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Complexes of a bio-molecule and a C_{60} cage

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Abstract

C_{60} is the most important fullerene cage and glycine is the simplest representative of a backbone unit of a protein. In this paper, the structures and the energies of glycine–C_{60} complexes were calculated at the B3LYP/6-31G(d) level DFT. It was found that the binding of glycine to C_{60} generated a slightly unstable complex via its amino nitrogen, a moderately unstable complex via its hydroxyl oxygen, and a very unstable complex via its carbonyl oxygen. This indicates that fullerene cages might be unable to form stable bindings to proteins via their amino nitrogen, hydroxyl oxygen and carbonyl oxygen active sites.

Keywords: Fullerene cage; Glycine; C_{60}; Amino acid; Density functional theory

1. Introduction

Fullerenes, the hollow carbon cages discovered in 1985 [1], have fascinated scientists. The most prominent representative of the fullerene class is C_{60}, which is the most abundant cluster in the solvent-extracted carbon soot and the smallest fullerene that satisfies the isolated pentagon rule. Since macroscopic samples of C_{60} became available in 1990 [2], many applications [3,4] have been suggested, particularly in the bio-area [5]. This class of compounds can be active as HIV-protease inhibitors [6], as antibacterial [7] and neuroprotective agents [8], and can also induce the photocleavage of DNA [9,10]. Proteins account for more than 50% of the dry weight of most cells, and they are instrumental in almost everything that the organism does. Information about how the fullerene cage chemically interacts with proteins is important for its applications to the bio-area. However, to the best of our knowledge, no such information is available. Glycine is the simplest of the 20 common amino acids and is often chosen as the simplest representative of a backbone unit of a protein. Therefore, glycine–C_{60} complex can be chosen as a model for studying the chemical interaction between a protein and a fullerene nano-cage. Furthermore, glycine (or other amino acid)–fullerene derivatives are of special interest as biologically active compounds [11–17], and several methods have been developed for the synthesis of C_{60} amino acid derivatives [11–17]. It was reported that glycine can directly react with C_{60} via its amino group in the presence of sodium hydroxide [16]. Very recently, by using semi-empirical (AM1) quantum chemical calculations, Messaouda et al. carried out interesting theoretical work regarding C_{60} $(Glycine)_n$ ($n = 1$–4) complexes formed via the amino nitrogen atom [18]. Their calculations showed that the addition of glycine to C_{60} via the amino group leads preferentially to structures in which the proton of the glycine is transferred to C_{60} with an energy gain (free energy of −27.5 kJ/mol). Furthermore, they found that, from a thermodynamic point of view, a bis-adduct C_{60} $(Glycine)_2$ forms easier than a mono-adduct.

Although semi-empirical quantum chemical calculations are widely applied to large molecules, the fullerene-based compounds are still challenging molecules for high-level quantum chemical calculations because of their sizes. The

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steep increase in the computational cost with the molecular size has prohibited the use of the most sophisticated ab initio methods for ordinary fullerenes. However, major progress has been achieved in the last few years towards the ab initio calculations for large molecular systems [19–23] by using the Hartree–Fock (HF) and the density functional theory (DFT), which are the least expensive ab initio methods. DFT is the method of choice for large clusters because it accounts for the electron correlation at an affordable computational cost, and this increases the accuracy of energy calculations. Furthermore, it was found that a major improvement over the standard DFT can be achieved by combining HF and DFT, leading to the so-called self-consistent hybrid (SCH) approaches. The B3LYP model, which is a combination of HF with DFT that is based on Becke's three-parameter exchange coupled with the Lee–Yang–Parr (LYP) correlation potential [24], is one of the most popular hybrid density functional methods. Furthermore, some studies have shown that the molecular structures and vibrational frequencies calculated by DFT methods are even more reliable than those provided by the MP2 method [25–27].

In this paper, we employed the B3LYP hybrid DFT method with the basis set superposition error (BSSE) correction to calculate the structure and the energy of the glycine–C_{60} complexes. The interactions between C_{60} and glycine were obtained for three active sites of glycine: the amino nitrogen (N), the hydroxyl oxygen (O), and the carbonyl oxygen (O) sites.

