Journal of Physical and Theoretical Chemistry
of Islamic Azad University of Iran, 12 (4) 289-296: Winter 2016
(J. Phys. Theor. Chem. IAU Iran)
ISSN 1735-2126

Investigation of nuclear magnetic resonance (NMR) and Binding Energies Clonidine Drug-Carbon Nano Tube: A Theoretical Study

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Received December 2015; Accepted January 2016

ABSTRACT

In this work, we have studied binding of Clonidine drug ($C_9H_9Cl_2N_3$) with zigzag single walled carbon nanotubes (SWCNT) (5, 0) by theoretical methods of theory using Gaussian 09 software package.
Binding energies, NMR parameters and HOMO- LUMO Gap energy were calculated. Results from binding energies indicate that it is possible thermodynamically to bind Clonidine drug to SWCNT.
The calculated NMR parameters exhibit that Cl57 and H83 atoms have the highest and smallest anisotropic magnetic shielding (σ_{aniso}) constants. The plots of σ_{iso}, σ_{aniso} and η indicatedall shielding values but $\Delta\sigma$, δ show more negative shielding values at the HFin ٦-٣1G* basis set.
The values of HOMO, LUMO and HOMO–LUMO Gap energies are calculation for Clonidine drug and Clonidine drug to SWCNT using HF method and 6-31G* basis set. From HOMO–LUMO Gap calculation, it can be seen that HOMO- LUMO Gap energy of decrease in the order: Clonidine >Clonidine-SWCNT and by decreasing of HOMO- LUMO Gap energy, would be more stable compound. So, Clonidine beside SWCNT can act better as an electron donor and probably all of its biochemical and molecular functions can be accounted for by this function.

Keywords: NMR; SWCNT; drug delivery; HOMO; LUMO; Gap energy

INTRODUCTION

Nano technology makes wide revolution in human's life. It comes rapidly to different fields of technology and becoming increasingly important in subjects such as engineering, construction, agriculture, medicine, and microelectronics. The application of Nano technology in the medical science has come under great attention. Applications such as disease diagnosis, tissue reconstruction, and drug delivery system are noticeable. One of the exciting classes of Nano materials is represented by carbon nanotubes [1, 2].

Carbon nanotubes were discovered almost 15 years ago. The first report by Iijima [3] was on the multi wall form, coaxial carbon cylinders with a few tens of nanometers in outer diameter. Two years later single walled nanotubes were reported [4, 5]. They are typically between 1 and 1.5 nm in diameter, but several microns in length. After a slow start in the mid 90's the field suddenly exploded two years ago. A first application – displays made out of field emitting multiwall tubes – is planned to be commercially available during the next years. Other proposed applications include, e.g., nanotubes in integrated circuits, nanotubes actuators, or nanotubes for hydrogen storage [6-10].

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From a physics point of view they are probably the best realized example of a one-dimensional system.

One type of carbon nanotubes is single-walled nanotubes (SWCNTs) [11]; that this has three conformation: armchair (n, n), zigzag (n, 0) and chiral (n, m) these conformations have individual properties [12]. Single wall carbon nanotubes (SWCNTs) are formed by the rolling of a single layer of sp^2 carbon, called a graphene layer, into a seamless hollow cylindrical tube with Nano scale dimensions. SWCNTs have been considered as the leading candidate for Nano device applications because of their one-dimensional electronic bond structure, molecular size, and biocompatibility, controllable property of conducting electrical current and reversible response to biological reagents [13-19].

On the other hand, the potential of nanotechnology to revolutionize medicine in particular seems endless. One significant application of this technology is use of nanotubes for the targeted delivery of drug molecules which was proposed at the beginning of the 20th century [20] but now, because of Nanotechnological advances, is fast becoming a reality. Ideally, the nanotubes will locate to a specific site in the body, through its functionalized surface, and release its contents. The major advantage with this form of targeted drug delivery is the possibility of reducing the many adverse side effects experienced by patients hence throughout various field of science and technology, a push towards the use of Nano- scale technology such as Single wall carbon nanotubes is on the move. One area where SWCNTs work is already well under way is within the field of drug delivery. SWCNTs make possible bonding to drugs.

