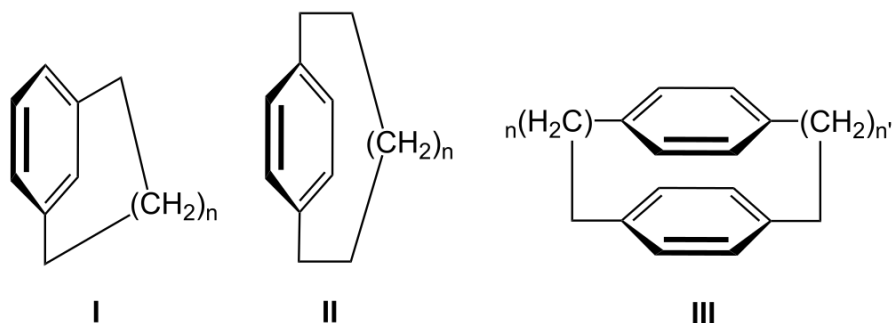


## Chemistry 478 — Molecular Modeling

### Laboratory #2 — Structures & Stabilities of *meta*- and *para*-Cyclophanes

Cyclophanes are a series of strained hydrocarbons, a surprising number of which have actually been prepared in the laboratory. In this lab you will find the relative energies of *meta*-cyclophane (I) structures with 4 to 7 carbon bridges, and compare to the energies of the corresponding dienes. You will also estimate the smallest size of the bridge (*i.e.*, the smallest value of “*n*”) for which the corresponding *para*-cyclophane (II) is stable. Additional known structures include the [*n,n'*]-cyclophanes (III) which we will not consider here.



#### Protocol

**(1)** Using Spartan Student, draw, and “clean up” via the Build/Minimize menu option, the structure of [4]-*meta*-cyclophane. Note that there are many “templates” available in Spartan which allow you to quickly generate aromatic and other rings, peptides, nucleic acids, inorganic and organometallic coordination compounds, *etc.*

**(2)** Find the minimum energy structure (*i.e.*, the “Equilibrium Geometry”) using the Hartree-Fock MO method with the 3-21G basis set. Repeat using the PM3 semi-empirical MO method, and using molecular mechanics (MM) with the MMFF force field.

**(3)** Perform the same three calculations (HF/3-21G, PM3 and MMFF) on the [5]-, [6]- and [7]-*meta*-cyclophanes. Then run calculations on the corresponding symmetric “diene” series of molecules, where the aromatic ring is replaced with a 1,4-cyclohexadiene. Make a plot of the energy difference between the cyclophane and the corresponding diene as a function of the bridge size, “*n*”.

**(4)** Begin by building [6]-*para*-cyclophane. Estimate the “strain energy” of this molecule. This can be done directly with the MMFF method, as molecular mechanics typically computes an estimate of the strain energy in terms of bond strain, angle strain, *etc.* Using QM calculations, the relative strain energy can be assessed by comparing the QM energy (try both PM3 and HF/3-21G) of the original cyclophane against an open chain analog. For example, by computing the QM energy difference between [6]-*para*-cyclophane and 1,4-di-*n*-propylbenzene. Perform such calculations as a function of “*n*”. For both MM and QM results, make a plot of the relative stability of [*n*]-*para*-cyclophane as a function of “*n*”.

## Questions

**(1)** Relative to the dienes as reference states, which of the meta-cyclophanes is the most strained? Based on your MMFF force field results, which energy components absorb most of the strain energy?

**(2)** How do the relative energies across the series of bridge lengths compare for the MMFF force field, PM3 semi-empirical MO, and HF/3-21G methods? Rationalize why your results turned out as they did.

**(3)** For each of your minimum energy *para*-cyclophane structures, compute a measure of the “non-planarity” of the aromatic ring. For example, you could determine the “out-of-plane” angle at the nominally  $sp^2$ -hybridized bridgehead carbon atoms (the aromatic carbons directly attached to the saturated bridge). Alternatively, you could angle between the C-C-C angle bisector at a bridgehead carbon and the plane containing the four non-bridgehead ring carbon atoms. Does the degree of *structural* deformation of the aromatic rings correlate well with your calculation of the *energetic* strain in these systems?

**(4)** Do a quick literature search to find the smallest values of “n” for the which the *meta*- and *para*-cyclophanes have been experimentally isolated.