Journal of Physical and Theoretical Chemistry
of Islamic Azad University of Iran, 10 (3) 153-160: Fall 2013
(J. Phys. Theor. Chem. IAU Iran)
ISSN 1735-2126

A Study on the Electronic and Structural Properties of C12X8 (X = C, B) and Their Interaction with Glycine with Potentially Drug Delivery Vessels

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Received February 2014; Accepted March 2014

ABSTRACT

In this paper, the structural properties of C_{20} and $C_{12}B_8$ fullerene interacting with glycine based on three active sites of glycine and one C atom or one B atom in $C_{12}B_8$ were analyzed through the density functional theory. It was found out that the binding of glycine to $C_{12}B_8$ generated a complex. Our results were extremely relevant in order to identify the potential applications of functionalized $C_{12}B_8$ as drug delivery systems. Glycine prefered to interact with the $C_{12}B_8$ cage via its carbonyl oxygen (B=O) active site. B atoms were relatively favored in energy over the C atoms in the $C_{12}B_8$ – glycine while the stable ordering of three active sites on glycine molecule was =O site> –O site> –N site.

Keywords: $C_{12}X_8$; glycine active site; DFT; HOMO-LUMO gap

INTRODUCTION

Long after the initial proposal by Osawa in 1970 [1], and the mass spectroscopic detection by Curl, Kroto, and Smalley in 1985 [2], the synthesis of a macroscopic quantity of fullerenes by Kra¨tschmer and Huffman in 1990 suddenly fueled the interest of experimentalists in fullerenes [3]. One of the future applications that came immediately to mind was their potential use in biology.

Then a variety of biocompatible fullerene-related materials have been widely considered in nanotechnology [4] and biomedical fields [5, 6].

Up to now much interest in their applications in electronics, materials science, chemistry and biochemistry as well as their unique physical properties such as electrical conductance, ferroelectricity, nonlinear optical properties, and so forth had been noted [7, 8] that could revolutionize industries. Substitutional doping fullerenes in which one or more carbon atoms replaced by heteroatoms like nitrogen, boron, germanium, and silicon, have been the subject of numerous experimental and theoretical investigations [9 - 13] opening a new window into the field of multicomponent systems.

Nitrogen- and boron-doped fullerenes were special important. Since B-doped fullerenes behave as positive hole carriers and N-doped fullerenes act as electron

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carriers. For example, Chen et al. further studied heterofullerene structures $C_{60-n}N_n$ for n =2, 4, 6 and 8 using MNDO, AM1, PM3, and the Hartee-Fock method.

Manaa [10] and Bryant et al. [11] have studied the structural stabilities of $C_{48}N_{12}$. Jindal et al. [12] reported the results of ab initio calculations of structural, electronic and, vibrational properties for nitrogen-doped fullerenes $C_{60-n}N_n$, n= 1-12.

Beside C_{60}, the smallest possible fullerene cage, i.e., C_{20} with 12 pentagons and no hexagons [14], can be doped with these methods. C_{20} is somehow different from C_{60} because of its extreme curvature and reactivity. This curvature leads to a higher ratio of sp^3 to sp2 bonding. Theoretical analysis shows that there are two kinds of carbon atoms in C_{20}. Atoms with the coordination number 4 (12 atoms) are sp3 hybridized, but is very distorted compared to the ideal sp3 hybridization in diamond. Atoms with coordination number 3 (8 atoms) are sp^2 hybridized.

The ideal goal of substitutional doping of fullerene cage is to improve its characteristics for special purposes while keeping its structural stability. In one of our previous work we were focusing our calculations on $C_{12}X_8$heterofullerenes where X = B, Al, Ga, C, Si, Ge, N, P, and As.

Results from molecular dynamics simulation, showed that it is dynamically stable up to 1000 K [15]. Tian et al [16] theoretically found that $C_{12}N_8$ is dynamically stable at ambient pressure.

Experimental studies demonstrate that the functionalization of C_{60} amino acids has the potential to provide greater interaction between the fullerene and a biological environment which is leading to novel medical applications [17, 18]. This has had further implications in the synthesis and biological activity of fullerene-containing bio molecules [19-22].

There are some theoretical studies using DFT and semi-empirical (AM1) methods about C_{60}-glycine [23-25] and C_{59}B-glycine [26] and the applications in their biological affinity have been experimentally observed.

