The Diels-Alder reaction is a powerful synthetic tool widely used by chemists to incorporate six member rings into compounds. Mechanistically, it goes through a \([4\pi+2\pi]\) cycloaddition, in which a diene interacts with an alkene (a dienophile) in a cyclic arrangement to create a six membered cyclohexene adduct. This process is largely driven by taking two reactive \(\pi\)-systems and creating two highly stable \(\sigma\)-bonds. (Scheme 1)

![Scheme 1- A Diels-Alder Reaction](image)

In order for the reaction to occur, the diene must be situated in the s-cis conformation. Dienes in the s-trans conformation can rotate about the single bond to form the s-cis conformation. (Figure 1)

![Figure 1- Diene conformation](image)

A normal electron-demand Diels-Alder reaction is favored by electron rich dienes and electron poor dienophiles, however electron poor dienes and electron rich dienophiles have been shown to work efficiently in inverse electron-demand Diels-Alder reactions. The Diels-Alder reaction can also be enhanced by the use of increased pressure or heat.

![Figure 2- Diels-Alder Mechanism](image)

The reaction goes through a syn-facial addition in which the dienophile approaches a single face of the diene, making a boat shaped transition phase. It also goes through a concerted mechanism where bonds are made and broken at the same time. (Figure 2)

In a single Diels-Alder reaction up to four new stereocenters can be formed. This is advantageous especially considering the fact that the Diels-Alder is diastereoselective and regioselective. A chemist can easily predict the stereochemistry of all four stereocenters using a few common trends the reaction follows.

First, the resulting cyclohexene product will either be a cis- or trans- diastereomer. As seen in
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(Table 1), the diastereomer can be predicted based on the spatial arrangement of the groups coming off the s-cis diene (inside or outside the diene), and the stereochemistry in the original dienophile.

Second, the Diels-Alder reaction primarily makes endo- diastereomers. Endo- and exo- are terms used to describe boat transition state stereochemistry. The dienophile can be attacked on two different faces. It can be attacked with its R groups situated away from the forming boat, resulting in exo- stereochemistry, or it can be attacked from the opposite face with its R groups situated underneath the forming boat, resulting in endo- stereochemistry. (Scheme 2) The endo-product is more favorable due to extra orbital overlap from the R groups during the transition state.

Table 1- Stereochemistry of starting materials is retained

Scheme 2- Endo- and Exo- Stereochemistry in the Diels-Alder
Finally, the Diels-Alder is highly regioselective, in that it will preferentially form 1,2- and 1,4-disubstituted adducts over 1,3- disubstituted adducts. (Scheme 3)

In today’s experiment you will use anthracene as the electron rich diene and maleic anhydride as the electron poor dienophile. There are several driving factors that make this reaction work so well. The reaction will be carried out in xylene, which has a boiling point of 140 °C, making it possible to reflux the reaction at high temperatures. Also, maleic anhydride is an excellent dienophile since it has strong electron withdrawing groups. (Scheme 4)
The Diels-Alder Reaction of Anthracene with Maleic Anhydride


Data Table: Have a copy of this table in your notebook prior to the beginning of lab. Fill in the amount, mmol, and mole ratio of each substrate when you actually complete that portion of the experiment. Sections with a “-” do not need to be filled in or included in your report.

<table>
<thead>
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<th></th>
<th>Anthracene</th>
<th>Maleic Anhydride</th>
<th>m-Xylene</th>
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<tbody>
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<td>Mole Ratio</td>
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Equipment:

Procedure:

To start, weigh out 100 mg of anthracene and 55 mg of maleic anhydride onto weigh papers and carefully transfer these into your 5 mL conical vial. Set up your reflux apparatus, by first filling the outside of your condenser with cold water and capping both outlets. Next take the med-large connector and make sure the condenser can connect to your 5 mL conical vial.
Next, using a pipette to transfer, measure out 1 mL of xylene into a 10 mL graduated cylinder and pour it into the 5 mL conical vial. Add a spin vane and set up the reflux apparatus seen in (Figure 2). Make sure to add cold water to the outside of your condenser and cap both outlets. Leave the top of the condenser uncapped.

Turn the hot plate on to medium high heat, and start stirring the reaction. The reaction should start boiling once your sand bath reaches 180-200 °C. Once your reaction starts boiling, turn the heat down to medium heat, and reflux for 30 minutes. If your reaction stops refluxing turn the heat up again.

Once 30 minutes has elapsed, remove your conical vial from the sand bath and let it cool to room temperature. While it is cooling, prepare an ice bath in a 100 mL beaker. Measure out 1 mL of xylene into a test tube and place the test tube into the ice bath to cool the xylene. This will be used to rinse your product when filtering.

Once your reaction reaches room temperature, place the conical vial in the ice bath for 5 minutes. This should produce white crystals. While it is cooling, set up your vacuum distillation apparatus using a 125 mL filter flask, a Hirsch funnel, and a filter paper.

Once 5 minutes has elapsed, turn the vacuum pump on and filter the contents of your conical vial. Use your metal spatula to scrape the crystals out of the conical vial into the Hirsch funnel, and the cold xylene to rinse any remaining crystals out of the vial. Once the crystals are dry on the filter paper, carefully transfer your crude product to a 100 mL beaker.

Next you should warm your sand bath again by turning the hot plate on medium-high. Measure out 3 mL of xylene into a test tube and place it in your sand bath. Once the xylene starts boiling, pipette some of the hot solvent into your 100 mL beaker with your crude product in it. The solvent cools down slightly while you are pipetting, so let it warm up to boiling again, swirling the beaker gently in the warm sand. Keep adding pipettes of hot solvent and warm in the sand until all of the crystals have dissolved in the boiling solvent.

Next remove the beaker of dissolved crystals from the heat and let it cool. Once it reaches room temperature, cool it further by placing it in your ice bath for 5 minutes. White crystals should start to fall out of solution as it cools, if no crystals fall out, try scratching the bottom of the flask with a glass stirring rod or spatula.

While your solution is cooling, prepare your vacuum distillation apparatus again using the same filter flask and Hirsch funnel. Measure 2 mL of xylene into a test tube and cool in your ice bath. Get a new filter paper and record the mass of the new filter paper. Once the crystals have cooled in the ice bath for 5 minutes, filter the crystals using your vacuum filtration apparatus. Use the cold xylene to rinse the remaining crystals from your beaker into the Hirsch funnel. Once the crystals are dry, carefully transfer your filter paper with your recrystallized product on it to a beaker, and leave the beaker in your drawer to dry until the next session.
Upon returning to lab, weigh the filter paper with your dry crystals on it, and find the weight of your product. Take an IR of your solid sample, and prepare an NMR sample using 1 mL of deuterated chloroform. Submit your NMR sample to your TA for analysis.


Pre-lab Questions:

1.) Predict the product. Make sure to show correct stereo- and regiochemistry.

2.) Suppose you did a Diels-Alder reaction and formed more than one product. How would you go about separating and identifying your products?