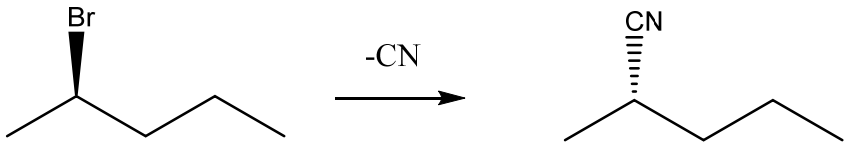
Discussion Worksheet #6
Substitution Reactions

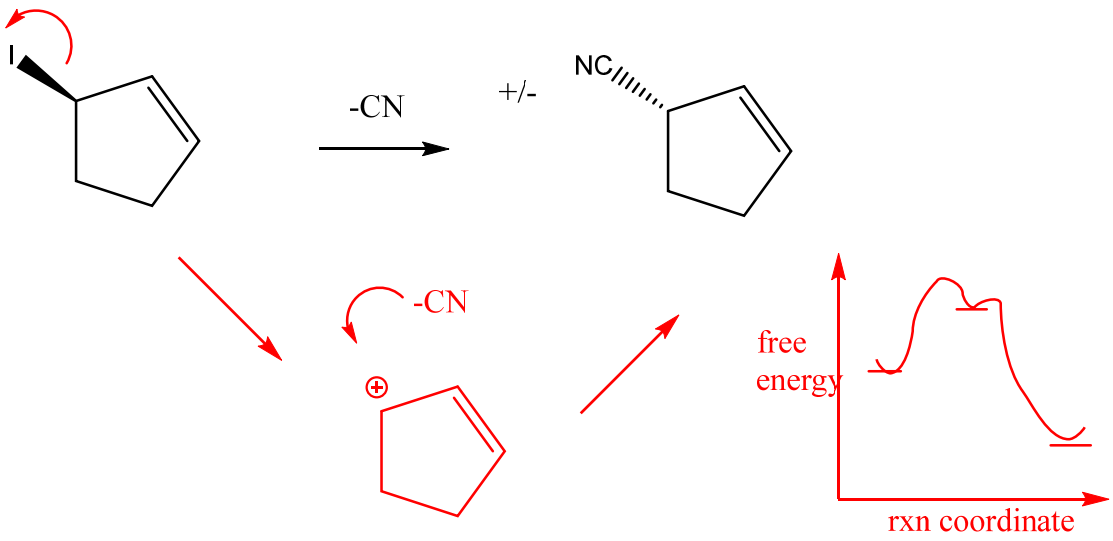
Skill 1: Draw arrow mechanisms for substitution reactions

- Given starting material and products, determine whether the reaction is Sn1 or Sn2 using stereochemistry and rearrangements
- Sn2 is a one step, 2 arrow mechanism with alkyl halides.
- Sn1 is a two step, 2 arrow mechanism (often followed by a deprotonation step) with alkyl halides.

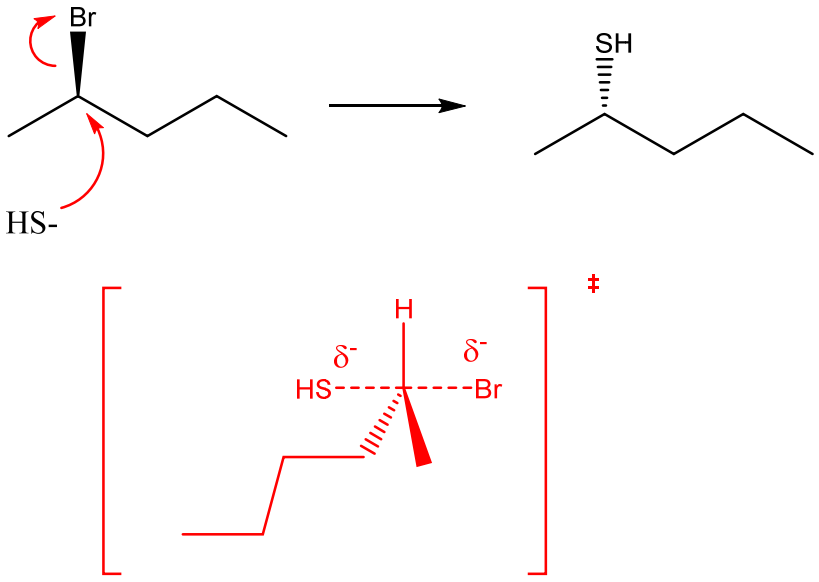
Problem 1: Label each as Sn1 or Sn2. Provide arrow mechanisms for each reaction, and draw an energy diagram assuming an overall exothermic process.



