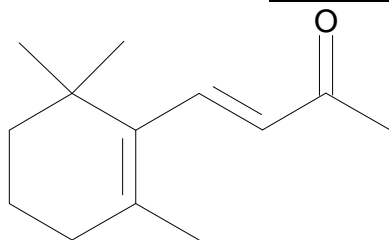


## Calculating NMR Chemical Shifts for beta-ionone



Molecular orbital calculations can be used to get good estimates for chemical shifts. In this exercise we will calculate the chemical shifts for beta-ionone. You can then compare the calculated shifts with the experimental shifts, and in so doing verify that you made the correct assignments. This calculation will be done using the GIAO method. GIAO is an acronym for Gauge Invariant Atomic Orbitals. This approach insures that the magnetic properties of the atoms are handled properly.<sup>1</sup> The GIAO approach is a time consuming calculation, and we will take some short cuts. Because of this, we will need to apply a scaling factor to our results. In other words, the shifts will be in the right order, but they will be off by a small factor. We will use EXCEL to find this scaling factor.

You will do two types of quantum mechanical calculations. The first is a semi-empirical calculation. In semi-empirical calculations the values for important integrals are taken from experimental measurements. The second is an *ab initio* calculation. In *ab initio* calculations the important integrals are done directly from first principles. First principles means that the integrals are done either using closed formulas or by doing the integrals numerically. The semi-empirical process is faster than *ab initio* calculations.

In semi-empirical calculations it is important to keep track of the experimental data that was used in finding the parameter for the integrals. For AM1 calculations, the molecules that were used were primarily hydrocarbons and simple oxygen containing compounds like alcohols, aldehydes, ketones, and carboxylic acids. AM1 calculations work very well for molecules that are in these classes. If you have nitrogen or heavy elements like sulfur or chlorine, PM3 calculations are better. The AM1 or PM3 simply signifies the sets of experimental parameters that are used. MOAPC is a semi-empirical program that extremely efficient.

The particular *ab initio* method that works best for calculating NMR properties is a variant of density functional theory, DFT, called B3LYP. We will talk about *ab initio* methods later in the course. The Gaussian program does semi-empirical and *ab initio* calculations.

The step-by-step instructions will take you through three stages, which are summarized below:

### *Summary Outline;*

Stage 1: You will draw the molecule and minimize the structure using molecular mechanics.

Stage 2: You will use GAUSSIAN at the PM3 semi-empirical level to minimize the structure to find a good geometry. Finding a good geometry is called geometry optimization, so "GEO" or "OPT" are used as the keyword (GEO in MOPAC and OPT in Gaussian).

Stage 3: You will do the NMR shift calculation using the GIAO method at the B3LYP level at the geometry found in Stage 2. A calculation where you hold the geometry fixed and just calculate the energy and associated properties of the molecule is called a "single point" calculation, so "SP" is used as the keyword.

## **Instructions**

### *Stage 1:*

1. This calculation will be easiest using the WebMO graphics front end Web application on the “schupflab” computer. WebMO makes the formation of the input files and viewing of the output files from MOPAC and Gaussian particularly simple. In other words WebMO doesn't do the calculations, but rather acts as a go-between you and the computational packages. A link to “schupflab” is available in the WebMo section of the PChem course Web home page (near the bottom, in the WWW Links listing: “<http://schupflab.colby.edu/cgi-bin/webmo/login.cgi>”).
2. Log in to WebMO using your normal Colby user name (e.g. “twshattu”). A temporary password will be e-mailed to you. Make sure to change this temporary password. You will see the Job Manager screen. Extensive help is available under Utilities in the top menu bar. An introduction to WebMo, which includes a quick start tutorial, is available at: [http://www.webmo.net/download/WebMO\\_Users\\_Guide.pdf](http://www.webmo.net/download/WebMO_Users_Guide.pdf)
3. Mouse over “New Job” and click on “Create New Job.” In the WebMO Editor window, draw  $\beta$ -ionone. Pull down the “Clean-Up” menu and choose “Add Hydrogens” and then “Comprehensive- Mechanics” to do a molecular mechanics minimization. Note the conformation of the side chain. Then click on the blue “>” button at the bottom-right of the editor window to close the Editor window.

### *Stage 2:*

4. Under the “Job Options” tab, enter a job name and choose the following options:
  - Calculation: Geometry Optimization
  - Theory: PM3
  - Charge: 0
  - Multiplicity: Singlet

To see the input file that is generated for Gaussian, click on the “Preview” tab and then the “Generate” button. Take a few moments to note the various sections and the keywords that are used.

5. Then click on the blue “>” button. The screen will switch back to the Job Manager screen. After less than a minute the status of your calculation should change to “Complete”. Click on the magnifying glass to see the results.
6. Your minimized structure should be displayed. You can rotate the molecule to observe the conformation. Click on the “Data Viewer” tab. Take a moment to notice the different sections, especially the PM3 Energy, and the Partial Charges. The atom numbers are listed in the Molecule Viewer.

### *Stage 3:*

7. Click on the “New Job Using this Geometry” button. Then click on the blue “>” button. Enter a job name and choose the following options:
  - Calculation: NMR
  - Theory: B3LYP
  - Charge: 0
  - Multiplicity: Singlet

8. Preview the input file. The Gaussian input file is then displayed. Take a moment to notice the different sections. Then click on the blue “>” button. The MO calculation will then start. You will be returned to the Job Manager. Your job should be listed. This calculation will take about 15 minutes to complete. When your job status is “complete”, click on the magnifying glass button. Your results should be displayed. Note the atom numbering in the 3D-display. Notice the numerical sections, especially the *B3LYP Energy*, the *Partial Charges*, and the *Relative NMR Shifts*. You can (should) copy and paste these shift values into Excel, where you can calculate the average shifts for each chemical environment. Note that the chemical shifts for protons in the same methyl group or methylene group aren’t equivalent. This is because the shifts are calculated for a motionally frozen structure. The motion of the methyl group averages these different chemical environments. So average the chemical shifts of the protons in each methyl group and each methylene to make a fair comparison with your experimental values. Arrange the averaged results in a column of your spreadsheet in order of chemical shift. Match up these calculated chemical shifts with your measured chemical shifts. Match methyls with methyls, methylenes with methylenes, etc.

