Predicting Magnetic Properties with ChemDraw and Gaussian

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Introduction

NMR chemical shifts are an important tool in characterizing molecular systems and structures. Accordingly, predicting NMR spectra is an essential feature of computational chemistry software. In this article, we'll look at two very different NMR facilities, each of which is very useful when applied to the appropriate sort of molecules.

ChemDraw Ultra includes the CS ChemNMR Pro facility which can be used to estimate the ^{13}C and ^{1}H (proton) chemical shifts with respect to TMS. This facility is accessed from the **Estimate** menu within the product. When a molecule has been selected, the two items on the menu become active, and selecting one of them causes the NMR chemical shifts for the corresponding atom type to be calculated.

Figure 1 illustrates the use of this facility; here we estimate the ^{13}C chemical shifts with respect to TMS for adenine. The **Estimate** menu and selected molecule appear on the left in the figure, and the resulting graphic output appears on the right. The latter consists of another copy of the molecule to which numbers denoting the chemical shift (in ppm) have been added at each atom location. Note that numbers are ordinary ChemDraw text labels and thus may be moved as needed in order to make them fully legible. Additional output is presented in text form via a Notepad document (which is opened automatically by ChemDraw).
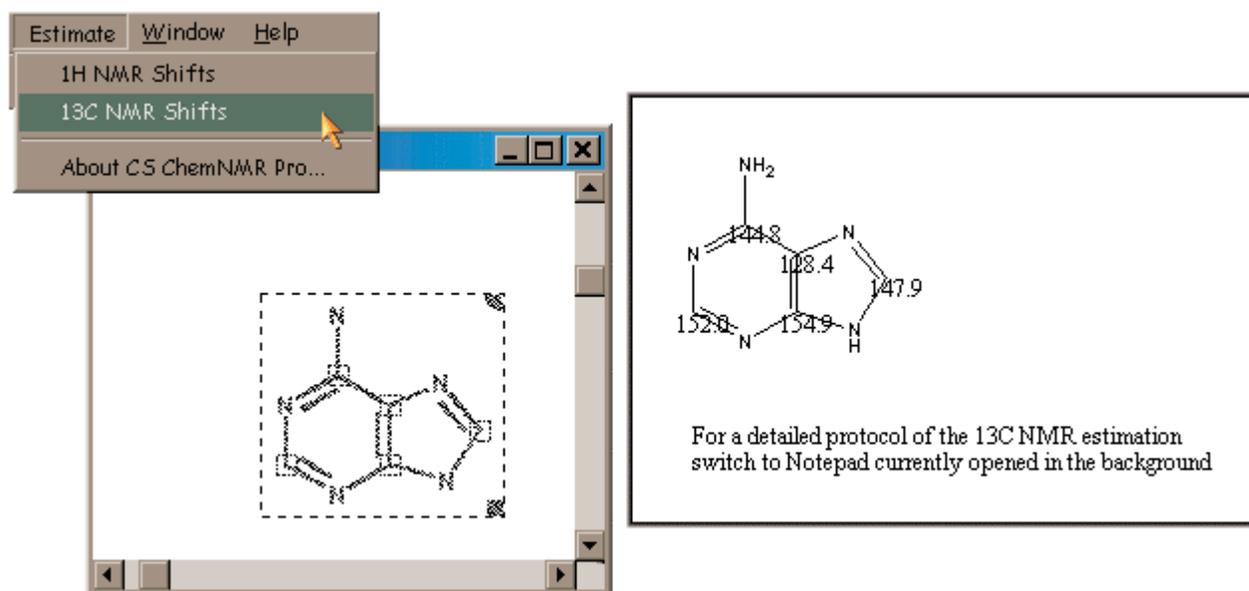

Figure 1. Example CS ChemNMR Pro Output

CS ChemNMR Pro uses a heuristically-driven procedure in order to estimate chemical shifts; it starts with a base value determined from the molecular mechanics atom type of the atom in question, and then applies corrections for each of the groups to which it is bonded in order to compute its final value. This process is illustrated in this excerpt from the textual output from a calculation on taxol:

```
Protocol of the 13C NMR Estimation

Node    Estim.    Base    Incr.      Comment (ppm rel. to TMS)
  C     138.5     123.3             1-ethylene
                           -8.9     1 -C-C-C-C
                           -7.4     1 -C
                           17.3     1 -C-C-C-C
                           14.2     1 -C-O
```

The main advantage of this approach to computing chemical shifts is its speed: chemical shifts can be computed almost instantaneously even for very large molecules. However, the method has an important weakness which must be kept in mind. Since it relies on a fixed set of parameters corresponding to atom types and subgroups, the method will be reliable only for molecules for which parameters are available and for which the assumptions about molecular structure and bonding which are built-in to the parameters are valid.

In simple terms, this NMR estimation method is appropriate only for ordinary organic molecules. It produces reasonable results for such systems, but becomes quite unreliable for systems with any unusual features: unusual bonding, strained systems, systems for which electron correlation is important for accurate modeling of the molecular structure or properties, and so on. In these cases, a more accurate computational method is required.

