ORGANIC LETTERS

2002
Vol. 4, No. 3
399−401

Predicting Experimental Complexation-Induced Changes in ^{1}H NMR Chemical Shift for Complexes between Zinc-Porphyrins and Amines Using the ab Initio/GIAO-HF Methodology

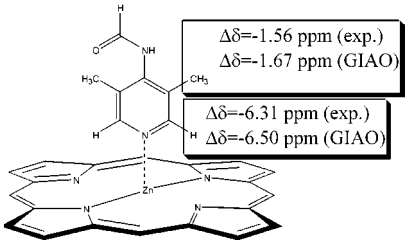
Rosa M. Gomila, David Quiñonero, Carmen Rotger, Carolina Garau, Antonio Frontera,* Pablo Ballester, Antonio Costa, and Pere M. Deyà*

Department of Chemistry, Universitat de les Illes Balears, 07071 Palma de Mallorca, Spain

tonif@soller.uib.es

Received November 22, 2001

ABSTRACT



Ab initio calculations were carried out on zinc-porphyrins complexed to several amines: *N*-(3,5-dimethyl-pyridin-4-yl)-formamide, 1,4-diazabiciclo-[2.2.2]octane (DABCO), and 1-azabiciclo[2.2.2]octane (quinuclidine). The proton chemical shifts of these complexes were calculated ab initio at the GIAO-HF/6-311G*//HF/3-21G level of theory, and the obtained values agree satisfactorily with experimental results. The complexation-induced changes in ^{1}H NMR chemical shifts correlate well with differences in association constants of several host–guest complexes.

Supramolecules containing metalloporphyrins have been widely used in host−guest chemistry.[1] Metalloporphyrins provide an advantageous class of building blocks for the construction of large multicomponent architecture as a result of their stability and facile synthesis. Oligomeric porphyrins and metalloporphyrins are under intensive investigation because of their potential application as new photonic and electronic materials.[2] For example, multiporphyrin arrays can be used as photon funnels,[3] molecular wires[4] and switches,[5] etc.

Zinc-porphyrins are often used as building blocks to create receptors with a range of cavity shapes and sizes. The strategy of this host−guest chemistry is based on the fundamental Zn−N recognition event.[6] The ^{1}H NMR chemical shift information is frequently used as a diagnostic tool in complex stoichiometry. The characteristic changes in the chemical shifts of the protons α to the nitrogen atom of the ligand (N_L) upon binding are used to determine the geometry of such complexes.

The interplay of theory and experiment in the field of NMR spectra has been very productive,[7] in particular for

(1) (a) Sanders, J. K. M. In *Comprehensive Supremolecular Chemistry*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Vogel, F., Eds.; Elsevier: Amsterdam, 1996; Vol. 9, pp 131−164. (b) Wojaczynski, J.; Latos-Grazynski, L. *Coord. Chem. Rev.* **2000**, *204*, 113.

(2) Gust, D.; Moore, T. A. *Top. Curr. Chem.* **1991**, *113*, 3638.

(3) Prathapan, S.; Johnson, T. E.; Lindsey, J. S. *J. Am. Chem. Soc.* **1993**, *115*, 4618.

(4) Wagner, R. W.; Lindsey, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 9759.

(5) Anderson, H. L.; Martin, S. J.; Bradley, D. D. C. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 655.

(6) Bampos, N.; Marvaud V.; Sanders, J. K. M. *Chem. Eur. J.* **1998**, *4*, 335.

10.1021/ol0170962 CCC: $22.00
Published on Web 01/05/2002

the elucidation of molecular structures and for the comprehension of chemical binding. Therefore, the computation of chemical shifts is an ideal link between theory and experiment, because it allows empirical proposal, as well as tests for theoretically predicted structures. The prediction of NMR parameters is a fundamental task during the process of computer-assisted structure elucidation.

