Suggested solutions for Chapter 17

PROBLEM 1
Draw mechanisms for these elimination reactions.

Purpose of the problem
Exercise in drawing simple eliminations.

Suggested solution
These are both E2 reactions as the leaving groups are on primary carbons. In fact both of these reaction are in the textbook (p. 387 and 391).

The structure of the amidine base, DBU, and why it is used in elimination reactions is discussed in the textbook on p. 387.
PROBLEM 2

Give a mechanism for the elimination reaction in the formation of tamoxifen, a breast cancer drug, and comment on the roughly 50:50 mixture of geometrical isomers (cis- and trans-alkenes)

\[
\text{H}_2\text{SO}_4 \quad \text{OH} \quad \text{O} \quad \text{NMe}_2
\]

\[
\text{H}_2\text{SO}_4 \quad \text{OH} \quad \text{O} \quad \text{NMe}_2
\]

Purpose of the problem

Thinking about the stereochemical consequences of E1.

Suggested solution

The tertiary alcohol leaving group, the acid catalyst, and the 50:50 mixture all suggest E1 rather than E2. There is only one proton that can be lost and, as there is very little difference between the isomeric alkenes, equilibration probably gives the 50:50 mixture.

\[
\text{H}_2\text{SO}_4 \quad \text{OH} \quad \text{O} \quad \text{NMe}_2
\]
PROBLEM 3
Suggest mechanisms for these eliminations. Why does the first give a mixture and the second a single product?

\[
\begin{align*}
\text{OH} & \quad \text{H}_3\text{PO}_4 \quad \text{heat} \\
\text{H}_3\text{PO}_4 & \quad \text{heat} \\
\text{H}_3\text{PO}_4 & \quad \text{heat} \\
\end{align*}
\]

\[
\text{64\% yield, 4:1 ratio}
\]

Purpose of the problem
Regioselectivity of eliminations.

Suggested solution
Whether the first reaction is E1 or E2, there are two sets of hydrogen atoms that could be lost in the elimination. The conditions suggest E1 and the major product may be so because of equilibration.

The second reaction produces a more stable tertiary cation from which any of six protons could be lost, but all give the same product. Repetition gives the diene.
PROBLEM 4

Explain the position of the alkene in the products of these reactions. The starting materials are enantiomerically pure. Are the products also enantiomerically pure?

Purpose of the problem

Examples of E1cB in the context of absolute stereochemistry.

Suggested solution

The first reaction is an E1cB elimination of a β-hydroxy-ketone. The product is still chiral although it has lost one stereogenic centre. The other (quaternary) centre is not affected by the reaction so the product is enantiomerically pure.

The second example already has an electron-rich alkene (an enol ether) present in the starting material so this is more of an E1 than an E1cB mechanism. The intermediate is a hemiacetal that hydrolyses to a ketone (p. 224 in the textbook). The product has two chiral centres unaffected by the reaction and is still chiral so it is also enantiomerically pure.
PROBLEM 5

Explain the stereochemistry of the alkenes in the products of these reactions.

Purpose of the problem

Display your skill in a deceptive example of control of alkene geometry by elimination.

Suggested solution

The first reaction is stereospecific cis addition of hydrogen to an alkyne to give the cis-alkene. The intermediate is therefore a cis,cis-diene and it may seem remarkable that it should become a trans,trans-diene on elimination. However, when we draw the mechanism for the elimination, we see that there need be no relationship between the stereochemistry of the intermediate and the product as this is an E1 reaction and the cationic intermediate can rotate into the most stable shape before conversion to the aldehyde.

The hydrogenation of alkynes to give cis alkenes is described on p. 537 of the textbook.
PROBLEM 6

Suggest a mechanism for this reaction and explain why the product is so stable.

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

Purpose of the problem

Exploring what might happen on the way to an elimination and explaining special stability.

Suggested solution

The obvious place to start is cyclisation of the phenol onto a ketone to form a six-membered ring. The product is a hemiacetal that will surely eliminate by a combination of hemiacetal hydrolysis and the E1cB mechanism.

The final product is particularly stable as the right hand ring is aromatic. It has two alkenes and a lone pair on oxygen, making six electrons in all. If you prefer you can show the delocalisation to make the ring more benzene-like.
**PROBLEM 7**

Comment on the position taken by the alkene in these eliminations.

![Chemical structures](image)

**Purpose of the problem**

Further exploration of the site occupied by the alkene after and elimination.

**Suggested solution**

The first is an E1cB reaction after methylation makes the amine into a leaving group. The alkene has to go where the amine was (and in conjugation with the ketone).

![Chemical structures](image)

The second is also E1cB and so the alkene must end up conjugated with the ketone. But this time the leaving group is on the ring so that is where the alkene goes. The stereochemistry is irrelevant as the enolate has lost one chiral centre and there is no requirement in E1cB for H and OH to be anti-periplanar.

![Chemical structures](image)

The third is an E2 reaction so there is now a requirement for H and Br to be anti-periplanar. This means that the Br must be axial and only one hydrogen is then in the right place.