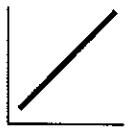
Analytical Cume November 2007

Correlations and NMR Spectroscopy

Correlation among data is well known and is currently of interest in NMR spectroscopy to achieve a number of improvements in time and resolution. We will explore some of these ideas in the following questions.

1. (20 pts) Draw a x-y scatter plot of data points (20-30 points, or alternatively a cloud of points) illustrating the following correlations:

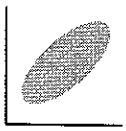
   a) 1.0 (highly correlated x- and y-data)

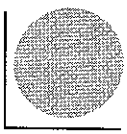
   b) -1.0 (negatively highly correlated data)

   c) 0.3

   d) 0.0

2. (30 pts) In Correlation Spectroscopy, commonly called COSY, a two-pulse sequence is used to identify connections among the J-coupled protons in the molecule. The pulse sequence is as follows:

Essentially, the pulse sequence is repeated for a number of different t_1 delay values and the signal (free induction decay, or FID) is collected. Fourier transformation (FT) is then performed twice, first as a function of the acquisition time t_2, and then along the so-called indirection or t_1 dimension. This leads to a 2D spectrum that chemists are very accustomed to seeing since 1976. (The combination of Fourier transform and 2D NMR led to a Nobel prize). Typically, 64 or 128 t_1 values are used, while there are often 16k points taken during a 2-second acquisition time.

a) Briefly, explain Fourier transformation. If you can write down a formula please do.

Fourier transformation is a mathematical method that is very often used to convert time dependent data to frequency dependent data, or vis-versa. The equation for Fourier transformation is the following:

$$S(\omega) = \int_0^\infty s(t)\exp(-i\omega t)dt$$

b) What is the Fourier transformation of a decaying exponential function?

A Lorentzian function. The mathematical form is: $L(\omega) = \frac{\lambda}{\lambda^2 + (\omega - \omega_o)^2}$**, with λ representing the line width. $\lambda = 1/T_2$ for NMR.**

c) What determines the spectral resolution in FT NMR?

The total acquisition time. Partial credit given for answers related to magnetic field strength of intrinsic line width of the spectra related to relaxation.

d) In the example above, what would the spectral resolution (in each dimension) be for a 10 ppm spectrum taken at 500 MHz? (you can give your answer either in Hz or ppm).

For the t1 dimension it is 1/(2 sec) or 0.5 Hz. For the second dimension, it is 500Hz/64 increments, or about 7.8 Hz. It would be 2 times smaller for 128 increments. To get the resolution in ppm, multiply by 10ppm/500Hz.

e) Normally, "zero-filling" is done along the indirect dimension to extend the data with zeros and double or even quadruple the number of t_1 increments. What does this accomplish?

This will increase the spectral resolution by a factor of 2 or 4. One cannot increase the resolution much more than this because there is no extra information available in the data.

3. (30 pts) A recently reported alternative approach for some 2D NMR experiments is called "Covariance NMR." In this approach, the data are collected as before, but instead of the Fourier transformation in the indirect direction, a cross-covariance calculation *between different frequencies* is performed to identify the couplings between the protons in the molecule.

a) (Hard) The correlation between x and y data is given by the following expression:

$$r_{xy} = \frac{\sum(x_i - \bar{x})(y_i - \bar{y})}{(n-1)s_x s_y},$$

where $\bar{x}$ is the mean of the x data, s_x is the standard deviation, and similarly for the y data. The covariance is the same expression without the normalization by the standard

deviations. Given the NMR data or signal is of the form S(freq, t_1), explain in words what is being correlated and what is being summed over.

Here the correlation is between signals x_i = S(freq1, $t1_i$) and y_i =S(freq2, $t1_i$) that have different frequencies. This is a essentially a cross correlation of the frequencies. The summation is over the different signals acquired as t1 is incremented, i.e., the indirect dimension in the 2D data set.

b) The big advantage of this approach is that the resolution is improved. Along what dimension does the improvement occur? Can you explain how?

The improvement occurs along the second dimension. Normally many increments are required to obtain good resolution, as indicated in problem 2d and 2e. With correlation, one often starts to see the correlated frequencies within a dozen increments or so.

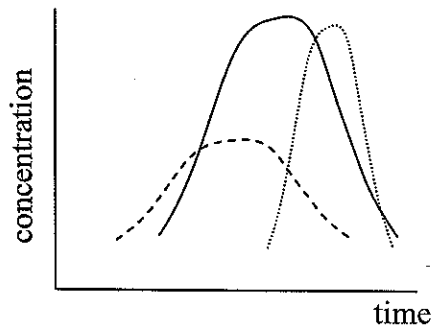
c) If n=16 for the covariance experiment, what would this represent compared to the Fourier transform approach? What is the advantage?

