

NIH Public Access

Author Manuscript

J Comput Chem. Author manuscript; available in PMC 2013 February 15.

Published in final edited form as:

J Comput Chem. 2012 February 15; 33(5): 490–501. doi:10.1002/jcc.22881.

Interaction and Protection Mechanism between Li@C₆₀ and Nucleic Acid Bases (NABs): Performance of PM6-DH2 on Noncovalent Interaction of NABs-Li@C60

Wenming Sun,

The Center for Modeling & Simulation Chemistry, Institute of Theoretical Chemistry, Shandong University, Jinan, 250100, People's Republic of China

Yuxiang Bu^{*}, and

The Center for Modeling & Simulation Chemistry, Institute of Theoretical Chemistry, Shandong University, Jinan, 250100, People's Republic of China

Yixuan Wang^{*}

Department of Natural Science, Albany State University, Albany, Georgia 31705, United States of America

Abstract

To discuss the protection mechanism of DNA from radiation as well as assess the performance of PM6-DH2 on noncovalent interactions, the interaction of four nucleic acid bases (NABs) such as adenine (A), cytosine (C), guanine (G), and thymine (T), with Li@C₆₀ was extensively investigated with the-state-of-art theoretical methods describing non-covalent systems, like M06-2x, PBE-D, and PM6-DH2 methods. In the gas phase, the binding strength of NABs to $Li@C_{60}$ from M06-2x decreases in the sequence, G>C>A>T. As dispersion was explicitly included, PBE-D relatively enhances the binding of A and T and corrects the sequence to, G>A>C~T. PM6-DH2 predicted similar binding energies to those from PBE-D within 0.5kcal/mol and the same binding sequence, suggesting that the PM6-DH2 method is promising for nano-scale systems. In the aqueous solution, binding of NABs-Li@C₆₀ is considerably decreased, and the M06-2X and PM6-D methods yield a different sequence from the gas phase, G>A>T>C. The encapsulation of Li atom results in a lower IP for $Li@C_{60}$ than those of NABs, and the dominant localization of single-occupied molecular orbital on Li@C60 moiety of the complexes NABs-Li@C₆₀ further indicates that an electron would be ejected from Li@C₆₀ upon radiation and Li@C₆₀ is therefore able to protect DNA bases from radiation. In addition, it was revealed that Li prefers coordination with the hexagonal ring at Li@C₆₀, which clarifies the existing controversy in this respect. Finally, Yang's reduced density gradient approach clearly shows that the weak and strong noncovalent interaction regions in the complexes, NABs-Li@C₆₀ and (NABs-Li@C₆₀)⁺.

Keywords

endohedral metallofullerene Li@C $_{60}$; noncovalent interaction; dispersion-corrected DFT; PM6-DH2; M06-2x

^{*}Correspondence to: Y. Bu; byx@sdu.edu.cn, Y. Wang; yixuan.wang@asurams.edu.

Supporting Information Available: Table S1 summarizes the charge population on Li atom in Li@C₆₀ and NAB-Li@C₆₀ complexes at different levels. The binding energies (E_b , kcal/mol) and ESP charge (e) for cationic complexes, (NABs-Li@C₆₀)⁺ were collected in Table S2. Figure S1 includes fragmental electron density isosurfaces (s=±0.004 au) for neutral Li@C₆₀ (a,b) and cation Li@C₆₀ (c,d) complexes. Figure S2 present SOMO and spin density of NABs-Li@C₆₀ in aqueous solution. This material is available free of charge via the Internet at www.

1. Introduction

Oxidative DNA damage could cause several diseases, such as cancer¹ and aging.² Radiation is one of the most general reasons for the oxidative DNA damage.³ We have recently investigated the interaction between nucleic acid bases (NABs) and C₆₀ molecule in their different charge states (neutral and cation) using the M05-2x, M06-2x and DFT-D methods,⁴ and revealed that the presence of C₆₀ fullerenes to some extent could protect NABs from radiation damage. In order to achieve the anticipated antiradiation drug application, it is suggested to synthesize new fullerene derivatives that have significant IP gap with guanine. This work was motivated partially by the recent interest in endohedral metallofullerene.

