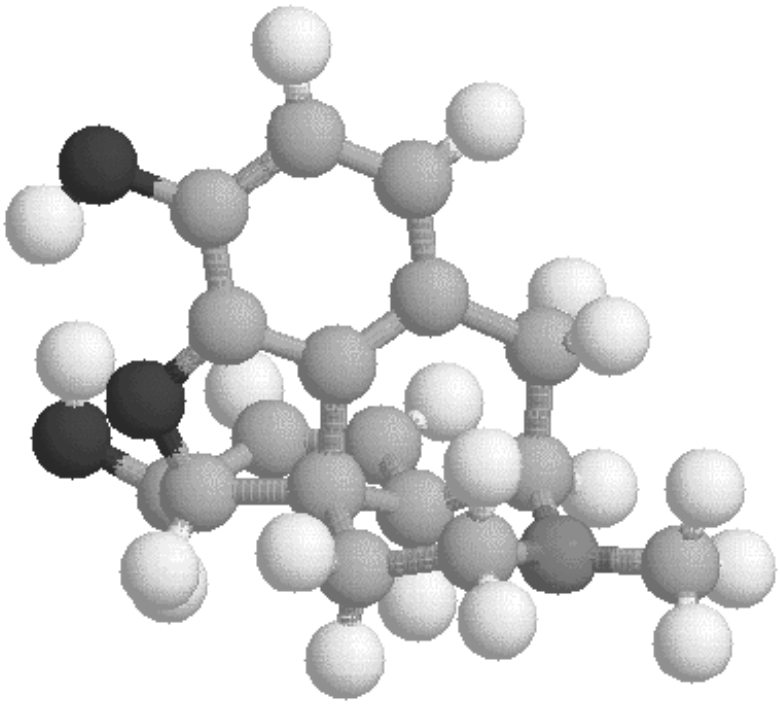
UNIVERSITY OF BATH

Department of Chemistry



YEAR 2 COMPUTATIONAL CHEMISTRY LAB

CH20023

Semester 2, 2003/2004

BSc and MChem in Chemistry

CH20023: COMPUTATIONAL CHEMISTRY LABORATORY

This Unit runs over seven weeks starting Monday 15 March but excluding the Bank Holiday Monday 3 May. The 3 South Computational Laboratory will be open from 9.15am to 5.15pm on Mondays and 9.15am to 12.15pm on Fridays. You must attend each Monday session, and you should take care to be present at the particular times specified for demonstrations and instructional sessions on Fridays; you will be notified in advance of these times. Otherwise you are free to organise your time as suits you best.

Professor Steve Parker will be responsible for the Unit, with assistance from Dr Mary Mahon (X-ray diffraction exercise), Postgraduate Demonstrators, and Linda Humphreys (Faculty Librarian).

The exercises in this Unit have been devised to complement the material presented during other parts of the chemistry course. The principal aims of this Unit are to:

(1) provide you with experience in computational chemistry,
(2) introduce you to a range of techniques in molecular modelling and chemical IT,
(3) consolidate knowledge from lectures by hands-on visualisation and calculation,
(4) improve your interpretative skills and report writing,
(5) enhance your time management skills.

The exercises are divided into "core" and "extra", with relative weightings as indicated.

Core exercises:		*Extra exercises:*	
Conformational analysis	(10)	Conjugation and colour	(15)
Qualitative MO theory	(10)	Bonding in nickel complexes	(15)
Molecular vibrations	(10)		
Peptide conformations	(10)		
Molecular dynamics	(10)		
X-ray diffraction	(10)		
Beilstein database	(5)		
ISIS/Draw	(5)		

You **must** complete all the core exercises in order to pass the Unit, but the maximum mark attainable from these exercises alone will be 70%. In order to achieve a mark potentially greater than 70% it will be necessary to complete one or more of the "extra" exercises. No student will be given a mark for an "extra" exercise unless they have already submitted reports for all the core exercises. The pass mark for the Unit is 40%. Any student failing to reach this will be instructed on the additional work required to gain credit for the Unit.

If you are unable to attend a Monday session (for example, due to illness or a placement interview) you **must** fill in an electronic Laboratory Absence form, which can be found on the web at:

http://www.bath.ac.uk/chemistry/notes.bpo/lababs.html

Completion of this form will give you the opportunity to take that session in a make-up class that will be time-tabled at the end of the semester, probably after the examinations. Students are entitled to complete two exercises/experiments per semester in a make-up class. However, there should be ample time for you to complete all of the exercises within the scheduled sessions.

Schedule

Monday 15 March:	X-ray diffraction
Friday 19 March:	no lab session
Monday 22 March:	Conformational analysis of six-membered rings
Friday 26 March – Friday 21 May:	You may work on the remaining exercises in any order, subject to the condition that no mark will be given a for an "extra" exercise unless reports for all core exercises have already been submitted.

IT skills

IT skills instruction sessions will be led by Lynda Humphreys on the following days, starting at 9.15am in the 3S Computational Laboratory. These sessions are an integral part of the Unit, and your participation will form part of the assessment.

26 March:	Introduction to chemical structure drawing with ISIS/Draw
30 April:	Introduction to the Beilstein electronic database

Prior to the session on the Beilstein database, you should register for use of the Athens and Crossfire services, as directed on the next page. Make a note of your Athens username and password!

Assessment

Each exercise will be assessed on the basis of a brief report. Read the instructions for each exercise carefully to make sure you know what is required in the report. In general you will be asked to provide answers to specific questions and you may be required to complete a particular assignment. If you are unsure about what you are being required to do, ask the supervising staff member or the demonstrator.

The report for the X-ray exercise must be submitted by 5pm Monday 22 March.

The report for the ISIS/Draw exercise must be submitted by 5pm Monday 19 April, and for the Beilstein exercise by 12 noon Friday 7 May.

You must submit **at least one** report for a 10-mark core exercise by 5pm of the following Mondays: 26 April, 10 May, 17 May.

All reports must be submitted by 5 pm Monday 24 May.

Reports should be word-processed and submitted on A4 sheets, either stapled together or placed in a folder to ensure that no pages are lost. You should submit your reports directly to Professor Steve Parker in return for a signed receipt.

Reports **must** be submitted on schedule, and failure to comply with this requirement will result in you being penalised in line with standard University regulations.

ATHENS REGISTRATION

Before you can use CrossFire, you must register for an ATHENS username and password. Go to the web page:

http://www.athens.ac.uk

click on 'self-registration'

enter username: batchu08

and password: ath14ehc

then set up your individual ATHENS username and password.

Note that the username is set to start with 'batch'...

CROSSFIRE REGISTRATION

You then need to register your ATHENS username and password with MIMAS, as follows:

On a Web browser, connect to:

http://www.mimas.ac.uk/crossfire/athens_reg.html

Click on Athens Registration. A certificate will appear (the form of this will depend on your browser) - you must accept this to proceed. Enter your ATHENS personal username and password and click on the Start Self-Registration button.

Click continue and follow the instructions until you see a page confirming that you can use your ATHENS username and password to access CrossFire.

Guidance for Working with VDUs

The use of Visual Display Units (VDU's) and other forms of Display Screen Equipment (DSE) is governed by the Health and Safety (Display Screen Equipment) Regulations 1992.

The Regulations aim to prevent problems associated with the use of Display Screen Equipment such as musculo-skeletal problems, visual fatigue, and stress. The likelihood of experiencing these is related mainly to the frequency, duration, intensity and pace of spells of continuous use of the display screen equipment, allied to other factors such as the amount of discretion the person has over the extent and methods of display screen use and, importantly, the provision of the correct equipment.

There is no convincing scientific evidence that VDUs are harmful to the eyes. However, since complaints of eye discomfort and fatigue are becoming more common as their use increases, safety concerns are receiving more attention. The levels of radiation from VDUs are well below those required to produce cataracts or other eye damage even after a lifetime of exposure.

As a student you may have limited control over the different working environments within the University in which you may be a VDU user, but you can take sensible measures yourself to avoid fatigue and strain: check your posture and take periodic rest breaks. The computational exercises you are asked to during this laboratory course should not require that you sit in front of a VDU for hours on end. Most students should find that they can each be completed within three or four hours, but you have the whole day scheduled for the lab class. If you need a break, why not write a section of the lab report, and then return to the VDU work later?

If you want further information on the subject of working with VDUs, you may wish to consult the following web sites.

University of Bath Safety Manual – Section 4.1.8
`http://www.bath.ac.uk/Admin/Safety/1section_4-1-08.htm`

Health and Safety Executive Leaflet on Working with VDUs
`http://www.open.gov.uk/hse/pubns/indg36.htm`

CONFORMATIONAL ANALYSIS OF SIX-MEMBERED RINGS

Molecular Mechanics

This exercise makes use of the SPARTAN program, which you will be using extensively in this course. Molecular modelling has evolved from a specialised research tool of limited availability, to an important, if not essential, means with which to explore chemistry. Computer-based models are now routinely able to supply quantitative information about the structures, stabilises and reactivates of molecules. SPARTAN comprises a series of independent modules tightly connected via a graphical user interface, thus provides a flexible and easy-to-use interface to a series of tools for building, manipulating, analysing and displaying molecular structures. In other exercises you will use SPARTAN for calculations using molecular orbital theory, but for the purposes of the present exercise you will use the simple approach sometimes called “molecular mechanics”. Briefly, this treats a molecule as if it were a set of atomic “balls” joined together by bonds, which act like “springs”. Distorting a molecule from its preferred geometry causes the springs to become stretched or compressed, and this “strain” leads to an increase in energy of the molecule. A preferred molecular geometry is one for which the strain energy is minimised.

The potential energy of a spring may be expressed by Hooke's Law for a small displacement away from the equilibrium position. Suppose the length of the spring at equilibrium is R_0, then a small compression or extension changes the length to a new value R; the size of the displacement ΔR is the difference $(R - R_0)$. According to Hooke's Law, the change $\Delta V_{\text{stretch}}$ in potential energy V for a harmonic oscillator displaced by $(R - R_0)$ is

$$\Delta V_{\text{stretch}} = \tfrac{1}{2}\, k_{\text{R}}\, \Delta R^{\,2}$$

Where k_{R} is the force constant describing the stiffness of the spring. This expression can be applied satisfactorily to small (strictly speaking, *infinitesimally* small) displacements in chemical bond lengths in molecules.

A similar expression can be used for the change in potential energy arising from a small change $\Delta\theta = (\theta - \theta_0)$ in a bond angle between three connected atoms in a molecule

$$\Delta V_{\text{bend}} = \tfrac{1}{2}\, k_{\theta}\, \Delta\theta^{\,2}$$

where θ_0 is the equilibrium bond angle and k_{θ} is the force constant for bending of this "angular" spring. To describe the change in potential energy arising from a small change in dihedral angle for a chain of four connected atoms (*e.g.* H-C-C-H in ethane), an expression involving the cosine of the angular displacement is usually employed.

Although the harmonic oscillator approximation is satisfactory for small distortions of covalent bonds, it is not at all suitable for describing the change in potential energy ΔV_{vdW} arising from a displacement in the relative positions of a pair of *non-bonded* atoms. To describe this type of interaction within a molecule, an expression is required which takes account of the very different distance dependencies of the attractive and repulsive contributions to van der Waals forces. Several functions may be used; we do not need to concern ourselves with the details here. Finally, there are expressions used to

Thus the potential energy of molecule, relative to an arbitrary zero of energy, may be expressed as the sum of contributions from all the bonded pairs of atoms, all the bond angles, and all the non-bonded pairs of atoms

$$\Delta V_{\text{total}} = \sum_{\substack{\text{all}\\ \text{bonded}\\ \text{pairs}}} \Delta V_{\text{stretch}} + \sum_{\substack{\text{all}\\ \text{bond}\\ \text{angles}}} \Delta V_{\text{bend}} + \sum_{\substack{\text{all}\\ \text{dihedral}\\ \text{angles}}} \Delta V_{\text{dihedral}} + \sum_{\substack{\text{all}\\ \text{non-bonded}\\ \text{pairs}}} \Delta V_{\text{vdW}}$$

In general it is not possible for all the individual covalent bonds and bond angles to adopt their ideal lengths R_0 and θ_0 simultaneously. In order to find the preferred geometry of a molecule at equilibrium, it is therefore necessary to find the minimum value of the potential energy ΔV_{total} as a function of all the geometrical parameters. This energy minimisation using a molecular mechanics method in which the "force-field" parameters (*e.g.* R_0, θ_0, k_R and k_θ) are determined empirically to give a "best fit" to a range of experimental properties of molecules; the resulting parameter set is called a "force field". SPARTAN uses a force field originally developed by computational chemists at Merck Pharmaceuticals: it is called "MMFF94", or just "MMFF".

The version of SPARTAN installed on most of the PCs in the 3S Computer Lab is the "Student Edition" (SPARTAN ST), but some have a slightly different version – the "Essential Edition" (SPARTAN ES). SPARTAN ES has a few more options and features than SPARTAN ST; in particular there is an alternative force field called "SYBYL", which was developed by Tripos Ltd. specifically for biological molecules. In this exercise use only MMFF, which is the default for SPARTAN ST.

Overview of the exercise

During this exercise you will use the molecular mechanics method within SPARTAN in order to:

- investigate the energy profile for internal rotation about the central bond in *n*-butane, using a spreadsheet making a plot;
- perform geometry optimisation to obtain fully relaxed minimum-energy structures for several conformations of *n*-butane and consider the reasons for their energetic differences;
- do likewise for conformers of cyclohexane;
- investigate the axial *vs*. equatorial preferences for a few monosubstituted cyclohexanes;
- explore the relative energetics of isomeric dimethylcyclohexanes.

Background reading

Jones, *Organic Chemistry* (2nd ed.)

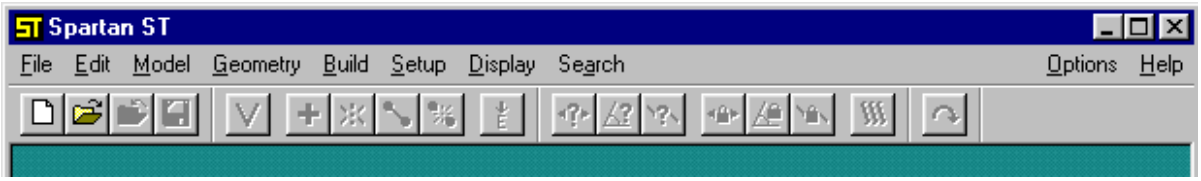
section 2.8: Butanes….and conformational analysis
section 5.3: Stereochemistry of cyclohexane: conformational analysis
section 5.4: Monosubstituted cyclohexanes
section 5.5: Disubstituted ring compounds

The instructions provided below are deliberately detailed, in order to direct you through the key steps involved in using SPARTAN. Please read them carefully and follow them closely, but in so doing do try not to lose sight of what it is that you are trying to do. Once you have mastered the basic skills, you will be able to perform simple tasks by yourself with the need for explicit directions.

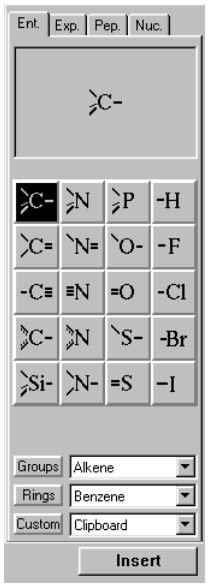
Conformations of n-butane: energy profile for internal rotation

You should recall that simple alkanes prefer conformations involving a staggered arrangement of bonds attached to a pair of C_{sp^3} atoms connected by single bond, and that conformations in which these bonds are eclipsed are unfavourable; furthermore, staggered *anti* conformations are lower in energy than staggered *gauche* conformations. Your first task is to use the SPARTAN program to evaluate the size of these energetic preferences.

To start, *click* on the **Start** button, the *click* on **Programs**, and finally *click* on **Spartan**. To quit, select **Exit** from File menu.



Click on **File** from the menu bar and then *click* on **New** from the menu which appears (or *click* on the icon in the toolbar beneath **File**).



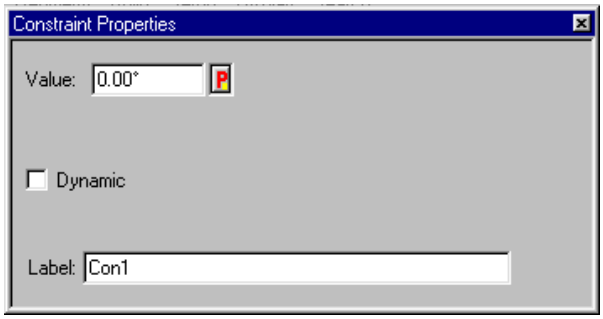
The **Entry** model building kit appears (as shown here on the right).

Click on the sp^3 hybridized carbon from the library of atomic fragments. The fragment icon is shown in reverse video, and the model of the fragment appears at the top of the model kit. Bring the mouse cursor anywhere on the green area of the SPARTAN window and *click*. Rotate the carbon fragment (move the mouse while holding down the left button) so that all four yellow free valences can been seen clearly; SPARTAN will automatically convert these to hydrogen atoms if you do not connect any other fragments to them.

Left click on the tip (yellow area) of one of the free valences of the sp^3 hybridized carbon: another sp^3 carbon should appear. The two fragments are now connected by a single bond, forming ethane. Continue in a zigzag fashion to construct a chain of four sp^3 carbons to comprise the backbone of *n*-butane.

Now you should set the CCCC dihedral angle to 0° (*syn* conformation). To achieve this, first *click* on the icon on the toolbar (or select **Measure Dihedral** from the Geometry menu). Now *click* on each of the four carbon atoms in sequence; they should turn olive-green in colour. Enter **0** (0°) into the text box to the right of "Dihedral…" in the bottom-right corner of the screen, and *press* the **Enter** key on the keyboard. You should see the *syn* conformer of butane appear in the window on the screen.

Click on the icon from the toolbar (or select **Constrain Dihedral** from the Geometry menu) *click* again on the same four carbons you used to define the dihedral angle, and then *click* on at the bottom right of the screen. The icon will change to indicating that a dihedral constraint is to be applied. Now exit the model building kit by clicking on the **View** icon. Select **Properties** from the Display menu and *click* on the constraint maker on the molecule in the window; this is a set of light-blue lines next to the central CC bond (in this case) which turn colour to olive-green when selected. The **Constraint Properties** dialog box appears.



