Lecture 4

Diastereoselective Hydroboration

Learning outcomes: by the end of this lecture you should be able to:

1. use conformational analysis to predict the diastereoselectivity of hydroboration reactions involving olefins containing α-stereogenic centres.

In the last lecture, we discussed how the reactive conformation of an alkene, undergoing a hydroboration reaction, differed (albeit rather subtly) from its ground-state conformation.

Based on this knowledge, we were able to rationalise the diastereoselectivity of a hydroboration reaction between borane, BH₃, and an alkene possessing an α-stereogenic centre. In that example, the small size of the substituents on the hydroborating agent (i.e. hydrogens in the case of BH₃), meant that we did not need to consider interactions between the alkene and the reacting borane. Unfortunately this is not always the case; there are plenty of occasions where interactions between the substrate and the reagent are significant and which then must also be taken into consideration.
Example 1

Rationalise the stereochemical outcome of the following hydroboration reaction:

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Hydroborating Agent</th>
<th>Anti Diastereoisomer</th>
<th>Syn Diastereoisomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>BH₃</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>BH₂</td>
<td>3.5</td>
<td>1</td>
</tr>
<tr>
<td>BH₂⁻</td>
<td>8.5</td>
<td>1</td>
</tr>
<tr>
<td>BH⁻</td>
<td>11</td>
<td>1</td>
</tr>
</tbody>
</table>

Note that the diastereoselectivity of this reaction is strongly dependent on the hydroborating agent used, which would suggest that interactions between the olefin substrate and hydroborating agent are now significant in controlling the stereochemical outcome of the reaction. To understand the stereoselectivity of these reactions, we need to:

1. draw the T.S.s leading to the anti and syn diastereoisomers (Newman projections will be most useful here).
2. identify the important interactions in the substrate alone that govern the relative energies of the two T.S.s.
3. identify the important interactions between the olefin and incoming hydroborating agent.
Example 2
The olefin geometry can also have profound effects on the diastereoselectivity of hydroboration reactions. Rationalise the stereoselectivity of the following examples. You should be able to explain why the Bu substituent in the (E)-stereoisomer has little effect on the diastereoselectivity of the reaction.

\[
\begin{align*}
\text{Bu} & \quad \text{OH} \\
\quad \downarrow \quad 9\text{-BBN} \\
\text{Bu} & \quad \text{OH} \quad \text{OH}
\end{align*}
\]

\[
\text{anti} \\
11:1 \text{ d.r.}
\]

\[
\begin{align*}
\text{Bu} & \quad \text{OH} \\
\quad \downarrow \quad 9\text{-BBN} \\
\text{Bu} & \quad \text{OH} \quad \text{OH}
\end{align*}
\]

\[
\text{anti} \\
9:1 \text{ d.r.}
\]
When we use the (Z)-stereoisomer, we observe a significant increase in the stereoselectivity of the hydroboration reaction. Draw T.S.s and identify the interactions that account for this increase in stereoselectivity.
Summary

Using two more examples of diastereoselective hydroboration, we have seen how we can rationalise the diastereochemical outcome of this reaction by:

i) understanding the difference between the reactive-state and ground-state conformations of alkenes;

ii) recognising the differences between the two possible T.S. geometries, principally by considering the 1,2- and 1,3-interactions present in the reacting substrate;

iii) recognising that interactions between the substrate and incoming reagent are sometimes also important and must then also be considered.