11.12: A SUMMARY OF REACTIVITY - SN1, SN2, E1, E1CB, AND E2

OBJECTIVES

After completing this section, you should be able to

1. determine whether a specified substrate is most likely to undergo an E1, E2, S_N1 or S_N2 reaction under a given set of conditions.
2. describe the conditions under which a given substrate is most likely to react by a specified mechanism (E1, E2, S_N1 or S_N2).

STUDY NOTES

This section summarizes much of what has been discussed in the chapter. It focuses on how a given substrate will behave under certain conditions, but does not deal with the stereochemistry of the products.

Having discussed the many factors that influence nucleophilic substitution and elimination reactions of alkyl halides, we must now consider the practical problem of predicting the most likely outcome when a given alkyl halide is reacted with a given nucleophile. As we noted earlier, there are multiple variables to be considered, **the most important being the substitution of the alkyl halide**. S_N2 reactions favor alkyl halides with little steric hindrance such as methyl halides and primary halides. In general, in order for an S_N1 or E1 reaction to occur, the relevant carbocation intermediate must be relatively stable such as with tertiary halides, secondary allylic halides, and secondary benzylic halides.

The next most import variable for predicting the outcome of a reaction is **the nature of the nucleophilic reactant**. Strong nucleophiles favor S_N2 substitution, and strong bases, especially strong hindered bases (such as tert-butoxide) favor E2 elimination. Weak nucleophiles that are also weak bases tend to favor S_N1 and E1 reactions.

- **Good Nucleophiles Which are Weak Bases:** I^-, Br^-, SCN^-, N_3^-, $CH_3CO_2^-$, RS^-, CN^-, Amines, etc.
- **Good Nucleophiles Which are Strong Bases:** HO^-, RO^-.
- **Poor Nucleophiles which are Weak Bases:** H_2O, ROH, RSH.

GENERAL RULES FOR PREDICTING A REACTION

Consider these in the order listed.

Methyl Alkyl Halides

- An S_N2 substitution occurs regardless if a good or poor nucleophile is used.

Primary Alkyl Halides

- An E2 elimination occurs if a strong, sterically hindered base is used.
- An E1cB elimination occurs if a strong base is used and the leaving group is two carbons away from a carbonyl group.
- An S_N2 substitution occurs if a good nucleophile is used.

Secondary Alkyl Halides

- An E1cB elimination occurs if a strong base is used and the leaving group is two carbons away from a carbonyl group.
- An E2 elimination occurs if a strong base is used.
- An S_N2 reaction occurs if a good nucleophile that is a weak bases is used in a polar aprotic solvent.
- An S_N1 reaction along with an E1 reaction occurs if a poor nucleophile that is a weak bases is used in a protic solvent.

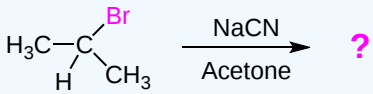
Tertiary Alkyl Halides

- An E1cB elimination occurs if a strong base is used and the leaving group is two carbons away from a carbonyl group.
- An E2 elimination occurs if a strong base is used.
- An S_N1 reaction along with an E1 reaction occurs if a poor nucleophile that is a weak bases is used in a protic solvent.

WORKED EXAMPLE11.12.1

1) For the following, please determine what kind of reaction is occurring and predict the product(s).

a)



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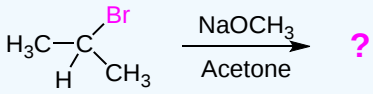

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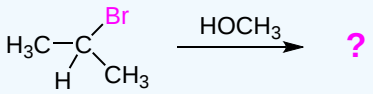
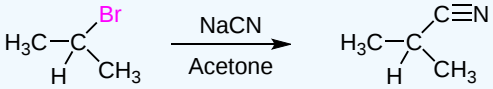
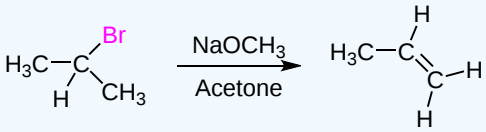


Answer

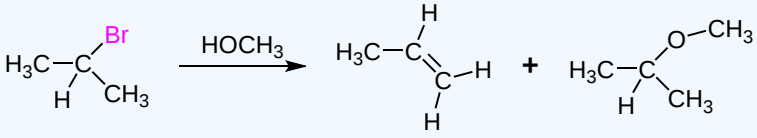
a) The substrate is a secondary halide so the product is determined by the nature of the nucleophile used in the reaction. Cyanide ($^-$CN) is a good nucleophile which is a weak base. The fact that the nucleophile is a weak base means that an E2 reaction is not favored. Also, the fact that cyanide is a good nucleophile means that S_N2 substitutions are favored over S_N1. When a secondary halide is reacted with a good nucleophile which is a weak base, the preferred reaction is S_N2. After S_N2 substitution the product is a nitrile.



b) The substrate is a secondary halide so the product is determined by the nature of the nucleophile used in the reaction. Methoxide ($^-OCH_3$) is a strong base so it could prefer to remove a hydrogen from the substrate. This makes an E2 elimination the preferred reaction and an alkene the product.