Compared to 64 increments along t1, this would imply a 4X decrease in the experimental time.

d) There is of course, no free lunch, and so this approach has a down side. The computation is a bit slower, but more importantly, if there are more peaks than n, one can get artifacts such as extra peaks. How would this be a problem for say biofluid samples?

In biofluids, there are many, many peaks in the NMR spectrum corresponding to the multitude of different molecules. Therefore, one runs the risk of identifying components that have a random correlation at small numbers of n with real correlations. Thus one has to be careful when using this approach to verify couplings, perhaps with more conventional NMR methods.

4. (20pts) A newly reported application of covariance processing is to de-convolve overlapped peaks in complex spectra such as in LC/NMR. Given 3 different compounds, each with its own NMR spectrum, and slightly different elution profile such that spectra are overlapped, how could you use covariance or correlation to figure out what the 3 different molecules are?



One could use correlation to identify the 3 different eluting peaks by correlating the peaks in the spectrum along the elution time dimension. 1D NMR spectra acquired during the chromatographic run would be correlated with one another to identify common peaks that could then be pulled apart, yielding isolated peaks at each time point.

No Biochemistry crib available yet

November 10, 2007

Written by Professor Das

Inorganic Chemistry Cumulative Exam

Purdue University

November 10, 2007

There are 100 possible points in this exam.

1. (30 points) The unit cell of MgO is shown below. The size of Mg^{2+} and O^{2-} ions are 0.086 nm and 0.126 nm, respectively. Estimate the volume (in cm^3) and density (in g/cm^3) of MgO. (No partial points will be given to incorrect or incomplete answers.)

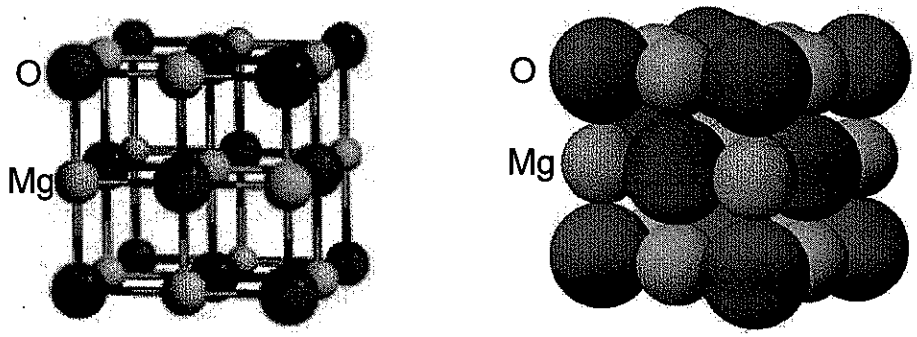
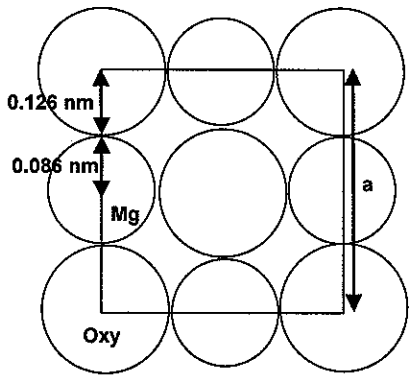


Figure 1. Two different representations of the MgO unit cell.

Answer:



- **a (length = width= height of a cube)= (0.126 nm + 0.086 nm) x 2 = 0.424 nm**
- **Volume of a unit cell = $(0.424\ nm)^3 = 0.0762 \times 10^{-27}\ m^3 = 7.62 \times 10^{-23}\ cm^3$**
- **Mass of a unit cell $=(40.3 \times 4 / 6.02 \times 10^{23})g = 26.8\ 10^{-23}\ g$**
- **(There are four Mg atoms and O atoms per unit cell)**
- **Density = m / v = $26.8\ 10^{-23}\ g / 7.62 \times 10^{-23}\ cm^3 = 3.51\ g/cm^3$**

<u>* I did not specify that "size" means "radius" in the question. Therefore, I gave full credit to those who solved this probem by interpreting size as diameter.</u>

2. (10 points) NaCl and MgO have the same crystal structure. Which compound do you predict to have a higher melting point? Explain. (Answers without explanation will not receive any points.)

