

## 7.19: COMPARING SUBSTITUTION AND ELIMINATION REACTIONS

### Learning Objective

- predict the products and specify the reagents for  $S_N1$ ,  $S_N2$ , E1 and E2 reactions with stereochemistry
- propose mechanisms for  $S_N1$ ,  $S_N2$ , E1 and E2 reactions
- draw, interpret, and apply Reaction Energy Diagrams for  $S_N1$ ,  $S_N2$ , E1 and E2 reactions

### Summary of Reaction Patterns

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, several variables must be considered, the most important being the structure of the alkyl group and the nature of the nucleophilic reactant. In general, in order for an  $S_N1$  or E1 reaction to occur, the relevant carbocation intermediate must be relatively stable. Strong nucleophile favor substitution, and strong bases, especially strong hindered bases (such as tert-butoxide) favor elimination.

The nature of the halogen substituent on the alkyl halide is usually not very significant if it is Cl, Br or I. In cases where both  $S_N2$  and E2 reactions compete, chlorides generally give more elimination than do iodides, since the greater electronegativity of chlorine increases the acidity of beta-hydrogens. Indeed, although alkyl fluorides are relatively unreactive, when reactions with basic nucleophiles are forced, elimination occurs (note the high electronegativity of fluorine).

The following table summarizes the expected outcome of alkyl halide reactions with nucleophiles. It is assumed that the alkyl halides have one or more beta-hydrogens, making elimination possible; and that low dielectric solvents (e.g. acetone, ethanol, tetrahydrofuran & ethyl acetate) are used. When a high dielectric solvent would significantly influence the reaction this is noted in red. Note that halogens bonded to  $sp^2$  or  $sp$  hybridized carbon atoms do not normally undergo substitution or elimination reactions with nucleophilic reagents.

Nucleophile	<b>Anionic Nucleophiles</b> ( Weak Bases: $I^-$ , $Br^-$ , $SCN^-$ , $N_3^-$ , $CH_3CO_2^-$ , $RS^-$ , $CN^-$ etc. ) $pK_a$ 's from -9 to 10 (left to right)	<b>Anionic Nucleophiles</b> ( Strong Bases: $HO^-$ , $RO^-$ ) $pK_a$ 's > 15	<b>Neutral Nucleophiles</b> ( $H_2O$ , $ROH$ , $RSH$ , $R_3N$ ) $pK_a$ 's ranging from -2 to 11
Alkyl Group			
Primary $RCH_2-$	Rapid $S_N2$ substitution. The rate may be reduced by substitution of $\beta$ -carbons, as in the case of neopentyl.	Rapid $S_N2$ substitution. $E2$ elimination may also occur. <i>e.g.</i> $ClCH_2CH_2Cl + KOH \longrightarrow CH_2=CHCl$	$S_N2$ substitution. ( $N \approx S \gg O$ )
Secondary $R_2CH-$	$S_N2$ substitution and / or $E2$ elimination (depending on the basicity of the nucleophile). Bases weaker than acetate ( $pK_a = 4.8$ ) give less elimination. The rate of substitution may be reduced by branching at the $\beta$ -carbons, and this will increase elimination.	$E2$ elimination will dominate.	$S_N2$ substitution. ( $N \approx S \gg O$ ) <b>In high dielectric ionizing solvents, such as water, dimethyl sulfoxide &amp; acetonitrile, <math>S_N1</math> and <math>E1</math> products may be formed slowly.</b>
Tertiary $R_3C-$	$E2$ elimination will dominate with most nucleophiles (even if they are weak bases). No $S_N2$ substitution due to steric hindrance. <b>In high dielectric ionizing solvents, such as water, dimethyl sulfoxide &amp; acetonitrile, <math>S_N1</math> and <math>E1</math> products may be expected.</b>	$E2$ elimination will dominate. No $S_N2$ substitution will occur. <b>In high dielectric ionizing solvents <math>S_N1</math> and <math>E1</math> products may be formed.</b>	$E2$ elimination with nitrogen nucleophiles (they are bases). No $S_N2$ substitution. <b>In high dielectric ionizing solvents <math>S_N1</math> and <math>E1</math> products may be formed.</b>
Allyl $H_2C=CHCH_2-$	Rapid $S_N2$ substitution for $1^\circ$ and $2^\circ$ -halides. For $3^\circ$ -halides a very slow $S_N2$ substitution or, if the nucleophile is moderately basic, $E2$ elimination. <b>In high dielectric ionizing solvents, such as water, dimethyl sulfoxide &amp; acetonitrile, <math>S_N1</math> and <math>E1</math> products may be observed.</b>	Rapid $S_N2$ substitution for $1^\circ$ halides. $E2$ elimination will compete with substitution in $2^\circ$ -halides, and dominate in the case of $3^\circ$ -halides. <b>In high dielectric ionizing solvents <math>S_N1</math> and <math>E1</math> products may be formed.</b>	Nitrogen and sulfur nucleophiles will give $S_N2$ substitution in the case of $1^\circ$ and $2^\circ$ -halides. $3^\circ$ -halides will probably give $E2$ elimination with nitrogen nucleophiles (they are bases). <b>In high dielectric ionizing solvents <math>S_N1</math> and <math>E1</math> products may</b>