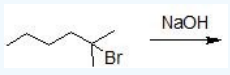


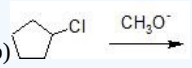
c) The substrate is a secondary halide so the product is determined by the nature of the nucleophile used in the reaction. Methanol ($HOCH_3$) is a weak nucleophile that is a weak base. Being a weak base means that methanol is not capable of actively removing a hydrogen to cause an E2 reaction. Also, because methanol is a weak nucleophile is not capable of attacking the substrate and causing an S_N2 reaction. For the methanol nucleophile to react the substrate must first eject it leaving group to form the highly reactive carbocation intermediate. Formation of the carbocation is the rate determine step for both the S_N1 and E1 reactions so they each form a separate product.

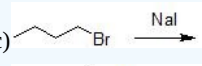


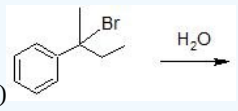
? EXERCISES 11.12.1

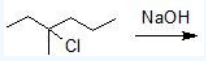
1. Identify the dominant reaction mechanism (S_N1, S_N2, E1, or E2) and predict the major product for the following reactions.

a) 

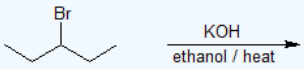
b) 

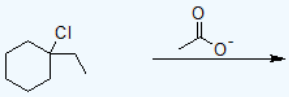
c) 

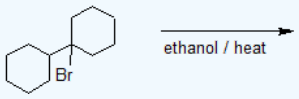
d) 

e) 

a) 

b) 

c) 

d) 

2) Identify the function of the following reagents. The reagents will be a strong/weak nucleophile and/or a strong/weak base.

a) Cl^-

b) NaH

c) t-BuO^-

d) OH^-

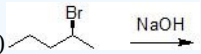
e) H_2O

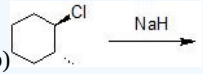
f) HS^-

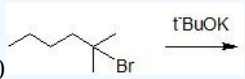
g) MeOH

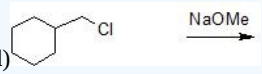
3) Identify which mechanism the following reactions would undergo.

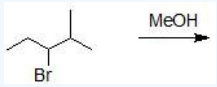
4) Identify all the products of the following reactions and specify the major product.

a) 

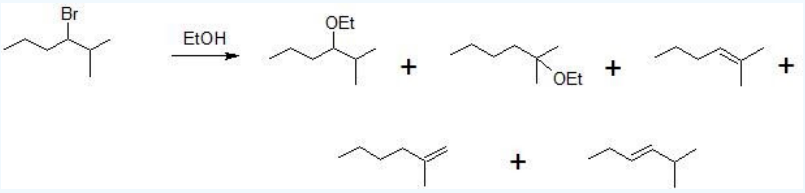
b) 

c) 

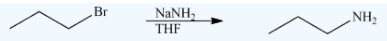
d) 

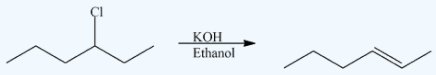
e) 

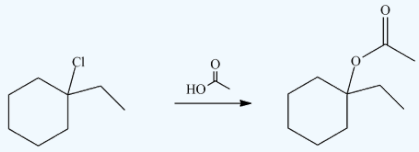
5) The following reaction yields five different products. Give the mechanisms for how each is formed.

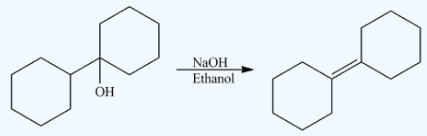


6) Label the following reactions as S_N1, S_N2, E1, or E2.

A) 

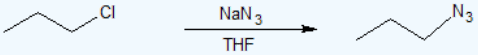
B) 

C) 

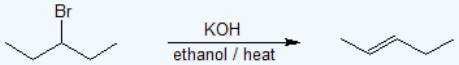
D) 

Answer

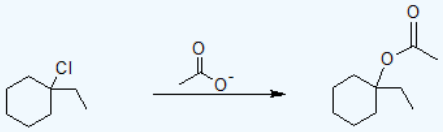
1)

a) 

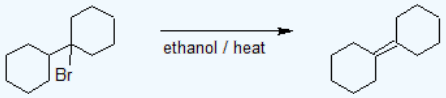
S_N2 b/c primary alkyl halide and strong nucleophile that is a weak base in a polar aprotic solvent

b) 

