

6.1 S_N1 vs S_N2 reactions

a) Which reaction(s) happen(s) in one step:

- S_N1
- S_N2
- None
- Both

b) In an S_N2 reaction, what is the stereochemical outcome at the carbon where substitution occurs?

- It stays the same
- It inverts
- It becomes racemic
- It depends on the reactants

c) Which reaction(s) involve(s) an intermediate species?

- S_N1
- S_N2
- None
- Both

d) What is the rate determining step of an S_N1 reaction?

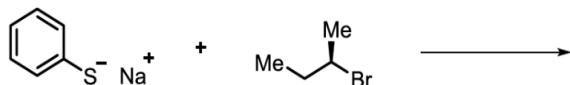
- Nucleophile attacking the electrophile
- Formation of a carbocation
- Loss of a proton
- Departure of the nucleophile

e) Which reaction(s) involve(s) a transition state?

- S_N1
- S_N2
- None
- Both

6.2 S_N2 Reaction Mechanism

a) Thiophenolate reacts with 2-bromobutane in a substitution reaction. Draw the resulting products. Name the reactants (nucleophile, electrophile, leaving group) and draw the electron displacement arrows.

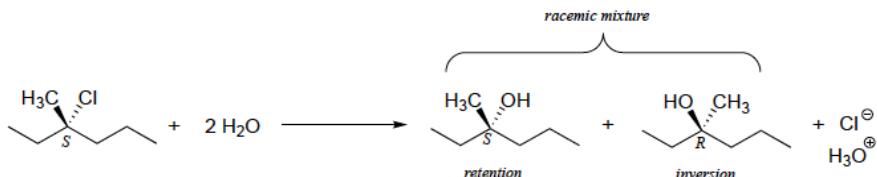


b) Draw the reaction profile diagram. Also label the axes correctly and draw the structure of the transition state of the reaction.

6.3 S_N1 Mechanism and Solvolysis

b) Draw a mechanism for the S_N1 solvolysis of tert-butyl chloride in methanol. What new functional group has been formed? Also draw the reaction profile of the S_N1 reaction diagram and label the axes correctly.

b) Now consider the solvolysis of (S)-3-chloro-3-methylhexane below:



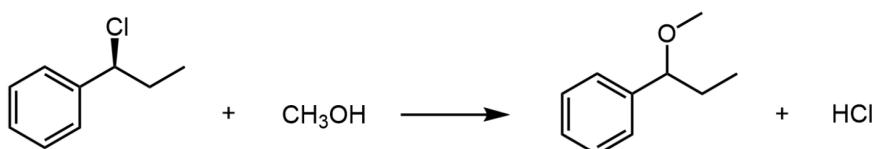
- i) Draw a complete mechanism for this hydrolysis reaction, showing all bond-breaking and bond-forming steps, and all intermediate species.
- ii) Draw structures representing TS1 and TS2 in the reaction. Use the solid/dash wedge convention to show three dimensions.
- iii) What is the expected optical rotation of the product mixture?
- iv) Could the two organic products be separated on a silica column chromatography?

6.4 S_N1 vs S_N2 reactions

a) Tick the factors that clearly favor the S_N1 mechanism over the S_N2 mechanism, and explain why (give at least one example):

- good nucleophile
- presence of a strong base
- bulky groups at the reactive center
- strong electron-donor substituents at the reactive center
- good leaving group
- basic leaving group

b) In order to increase the rate of the following reaction, I should:



- Add more electrophile (substrate)
- Add more nucleophile
- Increase the strength of the nucleophile
- Decrease the polarity of the solvent

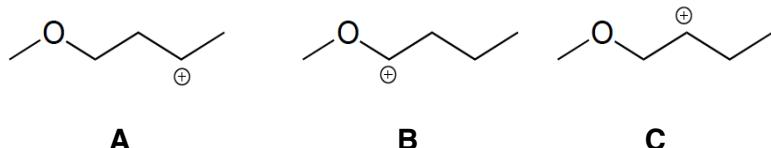
6.5 True or False ? (explain why)

- a) S_N2 reactions are favored by strong nucleophiles.
- b) A serine side chain is a better nucleophile than a threonine side chain
- c) S_N1 reactions proceed faster with tertiary alkyl halides than with primary alkyl halides.
- d) Stronger nucleophiles increase the rate of S_N1 reactions
- e) A weak nucleophile can still participate in an S_N1 reaction.
- f) Methanol (CH_3OH) is a better solvent for S_N2 reactions than DMSO.
- g) S_N2 reactions are favored in polar protic solvents.
- h) A cysteine side chain is a better nucleophile than a methionine side chain

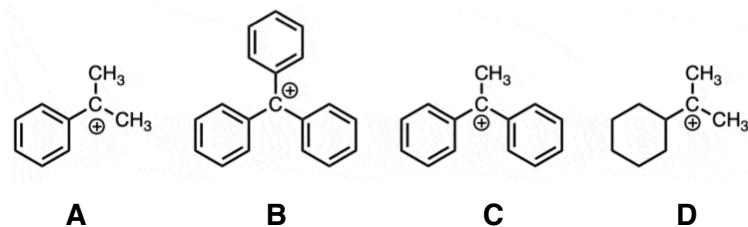
6.6 Carbocation Stability

a) Rank the following carbocations from most to least stable and explain.