In this letter we attempt to illustrate the capability of the theoretical method ab initio/GIAO at the HF/6-311G*//HF/3-21G level by comparing the calculated chemical shift (δ) values computed for free and complexed ligands with the data obtained experimentally. The proximity of the porphyrin π-system in these complexes causes the ^{1}H NMR signals to experience large ring-current-induced upfield shifts relative to the corresponding signals in free ligand.[8] The aforementioned method is able to reproduce these complexation-induced shifts in several zinc-porphyrin−amine complexes in good agreement with experimental data. Additionally, we report the influence that the geometric features of these complexes have on the computed complexation-induced shifts. This influence has been applied to explain differences in experimental association constants of two diporphyrin−dipyridine complexes.

Geometry optimizations[9] and energy calculations were done using the 3-21G basis set at the HF level by means of the GAUSSIAN 98 program,[10] since previous studies[11] have demonstrated that reliable quantitative results are obtained at this level of theory.[12] Furthermore, in one case (complex **7**) we have extended our calculation to HF/6-31G for the geometry optimization and no differences in the NMR shielding tensor were observed. No side chains were attached to the porphyrins evaluated in this study in order to keep the size of the calculations approachable. No symmetry constraints were imposed unless otherwise noted. Chemical shifts were determined by comparisons with the ^{1}H NMR isotropic shifts computed for tetramethylsilane at the same level. GIAO calculations were performed according to the reported method[13] at HF/6-311G*//HF/3-21G.

Computed and experimental ^{1}H NMR chemical shifts (δ) and complex-induced chemical shifts ($\Delta\delta$) of free ligands **1**−**3** and complexes **5**−**8** (see Figure 1) are present in Table 1. ^{1}H NMR spectra of free DABCO (**1**), quinuclidine (**2**), and *N*-(3,5-dimethyl-pyridin-4-yl)-formamide (**3**) are remarkably well reproduced at the GIAO-HF/6-311G*//HF/3-21G level of theory. Experimentally, when 1 equiv of ligand is added to form a 1:1 binary complex, the ^{1}H NMR resonance signals experience ring-current-induced upfield shifts. This upfield shift is especially significant in the ternary 1:2 complex **8** as a result of the proximity of the two porphyrin π-systems. It merits mention that these large experimental

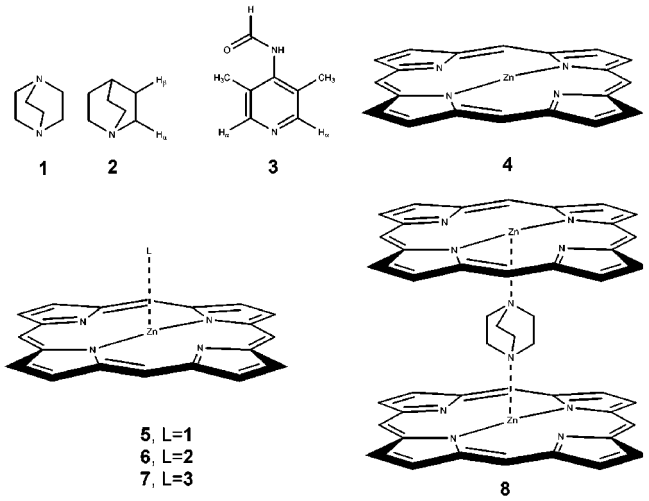


Figure 1. DABCO (**1**), quinuclidine (**2**), *N*-(3,5-dimethyl-pyridin-4-yl)-formamide (**3**), zinc-porphyrin (**4**), and its complexes (**5**−**8**).

