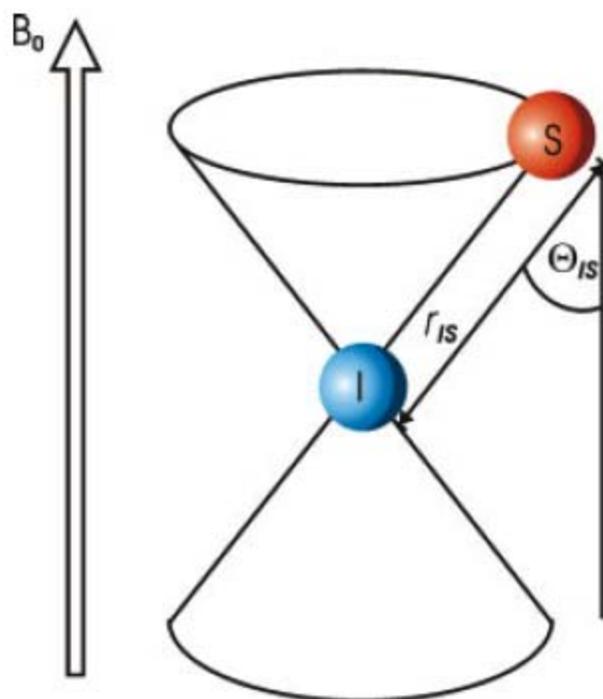


## NMR NEWS

August 2008

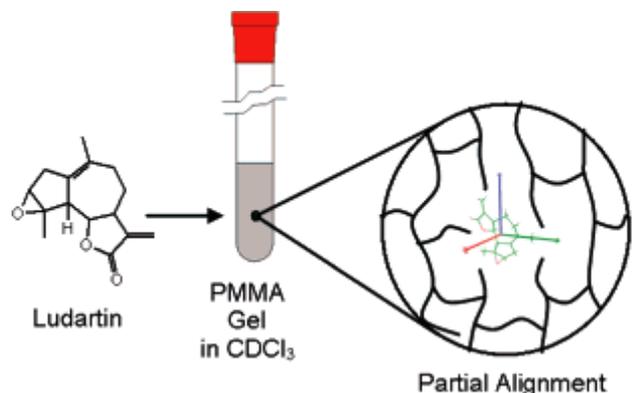
- \* To check on the [instrumental status](#) and the [reservation system](#), please, visit our website [www.chem.utk.edu/nmr](http://www.chem.utk.edu/nmr)
  
- \* [Tutorials](#) can now be downloaded from our NMR website (under Support Documents). At this time, tutorials for the AC250, Varian 300 and Bruker 400 are posted. Tutorials for the SS400 and V600 will be posted soon.
  
- \* [Measuring Residual Dipolar Couplings \(RDCs\)](#)  
In collaboration with Dr. Baker's group, in particular with Julio Gutierrez, I have been working for several months learning the know how about RDCs in small molecules. Around a month ago, we were able to measure RDCs in Julio's newly sensitized compound and used them to validate one of the proposed structures for his molecule.
  
- \* [What are RDCs?](#)  
RDCs are well known in the field of structural biology. They provide valuable information for the elucidation of the structure of proteins. The application of the method to small molecules, however, is still a new field.

**What is a dipolar coupling?** Is the dipole dipole interaction between two spins I and S (like a  $^1\text{H}$  and a  $^{13}\text{C}$  of a CH group). Its magnitude depends on the angle  $\Theta_{IS}$  between the line connecting both spins and the external magnetic field.

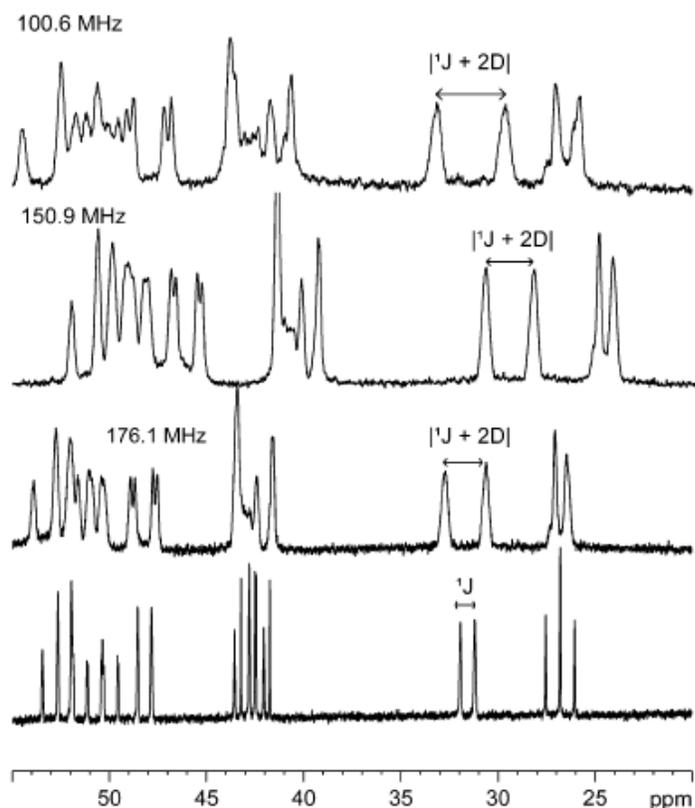


**Figure 1** The two cones covering the possible orientations of the vector connecting the spins I and S, which fulfil one value of a RDC for a given distance  $r_{IS}$ . For one-bond RDCs, this is equal to the possible orientations of the bond I-S. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

When a molecule is in liquid solution, it tumbles very fast, and then, the dipolar interactions between nuclear spins are average out. However, if we add an alignment media to the solution, like some liquid crystals that orient themselves in the presence of a magnetic field, then your solute becomes partially oriented in the media as shown in the figure;



As a consequence of the partial alignment of the solute, the dipolar interactions are not completely average out and a “residual dipolar couplings” (RDCs) remains. The RDCs cause the splitting of the NMR lines in the same way as a  $J$  coupling. Thus, for example, as shown in the following figure, the splitting  $\Delta$  of the  $^{13}\text{C}$  NMR line of a methine group (CH) caused by the bonded  $^1\text{H}$  is  $\Delta = J + 2D$ , where  $J$  is the  $^1J_{\text{CH}}$  scalar coupling constant and  $D$  is the RDC constant.