However the need for further study was crucial and relevant. The focus of the current research investigation was on the interaction of $C_{12}X_8$ (X = C and B) with amino acid species. Fullerene-functionalized derivatives were used in pharmacology. For example in neuroprotective effect, HIV-protease inhibitors [27] and antioxidant [28].

Bio molecules delivery introduces several chemical and biochemical problems concerning the interactions between the bio molecules and the fullerene or nanostructure. There were numerous studies on this problem, either experimental [29] or theoretical [30] Jiang and Zheng [31], in 2005, synthesized thefullerene-glycine derivative which displaysbetter antitumour activity in vitro against bone tumorcells.

These previous works allow us to make the assertion that fullerenes should interact with amino acids and act as potential drug delivery vessels.

The present study aims to investigate the stable binding sites between the C_{20} fullerene and $C_{12}B_8$ heterofullerenes (here after named as $C_{12}X_8$ (X=C, B)) with glycine based on three active sites of glycine and one X atom in $C_{12}X_8$ (X=C, B) (shown in Fig. 1 for C_{20}, $C_{12}B_8$ and glycine). The C_{20} cage, which consists solely by pentagons, is the smallest and unconventional fullerene [32–34]; it might generate the larger vibronic coupling than C_{60} cage. In the continuation of our interest in fullerene chemistry, it was very interesting for us to explore more detailed insights into the structural, and electronic properties of the interacting molecules with the aid of quantum chemical calculations.

COMPUTATIONAL METHODS

It is well known that a glycine molecule has three active sites, the amino nitrogen (N), the hydroxyl oxygen (OH) and the carbonyl oxygen (O) sites. The $C_{12}X_8$ (X=C, B) has two active sites, being C atom and B atom. As shown in Figure 2, six $C_{12}X_8$ – glycine conformers, weregenerated from the $C_{12}X_8$ cage and glycine at different binding sites. Full geometry optimizations were accomplished by means of hybrid functional B3LYP and the 6-31+G* basis set, as implemented in Gaussian 98 [35]. DFT methods were generally flawed when discussing dispersion forces, the methods employed appear to partially account for this. The strength of the dispersion forces for simple van der Waals complexes were adequately computed by the B3LYP method. The applied basis set was composed of Pople's well-known 6-31G* basis set and an extra plus due to the importance of diffuse functions.

This value was a measure of the stability of the complex however our calculations show that as this value increases entropy values decrease as a result of increased affinity for the fullerene surfaces.

Vibrational frequencies were calculated for $C_{12}B_8$ to establish the nature of stationary points as true minima. If the vibrational frequencies were positive then the structures calculated were minimum structures.

RESULTS AND DISCUSSION

The smallest fullerene that satisfies Euler's theorem is C_{20}. It is highly strained due to the extreme pyramidalization of the C=C double bonds. Cao et al. studied the stable binding sites between the C_{20} fullerene and glycine based on three active sites of glycine and an active top site and plane for C_{20}. Furthermore they considered and explored endohedral metallo fullerenes Gd@C_{20} – glycine [36].

Since The Gd@C_{20}-glycine is also carried out as a hypothetical system, not available, our interesting was exploration the structures, stabilities, and electronic properties of $C_{12}B_8$-glycine with the aid of quantum chemical calculations. Although proteins are much more complicated than glycine, however, all proteins contain amino nitrogen (–N), hydroxyl oxygen (–O), and carbonyl oxygen (=O) active sites. The equilibrium geometries for the C_{20}, $C_{12}B_8$ and isolated glycine molecule were as shown in Figure1. Therefore, from the calculation results involving in this paper, one can predict that proteins might form bindings with C_{20}. The calculated harmonic vibrational frequencies at B3LYP/6-31+G* level confirm that the optimized $C_{12}B_8$ and all of the complexes were true minima (NIMAG = 0).

All C–B bonds of $C_{12}B_8$ showed the similar length of 1.588 Å. The C–B bond lengths of $C_{12}B_8$ systems are quite close to the sum of covalent radii of C and B atoms. The covalent radius of B is about 0.84 Å. C–B–C angles were narrower than normal 120.0 (in a range of 104.8–109.2). C=C double bonds were expectedly shorter than those of C_{20} (1.394 vs. 1.445 Å, Table 1).

