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First-principles **investigation of the interaction between endohedral metallo [60] fullerene with glycine amino acid**

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Abstract: Density Functional Theory (DFT) calculations were used to investigate the possibility of formation of complexes between glycine and Li-doped C60 (Li@C60) fullerene and compared with those of pure C60 fullerene. It has been shown that the binding of glycine to Li@C60 fullerene generated the most stable complexes via its carbonyl oxygen (O) active site, with binding energy of about -18.24 kcal/mol. Our first-principles calculation results reveal also that heavier alkali metal atoms such as K cause a weaker interaction between the glycine molecule and alkali metal-doped fullerenes in comparison with the lighter atoms, Li in this work. Thus, Li-doped fullerenes could be a promising material for drug delivery and energy storage.

Keywords: Fullerenes; Metallo-doped C60; Amino acid; Adsorption; DFT

Introduction

There has been a steady increase in interest over the past few years in the interaction of biomolecules with carbon-based nanostructures, especially C_{60} fullerene. This hybrid system at the junction of the biological regime and the nanomaterials world possesses features which makes it very attractive for a wide range of applications [1-3]. The graphene-based nanosystems are important in the study of drug delivery due to their stability from a chemical point of view.[4-8] It has been shown that this class of compounds can be active as HIV-protease inhibitors [9], as antibacterial [10] and neuroprotective agents [11], and can also induce the photocleavage of DNA [12, 13]. Proteins are the main component 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. 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, amino acid–fullerene derivatives are of special interest as biologically active compounds [14-20], and several methods have been developed for the synthesis of C_{60} amino acid derivatives [14-19]. It was reported that glycine can directly react with C_{60} via its amino group in the presence of sodium hydroxide [19]. Recently, by using semi-empirical (AM1) quantum chemical calculations, Messaouda et al. carried out theoretical work regarding C_{60} (Glycine) $_n$ (n = 1–4) complexes formed via the amino nitrogen atom [20]. They found that the binding of glycine to C_{60} generated a slightly stable complex via its amino nitrogen active site with a binding energy of about -27.5 kJ/mol. It has been shown by using the hybrid density functional theory (B3LYP/6-31G(d)) calculations [21] that fullerene cages might be unable to form stable bindings to proteins via their active sites. Endohedral fullerenes, on the other hand, because of their robust carbon cage and its large hollow interior represent a new class of technologically relevant composites as they incorporate possible metallic and fullerenelike properties [22]. Charge transfer from the metal (*M*) into the unoccupied carbon cage orbitals, which is fostered by the high electron affinity of the fullerenes [23], raises expectations for *M*@fullerenes to exhibit metallic properties.

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It's well-known that charge-transfer effects increases its affinity to other molecular species capable of forming stronger and more specific chemical interactions with other materials such as peptides [24-27]. More recently, the interaction between amino acids and Li@C_{60} fullerene has been investigated at the DFT-BLYP/DND level of theory [27]. The calculated results indicated that when metals are encapsulated in fullerenes the charge-transfer to the surface increases and leads to favorable interactions with biological species [27]. Despite of extensive investigation carried out by researcher (the interaction between all twenty amino acids and Li@C_{60} fullerene has been evaluated) the various active sites in both amino acids (e.g. three active site in Gly) and fullerene (six-member and five-member rings) has not been considered in this work. In the present work we investigate the possibility of formation of complex between glycine and Li@C_{60} and K@C_{60} fullerenes by means of Density Functional Theory (DFT) based calculations. The interactions between fullerenes and glycine were obtained for three active sites of glycine: the amino nitrogen (N), hydroxyl oxygen (O), and carbonyl oxygen (O) sites. In view of the problems with designing life sciences-related tools employing these nano-materials and the relatively easiness of performing computations using standard density functional theory based program packages the results presented in this paper provide experiments with instructive information, thus contributing to a joint experiment and theory study.

