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COMPUTATIONAL STUDY OF ORGANIC COMPOUNDS – AN APPLICATION FOR LEARNING IN CHEMISTRY

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Abstract: Organic chemistry is a theme not so easy to understand by undergraduating students. The motivation of this work was carried out computational study of three different molecules by molecular modeling using classic and semi-empirical methods besides open-source softwares. The optimized structures were visualized through 3D representations which made the study more understanding. Physical chemistry properties were extracted from all molecules. For the molecule 01 there was good correlation between the calculation methods. For the molecule 02 and more complex structures like molecule 03 and 04 there was possible influence of steric effect showing that each method is applicable for each study system.

Keywords: Molecular Modeling; Organic chemistry; Physical-Chemistry.

1 INTRODUCTION

Computational chemistry has been gaining space and increasing recognition within research centers. This fact is due to the development of new computers with greater processing power and consequently the creation of new methods that make the results obtained through computational computations increasingly consistent with those obtained experimentally

(WALLER et al., 2013; ALLOUCHE et. al., 2011).

In addition to its application in scientific research, computational methods can be applied successfully within universities as a tool to aid students' learning process, making concepts more essential and more palpable. An abstraction that is not easily obtained by students and which makes the learning process more time-consuming and discouraging (QUEZADAA et. al. 2017; RAUPP et. al., 2008).

Understanding the structure of molecules in molecular level is important for chemistry because it is related to several properties such reactivity, stability and other physical-chemical properties (CAZALS, et. al., 2015; SOLOMONS et. al., 2009). In a molecule, the united atoms by sigma bonds can rotate freely, this causes parts of the molecule to have their positions varying with each other over time, that feature gives the molecule a range of temporary arrangements that we call conformers. The variation energy study associated with each of the conformers is known as conformational analysis (SOLOMONS et. al. 2009; RAMADAS, 2009). The identification and determination of the most stable and abundant conformer, besides the stability verification of a molecule are some of the subjects discussed in classes of organic chemistry that can be approached using conformational analysis besides geometry optimization. When this type of analysis is done using computational methods a door is opened to provide a more visual experience and enabling student experimentation by modifying variables and obtaining answers such as 3D molecular structures and thermodynamic properties, almost immediately, of a way that is not possible by traditional methods.

The visual experience is something that has been increasingly studied within the concept of teaching and learning, especially within the areas that require a certain level of abstraction. Chemistry is a science that at various times needs these abstractions and therefore can make computing its great ally (HASSINEN et al., 2001).

With the improvement of the computational chemistry tools the conformational analysis and geometry optimization have been developed to the point of obtaining calculated data that have great correlation with experimental data even in complex systems containing hundreds of atoms (HANWELL et. al., 2012). However, it is important to make the correct choice of the method to be used to obtain satisfactory results using various software packages available and the results that it may offer.

In computational chemistry we can choose between the classical methods that use Newton's mechanics to perform the calculations and data acquisition and semi-empirical methods that introduce concepts of quantum mechanics to make the system as close to the real as possible, obtaining more accurate data.

The treatment by means of quantum methods, different from the classical methods that consider each atom as simple spheres, takes into account the electrons of each atom. The arrangements of the free electron pairs in the atoms of the molecules lead to intra molecular attractions or repulsions by modifying the structure of the substance.

Structure optimization can be done and visualized through the use of free programs such as GHEMICAL (MOPAC2016), AVOGADRO (SCHAFTENAAR, et. al., 2000), MOPAC (VILAR, 1999), MOLDEN (CARACULACU, et. al., 2001), PyMOL (https://pymol.org/2/) among others. These programs can be run on computers with basic configurations for illustrating processes and obtaining simpler substance data. However, for more complex calculations computers with improved configurations will be necessary because, when it comes to computational methods, whatever the complexity, the higher the hardware requirements and the computational cost.

Understanding the performance differences and the results obtained through classical and semi-empirical methods makes it possible to further explore the potentialities and limitations of using computational chemistry as a tool to make it more visual and to facilitate the understanding of certain chemical concepts (RAUPP et. al., 2008).

