ORIGINAL ARTICLE

THEORETICAL AND EXPERIMENTAL EVALUATION OF THE ^{13}C NMR CHEMICAL SHIFTS FOR CARBONYL-CONTAINING COMPOUNDS

| Nadia Faska * | and | Fatima EL Baz |

Faculty of Applied Sciences Ait Melloul | University Ibn Zohr Agadir | Morocco |
LCAPE, Department of chemistry | Faculty of sciences | University Ibn Zohr Agadir | Morocco |

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ABSTRACT

Background: Numbers of methods have been developed for the calculation of molecular magnetic properties. It is generally accepted that accurate prediction of these properties within the finite basis approximation, requires gauge-invariant procedures. **Methods:** In this work, we calculate the ^{13}C nuclear magnetic resonance chemical shielding tensors of five cyclic ketones using three procedures: gauge including atomic orbitals (GIAO), the individual gauges for atoms in molecules (IGIAM) and continuous set of gauge transformations (CSGT) at both the Hartree-Fock (HF) and density functional theory (DFT) levels of theory using the 6-311G (d, p) basis set. **Results:** The statistical analysis shows that B3LYP combined with the GIAO NMR method are the best for the calculation of ^{13}C chemical shifts of carbonyl carbon in the considered cyclic ketones. **Conclusion**: The agreement between computed and experimental chemical shifts fully validates our approach.

Keywords*: ^{13C} NMR chemical shifts, carbonyl carbon group, DFT, HF, cyclic ketones, GIAO, CSGT, IGIAM.*

1. INTRODUCTION

NMR spectroscopy has proved to be a powerful experimental method for the characterization of electronic and structural properties of molecules [1,2,3]. A great attention has been devoted to the measurement of ^{13}C chemical shift of organic and bioorganic molecules [4,5,6]. A number of methods have been developed for the calculation of nuclear shieldings. It is generally accepted that accurate prediction of these properties within the finite basis approximation, requires gauge-invariant procedures [7,8]. This paper will focus on predicting NMR shielding tensors using three of these procedures, namely GIAO (gauge including atomic orbitals) [9,10,11], CSGT (continuous set of gauge transformations) [12-11] and IGIAM (individual gauges for atoms in molecules) [12] at both the Hartree-Fock and DFT levels of theory, which achieve "gauge-invariance" in different ways.

The importance of the carbonyl functional group, particularly the cyclic functionality, is demonstrated by the fact that this functional group is present in some antibiotics [13,14,15,16]. In the present work, theoretical and experimental NMR spectra of five cyclic ketones (Figure.1) have been studied both to collect a complete set of experimental NMR data and to test the performance of different NMR methods.

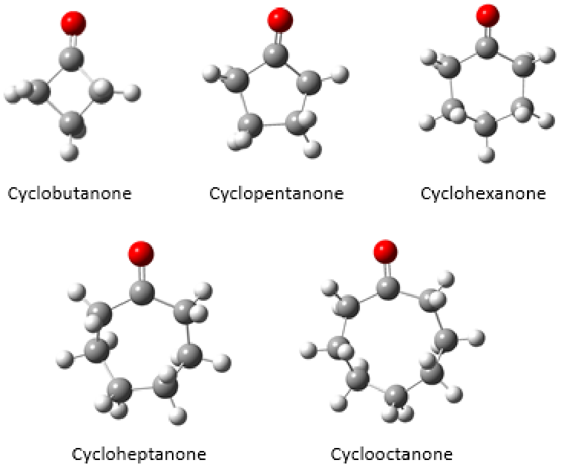

Figure 1: The figure presents the molecular structures of the cyclic ketones.

2. MATERIALS AND METHODS

2.1 Quantum-chemical calculations:

Calculations were performed with the use of the Gaussian 09 set of programs [17]. All structures were fully optimized with the density functional theory (DFT) using Becke's three parameter hybrid method [18] and correlation functional of Lee–Yang–Parr (B3LYP) [19, 20] in conjunction with the 6-311G (d, p) basis set. In all cases, the analytical vibrational frequencies were computed to confirm that the optimized structures correspond to real minima on the potential energy surface.

^{13}C nuclear shieldings of the considered cyclic ketones have been calculated over the fully optimized geometries within the gauge-including atomic orbital (GIAO), the individual gauges for atoms in molecules (IGIAM) and continuous set of gauge transformations (CSGT) methods. Absolute isotropic magnetic shieldings were transformed into chemical shifts by referencing to the shieldings of a standard compound (TMS) computed at the same level [21,22].