Click in the box alongside **Dynamic** inside the dialog box. This leads to an extended form of the **Constraint Properties** dialog box which allows the single value of the constraint upon the dihedral angle to be replaced by a range of values.

Leave the value of **0** (0°) as it is in the box to the right of "Value**"**, but change the contents of the box to the right of "to**"** to **180** (180°). You need to *press* the **Enter** key after you type in the value. The box to the right of **Steps** should contain the value **10**. (If not, type **10** in this box and *press* the **Enter** key.) What you have specified is that the dihedral angle will be constrained first to 0°, then to 20°, *etc*., and finally to 180°. *Click* on to dismiss the dialog box.

Select **Calculations…** from the Setup menu, select **Energy Profile** from the menu to the right of "Calculate**"**, and select **Molecular Mechanics** from the menu to the right of "with**"**. *Click* on **Submit** at the bottom of the dialog box. In the **Save As** dialog box, give a File name for the job in the form "**abc_butane**" (where "abc" are your own initials) and *click* on **Save**. A message appears to inform you that the job named "**abc_butane.spartan**" has started; *click* **OK** to remove this window.

It may take a few minutes for the computer to perform the ten dihedral-angle constraint calculations. At each value of the CCCC dihedral angle, all of the other bond lengths and angles are relaxed to determine their optimum values. Close "**abc_butane**" (**Close** from the File menu) to remove the original molecule from the screen, and wait for a message to appear informing you that the job has completed and then close this message window. Now open the file named "**abc_butane.profile1.spartan**", which you will find from the Open dialog box (*click* on the  icon or select **Open** from the File menu); this file contains the results of the calculations. Click on  the icon (or select **Align Molecules** from the Geometry menu and, one after the other, *click* on either the first three carbons or the last three carbons. Then click on the **Align** button at the bottom right of the screen, and finally *click* on  .

Select **Spreadsheet** from the Display menu, scroll to the bottom line and select **`Molecule010`**; the cell turns from green to purple, and the check box turns from yellow to blue. Now *click* on the header cell for the left-most blank column, and *click* on the **Add…** button. From the Add dialog box, select **rel.E**, and units of **kJ/mol** next to **Energy**; finally *click* on **OK**. To enter the dihedral angles, *click* on the  icon, then *click* on the purple constraint marker on the molecule, and *click* on the  button in the bottom-right corner. Finally select **`Molecule010`** again and *click* on **Sort** to ensure that the conformations are in the correct order. The relative energies may appear with at least 7 decimal places (d.p.) but you should consider that most of these are not significant figures. Similarly, the dihedral angles in the column headed **`Dihedral (Con1)`** have 7 d.p. and are not quite exactly equal to 0°, 20°, 40°, 60°, etc., but the difference is not significant. For clarity you might want to change a near-zero entry (*e.g.* `5.76234203e-008`) to 0, and (if necessary) change the sign angle the dihedral angle for **`Molecule010`** from –180 to +180.

Select **Plots…** from the Display menu, **Dihedral**(**Con1**) from the items in the X Axis menu and **rel.E (kJ/mol)** from the list in the Y Axis menu. *Click* on **OK** to dismiss the dialog and display a plot. Use the left and right scroll buttons at the bottom of the SPARTAN window to move through each of the conformations, from *syn* to *gauche* and on towards *anti*. Now you should take note of the energies and selected geometrical features of the maxima and minima in the energy profile for internal rotation. Scroll to the *anti* conformer, *click* on the icon (or select **Measure Angle** from the Geometry menu), *click* on three consecutive carbon atoms, and note the value of the CCC bond angle in the bottom-right corner. Now return to the *syn* conformer and repeat the procedure to determine the CCC bond angle, and check the energy (in kJ mol^{-1}) relative to the *anti* conformer. If you have followed all of the above instructions correctly, the energy profile should show a structure with CCCC dihedral angle = 120° lying almost exactly on top of the energy barrier between the

Anti:
- CCC bond angle =
- CCCC dihedral =
- relative energy =

Syn:
- CCC bond angle =
- CCCC dihedral angle =
- relative energy =

Transition state:
- CCC bond angle =
- CCCC dihedral angle =
- relative energy =

Approximate gauche:
- relative energy =

gauche and *anti* conformers; this represents the transition state for interconversion of the two staggered conformers. You should note the values of the CCC bond angle and of the relative energy for this *gauche* → *anti* transition state. Finally, note the energy of the structure nearest to the *gauche* conformer (CCCC dihedral ≈ 60°): this species does not lie at a minimum in the energy profile, so you will now perform a geometry optimisation to find the true local energy minimum.

Conformations of n-butane: geometry optimisation

Having scrolled to the approximate *gauche* conformer, *click* on the  icon (or select **Constrain Dihedral** from the Geometry menu) and then on the constraint marker; *click* on the  icon in the bottom-right corner of the screen; the icon will change to  indicating that the dihedral constraint has been removed. *Click* on the View icon  to remove any atom selections that may be in place (olive-green colours). Now drag a rectangle around the molecule on the screen (with both left and right mouse buttons depressed), *click* on **Copy** from the Edit menu, and **Close** the current window (from the File menu). Answer **No** to the question "Save changes to abc_butane.Profile1?", and *click* on the empty blue/green window to remove the white rectangle. Now *click* on **New** from the File menu, **Paste** from the Edit menu, and  to remove the model building kit. Select **Calculations…** from the Setup menu, select **Equilibrium Geometry** from the menu to the right of "Calculate", and **Molecular Mechanics** from the menu to the right of "with**"**. (If you are using Spartan ES, also make sure that MMFF is selected in the menu to the right of "Molecular Mechanics"). *Click* on **Submit** at the bottom of the dialog box and name the job appropriately (*e.g.* "**abc_syn**", *etc.*). Measure the value of the optimised CCC bond angle and CCCC dihedral angle using the  and  tools. The absolute value of the MMFF molecular mechanics energy (in kcal mol^{-1}) for the optimised *gauche* conformer may be found by selecting **Properties** from the Display menu. In order to determine the relative energy of this conformer, you will need also to find the absolute energy for the *anti* conformer; you will need to re-open the abc_butane.Profile1 file to do this.

N.B. *Absolute* values of molecular mechanics energies have no particular significance; it is only energy *differences* that are meaningful and which may be sensibly compared with experimentally derived values.

anti:
absolute MMFF energy =

gauche:
CCC bond angle =
CCCC dihedral angle =
absolute MMFF energy =
relative energy / kcal mol^{-1} =
relative energy / kJ mol^{-1} =

1 kcal mol^{-1} = 4.184 kJ mol^{-1}

Question 1

(a) Construct a Table containing the following results from your molecular mechanics optimisations on *n*-butane:
- relative energies (kJ mol^{-1} to 1 d.p.) of the *syn*, (optimised) *gauche* and *gauche* → *anti* transition-state conformations with respect to the *anti* conformation;
- CCC bond angles (degrees, 1 d.p.) for the *anti*, *gauche* → *anti* transition-state, *gauche* and *syn* conformations;
- CCCC dihedral angle for the *gauche* conformation.

(b) Account briefly for the trend in the CCC angles as between the four conformations, and comment upon the difference between the initial and final calculated values for the CCCC dihedral angle in *gauche* butane.

Conformations of cyclohexane: "all syn" and chair

A straight chain of six CH_2 (methylene) groups may adopt an extended "zigzag" conformation in which every C–C–C–C fragment is *anti*, with a dihedral angle of 180°. Imagine the two ends are brought together and linked to form a ring; this must necessarily involve twisting about the C–C bonds to give dihedral angles of 0° and all six C atoms coplanar. You can build this "all *syn*" species as follows.

Start by opening a **New** window within SPARTAN, and build a chain of six sp^3 carbon atoms. Then use the  and  tools to set each CCC bond angle to 120° and each CCCC dihedral angle to 0°; also set one HCCC dihedral angle to 0° at each end of the chain. Now select the  icon from the toolbar (or **Make Bond** from the Build menu) and *click* on each of the two yellow tips of the (almost superimposed) free valencies in order to complete the ring. *Click* on  to remove the model building kit. Select **Calculations…** from the Setup menu, select **Equilibrium Geometry**, and **Molecular Mechanics**. (If you are using Spartan ES, also make sure that MMFF is selected.). **Submit** the job and name it appropriately (*e.g.* "**abc_allsyn**"). Upon completion, make a note of the absolute energy (**Properties** from the Display menu). Make sure you save all the files from this job (and from the rest of this exercise: you may need to refer to them later, or in another exercise in this Unit.

This "all *syn*" conformation of cyclohexane is an unstable species, just as the *syn* conformation of *n*-butane is unstable in the sense that it corresponds to a maximum in the energy profile for rotation about the central C–C bond. The *gauche* and *anti* conformers of *n*-butane are both stable in the sense that each corresponds to a minimum in this energy profile, even though one is higher in energy than the other. In the same way, cyclohexane has two stable conformations, called "chair" and "twist-boat". You should now locate these two species – and also two other unstable species – in the following manner.

The chair conformer of cyclohexane is easy. Open a **New** window within SPARTAN, select **Cyclohexane** from the menu to the right of **Rings** in the model building kit, and click within the main window; the molecule should appear on the screen in the correct conformation, but now it must by optimised. As before, select **Calculations…** from the Setup menu, **Equilibrium Geometry**, and **Molecular Mechanics**; then **Submit** the job and name it appropriately ("**abc_chair**"). Once again, note the absolute energy (**Properties** from the Display menu). Also, measure the optimised values of the CCC bond angles, the CCCC dihedral angles, and the two different values of the CCCH dihedral angles. (Use the  and  tools.)

All syn:

absolute MMFF energy =

energy relative to chair / kJ mol^{-1} =

Chair:

CCC bond angle =

CCCC dihedral angle =

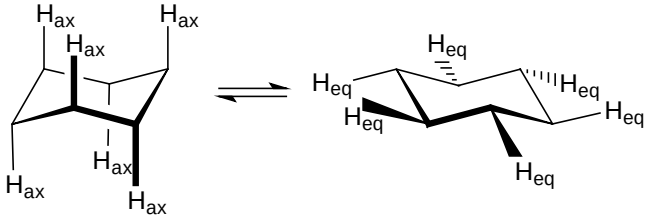
$CCCH_{ax}$ dihedral angle =

$CCCH_{eq}$ dihedral angle =

absolute MMFF energy =

- Observe that the twelve hydrogen's divide into two distinct groups of six, called "axial" and "equatorial", which may be distinguished according their CCCH dihedral (or "torsion") angles.

- Note that the set of equatorial H atoms can interchange with the set of axial H atoms if the chair conformer undergoes a "ring flip".



Conformations of cyclohexane: half chair and twist boat

Now you should attempt to construct an energy profile for the ring-flip process – or rather, of part of it. First ensure that all olive-green selections on chair cyclohexane are swiched off: do this by *clicking* on . Then select , *click* on three C atoms and an axial H atom, and *click* on . Select **Properties** from the Display menu and *click* on the constraint maker for the $CCCH_{ax}$ dihedral angle. Check the square alongside **Dynamic** in the **Constraint Properties** dialog box, enter **180** (180°) in the box to the right of "to**"**, and to *press* the **Enter** key. Type **13** in the box to the right of Steps and *press* the **Enter** again before closing this dialog box. Select **Calculations…** from Setup, **Energy Profile**, and **Molecular Mechanics**. **Submit** the job, close the message window, and **Close** the molecule from the File menu. Once the job has completed (and the message window closed), **Open** the file "**abc_chair.Profile1**". Select **Spreadsheet** from the Display menu, scroll to the bottom line and select **`Molecule013`**; *click* on the header cell for the left-most blank column, and *click* on the **Add…** button. Select **rel.E** and units of **kJ/mol** and *click* on **OK**. *Click* on , then *click* on the constraint marker, and *click* on the button. If the dihedral angle for **`Molecule013`** shows a negative value (*e.g.* –179.983891) whereas all the other values are positive, change the negative value to **+180** (and *press* **Enter**). Select **Plots…** from the Display menu, **Dihedral**(**Con1**) in the X Axis menu and **rel.E (kJ/mol)** in the Y Axis menu. *Click* on **OK** to dismiss the dialog and display a plot.

Inspect the conformation of highest energy in the profile: this is (approximately) the "half-chair". Observe that four consecutive carbon atoms are approximately coplanar. Note its energy relative to the chair.

Now inspect the conformations with CCCH dihedral angles between 140° and 180°. These are (approximately) "twist boats". Notice that they occur in mirror-image forms. Now find the minimum-energy structure for the twist-boat conformer. To do this, follow the procedure you used above for the geometry optimisation of *gauche* butane, but save the structure as, *e.g.*, "**abc_twistboat**". Note the absolute energy and the energy relative to the chair conformer, and note the various values of the CCC bond angles and CCCC dihedral angles. Notice that, viewed from one direction, the twist-boat has a "prow" and a "stern" to left and right sticking upwards (or downwards if it has turned turtle!) and that the bonds "amidships" in the foreground and background are skewed with respect to each other.

The "boat" conformer may be considered as the transition state for interconversion of enantiomeric twist-boats. To locate its structure by means of molecular mechanics, you will need to employ a trick. You will add a bridging CH_2-CH_2 unit across the twist-boat between the "prow" and the "stern". First save as a new file (*e.g.* "**abc_boat**"). Select **Add Fragment** from the Build menu on the toolbar and then select sp^3 hybridized carbon from the library of atomic fragments. *Click* on the yellow tip of the "flagpole" on the carbon at the "prow", and same on that of the carbon at the "prow". To form a bond between the two newly added carbons, *click* on the **Make Bond** icon (or select **Make Bond** from the Build menu), and then *click* on a free valency of each carbon. Now perform an **Equilibrium Geometry** calculation within Setup Calculations… to a produce a nicely symmetrical bicyclo-octane molecule with three identical CH_2-CH_2 bridges between two CH groups. The trick now is to delete one of the CH_2-CH_2 bridges and leave a symmetrical structure for boat cyclohexane. To do this, *click* on the **Delete** icon (or select **Delete** from the Build menu), and then *click* on two of the bridging carbons. Go back into the Setup Calculations… menu and re-do the **Equilibrium Geometry** calculation, but making sure that the **Symmetry** option is checked. The structure you obtain should not be the same as the twist-boat. Once you are sure that you do indeed have the boat, note its absolute energy and the energy relative to the chair conformer, and note the various values of the CCC bond angles and CCCC dihedral angles.

Half chair:

energy relative to chair / kJ mol^{-1} =

Twist-boat:

CCC bond angles =

CCCC dihedral angles =

absolute MMFF energy =

energy relative to chair / kJ mol^{-1} =

Boat:

CCC bond angles =

CCCC dihedral angles =

absolute MMFF energy =

energy relative to chair / kJ mol^{-1} =

Question 2

(a) Construct a Table containing the following results from your molecular mechanics optimisations on cyclohexane:
- relative energies (kJ mol^{-1} to 1 d.p.) of the "all *syn*", boat and twist-boat conformations with respect to the chair conformation;
- CCC bond angles and CCCC dihedral angles (degrees, 1 d.p.) for the four conformations.

(b) On the basis of these data account briefly for the energetic ordering of the four conformations.

Axial vs. equatorial substituent preferences

Conformations of substituted cyclohexanes

In many textbooks (including McMurry, section 4.12) the conformational preference of a substituent group X attached to a cyclohexane ring is discussed in terms of **1,3-diaxial interactions**. These may be understood simply in terms of the presence or absence of *gauche* butane-like XCCC fragments involving a substituent and part of the cyclohexane ring. The two approaches are equivalent.

Open a structure for chair cyclohexane and construct the equatorial conformer of methylcyclohexane as follows. Select a sp^3 hybridized carbon from the library of atomic fragments, and *click* on the yellow tip of one of the equatorial hydrogen atoms. Perform an **Equilibrium Geometry** calculation from within Setup Calculations…, saving the job as, *e.g.* "**abc_me_eq**". Note the absolute MMFF energy. Repeat the procedure starting afresh from chair cyclohexane to add a methyl group in an axial position. Determine the energy difference ($E_{axial} - E_{equatorial}$).

Absolute MMFF energy of equatorial methylcyclohexane = kcal mol^{-1}
Absolute MMFF energy of axial methylcyclohexane = kcal mol^{-1}
Energy of axial relative to equatorial = kJ mol^{-1}

Question 3

The two conformers are in equilibrium in a gaseous sample of methylcyclohexane ($C_6H_{11}Me$) at its boiling point, 101℃. Which conformer predominates in the sample? Calculate its mole fraction in the equilibrium mixture.

Hint: the equilibrium constant is given by $\exp(-\Delta E/RT)$, where R = 8.314 J K^{-1} mol^{-1}

Build ethylcyclohexane by changing a hydrogen atom on the methyl substituent of methylcyclohexane using the same procedure as above. For each conformer (equatorial and axial) of methylcyclohexane, there are two different positions in the substituent methyl where the new fragment could be attached; try them both and find which one gives the lowest energy conformation after geometry optimisation. Note the energies for the *preferred* equatorial and axial conformers of ethylcyclohexane. **Save** your optimised structures, with appropriate names,

Build the axial and equatorial conformations of *t*-butylcyclohexane by adding two more methyl fragments (in the manner described above) to your optimised ethylcyclohexane structures. Perform geometry optimisations and note the values of the energies.

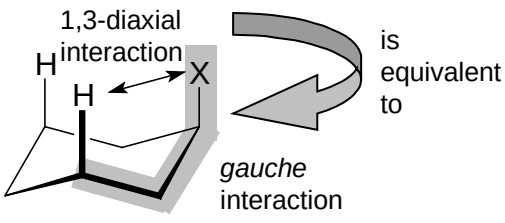
Question 4

(a) Tabulate the absolute molecular mechanics energies (kJ mol^{-1}, 1 d.p.) for equatorial and axial conformers of monosubstituted chair cyclohexanes $C_6H_{11}R$ (R = Me, Et & ^tBu) and the energy differences $\Delta E = E_{ax} - E_{eq}$.