The primary goal of this study was to examine the binding of Clonidine drug ($C_9H_9Cl_2N_3$) with zigzag single walled carbon nanotubes (SWCNTs) with (5, 0) structure and a length of 10^0A.

The secondary goal ofthis study was to investigate different parameters of Drug-SWCNT complex.

THEORETICAL AND COMPUTATIONAL METHOD

The carbon nanotube that used in this study containing 60 carbon atoms, with both ends opened. In our model, Clonidine drug was attached covalently to carbon nanotube (SWCNTs) with (5, 0) structure and a length of 10^0A.

All calculations were performed using Gaussian 09 software package. Geometrical optimizations of Drug, single point calculation and NMR, NBO and Electrical properties parameters were carried out in gas phase with the Hartee - Fock and B_3LYP methods coupled to 6-31g* and 6-31g basis sets for all atoms.

The most common type of ab initio calculation is called a Hartee- Fock calculation (abbreviated HF), in which the primary approximation is called the central field approximation. A method, which avoids making the HF mistakes in the first place, is called Quantum Monte Carlo (QMC). There are several flavors of QMC variational, diffusion and Green's functions. These methods work with an explicitly correlated wave function and evaluate integrals numerically using a Monte Carlo integration. In general, ab initio calculations give very good qualitative results and can give increasingly accurate quantitative results as the molecules in question become smaller. First, prepare a molecule with an appropriate starting geometry. Second, choose a calculation method and its associated options. Third, choose the type of calculation with the relevant options. For example we calculated H, C, N, Cl NMR spectral parameters for the

interaction of Clonidine drugwith the open end of a SWCNT in gas phase by the HF/6-31g*method. In general, the electron distribution around a nucleus in a molecule is more spherically symmetric. Therefore, the size of the electron current around the field, and hence the size of the shielding, will depend on the orientation of the molecule within the applied field B. The energy of a magnetic momentum, μ, in a magnetic field, B, is as follow:

$$E = -\mu. (1 - \sigma) B \quad (1)$$

that the σ refers to the differential resonance shift due to the induced motion of the electrons. The chemical shielding is characterized by a real three-by-three Cartesian matrix, which can be divided into a single scalar term, three anti symmetric pseudo vector components, and five components corresponding to a symmetric tensor. Only the single scalar and the five symmetric tensor elements can be seen in the normal NMR spectra of the solids. For brevity, these six values are usually pointed out as the shielding tensor:

$$\begin{bmatrix} \sigma_{xx} & \sigma_{xy} & \sigma_{xz} \\ \sigma_{yx} & \sigma_{yy} & \sigma_{yz} \\ \sigma_{zx} & \sigma_{zy} & \sigma_{zz} \end{bmatrix} \quad (2)$$

that can be obtained by averaging the off-diagonal values of the complete tensor. The chemical shielding tensor is commonly referred to the chemical shift anisotropy (CSA) tensor according to the possession of second rank properties. Calculation of the diagonal components ($\sigma_{xx},\sigma_{yy},\sigma_{zz}$) or ($\sigma_{11},\sigma_{22},\sigma_{33}$) in the principle axis system allows the complete description of the CSA tensor The CSA tensor can also be explained by three additional parameters as following, a: The isotropic value (or trace portion of the CSA tensor) σ_{iso}, of the shielding tensor which is defined as $\sigma_{iso}=0.33(\sigma_{11}+\sigma_{22}+\sigma_{33})$; b: The anisotropy ($\Delta\sigma$) of the tensor, due to the following expression: $\Delta\sigma= \sigma_{33} - 0.5(\sigma_{11}+\sigma_{22})$; c: The shielding tensor asymmetry parameter (η):

$$\eta = \frac{|\sigma_{22}-\sigma_{11}|}{|\sigma_{33}-\sigma_{iso}|} \quad (3)$$

RESULTS AND DISCUSSION

Molecular Geometry

Fig. 1, Shows the graphical representations of the optimized geometry of drug–SWCNT. In the figure, the Cl atoms are shown by green colors, white spheres are H atoms, blue sphere is N atoms and gray sphere is C. Selected geometrical parameters for Clonidine drug SWCNT are also shown in Fig.1.

