Certain types of reactions that are likely to occur with alkyl halides. 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.

1. \( \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br} + \text{CN} \xrightarrow{\text{alcohol}} \text{CH}_3\text{CH}_2\text{CH}_2\text{H}_2\text{CN} + \text{Br}^- \)

2. \( \text{CH}_3\text{CH}_2\text{CH}_2\text{H}_2\text{Br} + \text{CN} \xrightarrow{\text{alcohol}} \text{CH}_3\text{CH}_2\text{CH}_2\text{H}_2\text{CN} + \text{Br}^- \)

3. \( \text{CH}_3\text{CH}_2\text{Br} + \text{CN} \xrightarrow{\text{alcohol}} \text{CH}_3\text{CH}_2\text{CN} + \text{HBr} \)

4. \( \text{H}_2\text{C}=\text{CH}_2 - \text{Br} + \text{CN} \xrightarrow{\text{alcohol}} \text{No Reaction} \)

5. \( \text{H}_2\text{C}=\text{CH}_2\text{Br} \xrightarrow{\text{alcohol}} \text{CH}_3\text{CH}_2\text{CN} + \text{Br}^- \)

6. \( \text{H}_2\text{C}=\text{CH}_2\text{Br} \xrightarrow{\text{alcohol}} \text{CH}_3\text{CH}_2\text{CN} + \text{HBr} \)

7. \( \text{H}_2\text{C}=\text{CH}_2\text{Br} \xrightarrow{\text{H}_2\text{O}} \text{CH}_3\text{CH}_2\text{OH} + \text{HBr} \)

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.

\[ \text{R–X} + \text{Nu;} \xrightarrow{\text{Solvent}} \text{Products} \]

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
β-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.

Using the general reaction shown above as our reference, we can identify the following variables and observables.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Observables</th>
</tr>
</thead>
<tbody>
<tr>
<td>R change α-carbon from 1º to 2º to 3º</td>
<td>Products substitution, elimination, no reaction.</td>
</tr>
<tr>
<td>if the α-carbon is a chiral center, set as (R) or (S)</td>
<td>Stereospecificity if the α-carbon is a chiral center what happens to its configuration?</td>
</tr>
<tr>
<td>X change from Cl to Br to I (F is relatively unreactive)</td>
<td>Reaction Rate measure as a function of reactant concentration.</td>
</tr>
<tr>
<td>Nu: change from anion to neutral; change basicity; change polarizability</td>
<td></td>
</tr>
<tr>
<td>Solvent polar vs. non-polar; protic vs. non-protic</td>
<td></td>
</tr>
</tbody>
</table>

When several reaction variables may be changed, it is important to isolate the effects of each during the course of study. In other words: **only one variable should be changed at a time**, the others being held as constant as possible. For example, we can examine the effect of changing the halogen substituent from Cl to Br to I, using ethyl as a common R–group, cyanide anion as a common nucleophile, and ethanol as a common solvent. We would find a common substitution product, C₂H₅–CN, in all cases, but the speed or rate of the reaction would increase in the order: Cl < Br < I. This reactivity order reflects both the strength of the C–X bond, and the stability of X⁻ as a leaving group, and leads to the general conclusion that alkyl iodides are the most reactive members of this functional class.

**Contributors**