This article intends to illustrate the differences between the two types of analysis as well as to mention some software that can be used.

2 METHODOLOGY

CLASSICAL AND SEMI-EMPIRICAL TREATMENT

Initially, four organic compounds were drawn using the GHEMICAL software (HASSINEN et al., 2001)., Figure 1, to create the 3D coordinate of molecules C_5H_{12}, $C_{16}H_{18}$, $C_{13}H_{16}O_4N_3S$ and $C_{15}H_{10}O_2N_2$,, Figure 2. Classical energy minimization following by classical random conformational search, using TRIPOS 5.2 force field[15], were carried out to optimize the molecular geometries followed by semi-empirical optimization with PM7 method (VILAR, 1999), and keywords "PM7 PRECISE CHARGE = -1 PDBOUT" using the MOPAC (MOPAC2016) software. For the thermodynamic properties extraction were applied single point calculations using as input file the classical and semi-empirical optimized structures with "PM7 ROOT = 2 CHARGE = n FORCE LET THERMO = (100,400,10) COMPFG PDBOUT" keywords, where n is the formal charge of molecules. The output pdb files were superposes and visualized using the PYMOL program (https://pymol.org/2/). Finally, the results were extracted from output files and compared.

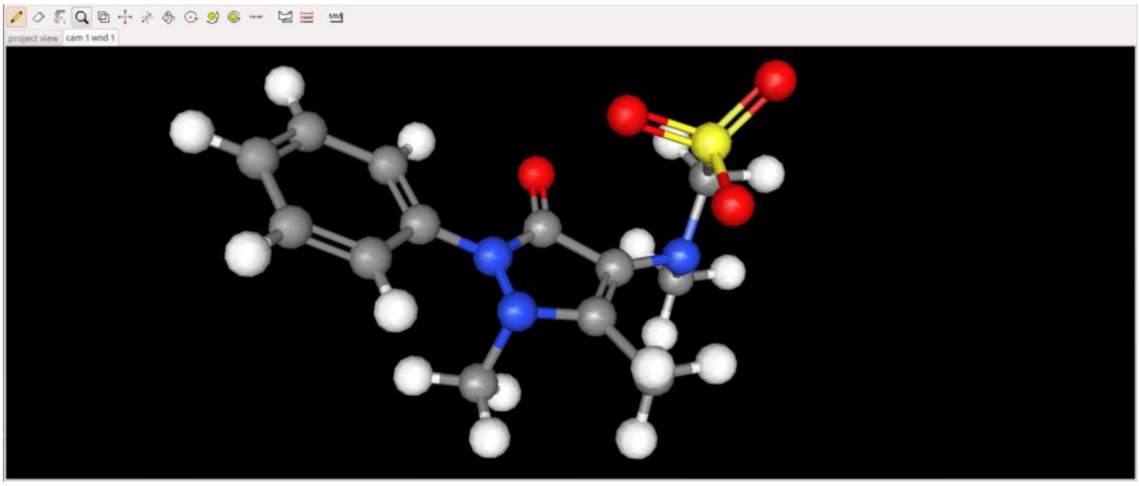
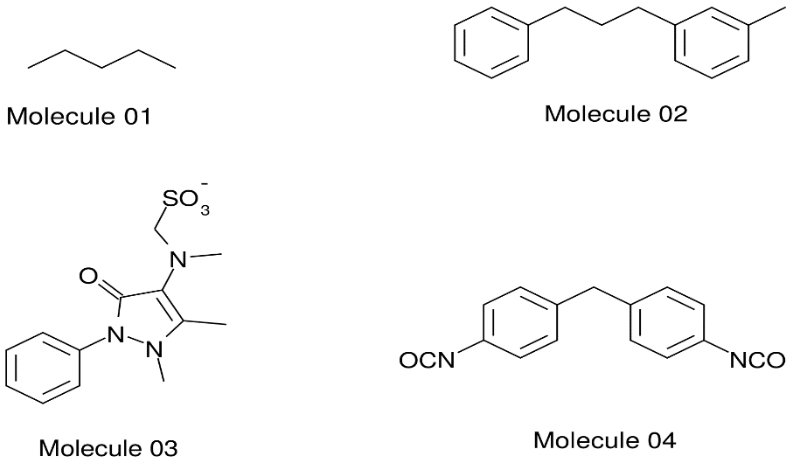


