Suggested solutions for Chapter 6

PROBLEM 1

Draw mechanisms for these reactions:

\[
\text{CH}_2=\text{CHOH} \xrightarrow{\text{NaBH}_4, \text{EtOH, H}_2\text{O}} \text{CH}_2\text{CH(OH)}_2
\]

\[
\text{CH}_3\text{C(=O)CH}_2\text{CHO} \xrightarrow{1. \text{LiAlH}_4, 2. \text{H}_2\text{O}} \text{CH}_3\text{CCH(OH)}_2\text{CH}_2\text{CH}_3
\]

Purpose of the problem

Rehearsal of a simple but important mechanism that works for all aldehydes and ketones.

Suggested solution

Draw out the BH\(_4^-\) and AlH\(_4^-\) anions, with the carbonyl compound positioned so that one of the hydrogens can be transferred to the carbonyl group, and the transfer the hydrogen from B or Al to C. A proton transfer is needed to make the alcohol: from the solvent in the first case and during the work-up with water in the second.

This reaction shows that you can reduce aldehydes with lithium aluminium hydride, even if you would usually prefer the more practical sodium borohydride.
**PROBLEM 2**

Cyclopropanone exists as the hydrate in water but 2-hydroxyethanal does not exist as the hemiacetal. Explain.

![Chemical structures](image)

**Purpose of the problem**

To get you thinking about equilibria and hence the stability of compounds.

**Suggested solution**

Hydration is an equilibrium reaction so the mechanism is not strictly relevant to the question, though there is no shame in including mechanisms wherever you can. To answer the question we must consider the effect of the three-membered ring on the relative stability of starting material and product. All three-membered rings are very strained because the bond angles are 60° instead of 109° or 120°. Cyclopropanone is particularly strained because the sp² carbonyl carbon would like a bond angle of 120°—there is ‘60° of strain.’ In the hydrate that carbon atom is sp³ hybridized and so there is only about ‘49° of strain.’ Not much gain, but the hydrate is more stable than the ketone.

The second case is totally different. The hydroxy-aldehyde is not strained at all but the hemiacetal has ‘49° of strain’ at each atom. Even without strain, hydrates and hemiacetals are usually less stable than their aldehydes or ketones because one C=O bond is worth more than two C–O bonds. In this case the hemiacetal is even less stable and, unlike the cyclopropanone, can escape strain by breaking a C–O ring bond.
**PROBLEM 3**
One way to make cyanohydrins is illustrated here. Suggest a detailed mechanism for the process.

```
   R\text{O}  \quad  \text{H}  \quad  \text{Me}_3\text{SiCN}  \quad  \text{catalytic KCN}  \quad  \text{H}  \quad  \text{CN}  \quad  \text{OSiMe}_3
```

**Purpose of the problem**
To help you get used to mechanisms involving silicon and revise an important way to promote additions to the carbonyl group.

**Suggested solution**
The silyl cyanide is an electrophile while the cyanide ion in the catalyst is the nucleophile. Cyanide adds to the carbonyl group and the oxanion product is captured by silicon, liberating another cyanide ion for the next cycle.

```
   \text{R}\text{O}  \quad  \text{CN}  \quad  \text{H}  \quad  \text{CN}  \quad  \text{Me}_3\text{SiCN}  \quad  \text{OSiMe}_3  \quad  +  \quad  \text{CN}
```

**PROBLEM 4**
There are three possible products from the reduction of this compound with sodium borohydride. What are their structures? How would you distinguish them spectroscopically, assuming you can isolate pure compounds?

```
   \text{H}  \quad  \text{H}  \quad  \text{O}  \quad  \text{O}
```

**Purpose of the problem**
To let you think practically about reactions that may give more than one product.
**Suggested solution**

The three compounds are easily drawn: one or other carbonyl group, or both, may be reduced.

The third compound, the diol, has no carbonyl group in the $^{13}\text{C}$ NMR spectrum or the infrared and has a molecular ion two mass units higher than the other two products. Distinguishing those is more tricky, and needs techniques you will meet in detail in chapter 18. The hydroxyketone has a conjugated carbonyl group (C=O stretch at about 1680 cm$^{-1}$ in the infrared spectrum) while the hydroxyaldehyde is not conjugated (C=O stretch at about 1730 cm$^{-1}$ in the infrared). The chemical shift of the C–OH carbons will also be different because the benzene ring is joined to this carbon in the aldehyde but not in the ketone.

