Answers to Chapter 7 Practice Problems

Question 1. A student had carefully prepared pure (R)-2-iodopentane, but in his/her haste had left the compound in solution overnight. When that student came back in the morning and took an optical rotation, the compound was racemic. It was also discovered that a small amount of sodium iodide was present in the solution. What happened?

*Racemization was achieved through a reversible SN2 reaction:*

\[
\text{Me Me} \quad \text{NaI} \quad \text{Me Me}
\]

\[\text{inversion}\]

\[
\text{Me Me} \quad \text{NaI} \quad \text{Me Me}
\]

\[\text{inversion}\]
Question 2. For each reaction shown below, provide the mechanism (i.e. draw in the curved arrows showing the movement of electrons) and identify the expected major product.

a) \[ \begin{align*}
\text{S} & \quad \text{Na}^+ \\
\text{H}_2\text{C} & \quad \text{Br} \\
\end{align*} \] 

\[ \rightarrow \] 

\[ \begin{align*}
\text{S} & \quad \text{CH}_3 \\
\end{align*} \]

b) excess Na\(^+\)I\(^-\) 

\[ \begin{align*}
\text{Br} & \quad \text{Br} \\
\text{Br} & \quad \text{Br} \\
\text{Br} & \quad \text{Br} \\
\text{Br} & \quad \text{I} \\
\end{align*} \] 

\[ \rightarrow \] 

\[ \begin{align*}
\text{Br} & \quad \text{Br} \\
\end{align*} \]

"Backside attack" is not possible (and will never be observed) on an sp\(^2\)-hybridized carbon because:
1. \(\sigma^*\) C-LG is shielded by the "in-plane" substituents
2. Inversion of configuration is impossible (in the above case it would lead to a trans-olefin in a 5-membered ring!)

\[ \begin{align*}
\text{KCN} & \quad \text{Br} \\
\end{align*} \] 

\[ \rightarrow \] 

\[ \begin{align*}
\text{Br} & \quad \text{H} \\
\text{Br} & \quad \text{C} \\
\text{N} & \quad \text{H} \\
\end{align*} \]

d) \[ \begin{align*}
\text{H} & \quad \text{O} & \quad \text{H} \\
\text{OH} & \quad \text{Br} & \quad \text{Br} \\
\end{align*} \] 

\[ \xrightarrow{\text{NaOH}} \] 

\[ \begin{align*}
\text{Br} & \quad \text{O} \\
\end{align*} \] 

\[ \rightarrow \] 

\[ \begin{align*}
\text{O} & \quad \text{C} \\
\end{align*} \]
e) \[
\begin{align*}
&\text{LiOH} \\
\xrightarrow{\text{LiOH}} \\
&\text{Cyclohexyl iodide} \\
\end{align*}
\]

f) \[
\begin{align*}
&\text{Cyclohexanone} \\
\xrightarrow{\text{LiOH}} \\
&\text{Cyclohexyl acetate} \\
\xrightarrow{\text{LiOH}} \\
&\text{Cyclohexyl acetate anion} \\
\xrightarrow{\text{LiOH}} \\
&\text{Cyclohexyl acetate cation} \\
\end{align*}
\]

g) \[
\begin{align*}
&\text{Cyclopentyl methyl sulfide} \\
\xrightarrow{\text{LiSEt}} \\
&\text{Cyclopentyl methyl sulfide} \\
\end{align*}
\]
Question 3. As mentioned in class, methyl tert-butyl ether (MBTE) is a common gasoline additive used to boost octane rating. Below are two reactions that are both attempts to form MBTE. Which reaction will be successful? Which reaction will fail to produce MBTE? Why will it fail?

(1) \((\text{CH}_3)_3\text{COK} + \text{CH}_3\text{Br}\) ?

(2) \((\text{CH}_3)_3\text{CBr} + \text{CH}_3\text{OK}\) ?

No \(S_n2\) on tertiary bromide!
Question 4. Below are a series of reactions that fail to give the indicated $S_N^2$ products. Explain why each reaction fails.

a) \( \text{NaOH} + \begin{array}{c}
\text{CH}_3 \\
\text{CH}_3 \\
\end{array} \rightarrow \begin{array}{c}
\text{OH} \\
\text{OH} \\
\end{array} \)
\( \oplus \)
\( \text{CH}_3 \text{ is a terrible leaving group} \)

b) \( \text{KCN} + \begin{array}{c}
\text{Br} \\
\text{Br} \\
\end{array} \rightarrow \begin{array}{c}
\text{CN} \\
\text{CN} \\
\end{array} \)
\( \null \)
\( \text{No } S_N^2 \text{ on tertiary center - } \alpha^+ \text{ C–Br is also blocked by the other rings.} \)

c) \( \text{NaI} + \begin{array}{c}
\text{Cl} \\
\text{Cl} \\
\end{array} \rightarrow \begin{array}{c}
\text{I} \\
\text{I} \\
\end{array} \)
\( \null \)
\( \text{There can be no } S_N^2 \text{ process at an } sp^2 \text{-hybridized carbon. See Question 2, part (b).} \)

d) \( \text{NMe}_3 + \begin{array}{c}
\text{Me} \\
\text{Me} \\
\end{array} \rightarrow \begin{array}{c}
\text{Me} \\
\text{Me} \\
\end{array} \)
\( \null \)
\( \text{No } S_N^2 \text{ at a neopentyl position} \)
Question 5. Rank the following sets of carbocations from most to least stable. Careful, part (c) is tricky!