Computational methods

To simulate the interaction between glycine molecule and fullerenes theoretically, the first-principles approaches using numerical atomic orbitals as basis set have been implemented. We have performed *ab initio* calculations based on the generalized gradient approximation (GGA) with the Perdew–Burke–Ernzerhof (PBE) functional [28] in density functional theory and the standard norm-conserving Troullier–Martins pseudo-potentials [29]. We have used the SIESTA code which solves the standard Kohn–Sham equations and has been demonstrated to be very efficient for large atomic systems [30-32]. In this code, the Kohn–Sham orbitals are expanded using linear combination of numerical pseudoatomic orbitals for the valence electron wave functions. The calculations are done using a split-valence double-zeta plus polarization function (DZP) as basis set for all simulated atoms. The relaxed atomic structures of the considered systems were obtained by minimization of the total energy using Hellmann–Feynman forces including Pullay-like corrections. Structural optimizations were performed using the conjugate gradient algorithm until the residual forces were smaller than 0.02 eV/Å. All total energy calculations were done with a double-ζ plus polarization (DZP) basis set. From the well known expression for calculating the molecular adsorption binding energies, E_{b} are obtained for various cases of our study.

$$E_b = E_{\mathrm{ful}-Glyc} - E_{\mathrm{ful}} - E_{Glyc} \tag{1}$$

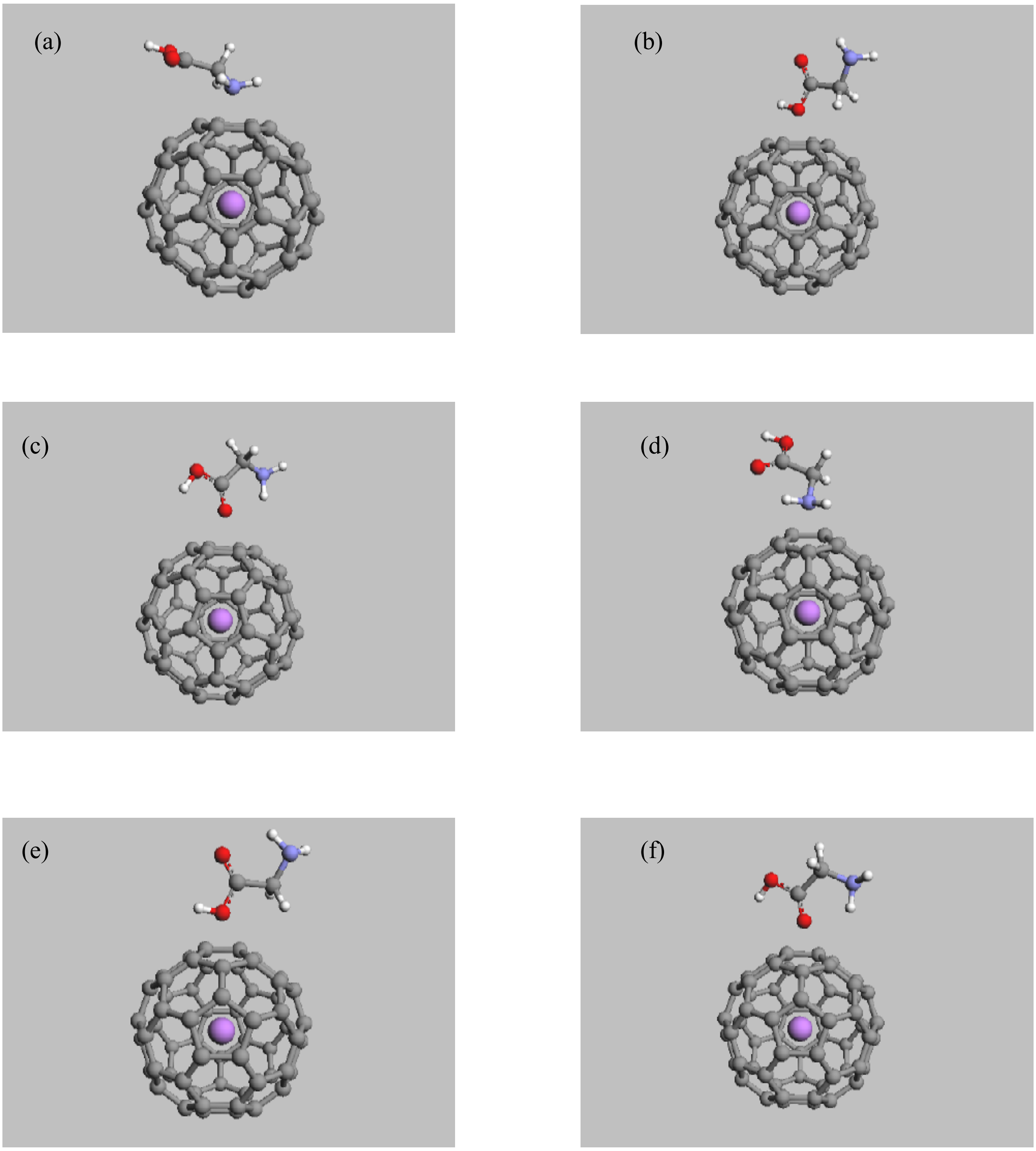
where $E_{\mathrm{ful}\text{-}Glyc}$ is the total energy of the fullerene with an adsorbed glycine molecule, E_{ful} is the total energy of the pure fullerene, and E_{Glyc} is the total energy of the isolated glycine molecule. It should be noted that the accuracy of our method has been evaluated in our previous works [33-36], hence reinforcing the reliability of theoretical method used in the present study.

