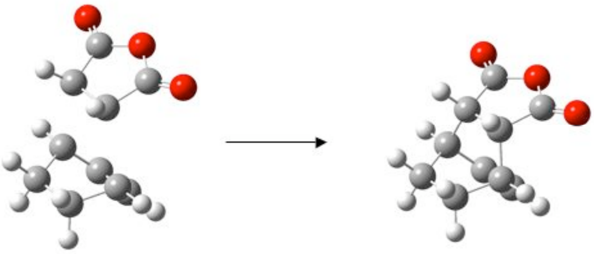
Exercise: ***To use Quantum Chemistry with transition structure modeling to study the regioselectivity of the Diels Alder reaction.***

The Diels Alder reaction



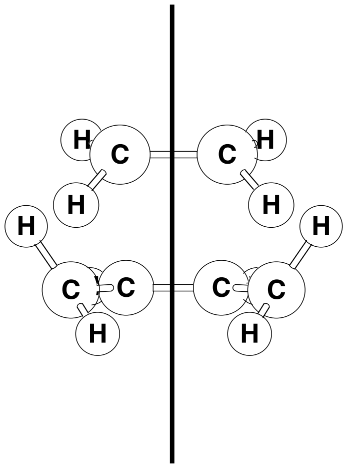
belongs to a class of reactions known as pericyclic reactions. The π orbitals of the dieneophile are used to form new σ bonds with the π orbitals of the diene. Whether or not the reactions occur in a concerted stereospecific fashion (**allowed**) or not (**forbidden**) depends on the number of π electrons involved. In general the HOMO/LUMO of one fragment interacts with the HOMO/LUMO of the other reactant to form two new bonding and anti-bonding MOs. The nodal properties allow one to make predictions according to the following rule:

If the HOMO of one reactant can interact with the LUMO of the other reactant then the reaction is ALLOWED.

The HOMO-LUMO can only interact when there is a significant overlap density. If the orbitals have different symmetry properties then no overlap density is possible.

If the dieneophile is substituted, with substituents that have π orbitals that can interact with the new double bond that is being formed in the product, then this interaction can stabilise the regiochemistry (i.e. head to tail versus tail to head) of the reaction. In this exercise we will study the nature of the transition structure for the Diels Alder reaction, both for the prototypical reaction and for the case where both diene and dieneophile carry substituents, and where secondary orbital effects are possible. Clearly, the factors that control the nature of the transition state are quantum mechanical in origin and thus we shall use methods based upon quantum chemistry.

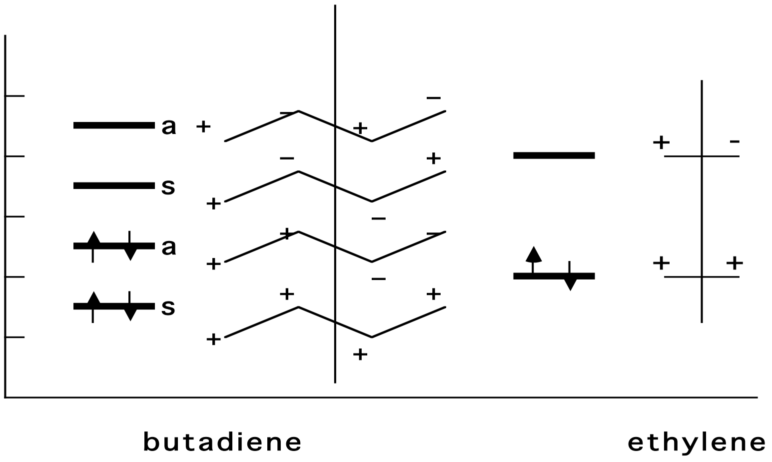
Shown below is a diagram of the transition state for the Diels-Alder reaction between ethylene and butadiene. The ethylene approaches the cis form of butadiene from above.



