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ARTICLE *in* JOURNAL OF MOLECULAR STRUCTURE THEOCHEM · MAY 2005

Impact Factor: 1.37 · DOI: 10.1016/j.theochem.2004.10.089

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CHIH-DFT determination of the electrical, optical, and magnetic properties and NICS aromaticity of megazol

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Received 24 August 2004; accepted 25 October 2004
Available online 30 December 2004

Abstract

The infectious diseases are one the most important causes of mortality in the world. Two of these are the American trypanosomiasis or Chagas disease and the African trypanosomiasis or sleeping sickness. At this moment there exist some medicines to fight them, but they are not effective in the chronic stage. Thus, there are a number of drugs being developed, among them megazol and its derivatives. In this work, some electrical, optical and magnetic properties have been determined for megazol, by using Density Functional Theory and a model chemistry called CHIH-DFT, which uses a modification of the hybrid functional PBE0 named PBEg, where *G* is a structure factor. Also, a NICS study of aromaticity is included.

Keywords: Megazol; Chagas disease; Sleeping disease; DFT; Molecular structure; Polarizability; Aromaticity

1. Introduction

There are two related diseases that causes the death of thousands of people every year. They are the disease of Chagas and the sleeping sickness or African trypanosomiasis [1]. Both diseases are caused by parasites of the mastigosphora class (flagellated) and pertaining to the Trypanosomatidae family [2]. The relevance of these diseases is given by the amount of infected people and the lack of adequate medicine to stop the disease in the chronic stages. The disease of Chagas is caused by the parasite, *Trypanosoma cruzi* and transmitted to the human beings by the bite of infected insects [3]. The sleeping sickness is caused by the parasite protozoarium *Tripanosoma brucei*, is transmitted to the human beings through the bite of the tse-tse fly [4].

The COST, European Cooperation in the Field of Scientific and Technical Research, in their final report about Action 9 called Chemotherapy of Infectious Diseases, dated March 27, 2002, confirms that the therapies available to fight the parasitic activity are extremely limited and for this reason it is necessary to continue with the development and investigation of the molecule of megazol, since it has been proven of great effectiveness in monkeys in the combat to the sleeping sickness and the disease of Chagas, even in the chronical stage [5].

The objective of this work is to characterize the megazol molecule, 2-amino-5-(1-methyl-5-nitroimidazol-2-yl)-1,3,4-thiadiazole, with the purpose of obtaining different electrical, magnetic and optical properties (dipole moment and multipolar moments, polarizability, hyperpolarizability, magnetic susceptibility and its components, as well as a study of the aromaticity and the solvation energy, as an answer to the call done by the SWG, Scientific Working Group on Tropical Diseases, TDR, (February of 2002), where a strong campaign is suggested to persuade the governments to give priority to the investigation and development of forms of control of the African Trypanosomiasis [6].

2. Theory and computational details

The computational characterization was carried out by using the Gaussian 03W program [7] and applying

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doi:10.1016/j.theochem.2004.10.089

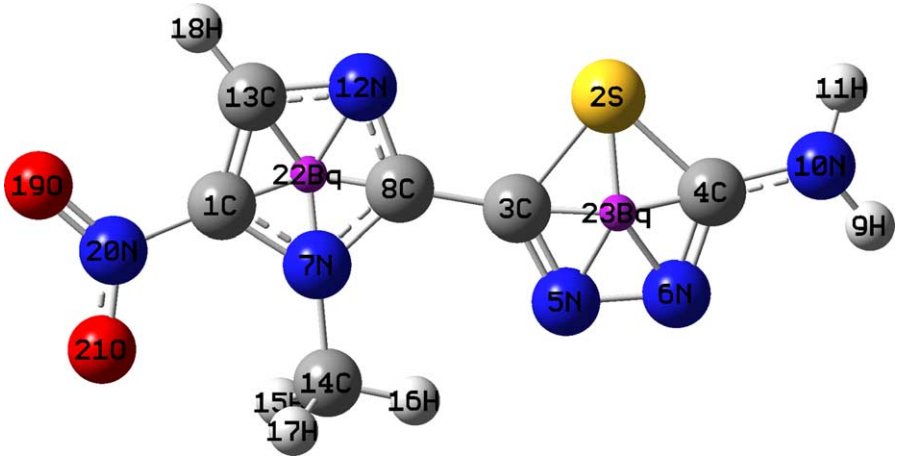

Fig. 1. Molecular structure of megazol calculated with the CHIH (large) model chemistry, showing the ghost atoms used in the NICS calculation of aromaticity.

the Density Functional Theory (DFT), with a model chemistry specially designed to work with heterocyclic systems This model that we have developed in our laboratory has been called CHIH-DFT (Density Functional Theory for Heterocyclic Systems–Chihuahua Heterocycles) and consists of an energy density functional of the hybrid type, with a structure factor G that depends on the structure of the heterocycle and measures the amount of Hartree–Fock exchange that is considered in the model [8–10].