E2 b/c secondary alkyl halide and a strong base heated

c) 

SN1 b/c tertiary alkyl halide with a weak nucleophile that is a weak base

d) 

E1 b/c tertiary alkyl halide with a weak base heated

2)

a) Cl^- ; strong nucleophile

b) NaH ; strong base

c) t-BuO^- ; strong base

d) OH^- ; strong nucleophile ; strong base

e) H_2O ; weak nucleophile ; weak base

f) HS^- ; strong nucleophile

g) MeOH ; weak nucleophile ; weak base

3)

a) E2, S_N1

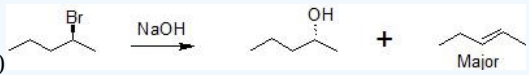
b) S_N2, E2

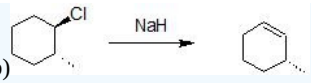
c) S_N2

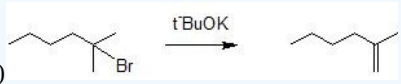
d) S_N1, E1

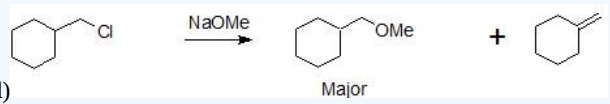
e) E2, S_N1

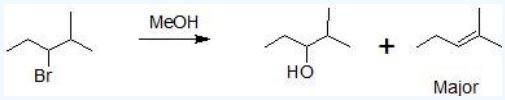
4)

a) 

b) 

c) 

d) 

e) 

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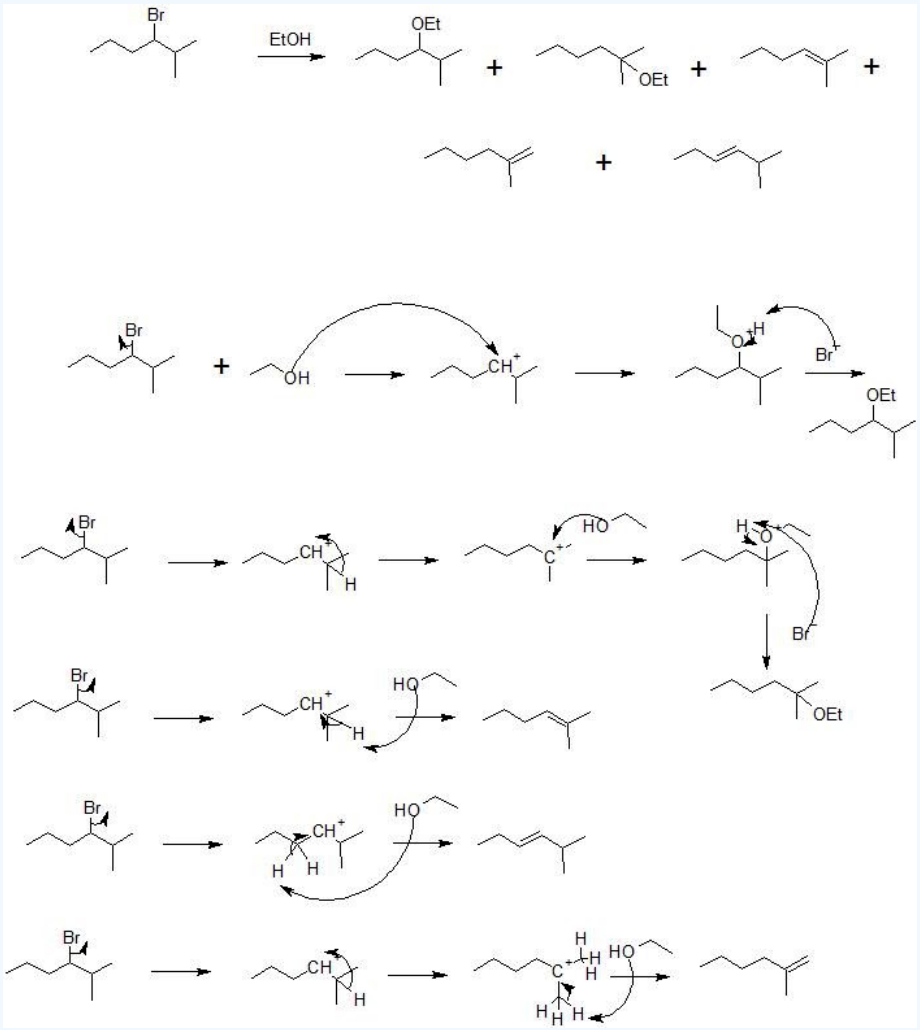

6)

A – S_N2

B – E1

C – S_N1

D – E2

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