Answer: MgO will have a higher melting point.
Explanation: Both NaCl and MgO are ionic compounds. The lattice energy in ionic compounds is proportional to the electrostatic interactions between the cations and anions for a given structure. The electrostatic interaction is proportional to the charges of cations and anions and inversely proportional to the distance between the cation and the anion. Both Mg^{2+} and O^{2-} in MgO have high charges than Na^+ and Cl^- in NaCl. Also the distance between Mg^{2+} and O^{2-} is shorter than the distance between Na^+ and Cl^- as Mg^{2+} is smaller than Na^+ and O^{2-} is smaller than Cl^-. Therefore Mg-O bond is stronger than Na-Cl bond.

3. (10 points) Explain what is wrong with the following statement, and correct it.

"Molecular weight of NaCl is 58.44 amu."

Answer: "Formula weight of NaCl is 58.44 amu."
Explanation: NaCl is not a molecular compound (There is no isolated molecule that is composed of one Na and one Cl). It is an ionic compound where Na^+ and Cl^- ions alternate infinitely along all the crystallographic axes. Therefore, NaCl is not a molecular formula but an empirical formula that shows the simplest Na to Cl ratio in this compound. In this case, formula weight is a proper term to use to describe its weight.

4. (10 points) NaCl is an ionic compound while H_2O is a covalent compound. The melting point of NaCl (804 °C) is much higher than that of H_2O (0 °C). Can you use these data to make a conclusion that in general ionic bonds are much stronger than covalent bonds? Explain.

Answer: No
Explanation: The the melting point of H_2O cannot be used to assess the strength of covalent H-O bonds in a H_2O molecule because when H_2O is melted, it is not the intramolecular H-O bond that is affected. Instead it is hydrogen bonding between water molecules (intermolecular bonding) that is affected. Therefore, the above data may be used to discuss the strength of ionic bond vs. hydrogen bond but not to discuss the strength the strength of ionic bond vs covalent bond.

5. (10 points) Fill in the banks (a-b) in the following statement.

"The effective ionic radius of Co^{2+} ions in a crystal structure is affected by (a) and (b) of Co^{2+} ions."

Answer: (a) coordination number and (b) spin sate (e.g. low spin or high spin)

6. (10 points) The crystal structures of NaCl and CsCl are shown below. Why would CsCl not adopt the same crystal structure as NaCl?

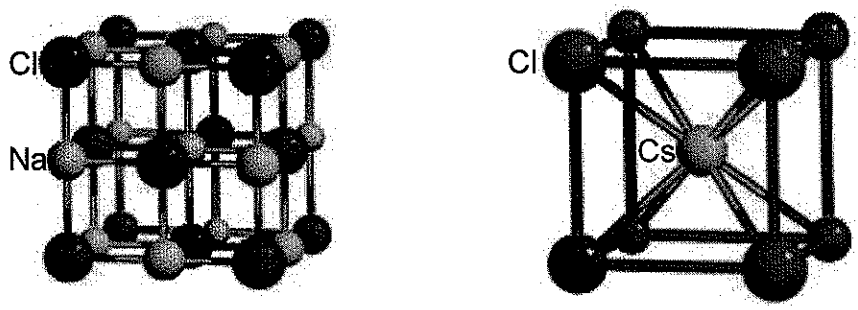


Figure 2. Crystal Structures of NaCl (left) and CsCl (right).

<u>Answer:</u> The cationic sites in NaCl structure are surrounded by 6 Cl^- ions while the cationic sites in CsCl structure are surrounded by 8 Cl^- ions. Cs ions are too big to fit in octahedral sites created by 6 Cl^- ions. Therefore Cs ions have to increase its coordination number to 8 to create enough space for them to form a stable crystal structure.

(Answers mentioning only the size of Cs ions as a reason without discussing (i) the difference in coordination numbers in these two structures or (ii) the importance of the cationic size to anionic size ratio for adopting crystal structures did not receive full credit.)

7. (20 points) A unit cell of calcium fluoride is shown below.

(a) What is the coordination number of fluoride ions?

<u>Answer: 4</u>

(b) What is the local environment of fluoride ions (e.g. octahedral, tetrahedral, square planar, trigonal pyramid, trigonal prism, etc.)?

<u>Answer: Tetrahedral</u>

(c) How many fluoride ions are present per unit cell?

<u>Answer: 8</u>

(d) How many calcium ions are present per unit cell?

