



FISHING MOLECULES: THE TALE OF HOW ART JOINED SCIENCE ON THE ROAD OF STRUCTURAL ELUCIDATION

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Structural elucidation is one of the most challenging task to be pursued in a Chemistry Laboratory, on the other hand, Nuclear Magnetic Resonance (NMR) spectroscopy is the most informative and suitable technique to infer information from solution samples. This poster shows several molecular structures solved through different NMR based key-techniques. Sometimes it is also possible to quickly change the solvent and general conditions in order to get more information completing the structural information and hopefully characterizing the biological function of these substrates. Sometimes in our group we took advantage of the heteronuclear NMR not only concerning the crucial ¹³C nuclei but also exploring other interesting and specific nuclei.

In several cases NMR analysis provided crucial information about the different conformation of molecules in polar protic media and in apolar media, these features are crucial in order to get a better insight into the biological mechanisms and activity which actually develops passing across cell membranes (apolar) and cytosol media (idrofili)

BENZODIAZEPIN-ONE DERIVATES

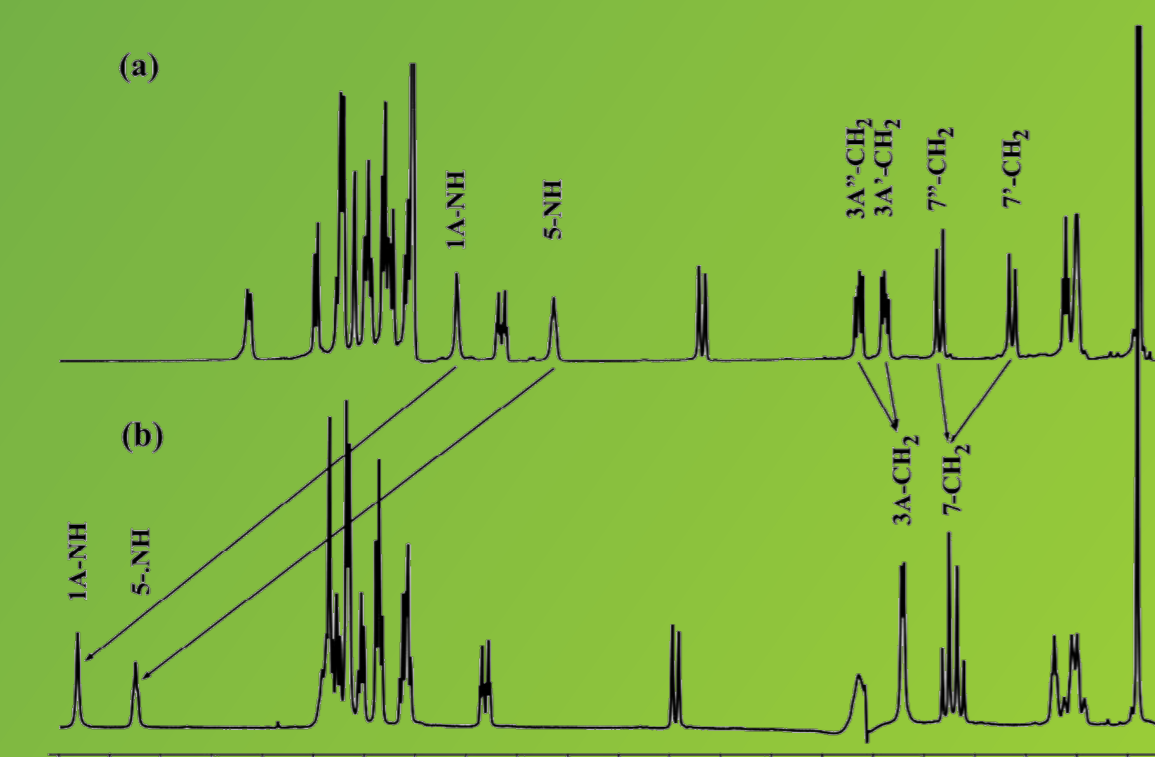


Fig. 1. ¹H NMR spectra at 500 MHz: (a) in KOH saturated CDCl₃ at 25 °C; (b) in CD₃OH at 5 °C with the O-H suppression. The complete ¹H assignment is possible showing the crucial differences.