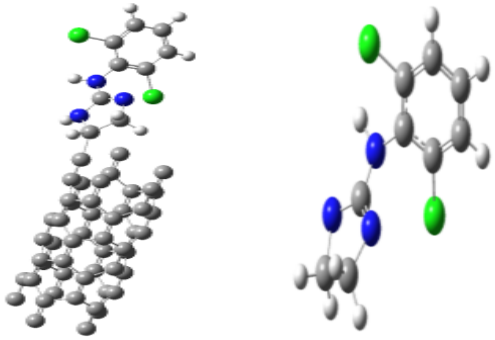

Fig.1. Optimized geometries of Clonidine and Clonidine drug-SWCNT obtained at HF/6-31G level.

Nuclear Magnetic Resonance Parameters

NMR spectroscopy is a research technique that exploits the magnetic properties of certain atomic nuclei to determine physical and chemical properties of atoms or the molecules in which they are contained. It relies on the phenomenon of nuclear magnetic resonance and can provide detailed information about the structure, dynamics, reaction state, and chemical environment of molecules. Ab initio

calculation of nuclear magnetic shielding has become an aid in the analysis of molecular structure and accurate assignment of NMR spectra of compounds. So, NMR is based on the quantum mechanical property of nuclei. The chemical shielding refers to the phenomenon, which is associated with the secondary magnetic field created by the induced motions of the electrons that surrounding the nuclei when in the presence of an applied magnetic field.

In the present paper, total dipole moments of drug interaction with SWCNT in gas phase have been explored and NMR computations were done by Gaussian 09 suite of programs. The calculated magnetic shielding tensor (σ ,ppm),magnetic shielding anisotropy (Δσ, ppm), shielding asymmetry (η) and the chemical shift tensor (δ) calculated for C, H, N and Cl nuclei in the active site of Clonidine drugand for carbon atoms of the open end of a SWCNT system in gas phase are presented in Table 1. Also, the graphs of calculated isotropic magnetic shielding constants σ_{iso} (ppm), anisotropic magnetic shielding tensors σ_{aniso} (ppm), Chemical shifts δ (ppm) and shielding asymmetry (η) versus the number of atomic centers for selected atoms of drug-SWCNT system are displayed in Figs. 2a-c ,respectively.

Table1. Components of the magnetic shielding tensor (σ, ppm), magnetic shielding anisotropy (Δσ, ppm), shielding asymmetry (η) and the chemical shift tensor (δ) calculated for C, H, N and Cl nuclei in the active site of Clonidine drugand for carbon atoms of the open end of a SWCNT in gas phases at HF level with the 6-31G* basis set