Systematic Prediction of Magnetic Properties

Gaussian 98 includes a facility for predicting magnetic properties, including NMR shielding tensors and chemical shifts. These calculations compute magnetic properties from first principles, as the mixed second derivative of the energy with respect to an applied magnetic field and the nuclear magnetic moment. As a result, they can produce high accuracy results for the entire range of molecular systems studied experimentally via NMR techniques.

Thus, *Gaussian 98*'s facility has several important advantages over the simple computation procedure used by CS ChemNMR Pro:

- Accurate prediction of magnetic properties for all types of molecular systems
- Ability to predict chemical shifts for atoms other than hydrogen and carbon (nitrogen, phosphorous, boron, and so on).
- NMR properties can be computed as part of a systematic and self-consistent study of the molecule.

Some Sample Results

As we've noted, CS ChemNMR Pro does an adequate job of estimating chemical shifts for ordinary organic compounds. Taxol provides an example of this. For this molecule, CS ChemNMR Pro's mean absolute error with respect to the observed ^{13}C chemical shifts is 3.8 ppm, with a standard deviation of 4.6, and the largest error is 19.0 ppm. *Gaussian* also does well for this molecule: its mean absolute error is 4.2, with a standard deviation of 3.8 and a maximum error of 23.6.

Observed and Predicted [13]C Chemical Shifts for Taxol
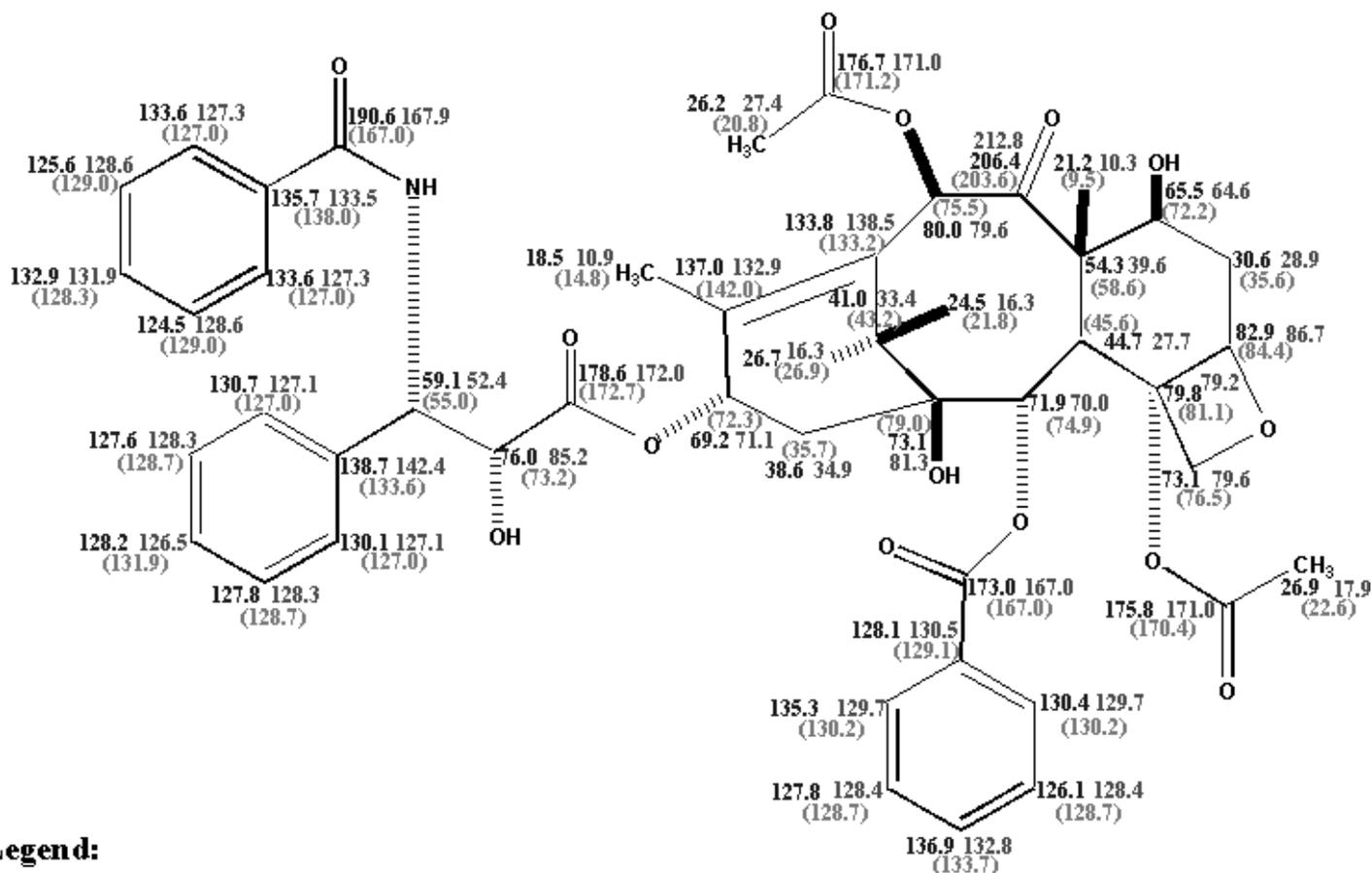
Legend:

Gaussian 98 **Shift**   CS ChemNMR Pro Shift
(Observed Shift)

Layout occasionally modified due to space constraints.