After computing the values of the ^{13}C chemical shifts using all the cited methods, a statistical analysis was carried out to determine which method produced the best results. Statistical analysis included the mean absolute error (MAE/ppm, Eq.1); the mean squared error (MSE/ppm2, Eq. 2); and the root mean squared error (RMSE/ppm, Eq.3). The error calculations were performed using Microsoft Excel 2013.

$$MAE = \frac{1}{n}\sum_{i=1}^{n}\left|\delta_i^{cal} - \delta_i^{exp}\right| \qquad (1)$$

$$MSE = \frac{1}{n}\sum_{i=1}^{n}\left(\delta_i^{cal} - \delta_i^{exp}\right)^2 \qquad (2)$$

$$\boldsymbol{RMSE} = \sqrt{\boldsymbol{MSE}} = \sqrt{\frac{\mathbf{1}}{\boldsymbol{n}}\sum_{\boldsymbol{i}=\mathbf{1}}^{\boldsymbol{n}}\left(\boldsymbol{\delta}_{\boldsymbol{i}}^{\boldsymbol{cal}} - \boldsymbol{\delta}_{\boldsymbol{i}}^{\boldsymbol{exp}}\right)^{\mathbf{2}}} \qquad (3)$$

2.2 Experimental section

NMR spectra were recorded on a Bruker 300 spectrometer at 300 K. ^{13}C NMR spectra were measured at 75 MHz. Chemical shifts were referenced to external TMS. Samples were contained in 5 mm tubes. For locking purposes, a 2 mm capillary coaxial tube containing $(CD_3)_2CO$ was used. The general reproducibility of chemical shifts data was estimated to be better than 0.01 ppm. All compounds used in this work were commercially available and were dried and purified before use by distillation. Their purities were checked from their ^{1}H and ^{13}C spectra. Samples were prepared by weight and volumetrically.

3. RESULTS AND DISCUSSION

Theoretical and experimental ^{13}C chemical shifts of the carbonyl carbon group, for all compounds studied are collected in Table 1.

Table 1: The experimental and theoretical ^{13}C chemical shifts (B3LYP/6-311G (d, p)) of carbonyl carbon in the considered cyclic ketones.

Cyclic ketones	**GIAO**		**CSGT**		**IGIAM**		**Exp**
	DFT	**HF**	**DFT**	**HF**	**DFT**	**HF**	
Cyclobutanone	208.076	213.325	206.358	212.056	206.364	212.067	209.829
Cyclopentanone	218.680	223.361	216.262	221.714	211.156	223.361	217.939
Cyclohexanone	209.419	215.110	206,857	212,972	206.862	224.382	211.887
Cycloheptanone	213.673	219.857	211.151	217.740	211.156	217.750	215.285
Cyclooctanone	218,294	223,595	216,508	222,158	216,513	222,168	218.300

GIAO: gauge-including atomic orbital; **CSGT**: continuous set of gauge transformations; **IGIAM**: individual gauges for atoms in molecules.

A comparison of the calculated NMR chemical shifts with the experimental values revealed that ^{13}C chemical shifts calculated at the Hartree-Fock 6-311G (d, p) level of theory are not much better, than those predicted at the density functional methods in the same level. The coefficients of linear correlations of the theoretical to the experimental data, which can be treated as a certain measure of goodness of theoretical values, are of the order of 0.99, 0.98 and 0.90 for GIAO, CSGT, and IGIAM methods, respectively. Among the three approaches for calculating chemical shifts, gauge including atomic orbital method has shown to provide results that are more accurate than those achieved by CSGT and IGIAM approaches at the same basis set size. The agreement between the experimental and calculated values is excellent as shown in Figure 2. The standard deviations remain close to zero.

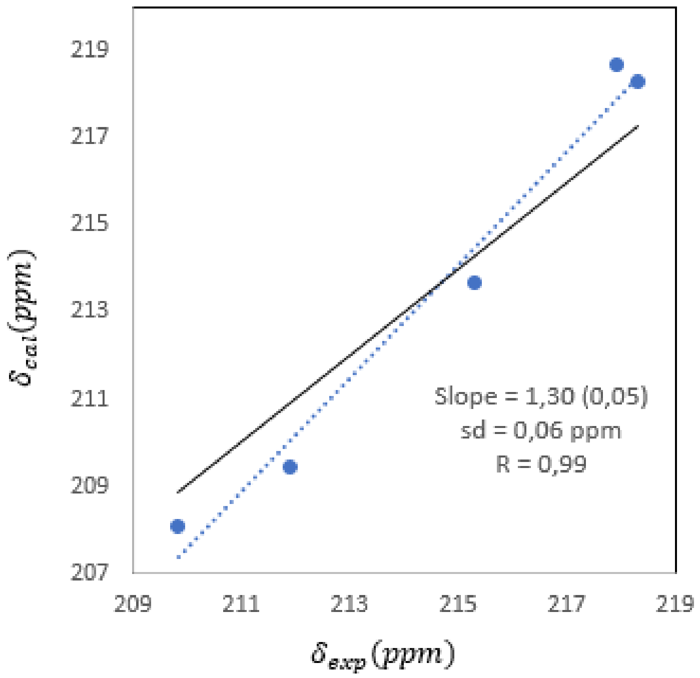

Figure 2: A plot of the relative experimental ^{13}C chemical shifts of the carbonyl carbon of cyclic ketones versus the theoretical (B3LYP/6-311G (d, p)).