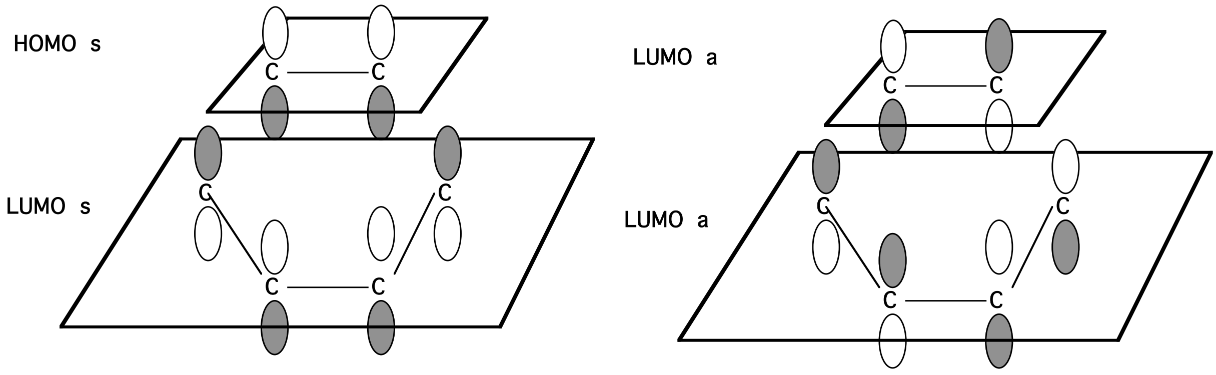
Before beginning our quantitative study, it is helpful to discuss the interaction of the π orbitals in a simple qualitative way.

You will confirm some of these considerations in your computations.

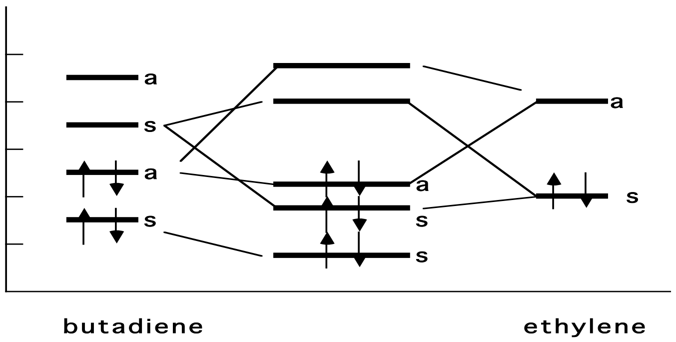
The principal orbital interactions involve the π/ π* orbitals of ethylene and the HOMO/LUMO of butadiene. It is referred to as [$4_S + 2_S$] since one has 4 π orbitals in the π system of butadiene. The orbitals of ethylene and butadiene and ethylene can be classified as symmetric **s** or anti-symmetric **a** with respect to a plane of symmetry as shown below. The + and - refer the phases of each p^{π} orbital and for butadiene they are easily remembered because they correspond to the harmonics of a plucked string. The MOs with the smallest numbers of nodes are lowest in energy and are occupied first according to the “aufbau” principle.



The HOMO of ethylene and the LUMO of butadiene are both **s** (symmetric with respect to the reflection plane) and the LUMO of ethylene and the HOMO of butadiene are both **a**. Thus it is the HOMO-LUMO pairs of orbital that interact as shown in the following diagram.



An orbital interaction diagram that shows the occupancies of the MO in the product transition state can be drawn as follows



The important point is that it is the HOMO of butadiene (**a**) that interacts with the LUMO of ethylene (**a**). The HOMO of the adduct is thus **a**.

Practical

1) Plot the HOMO and LUMO of cis butadiene and determine the symmetry (symmetric or anti-symmetric with respect to plane)

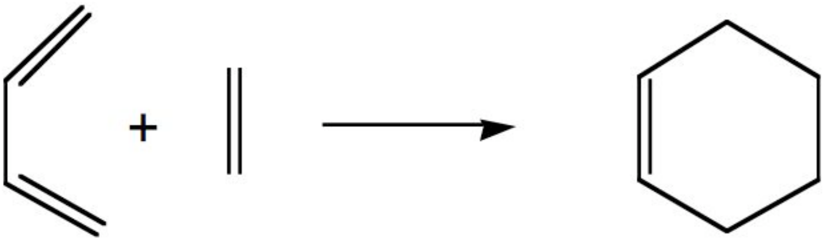
- Use GaussView to build cis-butadiene, and optimize the geometry using Gaussian, with the AM1 semi-empirical molecular orbital method.

