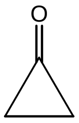
MOLECULAR MODELING:

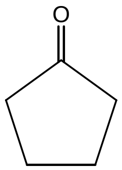
AROMATIC RESONANCE EFFECTS IN CYCLIC KETONES

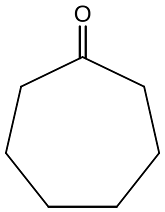
Goal: In this experiment, you will use computational chemistry to probe the effects of aromaticity upon bond strengths and lengths. The vibrational spectral frequencies for a variety of cyclic ketones will be predicted using molecular orbital methods, and the trends in bond length and C=O stretching frequency will be compared to expectations based on resonance theory and aromaticity models. If you wish you may work in groups of two or three, and share the results of your computations. Discuss the results amongst yourselves, but each person must write up and submit his or her own report.

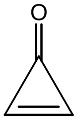
For the calculations, use the PC SPARTAN '02 computer program (Wavefunction Inc.) on PCs in the Chemistry Department (locations will be announced).

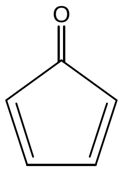
You will draw and calculate properties of each of the molecules shown below:

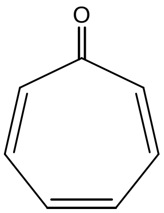








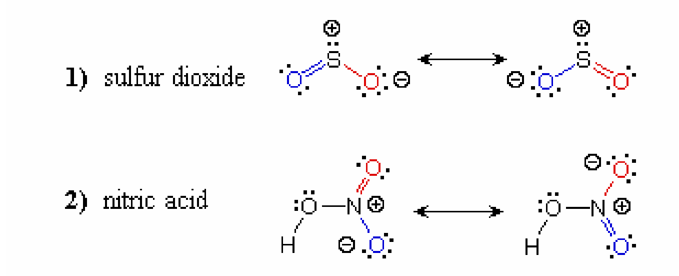




Background

Principles of Resonance

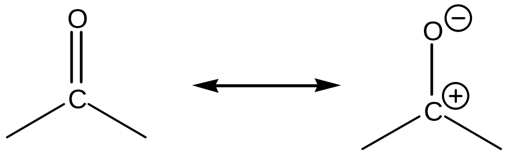
Kekulé structural formulas are essential tools for understanding organic chemistry. However, the structures of some compounds and ions cannot be represented by a single formula. For example, sulfur dioxide (SO_2) and nitric acid (HNO_3) may each be described by two equivalent formulas (equations 1 & 2). For clarity the two ambiguous bonds to oxygen are given different colors in these formulas.



If only one formula for sulfur dioxide were correct and accurate, then the double bond to oxygen would be shorter and stronger than the single bond. Since experimental evidence indicates that this molecule is bent (bond angle 120°) and has equal lengths of sulfur-oxygen bonds (1.432 Å), a single formula is inadequate, and the actual structure resembles an average of the two formulas. This averaging of electron distribution over two or more hypothetical contributing structures (canonical forms) to produce a hybrid electronic structure is called **resonance**. Likewise, the structure of nitric acid is best described as a resonance hybrid of two structures, the double headed arrow being the unique symbol for resonance.

The above examples represent one extreme in the application of resonance. Here, two structurally and energetically equivalent electronic structures for a stable compound can be written, but no single structure provides an accurate or even an adequate representation of the true molecule.

3) carbonyl



The principles of resonance are very useful in rationalizing the chemical behavior of many such compounds. For example, the carbonyl group of aldehydes and ketones reacts readily with many nucleophiles to give addition products. The course of these reactions can be explained by a small contribution of a dipolar resonance contributor, as shown in equation 3. Here, the first contributor (on the left) is clearly the best representation of this molecular unit, since there is no charge separation and both the carbon and oxygen atoms have achieved valence shell neon-like configurations by covalent electron sharing. If the pi-bond is broken heterolytically, formal charge pairs result, as shown in the other two structures. The preferred charge distribution will have the positive charge on the less electronegative atom (carbon) and the negative charge on the more electronegative atom (oxygen). Therefore the double-bonded formula represents a more reasonable and stable structure than the one on the right. The application of resonance to this case requires a weighted averaging of these canonical structures. The double bonded structure is regarded as the major contributor and the right structure a minor contributor. Since the right, charge-separated contributor has an electron deficient carbon atom, this explains the tendency of nucleophiles to bond at this site.

