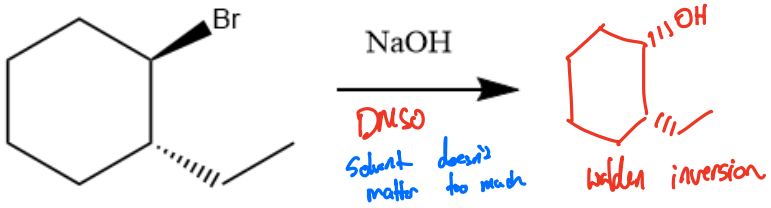
CHEM 223 (2024) SI Session #10

Learning Objectives: By the end of this session, students should be able to:

- Draw mechanisms & explain the rationale behind Sn1 and Sn2
- Use reactants and reaction conditions to differentiate between Sn1 and Sn2
- Begin compounding ideas from Chapter 4 and Chapter 6 to do basic synthesis

Section 1: Sn2

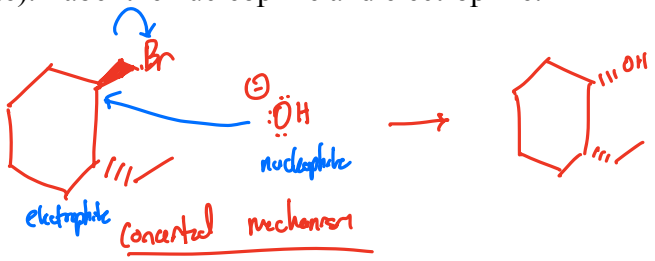
1. Using the following reaction, answer the questions



a. Predict the products of the reaction, including <u>correct stereochemistry</u>. Additionally, provide an adequate solvent for the reaction.

above

b. Draw the mechanism of the reaction (you do not need to include a transition state). Label the nucleophile and electrophile.



FQ: why "2" in S_N2?

FQ: What is a leaving group?

c. The reaction is repeated with sodium amide ($NaNH_2$) as the nucleophile. Will the reaction proceed faster or slower? Explain.

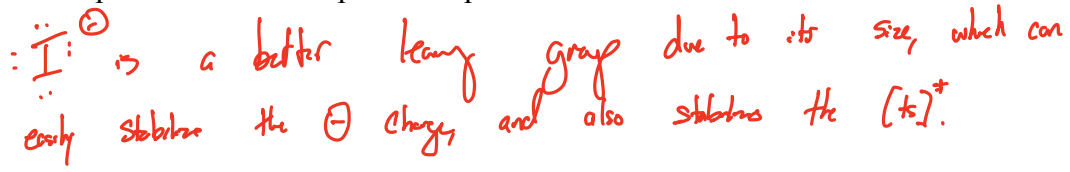
Faster; $:\ddot{N}H_2$ is a stronger nucleophile than $:\ddot{O}H$, so it will react much faster.

FQ: Base vs Nucleophile

↓ equilibrium constant of deprotonation

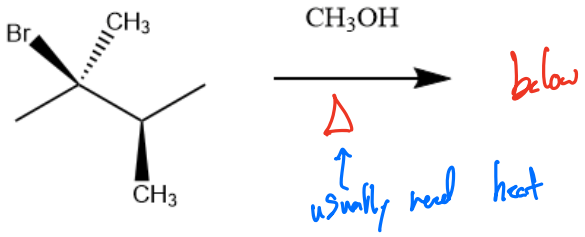
↓ rxn rate of S_N2

d. A chemist replaces Bromine atom with Iodine in this reaction and notices that the reaction proceeds faster. Explain this phenomenon.