Figure 1. Graphical interface of GHEMICAL software with Molecule 03 in ball and stick representation



Molecule 01 Molecule 02 Molecule 03 Molecule 04

Figure 2. 2D representation of molecules C_5H_{12}, $C_{16}H_{18}$, $C_{13}H_{16}O_4N_3S$ and $C_{15}H_{10}O_2N_2$

3 RESULTS AND DISCUSSION

After making the classical and semi-empirical treatment for Molecule 01 we observe that both methods provide similar geometries, Figure 3.

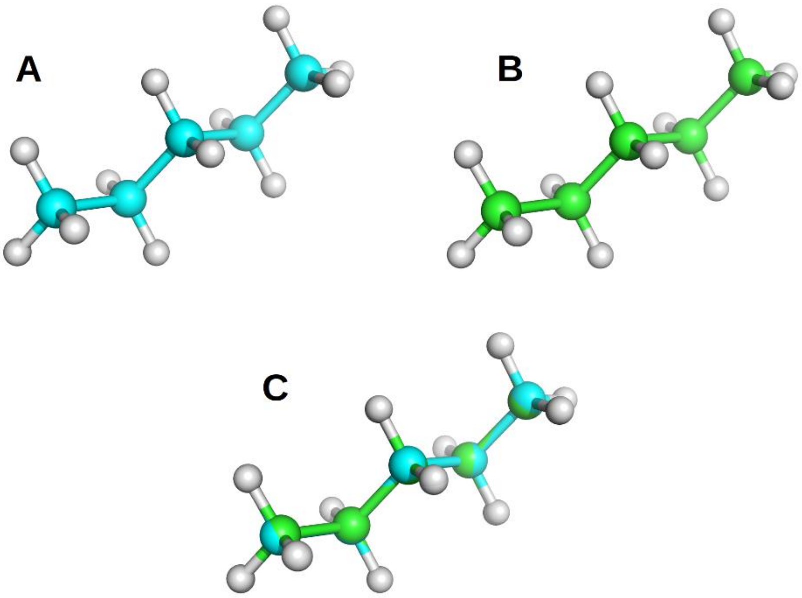


Figure 3 - Molecule 01 structure (A) obtained through semi-empirical optimization (B) classical optimization (C) overlap of structures.

Since Molecule 01 is a relatively simple hydrocarbon that does not have bulky electron clouds influencing the final geometry, the classical method achieves results with a good correlation with the method that considers interactions of quantum nature. Using the PYMOL program, it is possible to superimpose structures Figure 3 (C). By making the overlap, we obtain the Root Mean Square (RMS) deviation of 0.021 Å which means that the spatial conformations have almost no differences between them.

When the calculated physical-chemical parameters for Molecule 01 are analyzed, a small change in some values is observed, Table 1. Because the structures are very similar, the calculated properties have close values. This is also an indication that for the analysis of simple structures, the classical or semi-empirical methods can be used without great losses in the result.

Table 1. Thermodynamic properties of Molecule 01 calculated in MOPAC for structure obtained through classical and semi-empirical analysis.

Properties	Molecule 01	
	Classical	Semi-empirical
Heat of Formation / $kJ.mol^{-1}$	201.561	206.974
Enthalpy / $kJ.mol^{-1}$	21.760	23.595
Heat Capacity / $kJ.mol^{-1}.K^{-1}$	0.115	0.119
Entropy / $kJ.mol^{-1}.K^{-1}$	0.356	0.366

However, when the structures are larger and there are interactions that are better described through a quantum treatment, the classical methods begin to present greater deviations when compared to the semi-empirical methods which can be visualized by the structures obtained by each of the methods as shown in Figure 4.