9. To view the raw numerical results, you can click on the “Raw Output” button at the left-hand side of the screen. Now we can read off the absolute chemical shifts. Scroll down to the section that looks like this:

```
Calculating GIAO nuclear magnetic shielding tensors.
GIAO Magnetic shielding tensor (ppm):
 1 C   Isotropic = 158.9054   Anisotropy = 42.6840
    XX= 169.7778   YX= -16.5453   ZX= 12.9221
    XY= -21.3343   YY= 159.3514   ZY= -12.6809
    XZ= 4.7198    YZ= -1.1183   ZZ= 147.5870
    Eigenvalues: 144.3985 144.9562 187.3614
 2 C   Isotropic = -9.3932   Anisotropy = 181.9697
    XX= 15.0320   YX= 86.7475   ZX= -38.5124
    XY= 89.4731   YY= 18.7708   ZY= -13.1062
    XZ= -34.4217  YZ= -11.9061  ZZ= -61.9823
    Eigenvalues: -87.0712 -53.0283 111.9200
```

Scroll down until you find the hydrogens. For example:

```
Eigenvalues: 160.4333 165.4304 168.3726
15 H   Isotropic = 29.5760   Anisotropy = 5.0298
    XX= 32.4314   YX= -0.0761   ZX= -2.3382
    XY= 0.1015   YY= 26.9679   ZY= -1.1402
    XZ= -0.2352  YZ= -1.3542   ZZ= 29.3286
    Eigenvalues: 26.3873 29.4115 32.9292
16 H   Isotropic = 29.1019   Anisotropy = 5.4710
    XX= 30.7947   YX= 1.4534   ZX= 2.2040
    XY= 1.4384   YY= 30.2260   ZY= 1.0264
    XZ= 2.7856   YZ= -0.3504   ZZ= 26.2850
    Eigenvalues: 25.1608 29.3957 32.7493
```

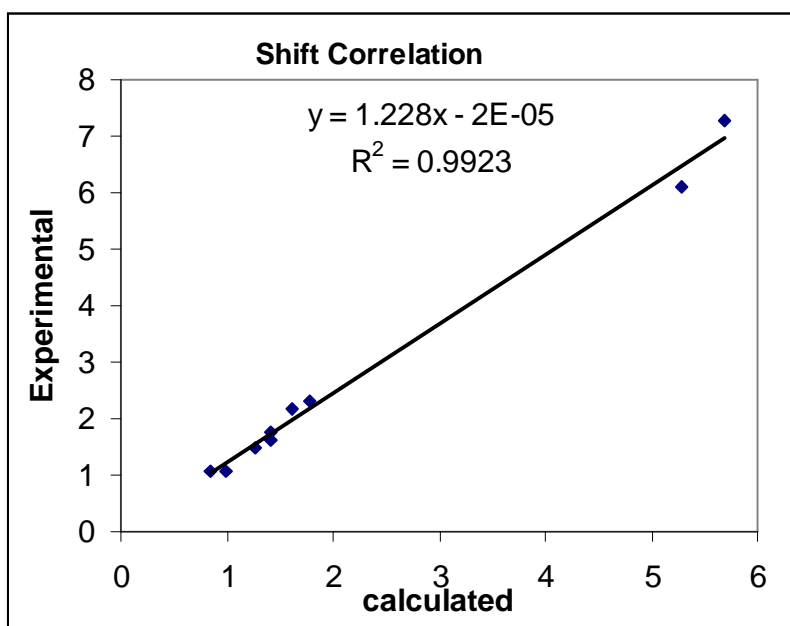
The chemical shift to note is the Isotropic value. For example, for hydrogen 15 the shift is 29.5760. To convert the shifts to ppm subtract the isotropic value from the isotropic chemical shift of the protons in TMS:

$$\delta_i \text{ (ppm)} = \text{isotropic(TMS)} - \text{isotropic}(i)$$

An appropriate value for the isotropic chemical shift for TMS is 31.9232 ppm at the B3LYP/6-31G(d) level.<sup>2</sup> The eigenvalues are the chemical shifts in three orthogonal directions around the nucleus. Note that the values can be rather different. The isotropic chemical shift is the average

of these three values. You don't need to do anything with this raw data. The point is to note that the chemical shift is very direction dependent, and the solution chemical shift is the average of rather widely varying directional values.

10. To see how well our calculation did, make a plot of the experimental chemical shift versus the calculated chemical shift (calculated on the horizontal axis). You should get a nice straight-line correlation. Here's an example plot:



**Questions:**

1. Do the calculated and experimental peaks come in the correct order? That is, do the methylenes and methyl groups come in the same order for theory and experiment?
2. How good is the correlation between the experimental and calculated shifts?

**Notes:**

1. The GIAO procedure is designed so the choice of coordinate axis does not change the magnetic properties of the atom.
2. You need to calculate the shift of TMS at the same level of calculation as you use for your molecule. This value is stored in WebMO and is used to calculate the *Relative Chemical Shift* for you automatically.

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