

NMR spectra interpretation of diastereomeric MacMillan imidazolidinones by DFT calculation of indirect spin-spin coupling constants

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The indirect spin-spin coupling constants (SSCC) along with chemical shifts are the most important parameters given by nuclear magnetic resonance (NMR) spectroscopy [1,2]. The SSCCs are very sensitive to any variation in molecular geometric structure [3]. DFT based

calculations are an efficient approach in the description of indirect SSCCs for various molecular structures in organic chemistry [2,4].

In this work we report the use of SSCC DFT calculations as an auxiliary tool for the interpretation of NMR spectra used in determining the relative configuration of diastereomeric imidazolidinones (1 and 2, figure 1) (MacMillan imidazolidinones) [5,6] synthesized by one of us (FGF). These diastereomers (*cis*, 1, and *trans*, 2) presented different spin coupling patterns that were difficult to assign based only on the experimental spectra obtained. One of them showed a signal with a doublet of



Figure 1 - (+)-2-terc-butyl-3-methyl-5-benzyl-4imidazolidinone. Diastereomers 1a and 1b (*cis* isomers *cis*); 2a and 2b (*trans* isomers).

triplet pattern while the other showed a doublet of triplets of doublets pattern.

With this objective, each one of the pair of configurations constructed for *cis* (1a,b) and *trans* (2a,b) isomers (figure 1) by inversion of the configurations of the N1 atom were submitted to a systematic conformational search at the B3LYP/6-31G(d,p) level of theory using the Gaussian '09 package. Each of the resulting potential energy minima found on the resulting potential energy surface were resubmitted to geometry optimizations, at the same level of theory, and characterized as energy minima by vibrational analysis. The coupling constants were then calculated for each of the individual conformers at the B3LYP/6-31G(d,p) level of theory and the final value of the coupling constant were obtained as weighted averages based on the Boltzmann distribution of its Gibbs free energies. These final absolute values of the



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coupling constants were then compared with the values obtained experimentally. All the calculations were performed in the gas phase.

Three conformers were found for each of the diastereomers 1a and 1b and four conformers for each of the diastereomers 2a and 2b. The contributions of each conformer according to the Boltzman distribution are shown in table 1. The final values of coupling constants are shown in table 2.

Our results show that, although it is not considered a totally reliable and robust level of theory, the popular and widely used hybrid functional B3LYP with the rather small basis set 6-31G(d,p) has led to calculated values of the SSCCs for the imidazolidinone derivatives in very close agreement with the values obtained by experiment, showing that its use, coupled with an adequate conformational analysis, may be very useful for the interpretation of NMR spectra. Being a rather economical level of theory, its use allows the extension of this protocol to larger molecular systems. The use of range-separated functionals, which is capable of capturing both shortrange and long-range interactions as wB97X-D, as well as greater basis sets, mainly, but not exclusively, in the conformational analysis stage, is being carried out and its results will be reported as soon as they are finished.

Diastereomer	Dihedral 1 (final) C4-C5-C6-C7	Dihedral 2 (final) C5-C6-C7-C8	Relative energy of the conformers (kcal/mol)	Boltzmann distribution (%)
1a (1 <i>S</i> , 2 <i>S</i> , 5 <i>S</i>)	92,8	117,1	3,04	0,46
	163,1	32,4	2,21	1,85
	-67,4	80,3	1,01	13,94
1b (1 <i>R</i> , 2 <i>S</i> , 5 <i>S</i>)	174,6	-91,6	0,00	76,47
	-63,1	-96,1	1,66	4,62
	95,4	-61,2	1,99	2,67
2a (1 <i>S</i> , 2 <i>R</i> , 5 <i>S</i>)	164,3	-149,9	1,46	4,21
	-178,0	100,1	0,84	11,91
	-67,9	-98,9	0,00	49,43
	93,2	114,7	2,14	1,34
2b (1 <i>R</i> , 2 <i>R</i> , 5 <i>S</i>)	176,2	-92,7	0,30	29,98
	-61,0	-88,4	1,78	2,45
	96,9	125,0	3,42	0,15
	95,6	-63,8	2,69	0,53

Table 2. Final value of the coupling constant weighted by the contributions of the conformers of the (+)-2-terc-butyl-3-methyl-5-benzyl-4-imidazolidinone.



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Coupling	JMEDIUM Cal	J Experimental (Hz)				
	Diastereomers la/lb (2R)	Diastereomers 2a/2b (2.5)	(2 <i>R</i>)	(2.5)		
¹ JC5H5	147,45	144,09	142,5	-140		
² JC5H6ab	-2,19	-2,14	Н	н		
³ JC5H2	1,98	-0,70	1,73	-		

Key-words: DFT, NMR, Indirect spin-spin coupling constant, imidazolidinone.

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References:

- [1] J. San Fabían, J. M. García de la Vega, E. San Fabían, J. Chem. Theory Comput. 10, 4938-4949, (2014).
- [2] Helgaker, T. et al. Prog. in NMR Spec., 53, 249-268 (2008).
- [3] Smith, L. J. J. Mol. Biol., 255, 494-506 (1996).
- [4] Rittner, R. et al. Chem. Phys. Let., 454, 129-132 (2008).
- [5] MacMillan, D. W. C. et al. J. Am. Chem. Soc., 122, 4243 (2000).
- [6] MacMillan, D. W. C. et al. J. Am. Chem. Soc., 122, 9874 (2000).