Chemical shifts are with respect to TMS.

Table 1 presents ^{13}C chemical shifts for adenine as computed by CS ChemNMR Pro and predicted by *Gaussian 98*, comparing them to the experimentally observed values. For this molecule, *Gaussian 98* performs slightly better than CS ChemNMR Pro. However, the errors that *Gaussian* makes are systematic, always over estimating the magnitude of the chemical shift. In contrast, the estimated shifts computed by CS ChemNMR Pro contain large errors with respect to the observed values in both directions.
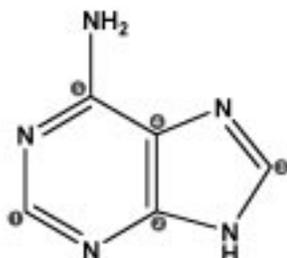

Table 1. Predicted ^{13}C Chemical Shifts for Adenine

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Atom    CS ChemNMR Pro   ΔExperiment   Gaussian 98   ΔExperiment   Experiment
C1      150.2              -2.2           161.2         +9.2          152.4
C2      154.9              +3.6           156.8         +5.5          151.3
C3      147.9              +8.6           139.5         +0.2          139.3
C4      128.4             +10.8           124.8         +7.2          117.6
C5      144.8             -10.5           160.7         +5.4          155.3
```

Table 2 lists the estimated and predicted ^{13}C chemical shifts for a series of three strained system, cyclopropane, bicyclobutane and [1.1.1]propellane, and for another unusual system, oxaspiropentene (left to right in the illustration). Both values for the carbon shift in cyclopropane are reasonable, but with the larger molecules, the limitations of the heuristically-based approach become clear. CS ChemNMR Pro cannot estimate either the values of the chemical shifts nor the difference in shift between the two different types of carbon atoms within the molecule. Finally, the results for oxaspiropentene are only fair. In contrast, the values predicted by *Gaussian 98*agree very well with with the observed values in all cases.

Table 2. Chemical Shifts for Three Strained Hydrocarbons

Molecule and Atom	CS ChemNMR Pro	*Gaussian 98*	Experiment
Cyclopane (C_3H_6)			
C1	-2.8	-6.7	-4.0
Bicyclobutane (C_5H_6)			
C1	6.6	26.6	32.0
C2	-0.2	-7.1	-5.7
Shift Difference	6.8	33.7	37.7

Molecule and Atom	CS ChemNMR Pro	*Gaussian 98*	Experiment
[1.1.1]Propellane(C_5H_6)			
C1	30.3	70.6	79.3
C2	26.0	-3.4	3.4
Shift Difference	4.3	74.0	82.7
Oxaspiropentene			
C1	46.0	39.2	38.9
C2	129.3	120.8	116.7
C3	44.6	31.13	30.76

Table 3 lists some sample results for predicted ^{15}N and ^{11}B chemical shifts as predicted by *Gaussian 98*. The predicted values are again in very good agreement with experimental observations.

Table 3. Predicted ^{15}N and ^{11}B Chemical Shifts

Molecule and Atom	*Gaussian 98*	Experiment
$C_2B_3H_5$		
C	99.9	103.3
B[b]	-0.1	3.5
CH_3CN		
C	-4.1	0.4
C	114.3	114.3
N[c]	290.8	272.6

[b]Shift with respect to B_2H_6.
[c]Shift with respect to NH_3.

Selected References

All reported *Gaussian 98* chemical shifts except those for taxol were computed via NMR calculations using the B3LYP/6-311+G(2d,p) level at the B3LYP/6-31G(d) optimized geometries. The taxol chemical shifts were computed from NMR calculations performed at the HF/6-31G(d) level using STO-3G optimized geometries.

"A comparison of models for calculating nuclear magnetic resonance shielding tensors," James R. Cheeseman, Gary W. Trucks, Todd A. Keith and Michael J. Frisch, *J. Chem. Phys.* **104** (1996) 5497. [A discussion of the method used to predict magnetic properties as well as results for a wide variety of molecules. See the references to this paper for the sources of the experimental values cited here.]

"Synthesis of Oxaspiropentene," W. E. Billups, Vladislav A. Litosh, Rajesh K. Saini and Andrew D. Daniels, *Org. Lett.* **1** (1999) 115. [NMR predictions are used to confirm the identiy of the synthesized compound.]

"NMR Chemical Shifts. 3. A Comparison of Acetylene, Allene, and the Higher Cumulenes," Kenneth B. Wiberg, Jack D. Hammer, Kurt W. Zilm and James R. Cheeseman, *J. Org. Chem.* **64** (1999) 6394. [An example of a recent application study using the *Gaussian* NMR facility.]

"NMR Methods Blossom," *Chemical and Engineering News*, 76:39, 28 September 1999. [Overview of a recent ACS symposium on NMR.]

Acknowledgments

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