



PERFORMANCE OF SEVERAL DENSITY FUNCTIONAL THEORY METHODS FOR COMPUTING ^{13}C NMR CHEMICAL SHIFTS OF KETONES CYCLIC

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ABSTRACT

^{13}C NMR chemical shifts were measured for a set of five ketones cyclic from four to eight-membered rings. ^{13}C NMR chemical shifts were computed at the B3LYP, B3PW91, B97D, BP86, CAM-B3LYP, LC-wPBE and PBE1PBE using the gauge-including-atomic-orbital (GIAO) method and 6-311G+(d, p) basis sets. The experimental versus computed chemical shift values for carbon were compared and evaluated using the linear regression and statistical analyses. From the results, it is revealed that DFT methods considered here showed good performance in the ^{13}C calculations and usually provided a better performance method. In particular, the CAM-B3LYP and B3LYP functionals afforded the best overlap between calculated and experimental outcomes. The linear regression analyses of the results indicate R^2 (correlation coefficients) values higher than 0.998 in the range for complete data set.

Keywords: ^{13}C NMR, DFT, cyclic ketones, GIAO.

1. INTRODUCTION

Nuclear magnetic resonance spectroscopy is a powerful technique for the determination of molecular structure [1,2,3]. The hydrogen and carbon NMR chemical shifts δ and spin-spin coupling constants J depending on the magnetic shielding of nuclei by electrons, other nuclei, and solvents are the major parameters designating the NMR spectra. In spite of the extensive capabilities of this method, the ambiguity in the interpretation of the spectra often occurs, mainly, in the assigning of the resonances to the corresponding proton and carbon atoms. Many predictive models have been advanced to assist in the interpretation of experimental chemical shifts [4, 5].

Currently, the development of theoretical models has provided a computational framework for the research of theoretical modeling of organic compounds, and it has become possible to determine their essential physicochemical properties by various theoretical methods. Density-functional theory (DFT) has become an important tool in modern molecular quantum chemistry. The best DFT functionals typically provide results comparable in quality with those of more elaborate ab initio methods at a fraction of the computational cost [6,7,8,9]. The computational expense of DFT is substantially less than that of second-order Moller-Plesset perturbation theory (MP2).

The aim of this work is to calculate the theoretical chemical shifts of some cyclic ketones (Figure.1) by using proper computational methods and basis sets. The calculated chemical shifts are then compared with the experimental values. Furthermore, it will be shown, via a comparative treatment, the performance of different DFT functionals to predict the chemical shifts with very satisfactory precision.

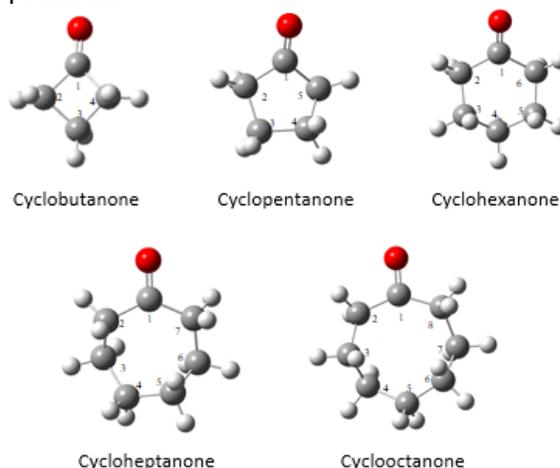


Figure 1: Molecular structures of the cyclic ketones.

2. MATERIALS AND METHODS

2.1 Quantum-chemical calculations:

All the calculations were performed with the use of the Gaussian 09 set of programs [10]. Geometry optimizations for all systems both in vacuum and in solution were performed on the basis of the density functional theory (DFT) using seven exchange-correlation XC functionals in the DFT benchmarking, including: B3LYP [11], B3PW91 [12], B97D [13], BP86 [14], CAM-B3LYP [15], LC-Wpbe [16], PBE1PBE [17]. The basis set used was the 6-311G+(d, p). Vibrational frequencies were calculated from analytic second derivatives to confirm the structures as local minima on their respective potential energy surfaces.

Calculations of nuclear shieldings were performed at the same level of the structural optimization, exploiting the gauge-including atomic orbital (GIAO) method [18]. Absolute isotropic magnetic shieldings were transformed into chemical shifts by referencing to the shieldings of a standard compound (TMS) computed at the same level.

To explore the influence of solvation on the chemical shifts we employed the (PCM) [19] model implemented in Gaussian 09. In this approach, the solute molecule is embedded in a cavity formed by the packet of spheres centred on solute atoms, the solvent is represented by an infinite dielectric medium characterized by the relative dielectric constant of the bulk and the so called UAHF radii are used for building the effective cavity occupied by the solute in the solvent. Furthermore, we have introduced several solvent molecules explicitly together with the PCM model. Then, we have optimized the geometrical structure of the solute-(solvent)_n to reproduce more or less correctly the effect of specific solute-solvent interactions, such as hydrogen bonds [20].

2.2 Experimental section

All compounds and solvents used in this work were commercially available and were dried and purified before use. ¹³C NMR spectra were obtained in (CD₃)₂CO on a Bruker 300 spectrometer at 75 MHz in 5 mm probes with direct detection, using TMS as internal standard ($\delta = 0.00$). The general reproducibility of chemical shifts data was estimated to be better than 0.01 ppm. Samples were prepared by weight and volumetrically.

3. RESULTS AND DISCUSSION

The measured carbon NMR spectrum of the selected ketones cyclic in the solution phase is compared with the simulated one obtained at GIAO/6-311G+(d, p)/PCM. The chemical shift values (in ppm) are reported relative to the chemical shift value of TMS standard. The experimental and theoretical chemical shifts are tabulated in Table 1. The labeling of atoms was used as per Fig.1. All carbon atoms of cyclic ketones are grouped by equivalent atoms.

Table 1: The table presents the experimental and calculated DFT ¹³C NMR shifts.

| Compounds | C _i | B3LYP | B3PW91 | B97D | BP86 | CAM-B3LYP | LC-wPBE | PBE1PBE | δ_{exp} |
|----------------|------------------|--------|--------|--------|--------|-----------|---------|---------|------------------------|
| Cyclobutanone | C ₁ | 208,76 | 204,12 | 200,44 | 204,68 | 207,11 | 208,29 | 201,91 | 209.829 ^(a) |
| | C _{2,4} | 49,35 | 46,26 | 48,97 | 49,65 | 48,59 | 45,52 | 44,08 | 48.321 |
| | C ₃ | 11,20 | 7,78 | 12,08 | 11,23 | 7,15 | 8,80 | 5,58 | 9.879 |
| Cyclopentanone | C ₁ | 218,68 | 214,53 | 210,24 | 215,06 | 218,94 | 212,06 | 212,37 | 217.939 ^(a) |
| | C _{2,5} | 39,71 | 36,20 | 39,09 | 39,65 | 36,25 | 29,51 | 34,07 | 38.028 |
| | C _{3,4} | 25,99 | 22,08 | 26,48 | 25,75 | 21,61 | 19,78 | 19,94 | 23.971 |
| Cyclohexanone | C ₁ | 209,54 | 205,56 | 201,05 | 205,67 | 209,42 | 203,74 | 208,42 | 211.887 ^(a) |
| | C _{2,6} | 44,34 | 40,22 | 43,85 | 44,38 | 43,34 | 32,53 | 45,34 | 42.876 |
| | C _{3,5} | 30,46 | 26,19 | 31,43 | 30,89 | 30,46 | 28,75 | 16,37 | 27.453 |
| | C ₄ | 28,12 | 23,54 | 28,51 | 27,76 | 28,12 | 27,77 | 14,53 | 25.754 |
| Cycloheptanone | C ₁ | 213,67 | 209,58 | 204,45 | 212,82 | 214,07 | 213,43 | 209,07 | 215.285 ^(a) |
| | C _{2,7} | 45,89 | 41,95 | 43,04 | 42,55 | 42,80 | 42,16 | 42,52 | 44.015 |
| | C _{3,6} | 26,92 | 25,85 | 20,73 | 21,71 | 23,50 | 25,72 | 21,27 | 24.712 |
| | C _{4,5} | 31,85 | 30,07 | 28,09 | 28,48 | 29,63 | 30,03 | 28,84 | 30.845 |
| Cyclooctanone | C ₁ | 218,29 | 215,83 | 210,16 | 215,70 | 217,91 | 217,08 | 214,36 | 218.300 ^(a) |
| | C _{2,8} | 40,60 | 41,45 | 32,56 | 41,45 | 43,20 | 41,70 | 40,05 | 42.913 |
| | C _{3,7} | 31,98 | 25,54 | 26,45 | 25,54 | 29,81 | 27,33 | 34,28 | 28.545 |
| | C _{4,6} | 28,22 | 24,24 | 24,59 | 24,24 | 27,32 | 25,39 | 27,79 | 26.611 |
| | C ₅ | 26,87 | 26,84 | 26,13 | 24,53 | 22,21 | 23,40 | 26,71 | 25.871 |

(a) Ref [21].

For ¹³C NMR chemical shifts, each functional showed different response for each type of C atom. For the carbonyl carbon atoms, the B3LYP functional presented values close to the experimental ones, while the B97D functional underestimated the values of δ , resulting in $\Delta\delta = \delta_{cal} - \delta_{exp} < 0$. For the methylene carbon in the α position, the best results were

obtained using CAM-B3LYP, with $\Delta\delta$ ranging from 0.27 to 1.78 ppm, and LC-wPBE reproduces well the chemical shift of C_3 carbon. As may be observed, the calculated values are in good agreement with the ^{13}C NMR chemical shift values measured experimentally in the same solvent.

The statistical treatment was performed, and the results are summarized in Table 2 in acetone solvent. The second column gives the mean difference between experimental and calculated values, with the corresponding standard deviation in column 3. Column 4 identifies the root-mean-square (RMS) difference, which is always larger than the mean difference. The last three columns document linear regression statistics for the direct correlation of calculated versus experimental shifts. All NMR shifts are in ppm relative to a TMS standard.

Table 2: The table presents the statistical diagnostics of NMR calculations of the considered cyclic ketones.

| | $\langle \delta_{exp} - \delta_{cal} \rangle$ | S.D. | RMS | R^2 | Intercept | Slope |
|------------|---|-------|-------|--------|-----------|-------|
| B3LYP | 1.732 | 0.004 | 1.870 | 0.9998 | 2.008 | 0.986 |
| B3PW91 | 2.549 | 0.004 | 3.033 | 0.9997 | -1.091 | 0.983 |
| B97D | 4.393 | 0.009 | 5.739 | 0.9992 | 1.003 | 0.951 |
| BP86 | 2.492 | 0.006 | 2.802 | 0.9996 | 0.464 | 0.980 |
| CAM- B3LYP | 1.722 | 0.005 | 1.882 | 0.9998 | -0.478 | 0.996 |
| LC-wPBE | 3.226 | 0.011 | 4.205 | 0.9992 | -2.141 | 0.992 |
| PBE1PBE | 4.421 | 0.012 | 5.354 | 0.9988 | -2.482 | 0.988 |

S.D.: standard deviation; **RMS:** root-mean-square.

They are comparing the differences between the experimental and theoretical values. B3LYP and CAM-B3LYP have proved to be the most efficient in predicting the ^{13}C chemical shifts of the compounds taken into consideration, displaying both the lowest RMS parameters and the highest R^2 coefficients, although CAM-B3LYP shows more precision to predict NMR shift for the different cyclic ketones. The most significant differences between experimental and theoretical values are found for PBE1PBE and B97D functionals with the maximum RMS equal to 5.305 (PBE1PBE) and 5.739 ppm (B97D). The experimental and computed correlation coefficients are both of excellent quality and the slopes are close to unity. This shows that there is an excellent linear correlation between calculated and NMR shifts experimentally observed, this is illustrated in Fig. 2 and is supported by the results in Table 2.

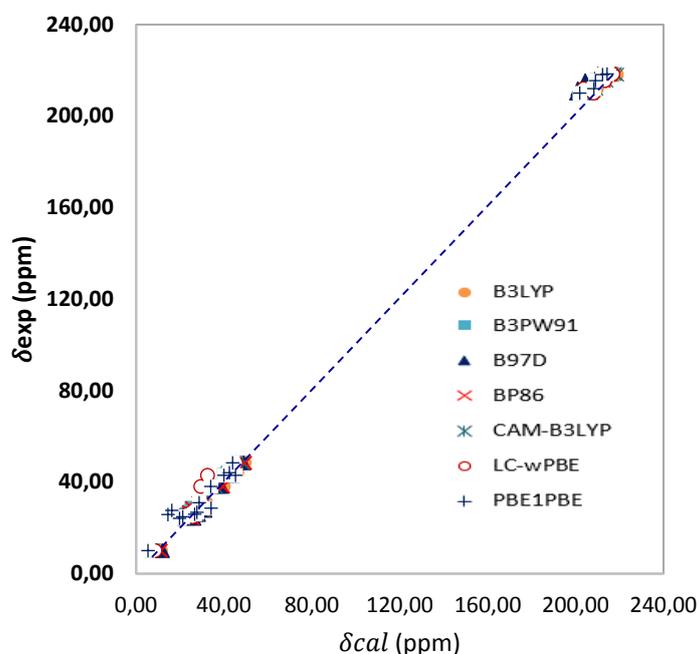


Figure 2: A plot of the relative theoretical ^{13}C chemical shifts of all carbon of cyclic ketones versus the experimental.

There is an excellent linear relationship between experimental and computed results. The experimental points, however, are above the line $y = x$, also shown. The correlation breaks down afterward, and the calculated values appear as smaller than the experimental ones. The linear relationship is very satisfactory.

4. CONCLUSION

In the current work, we have investigated and compared several density functional theory methods, which are often used or can be employed for chemical shifts prediction of cyclic ketones (Cyclobutanone, Cyclopentanone, Cyclohexanone, Cycloheptanone and Cyclooctanone), to find proper quantum models that satisfy both high accuracy and low cost. The correlations between experimental and calculated chemical shifts were subjected to statistical analysis to identify the best-performing functionals. The 6-311+G(d,p) basis set and GIAO NMR method combined with the B3LYP and CAM-B3LYP functionals showed the lowest values of RMS, better agreement of calculated values with the experimental ^{13}C NMR chemical shift.

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