- Draw up the HOMO and LUMO

There are two ways to do this in GaussView:
i) Select **Edit->MOs**. Select the HOMO and the LUMO from the MO list (highlights it yellow). Click the button **Visualise** (not Calculation), then **Update.**

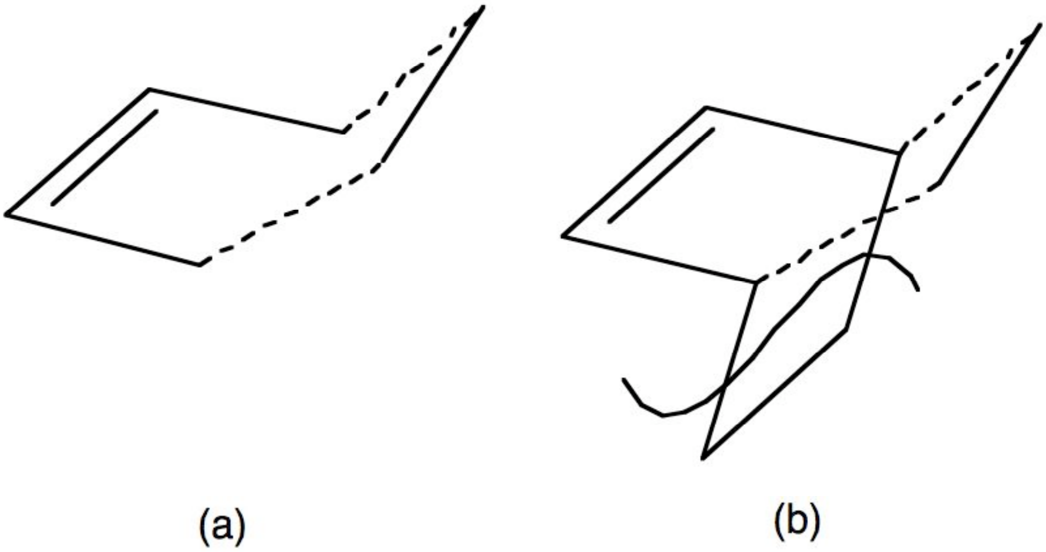
ii) Having calculated the surface for this orbital, you can alternatively display it in the main GaussView window for the molecule, from the **Results->Surfaces** menu. Select **Surface Actions->Show Surface**. Having displayed the surface this way, you can also select **View->Display Format->Surface**, and change **Solid** to **Mesh**.

2) Computation of the Transition State geometry for the prototype reaction



and an examination of the nature of the reaction path at the TS.

The transition structure has an envelope type structure indicated in (a) below (this maximizes the overlap between the ethylene π orbitals and the π system of butadiene. One way to obtain the starting geometry is to build the bicyclo system (b) below and then remove the $-CH_2-CH_2-$ fragment. One must then guess the interfragment distance (dashed lines) and optimize the structure in a manner similar to that used in the first exercise.



- the next step is to set the interfragment distances (dashed lines in (a) above) to a value appropriate to the TS. For a percyclic reaction, the partly formed σ C-C bonds in the transition state are around 1.9 to 2.3 Å. **It is suggested that you use a distance of 2.1Å**.

In order to carry out an OPT=TS calculation with Gaussian, you will need to supply an estimate of the initial force constants / second derivatives, using e.g. the FREQ keyword.

3) Analysis of the Diels Alder Transition State computed in 2

a) Geometry:

- Measure the bond lengths of the partly formed σ C-C bonds and the other C-C distances. Go to the proforma data sheet at the end of this exercise and attempt to complete the discussion suggested there.

b) Reaction Path at the transition state:

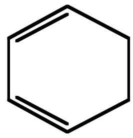
We can "animate" the vibrations of the molecule at the transition state. Select **Vibrations** from the **Results** menu. There is one special vibration that has a negative force constant (and an imaginary frequency) that corresponds to the reaction path as it passes through the transition state.

c) HOMO and LUMO at the TS.

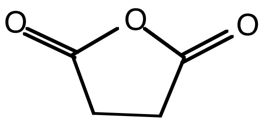
Plot the HOMO as in the previous exercise. Rotate the molecule so that the symmetry and nodal properties of the system can be interpreted and make a sketch. Now move to the data sheet and complete the discussion.