Endohedral metallofullerenes are an expand class of fullerenes known for their novel structures⁵ and promising applications ranging from biological tracer⁶ to qubits in quantum computers.⁷ Carbon atoms in these compounds form a cage enclosing a metal atom, which insulates the metal from the environment and modifies its properties. As a typical metallofullerene, Li@C₆₀ has been synthesized and characterized experimentally in several studies, $^{8-10}$ and theoretical calculations on these systems have also been carried out. $^{11-13}$ Theoretical investigations revealed that the alkali metal encapsulation into the fullerenes and single walled carbon nanotubes could promote external amino acid interaction because of the modification of surface properties through charger transfer. Jalbout et. al. did interesting research and trials in this topic.^{12,14–16} Both LDA and the conventional hybrid DFT B3LYP predicted the off-center position of the endo-Li in $\text{Li}@C_{60}$,^{13,17} but the two theoretical methods yielded the opposite global minimum for Li@C₆₀. The LDA predicted that pentagonal conformation (Li below the pentagon ring, referred to as η^5 -Li@C₆₀) is more stable by 0.01eV than the hexagonal one (Li below the hexagonal ring, referred to as η^6 -Li@C₆₀), while with the B3LYP/6-311G* η^6 -Li@C60 tends to be more stable by 0.027eV than the η^5 -Li@C₆₀. It is interesting to further clarify the difference with more accurate DFT methods. Broclawik found that the ionization potential of Li@C₆₀ is 6.06eV at LDA level, which is significant lower than the intrinsic C_{60} fullerene and guanine.¹¹ In view of the lower IP, it seems that Li@C₆₀ is a potential candidate for DNA protection from radiation. However, to the best of our knowledge the detailed mechanism of the interaction of Li@C₆₀ with NABs has not been yet available.

In the present study, the interaction between the NABs and $Li@C_{60}$ as well as cationic $Li@C_{60}$ will be extensively investigated using several computational methods well describing the non-covalent bonding. The objectives of the present work are multi-fold. Whether Li prefers binding to the pentagonal or the hexagonal ring will be established. Through the study the performance of several popular quantum mechanics methods on the non-covalent systems (NABs with $Li@C_{60}$) will also be assessed, including the hybrid-meta GGA M06-2X, the GGA PBE augmented by the empirical dispersion (referred as PBE-D), and a very recent empirical method PM6 enhanced by dispersion and hydrogen bond terms (PM6-DH2). In addition, electronic structures of the complex systems of NABs and $Li@C_{60}$ will be analyzed to shed the light on the biomedical implication of the systems.

2. Computational Methods

M06-2x

To locate the ground states for the open shell systems, several spin multiplicities have been considered for each neutral and cationic complexes of $\text{Li}@C_{60}$ and NAB-Li@C₆₀. Results show that the doublet and singlet states are ground states for the neutral and cationic complexes, respectively. To accurately account for non-covalent interaction in NAB-Li@C₆₀, we firstly adopted a hybrid meta-GGA DFT method, M06-2x ¹⁸ with 6-311G** basis set to fully optimize all of the relevant geometries. Single point energies were also

corrected at the M06-2x/6-311++G^{**} level. The basis set superposition error (BSSE) was estimated by the Boys-Bernardi counterpoise method.¹⁹ These calculations were carried out with Gaussian 09 suite of programs.²⁰

In aqueous solution nucleobases have a strong tendency to solvate, thereby resulting in nucleobases apart. Thus, it is necessary to take into account solvent effects on the binding of NABs with $(\text{Li}@C_{60})^{0,+}$. Since the conductor-like polarizable continuum model (CPCM)²¹ could give much more consistent errors on nuclear and electronic total polarization as compared with the dielectric PCM, NABs- $(\text{Li}@C_{60})^{0,+}$ were fully optimized with CPCM-M06-2X/6-311G** and energies were then improved with CPCM-M06-2X/6-311++G** together with a UAHF radius.