2. Calculation details

B3LYP has been proven to be a good method for the prediction of the fullerene structures [28]. In this work, the complexes formed between glycine and C_{60} were first calculated using semi-empirical AM1 method for preliminary geometry optimizations. The harmonic vibrational frequencies calculated at AM1 theory level were employed to confirm that the AM1-optimized geometries correspond to local minima on the potential energy surfaces. Then, the AM1-optimized geometries were subjected to further geometry optimizations and energy calculations by using the B3LYP method with the 6-31G(d) basis set. Furthermore, the basis set superposition error (BSSE), which is caused by the fact that the practical quantum chemical calculations are restricted to the use of finite basis sets, was taken into account for the complexes via the Boys–Bernardi counterpoise (CP) procedure. All calculations have been carried out using the Gaussian 03 program [29].

3. Results and discussion

3.1. Structures of glycine–C_{60} complexes

The structure of C_{60} has widely been examined theoretically using quantum chemical calculations [28,30–36]. All of these calculations have revealed that the C_{60} cluster has a unique icosahedral structure, consisting of only 5- and 6-membered rings, in which all the atoms are equivalent, with short-bonds between the 6- and 6-membered rings and longer-bonds between the 5- and 6-membered rings. The structure of C_{60} obtained (Fig. 1a) is consistent with the literature [28,30–36], and the prediction of bond lengths (1.4534 Å for single bond and 1.3955 Å for double bond) is in excellent agreement with the experimental values (1.458 and 1.401 Å, respectively) [37–39]. As the simplest representative of a backbone unit in a protein, glycine has been widely studied [40,41]. Its most stable structure, which we obtained using B3LYP/6-31G(d), is presented in Fig. 1b. The geometric parameters of this structure are consistent with the literature [40,41]. Furthermore, it is well known that a glycine molecule has three active sites, the amino nitrogen (N), the hydroxyl oxygen (O) and the carbonyl oxygen (O) sites. Therefore, it is

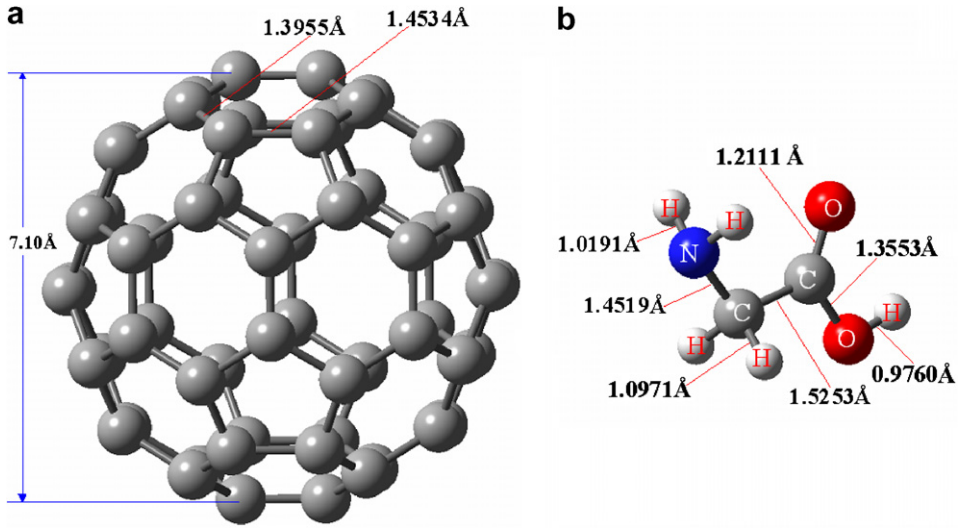

Fig. 1. (a) C_{60} fullerene cage and (b) glycine.

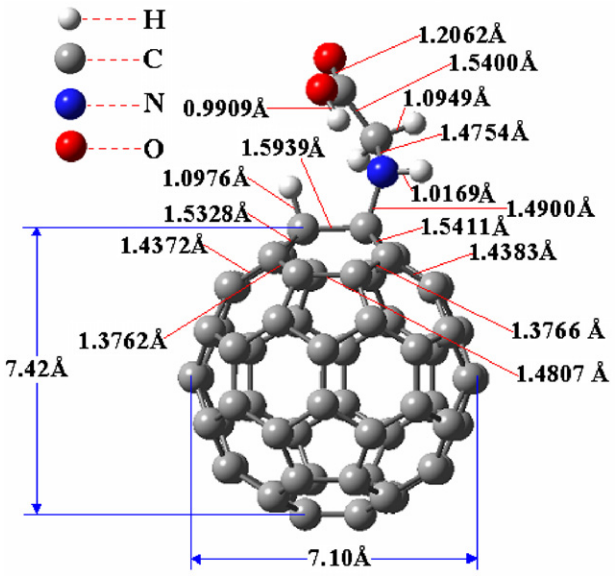

Fig. 2. Glycine–C_{60} complex via the amino nitrogen connection.