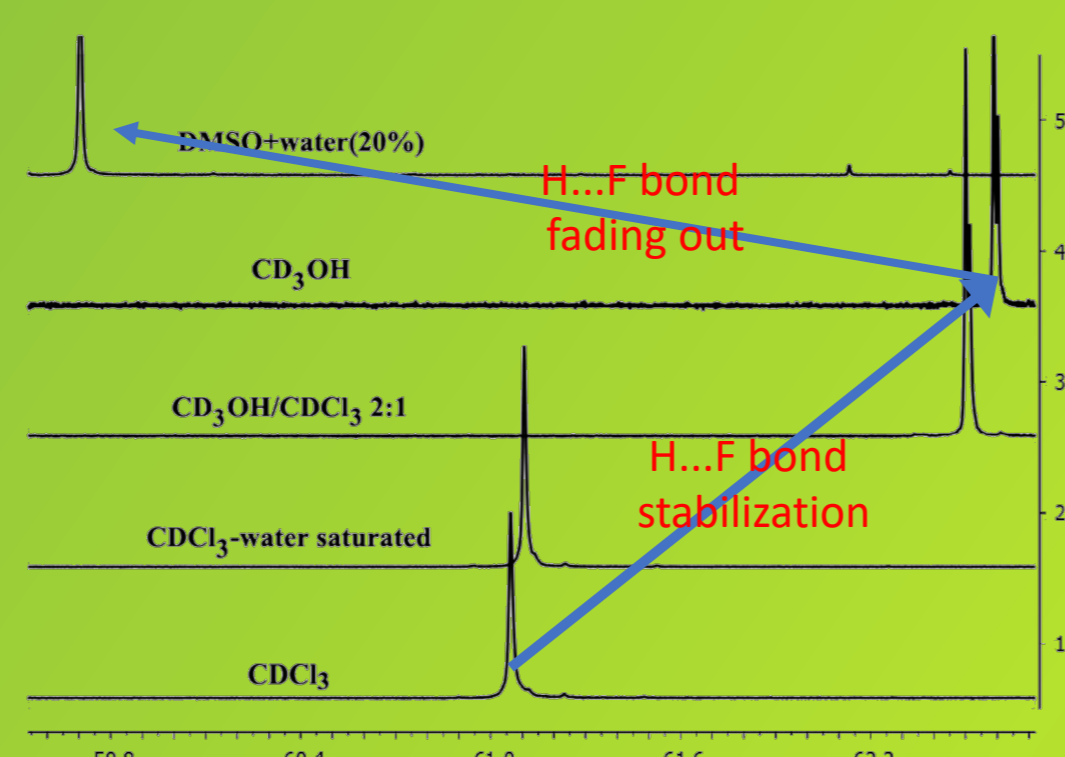