The basic principles of the resonance method may now be summarized.**For a given compound, a set of Lewis / Kekulé structures are written, keeping the relative positions of all the component atoms the same. These are the canonical forms to be considered, and all must have the same number of paired and unpaired electrons.**

The following factors are important in evaluating the contribution each of these canonical structures makes to the actual molecule.

The number of covalent bonds in a structure (the greater the bonding the more important and stable the contributing structure).

Formal charge separation (other factors aside, charge separation decreases the stability and importance of the contributing structure).

Electronegativity of charge bearing atoms and charge density (high charge density is destabilizing. Positive charge is best accommodated on atoms of low electronegativity, and negative charge on high electronegative atoms).

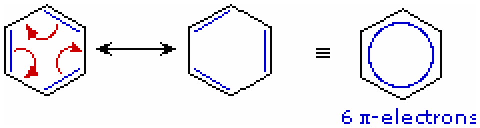
The stability of a resonance hybrid is always greater than the stability of any canonical contributor. Consequently, if one canonical form has a much greater stability than all others, the hybrid will closely resemble it electronically and energetically. This is the case for the carbonyl group (eq.3). The left hand C=O structure has much greater total bonding than either charge-separated structure, so it describes this functional group rather well.

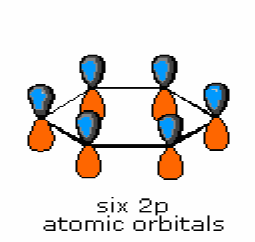
2) Aromaticity and The Hückel Rule

The adjective "aromatic" is used by organic chemists in a rather different way than it is normally applied. It has its origin in the observation that certain natural substances, such as cinnamon bark, wintergreen leaves, vanilla beans and anise seeds, contained fragrant compounds having common but unexpected properties. Cinnamon bark, for example, yielded a pleasant smelling compound, formula C_9H_8O, named cinnamaldehyde. Because of the low hydrogen to carbon ratio in this and other aromatic compounds (note that the H:C ratio in an alkane is >2), chemists expected their structural formulas would contain a large number of double or triple bonds. Since double bonds are easily cleaved by oxidative reagents such as potassium permanganate or ozone, and rapidly add bromine and chlorine, these reactions were applied to these aromatic compounds. Surprisingly, products that appeared to retain many of the double bonds were obtained, and these compounds exhibited a high degree of chemical stability compared with known alkenes and cycloalkenes (aliphatic compounds). On treatment with hot permanganate solution, cinnamaldehyde gave a stable, crystalline $C_7H_6O_2$ compound, now called benzoic acid. The H:C ratio in benzoic acid is <1, again suggesting the presence of several double bonds. Benzoic acid was eventually converted to the stable hydrocarbon benzene, C_6H_6, which also proved unreacive to common double bond transformations, as shown below. For comparison, reactions of cyclohexene, a typical alkene, with these reagents are also shown (green box). As experimental evidence for a wide assortment of compounds was acquired, those incorporating this exceptionally stable six-carbon core came to be called "aromatic".

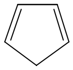
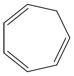
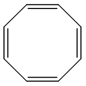
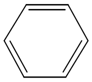
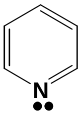
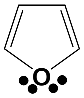
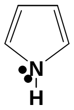
If benzene is forced to react by increasing the temperature and/or by addition of a catalyst, it undergoes **substitution reactions** rather than the addition reactions that are typical of alkenes. This further confirms the previous indication that the six-carbon benzene core is unusually stable to chemical modification. The conceptual contradiction presented by a high degree of unsaturation (low H:C ratio) and high chemical stability for benzene and related compounds remained an unsolved puzzle for many years. Eventually, the presently accepted structure of a regular-hexagonal, planar ring of carbons was adopted, and the exceptional thermodynamic and chemical stability of this system was attributed to resonance stabilization of a conjugated cyclic triene.