To quantify the performance of each functional, the statistical analysis using mean the absolute error (MAE), the mean squared error (MSE) and the root mean squared error (RMSE) was employed (Table 2).

Table 2: Statistical parameters defined in eq. 1-3. MAE = mean absolute error; MSE = mean squared error; RMSE = the root mean squared error of carbonyl carbon in the considered cyclic ketones.

	GIAO		**CSGT**		**IGIAM**	
	DFT	**HF**	**DFT**	**HF**	**DFT**	**HF**
MAE	1,316	4,402	3,221	2,680	4,238	5,298
MSE	2,462	20,190	12,092	8,260	20,702	42,314
RMSE	1,569	4,493	3,477	2,874	4,550	6,505

GIAO: gauge-including atomic orbital; **CSGT**: continuous set of gauge transformations; **IGIAM**: individual gauges for atoms in molecules.

The first three parameters (MAE, MSE and RMSE) are measures of the fitting error. These are used to estimate directly which functional gives a more accurate prediction, as smaller values indicate smaller error.

For ^{13}C NMR chemical shifts, the best results were obtained using DFT combined with GIAO, while IGIAM NMR method at the Hartree-Fock 6-311G (d, p) level of theory have the worst performance (figure.3).

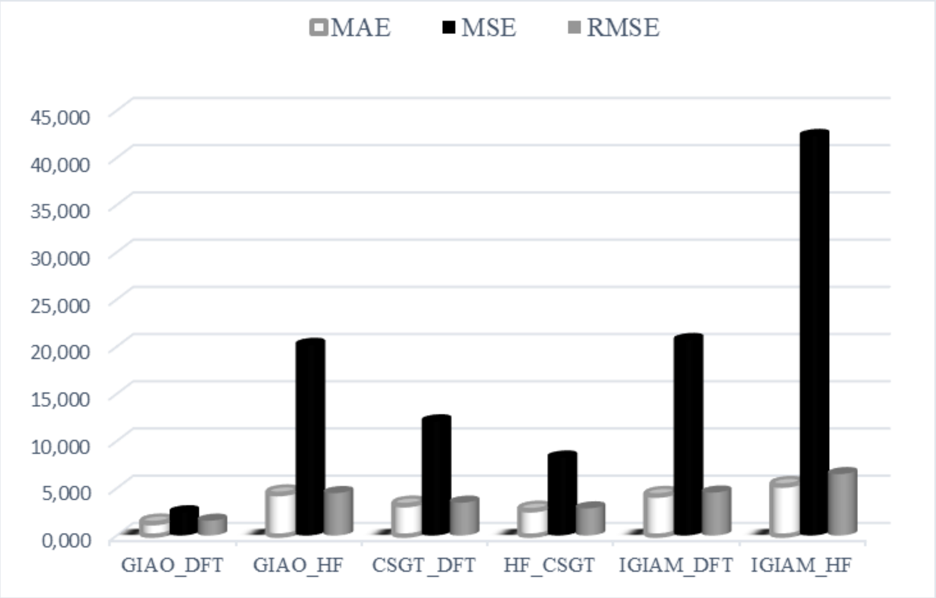

Figure 3: Results from the statistical treatment. **MAE**= mean absolute error, **MSE**= mean squared error and **RMSE**= root mean squared error of the theoretical calculations of ^{13}C NMR chemical shifts of carbonyl carbon in the considered cyclic ketones.

4. CONCLUSION

The examination of our results leads to the following conclusions: using the DFT/6-311G (d, p) based computational methodology employed in the present study it was possible to predict the ^{13}C NMR chemical shifts of carbonyl carbon in the considered cyclic ketones. The correlations between experimental and calculated chemical shifts were subjected to statistical analysis to identify the best-performing NMR methods. The GIAO method combined with the functional B3LYP, showed the lowest values of RMSE and MAE, i.e., better agreement of calculated values with the experimental ^{13}C NMR chemical shift. The information contained in this work can be used for the assignment of experimental NMR spectra and will motivate further studies involving the theoretical calculation of ^{13}C NMR organic compound.