<u>Answer: 4</u>

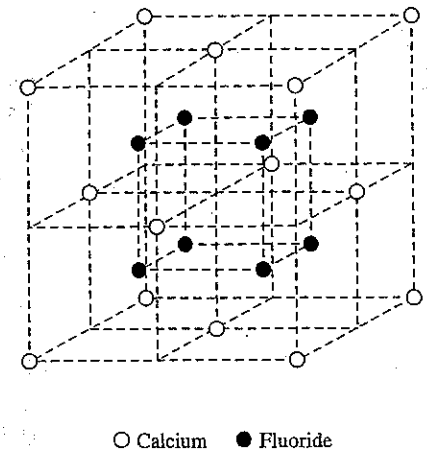


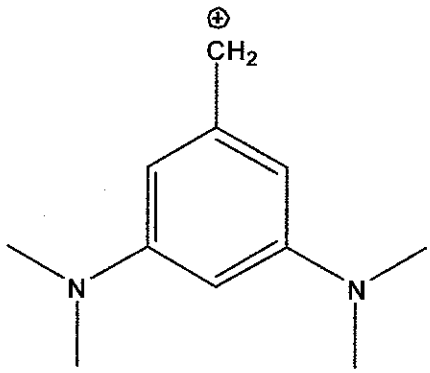
Figure 3. A unit cell of calcium fluoride.

total: 80 pts. → 100% $\times \frac{100}{80}$

ORGANIC CUMULATIVE EXAMINATION **Nov. 10th, 2007**

CRIB

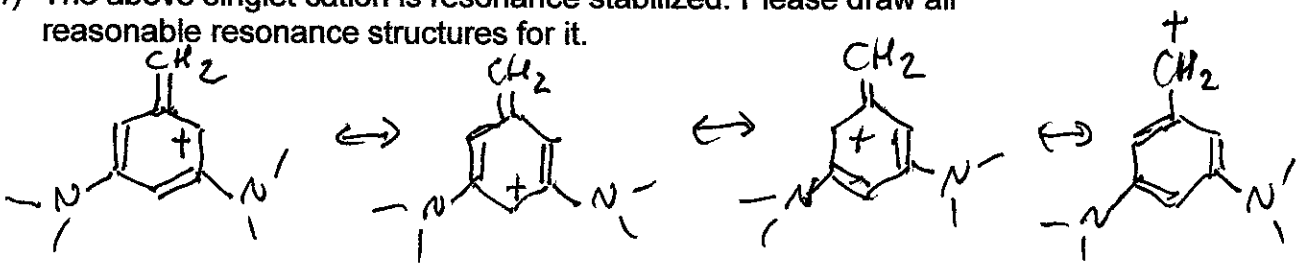
One long-standing interest of synthetic chemists has been in finding persistent high-spin organic molecules for use in ferromagnetic organic polymers. A recent JACS article ("*Benzylic Cations with Triplet Ground States: Computational Studies of Aryl Carbenium Ions, Silylenium Ions, Nitrenium Ions, and Oxenium Ions Substituted with Meta π Donors*", Arthur Winter, Daniel Falvey, Christopher Cramer and Benjamin Gherman, **2007**, *129*, 10113-10119) presents computational results that suggest that a π,π*-diradical state (triplet state) of benzyl cations is stabilized by π-donating *meta*-substituents. Notably, the 3,5-bis(N,N-dimethylamino)benzyl cation (shown below in its singlet state) is calculated to have a triplet ground state by 1.9 kcal/mol.



Please answer the following questions related to the above research:

10 pts.

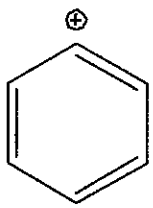
1) The above singlet cation is resonance stabilized. Please draw all reasonable resonance structures for it.

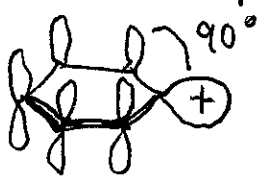


10 pts.

2) As opposed to benzyl cations, the phenyl cation (below) is not resonance stabilized. Why not?

Orthogonal orbitals; no overlap





10 pts. 3) Define a π-donating substituent. Give an example of a π-acceptor, σ-donor and σ-acceptor substituent.

Able to donate electron density to the π-system.