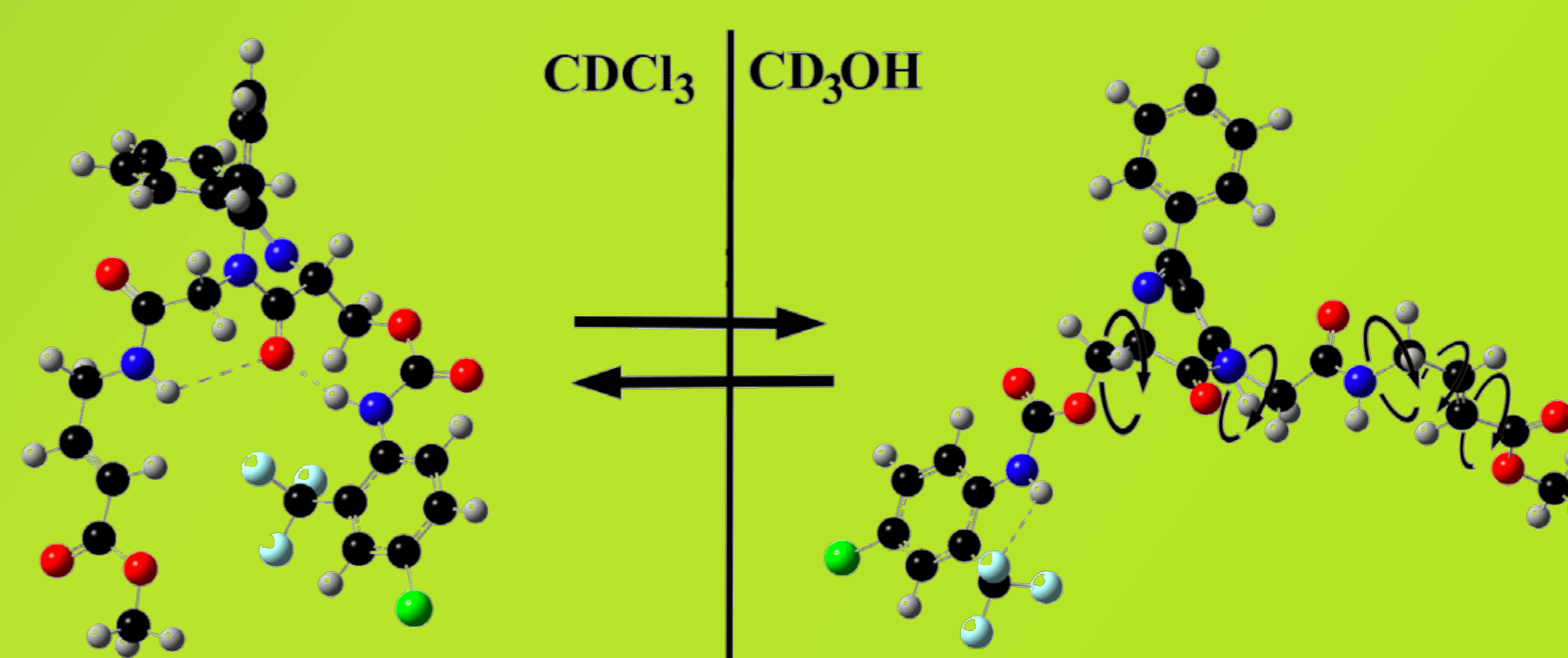
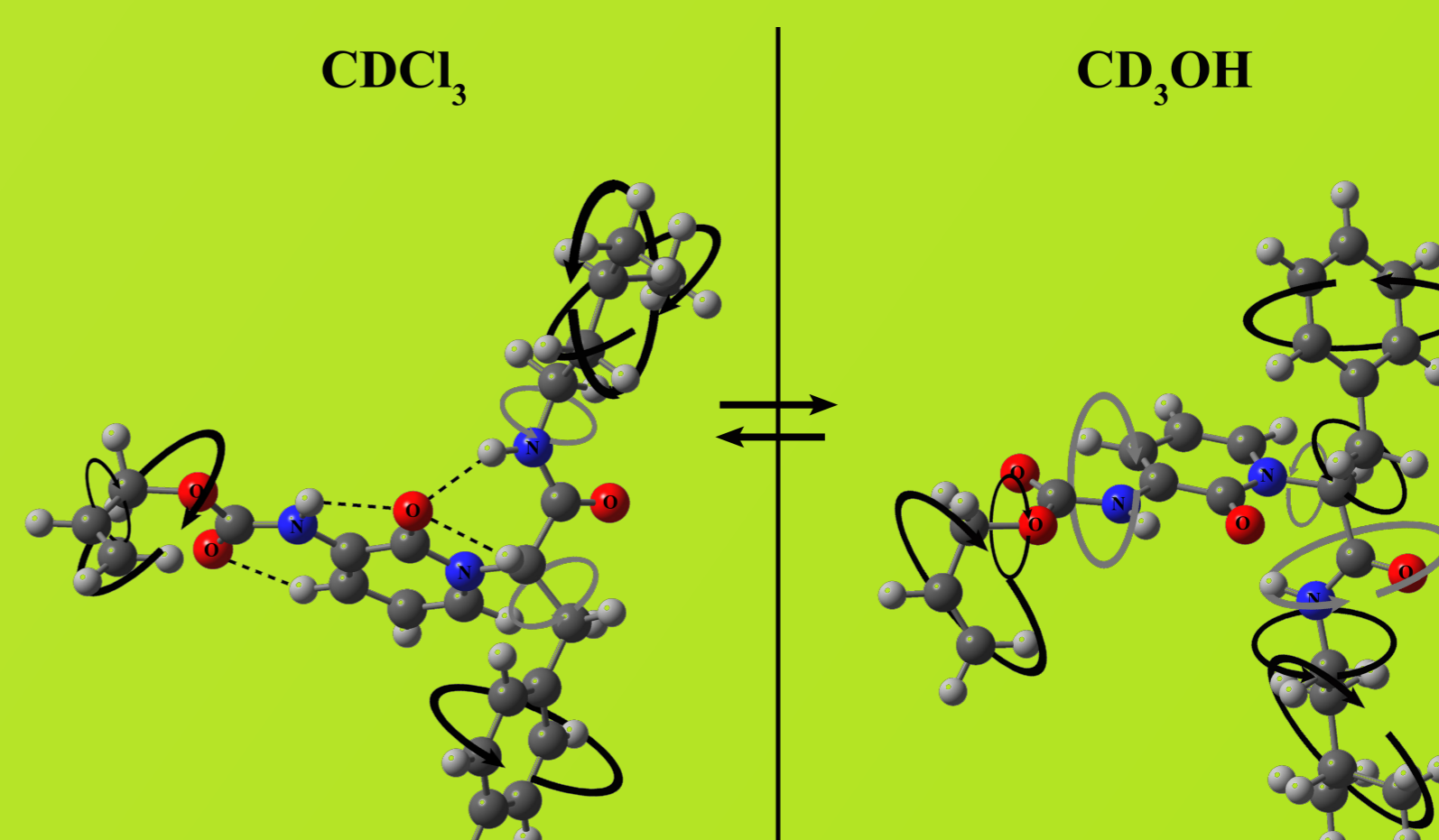