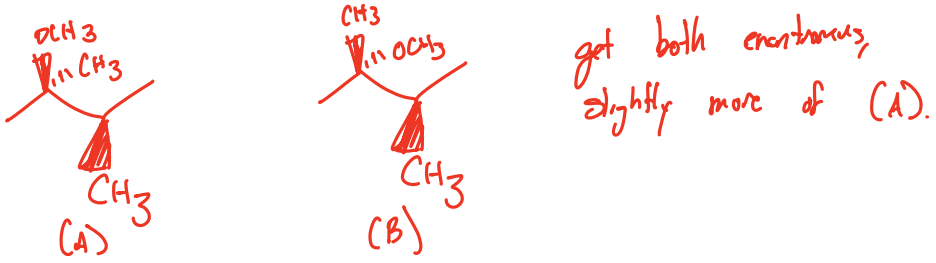


Section 2: Sn1

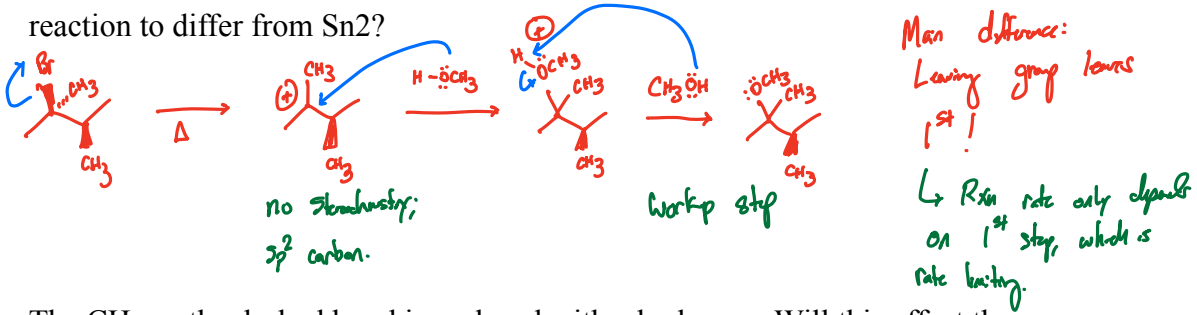
2. Using the following reaction, answer the questions below



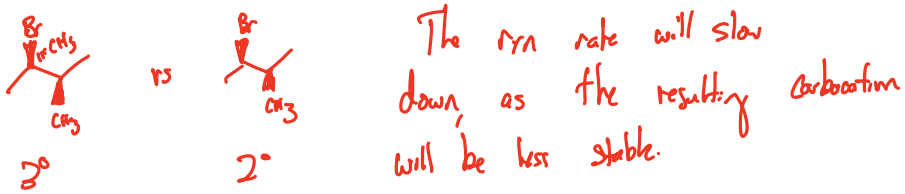
a. Predict the products of the reaction, including <u>correct stereochemistry</u> (if necessary). Additionally, provide an adequate solvent for the reaction and any other required reaction conditions.



b. Draw the mechanism of the reaction (you do not need to include a transition state). Label the nucleophile and electrophile. What causes the mechanism of this reaction to differ from Sn2?



c. The CH_3 on the dashed bond is replaced with a hydrogen. Will this affect the reaction rate, and if so, how? Provide a brief explanation.



Section 3: Differentiating between Sn1 and Sn2

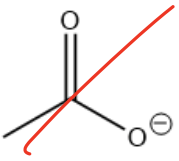
3. Explain how the reaction coordinate diagrams of Sn1 and Sn2 differ.

S_N2: 1 step, no intermediate

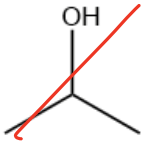
S_N1: 2 steps, carbocation intermediate, only 1st step contributes to rxn rate

4. Using the bank of nucleophiles below, order the nucleophiles in order of increasing reactivity within the Sn2 reaction. Explain your reasoning.

FQ: does nucleophile strength matter for S_N1? => no!
Prefer weak nucleophiles

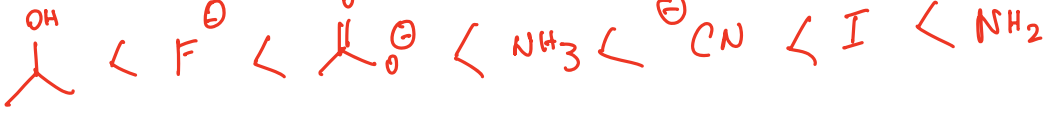


NH_3 I^- F^-



KNH_2 NaCN

See slide 27 for rankings



general: ⊖ = more nucleophilic
★ less stable = more nucleophilic (exception: polarizability)

5. Using the bank of leaving groups below, order the leaving groups in order of increasing leaving-group ability. Explain your reasoning.

