1. Determine which of the following groups can be leaving groups in a substitution reaction. The properties to look for in good leaving groups are: a weak bond to carbon (easy to leave), and stable as an independent entity once it does leave. Because the leaving group needs to be stable once it has left, it should be weakly basic (a weak base must also be stable).

   (a) H   (b) CH₃   (c) OH   (d) NR₂   (e) F   (f) Cl   (g) Br   (h) I   (i) OHMe

 Possible leaving groups:
 Cl, Br, I, °OHMe

 Not leaving groups:
 H, CH₃, OH, NR₂, F

2. Explain why sulfonates such as mesylates and tosylates are very good leaving groups.

   Once the sulfonate leaves, there is negative charge on the oxygen. This negative charge is shared over all three oxygens, by resonance, as shown below. Because the negative charge is delocalized, the anion is stabilized, and can exist as a stable anion. As an indicator of the stability, we can look at its basicity. The pKa table on page A-3 shows that the pKa of the conjugate acids of the mesylate and tosylate are -1.2 and -7 respectively. Since the conjugate acids are very strong, mesylates and tosylates are very weakly basic, making them good leaving groups.

3. Explain why the following substitution reaction does not occur:

   The bromine in the product has a positive formal charge, while lithium is neutral. While not completely unheard of, positively charged halogens are very high energy, and unlikely to occur.
4. Predict the products of the following S_N2 reactions. In some cases, there may be no reaction. Show the stereochemistry in the product where relevant.

(a) 
\[
\begin{array}{c}
\text{CH}_3 \overset{\text{O}}{\underset{\text{O}}{\text{SO}}} + \text{NaI} \\
\end{array}
\]

(b) No reaction (the 3° bromide is too sterically hindered to react by S_N2)

(c) 
\[
\begin{array}{c}
\text{Cl} \overset{\text{KCN}}{\rightarrow} \text{NC}
\end{array}
\]

(d) 
\[
\begin{array}{c}
\text{Br} \overset{\text{KO}}{\rightarrow} \text{O}
\end{array}
\]

(e) This reaction will not occur by S_N2, because OH is a very poor leaving group. Instead, the methoxide would probably deprotonate the OH in an acid/base reaction.

5. Determine which nucleophile to use to perform the following S_N2 reactions:

(a) 
\[
\begin{array}{c}
\text{Cl} \overset{\text{O}^-}{\rightarrow} \text{O}
\end{array}
\]

(b) 
\[
\begin{array}{c}
\text{C}_6\text{H}_{11} \overset{\text{MeLi}}{\rightarrow} \text{C}_6\text{H}_{11}
\end{array}
\]

(c) 
\[
\begin{array}{c}
\text{OTs} \overset{\text{NaCl}}{\rightarrow} \text{Cl}
\end{array}
\]
6. Propose a method to synthesize the following molecules using an $S_{N}2$ reaction, beginning with any alkyl halide any nucleophile you choose.

In order to answer this question, determine which bond was probably formed by the substitution reaction. Then, determine which half was from the nucleophile, and which from the electrophile.

(a) Carbon was the electrophile

(b) Two possibilities:

O was nucleophile

O was nucleophile

C was electrophile

(c) Two possibilities:

Carbon was the electrophile

Carbon of the alkyne was the nucleophile