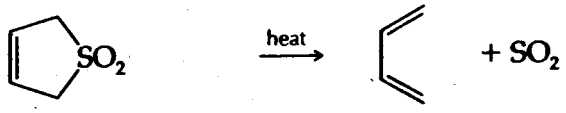
Laboratory #5 (Lab Handout#3)
Preparation of 4-cyclohexene-cis-1,2-dicarboxylic acid:
Example of the Diels-Alder reaction

16.2

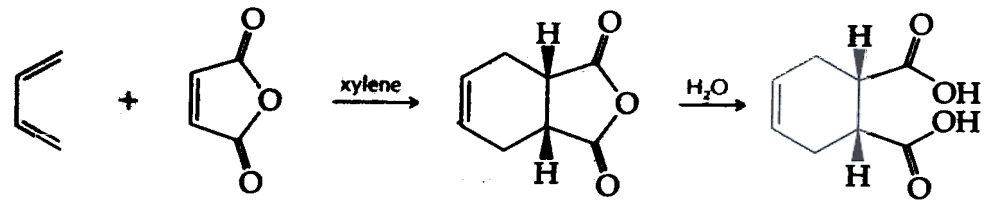
Synthesis of 4-Cyclohexene-*cis*-1,2-Dicarboxylic Acid from Butadiene Sulfone and Maleic Anhydride

Synthesize a cyclic compound by a Diels-Alder reaction.



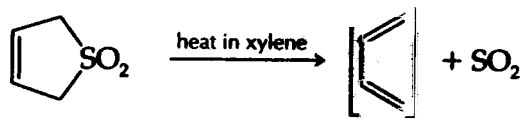
Butadiene sulfone
(2,5-dihydrothiophene-1,1-dioxide)
(3-sulfolene)
mp 65–66°C
MW 118.2

1,3-Butadiene
bp −4°C
MW 54.1



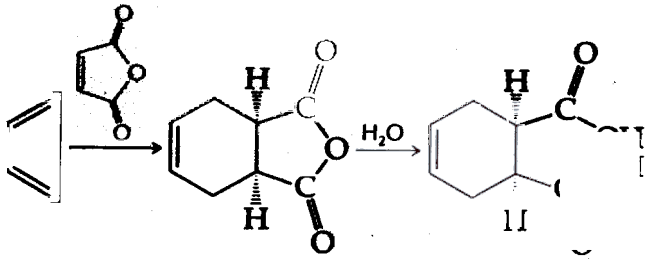
1,3-Butadiene | Maleic anhydride, mp 52°C, MW 98.1 | 4-Cyclohexene-*cis*-1,2-dicarboxylic anhydride, mp 105–106°C, MW 152 | 4-Cyclohexene-*cis*-1,2-dicarboxylic acid, mp 165°C, MW 70

This experiment demonstrates the use of 1,3-butadienesulfone (or 3-sulfolene) as an in situ source of 1,3-butadiene. Because butadiene is a gas, it presents some handling difficulties. We can, however, use the cyclic sulfone to produce 1,3-butadiene while all the reactants are dissolved in a solvent, xylene in this experiment:



Butadiene sulfone | Butadiene

While still in the reaction mixture, 1,3-butadiene rapidly reacts with maleic anhydride:



cis | *cis*

Two electron-withdrawing groups on the alkene double bond make maleic anhydride an excellent dienophile. Xylene (dimethylbenzene) is a convenient inert solvent, because the reaction proceeds readily at its reflux temperature (bp 139°C). The initial Diels-Alder product is an anhydride, which can easily be isolated. You will, however, hydrolyze the anhydride directly to the dicarboxylic acid.

The geometry of the two carbonyl groups is cis in both the anhydride and the dicarboxylic acid products, because the configuration of the two carbonyl groups is *cis* in the maleic anhydride starting material. The Diels-Alder reaction is a concerted *syn*

cycloaddition process that occurs stereospecifically with retention of configuration. The *cis* geometry is retained throughout the reaction.