4) To Study the regioselectivity of the Diels Alder Reaction

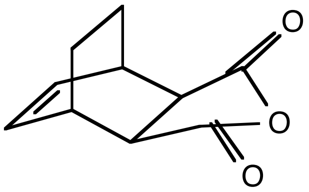
Cyclohexa-1,3-diene **1** undergoes facile reaction with maleic anhydride **2** to give primarily the **endo** adduct. The reaction is supposed to be kinetically controlled so that the **exo** transition state should be higher in energy.



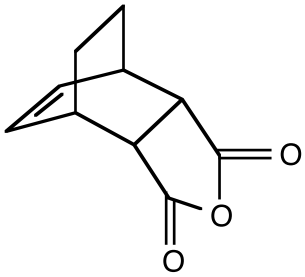
1



2



3 exo



4 endo

In this exercise we shall model the TS structure for both **3** and **4**. The technique is very similar to the previous exercise.

5) Analysis of the Diels Alder Transition State computed in 4

You should complete this analysis for both the **endo** and **exo** forms. The objective is to compare with the prototype example and to understand and document the differences between the endo and exo forms. Use the data sheet at the end of this exercise as a guide to your discussion.

a) Energy

Compare the energies of the endo and exo forms. Note that the energies printed out in Gaussian will be in atomic units.

b) Geometry:

- Measure the bond lengths of the partly formed σ C-C bonds and the other C-C distances. Make a sketch with the important bond lengths. Measure the orientation, (C-C through space distances between the C=O-CO-C=O- fragment of the maleic anhydride and the C atoms of the "opposite" -CH_2-CH_2- for the **exo** and the "opposite" -CH=CH- for the **endo**). The structure must be a compromise between steric repulsions of the -CH_2-CH_2- fragment and the maleic anhydride for the **exo** versus secondary orbital interactions between the π systems of -CH=CH- and -C=O-CO-C=O- fragment for the **endo.**

c) Reaction Path at the transition state:

- select **Vibrations** from the **Results** menu (as before) to see the vibrations of the molecule.

c) HOMO at the TS.

Plot the HOMO as in the previous exercise. Examine carefully the nodal properties of the HOMO between the -C=O-CO-C=O- fragment and the remainder of the system. What can you conclude about the so called "secondary orbital overlap effect"?

Data and Discussion Points

Exercise: ***To use Quantum Chemistry with transition structure modelling to study the regioselectivity of the Diels Alder reaction.***

Use this template as a guide. Screen images can be saved from the GaussView File menu.

1) Plot the HOMO and LUMO of cis butadiene and determine the symmetry (symmetric or anti-symmetric with respect to plane)

Sketch HOMO and LUMO labeling each as symmetric or anti symmetric

3) Analysis of the Diels Alder Transition State computed in 2

a) Geometry:

Sketch the geometry of the transition structure showing the bond-lengths of the partly formed σ C-C bonds.

What are typical sp^3 and sp^2 C-C bondlengths? What is the van der Waals radius of the C atom? What can you conclude about the C-C bondlength of the partly formed σ C-C bonds in the TS.

b) Reaction Path at the transition state:

Sketch the form of the vibration that corresponds to the reaction path at the transition state.

Is the formation of the two bonds synchronous or asynchronous?

Sketch the form of the lowest positive frequency.

c) HOMO and LUMO at the TS.

Is the HOMO **s** or **a**?

Which MO of Butadiene and Ethylene have been used to form this MO (e.g. LUMO butadiene + HOMO ethylene?)

Explain why the reaction is **allowed.**

5) Cyclohexa-1,3-diene raction with maleic anhydride ***2***

	EXO	**ENDO**
a) energy		
b) TS geometry		
c) TS vector		

You should observe that the structures are very similar but that the **endo structure** is .6 kcal mol^{-1} lower than the endo.

Comment on the structural difference between the endo and exo form. Why do you think that the exo form could be more strained.

c) HOMO at the TS.

Examine carefully the nodal properties of the HOMO between the -C=O-CO-C=O- fragment and the remainder of the system. What can you conclude about the so called “secondary orbital overlap effect”?