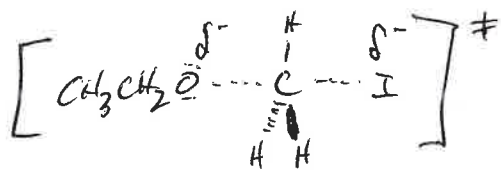
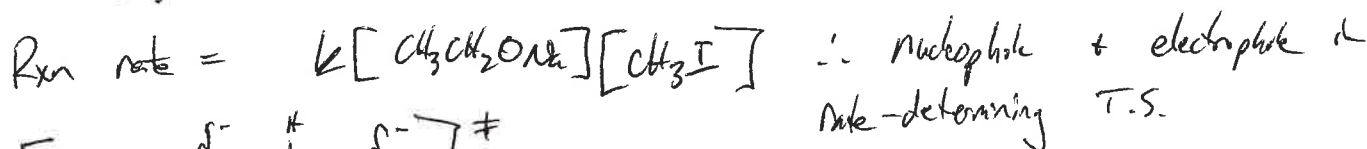
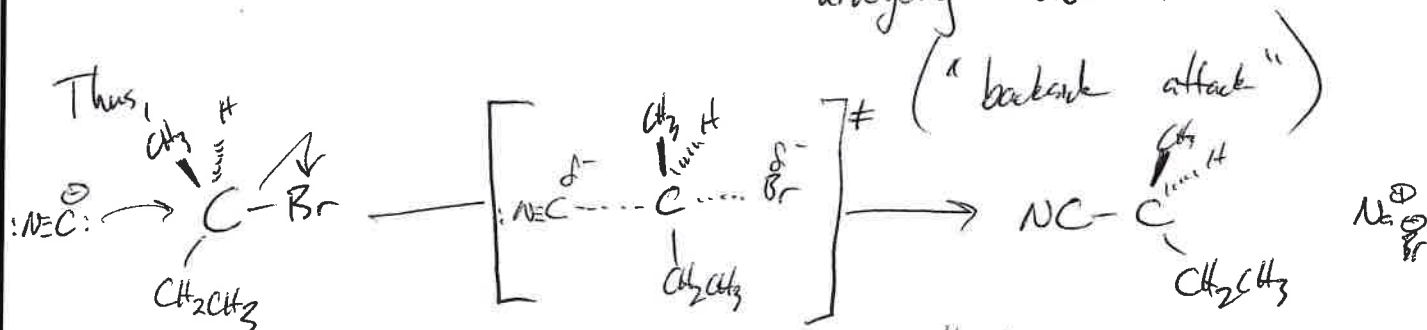
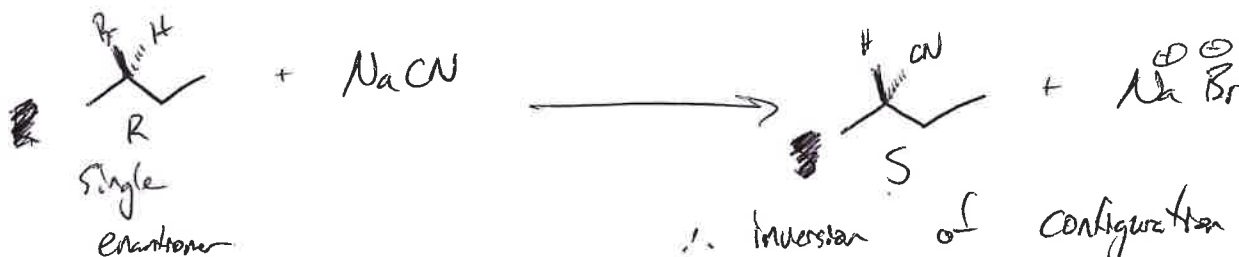