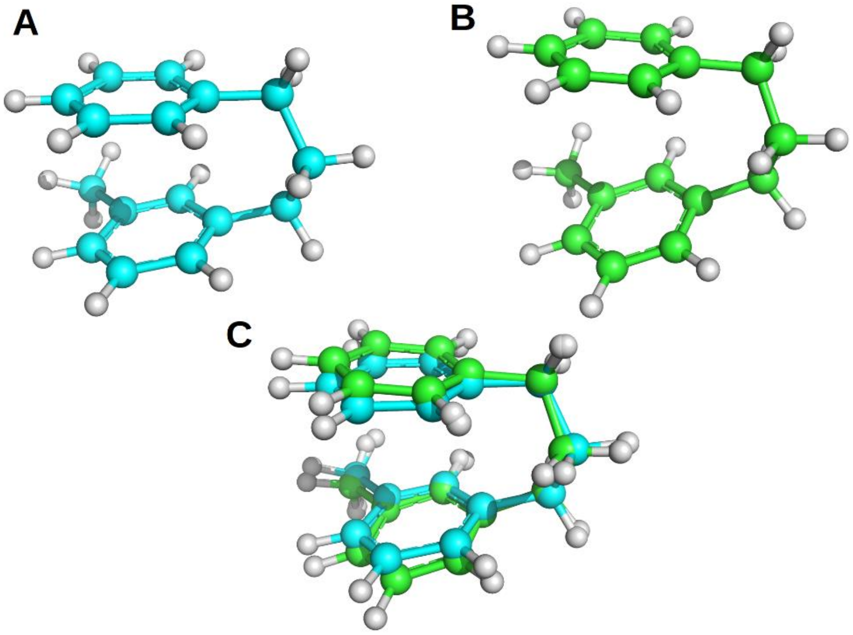


Figure 4 - Molecule 02 structure (A) obtained through semi-empirical optimization (B) classical optimization (C) overlap of structures.

Analyzing and overlapping the structures in PYMOL visually perceived that the structures do not completely overlap as shown in Figure 4 (C). This fact can be explained by the great electronic density of the aromatic rings that is not considered by the classical methods. For this molecule, the RMS calculated by the program was 0.342 Å confirming a less satisfactory relation between the structures.

When comparing the calculated properties for the optimized Molecule 02 in the two methods, it is possible to notice a more marked variation, mainly in the heat of formation, when compared with the data of Molecule 01, Table 2.

Table 2. Thermodynamic properties of the molecule 02 calculated in the MOPAC for structure obtained through classical and semi-empirical optimization.

Properties	Molecule 02	
	Classical	Semi-empirical
Heat of Formation / kJ.mol^{-1}	160.756	73.373
Enthalpy / kJ.mol^{-1}	40.948	41.428
Heat Capacity / kJ.mol^{-1}.K^{-1}	0.248	0.244
Entropy / kJ.mol^{-1}.K^{-1}	0.505	0.534

Increasing the complexity of the molecules, especially with respect to increasing the number of regions with electronic clouds, the correlation between the data obtained by classical methods and the semi-empirical methods decreases, making a simple classical optimization inefficient to make a conformational analysis with data close to the experimental ones. This is evident when we look at Molecule 03, Figure 5.

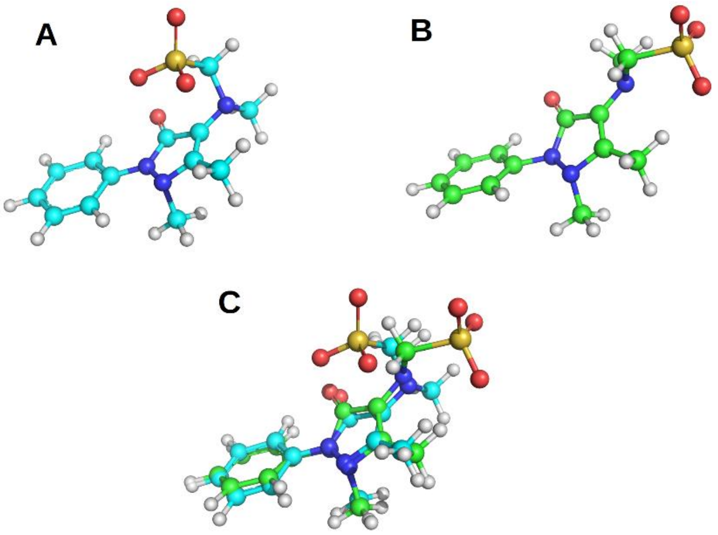


Figure 5 - Molecule 03 structure (A) obtained through semi-empirical optimization (B) classical optimization (C) overlap of structures.