The binding energy of $C_{12}B_8$ was 5.82 eV/atom which was not so far from that of C_{20} (6.34 eV/atom). Accordingly, the computed υ_{min} of $C_{12}B_8$ was 317 cm^{-1} which was noticeably high (compare to 32 cm^{-1} of C_{20}).The fullerene used initially had *Ci* symmetry but upon complexation it became slightly distorted. For stable complexes, the N – C bond length of glycine was lengthened from 1.447 Å to 1.460 A°. As well at the same time, the C=O and C–O bond lengths slightly increase, 0.02 Å. It means the binding between glycine and $C_{12}X_8$ also changed the structure of glycine.

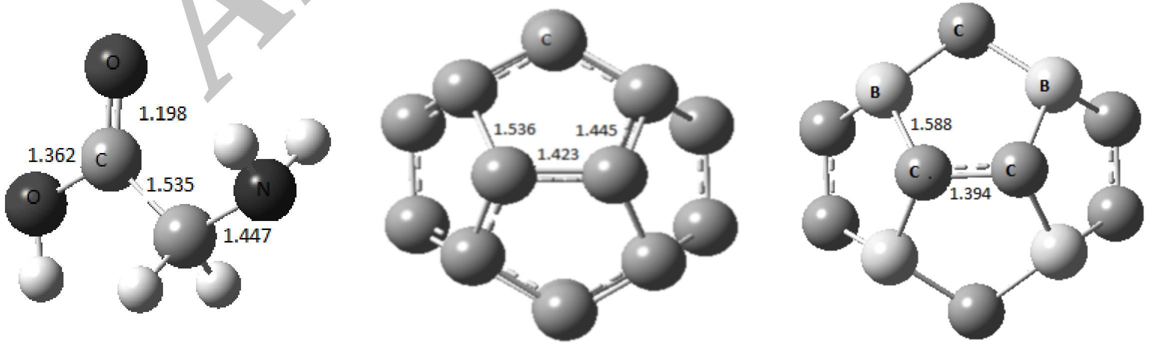
As shown earlier, glycine and $C_{12}X_8$ can form complexes by forming a new bond by breaking one of the original bonds of glycine. The new bond formation can increase the stability of the complexes, whereas the breaking of the original bond of glycine can decrease their stability. To evaluate the stability of $C_{12}X_8$– glycine complexes, we calculated the energy of formation of a complex between the glycine and $C_{12}X_8$ molecules (glycine + $C_{12}X_8$ = $C_{12}X_8$ – glycine), by using the equation:

$$E_b = E_{gly-\,C12X8} - E_{gly} - E_{\,C12X8} \qquad (1)$$

where E_{gly}, $E_{\,C12X8}$ and $E_{gly-\,C12X8}$ were the energy values of glycine, $C_{12}X_8$ and glycine– $C_{12}X_8$ complex, respectively. The results were listed as shown in Table 1. A negative E_b shows a thermodynamic stability; and the more negative the value of E_b, the more stables the complex. One can see that the formations of all six complexes were endothermic by 4.06 to 22.00 eV. This indicates that the binding of glycine to $C_{12}B_8$ was slightly unstable via its carbonyl oxygen (=O) sites and strongly unstable via its hydroxyl oxygen (–O) and amino nitrogen (–N) sites. Glycine prefered to interact with the $C_{12}B_8$ cage via its carbonyl oxygen (=O) active site, which was similar to the previous study of $C_{59}B$ – glycine [26] but disagrees with the C_{60}-glycine, [27] and C_{20}-glycine with the amino nitrogen (–N) active site [36]. Among two types of active atoms on the $C_{12}B_8$, it was easy to see that the B atoms were relatively favored in energy over the C atoms in the $C_{12}B_8$ – glycine while the stable ordering of three active sites on glycine molecule was =O site> –O site> –N site.