Results and discussion

We first examine the interaction between a glycine molecule and Li doped fullerene. To evaluate the binding of a glycine to the Li@C_{60} fullerene cage, six possible configurations were selected for a molecule approaching the six- and five-member ring of the cage via its amino nitrogen (N), hydroxyl oxygen (OH) and carbonyl oxygen (O) active sites, as represented in figure 1 (a)-(f), respectively.

The interaction of the glycine molecule with the exterior wall of the fullerene was studied by performing single point energy (SPE) calculation for the several orientations of the axis of the molecule. The optimized Li@C_{60} fullerene and glycine molecule were used for the molecule adsorption. To find the approximate stable adsorption configuration, the structures of the cage and the glycine molecule were fixed, while the distance between the tube and the molecule was varied, to obtain the system energy as a function of the separation. The obtained results indicate that the adsorption energies are slightly dependent on orientations and locations of the glycine molecule, and the interaction becomes rapidly repulsive as the molecule approaches the fullerene side wall. It has also been found that glycine molecule prefers to be adsorbed on the hollow site above the center of hexagon via its carbonyl (O) active site.

Figure 1. Model for six different adsorption states for a glycine molecule on the sidewall of the Li-doped C_{60} fullerene on the six-member ring of the cage via its (a) amino nitrogen (N), (b) hydroxyl oxygen (OH) and (c) carbonyl oxygen (O) active sites. The similar orientations schemes were selected for the glycine molecule approaching to the five-member ring of the cage, as depicted in (d)-(f). Atom colors: grey—carbon, white—hydrogen, blue—nitrogen and red—oxygen.