5. REFRENCES

1. Benn R., Brevard C., Rufinska A. and Schroth G. (1987) Direct and Indirect Recording of ^{183}W NMR Spectra and Structure Determination of (Diene),M (M = W, Mo) Compounds in Solution, Organometallics 6 938-942.
2. Dyson H. J. and Wrigh, P. E. (2004). Unfolded Proteins and Protein Folding Studied by NMR. Chemical Reviews, 104(8) 3607–3622.
3. Nerli S., McShan A.C. and Sgourakis N.G. (2018) Chemical shift-based methods in NMR structure determination, Progress in Nuclear Magnetic Resonance Spectroscopy 106 1-25.
4. Borkowski E. J., Fernando D. Suvire F. D. and Enriz R. D. (2010) Advances in correlation between experimental and DFT/GIAO computed ^{13}C NMR chemical shifts: A theoretical study on pentacyclic terpenoids (fernenes), Journal of Molecular Structure: THEOCHEM 953 83–90.
5. Iuliucci R. J., Facelli J. C., Alderman D. W., Grant D. E. M. (1995), Carbon-13 Chemical Shift Tensors in Polycyclic Aromatic Compounds. 5. Single-Crystal Study of Acenaphthene, Journal of the American Chemical Society, 117 2336-2343.
6. Johnston J. C., Iuliucci R. J., Facelli J. C., Fitzgerald G. and Mueller, K. T. (2009), Intermolecular shielding contributions studied by modeling the ^{13}C chemical-shift tensors of organic single crystals with plane waves. The Journal of Chemical Physics, 131(14), 144503.
7. Bifulco G., Dambruoso, P., Gomez-Paloma L. and Riccio R. (2007), Determination of Relative Configuration in Organic Compounds by NMR Spectroscopy and Computational Methods. Chemical Reviews, 107(9), 3744–3779.
8. Keith, T. A. and Bader, R. F. W. (1993). Calculation of magnetic response properties using a continuous set of gauge transformations. Chemical Physics Letters, 210(1-3), 223–231.
9. Ditchfield R. (1974), Self-consistent perturbation theory of diamagnetism. 1. Gauge-invariant LCAO method for N.M.R. chemical shifts, Molecular Physics, 27 789-807.
10. Wolinski K., Hilton J. F. and Pulay P. (1990), "Efficient Implementation of the Gauge-Independent Atomic Orbital Method for NMR Chemical Shift Calculations," Journal of the American Chemical Society, 112 8251-60.
(a) Cheeseman J. R., Trucks G. W., Keith T. A. and Frisch M. J. (1996), A Comparison of Models for Calculating Nuclear Magnetic Resonance Shielding Tensors, The Journal of Chemical Physics, 104 5497-509.
11. Keith T. A. and Bader R. F. W. (1992), Calculation of magnetic response properties using atoms in molecules, Chemical Physics Letters, 194 1-8. (b) Keith T. A. and Bader R. F. W. (1993), Calculation of magnetic response properties using a continuous set of gauge transformations, Chemical Physics Letters, 210 223-3.
12. Mandel G.L., Bennet J.E., Dolin R., Principle and Practice of Infectious Diseases, 4th ed., Churchilll Livingston, New York, 1995.
13. Wilhelm M. P. and Estes L. (1999), Vancomycin. Mayo Clinic Proceedings, 74(9), 928–935.
14. Ryffel B. (1992), The carcinogenicity of ciclosporin. Toxicology, 73(1), 1–22.
15. Eixeira L. R., Sasse S. A., Villarino M. A., Nguyen T., Mulligan M. E. and Light R. W. (2000), Antibiotic Levels in Empyemic Pleural Fluid. Chest, 117(6), 1734–1739.
16. Frisch M. J., Trucks G.W., Schlegel H. B. and al. Gaussian 0.9, Revision B.01. Wallingford, CT: Gaussian, Inc.; 2010.
17. Becke A. D. (1996), Density-functional thermochemistry. IV. A new dynamical correlation functional and implications for exact-exchange mixing, The Journal of Chemical Physics, 104 1040-46.
18. Lee C., Yang W. and Parr R. G. (1988), Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density, Phys. Rev. B, 37 785-89. (b) Becke, A. D. (1993), The Journal of Chemical Physics, 98, 5648.
19. Foresman J.B.; Frish, A., Exploring Chemistry with Electronic Structure Methods, Gaussian, Pittsburgh., 1996.

20. Alkorta I. and Elguero J. (1998), An initio hybrid DFT-GIAO calculations of the shielding produced by carbon-carbon bonds and aromatic rings in ^{1}H spectroscopy, New Journal of Chemistry, 22, 381–385.
21. Olsson L. and Cremer D. (1996), Prediction of Nitrogen and Oxygen NMR chemical shifts in organic compounds by density functional theory, Journal of Physical Chemistry. 100, 16881–16891.

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