Table 1. Binding energies (E_b in eV) and ranges of carbon–carbon, C – B and C–X bond lengths (Å), for the $C_{12}X_8$ – glycine at the B3LYP/6-31+G* level

Species	E_b	C=C	C–B	C–X	B–X
C12B8–Gly(C=O)	4.28	1.395	1/654	1/572	-
C12B8–Gly(C–O)	22.00	1/398	1/582	1/439	-
C12B8–Gly(C–N)	21.36	1/397	1/559	1/396	-
C12B8–Gly(B=O)	4.06	1/394	1/640	-	1/546
C12B8–Gly(B–O)	20.28	1/388	1/567	-	1/373
C12B8–Gly(B–N)	19.99	1/390	1/598	-	1/389

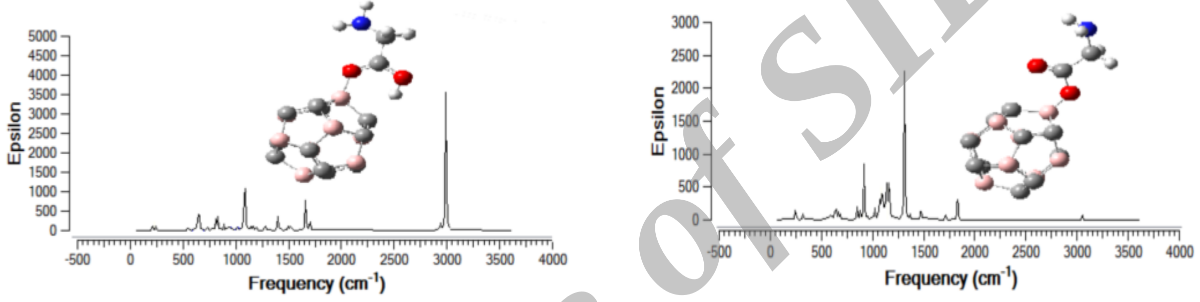


a b c

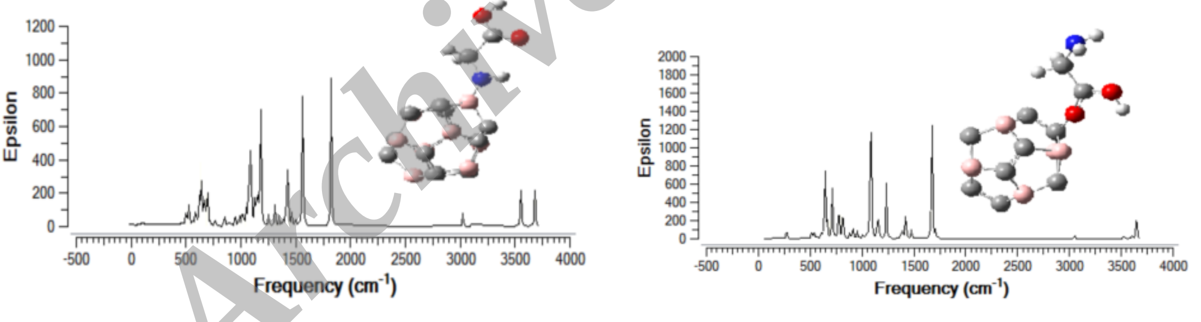
Fig. 1. Optimized structures of (a) glycine molecule (b) C20fullerene and (c) $C_{12}B_8$ heterofullerene obtained at the B3LYP/6-31+G*level of theory.

The lowest vibrational frequencies of $C_{12}B_8$ –glycine (B=O), being 9.32 cm^{-1}, involve mainly the wagging vibration of glycine backbone. The strongest band is found at 3299 cm^{-1}, which arise from the hydroxyl O–H stretching vibration. In order to further provide the distinctive spectroscopic fingerprints of our complexes, their calculated IR spectra were depicted in Fig. 2.