S_N1 because it forms a racemic mix



Problem 2. Provide a mechanism for each of these Sn2 reactions. Draw a transition state structure for each reaction.

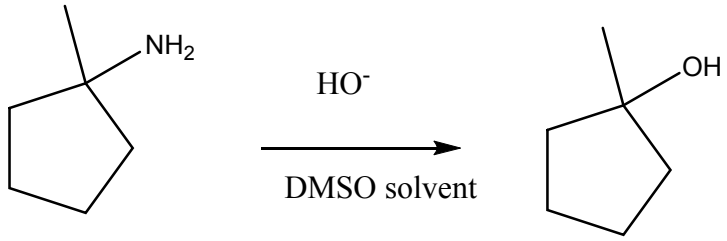


Skill 2: Weigh the factors that favor and disfavor substitution reactions. Predict whether a reaction will be Sn1 or Sn2

- First, consider the substrate.
  - Primary carbocations will not form (no Sn1)
  - Tertiary carbons are too hindered for direct attack (no Sn2)
  - Sp^2 centers will not undergo either Sn1 or Sn2
- Next, consider the nucleophile
  - Strong nucleophiles favor Sn2 if possible
  - Weak nucleophiles (typically solvolysis) must wait for Sn1
- Finally, consider solvent
  - Polar aprotic favors Sn2 by destabilizing the nucleophile
  - Polar protic favors Sn1 by stabilizing the carbocation

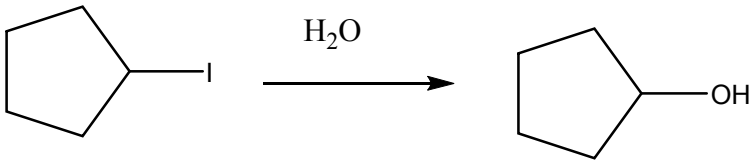
Problem 3. Consider all factors that would increase or decrease the rate of each of these substitution reactions (leaving group, nucleophile, solvent, substrate.) Predict whether each reaction will happen in a reasonable timeframe.

A. S_N2 reaction

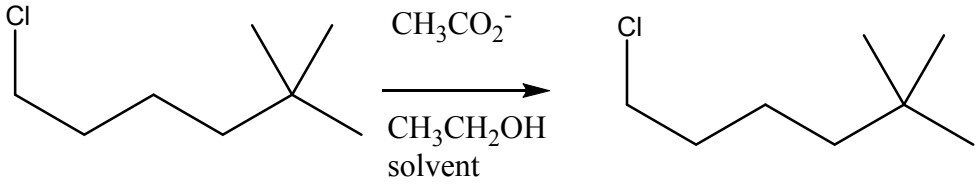


Very poor leaving group (strong base)
The tertiary substrate will sterically block the Sn2 attack. These two factors make Sn2 very slow (no perceptible reaction) even though the nucleophile is ok and the solvent is favorable for Sn2.

B. S_N1 reaction

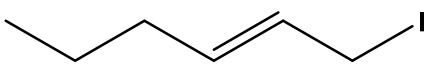


C. S_N2 reaction



Problem 4. Will the following reaction go through an Sn1mechanism, an Sn2 mechanism, or not proceed as written? Explain how you came to this conclusion.

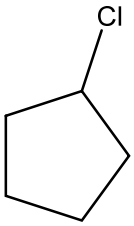
A.



HS-

Sn2. The substrate is unhindered, and the Nu:- is strong.

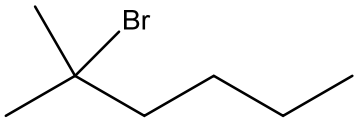
B.

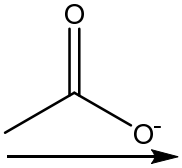


Ethanol

Sn1. The weak nucleophile is not strong enough for Sn2, and the 2° chloride can form a carbocation.

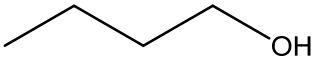
C.





acetic acid

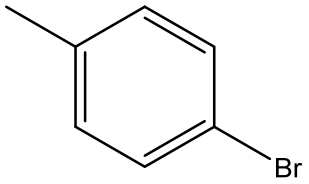
D.



NaCl

No reaction--hydroxide is too poor of a leaving group

E.



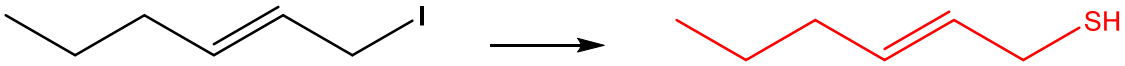
HO^-

Skill 3: Predict the products of a substitution reaction, including stereochemistry

- Sn2 reactions will lead to inversion of stereochemistry
- Sn1 reactions can lead to stereochemical mixtures

Problem 5. Predict the products of each of these substitution reactions, or write no reaction.