Benzene:





Many unsaturated cyclic compounds have exceptional properties that we now consider characteristic of "aromatic" systems. The following cases are illustrative:

Compound	Structural Formula	Reaction with Br_2	Thermodynamic Stabilization
1,3-Cyclopentadiene		Addition (0° C)	Slight
1,3,5-Cycloheptatriene		Addition (0° C)	Slight
1,3,5,7-Cyclooctatetraene		Addition (0° C)	Slight
Benzene		Substitution	Large
Pyridine		Substitution	Large
Furan		Substitution (0° C)	Moderate
Pyrrole		Substitution	Moderate

The first three compounds (cyclic polyenes) have properties associated with alkenes in general. Each reacts readily with bromine to give **addition products**, as do most alkenes. The thermodynamic change on introducing double bonds in to the carbon atom ring is also typical of alkenes (a destabilization of ca. 26 kcal/mol for each double bond). Conjugation offsets this increase in energy by a small amount (4-6 kcal/mol).

The remaining four compounds exhibit very different properties, and are considered **aromatic**. Benzene and pyridine are relatively unreactive with bromine, requiring heat and/or catalysts to force reaction, the result of which is **substitution** rather than addition. Furan and pyrrole react more rapidly with bromine, but they also give substitution products. This tendency to favor substitution rather than addition suggests that the parent unsaturated ring system has exceptional stability. Thermodynamic measurements support this conclusion. The enhanced stability, often referred to as **aromatic stabilization**, ranges (in the above cases) from a low of 16 kcal/mol for furan to 36 kcal/mol for benzene.

Factors Required for Aromaticity:

- A planar (or near planar) cycle of sp^2 hybridized atoms, the p-orbitals of which are oriented parallel to each other. These overlapping p-orbitals generate an array of π-molecular orbitals.

- These π-orbitals are occupied by 4n+2 electrons (where n is an integer or zero). This requirement is known as **The Hückel Rule**. All the aromatic compounds discussed above have 6 π-electrons (n=1).

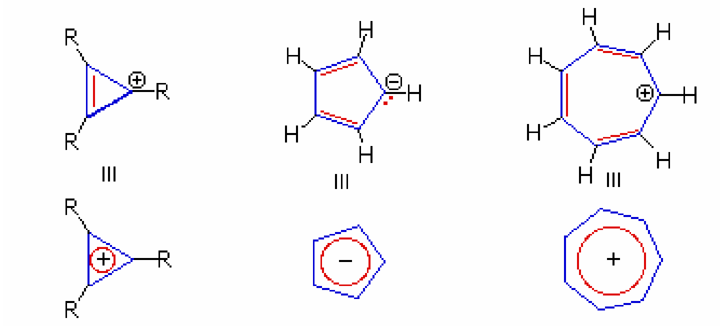
1,3-Cyclopentadiene and 1,3,5-cycloheptatriene both fail to meet the first requirement, since one carbon atom of each ring is sp^3 hybridized and has no p-orbital. Cyclooctatetraene fails both requirements, although it has a ring of sp^2 hybridized atoms. This molecule is not planar (a geometry that would have 135° bond angles). Angle strain is relieved by adopting a tub-shaped conformation; consequently, the p-orbitals can only overlap as isolated pairs, not over the entire ring. Furthermore, cyclooctatetraene has 8 π-electrons, a number not consistent with the Hückel Rule.

Benzene is the archetypical aromatic compound. It is planar, bond angles=120°, all carbon atoms in the ring are sp^2 hybridized, and the pi-orbitals are occupied by 6 electrons. Pyridine is similar to benzene, but it is essential to recognize that the non-bonding electron pair on nitrogen occupies a sp^2 orbital, and is not part of the π-electron system. Thus pyridine has 6 π-electrons and 2 non-bonding sp^2 electrons.

Furan and pyrrole have five-membered rings, in which one atom is not carbon (a heteroatom) and has at least one pair of non-bonding valence shell electrons. By hybridizing this heteroatom to a sp^2 state, a p-orbital occupied by a pair of electrons and oriented parallel to the carbon p-orbitals is created. The resulting planar ring meets the first requirement for aromaticity, and the π-system is occupied by 6 electrons, 4 from the two double bonds and 2 from the heteroatom, thus satisfying the Hückel Rule.

Four other examples of aromatic compounds are shown above. The sp^2 hybridized ring atoms are connected by blue bonds, the π-electron pairs are colored red. The first example is imidazole, a heterocycle having two nitrogen atoms. Note that only one of the nitrogen non-bonding electron pairs is used for the aromatic π-electron sextet. The other electron pair (colored black) behaves similarly to the electron pair in pyridine. The second and third compounds have ten-membered rings, which are forced to be planar, or nearly planar, by the bridging bond or methylene group (colored black). These are 10 π-electron systems that fit the aromaticity requirements. Finally, the last example has a fourteen-membered ring with 7 double bonds. The bridging atoms and bonds force it to be planar. The number of π-electrons in this aromatic system is 14.

