Electrophilic Aromatic Substitution: Regioselectivity in the Nitration of Methyl Benzoate

By carrying out the nitration of methyl benzoate and recording the M.P. of the isolated product(s), conclusions can be drawn about the directing effect of the ester substituent attached to the aromatic ring in the starting molecule.
General Mechanism For Nitration Of Benzene

The nitration of methyl benzoate is carried out using a mixture of sulfuric and nitric acid. Being the stronger acid, sulfuric acid protonates nitric acid, with subsequent loss of water giving the reactive nitronium ion \((\text{NO}_2^+)\) electrophile:

\[
\begin{align*}
\text{HO-} &\quad \text{H}_2\text{O} \quad \text{NO}_2^+ \quad \text{HSO}_4^- \\
\text{S-} &\quad \text{H}_3\text{O}^+ \quad \text{NO}_2 \quad + \text{H}_2\text{O} \\
\text{O} &\quad \text{HSO}_4^- \\
\end{align*}
\]

\(\text{HNO}_3\) is a poor electrophile and provides a low concentration of \(\text{NO}_2^+\). Sulfuric acid results in the essentially complete conversion of nitric acid into the nitronium ion, \(\text{NO}_2^+\).

When adding the mixture of acids to the ester, it is important to keep the temperature of the reaction below 15°C.
Electrophilic Attack On Mono-Substituted Benzene Derivatives

When considering the possible products of an electrophilic aromatic substitution reaction of a mono-substituted benzene derivative, the incoming electrophile may be incorporated at the ortho-, meta- or para-position.

In practice it is found that substitution occurs to yield either predominantly the \( m \)-isomer, or predominantly a mixture of the \( o \)- and \( p \)-isomers.

\[ \Rightarrow \text{Directing effect} \]

The overall rate at which substitution takes place may be faster or slower than with benzene itself.

\[ \Rightarrow \text{Activating effect} \]
Trends in Directing and Activating Groups

THE ATOM DIRECTLY ATTACHED TO THE RING HAS EITHER A POSITIVE OR PARTIAL POSITIVE CHARGE.

Y = NR₃, CCl₃, NO₂, CHO, COR, CO₂H, CO₂R, CONR₂, etc

THESE SUBSTITUENTS ARE RING DEACTIVATING (REDUCE ELECTRON DENSITY OF THE AROMATIC RING) AND DIRECT SUBSTITUTION AT THE META POSITION

THE ATOM DIRECTLY ATTACHED TO THE RING HAS A LONE PAIR AND IS NOT A HALOGEN.

Y = NR₂, OH, OR, OCOR, NHCOR, etc

THESE SUBSTITUENTS ARE RING ACTIVATING (INCREASE ELECTRON DENSITY OF THE AROMATIC RING) AND DIRECT SUBSTITUTION AT THE ORTHO AND PARA POSITIONS

OR

THE ATOM DIRECTLY ATTACHED TO THE RING IS A HALOGEN

Y = Cl, Br, I

THESE SUBSTITUENTS ARE RING DEACTIVATING (REDUCE ELECTRON DENSITY OF THE AROMATIC RING) AND DIRECT SUBSTITUTION AT THE ORTHO AND PARA POSITIONS
Product Isolation, Purification and Analysis

Pour reaction mixture onto crushed ice
The crude product will precipitate and can be easily isolated by vacuum filtration.
The crude product is subsequently purified by recrystallisation.

Record the M.P. of the product
The purity of the product is assessed by recording the M.P.
This will also allow the identification of the substitution product(s) formed in the reaction. Each of the three possible regioisomers has a distinct M.P.

Identifying the reaction product(s) allows the directing effect of the ester group to be determined.
Tips and Reminders

1. Ensure all glassware is dry and free of acetone before starting the experiment.

2. Try to keep the temperature of the reaction mixture in the range 5-15°C.

3. Use a **glass thermometer**!

4. Use the water aspirator as the vacuum source for isolating the crude product (note that the crude may be dried on the house vacuum if the Buchner flask is emptied).

5. Ensure the crude is thoroughly washed with ice-cold water (to pH > 5). This may require several washings.

6. A small **report of results** is required for this experiment.

7. The material in this lab will be covered by a quiz during the checkout week.