DFT-D

For an empirical dispersion-corrected density functional theory (DFT-D), Grimme's scheme was adopted,^{22–23} where the van der Waals interaction term is explicitly described by a damped inter-atom potential, accounting for long-range dispersion effects. The total density functional energy can be written as follows

 $E_{DFT-D} = E_{DFT} + E_{vdw} \quad (1)$

where E_{DFT} is the normal self-consistent density functional energy and E_{vdw} is the empirical dispersion correction term and is given by

$$E_{vdw} = -s_6 \sum_{i=i}^{N-1} \sum_{j=i+1}^{N} \frac{C_6^{ij}}{R_{ij}^6} f_{dmp}(R_{ij}) \quad (2)$$

where, s_6 is a global scaling factor only depending on the applied density functional method, and was determined by least-squared optimization of the deviations observed in the interaction energy values for the various weakly interacting systems. As usual, the combined

dispersion coefficient for atom pair *i* and *j*, C_6^{ij} , was estimated with a geometric mean of individual atomic C_6 coefficient, while R_{ij} , the interatomic distance between atoms *i* and *j*, is an arithmetic mean value of individual vdw radius. N is the number of atoms. $f_{dmp}(R_{ij})$, a damping function, is expressed by the following equation

$$f_{dmp}(R_{ij}) = \frac{1}{1 + e^{-\alpha(R/R_0 - 1)}} \quad (3)$$

where *a* is taken to be 20 in the exponent. In this work Perdew-Burke-Ernzerhof (PBE)²⁴ exchange-correlation functional in the DFT part was employed, and the DFT-D method was therefore referred to as PBE-D. The PBE-D/6-311G** was done with the ORCA suite of program.²⁵

PM6-DH2

Very recently, it was reported that the dispersion as well as hydrogen bonds corrected PM6 (referred to as PM6-DH2)^{26,27} is able to yield the most accurate results for non-covalent interactions of all the semiempirical quantum mechanical methods²⁸. Because of significant low computational demand, PM6-DH2 may be applied to macromolecular systems for describing H-bond and non-covalent interactions; however, it needs to be well validated before extensive application. Thus, PM6-DH2 implemented in MOPAC2009 package ²⁹ was

also employed to the neutral NAB-Li@ C_{60} complexes to further asses the method. To include solvent effect in the PM6-DH2 method, conductor-like screening model (COSMO) approach is applied.³⁰

sign(λ₂)ρ

In order to analyze and visualize the noncovalent interactions in these systems, an approach developed by Yang et al. was adopted.³¹ In this approach, the reduced density gradient, defined as $RDG=1/(2(3\pi^2)^{1/3})|\nabla \rho|/\rho^{4/3}$, together with electron density (ρ), were used to distinguish the covalent bonding and noncovalent interactions. The noncovalent interactions could be isolated as regions with low density and low RDG. In order to identify the noncovalent interaction types, the sign of the second largest eigenvalue (λ_2) of the electron-density Hessian was utilized as a tool to distinguish bonded ($\lambda_2<0$) from nonbonded ($\lambda_2>0$). The functions such as RDG and sign(λ_2) ρ were calculated with Multiwfn software.³² The gradient isosurface was plotted with VMD.³³

3 Results and Discussions

3.1 Structural and Electrical Properties of Li@C₆₀ and (Li@C₆₀)⁺

Figure 1 shows the fully optimized structures of η^6 -Li@C₆₀ and η^5 -Li@C₆₀, where the Li atoms are significantly shifted from the cage center towards the wall of C_{60} . At the η^6 -Li@C₆₀ and η^5 -Li@C₆₀, Li has the shortest distance to the coordinated hexagonal and pentagonal ring, respectively. As discussed below, the encapsulation of Li into C₆₀ induces a configuration $Li^+C_{60}^-$. Thus, the deviation of Li from the center of C_{60} is to maximize the attraction between the oppositely charged moieties. The M06-2x/6-311G** method turns out that the η^6 -Li@C₆₀ is more stable by 0.60kcal/mol than η^5 -Li@C₆₀, which excellently agrees with the predicted minimal separation of 0.62kcal/mol (217cm⁻¹) with the B3LYP/ 6-31G(d) by Zhang et. al..¹⁷ However, the present binding energy of Li to C_{60} of η^6 -Li@C₆₀, -38.8 kcal/mol is stronger than that from the B3LYP, -32.2 kcal/mol (11,260cm⁻¹). According to Figure 1, the distances between the Li atom and the center of C_{60} are 1.518 and 1.481 Å for η^6 -Li@C₆₀ and η^5 -Li@C₆₀, respectively. The distances are rather similar to the length of 1.5Å in Zhang et. al.'s report;¹⁷ yet is considerably different from the length of 1.26–1.43Å obtained by Slanina et. al..³⁴ The difference could be attributed to the discrepancy of calculation strategies. At η^6 -Li@C₆₀ and η^5 -Li@C₆₀, the Li atom locates under the hexagonal and the pentagonal rings with respective distances of 1.732 and 1.853 Å between Li and the ring centers. The off-center geometry is typical of endohedral metallofullerenes due to strong polarizability of alkali-metal. It was documented earlier that the barrier for the isomerization of η^6 -Li@C₆₀ and η^5 -Li@C₆₀ was rather low as 0.9 kcal/mol (~305 cm⁻¹).^{17,35} Therefore, to discuss the migration energy of Li in the cage we have limited our calculations to Li atom migrating along the 5-fold symmetry axis from the center of the pentagon to the center of cage. To determine the barrier for migrating, single point energy calculations were carried out at the M06-2x/6-311++G** level for different positions of Li. Results (Figure 2) indicate that Li atom has to overcome a energy barrier with a height about 12 kcal/mol as it crosses the center of cage.