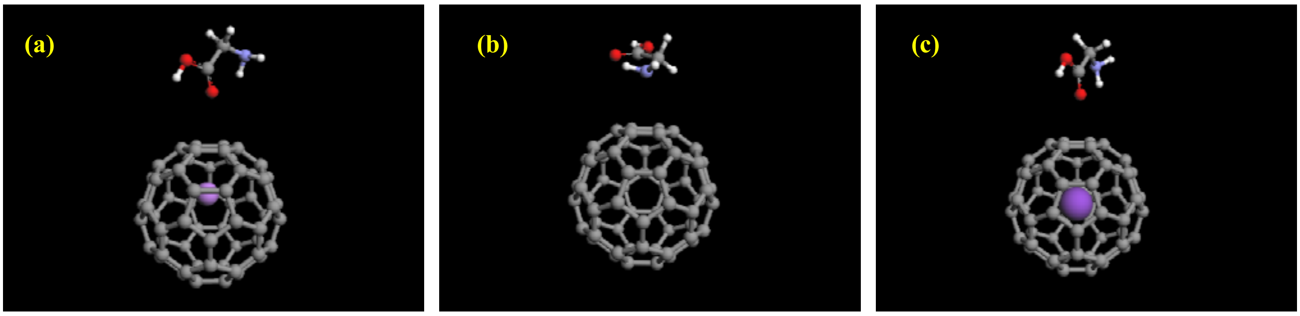
To further investigate the interaction between glycine and Li@C_{60} fullerene we carried out the full structural optimization of the most stable configuration. The obtained results show that the binding energy for the energetically most favorable configuration and the equilibrium distance between the closest atom between fullerene and glycine are about –0.79 eV (–18.24 kcal mol^{-1}) and 3.105 Å, respectively. Although our calculated binding energy is comparable with the DFT-BLYP/DND results of Jalbout [27] with binding energy of about –11.10 kcal mol^{-1} but the energetically most favorable configuration is however differs from their obtained result. It should be noted that in both study the Li atom moves towards the glycine molecule after full structural optimization of the complex, as depicted in figure 2 (a). Our first principles calculation results show also that the bond length of C–O in glycine changed to 1.210 Å, which is smaller than that in an isolated molecule (1.215 Å). The large distance of adsorbed glycine from the Li@C_{60} surface, the negative adsorption energy of −0.79 eV and the extension of C–O bond of the adsorbed glycine, all indicate weak interaction (physisorption) of glycine with the Li@C_{60} fullerene [37-40].

For comparison of the binding of glycine to the Li@C_{60} fullerene cage with the pure C_{60} cage we have also performed similar calculations for the possibility of formation of Gly–C_{60} complex. Six similar orientations were selected for the glycine molecule approaching the exterior surface of the C_{60} cage. The single point energy (SPE) calculations were performed for the several orientations of the axis of the molecule. The obtained results reveal that glycine molecule prefers to interact with the C_{60} cage via its amino nitrogen (N) active site on the hollow site of six-member ring of the C_{60} cage, consistence with both experimental observation [19] and theoretical results at B3LYP/6-31G(d) level of theory [22].

After full structural optimization of the energetically most favorable Gly–C_{60} complex we find that the binding energy and C–N equilibrium distance are about -0.27 eV (-6.38 kcal/mol) and 3.250 Å, respectively. The large distance of adsorbed molecule from the cage and the adsorption energy of -6.38 kcal/mol indicate a weak interaction of glycine with the C_{60} fullerene. The calculated binding energy and average C–N equilibrium distance are also comparable with those of amino acids and gas adsorption on CNTs [37-40]. The optimized geometric structures of the energetically most favorable Gly–C_{60} complex is represented in figure 2 (b).

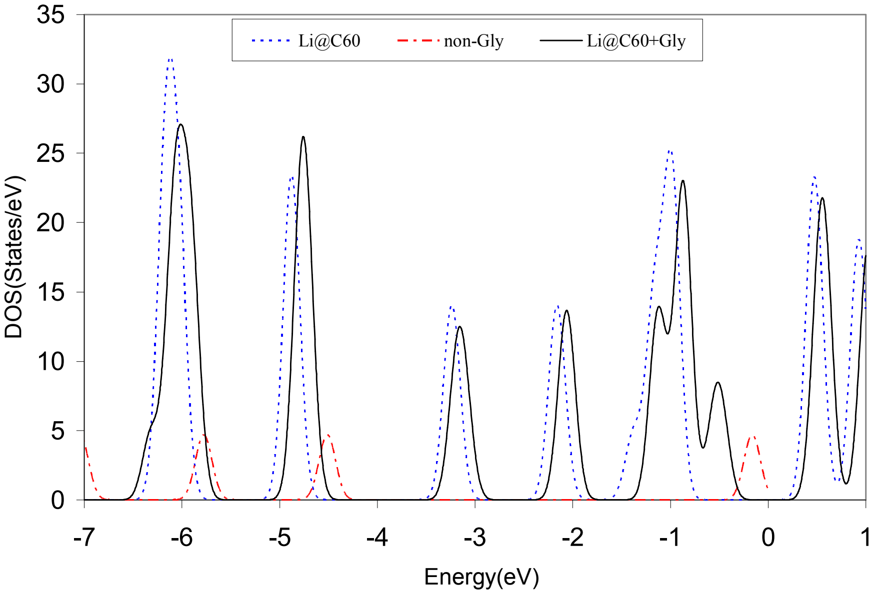
To further investigate the effect of incorporated alkali metals into the fullerenes on the adsorption properties of glycine amino acid, we also investigated the interaction between K doped C_{60} fullerene (K@C_{60}) and glycine molecule. The similar configurations and calculations procedures have been carried out for the glycine molecule approaching to the side-wall of the K@C_{60} fullerene. The SPE calculations reveal that glycine molecule prefers to be adsorbed on the exterior wall of the K@C_{60} fullerene on the hollow site of hexagon of the cage via its carbonyl (O) active site, similar to the Gly-Li@C_{60} system. The calculated binding energy and average C–N equilibrium distance of the fully optimized geometric structure of the most stable configuration are about -0.28 eV (-6.45 kcal/mol) and 2.941 Å, respectively. The optimized geometric structures of the energetically most favorable Gly–K@C_{60} complex is represented in figure 2 (c). These results indicate a weak interaction of glycine with the K@C_{60} fullerene. From the obtained results here one can conclude that larger alkali atoms doped into the C_{60} fullerene cause decrease in the interaction strength between fullerene and glycine amino acid.