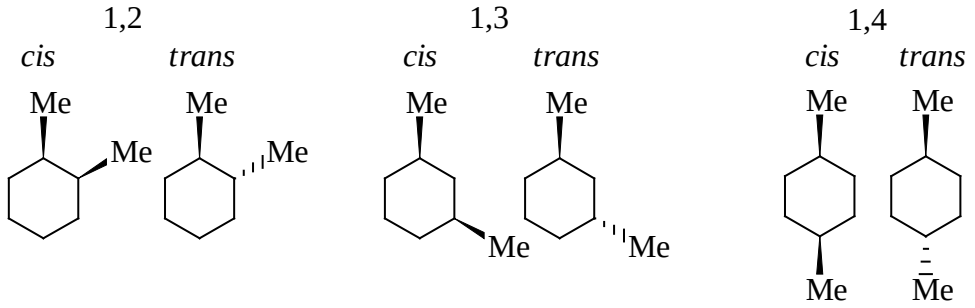
(b) Account briefly for the energy differences and conformational preferences.
In particular, why is the axial – equatorial energy difference ΔE for R = Et rather similar to that for R = Me, whereas that for R = ^tBu is much larger?

Note: Although in general the energies calculated by molecular mechanics for different molecules may not be compared directly, it is quite in order to compare the relative energies of isomers and conformers of species having the same molecular formula and the same type of functional groups.

In many textbooks (although not Jones) the conformational preference of a substituent groups X attached to a cyclohexane ring is discussed in terms of **1,3-diaxial interactions**. Thus one may speak of an "X…H 1,3-diaxial interaction". This is equivalent to a *gauche* interaction between an X substituent and part of the cyclohexane ring in an XCCC fragment, *i.e.* an "X-ring *gauche* interaction".

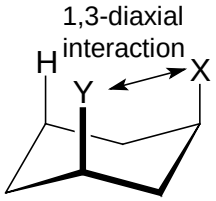


Isomers and conformers of dimethylcyclohexane



Build each of the above structures and determine the total energy of its optimum geometry. Start each structure by adding a methyl fragment to one of your saved methylcyclohexanes.

You may need to consider *gauche* interactions between an X and Y substituents in XCCY fragments, and also X…Y 1,3-diaxial interactions.



***Hint*: there may be more than one conformer for each isomer!**
You should consider all conformers with distinct energies.

Question 5

(a) Analyse each structure to identify how many 1,3-diaxial H···Me and Me···Me interactions and how many *gauche* MeCCMe interactions there are. Tabulate these results together with your total energies. Be sure to include all (chair) conformers of all isomers. Your Table should include a neat ISIS/Draw structure for each distinct isomer to illustrate clearly and correctly its stereochemistry.

(b) Comparing all the structures together, identify the most stable and the least stable, and provide a brief explanation for their relative stabilities.

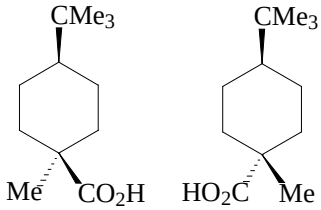
(c) Considering all the structures together, are the interactions analysed in (a) additive? How much energy is each type of interaction worth?

Reactivity of disubstituted cyclohexanes

Question 6

Consider the preferred conformation for each of the two isomers (a) and (b) shown on the right. Suggest a reason why acid-catalysed esterification in ethanol proceeds 20 times faster with isomer (b) than with isomer (a).

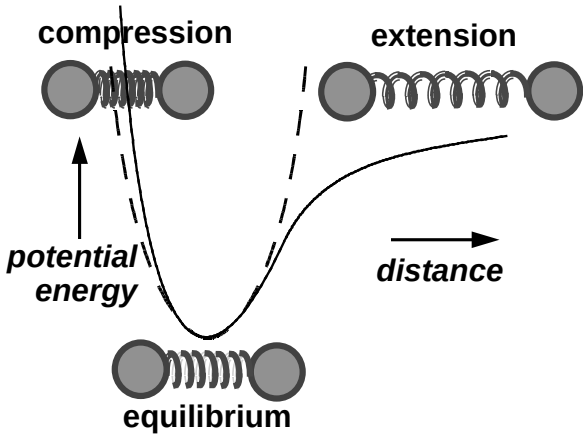
In your answer you should include suitable pictures from SPARTAN to illustrate your argument as simply as you can.



You can capture any image from SPARTAN by use of the **Copy** and **Paste** functions from the **Edit** menu to insert into a Word document. You can cut the unwanted borders away using the **Crop** tool in the **Picture** toolbar from the **View** menu of Word. Changing the **Wrapping** style (under **Format Picture**) to **Square** allows you to have text to right or left (or both sides of) your inserted picture.

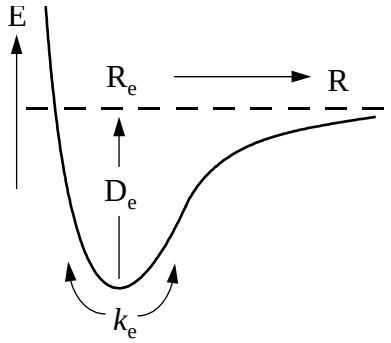
MOLECULAR VIBRATIONS

Let's think about how a diatomic molecule such as H_2 vibrates. The bond may be regarded rather like a spring: compression or extension of the spring away from its equilibrium length involves raising the potential energy of the molecule. If the spring obeyed Hooke's law, the increase in potential energy would be proportional to the *square* of the displacement, and the function describing how the energy varied with the interatomic distance would be a parabolic curve like the dashed line in the Figure on the right. Real molecules are harder to compress than would be predicted by a parabolic energy curve: the short-range repulsive interactions between the atoms make the energy rise more steeply as the interatomic distance is decreased. On the other hand, real molecules are easier to stretch than would be predicted for a harmonic oscillator obeying Hooke's law. Extension of the bond in the H_2 molecule leads eventually to dissociation, with the potential energy curve flattening out as the interatomic distance is increased.



The shape of the actual potential energy profile is closely approximated by a Morse function, which may be written in the following form.

$$E = D_e \{ 1 - \exp[-\beta (R - R_e)] \}^2$$



where R_e is the equilibrium bond length, at the minimum of the energy curve;

D_e is the bond dissociation energy measured from the energy minimum;

β is a coefficient describing the curvature of the function, given by

$$\beta = (k_e / 2D_e)^{½}$$

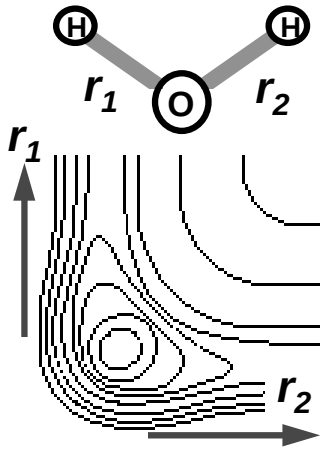
where k_e is the Hooke's law, harmonic oscillator force constant at the energy minimum.

The parabolic curve (dashed line in diagram at top right) with force constant k_e is a good approximation to both the Morse curve and the actual potential energy profile for *small* displacements $\Delta R = R - R_e$ away from the equilibrium bond length. The frequency ω with which the molecule vibrates about its equilibrium position may therefore be described approximately by the harmonic oscillator expression, as follows.

$$\omega = (1/2\pi) (k_e / \mu)^{½}$$

where μ is the reduced mass of the diatomic molecule A–B, given by $1/\mu = 1/m_A + 1/m_B$), and has dimensions of reciprocal time (units of s^{-1}). It is common, however, to express vibrational frequencies ν in units of cm^{-1}, where $\nu = \omega/c$ (velocity of light); to be strictly correct this means the 'frequencies' are actually 'wavenumbers'.

Now let's consider the H_2O molecule with two bonds of length r_1 and r_2. which may both be extended or compressed. To represent how the energy varies as function of these two



independent stretching coordinates requires a 2D potential energy surface, as shown in the Figure to the left. The bottom-left corner contains an energy well, corresponding to the geometry of the water molecule at equilibrium. Extension of just one of the bonds corresponds to movement along a valley, either horizontally or vertically, leading eventually to dissociation of the molecule. Small displacements away from the equilibrium geometry may be described by the harmonic approximation, as above, but the energy relative to the minimum is *not* simply the sum of two terms, one for stretching of each bond

$$\Delta E \neq \tfrac{1}{2} k_e \Delta \boldsymbol{r_1}^2 + \tfrac{1}{2} k_e \Delta \boldsymbol{r_2}^2$$

This because compression or extension of *both* bonds causes the energy to change due to an additional "cross-term".

$$\Delta E \neq \tfrac{1}{2} k_e \Delta \boldsymbol{r_1}^2 + \tfrac{1}{2} k_e \Delta \boldsymbol{r_2}^2 + k_{12} \Delta \boldsymbol{r_1} \Delta \boldsymbol{r_2}$$

The problem is yet more complicated because we still need to include energy changes due to displacement in the bond angle. The potential energy of the molecule is a function of three coordinates, and it would require a 4D surface to represent this graphically. For any molecule with more than three atoms the situation is worse: for an N-atomic molecule there are $3N - 6$ coordinates required to describe the energetics of displacements about the equilibrium geometry, and when all cross-terms are taken into account there are $\frac{1}{2}(9N^2 - 33N + 30)$ terms in the harmonic approximation for the potential energy. However, things are not actually quite as bad as they might appear to be!

Just as a tuning fork has a 'natural' frequency and motion (or *mode*) of vibration, so too does a molecule, except that any molecule larger than a diatomic has more than one 'natural' frequency. The motions of a molecule corresponding to its 'natural' frequencies are its **normal modes** of vibration. A normal mode is a motion with the property that, if each atom in a molecule is displaced from its equilibrium position by a displacement which corresponds to its maximum amplitude in that mode, then when the atoms are simultaneously 'let go' the atoms will all undergo a motion at the same frequency. Further, once having been 'let go' they will all simultaneously pass through the equilibrium configuration and, later, simultaneously again reach the positions of maximum amplitude. It turns out that the complicated and apparently random directions, amplitudes and phases of atomic motions in a vibrating polyatomic molecule can be regarded simply as the sum of normal-mode vibrations with different phases, provided the amplitudes are not too great. This just the same as regarding the complicated sound wave motion from a violin as the sum of different harmonic frequencies. The normal modes of a molecule are quantized, just like the harmonics of a vibrating stretched string, and it is possible to add a further quantum of vibrational energy to any mode. Absorption or emission of quanta of vibrational energy with frequencies characteristic of the normal modes is the basis of infra-red and Raman spectroscopies. A (non-linear) N-atomic molecule possesses $3N - 6$ normal modes $\boldsymbol{q}_i$ and, for small displacements from equilibrium, the change in potential energy is simply the sum of $3N - 6$ terms each involving the square of a normal-mode displacement. Each 'force constant' Φ_i corresponding to a particular normal-mode displacement $\Delta \boldsymbol{q}_i$ is related simply to the vibrational frequency: $\nu_i = (1/2\pi c)\, \Phi_i^{\frac{1}{2}}$.

$$\Delta E = \tfrac{1}{2} \sum_{i}^{3N-6} \Phi_i \Delta q_i^2$$

In this exercise you will use the SPARTAN program to compute vibrational frequencies and normal modes of vibration for the water molecule and its hydrogen-bonded dimer, and consider the consequences of deuterium substitution. SPARTAN employs molecular orbital (MO) theory to perform calculations to find the equilibrium geometry for a molecule and to determine the force constants required for the normal-mode treatment of molecular vibrations.

Getting started with SPARTAN:

To start, *click* on the **Start** button, then *click* on **Programs**, and finally *click* on **Spartan**. To quit, select **Exit** from file menu.

Normal modes and vibrational frequencies of the water molecule

Click on **File** from the menu bar and then *click* on **New** from the menu, which appears (or *click* on the icon in the tool bar).

The Entry model building kit appears, Select the icon for divalent oxygen (second from left in the second row of the Fragment panel) by *clicking* upon it with the left mouse button. Bring the cursor inside the Builder window and *click*. Divalent oxygen will appear on the screen with its unfilled valencies indicated by “yellow vectors”; if it appears "edge-on" you will need to rotate it (see below) in order to continue to build the structure. Unfilled valencies are automatically converted into hydrogen atoms upon exiting the builder.

At any stage during the building process, the molecule drawn in the work area can be rotated (middle mouse button, or middle mouse button with the **shift key** for rotation in the plane of the screen) or translated (right mouse button). It can also be enlarged or reduced in size (right mouse button with the **shift key**). If you discover that you have generated an unsatisfactory structure and wish to begin again, you may do so at any time by selecting **Clear** from the **Edit** menu. If you have a mouse with only two buttons, the function of the (missing) middle button is provided by pressing both right and left buttons together.

A molecule of water will be shown in the main screen, the appearance of which can be altered by selecting the various options from the **Model** menu: **Ball and Spoke** is recommended for this exercise.

SPARTAN ST:
Select **Calculations…** from the Setup menu. Select **Equilibrium Geometry** from the menu to the right of “Calculate”, and select **Hartree-Fock/3-21G** from the menu to the right of “with” and *click* in the box beside **Frequencies**. Make sure that the Total Charge is Neutral and the Multiplicity is Singlet (the default settings).

SPARTAN ES:
Select **Calculations…** from the Setup menu. Select **Equilibrium Geometry** from the menu to the right of “Calculate”, and select **Hartree-Fock** from the menu to the right of “with” and "**3-21G(*)**" from the menu next to it. In the line marked Compute:, *click* in the box beside **Freq**. Make sure that the Total Charge is Neutral and the Multiplicity is Singlet (the default settings).

[This specifies a particular level of MO calculation: the Hartree-Fock self-consistent-field method with a particular set of mathematical functions (the 'basis set') from which the MOs are to be constructed; the 3-21G basis is like a set of AOs, except that there are more of them. The 3-21G(*) basis provided by SPARTAN ES is actually identical to 3-21G for all the molecules throughout this exercise.]

Click on **Submit** at the bottom of the Calculations dialog box. In the **Save As** dialog box, name the job in the form "**abc_H2O**" (where "abc" are your own initials) in your own filespace on H: drive, and *click* on **Save**. A message appears to inform you that the job named "**abc_H2O.Spartan**" has started; *click* **OK** to remove this window. Once the calculation has completed (a message will appear on the screen; *click* on **OK** to remove it), the optimised structure will appear on the screen.

When the calculation is completed, perform the following operations and note the results.

(i) Inspect the OH bond length and HOH bond angle by means of the **Measure Distance** and **Measure Angle** tools from the **Geometry** menu.

> Question 1
>
> What are the O–H bond length (Ångström, to 3 d.p.) and HOH bond angle (degrees, 1 d.p) in the HF/3-21G(*) optimized geometry of the water molecule?

(ii) Select **Properties** from the **Display** menu. The energy of the molecule is given in "atomic" units (1 a.u. = 1 hartree = 2625 kJ mol^{-1}); this is the energy of the molecule relative to its component nuclei and electrons separated to infinity.

> Question 2
>
> What is the energy of the HF/3-21G optimized water molecule? (In a.u.)
>
> (*N.B*. retain 5 d.p. for energies in a.u. *throughout* this exercise.)

Select **Output** from the **Display** menu. Find the line that contains "Cycle Energy Max. grad. Max. Dist." The subsequent rows show the successive steps ("cycles") of energy minimisation towards the optimum geometry for the molecule. Note that the energy (in a.u.) decrease (becomes a larger negative number) in each step, and that the "Max. Grad." (the largest component of the gradient of the energy) and "Max. Dist." (the largest change in the geometry from the previous step) both approach values of zero.

(iii) Select the **Vibrations** option from the **Display** menu. Three vibrational frequencies are listed (in units of cm^{-1}) corresponding to the three normal modes of the H_2O molecule. *Clicking* on a frequency, causes the motion of the atoms in that normal mode of vibration to be animated on screen. For reasons of clarity, the amplitude of the motion as displayed is, by default, greatly exaggerated: remember, the harmonic oscillator approximation only holds good for *small* displacements away from equilibrium! Make sure you view the molecule from an appropriate angle that allows you to recognise its symmetry. To switch off the animation, *click* on the frequency again.

For each mode in turn, list the frequency (to 4 s.f. only) and sketch the form of the motion using arrows to show the relative directions and amplitudes of the atomic motions. Consider whether the motion is changed or unchanged by reflection in a mirror plane bisecting the molecule through the oxygen atom: an unchanged motion is 'symmetric', but one whose sign (direction) is reversed is 'antisymmetric'.

> Question 3
>
> For each vibrational mode of HOH in turn, list the frequency (to the nearest whole number) and sketch the form of the motion using arrows to show the relative directions and amplitudes of the atomic motions. Label each mode as

symmetric or antisymmetric, and indicate whether it is stretching or a bending mode.

Now close the window containing your "**abc_H2O.Spartan**" molecule, and open a new window to build a new water molecule. Once you have built the new molecule, select **Labels** from the Model menu. Then *click* on one of the hydrogen atoms and select the **Properties** option from the **Display** menu. Select **2 Deuterium** from the menu to the right of "Mass Number", and change the Label to "**D**", then press the **Enter** key and close the Atom Properties window. Run an **Equilibrium Geometry** calculation as before, with vibrational frequencies, and **Submit**, saving the file as (say) "**abc_HOD**". Inspect the energy, bond length, bond angle and vibrational frequencies of the optimised "heavy" water molecule.

Question 4

List briefly the similarities and differences between the calculated results for HOD and HOH. What effect does substitution of a heavier isotope have upon the energy, geometry, and vibrational frequencies?

(iv) Select **Surfaces** from the **Display** menu, *click* on **Add…**, and select **density** in the box to the right of "Surface:" and **potential** in the box to the right of "property" in the **Add Surface** window, then *click* on **OK**. Then *click* on **Submit** under the Setup menu. When the calculation is complete, *click* on **density** in the Surfaces window. The 3D-contour drawn around the molecule represents the electronic charge cloud surrounding the nuclei, as given by a preset value of the total electron density: this gives a good impression of the shape of the molecule from the steric point of view. The colours represent the electrostatic potential around the molecule at points on the electron-density contour surface. The red colour indicates a region where the energy of interaction between the molecule and a unit positive point charge (H^+) is attractive (its sign is negative). The blue colour indicates a region where the energy of interaction between the molecule and a unit positive point charge (H^+) is repulsive (its sign is positive).

