PROBLEM 1
Suggest mechanisms for the following reactions, commenting on your choice of S_N1 or S_N2.

Purpose of the problem
Simple example of the two important mechanisms of chapter 15: S_N1 and S_N2.

Suggested solution
NaOH (pK_a of water about 16) removes the proton from PhSH (pK_a about 7) rapidly as this is a proton transfer between electronegative atoms. Clearly the methyl group must be transferred from O to S and this must be an S_N2 reaction.

The first reagent in the second reaction resembles the reagent in the first reaction but it is the free sulfonic acid and not the ester. The ether product must come from the displacement of OH from one molecule of t-BuOH by the OH group of the other and this can only be an S_N1 reaction. The OH group leaves as H_2O after being protonated by the sulfonic acid.
PROBLEM 2

Draw mechanisms for these reactions, explaining why these particular products are formed.

Purpose of the problem

How to choose between $S_N 1$ and $S_N 2$ when the choice is more subtle.

Suggested solution

The first compound has two leaving groups – both secondary chlorides. The one that leaves is next to oxygen so that suggests $S_N 1$ (the oxygen lone pair can stabilise the cation) as does the reagent: surely MeO$^-$ would be used for $S_N 2$.

The second compound has only one leaving group and that must be protonated before it can leave. It has two possible sites for attack by the nucleophile (Cl$^-$), one primary and one secondary. As the primary is chosen, this must be $S_N 2$. 
**PROBLEM 3**

Draw mechanisms for these reactions and give the stereochemistry of the product.

\[
\begin{align*}
\text{Br} & \quad \text{Cl} \\
\text{Br} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\text{Br} & \quad \text{Cl} \\
\text{Br} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

1. \(\text{PhNMe}_2\) \(\text{CH}_2\text{Cl}_2\)
2. \(\text{NaH, DMF}\)

**Purpose of the problem**

Drawing mechanisms for two types of nucleophilic substitution in the same sequence to make a \(\beta\)-lactam antibiotic.

**Suggested solution**

We need an \(S_n2\) reaction at a primary carbon and a nucleophilic substitution at the carbonyl group with the amino group as the nucleophile in both cases. The carbonyl group reaction probably happens first. Don’t worry if you didn’t deprotonate the amide before the \(S_n2\) reaction. The stereochemistry is the same as that of the starting material (\(\text{CO}_2\text{Et up as drawn}\)) as no change has occurred at the chiral centre.

\[
\begin{align*}
\text{Br} & \quad \text{Cl} \\
\text{Br} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\text{Br} & \quad \text{Cl} \\
\text{Br} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]

\[
\begin{align*}
\text{Br} & \quad \text{Cl} \\
\text{Br} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\text{Br} & \quad \text{Cl} \\
\text{Br} & \quad \text{Cl} \\
\text{H}_2\text{N} & \quad \text{CO}_2\text{Et} \\
\end{align*}
\]
PROBLEM 4
Suggest a mechanism for this reaction. You will find it helpful first of all to draw good diagrams of reagents and products.

\[ t\text{-BuNMe}_2 + (\text{MeCO})_2\text{O} \rightarrow \text{Me}_2\text{NCOMe} + t\text{-BuO}_2\text{CMe} \]

Purpose of the problem
Revision of chapter 2 and practice at drawing mechanisms of unusual reactions.

Suggested solution
First draw good diagrams of the molecules as the question suggests.

With an unfamiliar reaction, it is best to identify the nucleophile and the electrophile and see what happens when we unite them. The nitrogen atom is obviously the nucleophile and one of the carbonyl groups must be the electrophile.

We must lose a \( t \)-butyl group from this intermediate to give one of the products and unite it with the acetate ion to give the other. This must be an \( S_{N1} \) rather than an \( S_{N2} \) at a \( t \)-butyl group.
PROBLEM 5
Predict the stereochemistry of these products. Are they diastereoisomers, enantiomers, racemic or what?

![Chemical structure](image)

Purpose of the problem
Revision of stereochemistry from chapter 14 and practice at applying it to substitution reactions.

Suggested solution
The starting material in the first reaction has a plane of symmetry so it is achiral: the stereochemistry shows only which diastereoisomer we have. Attack by the amine nucleophile at either end of the epoxide (the two ends are the same) must take place from underneath for inversion to occur. The product is a single diastereoisomer but cannot, of course, be a single enantiomer so it doesn’t matter which enantiomer you have drawn. The stereochemistry of the Ph group cannot change—it is just a spectator.

![Chemical structure](image)

The starting material for the second reaction is also achiral as it too has a plane of symmetry. The stereochemistry merely shows that the two OTs groups are on the same side of the molecule as drawn. Displacement with sulfur will occur with inversion and it is wise to redraw the intermediate before the cyclisation. This ‘inverts’ the chiral centre so that we can see that the stereochemistry of the product has the methyl groups cis. There are various ways to draw this.