By visualizing the overlap of the structures of Molecule 03, obtained by both methods, it can be seen that the region where a large electronic cloud is located, presented great variation when we consider the most stable conformer. In general terms, the RMS calculated by PYMOL between the two structures was 0.499 Å which indicates a large difference in structure which can be visually perceived.

By analyzing the calculated properties that are presented in Table 3, it is perceived that the difference in the calculated heat of formation for each method is quite high.

Table 3. Thermodynamic properties of the molecule 03 calculated in the MOPAC for structure obtained through classical and semi-empirical optimization.

Properties	Molecule 03	
	Classical	Semi-empirical
Heat of Formation / kJ.mol^{-1}	47.134	-591.737
Enthalpy / kJ.mol^{-1}	56.480	56.781
Heat Capacity / kJ.mol^{-1}.K^{-1}	0.327	0.329
Entropy / kJ.mol^{-1}.K^{-1}	0.622	0.639

Molecule 04 also presents difference between thermodynamic properties, more pronounced for the enthalpy of formation. The overlap of the structures (Figure 6 (C)) gives a deviation of 0.193 Å. The main discrepancy between the structures occurs in the isocyanate function present at the extremities of the structures. This occurs due to the high electronic density present in the 3 atoms involved in the bonds. In the isocyanate function, the electron density of the pi bond between carbon and oxygen tends to shift to oxygen, making the bonding characteristic of a sigma bond. This displacement is facilitated because the isocyanate function is attached to an aromatic group which is an electron acceptor.

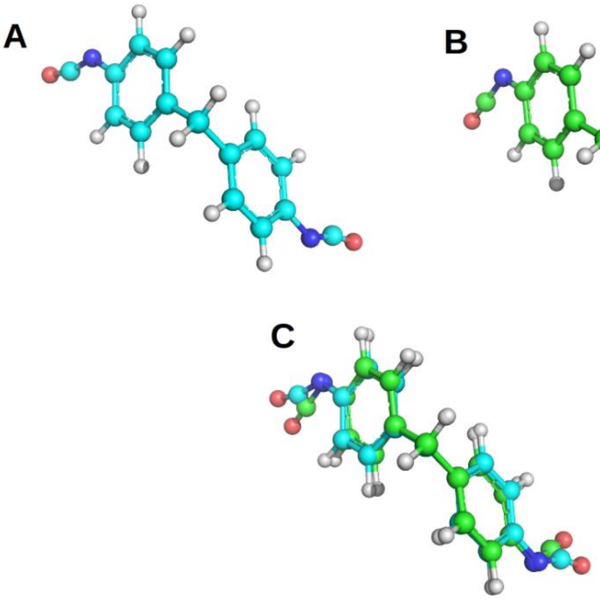


Figure 6 - Molecule 04 structure (A) obtained through semi-empirical optimization (B) classical optimization (C) overlap of structures.

It is observed that the angle formed between the nitrogen, carbon and oxygen is 165.2° in the isocyanate function for the semi-empirical method, already for the classic method the connection presents 180° in agreement with Caraculacu and Coseri[14]. This can be explained by the fact that the classical method does not consider the electronic contribution of the atoms and the effect is not observed.

The heat of formation were very far apart, while the other properties values remained relatively close suggesting that the chemical bonds present in the molecule affect the heat of formation values, Table 4.

The classical method does not provide satisfactory results for the geometry optimization when applied to molecules with double and triples bonds as we can see in this work. However, in cases that we have molecules with single bonds a classical analysis may be satisfactory.