We consider a modified version of the hybrid functional PBE0 [11] where there is only a correction in the Hartree–Fock exchange term, by using the G factor calculated for the megazole molecule which is 0.205. We considered the CBSB4 basis set which is equal to 6-31+G(d,p) for H to Si y and 6-31+G(df,p) para P,S and Cl. This basis set is a part of the CBS-QB3 method [12]. This level of theory has been called CHIH(medium) according to the levels developed in the QCOSMO group. We invite the interested reader to look for the details in the original articles [8–10].

3. Results and discussion

The dipole moment is of great importance to obtain data of the electronic distribution in a molecule since is one of the properties used traditionally to discuss and to rationalize the structure and reactivity of many chemical systems [13–15].

The values obtained for the dipole moment are 6.0818 Debye for the X coordinate, −0.4919 Debye for the Y coordinate and 1.0325 Debye for the Z coordinate, while the average result is 6.1884 Debye.

The results for polarizability are α are α_{xx}= 146.3474 a.u., α_{yy}=74.3377 a.u. and α_{zz}=256.7160 a.u., while the value average is 159.1337 a.u. For the first order hyperpolarizability, the values are β_{xxx}=75.8072241, β_{xxy}=4.4798216, β_{xyy}=−21.9094237, β_{yyy}=8.7525507, β_{xxz}=79.9826664, β_{xyz}=8.3072579, β_{yyz}=45.1465359, β_{xzz}=−272.7074205, β_{yzz}=18.55268, β_{zzz}=−2611.0835718. By using the formulas to obtain the average first order hyperpolarizability [15,16], we obtained value of 502.7203 a.u.

For the magnetic properties the values are: diamagnetic susceptibility −703.0616 a.u., paramagnetic susceptibility 681.2486 and −21.813 a.u. for the total magnetic susceptibility.

The NMR spectrum was calculated using a ghost atom in the center of each ring, with the purpose of analyzing the aromaticity of the molecule of megazol, by using the NICS aromaticity criterion based on the value of the shielding of that ghost atom. That is to say, if the value of the shielding is negative, the molecule is aromatic, while if it is positive, the molecule is nonaromatic [17]. The screening values for this calculation done with the basis set CBSB4 are −12.15 for the ghost atom called Bq22 and −10.08 for Bq23 (see Fig. 1). We can conclude that megazol is an aromatic molecule.

The calculation of energy was also done in the presence of water, simulated through the CPCM model. The solvation energy obtained in this way is equal to −7.72 kcal/mol. Although there are many factors that can contribute to the solubility of a molecule, we can conclude based on the solvation energy, that megazol is soluble in water.

A summary of the studied properties is shown in Table 1.

Table 1
Molecular properties of magazol calculated using density functional theory, and CHIH model chemistry with the PBEg functional and the CBSB4 basis set

Molecular property	Megazol
Diople moment (Debye)	6.1424
Energy gap (HOMO–LUMO gap	3.73248
Polarizability (a.u.)	159.1337
First order hyperpolarizability (a.u.)	502.7203
Diamagnetic susceptibility	−703.0616
Paramagnetic susceptibility	681.2486
Magnetic susceptibility	−21.813
Solvation energy (kcal/mol)	−7.72

4. Conclusions

The results for the polarizability α is of 256.7160 u a., the first order hyperpolarizability β of 502.7203 a.u., while for the dipole moment is 6.1884 Debye, thus being of greater polarity than the solvent water considered for the energy calculations. This explains the fact that the solvation energy is not so large (-72 kcal/mol), even though it is enough to consider the megazol molecule as soluble in water.

The value of the magnetic susceptibility -21.8774 is an indication that it is a diamagnetic material since $\chi < 0$ [14].

Finally, we can conclude that the molecule of megazol is aromatic, since the values of the shielding for the ghost atoms are negative, according to the NICS criteria, and close to the values for benzene itself.

Acknowledgements

This work has been supported by Consejo Nacional de Ciencia y Tecnología (CONACYT, Mexico) under Grant. No. 34697-U/2000. D.G.M. is a researcher of CONACYT and CIMAV. N.F.H. gratefully acknowledges a fellowship from CONACYT.

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