Normal modes and vibrational frequencies of the water dimer, $(H_2O)_2$

Hydrogen bonding is primarily a favourable electrostatic interaction between two species, one contains a donor hydrogen; the other is the hydrogen-bond acceptor.

Select the Expert model building kit, **O** from the periodic table, the  button, and *click* in the main window. Then select **H**, the  button and *double-click* on the "top" (vertical) yellow valency of the water molecule. Finally, select **O**, the  button, and *double-click* on the unfilled valency of the *divalent* hydrogen of the water molecule to produce an initial structure for the water dimer. Do try to arrange for the dimer to have a plane of symmetry containing the atoms of the hydrogen-bond donor monomer and bisecting the HOH angle of the acceptor monomer. If you follow the above instructions exactly (and without moving the molecule while you are building it) then all should be correct. Perform an **Equilibrium Geometry** calculation, with **Frequencies**, just as you did for the water molecule, saving the job as (*e.g.*) **abc_H2Odimer**. Note the energy, the bond lengths and angles, and inspect the vibrational frequencies, just as for the water monomer.

Question 5

What is the energy (in a.u.) of the optimized water dimer?

What is the potential energy ΔE (1 d.p. in kJ mol^{-1}) of hydrogen bond formation in the gas phase? (*Hint*: compare the dimer energy with the sum of the energies of two separate water molecules. Since you are determining the small difference between two large numbers: take care not to lose accuracy by truncation of significant figures.)

In the light of the electrostatic potential you calculated previously for the water monomer, account briefly for the structure of the water dimer.

Consider the OH bond lengths in each of the HOH fragments of the dimer. Comparing these values with those of the monomer, what is the most significant difference?

What is the bond angle O–H⋯O between the hydrogen-bond donor and acceptor fragments?

Each atom in a molecule may, in principle, move in three independent directions, *x*, *y*, and *z*. A triatomic molecule such as H_2O therefore has $3 \times 3 = 9$ degrees of freedom. Of these, six correspond to motion of the molecule as a whole either along ("translation") or around ("rotation") the *x*, *y*, and *z* axes. The remaining three degrees of freedom are internal motions of the atoms in the molecule, and correspond to vibrations. The water dimer is a single entity containing six atoms; of its $6 \times 3 = 18$ degrees of freedom, six correspond to overall translational or rotational motion of the dimer, and the remainder correspond to vibrations.

Question 6

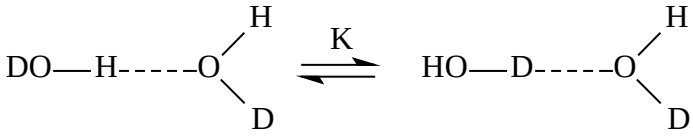
List the vibrational frequencies of the water dimer (to the nearest whole number).

By inspection of the vibrational modes, indicate which ones correspond to those of the component hydrogen-bond donor and acceptor fragments. Note the most significant difference in these frequencies caused by hydrogen bonding.

Provide a brief description of the motion in each of the vibrational modes that does *not* correspond to bending or stretching within a single H_2O fragment.

Isotopic substitution in the water dimer

Copy your optimised water dimer structure into two new files by using Save As with names such as "**abc_dimer_a**" and as "**abc_dimer_b**". For each of these dimers in turn perform the following. Select **Ball and Wire** and **Labels** from the **Model** menu. *Click* on either hydrogen atom of the hydrogen-bond acceptor fragment, select **Properties** from the **Display** menu, and on the drop down menu next to mass number, change the Mass Number to "**2 Deuterium**". Do the same for one of the hydrogens of the hydrogen-bond donor fragment. Check that the settings under **Calculations…** are the same as before (**Equilibrium Geometry**, **HF/3-21G(*)**, and **Frequency**) and **Submit**. Now repeat for the other new file, putting deuterium into the other position in the hydrogen-bond donor fragment. For each of the two possibilities, DO–H⋯OHD and HO–D⋯OHD, inspect **Output** from the **Display** menu.



For each of your two isotopically substituted water dimers, scroll down to the line reading "`Standard Thermodynamic quantities at 298.15K and 1 atm`". Note the values given for "`Free Energy (H-TS):`".

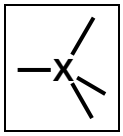
(The quantity given as "`....Total Enthalpy:`" is actually the sum of all the contributions to enthalpy *except* for the potential energy of the molecule; it would therefore be more accurate to label it as ($H° - E$). However, because the potential energy is the same for each of the two isotopic variants of the $(HOD)_2$ heavy water dimer, so $\Delta(H° - E) = \Delta H°$.)

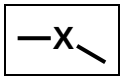
Now determine the Gibbs free energy change, $\Delta\mathbf{G}°$, for the equilibrium (*in the direction as shown in the equation above*) between the two "isotopomeric" forms of $(HOD)_2$.

> Question 7
>
> What is the value of the equilibrium constant (at 298K, 1 atm) for the equilibrium shown above? (Show your working.)
>
> Which position in the hydrogen-bond donor fragment does deuterium prefer to occupy in $(HOD)_2$?

[$K = \exp(-\Delta G°/RT)$, $R = 8.31\ J\ K^{-1}\ mol^{-1}$, $1\ kcal\ mol^{-1} = 4.184\ kJ\ mol^{-1}$]

Interconversion of water dimer structures



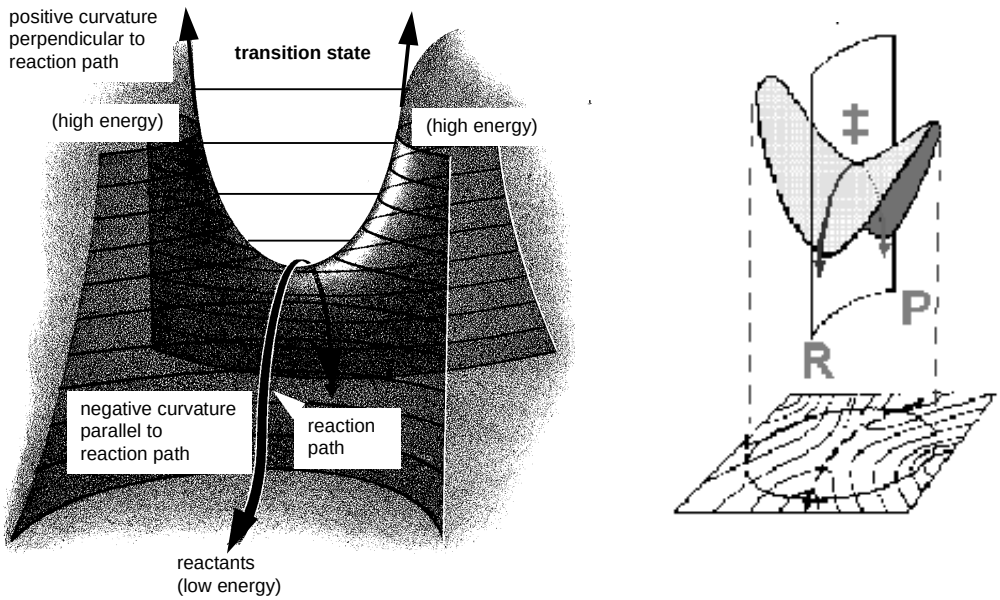


Select **New** from the **File** menu, and **Expert** from the **Fragment panel**. Select **C** from the periodic table and tetravalent **X** (see right), and *double-click* in the Builder window; select **O** from the periodic table and divalent **X** (see right), and *click* on two of the yellow unfilled valencies on carbon, then *click* one of the unfilled valencies on oxygen (*i.e.* three oxygens altogether). Select **Make bond** and click on both oxygen unfilled valencies in order to make a (distorted) four-membered ring. Select **Minimize** to obtain an initial trioxetane structure with C_{2v} symmetry. Now select **H** from the periodic table and divalent **X**, and *click* on both oxygens bonded to carbon. Finally, select select **O** from the periodic table, again, and tetravalent **X**, and click on the carbon. This procedure should produce a cyclic water dimer in which both hydrogens of one fragment are involved in hydrogen bonds to the other. **Minimize**, **Save As** a new name, **Submit** checking **Calculations…** are set to the same as before **Equilibrium geometry** from the menu to the right of "calculate", and select **Hartree-Fock** from the menu to the right of "with" and **3-21G(*)**. Once completed, submit again but checking **Frequency** under the column headed **Calculation**. (Sounds daft, but it should ensure that you obtain the correct answer when using SPARTAN ST.)

Inspect the frequencies and normal modes.

At the top of the list there should appear a frequency described as imaginary. This arises because the sign of Φ in the expression (see above, foot of page 2) for the frequency $\nu = (1/2\pi c)\ \Phi^{½}$ is negative: the square root of a negative number is an imaginary number. What does this mean? The quantity Φ_i is the force engendered in the molecule for a displacement of

unit length in the normal mode $\boldsymbol{q}_i$. A positive sign for Φ_i means that displacement away from equilibrium is met with a restoring force which tends to bring the molecule back to its equilibrium geometry; the potential energy rises as the atoms move along the normal mode away from the equilibrium geometry. A negative sign for Φ_i means that displacement away from equilibrium is accompanied by a force which tends to move the molecule further away from its equilibrium geometry; the potential energy decreases as the atoms move along the normal mode away from the equilibrium geometry.



The two diagrams above illustrate features of potential energy surfaces for a molecular species undergoing a chemical reaction, in terms of valleys and a mountain pass.

> Question 8
>
> What is the energy (kJ mol^{-1}) of this cyclic water dimer relative to the acyclic structure previously examined?
>
> List the value of the imaginary frequency and sketch the normal mode corresponding to it.
>
> How do the cyclic and acyclic water dimer structures correspond to features on the energy surface for the water dimer? What is the chemical significance of the cyclic structure?

Find your files from the "Conformational Analysis of Six-Membered Rings" exercise. Perform vibrational frequency calculations (at the Molecular Mechanics level) for *syn*-butane, boat cyclohexane, and "all-*syn*" cyclohexane, and inspect the results.

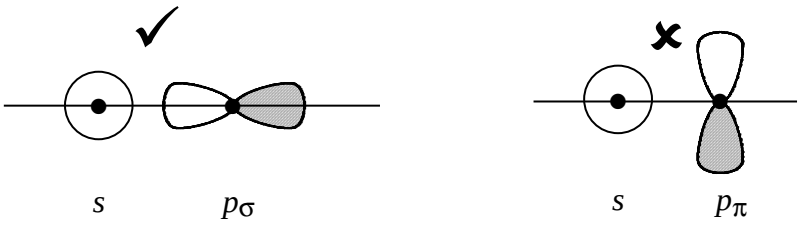
> Question 9
>
> Comment briefly upon how each of these three structures corresponds to either a valley, or a hilltop, or a mountain pass on an energy surface.

QUALITATIVE MOLECULAR ORBITAL THEORY

Two atoms may form a chemical bond if two atomic orbitals (AOs), one on each atom, combine to form a pair of molecular orbitals (MOs), one **bonding** and the other **antibonding**; if the bonding MO is occupied by a pair of electrons with opposite spins, and the antibonding MO remains unoccupied, the resulting molecule is lower in energy than the two separate atoms.

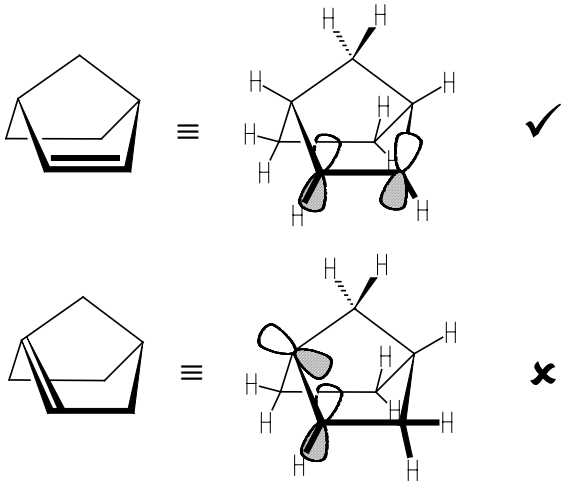
> Formation of a strongly bonding MO requires that the two AOs must:
> (1) be of the **same symmetry type**;
> (2) be of **similar energy**;
> (3) have a **strong overlap**.

Condition (1) means, for example, that a bonding MO may be formed by overlap of *s* and p_σ AOs, but **not** by overlap of *s* and p_π AOs.



Condition (2) means, for example, that a strong covalent bond may be formed by overlap between valence AOs (2*s* and 2*p*) of first-row elements (Li to Ne), but not between a 2*s* AO on Li and a 5*p* AO on I.

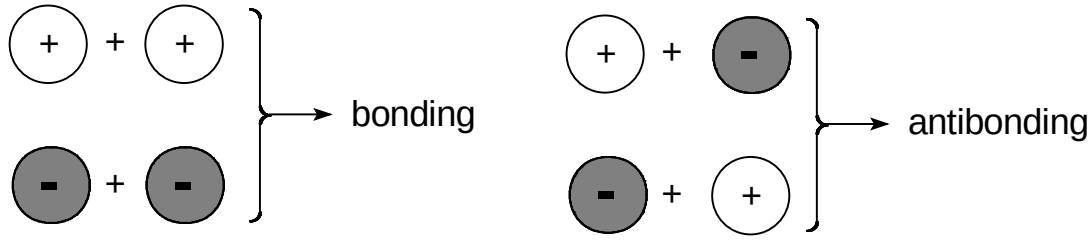
Condition (3) means, for example, that the p_π AOs of an alkene must be aligned with a dihedral angle close to zero degrees; twisting to larger dihedral angles reduces the strength of π-bonding, since the size of the overlap between the AOs diminishes. Thus the nearly perpendicular alignment of the *p* AOs in the second bicyclic alkene precludes formation of this isomer.

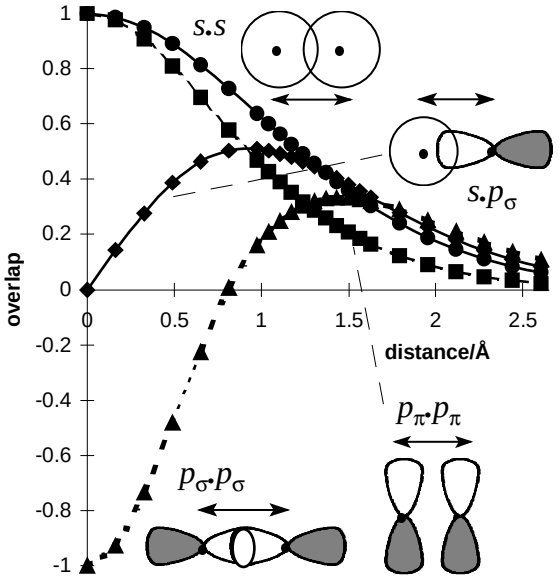


Remember that an AO is a wavefunction describing one electron in an atom. A wave has an amplitude and a **phase**; the latter is indicated mathematically by a sign (+ or –) or pictorially by an open or shaded lobe of the AO, as in the *p* orbitals shown above. The extent to which a pair of AOs overlap each other is measured by the value of their **overlap integral**. This is obtained by multiplying the values of the two AOs at every point in space and adding together all the products. If two AOs overlap perfectly – in the sense that they lie exactly on top of each other and have the same phase – their overlap integral has a value of +1. If the overlapping portions of the two AOs have different phases, the overlap integral has a negative value, which indicates

antibonding. A zero overlap means that the AO wavefunctions cancel each other out exactly. (Like the patch of calm water often encountered when the wakes of two motor boats cross in such a way that the peak of one wave coincides with the trough of the other.)

The phase of an AO is arbitrary, since the sign of the wavefunction varies with time, just like any wave. When two *s* orbitals overlap, as in the hydrogen molecule, only the relative phase of the one with respect to the other is important. Thus both + with + and – with – give rise to a bonding combination, whereas both + with – and – with + give rise to an antibonding combination. Note that the antibonding combination has a **nodal surface** between the two lobes of the MO; at every point on this plane the amplitude of the MO wavefunction is zero, meaning that the probability of finding an electron there is zero.





The diagram on the left shows plots of overlap integrals involving the various combinations of carbon 2*s* and 2*p* AOs as functions of the distance between the centres of the two orbitals. The overlap integral between two *s* orbitals is zero only at infinite separation, since the AO amplitudes tail off towards zero with an inverse exponential dependence on distance. Both the *s*/*s* and p_π/ p_π overlap integrals tend to a value of +1 as the distance between the two AOs decreases towards zero.

Question 1

(a) Why does the s/p_σ overlap integral tend to 0 at zero distance?

(b) Why does the p_σ/p_σ overlap integral tend to –1 at zero distance?

In this exercise you will discover how interactions between AOs affects the geometries of some simple molecules. You will use the SPARTAN program to perform molecular orbital (MO) calculations in order to determine molecular structures, energies, and MOs. We are not concerned at present with the theoretical details underlying these calculations; the program is being used as a tool, just as a spectrometer may be used to obtain a spectrum without the operator having any knowledge of the electronic gadgetry inside the instrument.

Getting started with SPARTAN:

To start, *click* on the **Start** button, then *click* on **Programs**, and finally *click* on **Spartan**. To quit, select **Exit** from file menu.

Molecular Orbital Shapes and Energies using SPARTAN

Ethene geometry optimisation

Select **New** from the **File** menu to enter the SPARTAN **Builder** window. Select the icon for trigonal sp^2 carbon (second from left in the top row of the **Fragment panel**) by clicking upon it with the left mouse button. Bring the cursor inside the **Builder** window and *click*. Trigonal carbon will appear on the screen with its unfilled valencies indicated by "yellow vectors"; if it appears "edge-on" you will need to rotate it (see below) in order to continue to build the structure. Now *click* again upon the double unfilled valence of the sp^2 carbon; a second trigonal sp^2 carbon will appear, with the carbons connected by a double bond. Unfilled valencies are automatically converted into hydrogen atoms upon exiting the builder.

At any stage during the building process, the molecule drawn in the work area can be rotated (middle mouse button, or middle mouse button with the **shift key** for rotation in the plane of the screen) or translated (right mouse button). It can also be enlarged or reduced in size (right mouse button with the **shift key**). If you discover that you have generated an unsatisfactory structure and wish to begin again, you may do so at any time by selecting **Clear** from the **Edit** menu. If you have a mouse with only two buttons, the function of the (missing) middle button is provided by pressing both right and left buttons together.