As one electron is ionized from Li@C₆₀, resulting in (Li@C₆₀)⁺, the Li atom gets closer to the center of C₆₀ with 1.488 Å, while it further deviates from the center of hexagonal ring by 1.762 Å. The adiabatic ionization potential of Li@C₆₀ is 5.98 eV, slightly lower than the vertical one obtained with LDA by Broclawik ¹¹ (6.06 eV). The encapsulated Li significantly decreases the IP of the intrinsic C₆₀ molecule (5.98 vs. 8.02 eV at the M06-2x/ 6-311G** level).

According to Figure 1, at η^6 -Li@C₆₀ and η^5 -Li@C₆₀ Li coordinates with 5 or 6 C atoms within approximately 2.1–2.3 Å. Together with the high binding energy of –38.0 kcal/mol, it

can be speculated that the valence electron of Li atom may considerably donates to the C_{60} cage, yielding a typical $\text{Li}^+\text{C}_{60}^-$ configuration. The scheme of population distribution is critical to investigate the charge transfer in the endohedral metallofullerene. The electrostatic potential (ESP) fitted charge shows that the charge carried by the Li in neutral and cationic complex is +0.840e and +0.529e, respectively, which roughly confirms the Li⁺C₆₀⁻ structure for the neutral Li@C₆₀. However, the different charge carried by Li does not follow Broclawik's conclusion that the charge on Li atom is nearly invariant with respect to the number of electrons in the systems.¹¹ The difference might be attributed to the different charge distribution analysis methods. In order to clarify this problem, we compared three charge population analysis methods: Mulliken, NBO and ESP, shown in the Supporting information. In addition, B3LYP/svp³⁶ level, which was used to calculate the properties of analogous systems in Froudakis' reports,^{36–38} was also applied for comparison. In the ESP scheme, atomic charges are fitted to the molecular electrostatic potential, which rigorously defines quantum mechanics property. The molecular electrostatic potential is calculated with the atomic wave function basis set.³⁹ In the non-ESP methods, such as Mulliken and NBO, atomic charges are determined by partitioning the electron density into atomic contributions. These non-ESP methods are very sensitive to the choice of basis sets,⁴⁰ which is also true for the current systems as shown in Table S1. The ESP predicted charge carried by Li does not change much with the theoretical methods and basis sets. Only ESP scheme was therefore used to estimate the amount of charge transfer. The difference of electron density plot was a good alternative to describe the process of charge transfer, and that would be discussed later. The B3LYP/svp predicted charge variation for the neutral and cationic complex (+0.813 vs + 0.637 e) is not as significant as that from the M06-2x (+0.840 e)vs +0.529e). The charge carried by Li at the un-relaxed $(\text{Li}@C_{60})^+$, +0.523e, indicates the variation is dominantly due to charge reorganization to relieve the repulsion between positively charged hexagonal ring of C_{60} and Li at $(Li^{(0)}C_{60})^+$, and geometry relaxation, e.g., the further separation between Li and surface of C₆₀ does not play much role in the charge variation. The frontier orbital plots of Li@C₆₀ were shown in Figure 3. It was clearly manifested that the single occupied molecular orbital (SOMO) almost localizes on the surface of fullerene. When an electron was removed from this complex, the ionization process is anticipated to occur in the fullerene surface exclusively. However, according to the ESP charge population variation, Li atom is also involved in the oxidation process. In order to analyze the ionization process more intuitively, the charge population of carbon atoms in fullerene in the three states: neutral, vertical ionization and adiabatic ionization were shown in Figure 4. As for the neutral state (red line), the donated electron from Li atom is generally assumed to be delocalized all over the cage due to the delocalization nature of π orbitals. Interestingly, the excess electron over the cage is found to be localized on the surface near Li rather than uniformly distributed on the cage, such as carbon 32, 43 and 58. This charge localization feature is attributed to the asymmetry location of Li in the cage and the strong electrostatic force between Li and cage. As for the vertical ionization state (black line), the amount of charge in Li is 0.532, which is nearly the same as the corresponding value in adiabatic ionization state (blue line). It could be inferred that the charge population has insignificant variation before and after the geometry optimization for the cationic complex. Given all that, the ionization process indeed primarily occur on the cage surface, and after that, the charge associated the geometry would be reorganized, yielding a new stable configuration. When an electron is removed from the complex, the charge in this system will be reorganized, coupling with the reorganization of geometry, reducing the charge amount on the Li and yielding the *Li...cage* interaction a feeble repulsion. In this sense, the Li atom is only partially insulated by the cage when an electron is removed from the complex.