a) 

\[
\begin{array}{ccc}
\text{Me} & \text{Me} & \text{Me} \\
\text{Me} & \text{Me} & \text{Me} \\
\hline
\text{most stable} & \text{least stable}
\end{array}
\]

b) 

\[
\begin{array}{ccc}
\text{Me} & \text{Me} & \text{Me} \\
\text{Me} & \text{Me} & \text{Me} \\
\hline
\text{most stable} & \text{least stable}
\end{array}
\]

Note: this cation is at a bridgehead. Carbocations are lowest in energy when sp²-hybridized (planar). This cation, however, cannot be planar (try building a model!). This forces the carbon into sp³-hybridization, and makes the cation very unstable.

c) The carbocation formed from ionization of the following iodides:

[Diagrams showing resonance structures]

These are resonance structures of the same compound.

most stable
Question 6. Starting with (S)-3-methyl-2-propanol, provide structures A-G for the following reactions. Pay attention to stereochemistry where appropriate.
Question 7. The reaction below does not proceed as written, but an $S_N2$ reaction does take place. What is the major product formed?

The reaction will proceed as:

This is an $S_N2$ reaction, so the displacement will proceed more rapidly at a primary position (either of them) over a secondary position.
Question 8. When cis-1-iodo-2-methylcyclohexane (A) is treated with potassium tert-butoxide, 1-methylcyclohexene (B) is formed as the major product (reaction 1). However, when trans-1-iodo-2-methylcyclohexane (C) is treated with potassium tert-butoxide, 3-methylcyclohexene (D) is formed (reaction 2) and the reaction proceeds more slowly than does reaction 1. Explain why the observed products are formed in reaction 1 and 2 and why reaction 2 proceeds more slowly.

\[ \text{cis-1-iodo-2-methylcyclohexane (A)} \rightarrow \text{1-methylcyclohexene (B)} \]  
\[ \text{trans-1-iodo-2-methylcyclohexane (C)} \rightarrow \text{3-methylcyclohexene (D)} \]

\[ \text{E2 elimination can only occur from axial iodide (needs anti-coplanar hydrogen atom)} \]

\[ \text{Only this hydrogen is anti-coplanar with the leaving group} \]

\[ \text{E2 elimination can only occur from axial iodide (needs anti-coplanar hydrogen atom)} \]

\[ \text{Compound C reacts more slowly because it must react through its diaxial conformation, which is much higher energy. At any given time only a small percentage of the molecules of C are in the diaxial conformation.} \]
Question 9. a) Explain why heating in primary bromide A in methanol does not produce the direct substitution product:

Substitution via $S_N1$ would have to result from a primary carbocation (without migration) – impossible. $S_N2$ is not favorable with weak nucleophiles.
b) When the reaction above is carried out, a complex mixture of products results as shown below.

Provide a mechanism showing how each of the above products is formed. Label each product as resulting from $S_N2$, $S_N1$, $E2$, or $E1$.

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Bromine ionizes with simultaneous hydride migration (avoids primary carbocation)

Bromine ionizes with simultaneous hydride migration (avoids primary carbocation)
Bromine ionizes with simultaneous **hydride** migration (avoids primary carbocation)

Bromine ionizes with simultaneous **carbon** migration (avoids primary carbocation)

A larger picture of the carbon migration:
Question 10. Explain the major difference in reactivity between the following pair of reactions:

\[
\begin{align*}
\text{I} & \quad \xrightarrow{\text{NH}_3\text{OH}} \quad \text{NH}_2 \\
\text{I} & \quad \xrightarrow{\text{NH}_4\text{Br}} \quad \text{Br}
\end{align*}
\]

"Ammonium hydroxide" (NH$_4$OH) is formed by dissolving ammonia in water:

\[
\text{NH}_3 + \text{H}_2\text{O} \quad \rightleftharpoons \quad \text{NH}_4^+ + \text{OH}^-
\]

This is not a favorable equilibrium (favors the left side of the above equation), since NH$_3$ is a weaker base than hydroxide ion. Therefore, the concentration of ammonia is much higher than the concentration of hydroxide. Since NH$_3$ and OH$^-$ have similar nucleophilicities, $S_N2$ with NH$_3$ as the nucleophile is the major pathway.

A similar equation can be drawn for the formation of ammonium bromide:

\[
\text{NH}_3 + \text{HBr} \quad \rightarrow \quad \text{NH}_4^+ + \text{Br}^-
\]

This time, the reaction strongly favors products, since HBr is a very strong acid. All of the NH$_3$ is protonated, and Br$^-$ is the sole nucleophile for $S_N2$.

Question 11. Explain the major difference in reactivity between the following pair of reactions:

\[
\begin{align*}
\text{I} & \quad \xrightarrow{\text{NaOH}} \quad \text{Hydroxide is a strong base and a moderate nucleophile. Elimination (E2) will be favored on secondary substrates.} \\
\text{I} & \quad \xrightarrow{\text{NaBr}} \quad \text{Bromide is a moderate nucleophile but a weak base. Substitution (S_N2) will be favored on secondary substrates.}
\end{align*}
\]