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Abstract

The structure assignment and conformational analysis of cinnamic derivative N-benzyl-N-(2-(cyclohexylamino)-2-oxoethyl) cinnamamide (NGI25) was carried out through Nuclear Magnetic Resonance (NMR) spectroscopy, Molecular Dynamics (MD) and Quantum Mechanics (QM), i.e., semiempirical and Density Functional Theory (DFT) calculations. Specifically, homonuclear (2D-COSY, 2D-NOESY) and heteronuclear (2D-HSQC, 2D-HMBC) spectra were obtained. Through them, the resonant values of the hydrogens and their constituent carbons were identified. After structure identification, NGI25 was subjected to computational calculations to reveal its most favorable conformations. QM, MD were in agreement with the spatial correlations that were observed in 2D-NOESY spectra.

Introduction

In this article Ugi-4R reaction was used to synthesize cinnamic adduct NGI25 [1,2].

Figure 1: N-benzyl-N-(2-(cyclohexylamino)-2-oxoethyl) cinnamamide, NGI25

In (Figure 1) Structure of NGI25 with carbons numbered as these are used in the assignment of NMR spectra Structure elucidation [3] was performed through NMR experiments and specifically, 1D and 2D experiments. A detailed conformational analysis was carried out via DFT [3,4] and MD [5]. These methods are the most appropriate for these organic compounds. A wide range of conformations has been examined through PM6 [6] and DFT calculations [7]. Finally, molecular dynamics calculations were used to study the mobility of NGI25 in DMSO.

Results

As a convenient starting point, the structure assignment was started by the protons H-10 and H-11. The final part was to identify the quaternary and carbonyls carbons through 2D-HMBC experiment. On the next stage, conformational analysis was carried out to find the most favorable configuration for NGI25. NGI’s conformations do not present important differences between the results of all the computational methods and experimental NMR results. In particular, the conformations provided by Grid Scan, MD, PM6 and DFT methodology are quite similar (see Figure 3), and only minor differences between the
conformers that derived from PM6 and DFT calculations are observed.

**Figure 2:** Overall diagram showing the identification strategy of the NGI25 compound in DMSO solvent.

![Overall diagram showing the identification strategy of the NGI25 compound in DMSO solvent.](image)

**Figure 3:** Conformation of NGI25 derived from (a) Grid scan (b) Molecular Dynamics (c) PM6 (d) DFT (B3LYP/6-31+G(d,p)) methodologies. The superimposition of these conformers is illustrated in the framed part of the figure.

![Conformation of NGI25 derived from (a) Grid scan (b) Molecular Dynamics (c) PM6 (d) DFT (B3LYP/6-31+G(d,p)) methodologies. The superimposition of these conformers is illustrated in the framed part of the figure.](image)

### Conclusion

Briefly, our findings demonstrate that cinnamic additives are very important compounds and in the future they will be used for molecular docking experiments to find some possible biological targets.

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### Conflicts of Interest:

The authors declare no conflict of interest.

### References

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For detailed references, please consult the full text of the article.