

Experiment 3

Diels-Alder Reaction

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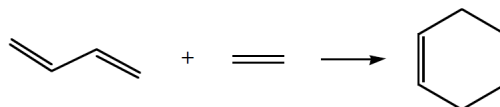
PURPOSE OF THE EXPERIMENT

In this experiment, isobenzofuranone derivative ((3aR,4S,5S,7aR)-1,3,3a,4,5,7a-hexahydro-5-methyl-3-oxoisobenzofuran-4-carboxylic acid) will be synthesized from E,E-2,4-hexadien-1-ol and maleic anhydride. Recrystallize the product and characterize it by using NMR.

BACKGROUND INFORMATION

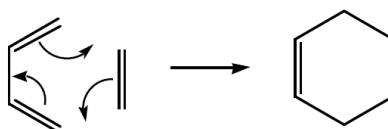
The Diels-Alder reaction is one of the most powerful tools used in the preparation of important organic molecules. When two carbon-carbon double bonds are positioned next to one another, a *conjugated diene* is formed. A non-conjugated diene is a molecule that has two olefins which are not next to each other. Conjugated dienes undergo a [4+2] cycloaddition reaction with certain double bonds to afford cyclohexenes and related compounds. This reaction is named for Otto Diels and Kurt Alder, who received the 1950 Nobel prize for discovering this useful transformation.

Figure1. The simplest Diels-Alder reaction is between 1,3-butadiene and ethylene.

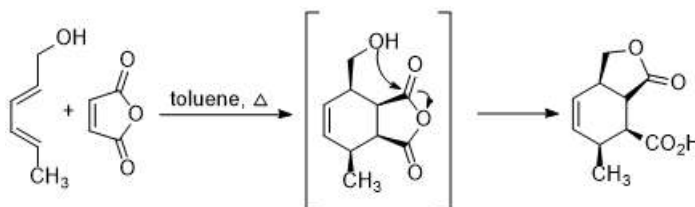


The mechanism of the reaction begins with the diene assuming the higher energy, but more reactive, *cis* conformation. As the diene and the *dienophile* (the mono-ene component) approach each other, the two terminal carbons of the diene meet the two carbons of the dienophile:

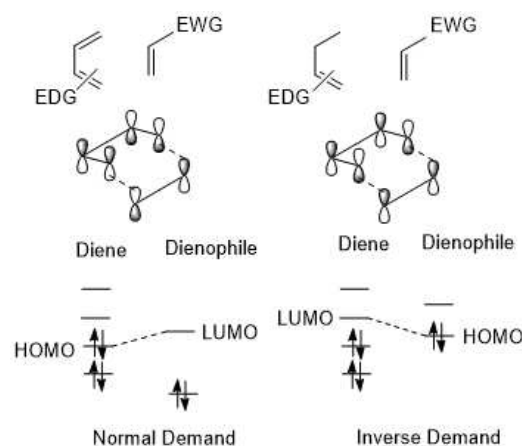
Figure2. The mechanism of the Diels-Alder reaction.



Our desired product can be produced by a Diels-Alder reaction between E,E-2,4-Hexadien-1-ol and Maleic Anhydride

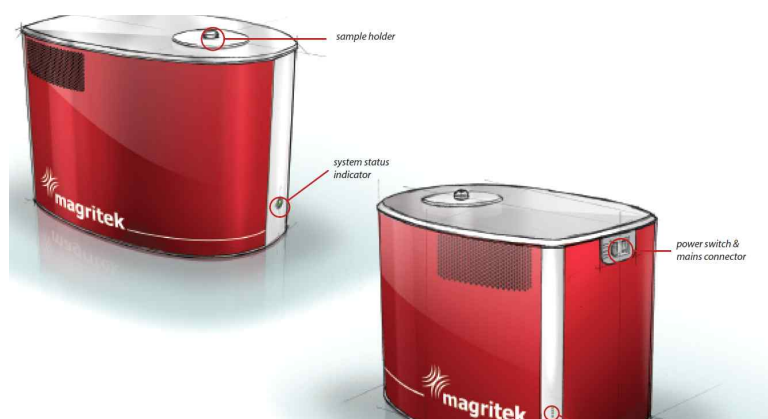


The Diels-Alder reaction proceeds as a suprafacial interaction between 4π electron system and 2π electron system. In case of 'normal' Diels-Alder reaction, the Ψ_2 of electron-rich diene is the HOMO and the π^* of electron-deficient dienophile is the LUMO. Diels-Alder reaction has regioselectivity and stereoselectivity. Among these, stereoselectivity is focused due to the reagents we use in this experiment.



The Diels-Alder reaction usually proceeds with *endo selectivity*. This means that the product in which the activating electron-withdrawing group of the dienophile is located in the endo position is formed faster than the alternative exo isomer. This happens even though the exo product is sometimes more stable than the corresponding endo product and is due to a variety of steric and electronic influences on the transition state of the reaction. Thus, we can expect the reaction between E,E-2,4-Hexadien-1-ol and Maleic Anhydride to form the *endo* product.

NMR
: Spinsolve



Frequency : 42.5 MHz

EXPERIMENT Diels-Alder Reaction.

Reagents and Properties

substance	quantity	molar mass (g/mol)	mmol [†]	mp (°C)	bp (°C)	density (g/mL)
E,E-2,4-Hexadien-1-ol	0.80 g	98.15				
Maleic anhydride	0.80 g	98.06		52.8		
Toluene	10 mL	92.14			110.6	0.867

CDCl₃

*product †calculate ‡you decide

PROCEDURE

1. Preparation of the Diels-Alder Adduct:

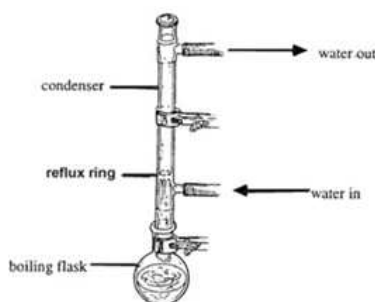
Note 1. Use available glass-ware. Specific choices are left to you. Two- or three-neck RBF equipped with rubber septa is suitable for the reaction flask.