3.2 Structural and Electrical Properties of NAB-Li@C₆₀ Neutral Complexes

Starting with displaced AB type of configuration like graphite layer and the NAB-SWCNT systems,⁴¹ where the hexagonal ring of NABs locates above the six-membered ring coordinated by the Li in Li@C₆₀, the geometries of the neutral complexes NAB-Li@C₆₀ were extensively searched for with M06-2x and PBE-D methods. The optimal geometries with M06-2x/6-311G** in Figure 5 show that NABs are almost parallel to the tangent plane of the Li@C₆₀ with approximately 3.4–3.6Å separation. Obviously, all NABs undergo physisorption processes when they interact with Li@C₆₀ fullerenes in the gas phase. The distance between the centre of fullerene and the centre of hexagonal ring of A, T, G, and C is 6.495, 6.418, 6.339, and 6.488 Å, respectively. The binding energy E_b for the neutral system is defined as:

 $E_b = E \cdot (NAB - Li@C_{60}) - E \cdot (NAB) - E \cdot (Li@C_{60})$ (4)

where E (NAB-Li@C₆₀), E (Li@C₆₀), and E (NAB) are the total energies for the complexes, Li@C₆₀, and NAB, respectively. According to Table 1, G-Li@C₆₀ complex is the strongest binding (E_b : -8.27 kcal/mol), followed by C-Li@C₆₀ (-7.36 kcal/mol) and A-Li@C₆₀ (-6.95 kcal/mol), and T-Li@C₆₀ complex is the weakest binding (-6.62 kcal/mol). The binding between NABs and Li@ C_{60} is generally stronger by 0.7–1.6 kcal/mol than that between the corresponding base with intrinsic C₆₀, which may be due to higher electrostatic interaction between the charged C₆₀ and NAB. The binding enhancement due to Li encapsulation into C₆₀ agrees well with Jalbout's finding that Li, Se and Te metallo endofullerenes promote external interactions with amino acids because of the modification of surface properties through charger transfer.^{15–16} The M06-2x predicted binding sequence for NABs-Li@C₆₀ is also different from the trend of interaction between NABs and C₆₀: G-C₆₀ $(-6.80 \text{ kcal/mol}) > A-C_{60}(-6.24) > C-C_{60}(-5.64) > T-C_{60}(-5.29)$.⁴ To clarify this difference, the binding for the complexes was also investigated at PBE-D/6-311G** level. After introducing the empirical dispersion correction term, the binding strength is enhanced to different extent, and the binding trend is changed to G-Li@C₆₀(-9.72kcal/mol)>A- $Li@C_{60}(-8.29)>C-Li@C_{60}(-7.28)>T-Li@C_{60}(-7.17)$. Similar to the NABs and C₆₀, the binding between A and Li@C₆₀ (BE: -8.29kcal/mol) was indeed predicted to be stronger than C-Li@C₆₀ (BE: -7.28 kcal/mol) by 1.0 kcal/mol. However, C-Li@C₆₀ still displays slightly stronger binding than T-Li@ C_{60} . The dominant force between NAB and C_{60} is dispersion force, while for the NAB-Li@C60 complexes the interaction may be complicated due to the charge delocalized over C_{60} surface. For the endohedral fullerene, the transferred electron from the Li atom makes the endohedral fullerene an almost ionic compound. In this sense, electrostatic force is non-negligible when analyzing the interaction between NAB and Li@C₆₀. Compared with the systems without intercalation of Li, the higher electrostatic interaction in NAB-Li@C₆₀ may switch the binding strength of C and T.