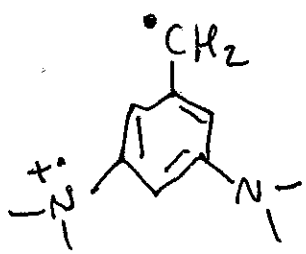
π-acceptor: CO, CN, NO_2

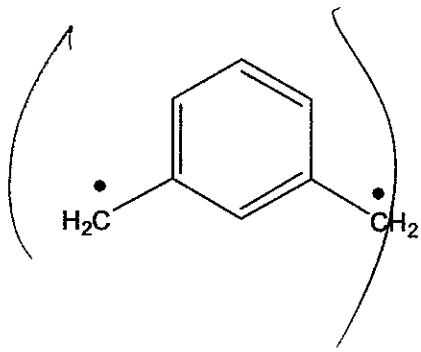
σ-donor: alkyl, SiR_3

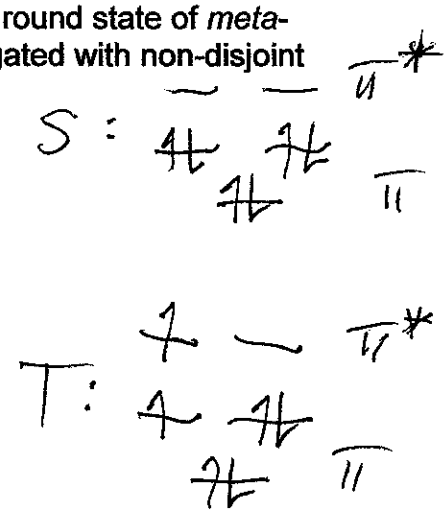
σ-acceptor: F, NO_2, CN

answer to question 1

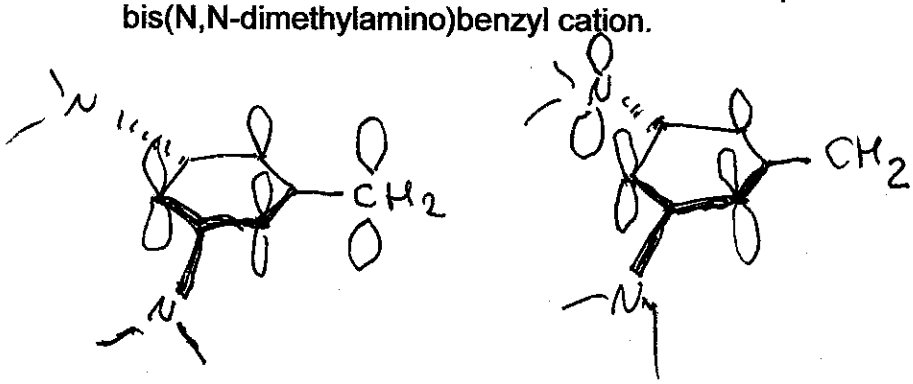
10 pts. 4) Illustrate the different electron distributions in the singlet and the π,π*-diradical states of the 3,5-bis(N,N-dimethylamino)benzyl cation (for the triplet state, promote an electron from the lone pair of the substituent into the LUMO formally associated with the benzylium based p-orbital). The π,π*-diradical state is analogous to the triplet ground state of *meta*-xylylene (below), a non-Kekule diradical conjugated with non-disjoint SOMOs.







10 pts. 5) Draw a three-dimensional picture to illustrate the relative orientations of the singly-occupied molecular orbitals in the triplet state of the 3,5-bis(N,N-dimethylamino)benzyl cation.



10 pts.

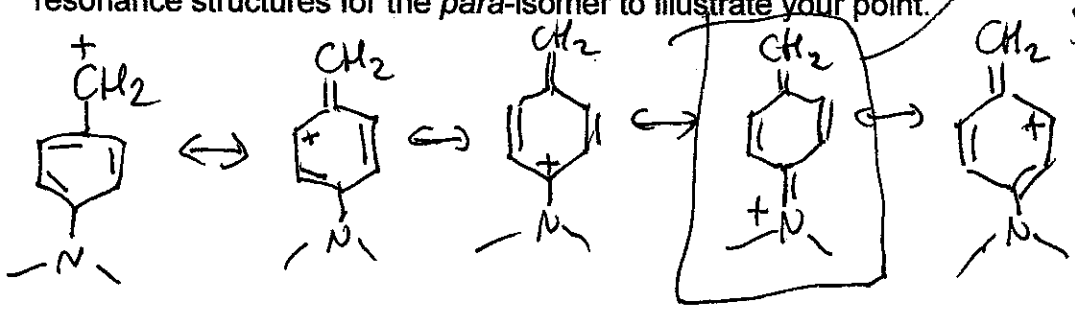
6) Why does the π,π*-diradical state-stabilizing substituent have to be a π-donor instead of a π-~~donor~~ acceptor, σ-acceptor or σ-donor?

σ-acceptor, π-acceptor: no electron donation to ring (ionization energy of the substituent increases)

σ-donor: does not lower the ionization energy of the ring system enough

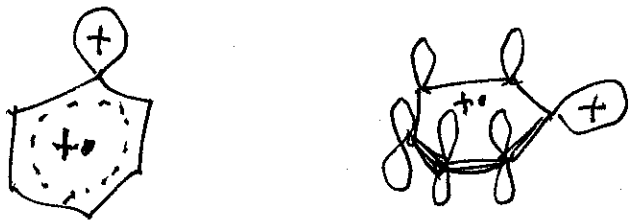
10 pts.

