CHEM 322: Diels-Alder Reaction: Preparation of cis-norbornene-2,3-endo-dicarboxylic anhydride

Introduction:

In 1921, Otto Diels and Kurt Alder discovered that certain alkenes and alkynes can undergo a 1,4-addition with conjugated dienes to give substituted cyclohexenes or 1,4-cyclohexadienes. In 1950, their work was recognized with a Nobel Prize in chemistry.

The mechanism of the reaction involves a cyclic flow of electrons in a single step in which the conjugated diene, commonly called the diene, supplies 4 π electrons and the alkene or alkyne, also called the dienophile, supplies 2 π electrons. In this process, two new sigma bonds which link the former dienophile to the diene and one new pi bond between the former double bonds of the diene are formed.

Due to the concerted mechanism, two kinds of selectivity are evident in Diels-Alder reaction products.

1. The stereochemistry of the dienophile is retained in the product. If the substituents of the dienophile are cis, they remain cis in the product. If they are trans, they remain trans in the product.

2. **“Endo” vs. “exo”:** if the diene is cyclic, and if the dienophile has cis substituents, then two stereochemical outcomes are possible. Look at the pictures below. In an endo isomer, the substituents lie fairly close to the newly-formed double bond. In an exo isomer, the substituents are as distant from the new double bond as possible.

The endo isomer is more sterically hindered than the exo. In spite of this, the endo tends to predominate in cases where the R substituents have a B system that is conjugated with that of the dienophile double bond. Woodward, Hoffman, and Fukui showed that favorable interaction between the substituent B system and that of the diene during cyclization overcomes the steric hindrance and thus favors the endo isomer over the exo.
Electron withdrawing groups on the dienophile and electron-donating groups on the diene can speed up this reaction. The dienophile is the part of the reaction that must be “hungry” for electrons from the diene. By having electron withdrawing groups on the dienophile, the dienophile’s alkene (or alkyne) is stressed by having to overly “share” electrons with the electron withdrawing groups. This makes the actual carbons in the alkene (or alkyne) part of the dienophile more positive looking than just a plain alkene (or alkyne), thus, they want electrons from the diene even more than a plain alkene (or alkyne).

Even though $s$-$trans$ conformation of dienes is more stable due to steric reasons, the $s$-$cis$ conformation is needed to carry out the Diels-Alder reaction. The $s$-$cis$ conformation of the diene would yield a six membered ring with a $cis$ double bond whereas a diene in $s$-$trans$ conformation would demand a $trans$ double bond in a six membered ring – an impossible feat. Cyclic dienes, which are locked into the $s$-$cis$ form, are particularly reactive.

Synthesis of several natural products, such as the powerful anti-inflammatory medication cortisone, takes advantage of the regioselectivity and stereoselectivity of the Diels-Alder reaction. In this experiment, you will synthesize $cis$-norbornene-$2,3$-$endo$-dicarboxylic anhydride, commonly called carbic anhydride, from cyclopentadiene and maleic anhydride. The product is used in unsaturated polyester, epoxy, alkyd, urea-formaldehyde, and melamine resins; and it is used in some insecticides, plastics, soaps, and textile finishing agents.

Cyclopentadiene, which is obtained from a light oil distilled from coal, is a very reactive diene and dienophile, so it readily dimerizes at room temperature to form “dicyclopentadiene”. However, this Diels-Alder reaction is reversible by “cracking” dicyclopentadiene using slow distillation and keeping the cyclopentadiene cold. At the boiling point of dicyclopentadiene, equilibration with the monomer is rapid; the monomer, being more volatile, may be removed from the dimer. The reaction for this reversible process is shown below:

\[
\text{2 Cyclopentadiene} \xrightarrow{\text{room temp.}} \text{Dicyclopentadiene}
\]

The reaction for this experiment is shown below:

\[
\text{Cyclopentadiene} + \text{Maleic Anhydride} \rightarrow \text{exothermic} \rightarrow \text{cis-norbornene-2,3-$endo$-dicarboxylic anhydride}
\]
**Safety:**

Dicyclopentadiene is both extremely flammable and toxic. It also has a very unpleasant odor—keep it in the hood as much as possible. Maleic anhydride is corrosive—avoid skin contact. Break up the large chunks in the main hood. Hexanes (petroleum ether) and ethyl acetate are flammable. Wear gloves and protective clothing throughout the experiment.

**Experimental Procedure:**

*Keep all containers covered at all times to retard evaporation!*

To a 50 mL Erlenmeyer flask, add 3 g of maleic anhydride, a small stir bar, and 8 mL of ethyl acetate. Place a *loose cork* in the Erlenmeyer flask. Stir and heat this mixture on a stirrer/hot plate only long enough to dissolve all of the maleic anhydride. Remove the solution from the stirrer/hot plate, cool the solution to room temperature; some maleic anhydride may precipitate.

Add 3 mL of dry cyclopentadiene (*how was this formed?*) dropwise (about 2 drops a sec) using a Pasteur pipette to the maleic anhydride/ethyl acetate mixture with constant good mixing. This reaction is exothermic, thus the reaction mixture may need to be cooled in an ice bath. After all of the cyclopentadiene has been added, the mixture will cool, and crystals should start to form. If none have formed by the time the solution reaches room temperature, add 8 mL of hexane or petroleum ether.

Once a solid forms, slightly warm and stir the reaction mixture to dissolve the solid. Proceed with one of the following two options.

- **Option 1:** If a solid is still present when the reaction mixture begins to boil, *hot filter* it (see instructor for technique) to remove insoluble impurities from the desired product. The white insoluble impurity is most likely a diacid, which comes from a reaction of maleic anhydride and water. Remove the filtered mixture from the heat and leave it covered.

- **Option 2:** If all the solids have dissolved, then transfer the reaction mixture to a 50 mL beaker. Rewarm the reaction mixture (keep it covered) to redissolve the solid.

Let the reaction mixture cool slowly to room temperature; then (and only then) move it into an ice bath. Swirl occasionally. Prepare a vacuum filtration set up, remove the beaker from the ice bath and dry its outside, swirl, and dump everything into the funnel. Using a Pasteur pipette, wash the crystals dropwise with 3 mL of cold hexane or petroleum ether. Pull air through for at least 5 minutes, then spread the crystals onto a clean paper towel (folded for safety!) so they can dry for at least a day. Measure yield, melting range, and obtain an IR spectrum of the product.

**Clean up:** All spent or excess reagents must go into the “organic non halogenated recycle” container.

**References:** (access dates provided by previous lab assistant)