Atoms	σ_{iso} σ_{aniso}	σ_{11} σ_{22} σ_{33}	$\Delta\sigma$ η δ	Atoms	σ_{iso} σ_{aniso}	σ_{11} σ_{22} σ_{33}	$\Delta\sigma$ η δ
41C	104.474	58.366	65.534	62N	241.9252	-109.6	241.925
	89.7976	106.8914	0.89		350.2511	107.0898	0.70
		148.1634	- 46.1082			240.6893	-188.9670
51C	61.7703	-29.22	112.31	63C	46.9402	-56.45	101.008
	165.8628	77.8861	0.64		170.7244	82.9864	0.30
		136.6438	-90.9893			114.2793	-103.3853
52C	75.3816	-20.75	-144.19	64N	177.681	128.82	-73.287
	204.3732	63.2723	0.77		113.7344	161.6631	0.50
		183.6229	108.2413			242.5571	64.8761
55C	59.63	-30.02	119.93	83H	25.8304	21.057	6.654
	169.6118	69.3270	0.78		9.2093	26.1681	0.85
		139.5873	-89.6545			30.2663	-4.7734
56C	71.3104	-16.07	-131.073	86H	29.7638	20.585	11.729
	176.14	69.9351	0.97		16.9981	31.1232	0.70
		160.0680	88.7576			37.5831	-9.1788
57Cl	814.559	662.79	-227.659	87H	26.5623	16.829	8.353
	402.4513	715.6539	0.21		15.3024	30.7270	0.14
		1065.2370	250.6780			32.1311	-9.7336
58Cl	835.1653	694.7	-210.705	88H	29.774	24.888	-7.329
	369.7232	746.3819	0.22		10.7943	28.7512	0.65
		1064.4186	229.2533			35.6825	5.9085
59N	207.198	167.72	-59.222	89H	28.8596	23.317	-8.314
	82.8595	203.2986	0.82		11.4076	28.5371	0. 89
		250.5780	43.3400			34.7246	5.8650
60C	152.866	116.08	51.613	90H	11.1004	22.0492	11.100
	71.1945	155.2430	0.87		15.2149	30.2780	0.89
		187.2748	-63.7857			37.2641	-7.8146
61C	147.6563	115.08	47.335				
	64.1307	148.6726	0.93				
		179.2135	-32.5732				

As was expected, the NMR shielding tensors of H, C, N, and Cl nuclei are drastically affected by the atom to which they are bonded and by the type of the bond to the neighboring atom. The results obtained give strong evidence that intermolecular interactions play a very important role in determining the H, C, N and Cl NMR chemical shielding tensors. Some systematic trends appeared from the analysis of the calculated values.

According to Fig.2a, it is obvious that one atom in drug-SWCNT system has maximumσ_{iso}value in compare to the other atoms of this structure and this value belongs to Cl58. Anisotropic chemical shielding is one of the other parameters that were checked in this work. From Figure 2b it has been found that the maximum value of σ_{aniso} in drug-SWCNT system is related to Cl57.