Figure 2. Stable structures for the adsorption states for a glycine molecule interacting with the (a) Li@C60, (b) pure C60 and (c) K@C60 fullerenes.



Finally, we analyzed the density of states (DOS) for the combined system of Gly–Li@C_{60} and compared with the corresponding DOS for the individual parts, *i.e.*, Li@C_{60} and glycine molecule separated (figure 3). It can be seen from the figure that the DOS of the combined system of Gly–Li@C_{60} is almost exactly the superposition of the DOS of the individual parts. Our finding highlights that the glycine amino acid and Li@C_{60} are interacting rather weakly, and that no significant hybridization between the respective orbitals of the two entities takes place thus, unveiling the small interaction obtained quantitatively in terms of binding energies. We also performed Mulliken charge analyses to evaluate the amount of electron transfers between the Li@C_{60} and glycine molecule. Charge analysis shows 0.04 *e* charge transferred from the glycine molecule to the fullerene cage for Gly−Li@C_{60} complex (about 0.01 *e* for Gly−C_{60} complex). Mulliken analysis emphasizes that there exists a weak interaction between Li@C_{60} and glycine amino acid. Therefore, from the calculation results involving glycine, one can predict that glycine amino acid might form rather stable bindings with Li-doped C_{60} fullerene via their carbonyl oxygen (O) active sites.

Figure 3. Comparison between the density of states for (a) an isolated glycine molecule (Gly), an isolated Li@C_{60}, and the combination of the two at equilibrium geometry (Gly– Li@C_{60}).



Conclusions

Interaction between a glycine molecule and Li-doped C_{60} fullerene (Li@C_{60}) has been theoretically investigated and compared with those of pure C_{60} and K@C_{60} fullerenes by using the *ab initio* density functional theory (DFT) treatments. Six possible configurations were selected for a glycine molecule approaching the six-/five-member rings of carbon atoms of the cage via their amino nitrogen (N), hydroxyl oxygen (OH) and carbonyl oxygen (O) active sites. The obtained results showed that the binding of glycine to Li@C_{60} fullerene generated more stable complex with binding energies of -0.79 eV via its carbonyl oxygen (O) active site. The interaction between K@C_{60} and glycine amino acid is as strong as pure C_{60} and glycine with the binding energy of about -0.28 eV. The study of the electronic structure suggests a mixing between electron states of the Li@C_{60} and glycine molecule in adsorption. Furthermore, the adsorption resulted in charge transfers from the glycine molecule toward the Li@C_{60} cage.

As we know, all proteins contain amino nitrogen, hydroxyl oxygen and carbonyl oxygen active sites therefore, from the calculation results involving glycine, one can predict that Li@C_{60} fullerene cages might be able to form stable bindings to proteins via their carbonyl oxygen (O) active sites.

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