Carbanions and carbocations may also show aromatic stabilization. Some examples:



The three-membered ring cation has 2 π-electrons and is surprisingly stable, considering its ring strain. Cyclopentadiene is as acidic as ethanol, reflecting the stability of its 6 π-electron conjugate base. Salts of cycloheptatrienyl cation (tropylium ion) are stable in water solution, again reflecting the stability of this 6 π-electron cation.

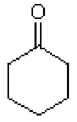
3) IR of Aldehydes and Ketones

For simple aldehydes and ketones the stretching vibration of the carbonyl group gives rise to a strong and distinctive infrared absorption at 1710 to 1740 cm $^{-1}$. As noted in the diagram on the right, the dipole moment of this function is increased on stretching (single bond character is greater), and this results in a strong absorption. Since alkyl substituents stabilize the carbocation character of the ionic contributer, ketone carbonyls have slightly lower stretching frequencies, 1715 ± 7 cm $^{-1}$, compared with aldehydes, 1730 ± 7 cm $^{-1}$. The values cited here are for pure liquid or CCl_4 solution spectra. Hydrogen bonding solvents will lower these frequencies by 15 to 20 cm^{-1}.

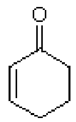
Three factors are known to perturb the carbonyl stretching frequency:

1. **Conjugation with a double bond or benzene ring lowers the stretching frequency.**

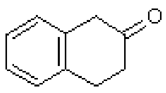
The 30 to 40 cm $^{-1}$ decrease in frequency is illustrated by the following examples. The stretching frequency of the conjugated double bond is also lowered (blue notation) and may be enhanced in intensity. The cinnamaldehyde example (far right) shows that extended conjugation further lowers the absorption frequency, although not to the same degree.



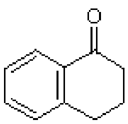
1716 cm^{-1}



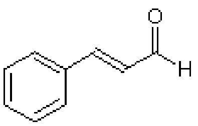
1685 cm^{-1}
1617 (C=C)



1716 cm^{-1}



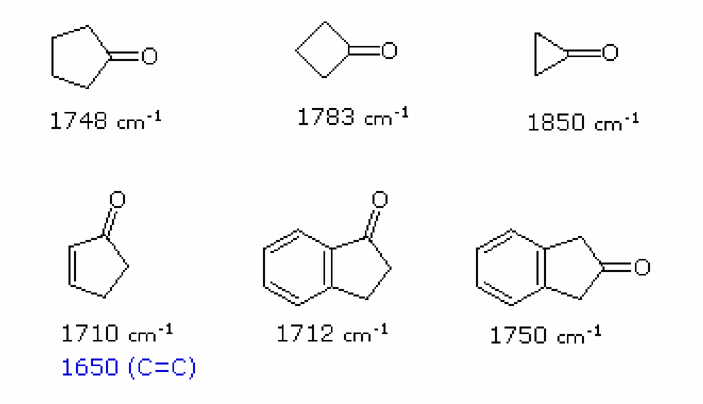
1683 cm^{-1}



1678 cm^{-1}
1627 (C=C)

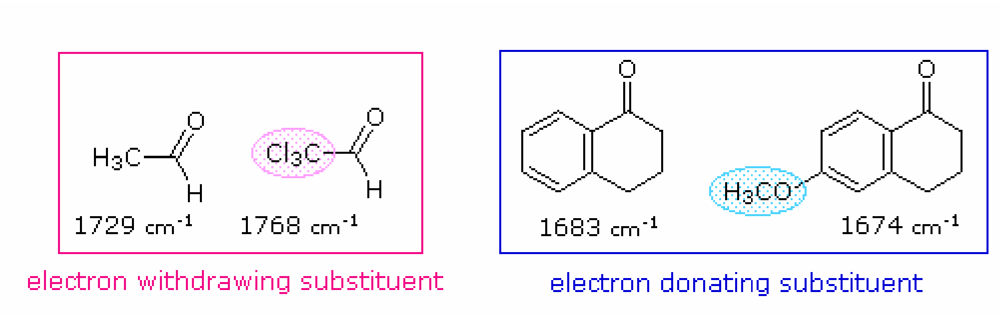
2. **Incorporation of the carbonyl group in a small ring (5, 4 or 3-membered), raises the stretching frequency.**

The increase in frequency ranges from 30 to 45 cm^{-1} for a 5-membered ring, to 50 to 60 cm^{-1} for a 4-membered ring, and nearly 130 cm^{-1} for a 3-membered ring. This shift also occurs in the presence of the previous conjugative lowering of the stretching absorption. Examples of this effect are shown below.