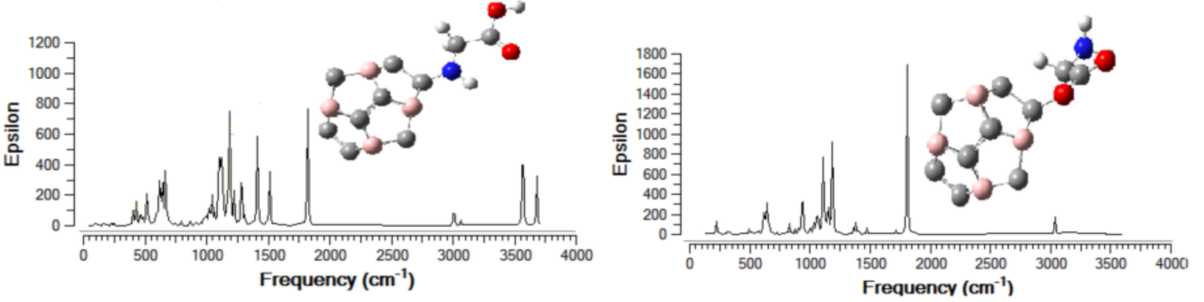
It worth to mentioned the HOMO – LUMO energy gap, (highest occupied molecular orbital (HOMO) - lowest unoccupied molecular orbital (LUMO), because it can be associated with the optical and electrochemical properties of complexes. The electrons donated by a molecule in a reaction should be from its highest occupied molecular orbital (HOMO), while the electrons captured by the molecule should be located on its lowest unoccupied molecular orbital (LUMO). Furthermore, the atom, on which the HOMO mainly distributes, should have the ability for detaching electrons, whereas the atom with the occupation of the LUMO



C12B8–B=O C12B8–B–O



C12B8–C=O C12B8–B–N



C12B8–C–O C12B8–C–N

Fig. 2. The calculated IR spectra and optimized structures of C12X8–gly at B3LYP/6-31+G*.

Table 2. the smallest vibrational frequencies (υmin), the number of imaginary frequencies (NIMAG), $\Delta E_{HOMO-LUMO}$, (eV)and $\Delta E_{reaction}$ for $C_{12}X_8$–gly at B3LYP/6-31+G*

System	υ_{min}	NIMAG	$\Delta E_{HOMO-LUMO}$ (eV)	$\Delta E_{reaction}$ (kcal/mol)
$C_{12}B_8$-Gly-C=O	23.69	0	2.76	-64.48
$C_{12}B_8$-Gly-C–O	27.97	0	1.86	-62.60
$C_{12}B_8$-Gly-C–N	24.89	0	1.86	-59.62
$C_{12}B_8$-Gly-B=O	9.32	0	2.71	-65.35
$C_{12}B_8$-Gly-B–O	18.44	0	2.91	-63.09
$C_{12}B_8$-Gly-B–N	13.84	0	2.86	-63.94

should gain electrons. The HOMO–LUMO gap is traditionally associated with chemical stability against electronic excitation, with larger gap corresponding to greater stability. The gap of $C_{12}B_8$ is calculated for comparison with the results of gap of complexes.

The energy gap of hollow $C_{12}B_8$ cage was 2.86 eV. As a result, the $C_{12}B_8$ – glycine (C–O) and $C_{12}B_8$-glycine (C–N) were 1.86eV, being smaller than that of $C_{12}B_8$ cage. The HOMO– LUMO gaps of $C_{12}B_8$ – glycine (C=O), $C_{12}B_8$ – glycine (B=O), $C_{12}B_8$ – glycine (B–O) and $C_{12}B_8$ – glycine (B–N) were 2.76, 2.71, 2.91 and 2.86 eV respectively. The results are shown in table 2. Molecular high-kinetic stability can be represented by a large HOMO – LUMO gap, because the molecule with large gap was unfavorable in energy to extract electrons from a low-lying HOMO orbital or to add electrons to a high-lying LUMO orbital; so it was relatively hard to form an activated compound.

CONCLUSION

We studied the interaction of the $C_{12}B_8$ fullerene with the smallest amino acid, glycine, by means of density-functional theory calculation. Six $C_{12}B_8$-glycine conformations, generated from the C12B8 cage and glycine at different active sites, were considered to be further explored. Glycine prefered to interact with the $C_{12}B_8$ cage via its carbonyl oxygen (=O) active site. The $C_{12}B_8$-glycine (C–O) and $C_{12}B_8$-glycine (C–N) were 1.86 eV, being smaller than that of $C_{12}B_8$ cage. The HOMO – LUMO gaps of $C_{12}B_8$ – glycine (C=O), $C_{12}B_8$ – glycine (B=O), $C_{12}B_8$ – glycine (B–O) and $C_{12}B_8$ – glycine (B–N) are 2.76, 2.71, 2.91 and 2.86 eV respectively so $C_{12}B_8$ – glycine (B–O) had the more molecular kinetic stability.

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