To gain further insight into the influence of the non-covalent interaction on the electronic structure of NABs-Li@C₆₀, single occupied molecular orbital (SOMO) plots of the complexes were given in Figure 6. For all these complexes, the SOMOs dominantly localize on the surface of C₆₀, indicating that it is most likely the ionization process would occur in the metallofullerene due to its low ionization potential. This implies that the Li@C₆₀ is able to well protect NABs from radiation. Similar to Li@C₆₀, the Mulliken spin density of C₆₀ cage is almost 1.0e, while those of Li and NABs approach to zero, which is another indication that an electron is transferred to the C₆₀. A close inspection of spin density distribution shows that the 10–12 atoms with high spin density (>0.04e) are located on the top half sphere close to NABs, and the total spin density of the top half sphere amounts to approximately 0.7e.

3.3 Performance of PM6-DH2 on NABs-Li@C₆₀

As a promising method that could deal with noncovalent interaction, PM6-DH2 method ^{26–27,42} was also utilized to investigate the binding of NABs with Li@C₆₀. Firstly, as suggested in the MOPAC manual NABs, Li@C₆₀, and their complex NABs-Li@C₆₀ were optimized with only PM6 method and calculate the heats of formation of each of the three systems with the single point PM6-DH2 (noted as PM6-DH2//PM6). The geometries were also optimized with PM6-DH2 and calculate the binding energies with the heat of formation (PM6-DH2//PM6-DH2). The optimized geometries with a few parameters were shown in Figure 7 and the binding energies were in Table 2. It is surprising to find that as dispersion term is explicitly included, the optimized geometries with PM6-DH2 display slight change from those with PM6. For instance, the PM6-DH2 predicted distances between the hexagonal ring of NABs and the Li coordinated hexagonal ring of C_{60} decrease by 0.11, 0.09, 0.22 and 0.20 Å for A, C, G, and T-Li@C₆₀, respectively, as compared with those from PM6. As a result of the similar structures, the PH6-DH2//PM6-DH2 predicted binding energies, G-Li@C₆₀(-10.12kcal/mol)>A-Li@C₆₀(-8.19)>T-Li@C₆₀(-7.90)>C-Li@C₆₀(-7.76), agree in the range of 0.5 kcal/mol with those from PH6-DH2//PM6, G- $Li@C_{60}(-9.47 kcal/mol) > A-Li@C_{60}(-8.50) > C-Li@C_{60}(-8.10) > T-Li@C_{60}(-7.94).$ Compared with the structures of PBE-D in Figure 5, the corresponding ones in Figure 7 show two striking features: first, the distances between the Li atom and coordinated hexagonal center of C_{60} increase by approximately 0.5–0.6Å, causing the Li atom closer to the cage center; the other one is that the NAB moieties well locate above the 6-membered ring of C_{60} that is coordinated by the Li atom. In spite of the differences, the PM6-DH2 predicted hexagonal ring separations between NABs and C_{60} agree very well with those from PBE-D/6-311G**, (3.334, 3.552 3.335, and 3.332Å vs 3.414, 3.485, 3.362 and 3.338 Å for G, A, C and T-Li@C₆₀ complexes). As shown in Figure 8, a variation of binding energies with the applied theoretical methods, the binding energies from PM6-DH2 only differ by the most 0.73 kcal/mol for T-Li@C₆₀ from those with the PBE-D. In above, the predicted geometry and binding energies from PM6-DH2 are very acceptable for the noncovalent systems. In view of dramatic low computational demand, the PM6-DH2 method is promising for nano-scale systems.