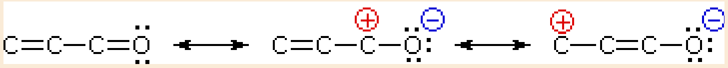
3. Changing an alkyl substituent of a ketone for an electron releasing or withdrawing group.

This effect, which may shift the carbonyl stretching frequency up or down, is particularly important when an alkyl substituent is replaced by a hetero atom such as N, O or X (halogen). Such cases will be discussed as carboxylic acid derivatives. The following examples show the influence of a strongly electron withdrawing group (-CCl_3) and a conjugatively electron donating group (-OCH_3).

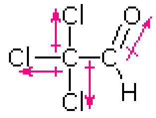


To understand the functioning of these factors consider the following analyses:

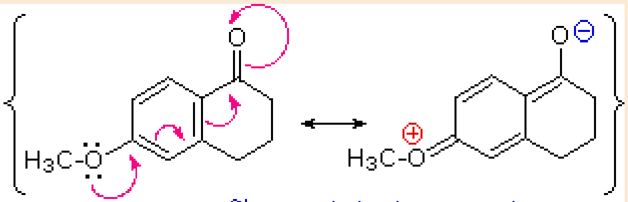
1. Conjugation extends the dipolar character of the carbonyl group to the double bond (or aromatic ring) so that the beta-carbon atom shares the positive character of the carbonyl carbon. As illustrated by the following resonance equation, this not only explains conjugate addition reactions of nucleophiles, but also suggests that the carbonyl double bond has slightly more single bond character than does an unconjugated function. The bond energy (and force constant) of the conjugated C=O group is correspondingly reduced, and this results in a lower stretching frequency.



2. Under ideal conditions the carbon atom of a carbonyl group is essentially sp^2 hybridized, which implies that the bond angles will be 120° and the C-O sigma bond has 33% s-character. If this group is incorporated in a small ring, the C-CO-C bond angle is reduced to 108° (5-membered ring), 90° (4-membered ring) or 60° (3-membered ring). When this happens, the C-C bonds of the ring assume greater p-character and the C-O sigma bond has correspondingly greater s-character. The double bond of the carbonyl group is therefore shorter and stronger, and exhibits a larger stretching frequency.
3. Electron donating substituents on the carbonyl group stabilize the ionic resonance contributor, and increase the single bond character of the C=O bond. The stretching frequency is therefore decreased, as noted in the right hand example below. Electron withdrawing groups have an opposite influence, and increase the stretching frequency of the carbonyl group. Trichloroacetaldehyde (left below) provides a good example.



C=O ν̃ stretch is increased



C=O ν̃ stretch is decreased

4) The IR frequency and the bond strength

The equation on the right describes the major factors that influence the stretching frequency of a covalent bond between two atoms of mass m_1 and m_2 respectively. The force constant (f) is proportional to the strength of the covalent bond linking m_1 and m_2. In the analogy of a spring, it corresponds to the spring's stiffness. For example, a C=N double bond is about twice as strong as a C-N single bond, and the C≡N triple bond is similarly stronger than the double bond. The infrared stretching frequencies of these groups vary in the same order, ranging from 1100 cm^{-1} for C-N, to 1660 cm^{-1} for C=N, to 2220 cm^{-1} for C≡N.

