

## Synthesis of 4-Cyclohexene-cis-dicarboxylic Acid Anhydride (Diels-Alder Reaction)

The Diels-Alder reaction is a powerful synthetic reaction because it joins two separate compounds and forms a cyclic compound that is still highly functionalized. A simple example of one of these reactions is shown in Figure 1.

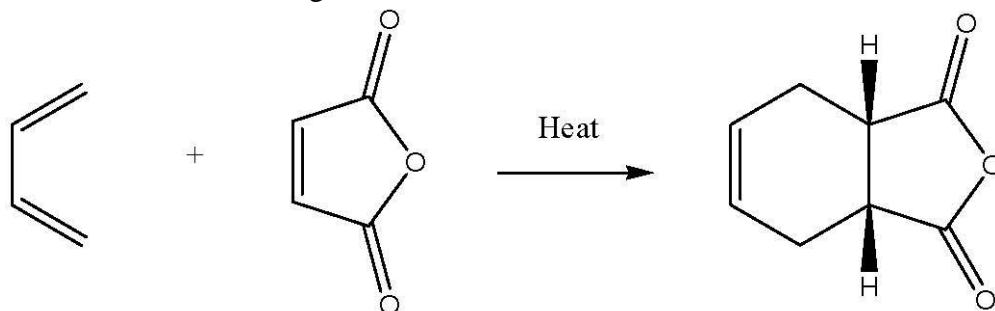


Figure 1: The overall equation.

The Diels-Alder reaction is a member of a larger class of pericyclic reactions. These are reactions with transition states in which the bonds being made or broken create a cyclic system of interacting orbitals. The number of electrons involved in this cyclic system of orbitals has been demonstrated to have a large effect on the facility with which these reactions occur. In the Diels-Alder reaction, six orbitals containing six electrons give way to a transition state that resembles the special, stabilized system of benzene. Thermal; pericyclic reactions involving six electrons are noted to be facile because of this stabilized transition state (shown in Figure 2).

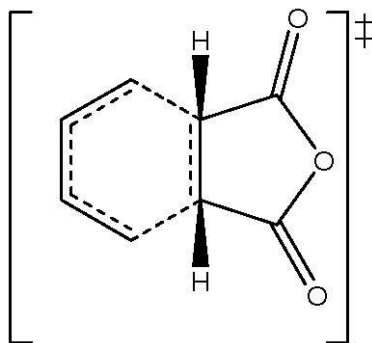


Figure 2: Suggested transition state structure for this experiment.

The 1,3-butadiene involved in the Diels-Alder reaction arises from another pericyclic reaction. While the Diels-Alder reaction described as a cycloaddition, the thermal loss of sulfur dioxide from 3-sulfolene to give 1, 3-butadiene (shown in Figure 3) is described as a chelotropic reaction-those in which two  $\mu$ -bonds are made or broken in concert to a single atom. Note again the absence of intermediates and the involvement of six electrons in a cyclic transition state:

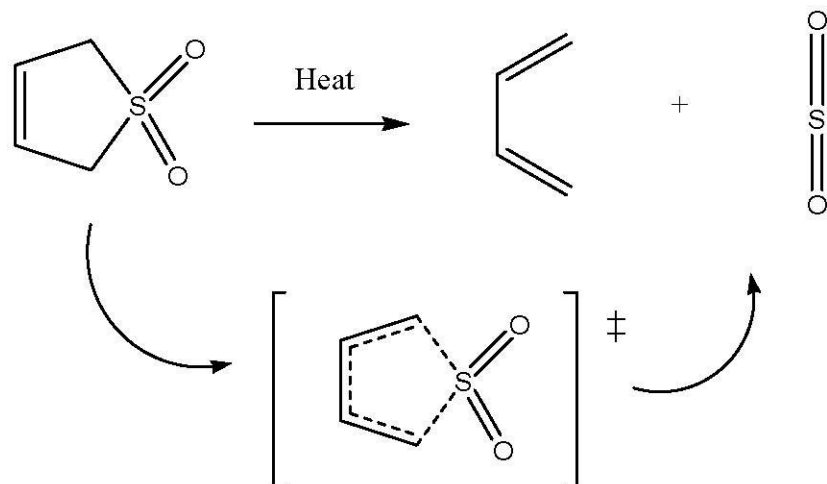


Figure 3: The equation, including the transition state structure, for the chelotropic process of generating a diene from sulfolene.