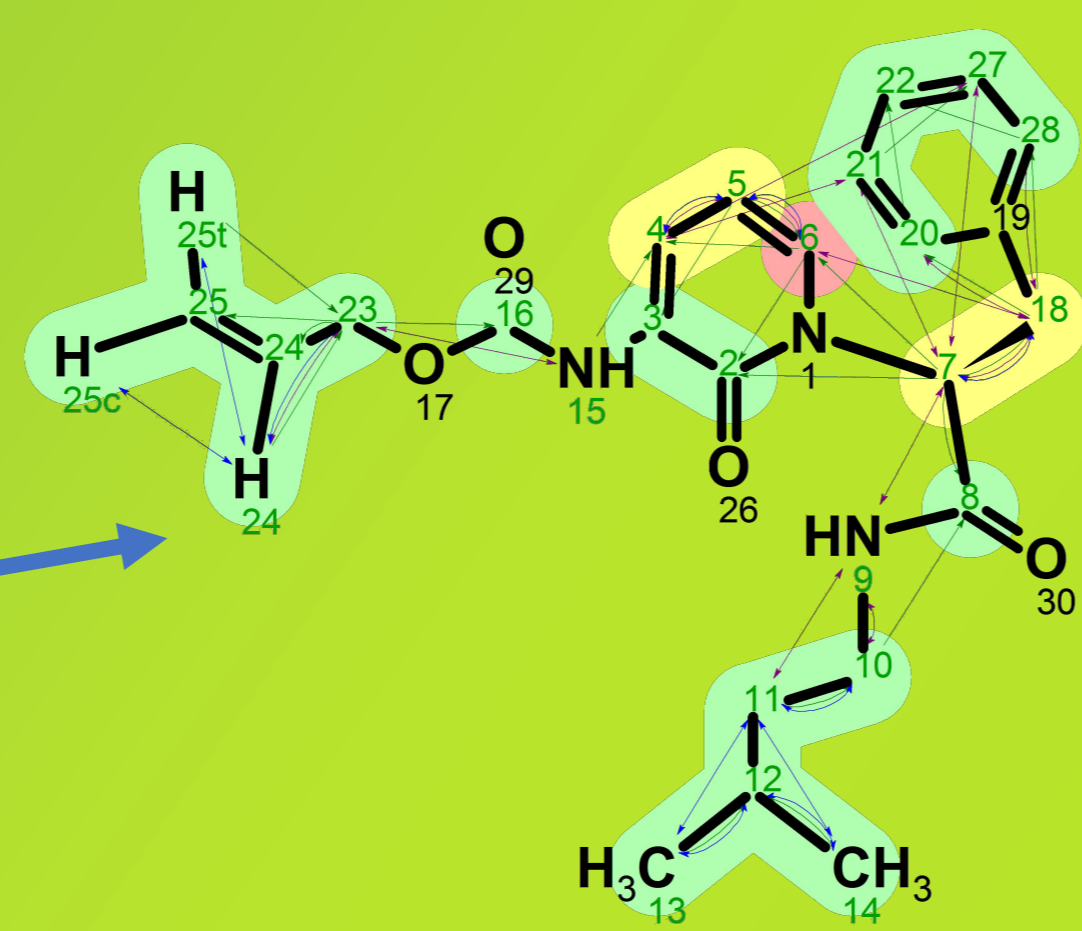