7) Why does the substituent have to be in the *meta*-position? Show resonance structures for the *para*-isomer to illustrate your point.



ortho- and para-substituents stabilize the singlet state relative to triplet

8) Illustrate the electron distributions in the σ,π-triplet state of the phenyl cation.



PChem Curve Nov. 10, 2007

Solutions

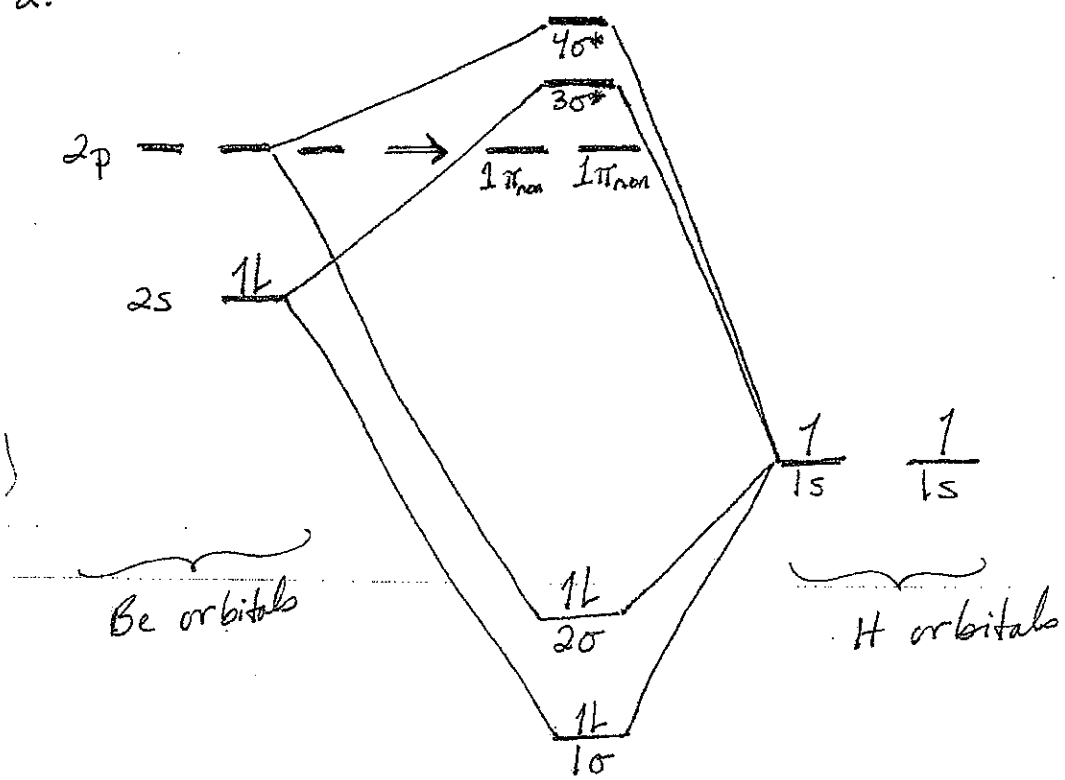
1.

