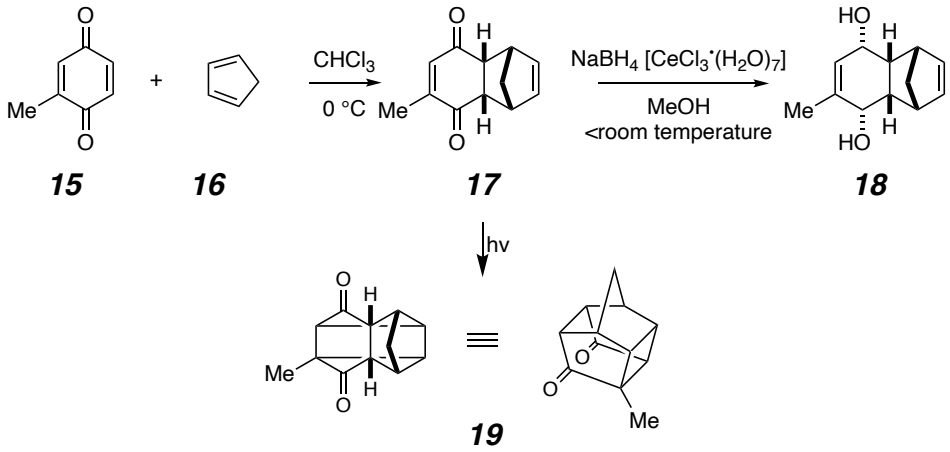
Chemistry 2312 October 3, 2024

Honors Organic Chemistry Laboratory T. R. Hoye

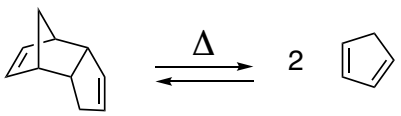
Experiment 5. Diels-Alder Reaction, Luche Reduction, and Photochemical 2+2 Cycloaddition

Reaction Sequence



You should read about the "Diels-Alder reaction" and the 2+2 photocycloaddition reaction, two of the most useful of the class of transformations known as cycloaddition reactions, in your organic chemistry textbook. The procedure outlined below for step one above, the Diels-Alder synthesis of **17**, is adapted from *Organic Syntheses*, Vol 73, pp 253-261, R. K. Boeckman, Jr., Ed. [You can find *Organic Syntheses* online at http://www.orgsyn.org/ (enter the last name of one of the authors of this procedure in the text search bar: Masaji Oda, Takeshi Kawase, Tomoaki Okada, and Tetsuya Enomoto to locate that procedure)] This reaction is also described in "Improved synthesis of pentacyclo-[5.4.0.02,6.03,10.05,9]-undecane." Marchand, A. P.; Allen, R. W. *J. Org. Chem*. **1974**, *39*, 1596-1596.

You will need to use freshly prepared (thermally "cracked") cyclopentadiene (CpH, **16**). The TA's have set up a cracking column fitted with a distillation head in the hood in which to heat dicyclopentadiene (DCP), distilling the volatile cyclopentadiene monomer into the receiving flask. Let the TA know in advance if you plan to use CpH that day and they will turn on the heating bath for the cracking apparatus. CpH is unstable at room temperature; it dimerizes back to DCP at a reasonably fast rate ($t_{1/2}$ of hours at room temperature). You should plan to use the CpH (**16**) that has been freshly made on the same day that you prepare/crack it.



Cycloaddition reaction to make 17. Plan to run the Diels-Alder reaction on a scale of *~2 g* of recrystallized methylbenzoquinone (MBQ, **15**, the dienophile) and a concentration of 1 M using chloroform (not methylene chloride, which is used in the *Organic Syntheses* procedure referenced above) as the solvent. The commercial source of MBQ is rather impure. First, recrystallize ca. 4 g of this dark-colored material from ethanol. Because EtOH is flammable, use the sand in a heating mantle that the TAs have set up in a hood. An Erlenmeyer flask is a good choice of vessel for this recrystallization. Pure MBQ is a yellow crystalline substance. Wear gloves during this procedure. The quinone will stain your skin brown if you would happen to contact a solution containing the quinone.

Combine the MBQ and CpH in chloroform at 0 °C. Use *1.3 equivalents* of CpH. Monitor the reaction by tlc to observe complete consumption of **15**; the CpH is too volatile to identify on the tlc plate. When the MBQ is gone, remove most of the $CHCl_3$ on a rotary evaporator. Model your purification of the product **17** (a crystallization) after that used in the *Organic Syntheses* article referenced above. It is important to not heat **17** too aggressively. Record the melting point (range), spectral data, and yield for your purified **17**.