Macroscale Procedure

Techniques Drying tube used as a gas trap: Technique 3.3
IR Spectrometry: Spectrometric Method 1

SAFETY INFORMATION

Conduct the experiment in a hood, if possible.

Butadiene sulfone (3-sulfolene) is an irritant. Wear gloves and avoid contact with skin, eyes, and clothing. This compound emits toxic, corrosive sulfur dioxide when it is heated. Be sure that the gas trap is positioned before you begin heating the reaction mixture.

Maleic anhydride is toxic and corrosive. Avoid breathing the dust and avoid contact with skin, eyes, and clothing.

Xylene is flammable.

Solid sodium hydroxide absorbs moisture from the atmosphere; spilled pellets can form droplets of concentrated NaOH solution rapidly.

Sodium hydroxide is corrosive and causes burns. Wear gloves and avoid contact with skin, eyes, and clothing. Clean up any spilled pellets immediately. Keep the jar tightly closed.

Synthesis of the Diels-Alder Adduct

Prepare a gas trap, using a drying tube. Place a small piece of cotton in the bottom of the tube, fill it approximately three-fourths full with 20–40 mesh sodium hydroxide pellets, and put a piece of cotton on top of the NaOH pellets.

Combine 2.0 g of butadiene sulfone, 1.2 g of finely ground maleic anhydride, 0.80 mL of xylene (a mixture of isomers is all right), and a boiling stone in a 25-mL round-bottomed flask. Fit a water-cooled condenser in the flask and place a thermometer adapter in the top of the condenser with the gas trap set in the rubber thermometer holder [see Technique 3.3]. Begin heating the mixture gently with a heating mantle. After the solids dissolve, continue heating the mixture at a gentle reflux for 30 min. Remove the heating mantle and cool the reaction mixture for about 5 min before proceeding immediately with the hydrolysis of the anhydride product.

Hydrolysis of the Diels-Alder Product to the Dicarboxylic Acid

Remove the thermometer adapter and the NaOH-filled drying tube. Pour 4 mL of water down the condenser, add another boiling stone, and heat the mixture under reflux for 30 min. Cool the solution to room temperature. If crystallization of the product does not occur, add 3 or 4 drops of concentrated sulfuric acid, stir the contents of the flask, and cool the resulting mixture in an ice-water bath for 5 min. Collect the product by vacuum filtration. Wash the crystals twice with 1-mL portions of ice-cold water. The dicarboxylic acid is usually quite pure without recrystallization. If time permits, the product can be recrystallized from water [see Technique 5.3]. Allow the product to dry overnight before determining the melting point, percent yield, and IR spectrum.

Cleanup: Wearing gloves, remove the cotton from the top of the drying tube and pour the NaOH pellets into a 600-mL beaker containing 300 mL of water. Add the aqueous filtrate from the reaction mixture. Stir the mixture until the NaOH dissolves, add some crushed ice, then add 6 M HCl solution until the pH is between 6 and 8, as indicated by pH test paper. Wash the neutralized solution down the sink or pour it into the container for aqueous inorganic waste. Rinse the cotton with water before discarding it in the container for nonhazardous waste.

microscale Procedure

Techniques Drying tube used as a gas trap: Technique 3.3
IR Spectrometry: Spectrometric Method 1

SAFETY INFORMATION

Conduct this experiment in a hood, if possible.

Butadiene sulfone (3-sulfolene) is an irritant. Wear gloves and avoid contact with skin, eyes, and clothing. This compound emits toxic corrosive sulfur dioxide when it is heated. Be sure that the gas trap is positioned before you begin heating the reaction mixture.

Maleic anhydride is toxic and corrosive. Avoid breathing the dust and avoid contact with skin, eyes, and clothing.

Xylene is flammable.

Sodium hydroxide is corrosive and causes burns. Wear gloves and avoid contact with skin, eyes, and clothing. Clean up any spilled pellets immediately. Keep the jar tightly closed.

Solid sodium hydroxide absorbs moisture from the atmosphere; spilled pellets can form droplets of concentrated NaOH solution quite rapidly.