$$\psi_1 = \frac{1}{\sqrt{3}}\psi_{2s} + \sqrt{\frac{2}{3}}\psi_{2p_z}$$

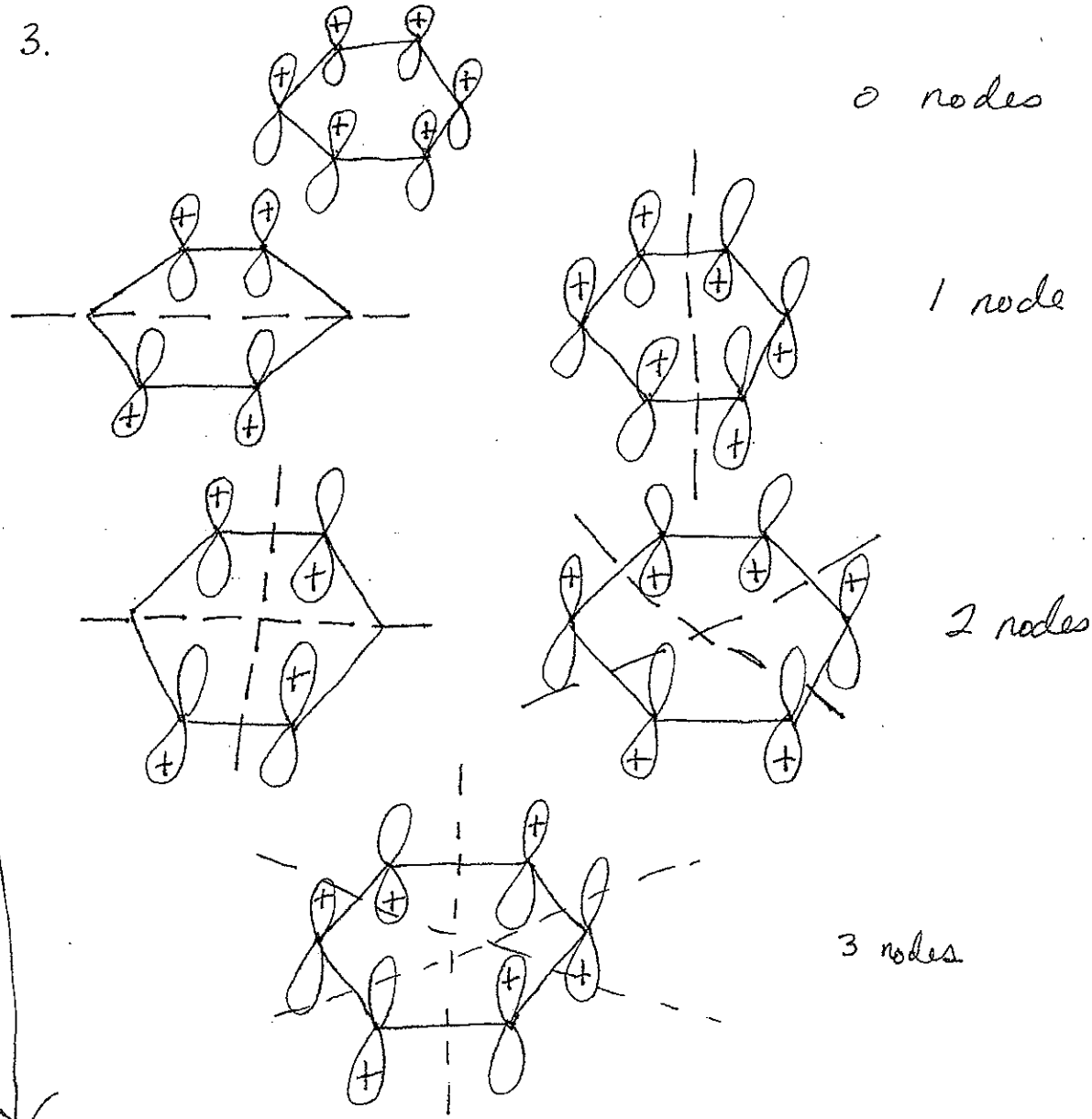
$$\psi_2 = \frac{1}{\sqrt{3}}\psi_{2s} - \frac{1}{\sqrt{6}}\psi_{2p_z} + \frac{1}{\sqrt{2}}\psi_{2p_x}$$

$$\psi_3 = \frac{1}{\sqrt{3}}\psi_{2s} - \frac{1}{\sqrt{6}}\psi_{2p_z} - \frac{1}{\sqrt{2}}\psi_{2p_x}$$

2.



3.



Explanation – these come from solving the Hückel secular determinant for benzene, which correspond to the following:

$\psi_1 = \frac{1}{\sqrt{6}}(2p_{z1} + 2p_{z2} + 2p_{z3} + 2p_{z4} + 2p_{z5} + 2p_{z6})$ $\quad E_1 = \alpha + 2\beta$ (lowest E)

$\psi_2 = \frac{1}{\sqrt{4}}(2p_{z2} + 2p_{z3} - 2p_{z5} - 2p_{z6})$ $\quad E_2 = \alpha + \beta$] degenerate

$\psi_3 = \frac{1}{\sqrt{3}}(2p_{z1} + \frac{1}{2}2p_{z2} - \frac{1}{2}2p_{z3} - 2p_{z4} - \frac{1}{2}2p_{z5} + \frac{1}{2}2p_{z6})$ $\quad E_3 = \alpha + \beta$

$\psi_4 = \frac{1}{\sqrt{4}}(2p_{z2} - 2p_{z3} + 2p_{z5} - 2p_{z6})$ $\quad E_4 = \alpha - \beta$] degenerate

$\psi_5 = \frac{1}{\sqrt{3}}(2p_{z1} - \frac{1}{2}2p_{z2} - \frac{1}{2}2p_{z3} + 2p_{z4} - \frac{1}{2}2p_{z5} - \frac{1}{2}2p_{z6})$ $\quad E_5 = \alpha - \beta$