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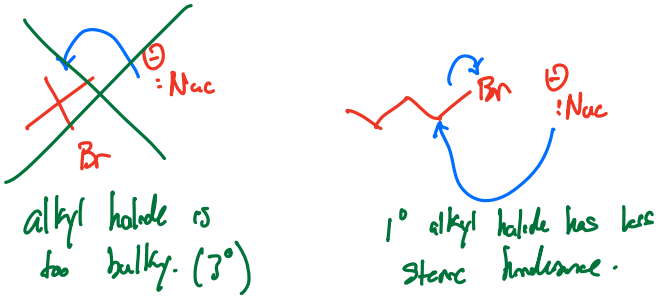
Cl^- PO_4^{3-}

I^- H_2O

Relationship is unclear

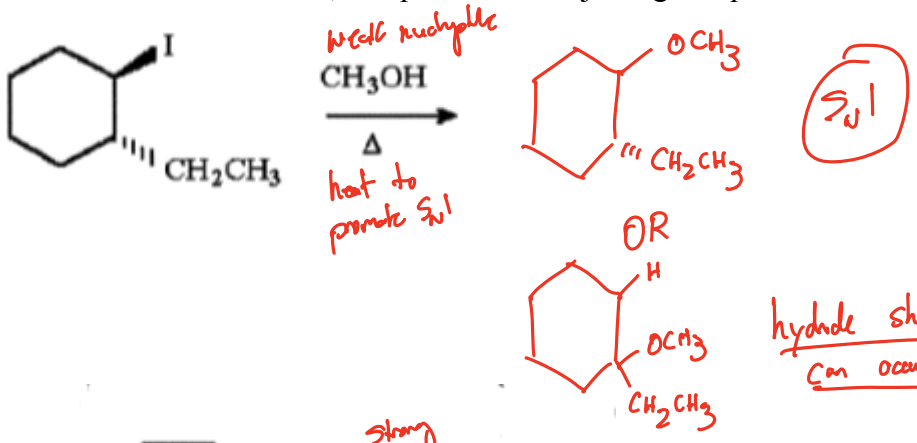
more stable = better leaving group capacity

6. Explain why t-butyl bromide cannot undergo Sn2, but 1-bromobutane can. Explain why this constraint does not exist for Sn1.

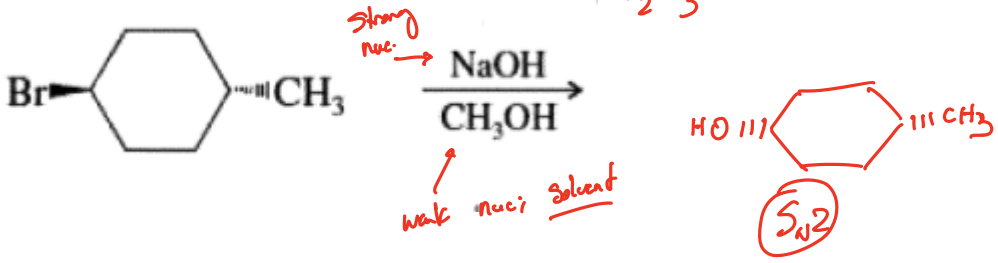


7. (From 2023's Exam) For each of the following reactions, predict which nucleophilic substitution mechanism will occur, and predict the major organic products.

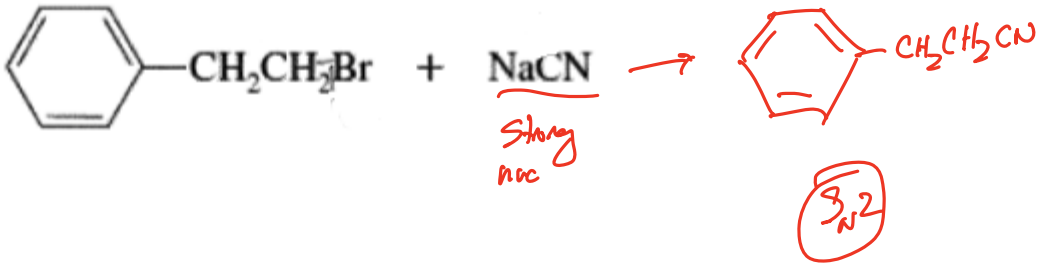
a.