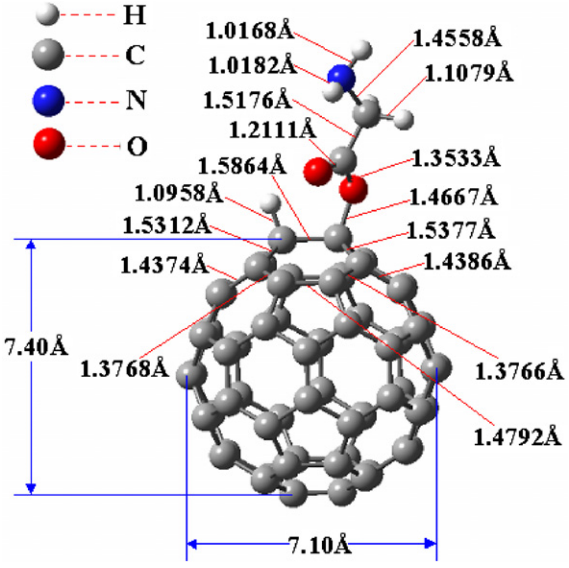

Fig. 3. Glycine–C_{60} complex via the hydroxyl oxygen connection.

expected for glycine to interact with the C_{60} cage via these three active sites.

As shown in Fig. 2, when glycine was attached to the C_{60} cage via the amino nitrogen (N), the H—N bond of glycine was broken and two new bonds between glycine and C_{60}, namely H—C (1.0976 Å) and N—C (1.4900 Å), were formed. Furthermore, the length of the C=C bond, which was saturated with the H and N of glycine, changed from 1.3955 to 1.5939 Å, indicating that the C=C double bond was transformed into a C—C single bond. Furthermore, the lengths of the other C—C single bonds, which are connected to those two C atoms that bind to H and N of glycine, also became longer (increasing from 1.4534 to about 1.54 Å). As a result, the spherical C_{60} cage acquires an oval shape with a length of 7.42 Å and a width of 7.1 Å. On the other hand, the binding between glycine and C_{60} also changes the structure of glycine. The lengths of the N—C and C—C bonds of glycine become longer (increasing from 1.4519 to 1.4754 Å and from 1.5253 to 1.5400 Å, respectively).

When the hydroxyl oxygen (O) site of glycine was attached to the C_{60} cage, the H—O bond of glycine was broken and two new bonds between glycine and C_{60}, H—C (1.0958 Å) and O—C (1.4667 Å), were formed (Fig. 3). The original C=C double bonds of the C_{60} cage that was saturated with the H and O of glycine was transformed to a C—C single bond with a length-increase from 1.3955 to 1.5864 Å. Furthermore, the saturation of the C=C double bond with H and O affected its neighboring C—C single bonds, leading to changes in their bond lengths from 1.4534 to about 1.53 Å. Consequently, the C_{60} cage was transformed from a spherical to an oval shape with a length of 7.40 Å and a width of 7.1 Å. The bond lengths of glycine exhibit only small changes during its binding to the C_{60} cage.

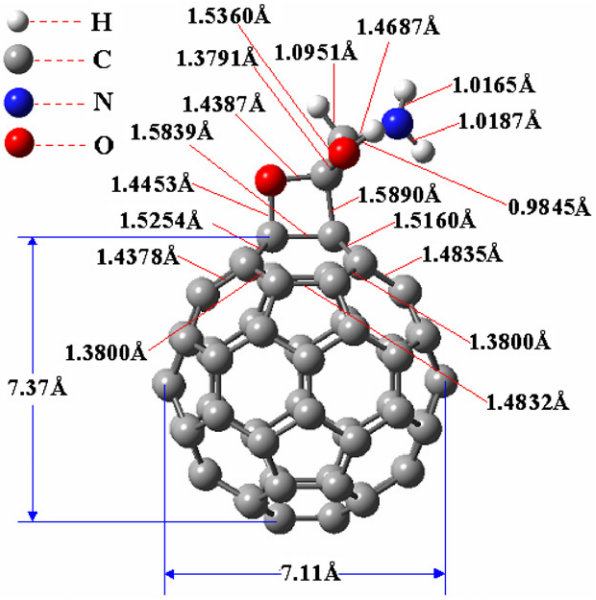

Fig. 4. Glycine–C_{60} complex via the carbonyl oxygen connection.