be formed. Water hydrolysis will be favorable for 2° & 3°-halides.

Benzyl  
C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>–

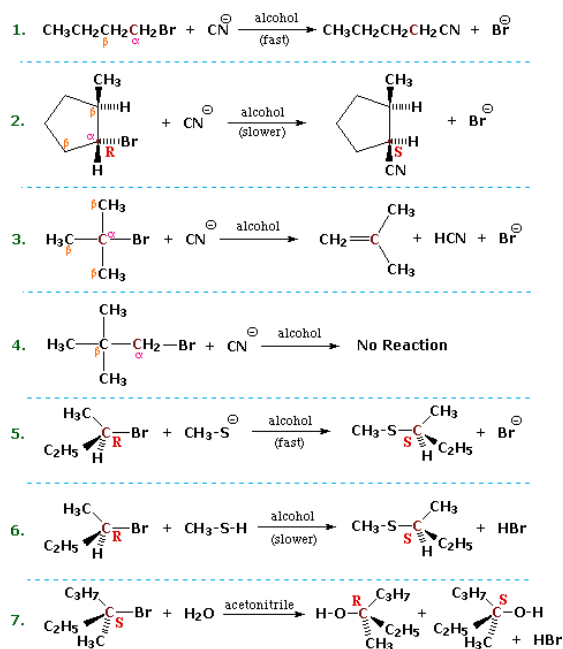
Rapid S<sub>N</sub>2 substitution for 1° and 2°-halides. For 3°-halides a very slow S<sub>N</sub>2 substitution or, if the nucleophile is moderately basic, E2 elimination. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S<sub>N</sub>1 and E1 products may be observed.

Rapid S<sub>N</sub>2 substitution for 1° halides (note there are no β hydrogens). E2 elimination will compete with substitution in 2°-halides, and dominate in the case of 3°-halides. In high dielectric ionizing solvents S<sub>N</sub>1 and E1 products may be formed.

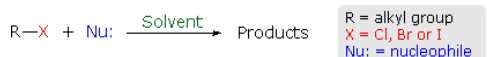
Nitrogen and sulfur nucleophiles will give S<sub>N</sub>2 substitution in the case of 1° and 2°-halides. 3°-halides will probably give E2 elimination with nitrogen nucleophiles (they are bases). In high dielectric ionizing solvents S<sub>N</sub>1 and E1 products may be formed. Water hydrolysis will be favorable for 2° & 3°-halides.