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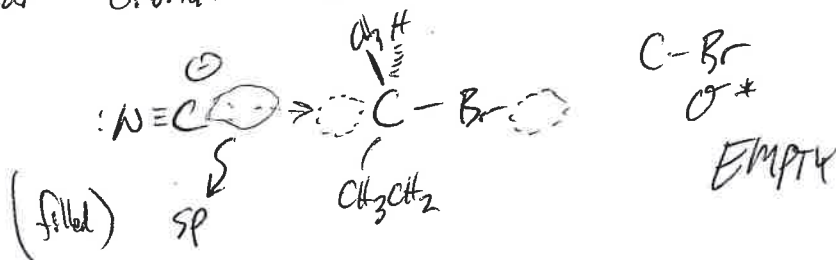
Recall:  $S_N2$  Rxn



Stereochemical outcome affords supports mechanistic hypothesis



Molecular orbital rationale for backside attack:

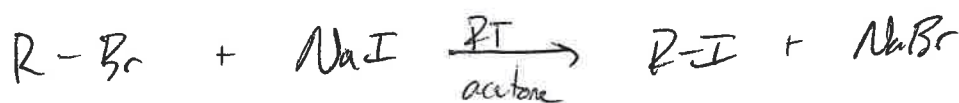


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Factors that influence S<sub>N</sub>2 Reactivity

- Structure of alkyl halide (steric effects)
  - Nucleophile reactivity
  - Solvation
  - Leaving group
- } Strong interplay

1) alkyl Halide structure (Table 9.3)




<u>SM (R-Br)</u>	<u>Relative Rate (S<sub>N</sub>2)</u>
CH <sub>3</sub> -Br	145
CH <sub>3</sub> CH <sub>2</sub> -Br (1°)	1.0 (reference)
CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> -Br (1°)	0.8
(CH <sub>3</sub> ) <sub>2</sub> CH-Br (2°)	0.008
(CH <sub>3</sub> ) <sub>3</sub> C-Br (3°)	~0

(Trends are what is important!)

Trends

1) Methyl > 1° > 2°. 3° do not react

2) Adding "steric bulk" away from

However: "Neopentyl effect" 

substitution site has little effect (↖ vs. ↘)   
 i. slow to react

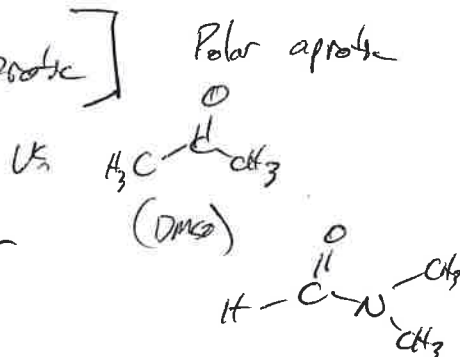
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2) Nucleophile reactivity + 3) Solvation

[Recall: polar aprotic solvents vs. polar protic]

Examples:  $\text{CH}_3\text{-OH} \equiv$  "polar protic"  
 $pK_a \sim 16 \Rightarrow$  good H-bond donor



DMF  
 No H-bond donor

Some data....

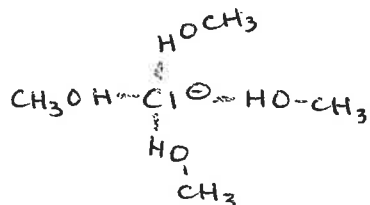


parameter: time to 97% rxn (table 9.6)  
 @ RT

In  $\text{CH}_3\text{OH}$  : 13 days  
 In DMF : 1.4 seconds }  $10^6$ -fold

origin of this "solvent effect"?

$\text{Cl}^\ominus$  strongly solvated  
 in  $\text{CH}_3\text{OH}$



$\Rightarrow$  But, in DMF, no H-bond donors

$\Downarrow$

"naked anion"

$\Downarrow$

highly reactive

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General Trend :  $S_N^2$

- rxns much faster in polar aprotic than in polar protic

Differences in nucleophile reactivity are most pronounced in polar protic solvents (eg  $CH_3OH$ )

Nuc. reactivity trends  $\rightarrow$  Tables 9.5 + 9.6

Key trends :

Nucleophilic atoms in same column

- Lower  $\Leftrightarrow$  more reactive

Thus,  $R\ddot{S}:\ominus > R\ddot{O}:\ominus$  or  $I^\ominus > Br^\ominus > Cl^\ominus$

Leaving group