Select **Calculations…** from the setup menu. Select **Equilibrium Geometry** from the menu to the right of "Calculate", and select **Hartree-Fock/3-21G** from the menu to the right of "with". Click in the box between **Print** and **Orbitals**.

Check that **Charge** is **Neutral**, and **Multiplicity** is **Singlet** (the default settings) and change if necessary. *Click* on **Submit** at the bottom of the dialog box. In the **Save As** dialog box, give the filename for the job in the form "**abc_C2H4**" (where "abc" are your own initials) and *click* on **Save**.

Remove the message that appears on the screen by *clicking* on **OK**. The optimization will take only a few seconds for this small molecule. Once completed (a message will appear on the screen; *click* on **OK** to remove it), the optimized structure will replace the original structure from the Builder on the screen.

Now perform the following operations. Select **Distance** from the **Geometry** menu. *Clicking* on the two carbon atoms of the ethene molecule will result in each being marked with a yellow sphere, and the distance between the two being displayed in a box. An alternative is to *click* on the double bond.

Question 2

(a) What is the carbon–carbon bond length (Ångström, to 3 d.p.) in your optimised structure for ethene?

(You must state which MO model you have used, *e.g.* HF/3-21G.)

(b) Look again at the graphs of overlap integral *vs.* distance on page 2. Suggest a reason why the σ bond and the π bond of ethene have different bond energies.

Ethene molecular orbitals

Select **Surfaces** from the **Setup** menu. A **Surfaces** dialog box appears. *Click* on **Add…** and select **LUMO** from the Surface menu, and check that **Property** = **none**. (If you are using SPARTAN ES, also check that **Resolution** = **med**.) *Click* on **OK**; the line "LUMO pending" appears in the text box. Now *click* on **Add…** again, this time selecting **HOMO** from the Surface menu, and repeat. Then select **HOMO{**–} and **1** and repeat. [If you make a mistake, *click* on the line describing the unwanted surface (it will then be highlighted), and then *click* on **Delete**.] Continue to select and **Add** all the orbitals from **HOMO**–**2** to **HOMO**–**5** to the list of MOs to be displayed. Finally, select **Submit** from the Setup menu. When the calculation is complete, select which orbital you wish to display by *clicking* on the appropriate line in the Surfaces dialog box. You may change the appearance of the MO surface by selecting **Properties** from the **Display** menu, and then *clicking* on the orbital itself. You might want to select **Transparent** from the Surface Properties dialog box that appears. To display another orbital, turn off the first orbital by *clicking* on the appropriate entry in the Surfaces dialog box and then select the new orbital. Each orbital may be rotated into a convenient view using the left mouse button. The red and blue regions represent the different phases of the lobes of each orbital.

To inspect the MO energies, select **Output** from the **Display** menu. You can scan the output from the MO calculation by *scrolling* with the vertical bar to the right-hand side. The information at the "top" of the output file includes the number of electrons in the molecule. Ethene possesses a total of sixteen electrons, so the highest occupied molecular orbital (HOMO) is the eigth MO and the LUMO is the ninth. The `Closed-Shell Molecular Orbital Coefficients` are printed out midway down the output file, in columns, five or six at a time; the orbital energy (**Eigenvalue**) appears at the head of the column in atomic units and beneath in electron-volts (1 eV = 96.5 kJ mol^{-1}). Inspect the MOs for ethene, from that of lowest energy through to the LUMO, and decide which are σ and which are π. (Be careful: these labels refer simply to whether the MO is symmetric or antisymmetric with respect to reflection across the molecular plane.)

> Question 3
>
> Tabulate the molecular orbital energies (in eV), indicate whether each is σ or π, and note how many nodal planes each possesses.
>
> Comment qualitatively upon how the MO energy is related to the σ or π character of the orbital and to the number of nodal planes separating the lobes of the orbital.

The H_3^+ cation

Select **New** from the **File** menu, *click* on the **Expert** button; select "H" from the periodic table, and divalent "–•\" from the list of bonding options (make sure you have the *bent* option, not the linear one "–•–"). Select **Calculations…** from the Setup menu, **Equilibrium Geometry** from the menu to the right of "Calculate", **Hartree-Fock/3-21G** from the menu to the right of "with", and check the box between Print and Orbitals. Check that **Multiplicity** is **Singlet** and **Total Charge** is **Cation**. **Submit**, and **Save As** with an appropriate filename (*e.g.* **H3_plus**). After completion of the calculation, use the tools (**Distance**, **Angle**) from the **Geometry** menu to determine the optimised geometrical parameters of the molecule. (*Hint*: don't only check the two bond lengths and one bond angle displayed; is the molecule really symmetric?)

Note the total energy (in atomic units; 1 a.u. = 2625 kJ mol^{-1}) for the optimised structure of the H_3^+ cation in **Properties** from the **Display** menu. Check the MO energies (in eV) towards the bottom of **Output** from the **Display** menu and note the values of the first three orbitals. **Save** the **H3_plus** file.

(N.B. Surprisingly, perhaps, there are six MOs listed for this species. The last three have very high energies and have no physical role; they arise because the 3-21G basis set has two "basis functions" to represent each 1s(H) AO instead of just one.)

The aim of the next section of the exercise is to explore how the total energy and the HOMO and LUMO energies of the H_3^+ cation vary as the angle at the central H atom is changed. You should do this by performing an **Energy Profile** calculation. Select the **Constrain Angle** icon from the toolbar, *click* on the each of the three atoms (in the order: end, centre, other end), and *click* on the padlock icon in the bottom-right corner. Now *click* on the purple angle constraint marker beside the molecule, and select **Properties** from the Display menu. *Click* alongside **Dynamic**, and *enter* **Values** from **50°** to **180°** in **14 Steps**; close the **Constraint Properties** dialog box. Select **Energy Profile** in **Calculations…** from the Setup menu, using **Hartree-Fock/3-21G**, **Cation** and **Singlet**; then **Submit**. Close **H3_plus**, and upon completion of the job, open the new file **H3_plus.Profile**. Select **Spreadsheet** from the Display menu, *click* on the icon, *click* on the three atoms as before, and click on the icon in the bottom-right corner in order to enter the values of the angles against the molecules. *Click* on `Molecule001` and then *click* on **Sort**. Now *click* on the header cell of the next free column, then *click* on **Add…**, and select **E** in units of **au**. Similarly, **Add… E HOMO** and **E LUMO**, each in units of **eV**. Finally select **Plots…** from the Display menu, select **Angle** on the **X Axis** and **E**, **E HOMO** and **E LUMO** together (while depressing the **Shift** key). You can change the colour of the background to white by selecting **Colors** from the **Options** menu, and moving each of the Red, Green and Blue sliders to 100%. You may **Copy** the plot from SPARTAN and **Paste** it into WORD. Alternatively, you could copy the contents of the spreadsheet into EXCEL and produce your own plot using the Excel **Chart Wizard**.

Question 4

(a) Show the plot of total energy, and HOMO and LUMO energies against bond angle.

(b) Comment qualitatively upon how the total energy E, the HOMO energy, and LUMO energy vary with the bond angle between bent and linear geometries.

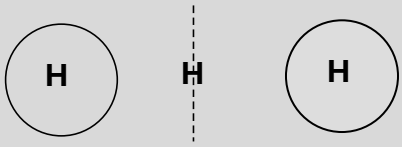
(c) What is the optimum geometry for the H_3^+ cation? (Quote bond lengths to 3 d.p. and bond angles to 1 d.p.) Comment upon any difference you notice between the results of the constrained energy profile and the equilibrium geometry calculations in the light of the total energies obtained.

Now you should take a closer look at the LUMO and LUMO+1 orbitals as the molecule passes through the 60° angle. From the energy profile, right-drag a rectangle around each of the structures at 50° and 70° in turn, and **Copy** and **Paste** them into new files. For each one, **Add… LUMO** and **LUMO+1** from **Surfaces** under the Setup menu; select **Single Point Energy** in the **Calculations** dialog box, check **Print Orbitals** and **Submit**. Inspect each orbital in turn using **Surfaces** from the Display menu, compare with the same two orbitals for the 60° structure, and consider the orbital energies (in **Display Output**) carefully.

Question 5

(a) Sketch the forms of the three MOs (HOMO, LUMO and LUMO+1) for the 60° and 180° structures in terms of the contributions of the individual AOs; note the relative phases of the contributing AOs and the presence of any nodal plane(s). (Copies of the MOs from Display Surfaces are *not* required.)

e.g.



(b) Account qualitatively for the trends noted in Q5 in terms of the changing forms of the HOMO and LUMO determined for the optimum geometry and for the linear structure.

(Hint: *consider how the overlap between the AOs changes with angle.*)

(c) What happens to the LUMO and LUMO+1 as the HHH angle passes through 60º?

The H_3^- anion

The final part of the exercise is to perform a similar investigation for the H_3^- anion. Essentially you should repeat everything you have done for H_3^+ but using a **Total Charge** = **Anion**, with **Hartree-Fock/3-21G** and **Singlet**. However, it is also necessary to constrain the HH bond lengths at the (equal) values they have for H_3^+. Run your energy profile from 75° to 180° in 8 steps, and plot the total energy, HOMO and LUMO energies against the HHH angle, as before.

Question 6

(a) Show the plot of total energy, and HOMO and LUMO energies against bond angle for the H_3^- anion.

(b) How is the H_3^- HOMO related to the H_3^+ LUMO? Comment qualitatively upon the relationship between the total energy for H_3^- and the HOMO energy for the anion as functions of the bond angle.

Question 7

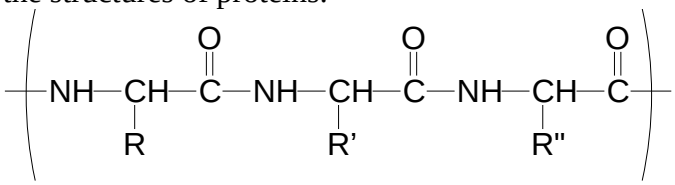
By generalising your results, suggest how a qualitative consideration of the variation of the MO energies with geometry for a molecule HAH (A = Be to Ne) could be used to predict the preferred geometry for any particular $(HAH)^q$ species (where q is the charge).

Hint: you are discovering for yourself what is known as Walsh's Rule!

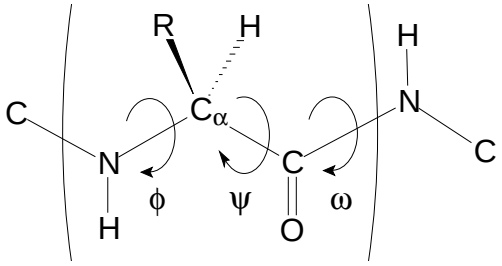
CONFORMATIONAL ANALYSIS OF PEPTIDES

Introduction

Peptides are chains of amino acids linked together by amide bonds between the $–NH_2$ of one amino acid and the $–CO_2H$ group of the next. A protein is a polypeptide comprising more than about 50 amino acids. You can read more about the chemistry of amino acids and peptides in chapter 25 of Jones (2nd ed.). In this practical we will cover some of the basic conformational properties of peptides that determine the structures of proteins.



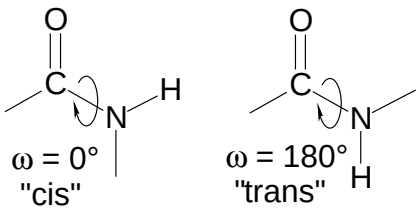
This segment of a peptide contains three amino acids with different side-chains R, R', and R". The middle carbon of the amino acid (the C of CH(R)-) is named the C_α carbon; this is a crucial atom in defining the conformations of peptides. The carbonyl group (C=O) and secondary amine group (NH) are the other constituents of the peptide backbone; the C=O carbon and the NH nitrogen are also important atoms for defining peptide conformations.



The conformation of the peptide backbone is determined by the three torsion angles, as shown on the left.

ϕ (phi) = dihedral angle $C–N–C_\alpha–C$
ψ (psi) = dihedral angle $N–C_\alpha–C–N$
ω (omega) = dihedral angle $C_\alpha–C–N–C_\alpha$

These dihedral angles have values of 0° for the *syn* conformation of the four-atom chain that defines it, and 180° for the *anti* conformation. Note that the amide bond is often labeled as being *cis* or *trans*, as shown here.



Other groups mentioned in this practical are the acetyl group ($CH_3–CO–$) and the methylamide group ($CH_3–NH–$).

Ramachandran Map

One of the very first calculations of peptide and protein conformation was performed by the Indian group of Ramachandran, who studied rotation through 360^o of the two main flexible torsion angles ϕ and ψ of the peptide backbone. In this exercise you will perform a similar calculation using the MMFF molecular mechanics method in SPARTAN ESSENTIAL EDITION (ES). Remember to save your work frequently in case of computer problems.

Building the blocked alanine residue

Select **New** from the **File** menu to enter the SPARTAN Builder window. Select the **Pep.** tab from the model kit on the right of the screen, select **Ala** from the palette of amino acids, and *left-click* in the the main viewing window. As we wish to investigate the conformations of alanine as part of a peptide chain, we need it to be preceded and succeeded by amide groups. To approximate this we add an acetyl (CH_3CO) blocking group to the *N*-terminus and a methylamino (CH_3NH) blocking group to the *C*-terminus, as follows. Select **Gly** from the amino acid model kit; *click* on the yellow free valency attached to the nitrogen atom of the alanine fragment, and *click* again on the yellow free valency attached to the carbonyl carbon atom. Now **Delete** the unwanted carbonyl C and O atoms from the end of the glycine fragment you have just added, and the unwanted N atom from the

end of the other glycine fragment you added first. Select **View** to complete the building of the blocked alanine amino acid, $CH_3CO–NH–CH(CH_3)–CO–NHCH_3$.

In principle, the conformational energy surface of this molecule could be explored completely by computing scanning each of the two torsion angles ϕ and ψ over the range from 0º to 360º. However, SPARTAN does not allow us to do this simply to obtain a 2D energy contour map. Instead, you should perform a series of constrained energy minimisations for a set of nine selected points, with the following pairs of (ϕ, ψ), using the same procedure for each conformation.

Point #:	1	2	3	4	5	6	7	8	9
(ϕ , ψ):	120, 120	–120, 120	0, 0	–70, 60	70, –60	0, 180	180, 0	60, 0	-60, –60

Select **Measure Dihedral** from the **Geometry** menu, or its toolbar icon. Select **Labels** from the **Model** menu. Select the following four atoms: **C, N, CA, C**; these define the ϕ torsion angle of the blocked peptide. Specifically these are the carbonyl C of the CH_3CO, the amide N, the C_α (CA) carbon, and the C of the second carbonyl group. Type in a value for the dihedral angle ϕ. Repeat for **Constrain Dihedral**: *click* on the padlock icon in the bottom-right corner to close it. Now select the four atoms: **N, CA, C, N**; these define the ψ torsion angle. Specifically this is the amide N of the alanine residue, the C_α (CA) carbon, the C of the second carbonyl group, and the second amide N in the $NHCH_3$ group. Use **Measure Dihedral** and **Constrain Dihedral** to set the value of and constrain this angle.

Now prepare for each of the energy calculations. Select **Calculations** from the **Setup** menu, **Equilibrium Geometry** and **Molecular Mechanics**. Check the **Constraints** box to the right of **Subject to:**, the **Freq.** box labeled in the list to the right of **Compute:**, and the **Thermodynamics** and **Atomic Charges** boxes in the list to the right of **Print:**. Now **Submit** and **Save** with a suitable name on your H: drive. Once the calculation has completed, select **Properties** from the **Display** menu and note the value of **Energy**. Also measure the hydrogen bond distance between the carbonyl O of the $CH_3C=O$ group and the amide H of the $NHCH_3$ group.

Repeat this procedure for each of the nine conformations listed above and note the data required to answer Question 1 below.

Vibrational modes of the blocked amino-acid

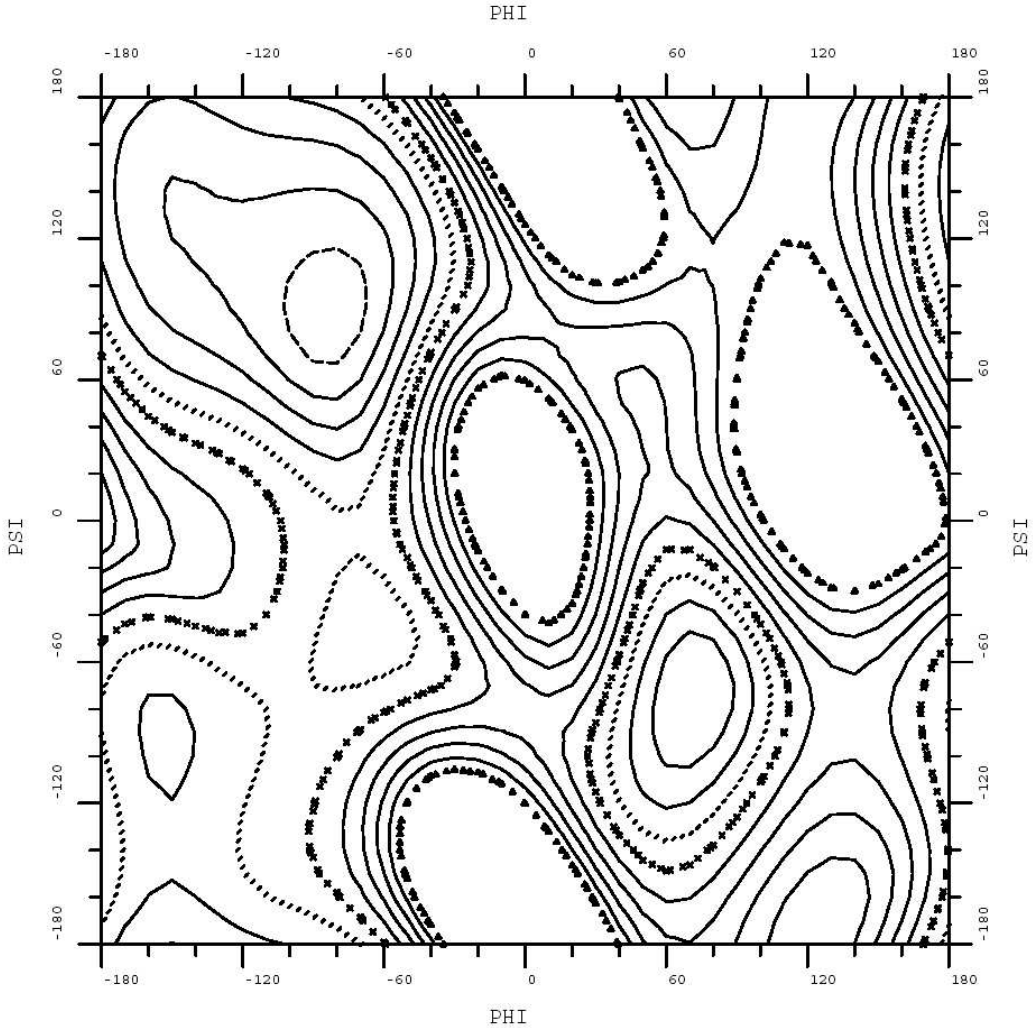
Now select the **Vibrations** entry of the **Display** menu. A new dialog box opens which contains a scrollable list of items labeled at the top **Frequency**. These are the vibrational modes for the molecule in this conformation. The frequencies are listed from lowest (smaller numbers) to highest (larger positive numbers). Select the yellow box next to a frequency. The molecule will start an animation of the motion of the molecule when exited by this frequency. (The animation is stopped by clicking on the same frequency yellow box again.) These frequencies correspond to motions that are excited by exposing the molecule to infra-red radiation and the frequencies are measured in reciprocal centimetres, exactly as measured by the infra-red spectrometer. Explore the motions of this conformation of this molecule, in particular selecting some low frequencies and some high frequencies. Note that for the low frequencies you may be able to see the motion better by increasing the value in the **Amp.** field of the **Vibrations** dialog. In Question 3 you are asked to comment on these motions for selected conformations of the 9; it is easier to do this as you calculate each conformation, rather than just getting the energies for Question 1 and then having to redo the calculation for Question 3.

