

Friday 9th December 2011

2.00pm - Room 531

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### ***NMR Structure elucidation without using chemical shifts or couplings – Can it be true?***



Determining the precise 3-dimensional structure of complex 'small' molecules in solution, such as natural products, is a challenge which still often defeats chemists and spectroscopists alike. One solution to these structure determinations is a lengthy and extremely expensive total synthesis costing tens or hundreds of thousands of pounds and many person-years of effort. Another solution is just to get better data from your spectroscopy in the first place!

We have recently reported the reliably high accuracy of interproton distances obtained by analysis of NOESY measurements in both rigid [1] and flexible [2] small molecules – which is illustrated in Figure 1. If one assumes (and it is perhaps a big assumption!) that NOE-distance relationships of this sort are therefore valid under the conditions employed, then some quite remarkable structural details can be extracted from solution data, including:

Computer-assisted 2D- and 3D- structure elucidation directly from NMR spectroscopic data, without the need for human intervention or interpretation [3]. Software in development can achieve this in ~20 seconds from peak-picked spectra, without employing chemical shift or coupling constant interpretation.

Assessment of conformer populations in flexible molecules with levels of accuracy beyond that achieved by standard DFT energy assessments.

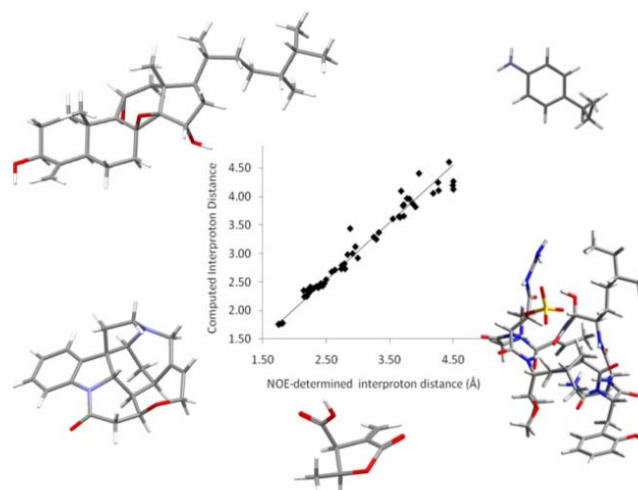
Determination of the relative configuration and conformation of novel natural products, which would otherwise fail if applying only qualitative NOE analysis methods.

The talk will describe how such measurements are made, how these are analysed, where the pitfalls lie and how these last can be avoided. If I'm lucky, it will also include a (successful?) demonstration of our latest software to achieve structure determination in seconds.....

[1] C.P. Butts, C.R. Jones, E.C. Towers, J.L. Flynn, L. Appleby and N.J. Barron, *Org. Biomol. Chem.*, 9, 177 – 184 (2011).

[2] (a) C.P. Butts, C.R. Jones, J.N. Harvey, *Chem. Commun.*, 1193 – 1195 (2011). (b) C.P. Butts, C.R. Jones, J.N. Harvey, *Beilstein J. Org. Chem.*, 145 – 150 (2011).

[3] J. N. Harvey, C. P. Butts, PCT/GB2009/051105.



**Fig. 1** Plot of NOE-determined interproton distances in solution against their expected values (computed and/or crystallographic). Surrounding molecules are examples of those which we have examined to date.