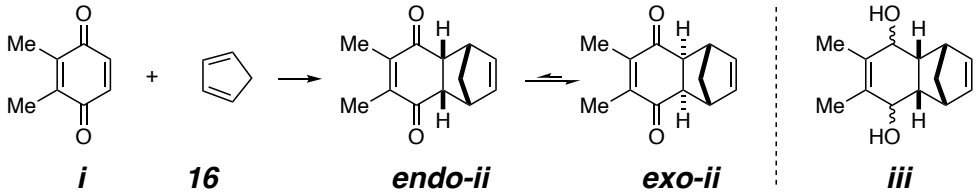
Reduction to Diol 18. Look up a procedure for the Luche reduction ($NaBH_4$, $CeCl_3$) of **17** to **18** using Reaxys. In a paper published in the *Journal of Organic Chemistry* (*J. Org. Chem.* **1998**, *63,* 7687–7693) this precise transformation was reported. Use ca. 500 mg of **17** in this reduction reaction. Combine the $CeCl_3$ with the diketone **17** *before* adding the $NaBH_4$. You may observe a substantial amount of gas evolution when you initially begin adding the $NaBH_4$, so add it in small portions until you get a feel for that. Monitor the consumption of **17** by tlc. Remove most of the methanol on a rotary evaporator and then quench the remaining reaction mixture by adding saturated, aqueous NH_4Cl. Use EtOAc to extract the product diol, which is more polar than Et_2O and the diol product **18** is a fairly polar compound. Recrystallize or chromatograph the crude product, your choice, to give the sample of purified diol **18**; you could consider splitting your crude sample into two portions and explore purifying one portion by chromatography and the other by recrystallization.

Photocycloaddition to 19. We will us a Rayonet photochemical reactor for the transformation of **17** to **19**. ***Caution****: it is critical that you never look directly at the light produced by a uv lamp, including those used inside this reactor; the wavelengths of light being produced renders that radiation dangerous and damaging to your eyes.* Use ethyl acetate as your reaction solvent. This is a unimolecular reaction (i.e., intramolecular) so the concentration is not so critical. Use a culture tube as your reaction vessel; the geometry (tall and cylindrical) allows for a better flux of photons into the solution. I recommend filling the tube ca. ¾ full with solvent, regardless of the amount of **17** you use. Once TLC analysis indicates that your starting material has been consumed (you may need to search for a stain that will show the product, but consumption of **17** should be readily seen by UV visualization), remove the reaction solvent and chromatogaph your product to isolate pure **19** and carry out your battery of characterization experiments.
Here are two citations to studies in which the NMR data for **19** are reported:

J. Org. Chem. **1984**, *49*, 670–675 (used medium pressure Hanovia; Pyrex in EtOAc or acetone)
Magn. Reson. Chem. **2012**, *50*, 803–808 (used 360 nm; Pyrex in acetone)

Lab Report 5 Questions (Please answer in your own words):

1. Draw a three-dimensional representation of the *endo* and the *exo* diastereomers of the Diels-Alder adducts **endo-ii** and **exo-ii** (see below) produced by reaction of cyclopentadiene (**16**) with 2,3-dimethylbenzoquinone (**i**). Feel free to create a 3D image with, e.g., Chem 3D or to first make a molecular model of each isomer to help you draw each molecule .Notice that 2,3-dimethylbenzoquinone (**i**) has higher symmetry than 2-methylbenzoquinone (**15**), the dienophile you are using in this experiment.



i ***16*** ***endo-ii*** ***exo-ii*** ***iii***

2. When pure **endo-ii** is heated in refluxing xylene in a sealed vessel (so as to not lose any volatile CpH) and then cooled, **exo-ii** is observed as the predominant species (ca. 10:1 **exo-ii:endo-ii**). If one uses pure **exo-ii** at the start of an analogous experiment, the same result is obtained – namely, a final 10:1 ratio of **exo-ii:endo-ii** is observed. Explain this phenomenon *using an energy diagram* and the concepts of kinetic vs. thermodynamic control (*hint*: recall what you learned and observed in the equilibration of your samples of menthone and isomenthone).

3. Compound **iii** has four stereoisomers. Draw the structure of each. Place a box around those that are a meso compound and a circle around those that are chiral.

4. How many resonances (*i.e.*, unique carbon atoms) would you expect to observe in the ^{13}C NMR spectrum of each of the additional three isomers of **iii** you drew above in your answer to question 2 you drew in your answer to question #3? What symmetry element, if any, is present in each of these molecules?

5. Why is the reduction of **endo-ii** highly diastereoselective for the formation of largely one isomer of **iii**?

6. Which of diketone **endo-ii** and diol **iii** is white and which is yellow? Explain, briefly, this difference in visual appearance.