Table 4. Thermodynamic properties of the molecule 04 calculated in the MOPAC for structure obtained through classical and semi-empirical optimization

Properties	Molecule 04	
	Classical	Semi-empirical
Heat of Formation / kJ.mol^{-1}	159.778	18.033
Enthalpy / kJ.mol^{-1}	42.152	45.462
Heat Capacity / kJ.mol^{-1}.K^{-1}	0.257	0.260
Entropy / kJ.mol^{-1}.K^{-1}	0.512	0.573

4 CONCLUSIONS

The theoretical conformational study is a fertile one with great potential both in the field of research and for educational purposes. This is because it presents satisfactory results by reducing costs and making certain themes more attractive and visual. The choice between the classical or semi-empirical method must be made based on the purpose of the analysis and the type of results to be obtained. For a conformational analysis of a simple substance or when close to real data is not needed, a classical analysis is sufficient, however when searching for more accurate data semi-empirical treatment is the best option. In general, regardless of the method, conformational analysis still has much to offer within schools and universities because it is a relatively simple, inexpensive and free-access tool that can aid research and educational processes by improving and facilitating the achievement of results. In this context it is important to report that all the components of the class ended up doing a self-evaluation participating from the making of the molecules to the extraction of thermodynamic properties without the need for a questionnaire application.

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REFERENCES

ALLOUCHE, A. Software News and Updates Gabedit—A Graphical User Interface for Computational Chemistry Softwares. **Journal of Computational Chemistry**. 2011, 32, 174–182.

CARACULACU, A. A.; COSERI, S. Isocyanates in polyaddition processes. **Structure and reaction mechanisms**. 2001, 26, 799-851.

CAZALS, F.; DREYFUS, T.; MAZAURIC, D.; ROTH, C.; ROBERT, C. H. Conformational Ensembles and Sampled Energy Landscapes: Analysis and Comparison. **Journal of Computational Chemistry**. 2015, 36, 1213–1231.

HANWELL, M. D.; CURTIS, D. E.; LONIE, D. C; VANDERMEERSCH, T.; ZUREK, E.; HUTCHISON, G. R. Avogadro: An advanced semantic chemical editor, visualization, and analysis platform. **Journal of Cheminformatics**. 2012, 4, 1-17.

HASSINEN, T.; PERÄKYLÄ, M. New energy terms for reduced protein models implemented in an off-lattice force field. **Journal of Computational Chemistry**. 2001, 22(12), 1229-1242.

JEFFREY P. Fitzgerald; CYCLOOCTANE Conformational Analysis Via Mechanical and Computational Models; **Journal of Chemical Education**; Volume 70 Number 12 December 1993.

MOPAC2016, JAMES J. P. STEWART, Stewart Computational Chemistry, Colorado Springs, CO, USA, HTTP://OpenMOPAC.net (2016).

QUEZADAA, C. T.; GANGASB, P. V.; FRÍASC, M. V.; MORALES, P. F.; Implementación de Avogadro como visualizador y constructor de moléculas para alunos deprimer año de Odontología em la asignatura Química General y Orgánica. **Educación Química**. 2017, 28, 22-29.

RAMADAS, Jayashree; Visual and spatial modes in science learning; **International Journal of Science Education** · February 2009.

RAUPP, D.; SERRANO, A.; MARTINS, T. L. C. A evolução da química computacional e sua contribuição para a educação em Química. **Revista Liberato**. 2008, 9(12), 13-22.

SCHAFTENAAR, G.; NOORDIK, J. H. Molden: a pre- and post-processing program for molecular and electronic structures. J**ournal of Computer-Aided Molecular Design**. 2000, 14, 123-134.

SOLOMONS, T.; W.; G.; Fhyhle, C. B. Química orgânica, 9 ed.; LTC: Rio de janeiro, Brazil, 2009; pp 142.

VILAR, W. D. Chemistry and Technology of Polyurethanes. Rio de janeiro Brazil:Vilar Consulting, 1999, 400 p.

WALLER, M. P.; DRESSELHAUS, T.; YANG, J. JACOB: An Enterprise Framework for Computational Chemistry. **Journal of Computational Chemistry**. 2013, 34, 1420–1428.