Course 343-5 Lecturer Prof. Gellman

Day Monday! Yes! Date 10/31/2016

Notes Taken By Sungho Total # of Pages Four

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Exam 2 on Wednesday

Students with last names beginning w/ I or J → take exam here

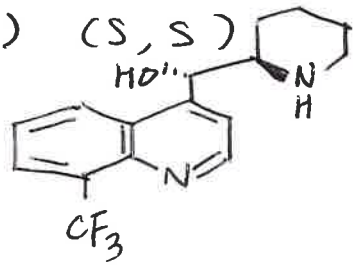
Office hour today, until 3 PM

Review session tomorrow 5 PM (Chem B371)

"Mefloquine" anti-malaria drug

(R,R isomer causes psychosis)

(+) (S,S)



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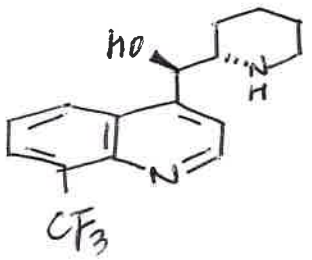

(−) (R,R)

Recall Rxns of alkyl halides: substitution vs elimination

Focus: S_N2 rxn (rate = $k[CH_3I][CH_3CH_2ONa]$)

Mech: "backside attack", "concerted"

Major factors that influence S_N2 reactivity

- Structure of alkyl halide (steric effects)
- Leaving group
- Nucleophile reactivity } intertwined
- Solvent }

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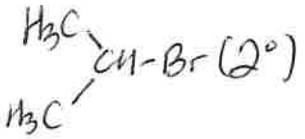
1) Alkyl halide structure (Table 9.3)

SM	Rel. rate S_N2 rxn
CH_3-Br	~~1.0~~ 145
CH_3CH_2-Br (1°)	1.0
$CH_3CH_2CH_2-Br$	0.8



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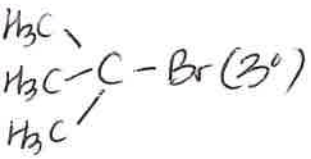


~0
no S_N2

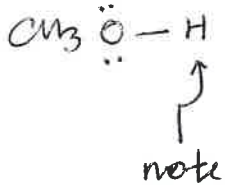
Trends: Methyl > 1° > 2° ⇏ (reactivity)

3° does not react (S_N2)

2) Nucleophile + solvation

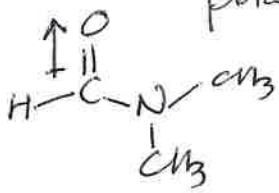
Important distinction: Polar protic vs polar aprotic among solvents

Examples: polar protic

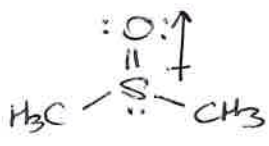


vs

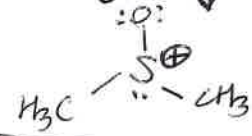
polar aprotic



DMF



DMSO



H-bond donor → "protic"
- contains a mildly acidic proton (pKa ≤ 20) → participate in H-bonding

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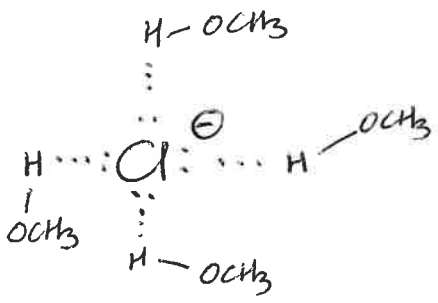
Impact - $NaCl + CH_3I \longrightarrow NaI + CH_3Cl$

Time to 97% completion ...

... in CH_3OH = 13 days

in DMF = 1.4 seconds

Crucial factor is nucleophile ~~solvation~~ solvation



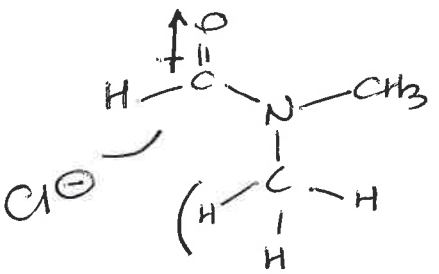
Solvent = H-bond donor

Solvent molecules interact strongly; must be stripped off before nucleophile reactivity is possible

Contrast: DMF

Cannot strongly interact w/ anions ($:\ddot{Cl}:^{\ominus}$)

("naked anion")



Considerations

1) Polar aprotic solvents
   - Maximize nucleophile reactivity
   - Expensive

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2) Larger reactivity differences among nucleophiles in polar protic (Tables 9.5 & 9.6)
CH_2O, CH_3OH, CH_3CH_2OH)

Trends in nucleophile reactivity

- Atoms in a column (P.T.), lower = more reactive

Ex: $I^\ominus > Br^\ominus > Cl^\ominus \gg [F^\ominus]$

$RS^\ominus > RO^\ominus$

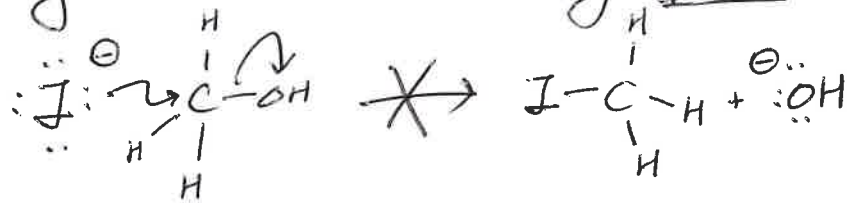
Leaving groups: $I^\ominus$ is best L.G.

$I^\ominus > Br^\ominus > Cl^\ominus$ [$F^\ominus$ never a L.G.]

In general, recognize good L.G.'s as the conjugate bases of strong acids (i.e., weak base)

HCl, HBr, HI are strong acids

Recognize $^\ominus OH$ as a very <u>poor</u> L.G.



$^\ominus OH$ NEVER an S_N2 L.G.