Question 1.

For the ϕ and ψ angles specified below, find the energy of these points and the distance between the carbonyl oxygen of the acetyl group and the amide hydrogen of the methylamide group - the hydrogen bond length. Make a table of these values converting the energies to relative values by subtracting the lowest energy of all of these points (which therefore will become 0). Convert all energies from kcal mol^{-1} to kJ mol^{-1}.

(ϕ,	ψ)	Energy/kcal mol^{-1}	Rel energy /kJ mol^{-1}	C=O···H–N distance/ Å
120º	120º			
–120º	120º			
0º	0º			
–70º	60º			
60º	–70º			
0º	180º			
180º	0º			
60º	60º			
–60º	–60º			

The Ramachandran ϕ,ψ map for alanine



Solid contour lines —— are at 6.7, 10.9, 15.0, 27.6, 31.8, 36.0, 40.2 kJ mol^{-1}.

Dotted line …… is at 2.5 kJ mol^{-1}.

Dashed line ----- is at 19.2 kJ mol^{-1}.

Crossed line ×××××× is at 23.4 kJ mol^{-1}.

Triangles line ▲▲▲▲ is at 44.3 kJ mol^{-1}.

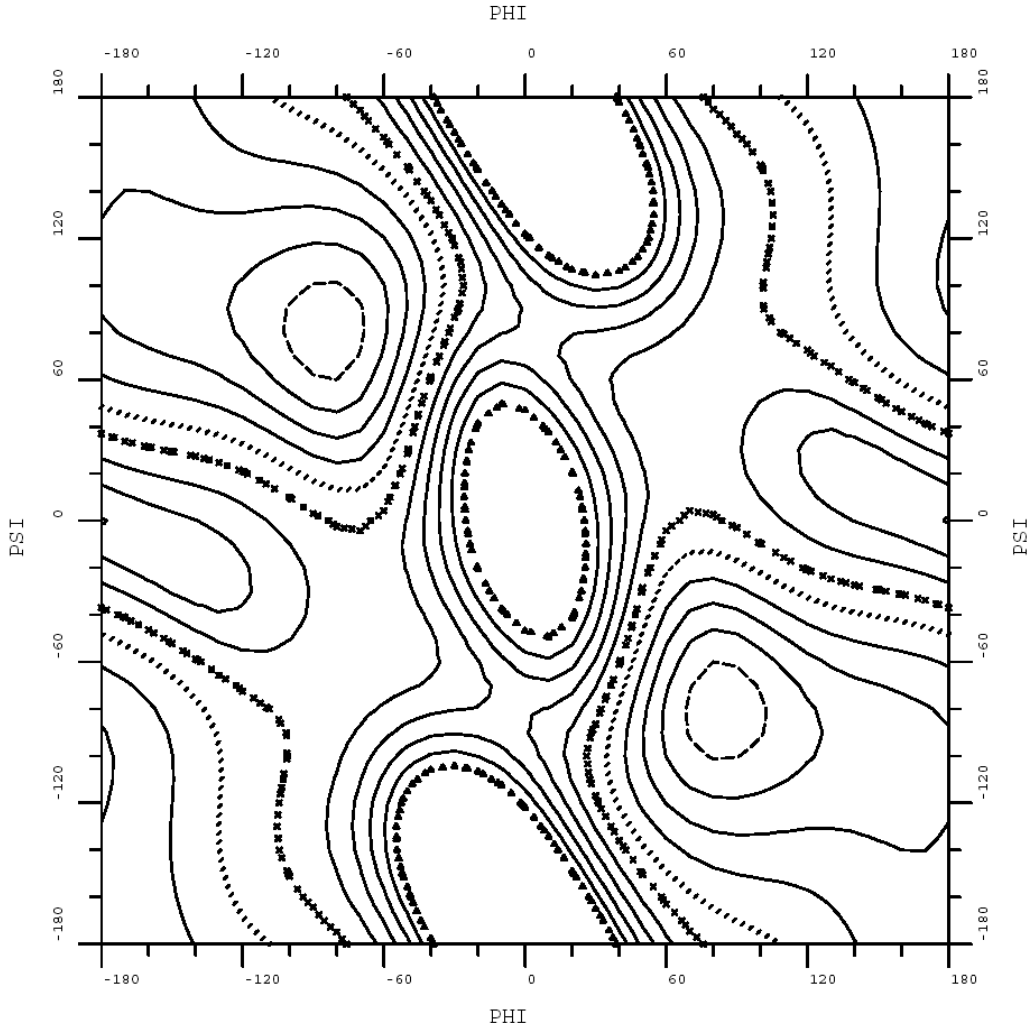
Features of the ϕ,ψ map

The notable features of the ϕ, ψ maps for amino-acids are the high energies found down the centre line of the map and the major low energy region seen in the upper left-hand area of the map. The high energy found at the centre of the map is due to steric clashes between a carbonyl O and an amide N of the two amide groups. As any residue in a peptide chain will have these *N*- and *C*-terminal amide groups this region of the map is the same for all amino-acids and prevents any peptide or protein from having such a conformation ϕ and ψ both approx. 0. The main low energy centre in the upper left-hand region of the map is the lowest energy minimum of the map and represents the most favourable conformation for amino acids. Residues in the *sheet* secondary structure of proteins have ϕ, ψ angles that fall in this region of the map.

Conformational analysis of blocked glycine

Now repeat this whole exercise for blocked glycine, by replacing Gly for Ala in the procedure detailed above for blocked alanine.

The Ramachandran ϕ,ψ map for glycine



The contour levels in this plot are as for the alanine map.

Question 2.

a. What is the main difference between the Ramachandran maps for blocked alanine and for blocked glycine?

b. Account for the difference between the two maps in terms of the chemical structure differences between the two molecules.

For question 3 restrict the conformations chosen to -70,60 and -60,-60.

Question 3.

a. Describe the motion of the highest frequency (e.g. is it a bond vibrating, an angle bending, a torsion angle rotating,or a global motion of the whole molecule).

b. Describe the motion of the lowest frequency.

c. For which of the two conformations does the lowest frequency motion appear more constrained.

d. Which of the two conformations has the lowest frequency?

Poly-alanine Conformation and Vibrational Modes

In this phase you will build a 16-residue polypeptide made of all alanine residues. Select **New** from the **File** menu to enter the SPARTAN **Builder** window. Select the **Pep.** tab from the model kit, and select **Gly**. Ensure that the label α **HELIX** is selected, and *left-click* in the main viewing window. Now add an **Ala** residue to the carbonyl C of glycine residue, and then extend the peptide chain with another 15 alanine residues, adding each one to the same C-terminal end. Finally add another **Gly**. Now **Delete** the *N*-terminal amide N and the C-terminal carbonyl O, as you did before for blocked alanine itself. This has created a blocked poly-alanine molecule in the α-R helical conformation, or helix conformation for short. Now prepare for each of the energy calculations. Select **Calculations** from the **Setup** menu, **Equilibrium Geometry** and **Molecular Mechanics**. Ensure that the box labeled **Constraints** is *NOT* checked. Check the **Freq.** box labeled in the list to the right of **Compute:**, and the **Thermodynamics** and **Atomic Charges** boxes in the list to the right of **Print:**. Now **Submit** and **Save** with a suitable name on your H: drive.

Once the calculation has completed (it may take a little while), select **Properties** from the **Display** menu and note the value of **Energy**. Record the dipole moment of the molecule, which you may find by scrolling through the **Output** under the **Display** menu looking for the line "Dipole Moment:". Explore the low-frequency vibrational motions of this conformation.

Now repeat this whole build procedure except that instead of ensuring the α **HELIX** button is pressed, click the **OTHER** button and enter 60.0 in the box labeled ψ and −70.0 in the box labeled ϕ. This generates a conformation for each alanine amino acid that is the lowest energy point of the ϕ, ψ map for the blocked amino acid (see Question 1.). Compute the energy and vibrations and record the energy and dipole moment as previously. If the calculation gives an error indicating the run has failed, look in **Output** for a message like "RUN OUT OF CYCLES" (or similar). If so, change the entry labeled **Start from:** from **Initial** to **MMFF Conformer** in the **Calculations** dialog under the **Setup** menu, and **Submit** the calculation again.

Question 4.

a. Which is the more stable conformation of ~70, 60 and ~60, ~60 for the single blocked amino acid?
b. Which is the more stable conformation of ~70, 60 and ~60, ~60 for the 16 amino acid polymer?
c. Suggest a reason for the extra stability of the more stable conformation of the 16 amino acid polymer.
d. Describe the 3 lowest frequency motions of the helical conformation ~(60, ~60).
e. Which of the two conformations is the more constrained?

Using *RasMol* to look at Protein Structures

There are two main experimental methods for determining protein structure, X-ray crystallography and NMR. The Protein Data Bank (PDB) was setup in the USA to provide a central place for the deposition of protein structures created by scientists for the distribution to other scientists. Currently there are something like 16,000 structures available in this database, and most scientific journals that publish papers on the determination of a protein structure make it a requirement that a copy is lodged with the PDB. The PDB is currently run by the RCSB organisation and the whole database is available via the WEB. We will use the PDB database to download some sample protein structures and view them with the RASMOL program. This program is available under drive **G:** in the directory **rasmol**.

Using your favourite browser, go to the page **http://www.rcsb.org/pdb/**. This is the main starting page for the PDB. In these examples you will be given the PDB ID number which can typed straight into the **Search the Archive** box on this page.

The first protein you should look at is myoglobin, one of the first protein structures solved. This is an oxygen carrying protein found in the blood of mammals, in this particular case the sperm whale. It is similar in function and structure to haemoglobin. In the main RCSB page type **1MBD** in the search box and click in the **Find a Structure** box. The page will change to a list of entries found, find the entry labeled **1MBD** and click on the **EXPLORE** link. A new page appears describing this specific structure. To the left of the page is a list of links, one of which is labeled *Download/Display File*. Click on this link. The new page that appears is split into 2 sections, **Display the Structure File** and **Download the Structure File**. Look at the **Download the Structure File** section, in the table of formats and compression click on the **X** in the first leftmost box, labeled **none** for compression horizontally and **PDB** vertically. A pop-up window will appear asking where you want to save this file, which can be either the **C:** drive or your **H:** drive. Save the under the name given. Now activate the RASMOL program. Under the **File** menu item *click* on **Open** and in the file selection box that opens find the file you just saved and click on **OK**. You should see a so-called **wireframe** view of the chosen protein structure. Explore the various views in the **Display** menu. In particular the **Spacefill** view type displays the protein structure as spheres which represent the van der Waals radii of the atoms, and show how proteins are close packed structures. Another important display is the **Strands** which displays the backbone as a ribbon emphasising the conformations of the residues. This should be used in conjunction with the **Structure** item of the **Colours** menu, which colours the helix conformation purple (magenta) and the sheet conformation yellow. Myoglobin is an example of a protein in the *all-helical* class as most of its residues are in the helix conformation and there are no residues in the sheet conformation.

We will now look at a protein from the immunoglobin family, the antibodies, which are part of the immune system. Follow the procedure above to download and view the protein with PDB ID **1MCP**. This protein is an example of a sheet protein with most residues in the sheet conformation.

The third protein to look at is Dihydrofolate Reductase, PDB ID **3DFR**. This is an example of proteins that have both the helix and sheet conformations in their structure, the so-called mixed proteins.
Finally, download the **1TIM** structure, an example of a mixed structure protein with alternating helices and sheets in a so-called barrel motif. Structures of this type (the most frequently occurring protein structure style in the PDB database) are called TIM barrels.

Question 5.

Go to the RCSB home page (**http://www.rcsb.org/pdb/**) and click on the **Searchlite** link. Type in a word relating to a protein name, disease or biological organism you have come across and perform a **Search** on the PDB. Having found a PDB ID, download the structure and answer the following questions. The protein must be different from one of above 4 examples.

(a) Record the PDB ID.

(b) Record the Resolution and R-Value of this structure if it is an X-ray structure; otherwise note that it is an NMR structure.

(c) Count and record the number of helices and sheet strands.

(d) Determine if the protein is an all-helix, all-sheet or mixed helix/sheet structure.

Introduction to Molecular Dynamics

Molecular dynamics is a powerful method for exploring the structure of solids, liquids and gases. Though a very modern method, requiring computers, it would not have appeared strange to Isaac Newton, the founder of modern physical science. The idea is a simple one: calculate the forces acting on the atoms in a molecular system and analyse their motion. When enough information on the motion of the individual atoms has been gathered, it is possible to deduce the bulk properties of the material. These properties include the structure (*e.g.* crystal structure, predicted x-ray and neutron diffraction patterns), thermodynamics (*e.g.* enthalpy, temperature, pressure) and transport properties (*e.g.* thermal conductivity, viscosity, diffusion). In addition molecular dynamics can be used to investigate the detailed atomistic mechanisms underlying these properties and compare them with theory. It is a valuable bridge between experiment and theory.

You will use the Molecular Dynamics program DEMOCRITUS, which was written by A. S. Côté, W. Smith and P.J. Lindan (CCLRC Daresbury Laboratory, Daresbury, Warrington), to control the motion of a group of atoms. In addition, you have the ability to change the temperature and the density, and study the effects this has to the system.

All of the information you need to run the program, the program itself, eight tutorials and the background theory are available in a series of `html` pages. We would like to work through the tutorials, although we want you to answer the questions below as you go though the experiments

Actions:

1. Start the viewer and you will see a molecular dynamics simulation in progress. You can vary the Temperature and Density. You can ask the program to generate some graphical data from the simulation. These include:
   (a) RDF, Radial Distribution Functions
   (b) MSD, Mean Square Displacements
   (c) VAC, Velocity Autocorrelation Function
2. Work your way through the experiments, enter the data on the attached sheets and for the 'write-up' provide answers to the questions given below.

Opening the viewer

1. In the computer lab, follow the instructions given by the demonstrators.

   OR (from anywhere on campus)

   a. Open the internet browser at http://internal.bath.ac.uk/~chsscp/teach/md.bho
   b. *Double-Click* on Copy of Democritus.html and then Experiments to begin running the program from its current location

   OR (from anywhere on campus that does not have "Java 2 runtime environment" installed.

   a. Open the internet browser at http://internal.bath.ac.uk/~chsscp/teach/md.bho
   b. *Double-Click* on the self-extracting zip md ZIP File.exe. Run the program from its current location. An authentification window will open, click on YES. When you get the 'self extracting archive' box, change the top line to H:\md
   c. Open the windows explorer, find the directory H:\md and double click on md.bat. Note: if the program freezes, close the viewer down and re-open by clicking on md.bat.

To Learn about the background and theory go back to your browser and *double click* on Democritus.html then Experiments

Hand-in the answers to the following questions:

1. Condensation

a. What is the condensation experiment attempting to show?

b. After drastically cooling the sample record the time, number of clusters, cluster size, typical shape on the DATA SHEET (1) – approximately, every two minutes.

c. Comment on the evolution of the size and shape as a function of time, including for example, whether they are the same shape for the same size? Are the shapes much as you would have predicted?

CONDENSATION DATA SHEET (1)

time	number	size	Shape

2. RDF

a. How does an RDF (radial distribution function) differ between a solid, liquid and gas?

b. Why does the RDF not go through the origin?

c. Choose 3 different conditions of density and temperature and record these with the positions of the peaks in RDF in DATA SHEET (2)

d. Suggest what state of matter is your simulated material in.

RDF - [1]DATA SHEET (2)

Expt1		**Expt 2**		**Expt3**	
Conditions		**Conditions**		**Conditions**	
R	**G(r)**	**r**	**G(r)**	**r**	**G(r)**

[1] Signed _____

3. MSD

a. Choose a minimum of three different temperatures at a fixed density and estimate the slope of the MSD from the screen (time is in fs). DATA SHEET (3)

b. The slope of the MSD represents the diffusion constant (rate constant for diffusion). Assuming the Arrhenius equation estimate the activation energy for diffusion of the particles.

c. Comment of the results obtained.