**PROBLEM 5**

The triketone shown here is called ‘ninhydrin’ and is used for the detection of amino acids. It exists in aqueous solution as a hydrate. Which ketone is hydrated and why?

**Purpose of the problem**

To let you think practically about reactions that may give more than one product.

**Suggested solution**

The two ketones next to the benzene ring are stabilised by conjugation with it but also destabilised by the central ketone—two electron-withdrawing groups next to each other is a bad thing. The central
carbonyl group is not stabilised by conjugation and is destabilised by two other ketones so it forms the hydrate. Did you remember that hydrate formation is thermodynamically controlled?

\[
\text{OH} \quad \text{OH}
\]

\[
\text{O} \quad \text{O}
\]

**PROBLEM 6**

This hydroxyketone shows no peaks in its infrared spectrum between 1600 and 1800 cm\(^{-1}\), but it does show a broad absorption at 3000–3400 cm\(^{-1}\). In the \(^{13}\text{C}\) NMR spectrum there are no peaks above 150 ppm but there is a peak at 110 ppm. Suggest an explanation.

\[
\text{HO} \quad \text{O}
\]

**Purpose of the problem**

Structure determination to solve a conundrum.

**Suggested solution**

The evidence shows that there is no carbonyl group in the molecule but that there is an OH group. The peak at 110 ppm looks at first sight like an alkene, but it could also be an unusual saturated carbon atom bonded to two oxygens. You might have argued that an alcohol and a ketone could combine to give a hemiacetal, and that is, of course, just what it is. The compound exists as a stable hemiacetal because it has a favourable five-membered ring.

\[
\text{HO::} \quad \text{H} \quad \text{O} \quad \text{O} \quad \text{O}
\]

\[
\text{O} \quad \text{O}
\]

\[
\text{P. 136 of the textbook explains why cyclic hemiacetals are stable.}
\]
PROBLEM 7

Each of these compounds is a hemiacetal and therefore formed from an alcohol and a carbonyl compound. In each case give the structures of the original materials.

![Chemical structures](image)

Purpose of the problem

To give you practice in seeing the underlying structure of a hemiacetal.

Suggested solution

Each OH group represents a carbonyl group in disguise (marked with a grey ring). Just break the bond between this carbon and the other oxygen atom and you will see what the hemiacetal was made from. The first example shows how it is done.

![Chemical reaction](image)

The next is similar but the alcohol is a different molecule.

![Chemical reaction](image)

Do not be deceived by the third example. There is one hemiacetal (two oxygens joined to the same carbon atom) but the other OH is just a tertiary alcohol.
The last two examples are not quite the same. The first is indeed symmetrical but the second has one oxygen atom in a different position so that there is only one hemiacetal. Note that these hemiacetals may not be stable.

PROBLEM 8

Trichloroethanol may be prepared by the direct reduction of chloral hydrate in water with sodium borohydride. Suggest a mechanism for this reaction. Take note that sodium borohydride does not displace hydroxide from carbon atoms!

Purpose of the problem

To help you detect bad mechanisms and find concealed good ones.

Suggested solution

If sodium borohydride doesn’t displace hydroxide from carbon atoms, then what does it do? We know it attacks carbonyl groups to give alcohols and to get trichloroethanol we should have to reduce chloral. Hemiacetals are in equilibrium with their carbonyl equivalents, so...
PROBLEM 9
It has not been possible to prepare the adducts from simple aldehydes and HCl. What would be the structure of such compounds, if they could be made, and what would be the mechanism of their formation? Why can’t these compounds be made?

Purpose of the problem
More revision of equilibria to help you develop a judgement on stability.

Suggested solution
This time we need a mechanism so that we can work out what would be formed. Protonation of the carbonyl group and then nucleophilic addition of chloride ion would give the supposed products.

```
\[ \text{HCl} \quad \text{H} \quad \text{Cl} \]
```

There’s nothing wrong with the mechanism, it’s just that the reaction is an equilibrium that will run backwards. Hemiacetals are unstable because they decompose back to carbonyl compounds. Chloride ion is very stable and decomposition will be faster than it is for hemiacetals.

PROBLEM 10
What would be the products of these reactions? In each case give a mechanism to justify your prediction.

Purpose of the problem
Giving you practice in the art of predicting products—more difficult than simply justifying a known answer.

Suggested solution
The Grignard reagent will add to the carbonyl group and the work-up will give a tertiary alcohol as the final product.
The second reaction should give you brief pause for thought as you need to recall that borohydride reduces ketones but not esters.