Table 1. Calculated and Experimental ^{1}H NMR Chemical Shifts (δ) and Complex-Induced Chemical Shifts ($\Delta\delta$) in ppm

	GIAO/6-311G*//HF/3-21G			experimental	
compound	AS[a]	δ[b]	$\Delta\delta$	δ[b,c]	$\Delta\delta$
TMS	32.77	0		0	
1	30.44	2.31		2.80	
2 (H_α)	30.27	2.50		2.85	
2 (H_β)	31.53	1.24		1.51	
3 (H_α)	24.04	8.73		8.38	
3 (CH_3)	30.51	2.26		2.26	
5	36.75	−3.98	−6.29	−3.10	−5.90
6 (H_α)	36.60	−3.83	−6.33	−3.49	−6.34
6 (H_β)	33.82	−1.05	−2.29	−0.64	−2.15
7 (H_α)	30.54	2.23	−6.50	2.07	−6.31
7 (CH_3)	32.18	0.59	−1.67	0.70	−1.56
8	39.17	−6.40	−8.71	−5.20	−8.00

[a] Absolute shielding. [b] Relative to TMS. [c] In $CDCl_3$ at 20 °C.

(7) (a) Fleisher, U.; Kutzelnigg, W.; Lazzeretti, P.; Mühlekampp, V. *J. Am. Chem. Soc.* **1994**, *116*, 5298. (b) Arduango, A. J., III; Dixon. D. A.; Kumashiro, K. K.; Lee, C.; Power, W. P.; Zilm, K. W. *J. Am. Chem. Soc.* **1994**, *116*, 6361.

(8) Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5773.

(9) Geometries and energies for the optimized structures are available upon request by contacting tonif@soller.uib.es.

(10) *Gaussian 98*, Revision A.7; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Forestman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 1998.

(11) Gomila, R. M.; Quiñonero, D.; Frontera, A.; Ballester, P.; Deyà, P. M. *J. Mol. Struct. (THEOCHEM)* **2000**, *531*, 381.

(12) Several studies indicate that correct geometries require the inclusion of electron correlation, see for example: Malsch, K.; Roeb, M.; Karuth, V.; Hohlneicher, G. *Chem. Phys.* **1998**, *227*, 331.

(13) Wolinski, K.; Hinto, J. F.; Pulay, P. *J. Am. Chem. Soc.* **1990**, *112*, 8251.

(14) Synthesis and characterization of **9**−**13** will be published elsewhere, including the UV−visible absorption titrations.

upfield shifts are in excellent agreement with the computed $\Delta\delta$, see Table 1. In no case is the difference between theory and experiment greater than 0.4 ppm for the 1:1 complexes **5**−**7**. The agreement for the ternary complex **8** is also remarkable; the computed $\Delta\delta$ is −8.71 ppm, which is comparable to the experimental value (−8.00 ppm).

As an example for the diagnostic capacity of the theoretical method, we studied experimentally[14] the behavior of the complexes shown in Figure 2 using UV−visible absorption

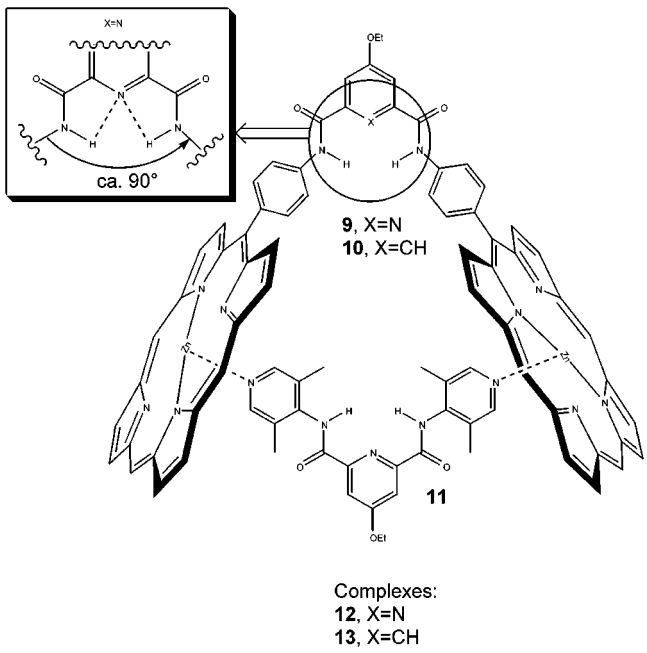


Figure 2. Porphyrin dimers **9** and **10**, pyridine dimer **11**, and its complexes **12** and **13**.

