THE DIELS-ALDER REACTION

The Diels-Alder reaction occurs with high levels of stereoselectivity. The reaction proceeds via a syn addition, and as such, the relative stereochemistry of substituents contained on the diene and the dienophile is maintained over the course of the reaction. Thus, reaction of butadiene with a cis-substituted dienophile leads to the cis product, whereas reaction of butadiene with a trans-substituted dienophile leads to the trans product. By the same token, dienes in which the substituents at the 1 and 4 positions occupy the same orientation in the s-cis configuration (both groups either $R_{outside}$ or $R_{inside}$) will give the cis product, whereas those having substituents that occupy different orientations (one substituent $R_{outside}$ and one substituent $R_{inside}$) will give the corresponding trans product.

• Stereochemistry of the dienophile is maintained:

\[
\text{cis product}
\]

\[
\text{trans product}
\]

• Stereochemistry of the diene is maintained:

\[
\text{symmetrical orientation}
\]

\[
\text{unsymmetrical orientation}
\]
The same principles hold true when looking at a Diels-Alder reaction in which both the diene and the dienophile bear substituents. Thus, for the reaction below, note that the stereochemistry of the diene is maintained (symmetrical orientation of groups leads to cis relative stereochemistry in the product), as is that of the dienophile (cis dienophile leads to cis relative stereochemistry in the product).

\[
\text{CH}_3 + \text{CO}_2\text{CH}_3 \xrightarrow{\Delta} \text{cis relationship in product}
\]

\[
\text{CH}_3 + \text{CO}_2\text{CH}_3 \xrightarrow{\Delta} \text{cis relationship in product}
\]

**Putting it all together**

When looking at the relative stereochemistry of substituents on the diene vs. those on the dienophile, consider that the dienophile can approach the diene in either of two orientations:

a. the dienophile approaches the diene such that its electron withdrawing substituents are oriented away from the diene \(\pi\) system (the exo orientation).

\[
\text{exo transition state} \xrightarrow{\text{heat}} \equiv \text{exo product (minor)}
\]

b. the dienophile approaches the diene such that its electron withdrawing substituents are oriented toward the diene \(\pi\) system (the endo orientation); \(E = \text{CO}_2\text{CH}_3\).

\[
\text{endo transition state} \xrightarrow{\text{heat}} \equiv \text{endo product (major)}
\]

In most cases, formation of the endo product is favored.
Practice Problems

Show the product(s) you would obtain for each of the following reactions. Clearly depict any relative stereochemistry. Where appropriate, identify the major and minor products.

1. 

\[
\text{OCH}_3 + \text{CH}_3 + \text{NC} = \text{NC} = \text{NC} \xrightarrow{\Delta} \]

2. 

\[
\text{CO}_2\text{H} + \text{CH} = \text{CH} \xrightarrow{\Delta} \]

3. 

\[
\text{CH}_3\text{CH} = \text{CH} + \text{CH}_3\text{CHO} \xrightarrow{\Delta} \]

4. 

\[
\text{CH}_3 + \text{CO} = \text{O} = \text{O} \xrightarrow{\Delta} \]

5. 

\[
\text{CH}_3\text{CH} = \text{CH} + \text{CH} = \text{CH} = \text{CHO} \xrightarrow{\Delta} \]

6. 

\[
\text{CH}_3\text{CH} = \text{CH} + \text{CH}_3\text{O} = \text{C} = \text{C} = \text{OCH}_3 \xrightarrow{\Delta} \]