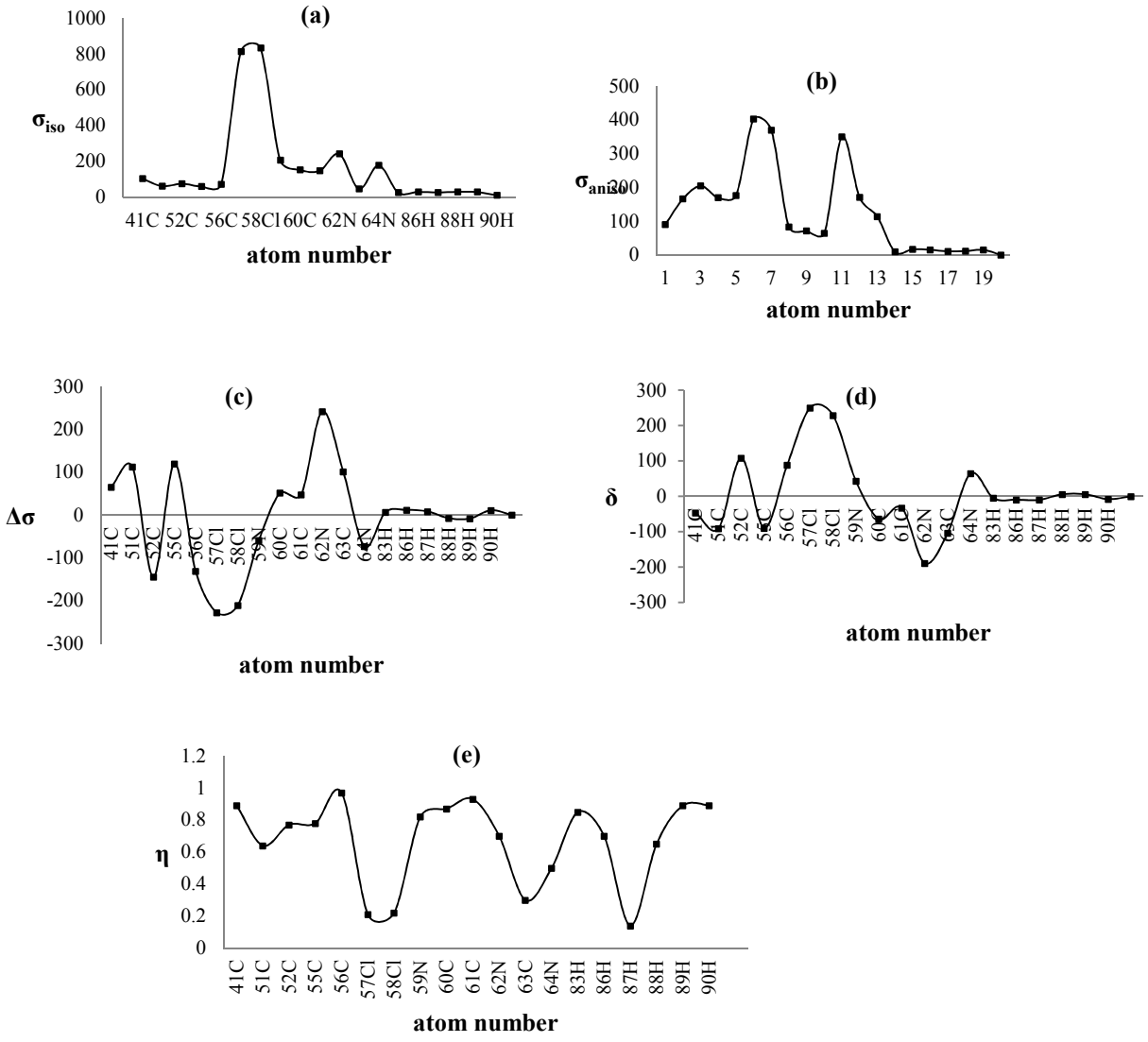

Fig. 2. The graphs of **a)**σ_{iso}, **b)**σ_{aniso} ,**c)** Δσ,**d)** δ and**e)** η (ppm) of propose atoms of drug binding to SWCNT in gas phase at HF/6-31G* basis set.

The maximum value of Δσhas been observed for N62 nuclei in drug-SWCNT system. The results of investigating chemical shift tensor indicate that Cl57 have been shown to be the largest value of (δ) in system as drug interacted with SWCNT and our knowledge about drug interacted to SWCNT has been specified that C number 56 show the largest intermolecular effects in (η) component(Fig. 2e).

HOMO, LUMO and HOMO- LUMO Gap Energies

Table 2 shows the values of HOMO, LUMO, HOMO–LUMO Gap energies for drug-SWCNTusing HF with 6-31G* basis set. Table 2 demonstrates that from HOMO–LUMO Gap calculation, it can be seen that HOMO- LUMO Gap energy of decrease in the order: Clonidine >Clonidine-SWCNT and by decreasing of HOMO- LUMO Gap energy, would bemore stablecompound. So, Clonidine beside SWCNT can act better as an electron donor and probably all of its biochemical and molecular functions can be accounted for by this function [38-41]. Also, the graphs of calculated HOMO, LUMO, HOMO–LUMO Gap energies for Clonidine and Clonidine-SWCNT system are displayed in Fig. 3.