$\psi_6 = \frac{1}{\sqrt{6}}(2p_{z1} - 2p_{z2} + 2p_{z3} - 2p_{z4} + 2p_{z5} - 2p_{z6})$ $\quad E_6 = \alpha - 2\beta$ (highest energy)

4. The probability is found from the integral:

$$\int_0^{a_0} R_{1s}^2(r)\, r^2\, dr$$

Since

$$\Psi_{100} = \frac{1}{\sqrt{4\pi}} R_{1s}(r) = \frac{1}{\sqrt{\pi}}\left(\frac{1}{a_0}\right)^{3/2} e^{-r/a_0}$$

then $R_{1s}(r) = 2\left(\frac{1}{a_0}\right)^{3/2} e^{-r/a_0}$

The integral then becomes

$$\frac{4}{a_0^3}\int_0^{a_0} r^2 e^{-2r/a_0}\, dr.$$

It was given that $\int_0^1 x^2 e^{-2x}\, dx = \frac{1}{4} - \frac{5}{4}e^{-2}$

Therefore:

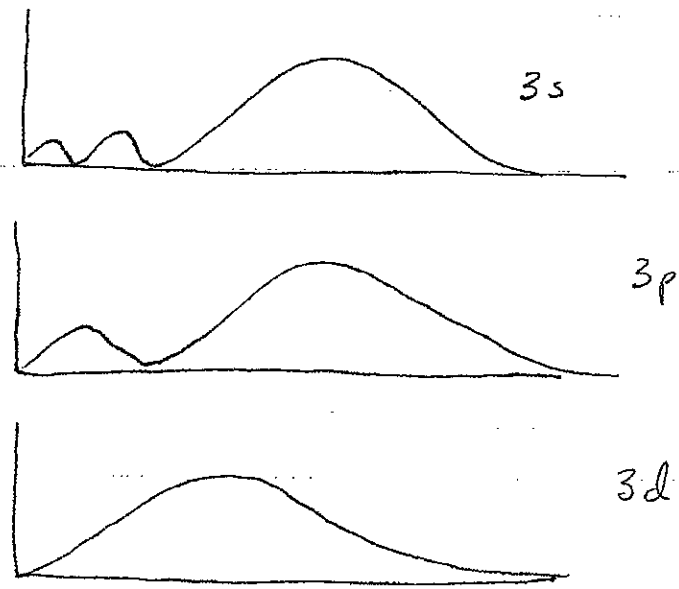
$$\frac{4}{a_0^3}\int_0^{a_0} r^2 e^{-2r/a_0}\, dr = 4\int_0^1 x^2 e^{-2x}\, dx$$

$$= 1 - 5e^{-2}$$

$$= 0.323$$

or 32.3%

5. The problem asks only for the radial probability densities, $r^2 R_{nl}^2(r)$ versus r.



6a. $[\hat{L}_z, \hat{L}_+] = \hat{L}_z \hat{L}_+ - \hat{L}_+ \hat{L}_z$

$$= \hat{L}_z(\hat{L}_x + i\hat{L}_y) - (\hat{L}_x + i\hat{L}_y)\hat{L}_z$$

$$= \hat{L}_z \hat{L}_x + i\hat{L}_z\hat{L}_y - \hat{L}_x\hat{L}_z - i\hat{L}_y\hat{L}_z$$

$$= (\hat{L}_z\hat{L}_x - \hat{L}_x\hat{L}_z) - i(\hat{L}_y\hat{L}_z - \hat{L}_z\hat{L}_y)$$

$$= [\hat{L}_z, \hat{L}_x] - i[\hat{L}_y\hat{L}_z]$$

$$= i\hbar\hat{L}_y - i(i\hbar\hat{L}_x)$$

$$= \hbar(\hat{L}_x + i\hat{L}_y)$$

$$\boxed{[\hat{L}_z, \hat{L}_+] = \hbar L_+}$$

6b. $[\hat{L}^2, \hat{L}_+] = \hat{L}^2\hat{L}_+ - \hat{L}_+\hat{L}^2$

$$= \hat{L}^2(\hat{L}_x + i\hat{L}_y) - (\hat{L}_x + i\hat{L}_y)\hat{L}^2$$

$$= \hat{L}^2\hat{L}_x + i\hat{L}^2\hat{L}_y - \hat{L}_x\hat{L}^2 - i\hat{L}_y\hat{L}^2$$

$$= (\hat{L}^2\hat{L}_x - \hat{L}_x\hat{L}^2) - i(\hat{L}_y\hat{L}^2 - i\hat{L}_y\hat{L}^2)$$

$$= \underbrace{[\hat{L}^2, L_x]}_{=0} - i\underbrace{[\hat{L}_y, \hat{L}^2]}_{=0} = 0$$