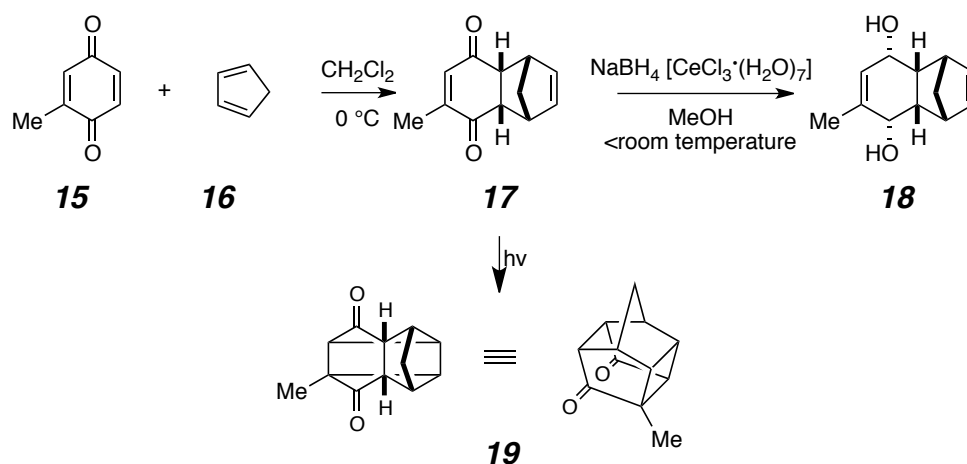


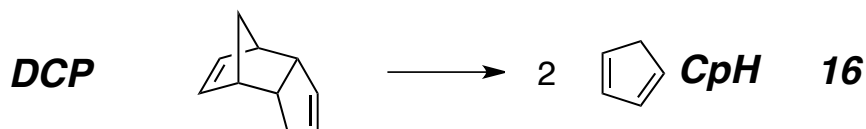
Experiment 5. Diels-Alder Reaction, Luche Reduction, and Photochemical 2+2 Cycloaddition

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[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]-undecane." Marchand, A. P.; Allen, R. W. *J. Org. Chem.* **1974**, *39*, 1596-1596.

You will need to use freshly (thermally) cracked dicyclopentadiene (DCP), which generates the cyclopentadiene (CpH, **16**). The TA's have set up a cracking column fitted with a distillation head in the hood that each of you can use, in turn, for collecting your cyclopentadiene monomer. 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 use 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 methylene chloride as 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.

Combine the MBQ and CpH in DCM 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 CH₂Cl₂ on a rotary evaporator. If the crude residue solidifies, record the melting point (as a temperature range) of this crude product.

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) and spectral data for purified **17**.

Reduction to Diol 18. Look up a procedure for the Luche reduction (NaBH₄, CeCl₃) 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 CeCl₃ with the diketone **17** before adding the NaBH₄. You may observe a substantial amount of gas evolution when you initially begin adding the NaBH₄, 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 NH₄Cl. Use EtOAc to extract the product diol, which is more polar than Et₂O 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 use 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 it 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. I recommend ca. 0.1 M initial concentration of **17**. Use a culture tube as your reaction vessel; the geometry allows for a better flux of photons into the solution. Once TLC analysis indicates that your starting material has been consumed, remove the reaction solvent and chromatograph your product to isolate pure **19** and carry out your battery of characterization experiments.

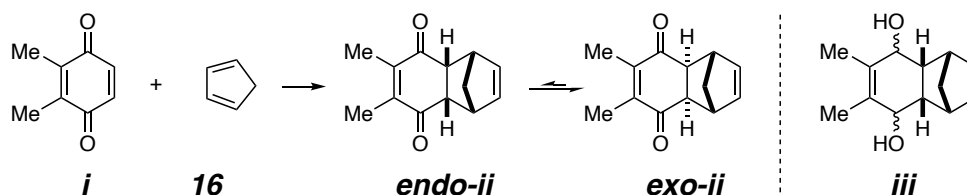
Here are two citations to studies in which the NMR data for **19** are reported:

J. Org. Chem. **1984**, *49*, 670–675.

Magn. Reson. Chem. **2012**, *50*, 803–808.

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

1. Draw a three-dimensional representation of the *endo* and the *exo* isomers 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 sketcher in Maestro). Notice that 2,3-dimethylbenzoquinone (**i**) has higher symmetry than 2-methylbenzoquinone (**15**), the dienophile you are using in this experiment.



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 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 stereoselective 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 to the human eye.