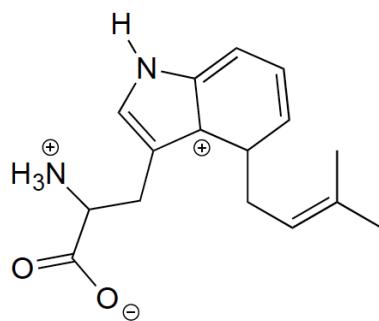
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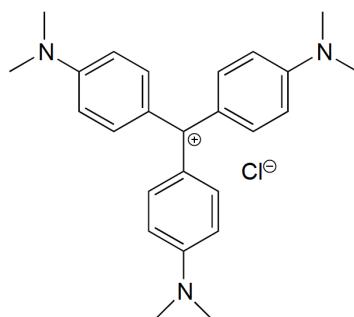
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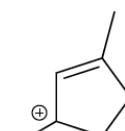
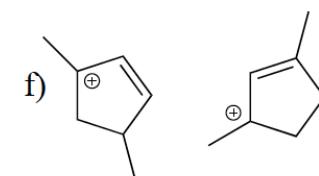
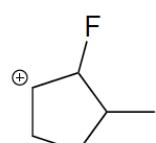
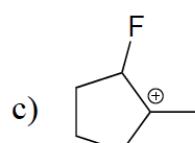
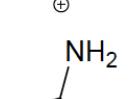
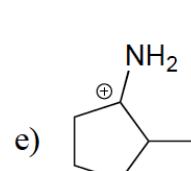
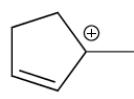
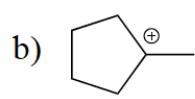
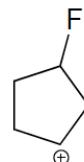
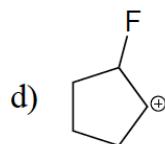
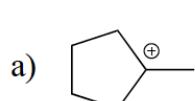
b) The carbocation below is an intermediate species in a reaction that is part of the biosynthesis of a hallucinogenic compound in a fungus. Draw a resonance contributor that shows how it is stabilized by resonance with the nitrogen atom.



c) Consider the structure of crystal violet given below. Draw a resonance structure of the crystal violet cation in which the positive charge is delocalized to one of the nitrogen atoms.

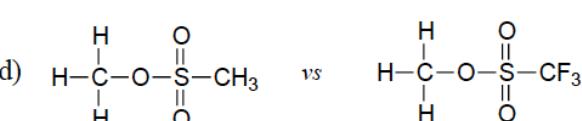
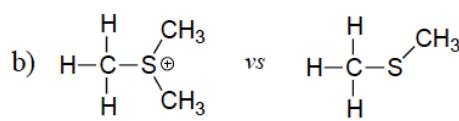
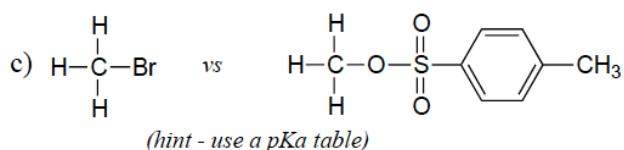
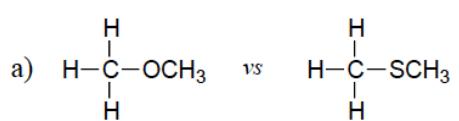


d) State which carbocation in each pair below is more stable, or if they are expected to be approximately equal. Explain your reasoning.



6.7 Electrophilicity

In each pair (A and B) below, which electrophile would be expected to react more rapidly with cyanide ion nucleophile in acetone solvent? Explain your reasoning.



6.8 Nucleophilic Substitution in Biology

a) S-adenosyl methionine (SAM) is formed by a nucleophilic substitution reaction between methionine and adenosine triphosphate (ATP). Draw a mechanism for this reaction, and explain why you chose either an SN1 or and SN2 pathway.

6.9 Nucleophilic Substitution Reactions

Indicate whether the reactions take place according to S_N1 , S_N2 or not at all (extremely slow) and complete the reaction equations.