$$\tilde{\nu} = \frac{1}{2\pi c}\sqrt{\frac{f(m_1+m_2)}{m_1 \cdot m_2}}$$

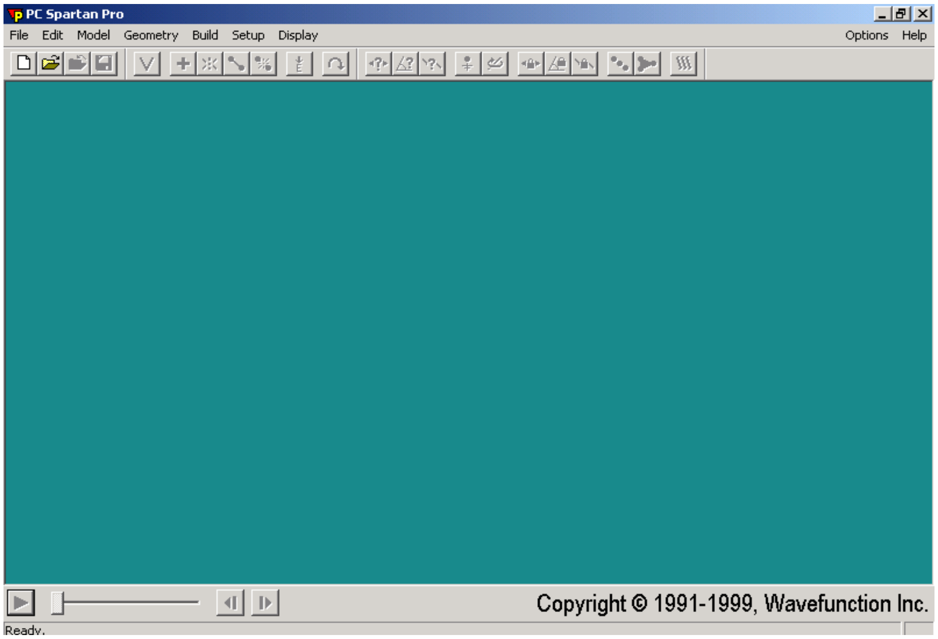
$\tilde{\nu}$ = frequency in cm^{-1}
f = the force constant
c = the velocity of light

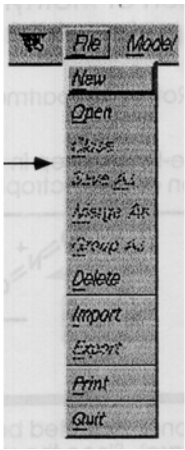
5) Dipole Moment:

When two different atoms are bonded covalently, the shared electrons are attracted to the more electronegative atom of the bond, resulting in a shift of electron density toward the more electronegative atom. Such a covalent bond is **polar**, and will have a **dipole** (one end is positive and the other end negative). The degree of polarity and the magnitude of the bond dipole (which is measured by the **dipole moment**) will be proportional to the difference in electronegativity (or charge separation) of the bonded atoms and the distance between these atoms.

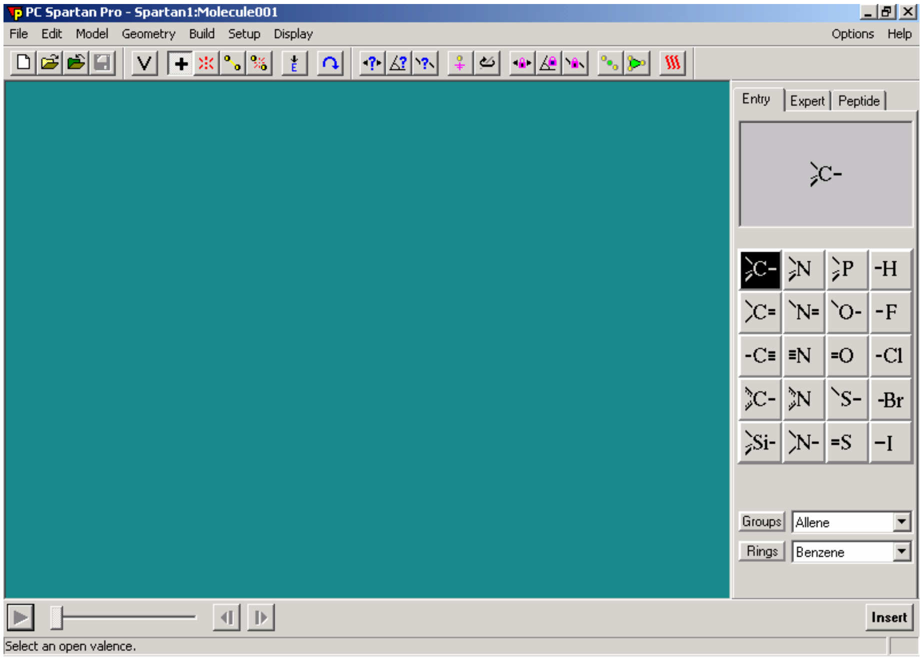
SAMPLE PROCEDURE FOR DRAWING CYCLOPROPANONE

1) Double click on *PC Spartan Plus* icon to open the program.