### Method of Purification:

1. 3-Sulfolene as an alternative reactant for 1,3-butadiene in diene syntheses has the following advantages: (1) it is practically nontoxic and presents no particular flammability hazard; (2) it is an odorless, crystalline, nonhygroscopic solid which may be stored without inhibitor at ordinary temperatures for years with no evidence of deterioration; (3) it assures the thermally controlled release of the 1,3-butadiene. The substantial excess of free diene that is often employed to force the usual reaction is not required; therefore, formation of troublesome polymeric by-products is greatly diminished.
2. During the distillation process, the 3-sulfolene was decomposed to form 1,3-butadiene and sulfur dioxide. The excess 1,3-butadiene and the sulfur dioxide are gases at room temperature and were distilled away during reflux.
3. The remaining sample was diluted with toluene and the petroleum ether was used to induce crystallization by reducing the solubility of the anhydride. The anhydride was then recovered via vacuum filtration.

### Safety:

Caution! Experiment should be conducted in an efficient fume hood to avoid exposure to sulfur dioxide generated in the reaction.

### Procedure:

1. To a 5mL conical vial containing a spin vane, add 170 mg of 3-sulfolene (which can form  $SO_2$  - toxic by inhalation; do not breathe fumes) and 90 mg of maleic anhydride (maleic anhydride will hydrolyze to maleic acid on prolonged exposure to the atmospheric moisture. Do not breathe dust; it may react with water in your lung. Clean up the weighing area with damp paper towels). Transfer to the same conical vial 80  $\mu$ -L of tert-butylbenzene (keep container tightly closed; toxic by inhalation or skin contact) and equip the conical vial with an air condenser (no water line needed).

2. Heat this mixture slowly to reflux (boiling) using a hot plate/stirrer. Before coming to reflux, be careful to avoid vigorous heating so the 1,3-butadiene is not distilled away before it has a chance to react. Heat gently (set the hot plate at low numbers such as 1 or 2) to allow a slow release of 1,3-butadiene from 3-sulfolene for reaction. Also, heat gently to avoid excess of free 1,3-butadiene which otherwise will form troublesome polymeric by-products through dimerization and polymerization.
3. Allow 20 minutes of reflux and keep the block temperature below 150°C -160°C. Carefully remove the reaction apparatus from the heat source and allow it to cool to room temperature. In the following steps, the Diels-Alder adduct will be recrystallized from the reaction mixture.
4. Remove the spin vane and rinse the spin vane while adding 0.5 mL of toluene to completely dissolve the cooled reaction mixture. Mix gently (*you could use a pipette to help mixing the solution up and down*). Add in more toluene as needed until you get a clear solution that doesn't show any crystals.
5. If there are solids such as dimers or polymers at the bottom, use pipette to remove the bottom brown layer that should be sticky to the pipette. (*If this experiment is to be done in two days, you can stop here for the first day and parafilm the vial for storage.*)
6. Into the clear solution, add in dropwise manner petroleum ether (about 0.40 mL or more if you had added more toluene in step 4) until a slight cloudiness is observed and persists.
7. Heat the resulting solution until it clarifies (to completely dissolve both crystals and impurities at high temperature), and then allow it to cool slowly to room temperature and *without any agitation*. The crystals will be finer and cleaner with no trapped impurities. Once this has occurred, cool the conical vial in an ice bath. Scratching the sides of the vial with a small, glass stirring rod will help initialize crystallization.
8. Collect the resulting crystals of the product by vacuum filtration with a low vacuum, and wash them with 0.5 mL of cold (*pre-cooled in the same ice bath*) petroleum ether.
9. After allowing the crystals to air dry, calculate the yield of 4-cyclohexene-cis-1,2-dicarboxylic anhydride. Determine the melting point of your product and also obtain an IR spectrum.

**For your report:**

Calculate your percent yield.

Discuss the results of your percent yield, your melting point and IR spectrum.

Predict the <sup>1</sup>H-NMR spectrum for the product.