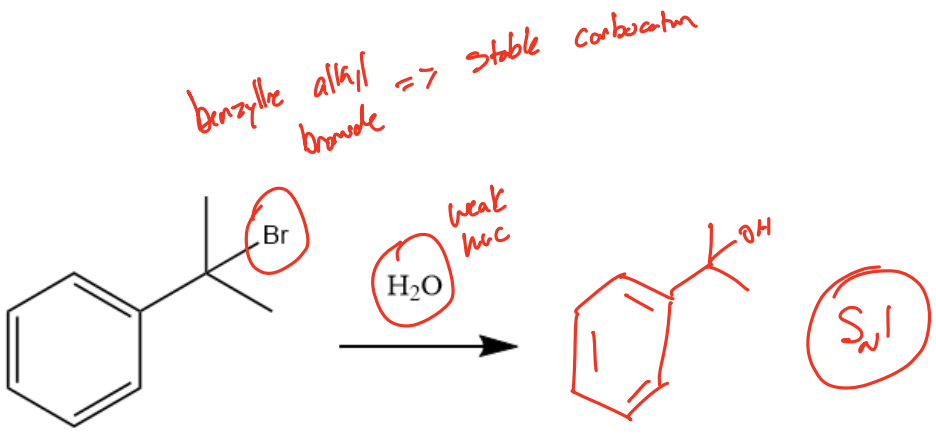
b.



c.

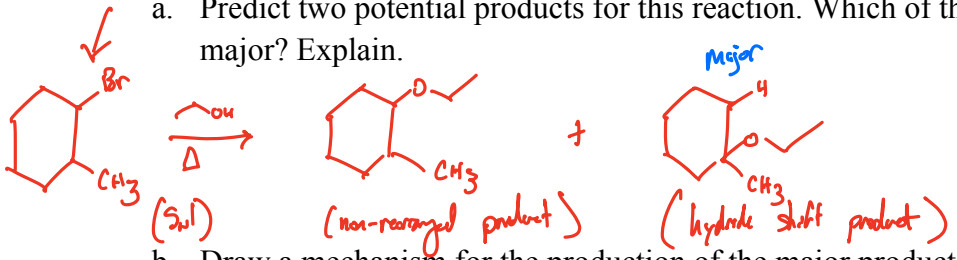


d.

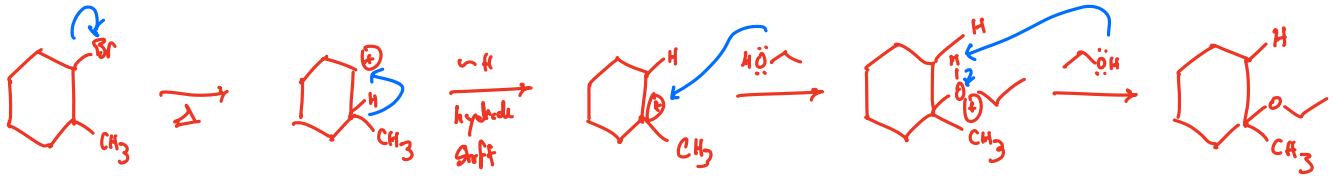


Section 4: Complications within Sn1 & Basic Synthesis

8. 1-bromo-2-methylcyclohexane reacts with ethanol in the presence of heat.
   a. Predict two potential products for this reaction. Which of these will be more major? Explain.



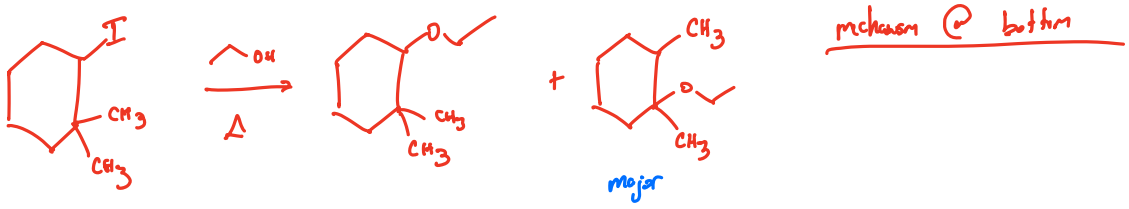
   b. Draw a mechanism for the production of the major product.



FQ: why? → 2° to 3° Carbocation!

Can ignore if we run out of time

   c. 1-iodo-2,2-dimethylcyclohexane also reacts with ethanol in the presence of heat. Predict the major product and draw a mechanism for its production.



mechanism @ bottom

9. Starting with cyclohexane, synthesize cyclohexanol.