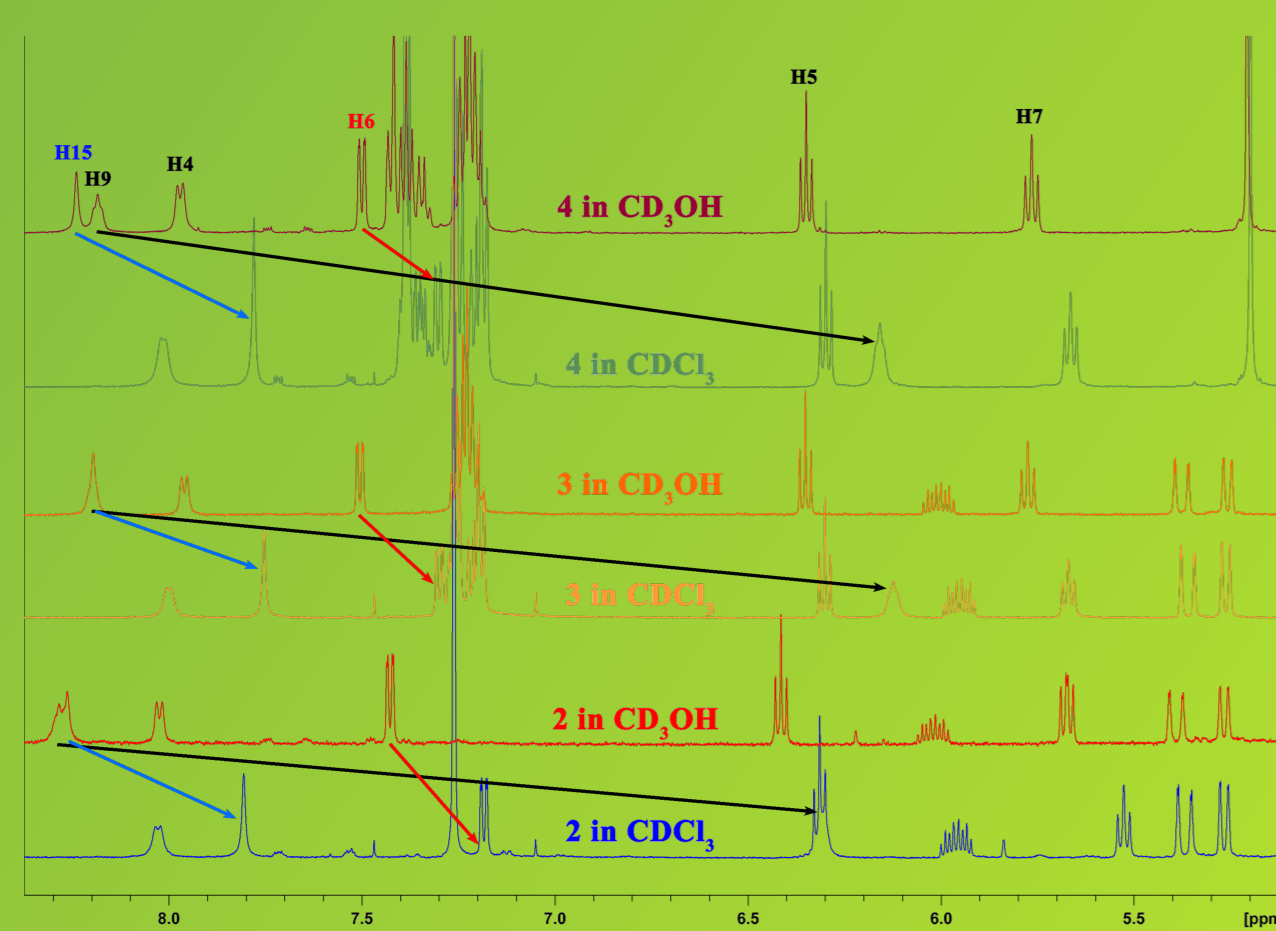