MSD - DATA SHEET (3)

Expt 1		**Expt 2**		**Expt3**	
Conditions		**Conditions**		**Conditions**	
Slope		**Slope**		**Slope**	
Comment					
Expt 4		**Expt 4**		**Expt 5**	
Conditions		**Conditions**		**Conditions**	
Slope		**Slope**		**Slope**	
Comment					

[2]Signed _____

4. PRESSURE

a. Perform the relevant experiments,

b. Record Pressure versus Density - DATA SHEET (4)

c. Record Pressure versus Temperature - DATA SHEET (4)

d. Use the data in the DATA SHEET (4) to generate plots *via* EXCEL.

e. Comment on the deviation, if any, from the behaviour of a perfect gas, i.e. where it is evident and the reasons.

PRESSURE - DATA SHEET (4)

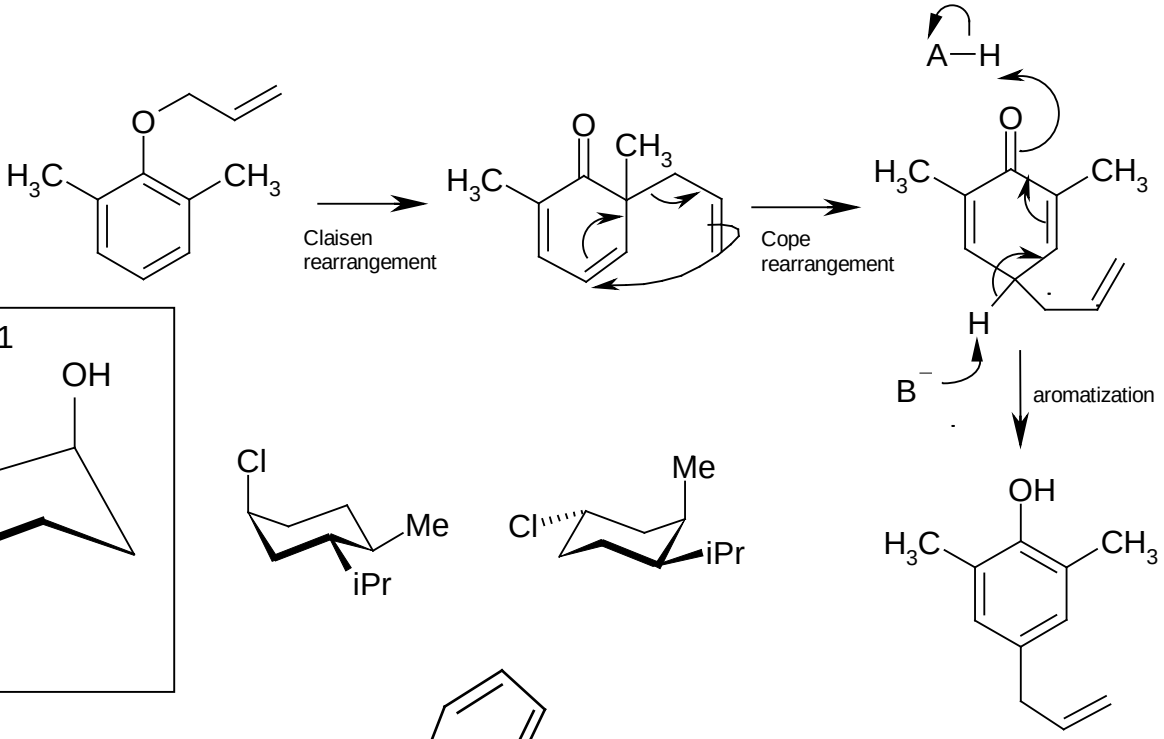
Density/Pressure		Temperature/Pressure	
Conditions		Conditions	
Density	Pressure	Temperature	Pressure

[a] [3]Signed _____

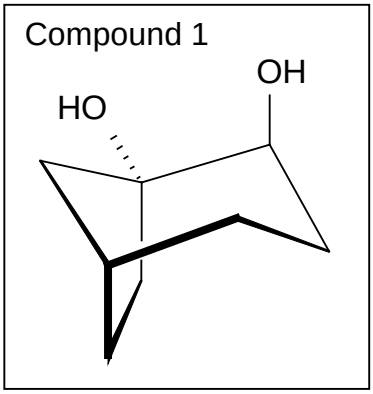
ISIS/Draw Exercise **YOUR Name: ……**

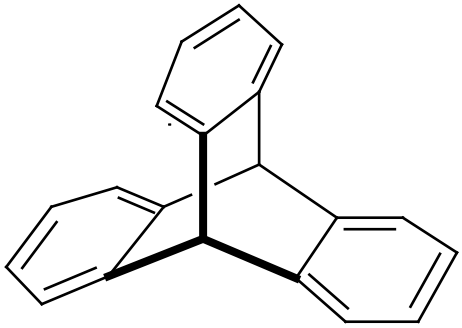
Draw the structures and reactions on this sheet using ISIS/Draw; copy and paste into a Word document (using text boxes where necessary); email as an attachment to chsihw@bath.ac.uk

Reaction 1

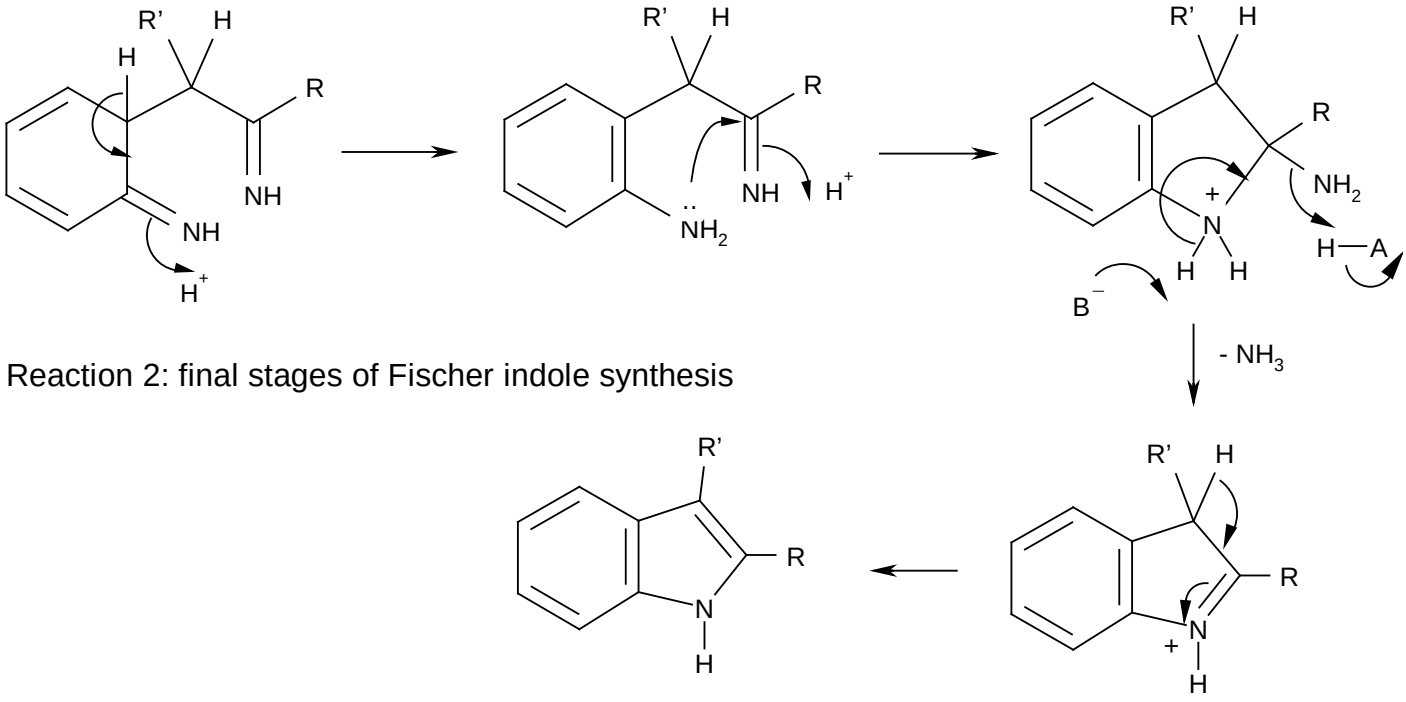


Compound 1





Reaction 2: final stages of Fischer indole synthesis



Beilstein/Gmelin Exercises *Name*……..

Question 1 - Fact Search

What is the molecular weight of **Ferrocene**?

Question 2 - Fact Search

a) What is the decomposition temperature of **$Zn(N_3)_2$**?

Question 3 - Fact search

What is the IR spectral peak range for $[Mo(CO)_4(PPh_3)_2]$ in the solvent methylene dichloride?

Question 4 - Fact search

Find a method for the preparation of **1,3-adamantanedicarboxylic acid** from the reactants **formic acid** and **adamantane**.

a) What is the yield of the product?

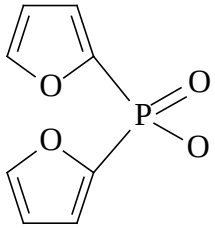
b) Give the literature reference where you would find details of this reaction.

Question 5 - Fact Search

Give a reference to an article where you will find the solubility of **benzocaine** [also called **4-amino-benzoic acid ethyl ester**] in pure **ethanol**.

[HINT: The field name for solubility of a solute in a solvent is: **SLB.SOL**]

Question 6 - Structure Search



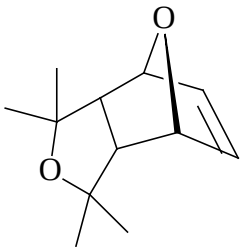
Construct the following molecule:

Search for the molecule "as drawn"
(*i.e.* fully saturated with hydrogens).

a) What is the name of this compound?

b) What is its melting point?

Question 7 - Substructure Search



Construct the following molecule:

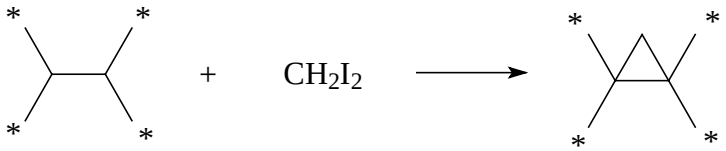
Do a substructure search, to find **any substituent** on **any of the carbon** atoms.

a) How many compounds did you find?

b) What is the name of the first compound?

Question 8 - Reaction search

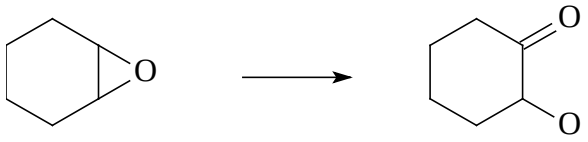
This is an example of the Simmons-Smith reaction:



a) How many reactions of this type can you find?

b) Look at the first 10 reactions. What reagent is most commonly used in this reaction?

Question 9 - Reaction search



Draw the reaction:

a) What are the names of these two compounds?

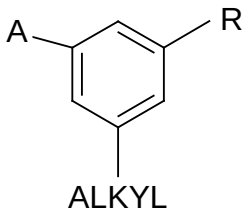
b)You should find two reactions. For the first reaction listed, the yield is 59%. What is the reagent used, and what is the solvent?

c) Give the literature reference where you would find details of this reaction.

Question 10 - Generic Search

You wish to search for a 1,3,5 substituted benzene, where one substituent is an **alkyl group**, one substituent is a **hydroxyl**, **thiol** or **amine** and the other substituent is a **carboxylic acid**, **nitrile** or **nitro** group.

A = OH, SH or NH
R = COOH, CN or NO_2



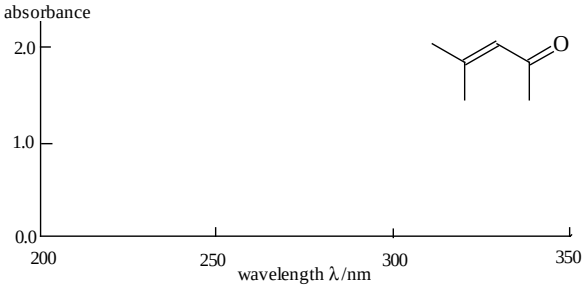
a) How many compounds did you find?

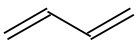
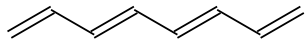
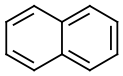
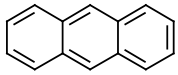
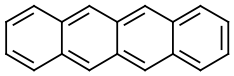
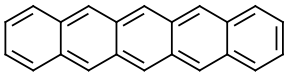
b) Draw and name the first compound:

CONJUGATION AND COLOUR

Ultraviolet Spectroscopy

The UV region of the spectrum is of short wavelength (higher energy) than visible light, and the portion of most interest to organic chemistry is the range 200-400 nm. Energies of this magnitude (~630-315 kJ mol^{-1}) correspond to those required to raise the π electrons of conjugated molecules from their lowest (ground) state to an excited state. UV spectra are usually quite simple, with a small number of broad absorption maxima which are characterised by their wavelength λ_{max} and intensity. For example, the spectrum of 4-methyl-3-penten-2-one is as follows.

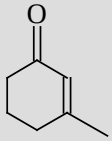


	λ_{max}/nm
	171
	220
	258
	287
	260
	280
	375
	450
	575

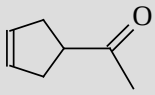
Molecules with no double bonds or only one double bond (or more than one isolated double bonds) only absorb UV light of wavelength even shorter than 200 nm. Unsaturated molecules containing conjugated double bonds do absorb UV light in the 200-400 nm region: the more extended the conjugation the longer the wavelength of maximum absorption. The λ_{max} for a particular UV-absorbing group ("chromophore") is also affected by substituents, conformation, and other structural characteristics of the conjugated π-electron system. The nature of the solvent may also have a small effect.

Question 1

(a) How could you use UV spectroscopy to distinguish between these two compounds?



and



(b) Which of the following compounds show UV absorptions in the range 200-400 nm?

(a) 1,3-cyclohexadiene
(b) 1,4-cyclohexadiene
(c) methyl propenoate
(d) 4-bromotoluene
(e) 2-methylcyclohexanone
(f) 2-methyl-2-cyclohexenone

Types of Electronic Transition

The ground state of an organic molecule contains valence electrons in three principal types of molecular orbitals: sigma (σ), pi (π), and non-bonding, lone-pair (*n*). Both σ and π orbitals

are formed from the overlap of two atomic or hybrid orbitals, each therefore has an antibonding σ* or π* orbital associated with it. An orbital containing *n* electrons does not have an antibonding orbital (because it is not formed from two orbitals). Electron transitions involve the promotion of an electron from one of the three ground state orbitals (σ, π and *n*) to one of the two excited-state orbitals (σ* or π*). The following transitions give rise to absorption in the non-useful 100 – 200 nm region of the UV spectrum: $\pi \rightarrow \pi^*$ for an isolated double bond, and $\sigma \rightarrow \sigma^*$ for an ordinary carbon–carbon bond. The useful transitions (200 – 400 nm) are $\pi \rightarrow \pi^*$ for compounds with conjugated double bonds, and some $n \rightarrow \sigma^*$ and $n \rightarrow \pi^*$ transitions.

In this exercise you will use the SPARTAN program to perform molecular orbital (MO) calculations to investigate the properties of some conjugated molecules. You will need to recall what you have learnt from earlier exercises regarding how to use the program.

Frontier orbitals for substituted ethenes

Build ethene and perform an **Equilibrium Geometry** calculation using the **Hartree-Fock HF/3-21G** method, with **Charge** = **Neutral** and **Multiplicity** = **Singlet**. Note the energies of the HOMO and LUMO (the "frontier" orbitals) of ethene and determine the HOMO – LUMO energy gap, ΔE.

Now investigate the effect of three types of substituent X which may replace a hydrogen atom in ethene to give a substituted molecule CH_2=CHX. You should consider X = $CHCH_2$ (*i.e. trans*-butadiene), X = NH_2, and X = CF_3. For each molecule you should note the HOMO and LUMO energies and the HOMO – LUMO energy gap, ΔE. You should also compute the electrostatic potential and display it on the electron density surface (Surface = Density, Property = Potential). Remember, the electrostatic potential measures the interaction between the molecule and a positive charge (*e.g.* a proton); a red colour indicates a region of attractive interaction, and a blue colour indicates a region of repulsive interaction, with an electrophile. Look carefully at the regions of high π-electron density in the original ethene fragment.

Question 2

(a) Tabulate the HOMO and LUMO energies and the HOMO – LUMO energy gap, ΔE, for ethene and the three substituted ethenes.

(b) Comment upon how substitution affects the frontier orbital energies and the ΔE gap.

(c) By inspection of the electrostatic potentials, comment upon the electron-withdrawing or electron-donating nature of the NH_2 and the CF_3 substituents.

Coloured Organic Materials

When an electron transition is caused by absorption of light in the visible region of the spectrum (about 400 – 750 nm), the colour of the compound absorbing the light is perceived by the human eye and brain as the complementary colour to that of the absorbed light. Some

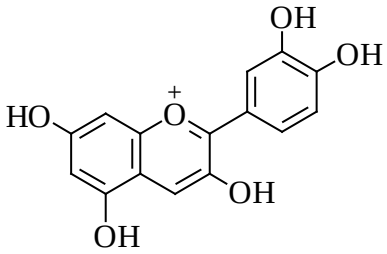
compounds appear to have a yellow colour even though their λ_{max} are all in the UV region; in such cases a "tail" of an absorption band stretches into the visible. Absorption of visible light by intensely coloured materials generally involves $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transitions and conjugated systems of π-electrons. If an absorption band is narrow and sharp, the colour will appear to us as brilliant and clean. A broad absorption band, or more than one band in the visible region, gives colours that we perceive as dull or "muddy".

Colour and wavelength

λ/nm	colour	complementary colour
400 – 430	violet	green-yellow
430 – 480	blue	yellow
480 – 490	green-blue	orange
490 – 510	blue-green	red
510 – 530	green	purple
530 – 570	yellow-green	violet
570 – 580	yellow	blue
580 – 600	orange	green-blue
600 – 680	red	blue-green
680 –750	purple	green

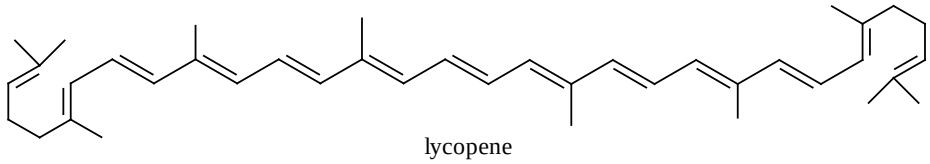
Natural Coloured Materials

Anthocyanins provide much of the colour of the plant world; they are responsible for the red colour of buds and the purple of autumn leaves. Their colours depend in part on the pH of their environment. Thus blue cornflower and red rode have the same pigment (cyanin), the blue colour being due to the potassium salt. Hydrolysis of cyanin yields cyanidin ,which colours crimson to blue-red flowers and cherries.

