

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 cahracterizing 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 mechanismas and activity which actually develops passing across cell membranes (apolar) and citosol media (idrofilic)

BENZODI&ZEPIN-ONE DERIVATES

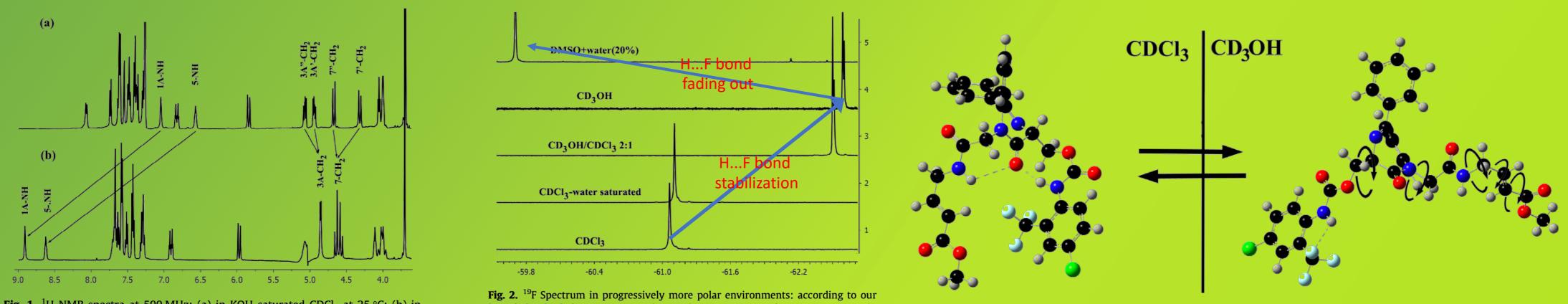


Fig. 1. ¹H NMR spectra at 500 MHz: (a) in KOH saturated CDCl₃ at 25 °C; (b) in CD₃OH at 5 °C with the O—H suppression. The complete ¹H assignment is possible showing the crucial differences.

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 derivates 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.

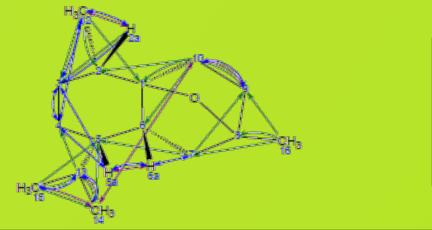
C. This is especially true for the species 3 which is supporting its remarkable biological activity

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 straightforward resolution 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





	Atom#	Glabel	26 31 M	2010	Histel	H 3100	HIMark.	Contention	H Made Stiff	H Multiplicity	15537	TRESHY	NOESY	HIHMEC	S HMEC
1	12	612	16.085	CH3	H 12	1 JIE 1		15.013	1.999	d (6.83)	23	3, 4, 23, 3	25		3,2,1
2	15	61	16.293	6113	H 1	12721		2117-52	1.975	d (6.88)	13		- 14	14	14, 13, 5
3	16	68	21.712	CHB	H 16	1.868		21,995	1.335	bit. si					9,7,8
4	14	6:14	21.896	6113	112	0.885		20.752	0.875	đ	13		15, 10, 13	15,13	15, 13, 5
2	ų.	64	24.431	2113	H4	0.908	33	24,888	1.389		4			13	
	ধ	64	24.431	2113	H4	1.540	ΞĮ	24,559	1,453			53, 12, 3		13	10
3	10	C 13	27,480	6H	H 12	1.540		26,688	1.995	a de la companya de la compa	15, 14		- 14	15,14	ીચ, ચ
8	3	63	21.875	2113	Ha	1.310	311	30,305	1,498			12,4,21		12, 35	
9	19	63	21.876	2113	Ha	1.638	æq	30,305	1.000			23,12		12, 35	25
11	10	61	34.707	SH2	H 10	1,229	e.	28,579	1.798	61 (12.08, 12.08, 3.84)	10	11,9	11,9	2	2,9,5,1
11	10	61	34.707	2HB	H 10	1.254	•	28,579	1298		10	9,10	14,10		8
12	20	62	34,843	CH	112	1.628		36.521	1.534		12	12,3	12	12,10	3
13		69	37.566	SHE	H9	1.834		36,535	1.218			10, 10		16, 7, 10	
18		69	37.566	SHE	H9	1,415		36.535	1.218				10	16, 7, 10	
15	3	67	441,789	SHE	117	1/825		411928	1,458	dd (11.50, 8.23)	3	7,81	ক	16	3,5
15	3	67	441789	SHB	Ш7	1.132		40.923	1.152		3	83,7	ক	16	
17	83	66	49,137	CH	HG	1.506	31	43.328	1,443	a de la companya de la compa	53	3,3	Sa	10, 10	
10	53	65	48.687	CH	HS	0.997	31	42.009	1,425		Ea	4,3	Sa	15, 14, 7	
19	m	68	33,499	8				83,904						16	
20	1	@1	280.78	8				87.919						12,10	

	2D - PREDICTED VALUES	GAUSSIAN CALCULATED SHIFTS FOR THE 5 STEREOISOMERS										
	ACCORDING TO DATABASES	1-КККК	2-RRRS	3 - RRSR	4-RRSS	5- RSRR	6-RSRS	7-RSSR	8-RSSS			
	QUADRATIC DEVIATIONS RESPECT TO EXPERIMENTAL SHIFTS											
¹³ C	149.65	143.38	154.58	180.70	45.80	311.42	169.07	303.65	100.42			
¹ H	98.44	97.22	177.93	214.99	10.06	227.44	452.12	173.45	353.43			