#### Experimental Observations

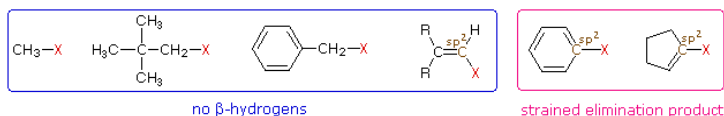
Experimental observations are reported for the following reactions. These reactions include a range of alkyl halide structures in a variety of reaction conditions to illustrate the reaction patterns summarized above. In describing these, it is useful to designate the halogen-bearing carbon as **alpha** and the carbon atom(s) adjacent to it as **beta**, as noted in the first four equations shown below. Replacement or substitution of the halogen on the α-carbon (colored maroon) by a nucleophilic reagent is a commonly observed reaction, as shown in equations **1, 2, 5, 6 & 7** below. Also, since the electrophilic character introduced by the halogen extends to the β-carbons, and since nucleophiles are also bases, the possibility of base induced H-X elimination must also be considered, as illustrated by equation **3**. Finally, there are some combinations of alkyl halides and nucleophiles that fail to show any reaction over a 24 hour period, such as the example in equation **4**. For consistency, alkyl bromides have been used in these examples. Similar reactions occur when alkyl chlorides or iodides are used, but the speed of the reactions and the exact distribution of products will change.



In order to understand why some combinations of alkyl halides and nucleophiles give a substitution reaction, whereas other combinations give elimination, and still others give no observable reaction, we must investigate systematically the way in which changes in reaction variables perturb the course of the reaction. The following general equation summarizes the factors that will be important in such an investigation.

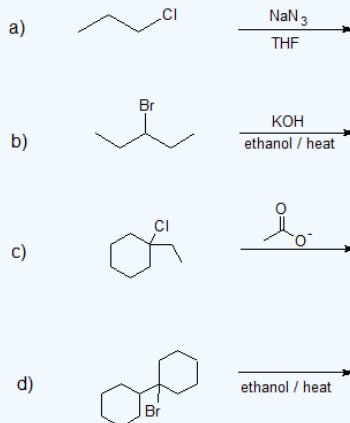


Friendly Reminder: One conclusion, relating the structure of the R-group to possible products, should be immediately obvious. **If R- has no beta-hydrogens an elimination reaction is not possible**, unless a structural rearrangement occurs first. The first four halides shown on the left below do not give elimination reactions on treatment with base, because they have no  $\beta$ -hydrogens. The two halides on the right do not normally undergo such reactions because the potential elimination products have highly strained double or triple bonds. It is also worth noting that  $\text{sp}^2$  hybridized C-X compounds, such as the three on the right, do not normally undergo nucleophilic substitution reactions, unless other functional groups perturb the double bond(s).



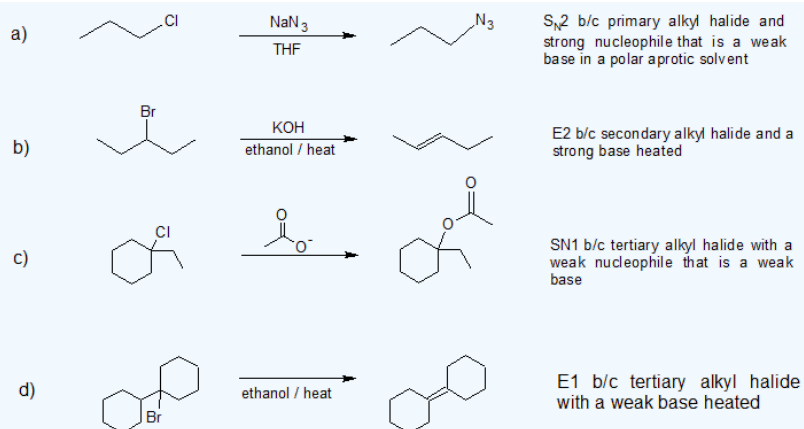
### Exercise

1. Identify the dominant reaction mechanism ( $\text{S}_{\text{N}}1$ ,  $\text{S}_{\text{N}}2$ , E1, or E2) and predict the major product for the following reactions.



Answer

1.



## CONTRIBUTORS

- William Reusch, Professor Emeritus ([Michigan State U.](#)), [Virtual Textbook of Organic Chemistry](#)

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