and ^{1}H NMR spectroscopy. To obtain the binding constant for complexes **12** and **13** we performed titrations of the porphyrin dimers **9** and **10**, adding the pyridine dimer **11** and studying the coordination shift of the Soret band in the UV−visible absorption spectrum in methylene chloride. Good isosbestic points were observed. Analysis of the binding curves showed that simple 1:1 complexes were formed with binding constants of 1.27×10^7 M^{-1} for complex **12** and 1.26×10^5 M^{-1} for complex **13**. A likely explanation for this considerable difference in binding constants (the difference is 2 orders of magnitude) is that the geometry of the porphyrin−pyridine interaction is different. Porphyrin dimer **9** has a 2,6-pyridine-dicarboxamide group, which connects both porphyrins. This linker has internal hydrogen bonds, which reduces the 120° angle expected for meta-substituted arenes to 96° (Figure 2).[15] This linker has been also used to connect the two pyridine units in dimer **11**. Therefore the geometries of host and guest prior to complex formation **12** (**9** + **11**) are almost optimal. On the contrary, in complex **13** (**10** + **11**), the linker of the porphyrin dimer **10** does not have the intramolecular hydrogen bonds (instead it has a repulsive C−H···H−N interaction), and thus the geometric complementarity of the porphyrin to the diamine unit is reduced.

This explanation has been corroborated using theoretical calculations. Clearly, the complexation-induced shift is influenced by the geometries of host and guest in the complex. We have calculated the $\Delta\delta$ of complex **7** at several orientations, varying the angle formed by the porphyrin N_4 plane and the molecular plane of the ligand from 90° to 70° in steps of 5°. Figure 3 shows the obtained relation (r^2 =

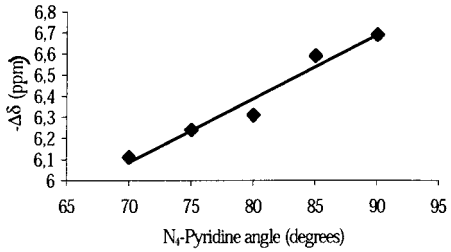


Figure 3. Plot of the regression between the angle defined by the N_4 plane and the pyridine molecular plane in degrees and the complexation-induced shift of the α hydrogen atom in ppm computed for complex **7**.

0.96) between the orientation angle and the complexation-induced chemical shift ($\Delta\delta$). The optimum orientation is achieved when the pyridine ligand is perpendicular to the N_4 plane of porphyrin. In this orientation the $\Delta\delta$ is maximum (in absolute value). Experimentally, the $|\Delta\delta|$ (upfield shifted) for complex **12** are 6.31 ppm for H_α and 1.55 ppm for the methyl group. The values for complex **13** are smaller in absolute value, 6.15 ppm for H_α and 1.52 ppm for the methyl group, indicating that the geometrical orientation of this complex is not as good as in complex **12**, as reflected in the experimental binding constants.

In conclusion, we have shown that the GIAO method at the HF/6-311G*//HF/3-21G level of theory is able to reproduce effectively experimental chemical shifts. Moreover, it has been successfully applied to the theoretical calculation of complexation-induced shift of zinc-porphyrin complexes, where the ^{1}H RMN resonance signals experience large ring-current-induced upfield shifts. Finally, we have found a linear correlation between the orientation of the ligand over the porphyrin plane and the computed complexation-induced shift. The influence of this orientation on the $\Delta\delta$ has been verified experimentally.

Acknowledgment. We thank the DGICT (project PB98-0129) for financial support. We thank the CESCA for computational facilities. A.F. and M.C.R. thank the MCT for postdoctoral grants. D.Q. and C.G. thank the UIB and the FSE, respectively, for predoctoral fellowships.

OL0170962

(15) (a) Hunter, C. A.; Purvis, D. H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 792. (b) Hamuro, Y.; Geib, S. J.; Hamilton, A. D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 446. (c) Hunter, C. A.; Sarson, L. D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2313.