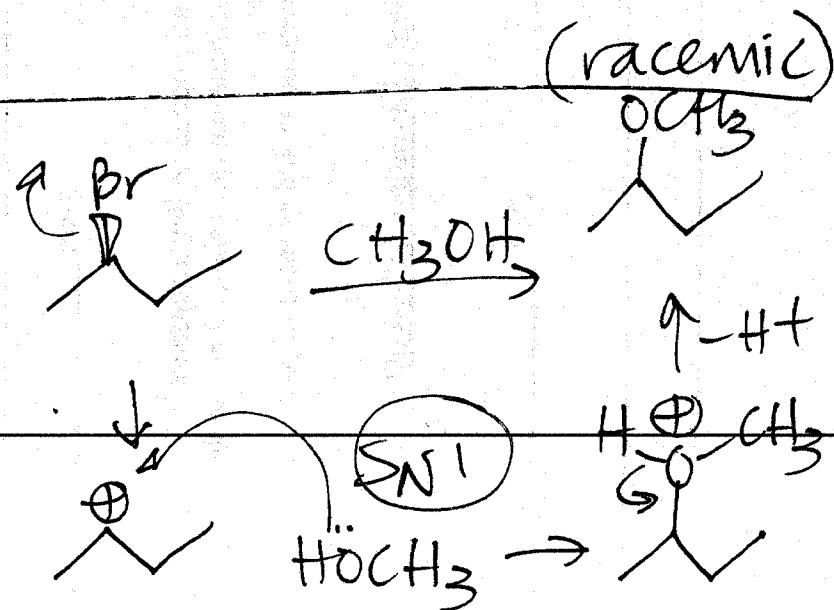
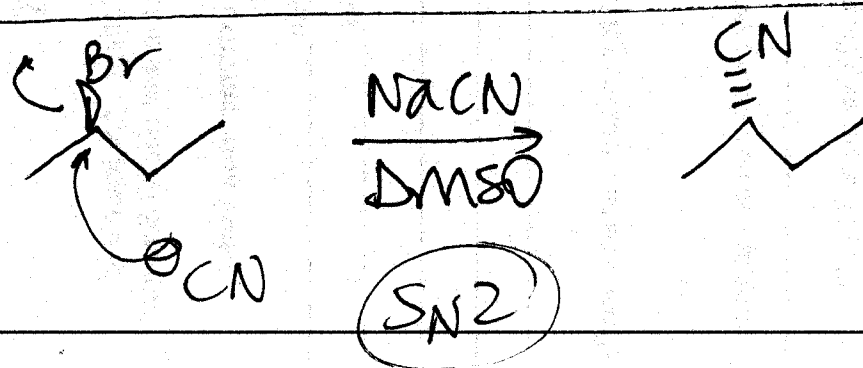
$CH_3OH / CH_3O^- Na^+$

$EtOH / EtO^- Na^+$

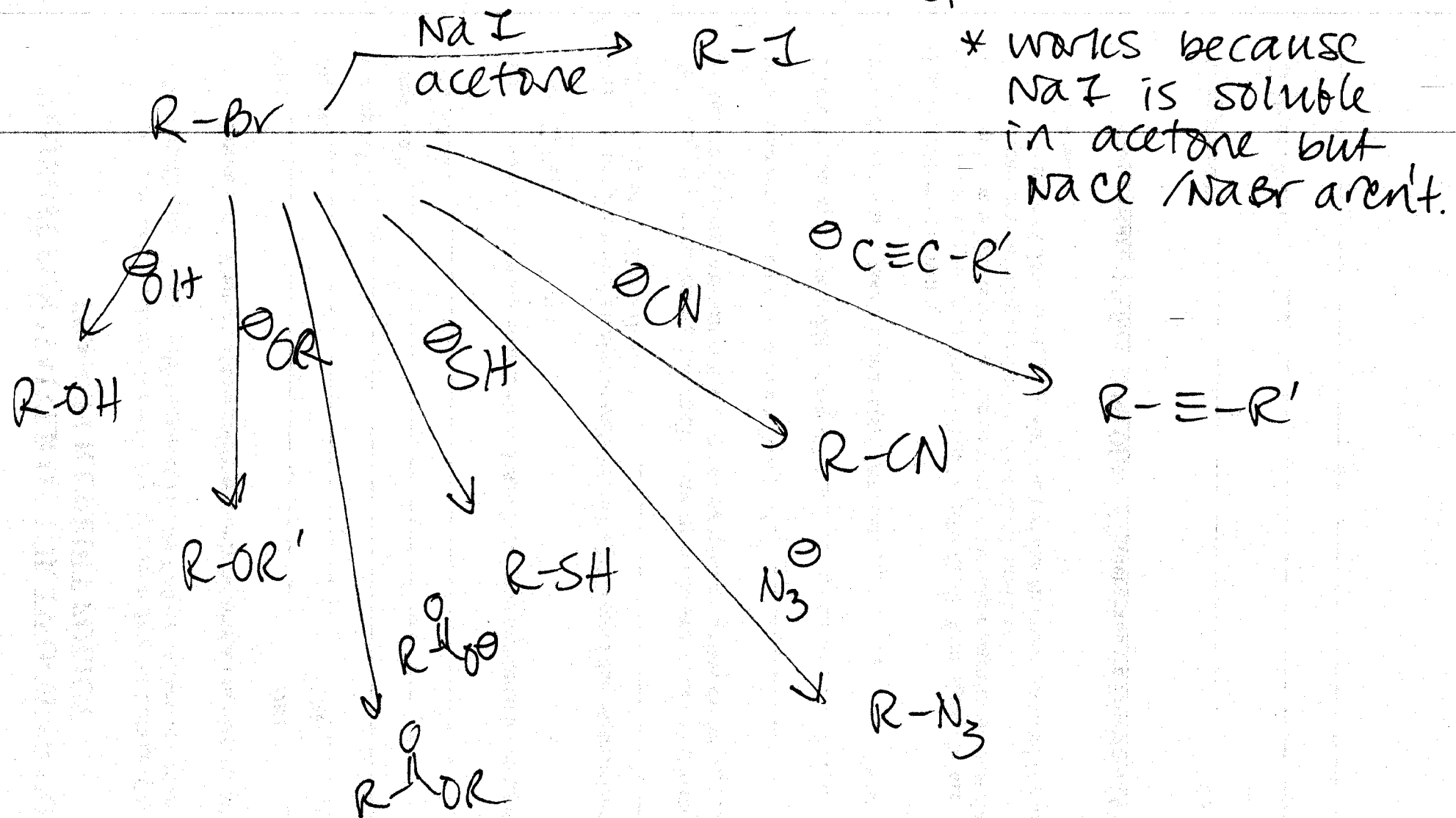
$tOH / tO^- K^+$

summary:

	S_N1	S_N2
substrate	$3^\circ > 2^\circ > 1^\circ > CH_3$ * cation stability	$CH_3 > 1^\circ > 2^\circ > 3^\circ$ * sterics
Nu	weak (neutral molecules; can be solvent)	strong (anions, high concs. of Nu preferred)
solvent	polar protic	polar aprotic
LG	$I > Br > Cl > F$	same



S_N2 - used for functional gp. transformation.



* can't be done w/ 3° RX / aryl / vinyl