A.



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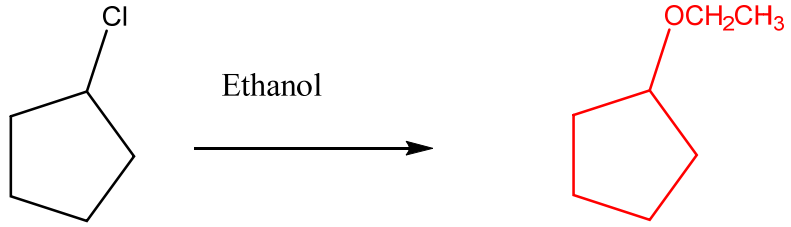
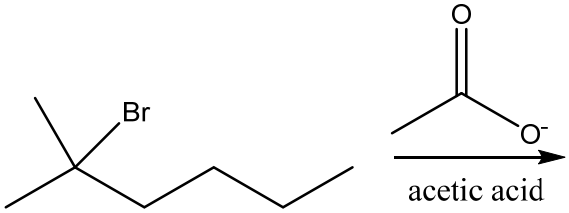
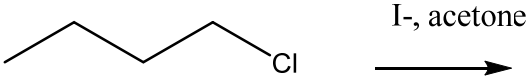


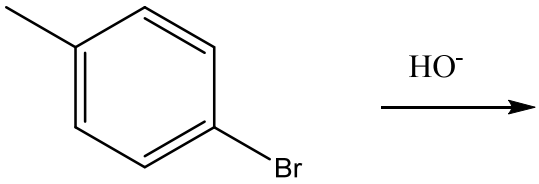
C.



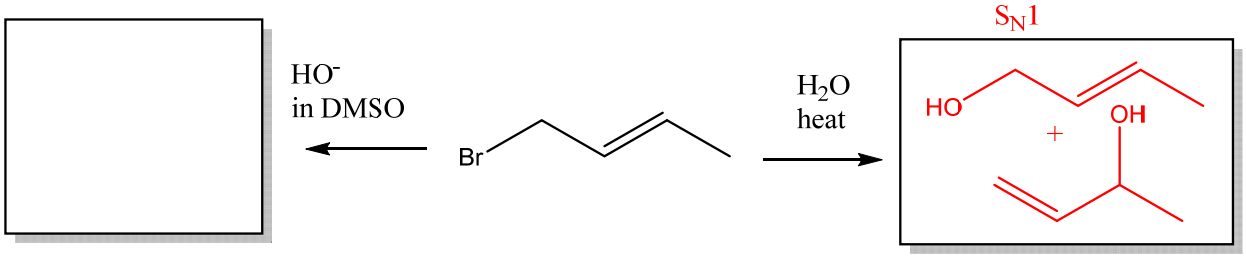
D.



E.



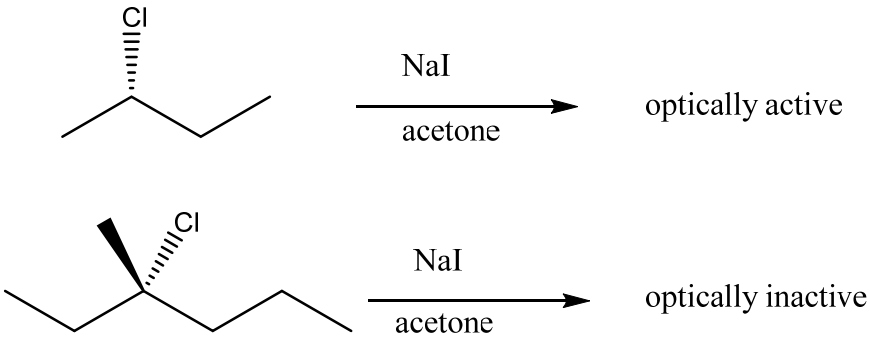
Problem 6. A slight change in the nucleophile used in this reaction leads to difference in products because the mechanism changes. Draw the product(s) of each reaction.



Skill 4: Provide reagents for substitution reactions

- Be sure to consider stereochemical outcomes in determining the starting material to use for a substitution
- If the starting material is a nucleophile, add an electrophile, and vice versa
- You must use an acid if the leaving group is poor (hydroxyl group.)

Problem 7. Treating S-2-chlorobutane with NaI leads to an optically active product, but the same reaction with S-3-chloro-3-methylhexane does not. Explain.



Problem 8. Provide the reagents or starting materials necessary to produce the indicated products.