Calculation of Binding Energies for Clonidine drug and Clonidine drug – SWCNT

Binding parameters such as binding energy, Enthalpy, Free Gibbs energy and Energy are calculated for Clonidine drug and Clonidine drug-SWCNT.The results are shown in table3. Results in table 3 indicate that energy and enthalpies values as well as free Gibbs energies obtained are negative, signifying that such interaction is favorable thermodynamically.

Table 2. HOMO, LUMO and Gap energies for Clonidine drug and Clonidine drug -SWCNT in gas phases at HF level with the 6-31G* basis set

System	HOMO energy(eV)	LUMO energy(eV)	Gap energy(eV)
Clonidine	-0.32028	0.11571	0.43599
Clonidine-SWCNT	-0.21780	0.03525	0.25305

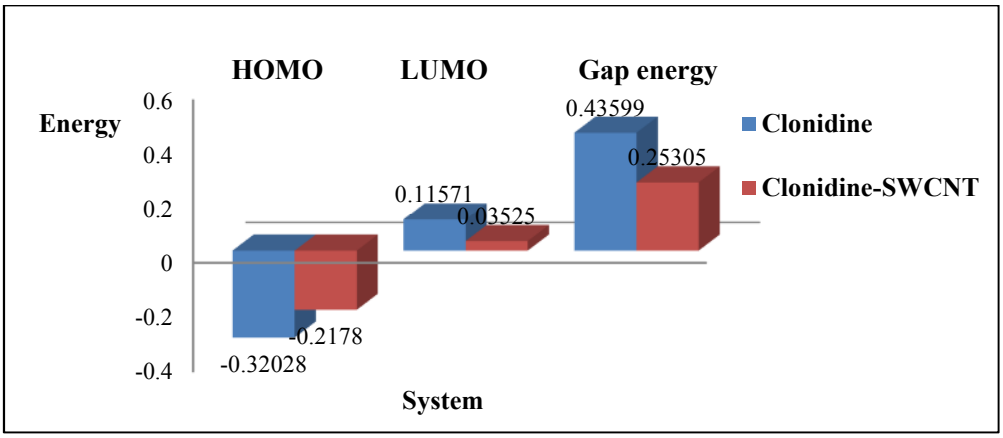

Fig. 3. The graphs of a) HOMO, b) LUMO, c) Gap energy for Clonidine drug and Clonidine drug -SWCNT in gas phases at HF / 6-31G* basis set.

Table 3. Binding energies for Clonidine drug and Clonidine drug -SWCNTin gas phases at HF level with the 6-31G* basis set

System	energy(J/mol)	Enthalpies(J/mol)	Free Gibbs Energies(J/mol)
Clonidine	-1428.890237	-1428.889293	-1428.937863
Clonidine-SWCNT	-2349.149574	-2349.148630	-2349.211260

CONCLUSION

In this study, interaction between some molecules and ionsand Si_5O_{10} cave have been investigated with density functional theory using HF method and 6-31G* basis set.

We analyze binding parameters and binding energies, HOMO, LUMO, HOMO- LUMO GAP energies, ΔE, ΔH and enthalpies ΔG are calculated. The obtained large negative values of the ΔG confirmed the structural stability of theClonidine drug and Clonidine drug -SWCNTin gas phase. From HOMO–LUMO Gap calculation, it can be seen that HOMO- LUMO Gap energy of decrease in the order: Clonidine >Clonidine-SWCNTand by decreasing of HOMO-LUMO Gap energy, would bemore stablecompound.

NMR chemical shielding tensors in the methods framework makes it possible to study the chemical shift of carbon nanotubes. The calculated parameters reveal that Cl57 and H83 atoms have the largest and smallest anisotropic magnetic shielding (σ_{aniso}) constants among the other nuclei, respectively.

The Cl57 has the largest but N62has the smallest chemical shift (δ) constants among the other atoms, respectively.The diagrams consist of σ_{iso}, σ_{aniso} and η showall shielding values but $\Delta\sigma$, δ show more negative shielding values at the HFin 6-31G* basis set.

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