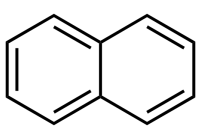
D1CH9116 - MMCO
Molecular Modelling applied to organic chemistry

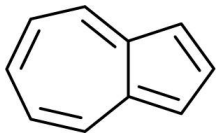
Practical 2: Molecular isomers

A/ Electronic structure of isomers

Determine the optimal geometry and the electronic structure of the naphtalene and azulene isomers at the AM1 level. Check the dipole moment and the HOMO-LUMO gap for the two structures, and comment.



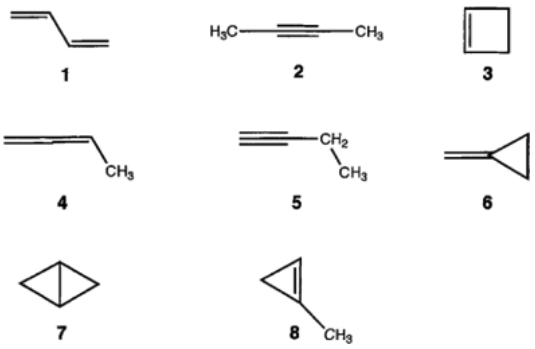
Naphtalene



Azulene

B/ Relative energies of isomers

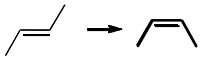
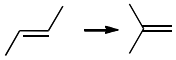
Optimize the structures of isomers **1**-**8** at the AM1 and PM6 levels, and compare their relative energy (heats of formation) to the experimental results.



Isomer	Energies relative to 1 (kcal/mol)
2	8.6
3	11.2
4	12.4
5	13.2
6	21.7
7	25.6
8	31.9

C/ Isomerization reactions

The Table below reports isomerization reactions together with the experimental heats of isomerization. Optimize in each case the two equilibrium structures at the AM1 and PM6 levels and note their energy (heats of formation). Calculate the heats of isomerization and compare to experimental results.

Isomerization reaction	Experimental heats of isomerization (kcal/mol)
$H_3C-C\equiv CH \rightarrow$ 	21.8
$H_3C-\underset{H}{C}=CH_2 \rightarrow$ 	7.8
	1.1
	2.8
	–1.3

D/ Relative populations of conformers

The population of a conformer *i* at a given temperature T can be evaluated using the Boltzmann distribution:

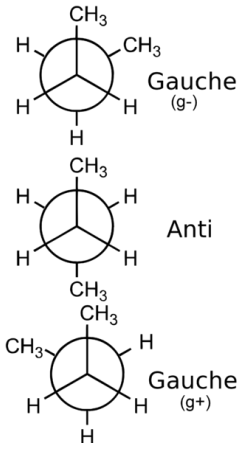
$$\frac{N_i}{N_{total}} = \frac{\exp\left(-E_i/RT\right)}{\sum_{k=1}^{N_{total}} \exp\left(-E_k/RT\right)}$$

where N_{total} is the total number of conformers, E_k is the relative energy of the k-th conformer with respect to the minimum energy conformer (J/mol), R the molar ideal gas constant equal to 8.31 (J/mol/K) and T the temperature in kelvins (K).

1/ Considering a 2-conformation Boltzmann distribution, plot the population of the lowest-energy conformer at room temperature as a function of their energy difference.

2/ Calculate the energy difference necessary to obtain a population ratio larger than 99% for the most stable form.

3/ Evaluate the relative population of the *gauche* and *anti* rotamers of butane at the AM1 and PM6 levels.



E/ Chiral molecules

The 2-bromo-3-fluorobutane molecule, which contains two chiral centers, has four possible stereoisomers:

- **1**. (2R,3R)
- **2**. (2R,3S)
- **3**. (2S,3R)
- **4**. (2S,3S)

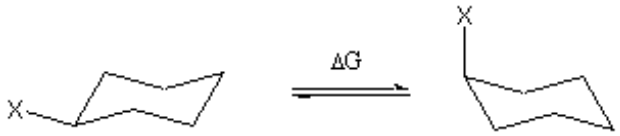
The pairs of compounds (1,3) and (2,4) are enantiomers (mirror images), and are therefore equally stable. The pairs (1,2) and (3,4) are diastereomers (non-mirror images), and have different energies.

1/ Calculate the total energy (heat of formation) of compounds **1** and **2** at the PM6 level and deduce the most stable configuration. *Use the tool "switch about an atom" of AGUI to change the configuration of carbon 3.*

2/ Evaluate the relative populations of **1** and **2** using a Boltzmann distribution at room temperature.

F/ Axial-equatorial conformations in methylcyclohexane

The amount of energy it "costs" to move a substituent group from the equatorial to the axial position is sometimes referred to as the A-value of that substituent group. The A-values of several substituent groups are listed below. Calculate the energy difference between the equatorial and axial conformers at the AM1 and PM6 levels, and compare to experimental results.



X	ΔG (kcal/mol)
H	0
Me	1.8
Et	1.8
i-Pr	2.1
t-Bu	> 4.5
F	0.25
Cl, Br, I	0.5
OH	0.9