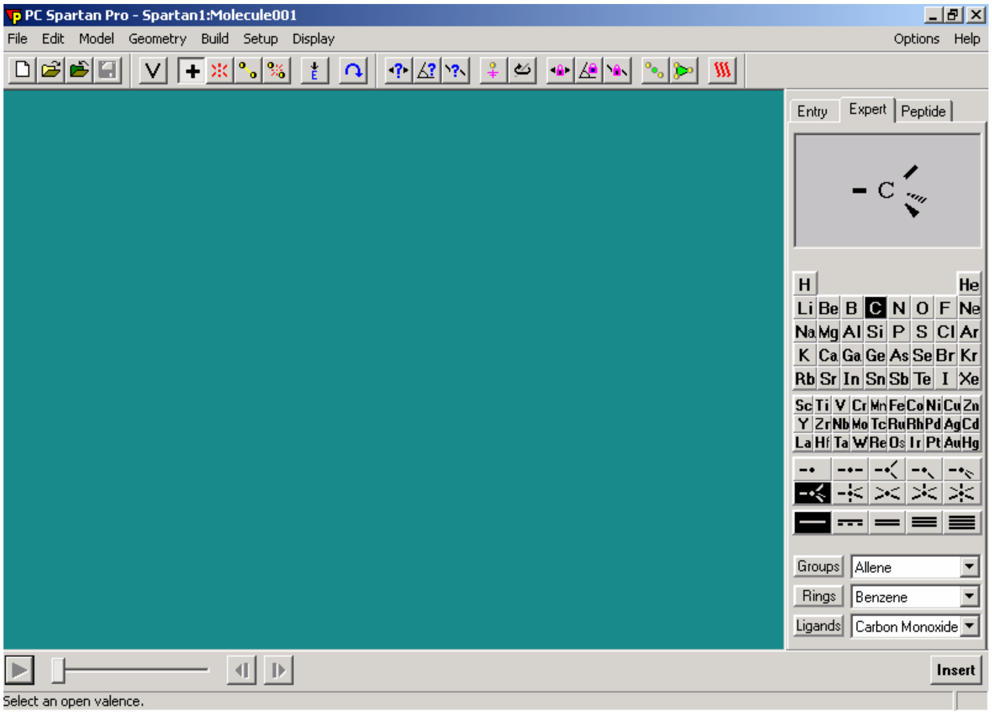
2) Under *File* menu choose *New* (or *Control+N*) to open the *Builder Window* and under *Build* menu choose *Add Fragment* (A *Fragment Panel* will appear on the right side of the screen)



Select an open valence.

The appearance of the screen in PC Spartan Plus

3) Choose the *Expert* mode on the *Fragment Panel*



Select an open valence.

The *Fragment Panel* (the *Expert* mode) in PC Spartan Pro, (*Add, Bond, Delete, Move*, etc. do not appear in the *Fragment Panel* , but can be found under the *Build Menu* or as the small icon short-cut buttons under the menu toolbar which contains *File, Model, Geometry, Build* etc. menus.

4) Click on the *Groups* menu (located close to the bottom right of the *Fragment Panel*) and choose *Carbonyl* form this menu (You will also see Rings

5) Move the cursor to the black area on the screen and click on this area once to add a Carbonyl group
6) Then choose C (Carbon) and sp^3 hybridization on the *Expert* menu (from the *Fragment Panel*)
7) Click on both of the yellow-colored Hydrogens on the previously drawn Carbonyl group to convert the Hydrogens to Carbon atoms.
8) Then under the *Build* menu choose Make Bond and click on one of the Hydrogens on each of the sp^3 hybridized added in step 7 to connect these two Carbon atoms with a single bond
9) Choose *Minimize* under *Build* menu
10) Choose *Save* under *File* menu and save the molecule after giving it a name.
11) Choose *Quit* under *File* menu and continue with step 5 in the procedure given in page 2 of the Molecular Modeling experiment.

Other Useful Things to Know:

In order the rotate the molecule, hold down the left mouse button and drag the mouse in any direction until the desired view of the molecule is obtained. You can move the molecule drawn to anywhere on the screen by clicking on the molecule with the right mouse button and dragging it on the screen while holding the right mouse button down.

You can always undo a mistake by choosing *Undo* under the *Edit* Menu

It is possible to erase everything drawn on the screen by clicking on *Clear* under the *Edit* Menu.