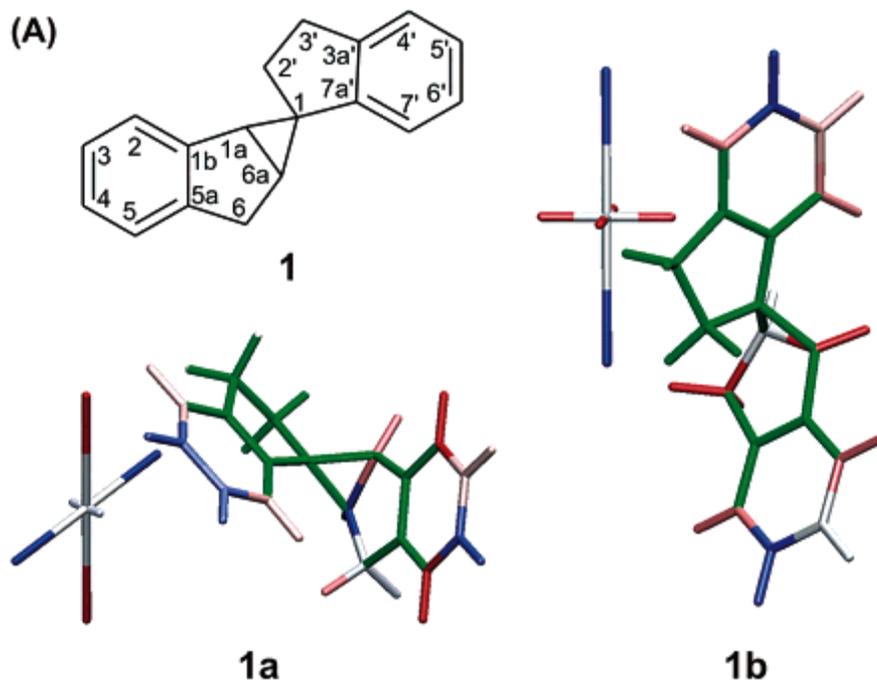


**Figure 2.** Expansion of the aliphatic region of gated decoupled  $^{13}\text{C}$  NMR spectra of strychnine at 300 K.<sup>19,22</sup> First (from top to bottom): strychnine in PBLG/ $\text{CDCl}_3$  at 100.6 MHz; second at 150.9 MHz; and third at 176.1 MHz. For comparison, the spectrum of an isotropic solution of strychnine in  $\text{CDCl}_3$  at 176.1 MHz is depicted at the bottom.

**Why to bother with RDCs?** The nice thing about RDCs is that D depends on the orientation of the C-H bond respect to the external magnetic field. Thus, if five or more RDCs can be measured in a molecule, one gets information on the orientation of these bonds and they can be used to either confirm or rule out a proposed structure.

**How the results look like. One example.** Since we are still working on the project and the results were not published yet, this example comes from the literature, *J. AM. CHEM. SOC.* **2004**, 126, 14690-14691

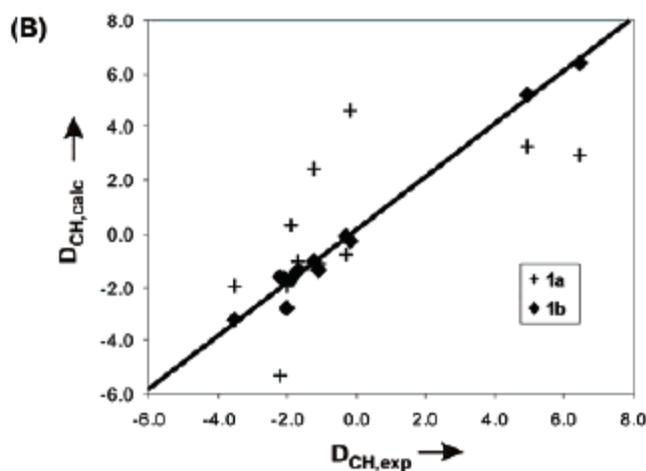
**Two possible diastereomers for molecule 1; 1a and 1b.**



## What do we do?

- 1) We measure the RDCs and calculate the experimental D values.
- 2) The set of D values along with the proposed structure are used to calculate the alignment tensor for the molecule.
- 3) The alignment tensor is used to back calculate the D values.
- 4) Calculated and experimental values are compared.

If the proposed structure matches the real one, the correlation between experimental and calculated D values is very good as shown in the figure shown below (1b points). If the structure is incorrect, the correlation is bad (1a points). At the end, it is that simple!



**Figure 2.** Top: Structures of the two possible diastereomers of **1**. The RDCs determined in a PDMS/ $CDCl_3$  gel are color coded to the structures (red, negative RDCs; blue, positive RDCs; green, no RDCs or RDCs not used in analysis). The axis systems to the left of each structure represent the corresponding alignment tensors. Bottom: Correspondence of experimental vs back-calculated RDC values for structures **1a** and **1b**.