Caution: Wear lab coats and safety goggles at all times while in the lab. Many chemicals are potentially harmful. Prevent contact with your eyes, skin, and clothing. Wearing contact lens is strictly prohibited.

Measure 0.80 g of maleic anhydride and 0.80 g of E,E-2,4-Hexadien-1-ol and place them in a 25-mL round-bottom flask (RBF). Add 10 mL of toluene in the 25-mL RBF.

Caution: Make sure that the reactant should not to be exposed to the air. It is recommended to use a nitrogen-substituted balloon.

Reflux the reactants. Allow water to flow from bottom to top during reflux.



Caution: The temperature of sand bath should be lie between 80°C and 90°C. Since the boiling point of toluene is 110°C, the temperature of the sand bath should not exceed 110°C.

Heat the RBF in a sand bath for 30 min. During the reaction, check whether the reaction is finished or not with the TLC plate. It is necessary to develop a co-spot in which the product and the reactant are taken together. Record the ratio of ethyl acetate (EA) and hexane used as TLC developing solvent.

Cool the solution slowly to room temperature. After white crystalline material start to be seen, cool the reaction mixture in ice bath for 10 min to complete crystallization of the product.

Caution: If you do not cool slowly, crystals may not appear.

Isolate the white crystalline solid by vacuum filtration. Rinse with a small amount of cold toluene and allowed to air dry. Record the mass and percentage yield of your product. (If it is difficult, rinse the RBF with toluene and concentrate by vacuum pump.)

2. Characterizing the Product

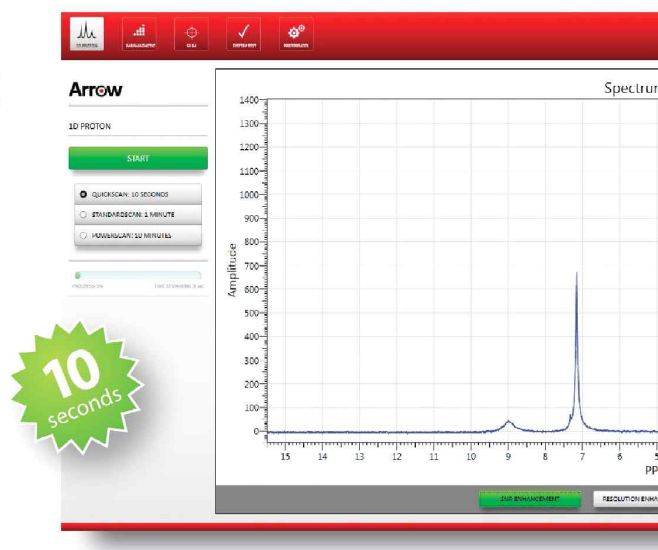
Characterize the product by NMR spectroscopy.

NMR Prepare and load a sample

1. Put sample in tube.
2. Put tube in tube holder.
3. Check sample level.
4. Put tube and holder into Spinsolve.

To run a protocol

Fast



1. Prepare and load a sample.
2. Select a protocol at the top of the screen.
3. Select protocol setting, as required.
- **Quickscan**
4. Press the green **Start** button.

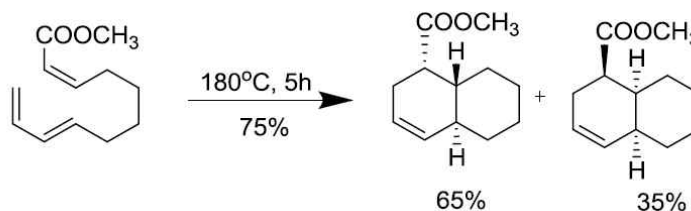
Post-Laboratory Questions

1. Calculate the percent yield of the Diels-Alder product based on the mass of maleic anhydride used.
2. How many peaks are expected in carbon NMR of your final product?

- Analyze your NMR data of each product.
- Draw the structures for the “endo” and “exo” products from the reaction of E,E-2,4-Hexadien-1-ol with maleic anhydride.
- In this reaction, the endo-adduct is preferred even though it has higher steric hindrance in the transition state. Why?

Pre-Laboratory Questions

- MSDS
- What is the Diels-Alder reaction? Explain it with mechanism briefly.
- Cycloaddition, such as Diels-Alder reaction, is a type of pericyclic reaction. Show 2 more different types of pericyclic reaction examples and count how many sigma-bonds and pi-bonds are formed or broken in each reaction.
- How is the “exo” and “endo” of a bridged bicycle compound defined? Draw the two transition states leading to each products in the following reaction:



- What is the recrystallization? Briefly explain it with its principle.

PPT REPORT FORM

The Diels-Alder Reaction

Name

Date

Calculation

a) E,E-2,4-hexadien-1-ol (M.W. = 98.15 g/mol) _____ g _____ mol
(calculation)

b) Maleic anhydride (M.W. = 98.06 g/mol) _____ g _____ mol
(calculation)

c) The limiting reagent (smaller moles reagent) is _____

d) Theoretical yield of product (M.W. = 196.20 g/mol) _____ g _____ mol
(calculation)

e) Actual yield of product (collected solid product) _____ g

f) Percentage Yield (% Recovery) _____ %

g) Ratio of EA and hexane (TLC) EA : Hexane = _____ :