The *Build* Menu contains the following under it:

Delete [deletes the highlighted portion of the molecule]
Make Bond [makes a bond between the desired two atoms in the molecule- the atoms may be selected by clicking on them (a green ball appears on the selected atom)]
Break Bond (breaks the bond between two atoms- just click on the bond to choose the bond you wish to be broken)
Minimize
Reaction

Important Note:

When building the desired molecule using appropriate molecular fragments, note that, for some molecules, before connecting the next fragment or closing a ring, you may have to rotate a bond to get the atoms in the approximately correct positions. Otherwise, undesired, strange-looking geometries may result (e.g., for rings, cis-, not trans- double bonds are desired). Also as you are building a ring, some atoms may overlap and make building difficult. To make the cyclopropenone, first make the C=O then attach one sp^2 carbon to one side and one to the other side of the carbonyl, and without rotating any bonds, connect the double bonds to make the ring. This should result in the correct geometry. With any of the structures apply the test of reasonability - see if what you made after minimization looks like a reasonable geometry.

Procedure for Running Calculations:

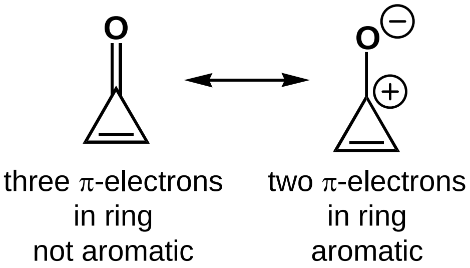
1) Under *Set-up* choose *Calculations*.
2) Click on the boxes to choose *Equilibrium Geometry*, *Semi-empirical*, *AM1*, *Frequencies*, *Vibrational Modes*, *Atomic Charges* in the *Calculations* window.
3) Then click on *Set-up* menu and under *Set-up* choose *Submit*.
4) Then under *Display* menu, choose *Properties* to read the energy in kcal/mol and Dipole (in Debyes).
5) Under *Display*, click on *Display Vibrations* and click on different frequency values to view the bond vibrations. Find the C=O stretching vibration and record its frequency.
6) Under *Geometry*, choose *Measure Distance* and then click on the C=O bond on the molecule. Record the distance in Angstroms (A^o).
7) Under *Model*, select *Dipole* and visualize the direction of the dipole moment.
8) Under ***Display***, select *Properties* and click on the C and O atoms of the Carbonyl (C=O) group to find their charges. Record the <u>Mulliken charges</u> for C and O of C=O group.

In order to modify the structure or to add anything to it, return to *Builder* menu and choose *Add Fragment* under Build

Results and Discussion

Part I (Resonance Forms and Aromaticity)

Draw the resonance forms (neutral and charge separated) for each cyclic ketone studied in this experiment. Also, indicate the number of π-electrons that are present in each ring <u>and</u> indicate whether or not a resonance form is aromatic. An example is as follows:



Part II (Calculated Frequencies)

Comment on the nature of the trend observed in the C=O stretching frequencies for the saturated cyclic ketones that you calculated. Likewise, comment on the nature of the trend observed in the frequencies for the unsaturated cyclic ketones. Arrange the saturated and unsaturated molecules according to increasing C=O stretching frequency.

Part III (Rationalization of Trends)

Discuss the trends observed in the C=O stretching frequencies for the saturated and unsaturated cyclic ketones (neutral and charge separated) that you calculated in terms of ring size and aromaticity. Provide a description that explains why the various trends are observed.

Part IV (Literature Frequencies)

The literature C=O stretching frequencies for the molecules studied in this experiment are:

cyclopropanone: 1813 cm^{-1} cyclopentanone: 1700 cm^{-1} cycloheptanone: 1700 cm^{-1}
cyclopropenone: 1840 cm^{-1} cylcopentadienone: 1870 cm^{-1} cycloheptatrienone: 1651 cm^{-1}

Is the trend observed in the literature for the saturated and unsaturated cyclic ketones consistent with the trends observed in your calculated structures? Explain.

Part V (Bond Lengths and Dipole Moments)

Compare the calculated bond lengths of your calculated molecules for those saturated and unsaturated ring systems: 1) of same size and 2) of increasing size. Discuss whether or not the trends are consistent with your rationalization of your calculated C=O stretching frequencies.

Compare the calculated dipole moments of your calculated molecules. Can you recognize a trend?