Fig. 2. ¹⁹F Spectrum in progressively more polar environments: according to our knowledge [26] the 1A-NH...CF₃ interaction gets more and more permanent in pure CD₃OH eventually fading out in strong polar environments.



PYRID-ONE DERIVATES



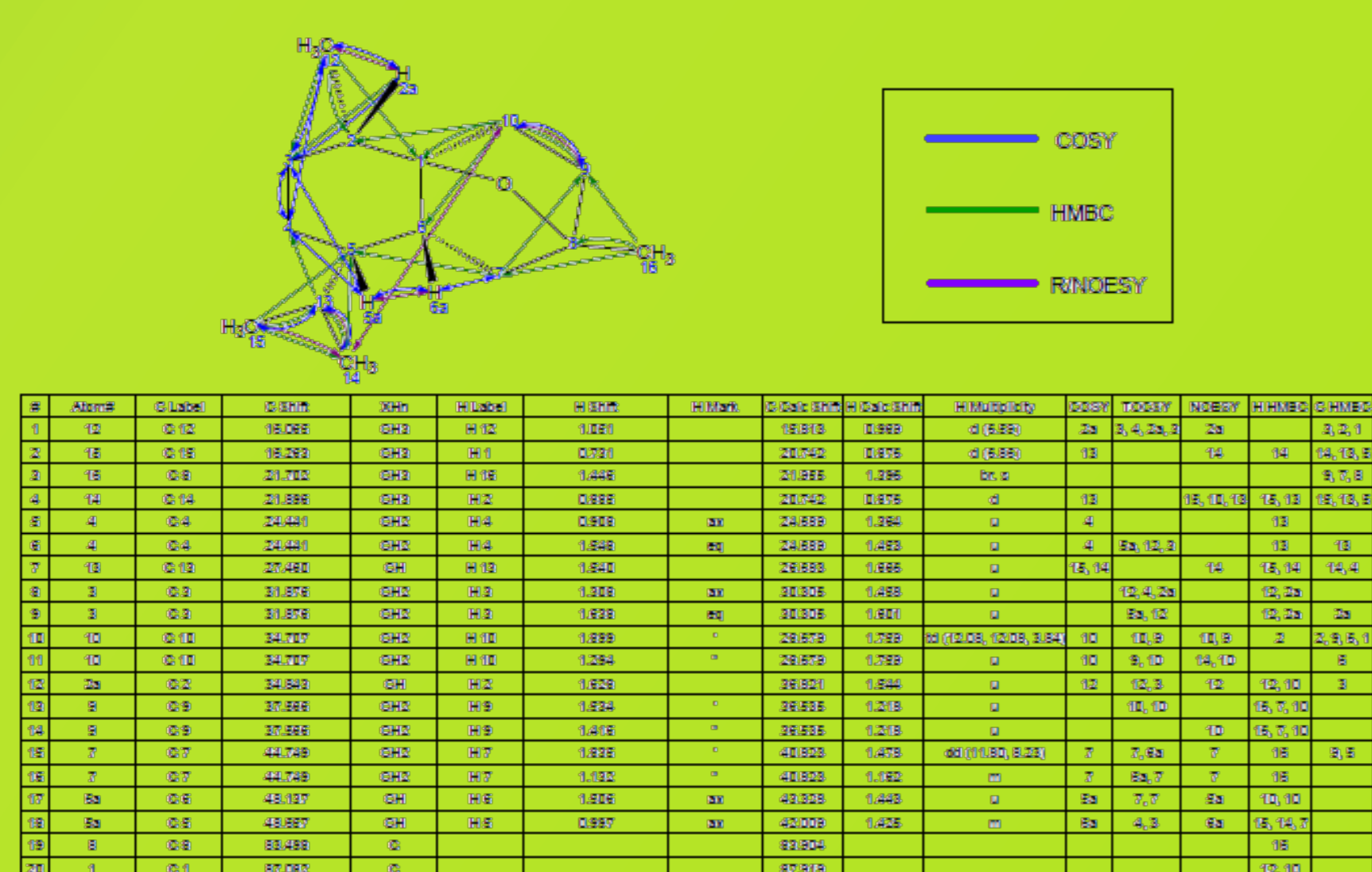
- A. Spectra of pyridone derivatives show that the NH take a great shift getting from Methanol to Chloroform medium (at a lesser extent also followed by 6-CH).
- B. The assignment and 2D-NMR connection (TOCSY, NOESY, HSQC, HMBC) show a pretty locked conformation in chloroform stabilized by intramolecular interactions.
- C. This is especially true for the species 3 which is supporting its remarkable biological activity

AMORPHANE DERIVATES

Lately our group has focused its efforts toward an other appealing tool to verify the correct molecular structure with selection of specific stereo-isomers even in case of missing NOE data or unresolvable overlaps: the selection through theoretical spectroscopical data. As a matter of this fact we have found that theoretical predictions based on the 3D structural data are much more effective than any other empirical prediction which usually can just forecast 2D arrangements. Herein we just show the first two chiral molecules characterized through the matching between experimental NMR and GAUSSIAN calculated chemical shifts. According to my opinion this could pave the way for a new eve in the field of structural characterization provided that eventual solvent-effects and conformational changes are accounted for the final results. These two new molecules isolated from natural matrices were characterized according to the structural elucidation by NMR, confirmed by the elucidation and resolved as relative configuration according to the GAUSSIAN prediction best fitting to the experimental values (this is perfectly consistent with the other NMR data provided that signal overlapping is hampering the straightforward resolution of these structures)

Despite the spin systems featured by very similar group and general overlaps, 3D minimization modelling and calculations open the way to the right selection of the stereoisomer (of course both couples) for the two closed structures shown below

2D-Characterization → STEREOISOMER SELECTION → 3D-STRUCTURAL ELUCIDATION



ACCORDING TO DATABASES	GAUSSIAN CALCULATED SHIFTS FOR THE 5 STEREOISOMERS							
	1-RRRR	2-RRRS	3-RRSR	4-RSSS	5-RSRR	6-RSRS	7-RSSR	8-RSSS
¹³ C	149.65	143.38	154.58	180.70	311.42	169.07	303.65	100.42
¹ H	98.44	97.22	177.93	214.99	45.80	227.44	452.12	173.45

