Suggested solutions for Chapter 11

PROBLEM 1
Draw mechanisms for these reactions, both of which involve loss of carbonyl oxygen.

Purpose of the problem
To see if you can draw mechanisms for two of the main classes of reactions in the chapter.

Suggested solution
As MeOH is present in large excess as the solvent, it probably adds first. This also makes the intermediate for the addition of chloride a stable oxonium ion. The mechanism is very like that for acetal formation and, if you added chloride first, that is also a reasonable mechanism.

The second example is imine formation—attack by an amine nucleophile and dehydration of the intermediate. Don't forget to protonate the OH group so that it can leave as a water molecule.
PROBLEM 2
Each of these compounds is an acetal, that is a molecule made from an aldehyde or ketone and two alcohol groups. Which compounds were used to make these acetals?

Purpose of the problem
Practice at the recognition of acetals and working out how to make them.

Suggested solution
All we have to do is to identify the hidden carbonyl group by finding the only carbon atom having two C–O bonds. This atom is marked with a grey circle. If you imagine breaking the two C–O bonds you will discover the carbonyl group and the alcohols.
PROBLEM 3
Suggest mechanisms for these two reactions of the smallest aldehyde, formaldehyde (methanal CH₂=O).

![Chemical structures]

Purpose of the problem
Extension of simple acetal chemistry into related reactions with nitrogen.

Suggested solution
Both reactions start in the same way by attack of a nitrogen nucleophile on formaldehyde. Acid catalysis is not necessary for this step. The first reaction ends with the formation of the iminium ion by acid-catalysed dehydration.

![Chemical structures]

In the other reaction a second amino group is waiting to capture the iminium ion by cyclisation to form a stable five-membered ring.

![Chemical structures]
PROBLEM 4
In the textbook (p. 104) we showed you a selective hydrolysis of an acetal. Why were the other acetals (one is a thio-acetal) not affected by this treatment? How would you hydrolyse them? Chloroform (CHCl₃) is the solvent.

Purpose of the problem
Revision of the different types of acetal and their relative reactivity.

Suggested solution
Cyclic acetals are more stable than non-cyclic ones as we explain on p. 228 of the textbook. Hydrolysis needs more vigorous conditions. Thioacetals are much harder to hydrolyse because sulfides are even less basic than ethers. They can be hydrolysed using electrophiles that attack sulfur readily, such as Hg(II) or methylating agents. This is one possible solution:
PROBLEM 5

In the textbook (p. 228) we say that the Grignard reagent below is ‘an unstable structure – impossible to make.’ Why is this? What would happen if you tried to make it?

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

Purpose of the problem

Revision of the danger of mutually destructive functional groups.

Suggested solution

There are various possibilities that all arise from the presence of a carbonyl group and a Grignard in the same molecule. These two would react together. They might cyclise to form a four-membered ring or a bimolecular reaction might lead to a dimer and perhaps polymerisation.

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

PROBLEM 6

Suggest mechanisms for these reactions.

Purpose of the problem

Extension of acetal and imine formation into examples where the intermediate is trapped by a different nucleophile.
Suggested solution

The first reaction starts with the usual attack of an alcohol on the aldehyde but the second nucleophile is the carboxylic acid. Though a poor nucleophile, it is good enough to react with an oxonium ion, particularly in a cyclisation.

The second reaction starts with nucleophilic attack by the amine on the more electrophilic carbonyl group – the ketone. Imine formation is followed by cyclisation and this second step is normal nucleophilic substitution of an ester (chapter 10). The imine double bond moves into the ring to secure conjugation with the ester.

The third example uses very simple molecules and again starts with imine formation. Cyanide is the nucleophile that captures the iminium ion and a second imine formation completes the mechanism.
PROBLEM 7
Don’t forget the problem in the summary on p.238 of the textbook: suggest a mechanism for the formation of this thioacetal.

![Mechanism diagram]

Purpose of the problem
Extension of the mechanism for acetal formation to dithioacetal (dithiane) formation.

Suggested solution
The mechanism is a direct analogue of acetal formation. The dehydration step is more difficult: the C=S bond is less stable than the C=O bond because overlap of 2p and 3p orbitals is not as good as overlap of two 2p orbitals of similar size and energy.

![Mechanism steps diagram]