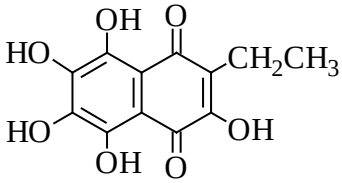


cyanidin

Carotenoids occur in many organisms, from bacteria and fungi to complex plants and animals. The red colour of boiled lobster arises as a carotenoid is released from a protein complex as it is denatured by boiling water. Lycopene gives colour to tomatoes and ripe fruit.

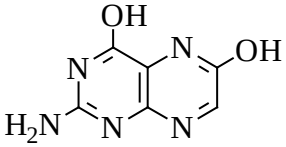

lycopene

Quinones are found in both animals and plants; echinochrome is a red pigment occuring in sea urchins. *Melanins* are polymeric quinoidal compounds occuring in feathers, hair, eyes, and the ink of cephalopods; they are responsible for the varied skin colouration among the races of mankind.



echinochrome

Pterins include xanthopterin, a yellow pigment found in butterfly wings and animals.



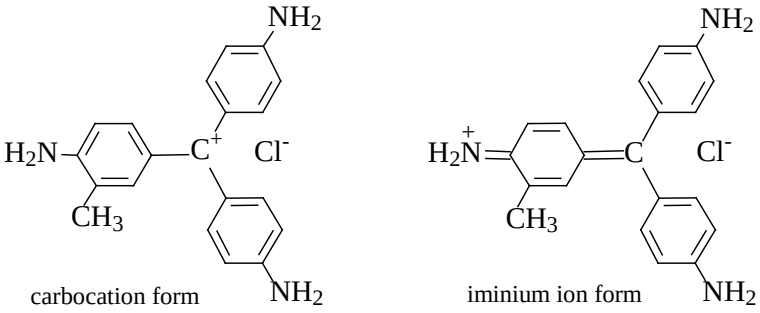
xanthopterin

Other naturally occuring pigments include *porphyrins*, such as haemin and chlorophyll, and *indigoids*, from which the first dyes were obtained.

Synthetic Dyestuffs

In 1856, when W.H. Perkin (an 18-year-old student at the Royal College of Chemistry) prepared mauve from (impure) aniline, he started a mad race to develop other commercially profitable dyes from aniline and related compounds. A few years later, Verguin heated the crude aniline of the day with stannic chloride and produced a beautiful fuchsia-coloured substance fuchsin (λ_{max} = 547 nm) that was the first of the triphenylmethane dyes. (Repeating this experiment with today's aniline would not produce fuchsin, because its formation was due to the presence of *p*-toluidine, $CH_3C_6H_4NH_2$, as an impurity!)

Alternative structures for fuchsin, a triphenylmethane dye



The triphenylmethane dyes come in all colours of the rainbow, from the red of fuchsin through malachite green and Victoria blue to crystal violet. The chromophores responsible for these colours are essentially nitrogen-substituted triphenylmethyl (trityl) cations, but they are not true carbocations, because most of the positive charge is distributed to the ring nitrogen atoms, as in the iminium ion form of fuchsin. Such charge delocalization stabilizes the dyes so that most of them will keep indefinitely, even in aqueous solution. Unsubstituted trityl salts, which are true carbocations, are nearly 10^{12} times less stable than crystal violet, and they hydrolyze rapidly to triphenylmethanol in water. Nevertheless, the trityl cation is unusually stable for a carbocation; when protected from atmospheric moisture, it is stable enough to keep almost indefinitely.

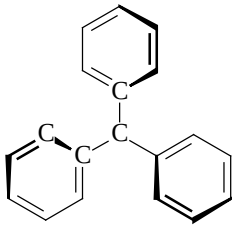
In the early days, the triphenylmethane dyes were represented by quinonoid (iminium ion) structures like the one shown above for fuchsin. However, when triphenylmethanol – which, having no nitrogen-containing substituents, cannot form iminium ions – was treated with strong acid, it also produced a coloured solution. This led to the suspicion that the coloured product, and by extension the triphenylmethane dyes as well, were actually carbocations having the positive charge located on the central carbon atom. Some heated arguments ensued between the supporters of the iminium ion structure and those of the carbocation structure. Their differences were eventually reconciled by resonance theory, by which the two forms are regarded as contributing structures of a resonance hybrid that has some characteristics of each.

Trityl cation geometry

First build triphenylmethanol (Ph_3COH) and perform an Equilibrium Geometry calculation using the **Semiempirical PM3** method (the default semiempirical method in SPARTAN ST, but an option in SPARTAN ES) with **Charge** = **Neutral** and **Multiplicity** = **Singlet**. Note the average C–C bond length around the central carbon and the HOMO – LUMO energy gap. (You are advised *not* to check the **Print Orbitals** box in **Setup Calculations** in order to avoid generating a very large output file; this advice applies also to subsequent calculations in this exercise. Instead, you may find the HOMO and LUMO energies simply by going into **Spreadsheet** from the **Display** menu and **Add**ing the appropriate quantities.)

Next build the triphenylmethyl cation in a *planar* geometry. (Just add three benzene rings to a trigonal planar carbon in the model kit.) Perform an Equilibrium Geometry calculation using the **Semiempirical PM3** method with **Charge** = **Cation**, **Multiplicity** = **Singlet** and **Compute** = **Frequencies**. Note the C–C bond lengths around the central carbon and the HOMO – LUMO energy gap. Note also the number and nature of the vibrational modes with imaginary frequencies.

Finally, twist each of the phenyl groups (in the same direction) to a dihedral angle of about 30º for the CCCC atoms indicated in the Figure, so that the molecule resembles a propeller with angled blades. Optimise the geometry once more, and note the same quantities as before together with the optimum value of the dihedral angle.

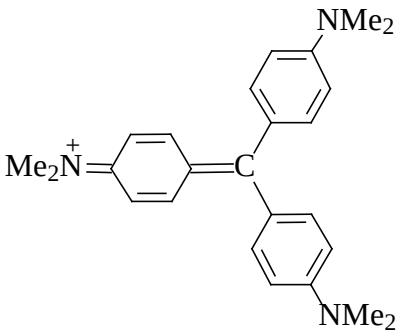


Question 3

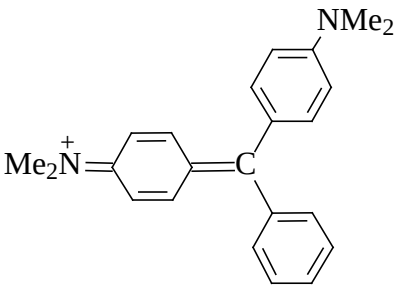
Suggest an explanation for the difference in C–C bond lengths to the central carbon in the three species. What is the optimum geometry for the trityl cation and why is this preferred?

Effect of substituents upon colour

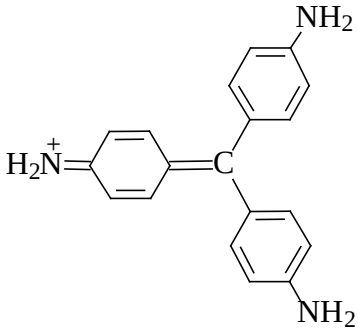
Build and optimise the geometries of the following two compounds **A** and **B**, using the semiempirical PM3 method. (*N.B.* Consider all three phenyl rings as equivalent when constructing these molecules. That the resonance contributors shown her for A and B are drawn with one double-bonded ["quinoid"] ring is irrelevant for the MO calculations.)



A



B



parafuchsin

Question 4

One of these compounds is blue-green (λ_{max} = 614 nm) and the other is violet (λ_{max} = 588 nm) at pH 7. On the basis of PM3 calculated results, which is which? Explain your answer briefly.

Now optimise the geometry for tri-(4-aminophenyl)-methyl cation (parafuchsin, λ_{max} = 544 nm) also using the semiempirical PM3 method.

The final stage of the investigation can only be performed using Spartan Essential Edition, since the Student Edition does not permit enough basis functions to be used in the Hartree-Fock/3-21G calculations. If you have been using Spartan ST up to this point, you should now find a PC with Spartan ES in order to complete the work.

Perform **Single Point Energy** calculations for trityl cation, compounds **A** and **B**, and parafuchsin, using the **Hartree-Fock/3-21G** method for the semiempirical PM3 geometries that you have already obtained. Make sure each species is a **Cation**, and do *not* check any other boxes in **Setup Calculations**. In each case note the HOMO- LUMO energy gap.

N.B. This type of calculation, in which a slower but more reliable method is used to evaluate a single-point energy at a geometry optimised using a faster method, is often described by the notation "energy-method//geometry-method". In the present case we may denote the calculation as HF/3-21G//PM3.

Question 5

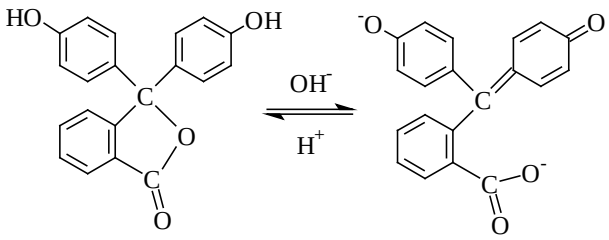
(a) Use Excel to make a plot of HF/3-21G//PM3 calculated HOMO – LUMO energy gaps ΔE against the experimental wavelength of maximum absorption for the three compounds (A, B & parafuchsin) for which you have a value of λ_{max}.

(b) Determine a linear regression equation relating λ_{max} to ΔE.

(c) Predict the colour of the trityl cation.

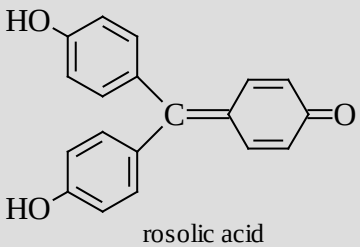
Indicators

An acid-base indicator is an organic compound that changes colour with a change in pH. These compounds are most frequently encountered as titration endpoint indicators. Test papers, such as litmus, are impregnated with one or more of these substances. Indicators change colour because the chromophoric system is changed by an acid-base reaction. In acidic solution, phenolphthalein is a colourless lactone in which the three benzene rings are not conjugated, owing to the sp^3-hybridisation of the central carbon atom. At pH > 8.3, the phenolic protons are removed, the lactone ring is opened, the central carbon is sp^2-hybridised, the molecule is conjugated, and is coloured red.



Question 6

Rosolic acid has the structure shown here, but when protonated, it is the tri-(4-hydroxyphenyl)-methyl cation. By means of appropriate calculations, predict its colour in neutral and in acidic solutions.



rosolic acid

(N.B. Once again, when constructing these molecules you should consider all three rings as phenyls. Do not attempt to build the particular pattern of double bonds implied by the resonance structure. This would only be necessary for a molecular mechanics calculation, but not for a molecular orbital calculation which will itself determine the best arrangement of the electrons.)

NICKEL CARBONYL COMPLEXES

In the course of studying the corrosion of nickel valves in process gas containing carbon monoxide, Mond, Langer and Quincke found in 1890 that an unusual volatile compound $Ni(CO)_4$ (colourless, mp 19 ºC, bp 42 ºC) was formed. This compound, tetracarbonylnickel(0), is readily decomposed to Ni + 4CO by gentle heating, and its formation and decomposition became the *Mond process* for nickel refining which was used for many years.

$$Ni(s) + 4\ CO(g) \xrightarrow[1\ atm]{30\ ^oC} Ni(CO)_4(l)$$

Since then it has been found that most transition metals form one or more carbonyl complexes. These are best regarded as forming from neutral CO and the metal in an oxidation state of zero. Each CO provides 2 electrons and these, with the metal valence shell electrons, add up to the rare gas configuration of 18 electrons in nearly every case. Thus Ni(0) has 10 valence electrons [d^{10}] and the 8 from the four CO groups gives the configuration of Kr. Since the metal is zero-valent, and the CO group is a very poor lone pair donor, it is clear that a simple electrostatic approach cannot account for the structure and bonding in metal carbonyls. You have been introduced to these species in CH20015 Transition Metal Chemistry and in CH20020 Inorganic Chemistry Laboratory; further information may be found in chapter 23 of Housecroft and Sharpe, *Inorganic Chemistry*.

In this exercise you will use the SPARTAN program to perform molecular orbital (MO) calculations to investigate the properties of some nickel carbonyl complexes of general formula $Ni(CO)_3X$, where X is some other ligand. You will need to recall what you have learnt from earlier exercises regarding how to use the program. What follows below is not a comprehensive set of instructions but rather guidelines and hints to help you obtain the data necessary to answer the questions. Note that the semiempirical PM3 (or PM3D for transition metals) method treats only the valence-shell electrons and atomic orbitals.

Frontier orbitals and bonding interactions for $[Ni(CO)_3Br]^-$

Use the **Expert** model kit to build tetrahedral $[Ni(CO)_3Br]^-$ and then perform an **Equilibrium Geometry** calculation using the **Semiempirical (PM3)** method, with **Charge** = **Anion**, **Multiplicity** = **Singlet**, **Compute: Frequencies** and **Print: Orbitals**. Prior to submitting the calculation, you should also **Add… HOMO-1**, **HOMO**, **LUMO** and LUMO+1 from Setup Surfaces. Note the optimised lengths of the Ni–Br, Ni–C, and C≡O bonds; the HOMO and LUMO energies, and the frequencies of the carbonyl stretching vibrations. From the data provided in **Display Output** and **Display Vibrations** you should note the symmetry labels (A_1 or E) of the HOMO and LUMO and of the carbonyl stretching vibrations, and the relative intensities of the infrared absorptions corresponding to these vibrational modes. The latter information is listed under "`IR Transition Moments`": the infrared absorption intensity is proportional to the magnitude of the "`Moment`".

Consider the interaction between the $Ni(CO)_3$ and Br^- fragments. To do so, you may wish to constrain the three (equal) values of the C–Ni–C angles, delete the Br atom, **Save As** a different filename, and perform a Single Point Energy evaluation on the **Neutral** fragment. Also, a Single Point Energy evaluation on the bromide anion might be helpful.

In order to enable you to evaluate the binding energy of Br^- to $Ni(CO)_3$ it would help to release the constrains from the $Ni(CO)_3$ fragment so that it may relax from a pyramidal to a trigonal planar geometry.

Constrain the Ni–Br bond length dynamically to start at 2.5 Å and go to 4.5 Å in 5 steps, and perform an **Energy Profile** calculation using the same settings as before. As you inspect each structure, check the form and symmetry of the frontier orbitals to make sure that you are still looking at those you selected in answer to Question 1; the identities of the HOMO and the LUMO may change to something not relevant to the bonding interaction. Note the optimised lengths of the Ni–Br, Ni–C, and C≡O bonds; the energies of the relevant frontier orbitals (whether or not the actual HOMO and LUMO), the charge on the Br atom, and the frequency of the infrared-active carbonyl stretching vibration.

Structural and vibrational effects in $[Ni(CO)_3X]^-$

Obtain optimised (equilibrium geometry) structures for $[Ni(CO)_3F]^-$, $[Ni(CO)_3Cl]^-$ and $[Ni(CO)_3I]^-$, just as you did for $[Ni(CO)_3Br]^-$ - except that it is not necessary to repeat the energy profile calculation. Note the same data as before, including the charge on the halogen atom, but beware that the actual HOMO and LUMO may not necessarily be the orbitals of interest. Determine the binding energies relative to $Ni(CO)_3$ and X^-.

Structural and vibrational effects in $Ni(CO)_3PX_3$

Obtain optimised structures for the series of phosphine complexes with X = H, CH_3, F and Cl. Take care to check whether a staggered or an eclipsed conformation is preferred about the Ni–P bond. Once again, beware that the actual HOMO and LUMO may not necessarily be the orbitals of interest. Note the same data as before, including the charges on the PX_3 and $Ni(CO)_3$ fragments. Determine the binding energies relative to $Ni(CO)_3$ and PX_3.

Structural and vibrational effects in $Ni(CO)_4$

Finally, consider the bonding in tetracarbonylnickel(0) itself.

The purpose of this exercise is for you to abstract relevant results from the data you obtain and to present them in a clear and concise manner in order to support your arguments in answer to the questions listed below. Your report should therefore only contain the results you consider necessary to include for this purpose. There is no point in tabulating results that you do not mention in your discussion. The report will be assessed on the basis of its quality, not its quantity.

Question 1

With the aid of a simple MO diagram showing the relevant frontier orbitals, explain briefly how bromide anion interacts with tricarbonylnickel(0) to form $[Ni(CO)_3Br]^-$.

Question 2

Provide a concise account to explain the variations in the calculated infrared-active carbonyl stretching frequencies in $[Ni(CO)_3X]^-$ and $Ni(CO)_3PX_3$ complexes in terms of a simple model for the bonding, illustrating your answer with appropriate results from your calculations.

Question 3

Briefly compare the properties of CO as a ligand with those of halide anions and phosphines.

COMPUTATIONAL CHEMISTRY LABORATORY

STUDENT QUESTIONNAIRE

We would be grateful for feedback upon your experience of this component of the laboratory course. Please assess each of the following points by placing a tick in the appropriate column. If you consider a question to be unsound, or you are unsure that your response would be meaningful, please tick the column headed "U". (For example, you may consider it too premature to judge the value of the course for you.)

	very good		*average*		*very poor*	*unsound*
	5	**4**	**3**	**2**	**1**	**U**
1 Reasonable assumptions were made about prior knowledge of chemistry						
2 Reasonable assumptions were made about prior experience of computers						
3 Concepts covered were understandable						
4 Quality of handouts and instructions						
5 Quality of supervision by academic staff						
6 Quality of support from postgraduate demonstrators						
7 Interest of the course						
8 Value of the course						

Other comments: