Density Functional Theory based study on structural, vibrational and NMR properties of cis - trans fulleropyrrolidine mono-adducts

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Abstract

Since the early nineties, countless publications have been devoted to the study of possible uses of [60] fullerene (C_{60}) and its derivatives in the fields of materials and nano-biomedical sciences. However, in spite of the importance of conformers notably from the pharmacological point of view, the cis/trans isomerization of C_{60} mono-adducts has been rarely seldom investigated. Here we present the results of DFT calculations of the structural, vibrational and NMR properties of both cis and trans isomers of fulleropyrrolidine mono-adduct obtained by photo-addition of glycine methyl ester to C_{60}. Taken together, our results have shown that the cis isomer is more stable than the trans one. For the cis conformation, the simulated vibrational spectrum shows a more intense peak at 1298 cm^{-1}. While 13C spectra revealed no significant differences between the two isomers as compared to experimental results, the calculated 1H chemical shifts show a significant difference between the two conformers in both the gas phase and in solution. The trans isomer presents a proton at 5.86 ppm, which is more deshielded than the proton of the cis conformer (5.24 ppm).

Introduction

More than 30 years after its discovery, [60] fullerene or C_{60} and its derivatives have continued to fuel research in the fields of materials and biomedical sciences [1,2]. Moreover, although the chemical reactivity of C_{60} has been well apprehended for years, some important chemical reactions have never been carried out on the surface of the fullerene [3]. Indeed, chemists still continue to exploring alternative ways of C_{60} derivatization [4].

Several important aspects of C_{60}-derivatives characterization still remain to be investigated. This is true not only for poly-adducts and their isomers but also for simple mono-adducts. For instance, while the mechanism of sequential photo-addition of glycine methyl ester (GME) to C_{60} has been well understood [5,6,7], the separation and characterization of the whole of the...
obtained fulleropyrrolidine poly-adducts remain to be achieved. It is the same for the separation and the characterization of the cis-trans isomers of the fulleropyrrolidine mono-adduct [8]. This is an important issue notably because of the difference of reactivity of such a kind of conformers at the pharmacological level.

As a matter of fact, the cis/trans isomerisation of C_{60} derivatives has been rarely investigated. Only few studies have been devoted to this aspect of fullerene chemistry [9, 10, 11]. More recently, based on experimental results and DFT calculations a mechanism of stereo-chemical outcome of cis-trans isomerization involving the H-bonding assistance of the inner water molecule in the carbanion stabilization of H20@C_{60} fulleropyrrolidine has been proposed [12].

Here we present the results of a density functional theoretical study on the structural, vibrational and NMR properties of both cis and trans isomers of the fulleropyrrolidine mono-adduct obtained by photo-addition of GME to C_{60} [5]. The obtained results are also compared to the previously published experimental results [5].

**Methodology**

Gaussian 09 has been employed for all the theoretical calculations [13]. Geometries of structures were optimized using the DFT at B3LYP [14,15] level along with 6-31G (d) basis set [16–19]. The 6-31G (d) basis set [20,21] was chosen to provide accurate results for conjugated derivatives [22]. The Geometry optimizations and frequencies were performed in the gas phase. Frequencies were scaled by a factor amounting to 0.96 to best compare with experiment [23]. The calculation of NMR spectrum of the different structures was performed using the GIAO (Gauge-Including Atomic Orbitals) method [24, 25], implemented in the Gaussian, with the B3LYP functional, in conjunction with 6-31G(d) and 6–311+g(2d,p) basis sets. In order to express the chemical shifts in ppm, the geometry of the tetramethysilane (TMS) molecule has been optimized. The calculations of NMR spectrum were performed in the presence of CDCl$_3$ solvent with the PCM model and in the gaseous phase.

**Results and discussion**

**Structures of GME added to C$_{60}$**

We optimized the geometry of the two structures (cis and trans, S1 and S2 Tables) of the mono adduct by the DFT method at B3LYP 6–31 G(d) Level. The optimized geometry is represented in Fig 1.

The optimization of the two structures of the mono adduct (cis and trans) shows that the distances inside the two molecules are similar.

We were particularly interested in C-C bonding or grafting of the adduct. We note that the length values of these bounds are slightly shorter for the trans form compared to cis form (1.612 Å for C-C CIS versus 1.607 Å and 1.608 Å). This may suggest that adsorption energy for the trans form is the most important.

In the cis structure there is almost a Cs symmetry in the plane containing N and parallel to the two bonds between C$_{60}$ and the Indole ring. trans structure is almost a C2 symmetry.

The calculated energies of the cis and trans isomers of the mono adduct in the gas state and in solution are presented in Table 1.

The formation of the cis form of the mono adduct is slightly more favorable than the formation of the trans, it’s worthy to note at room temperature, the difference between the two structures is about 1 kcal. This suggests that the proportions of the two molecules are almost equal. This result is in agreement with Maroto et al. who showed that trans isomer is less stable than cis for theses Fulleropyrrolidines [12]. The less favorable energy of the trans product could be
mainly attributed to the higher repulsion of the lone pairs of the nitrogen atom of the pyrrolidine ring and the carbonyl group of the substituent.

Calculation of IR spectra

The simulation of the IR spectra of the cis and trans isomers of the mono adduct is shown in Fig 2. The two spectra were superposed in order to identify the differences.

All characteristic frequencies of vibration assigned to the mono-adduct were determined and are summarized in Table 2.

The comparison between the cis and the trans IR spectra (Table 2) shows a remarkable difference in the vibration frequency of 1298 cm$^{-1}$. The latter is attributed to C-H bond, it has a higher intensity in the cis isomer IR spectrum. At the same time, this frequency value (1298 cm$^{-1}$) is lower than the C-N frequency value that experimentally appears at 1428 cm$^{-1}$. This is allows to suggest that we are in the presence of both cis and trans isomers [5].

Calculation of chemical shifts

a) Calculation of $^1$H chemical shifts. For the optimized structures, the calculation of the $^1$H NMR spectra of the two isomers cis and trans of the mono adduct and their comparison with the experimental results is presented in Table 3.

Enlarging the basis allowed us the improvement of the shielding values. In addition to the 6–31 G(d) basis, we have used a larger basis, the 6–31 G (2d,p), to optimize the geometry and to simulate the NMR results [26].

Calculation of the shielding parameters was performed at the same level of theory as for the protons of the Tetra Methyl Silane (TMS) molecule, chosen as a reference, in order to obtain the chemical shifts for the protons and carbons under consideration through the following

| Structure      | $\Delta E$ (gas phase) | $\Delta E$ (solvent CDCl$_3$) |
|----------------|------------------------|-------------------------------|
| Mono-adduct (cis) | 0                      | 0                             |
| Mono-adduct (trans) | 4.07                   | 5.25                          |

Table 1. Energy difference between the cis and trans isomers (kJ mol$^{-1}$).
relation [27]:

\[ \delta = \delta(TMS) - \delta(Structure) \]  

Where, \( \delta \) is the chemical shift in ppm.

The root mean square (rms) deviations between calculated and experimental values for the chemical shifts have been calculated using the following equation (27).

\[
\text{rms}(P) = \sqrt{\frac{\sum_{K=1}^{N} (P_{\text{Exp}}(K) - P_{\text{Calc}}(K))^2}{N}}
\]

Where \( N \) is the number of data. These rms values calculated for \( \delta \) are displayed in Table 3 and Table 4.

We have considered that the nitrogen inversion in the Fulleropyrrolidines is a fast event at the operating temperatures, so we have calculated the average between the two chemical shifts of the two methine protons for the trans isomer [12].

Fig 2. (a) Superposition of the two simulated IR full spectra of the cis and trans mono-adducts (b) Zoom in on the range from 0 to 2000 cm\(^{-1}\) of the same superposition.

Table 2. Comparison between experimental and calculated IR spectra for the cis and trans compounds with significant intensities (cm\(^{-1}\)).

| Attributions | cis  | trans | EXP * |
|--------------|------|-------|-------|
| -            | 323  | -     | -     |
| -            | 737  | 737   | -     |
| -            | 783  | 783   | -     |
| -            | 806  | -     | -     |
| -            | 852  | -     | -     |
| -            | -    | 883   | -     |
| -            | -    | 1136  | -     |
| C-O          | 1167 | 1167  | -     |
| C-O          | 1190 | 1198  | 1255  |
| C-H          | 1259 | 1251  | -     |
| C-H          | 1298 | 1313  | -     |
| C-N          | 1367 | 1359  | 1428  |
| C = O        | 1756 | 1751  | 1740  |
| N-H          | 3340 | 3356  | 3288  |

* According to Skanji et al [5].

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We observe that for the cis isomer we have just one chemical shift at 5.24 ppm for the methine proton but for the trans isomer we have two chemical shifts at 5.34 and 6.39 ppm for the same proton we have averaged the two values in order to compare our results to the experimental results. Our system is non-symmetrical; we then have two different chemical shifts of the two methine protons. The deshielding of one of the protons from the other is due to the combination of the electronegative effect of nitrogen and the magnetic anisotropy created by the inhomogeneity of the electron density and the magnetic fields induced by the electron circulation within the fullerene cage [28].

Some studies with different experimental conditions have shown the protons in the trans form more deshielded than those in the cis form. In our case, we have shown the same trend [29,30]. For the basis 6-31G(d) The mean square error varies between 0.47 and 0.64 while for the basis 6–311+g (2d,p) it varies from 0.4 to 0.77. This suggests that hydrogen in CH trans is more deshielded than the proton of the CH cis.

b) Effect of solvent. We have studied the effect of the CDCl₃ solvent which is used for the NMR analysis. The results of calculated NMR chemical shift for the most stable cis isomer of mono-adduct using the basis 6-31G(d) and the comparison with the results in gas phase are presented in Table 4.

The chemical shift for the cis structure has increased for the hydrogen of CH cis.

c) Calculation of ¹³C chemical shifts. The calculation of the predicted ¹³C chemical shifts in the gas phase, ¹³C of the characteristic groups (Fig 3), is illustrated in Table 5.

We have averaged the two values of ¹³C in order to compare our results to the experimental results.

In the ¹³C NMR experimental spectrum suggests that it is a cis—and trans- isomer mixture; The Methine carbon is at 74 ppm, two fullerene sp2 carbons at 149,84 and 152.1 ppm, and Carboxylic Ester carbons between 160 and 170 ppm.

Considering the experimental results, the mean square error of the calculated NMR spectra of cis isomer is about 4.67 and is about 4.11 for the trans isomer.[5]

Table 4. Chemical shifts (ppm) calculated for the cis isomer in CDCl₃.

| δ (ppm) cis | RMSD | δ (ppm) trans | RMSD |
|-------------|------|---------------|------|
| CH₃ | CH | NH | CH₃ | CH | NH |
| B3LYP/6-31g(d) | 4.01 | 5.24 | 4.15 | 0.47 | 3.98 | 5.86 | 3.65 | 0.64 |
| B3LYP/6-311+g (2d,p) | 4.11 | 5.97 | 4.68 | **0.40** | 4.14 | 6.5 | 4.31 | 0.77 |
| EXP * | 3.93 | 5.59 | 4.54 | | 3.93 | 5.59 | 4.54 |

*: According to Skanji et al [5].

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Conclusion

Using B3LYP/6-31G(d), we have been able to model two configurations of the fulleropyrrolidine mono-adduct. We have notably shown that the cis isomer is more stable than the trans conformer. For the cis conformation, the simulated vibrational spectrum shows a more intense peak at 1298 cm⁻¹. Also, the comparison with previously published experimental results has shown that the calculated ¹H chemical shifts exhibit a significant difference between the two structures in both gas and solution phases. The trans isomer presents a proton at 5.86 ppm, which is more deshielded than the proton of the cis conformer (5.24 ppm). However ¹³C spectra has revealed no significant differences between the two isomers. These results will help rationalize the interpretation of the spectra of Fulleropyrrolidine structures.

Supporting information

S1 Table. XYZ coordinates of the optimized geometry: cis.
(DOCX)

S2 Table. XYZ coordinates of the optimized geometry: trans.
(DOCX)

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Table 5. Experimental and calculated ¹³C NMR spectra.

|        | C₁  | C₂  | C₃  | C₄  | Carboxylic Ester | CH₃  | RMSD |
|--------|-----|-----|-----|-----|-----------------|------|------|
| δ (ppm) EXP a | 74.0 | -   | 149.84 | 152.1 | 160–170         | 52.9 | -    |
| δ (ppm) cis    | 74.45 | 81.84 | 148.97 | 151.48 | 162.17         | 51.40 | 4.67 |
| δ (ppm) trans  | 74.74 | 81.58 | 148.80 | 153.07 | 164.24         | 51.40 | 4.11 |

a: According to Skanji et al. [5].

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