As shown in Fig. 4, when glycine was attached to the C_{60} cage via the carbonyl oxygen (O), two new bonds between glycine and C_{60}, O—C (1.4453 Å) and C—C (1.5890 Å), were formed, which generated a 4-membered ring. The length of the C=C double bond, which was saturated with O and C of the glycine, increased from 1.3955 to 1.5839 Å, indicating that the C=C double bond was transformed into a C—C single bond. Furthermore, the lengths of the other C—C single bonds, connected to those two C atoms saturated by the O and C of glycine, also became much longer (from 1.4534 to about 1.52 Å). As a result, the spherical C_{60} cage acquired an oval shape with a length of 7.37 Å and a width of 7.11 Å. Furthermore, the binding between glycine and C_{60} also changed the structure of glycine.

Table 1
Formation energies of glycine–C_{60} complexes

Connection type	Energy (Hartree)[d]			Formation energy[e] (kcal/mol) ΔE
	Glycine E_{gly}	C_{60} $E_{C_{60}}$	Glycine–C_{60} $E_{gly-C_{60}}$	
Amino nitrogen (N)[a]	−284.4234	−2286.1743	−2570.5901	4.8
Hydroxyl oxygen (O)[b]	−284.4234	−2286.1743	−2570.5803	10.9
Carbonyl oxygen (O)[c]	−284.4234	−2286.1743	−2570.5383	37.3

[a] See Fig. 2.
[b] See Fig. 3.
[c] See Fig. 4.
[d] Obtained from B3LYP/6-31G(d) calculations with the BSSE correction.
[e] $\Delta E = E_{gly-C_{60}} - E_{gly} - E_{C_{60}}$.

The length of the O—C bond of the carbonyl group increased from 1.2111 to 1.4387 Å, and the C—O of the hydroxyl group changed from 1.3553 to 1.3791 Å. In addition, the C—C and C—N bonds increased from 1.5253 and 1.4519 Å to 1.5360 and 1.4687 Å, respectively.

3.2. Stabilities of glycine–C_{60} complexes

As shown above, glycine and C_{60} can form complexes by forming some new bonds and by breaking (or weakening) some of the original bonds of glycine and C_{60}. The new bond formation can increase the stability of the complexes, whereas the breaking or weakening of some of the original bonds of glycine and C_{60} can decrease their stability. To evaluate the stability of glycine–C_{60} complexes, we calculated the energy of formation of a complex between the glycine and C_{60} molecules (glycine + C_{60} = glycine–C_{60}), by using the equation:

$$\Delta E = E_{gly-C_{60}} - E_{gly} - E_{C_{60}}$$

where E_{gly}, $E_{C_{60}}$ and $E_{gly-C_{60}}$ are the energy values (obtained during the geometry optimization routine) of glycine, C_{60} and glycine–C_{60} complex, respectively. The results are listed in Table 1. One can see that the formation of all three complexes (via the amino nitrogen, the hydroxyl oxygen and carbonyl oxygen active sites) increases the energy of the system by 4.8, 10.9 and 37.3 kcal/mol, respectively. This indicates that the binding of glycine to C_{60} is slightly unstable via its amino nitrogen, moderately unstable via its hydroxyl oxygen, and very unstable via its carbonyl oxygen. However, Messaouda's results showed that the addition of a glycine on C_{60} via amino group leads to a stable complex [18]. This occurs because we used B3LYP/6-31G(d) DFT method for calculations, whereas Messaouda et al. carried out their calculations with a semi-empirical method (AM1).

Although real proteins are much more complicated than glycine, all proteins contain amino nitrogen (N), hydroxyl oxygen (O) and carbonyl oxygen (O) active sites. Therefore, from the calculation results involving glycine, one can predict that proteins might not readily form stable bindings with C_{60} via their amino nitrogen (N), hydroxyl oxygen (O) and carbonyl oxygen (O) active sites. In other words, the C_{60} cage may have no permanent effects on the protein structure and function. This is consistent with the experimental observation that C_{60} without functional groups seems not to be toxic [5,42].

4. Conclusions

Hybrid density functional theory (B3LYP/6-31G(d)) calculations showed that the binding of glycine to C_{60} generated unstable complexes with destabilization energies of 4.8, 10.9 and 37.3 kcal/mol via its amino nitrogen (N), hydroxyl oxygen (O) and carbonyl oxygen (O) active sites, respectively. Therefore, fullerene cages might be unable to form stable bindings to proteins via their active sites.

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