3.4 Structural and Electronic Properties of Cationic Complexes (NAB-Li@C₆₀)+

In order to further analyze electron transfer mechanism as an electron is ejected, M06-2x and PBE-D methods were also applied to the cationic complexes, $(NAB-Li@C_{60})^+$. According to the optimized structures presented in Figure 9, all geometries obviously keep the stacked π - π stacked configurations except for $(C-Li@C_{60})^+$, which transforms to the σ - π conformation via the lone electron pair of oxygen at cytosine. Compared with their counterparts in neutral complexes, both the equilibrium distance between hexagonal rings of NABs and C₆₀, and that between the hexagonal rings and the Li did not display clear change. Since Li@C₆₀ has lower IP than NAB molecules, the binding energy for (NAB-Li@C₆₀)⁺ was defined as:

 $E_{b}^{+}=E \cdot [(NAB - Li@C_{60})^{+}] - E \cdot (NAB) - E \cdot [(Li@C_{60})^{+}]$ (5)

the superscript "+" represents the cationic system, the other notations are the same as them in Equation (4). In the cationic complexes, because of the predictable higher electrostatic force, the binding energies listed in Table 3 are higher negative than those in neutral complexes NAB-Li@C₆₀, i.e., the binding of NABs to positively charged $(\text{Li}@C_{60})^+$ is stronger than that to the neutral Li@C₆₀. Analyzing the results shown in Table 3, it is clear that the binding trend is C>G>A>T. Obviously, the binding energy of C-Li@C₆₀ is the largest. As for C-Li@C₆₀ cationic system, the shortest distance between oxygen atom and cage surface is 2.710Å. This σ - π interaction is very similar to its counterpart in C-C₆₀

cationic complex.⁴ This configuration is responsible for the strong electrostatic force between the oxygen atom and its nearby carbon atoms in the cage. To discuss their electronic properties, frontier orbitals are plotted in Figure 10. LUMOs dominantly localize on the surface of cage, while HOMOs localize on the NABs. The frontier orbital distributions further show that for the neutral states NABs-Li@C₆₀ an electron would be ejected from C₆₀ rather than NABs upon radiation.

It was known that the atomic dispersion coefficients (C_6) in DFT-D method are highly empirical molecular-mechanics-like parameters. They depend only on atom type and do not respond to changes in an atom's electronic environment. As a result, atomic dispersion coefficients in charged molecules may be quite different from their counterparts in neutral ones. Consequently, DFT-D methods tend to perform very well for dispersion interactions involving neutral systems, yet questionable for charged ones. In this sense, the utility of DFT-D scheme in these systems is uncertain. In this part, the PBE-D scheme was also employed to optimize the geometries of the complexes. Optimal geometries are also shown in Figure 9. The type of adsorption from the DFT-D remains consistent with geometries obtained through M06-2x, among which only the cytosine is chemisorbed on the surface of Li@C₆₀. It is difficult to calibrate the geometries and binding energies of such large complexes with MP2 or higher level post-HF methods, but apparently, the trends of binding energy obtained by the two methods are consistent. In this sense, the utility of PBE-D method in our system is acceptable.

3.5 Solvent Effects on the Binding of NABs and (Li@C₆₀)^{0,+}

For the biomedical implication the solvents effects on the geometry, binding and electronic structure are important. Thus, CPCM model with the UAHF radius was also used to optimize the complexes, consisting of NABs with neutral as well as cationic $\text{Li}@C_{60}$, $(\text{Li}@C_{60})^{0,+}$. In the aqueous solution the electrostatic attraction between negatively charged C_{60} and positively charged Li is so significantly reduced that Li locates rather close to the center of C_{60} with respective distance of 0.31 and 0.29Å for $(\text{Li}@C_{60})^{0,+}$. It is interesting to note that the charge of Li at Li@C₆₀ is increased to +1.521e in aqueous solution from +0.84e in the gas phase. The negative charge is more delocalized as shown in Figure S2 and is stabilized by solvent effect.

The CPCM-M06-2X optimized geometries for $(NABs-Li@C_{60})^{0,+}$ were demonstrated in Figure 11 with the distance between hexagonal rings of NABs and C_{60} . The Li remains close to the center of C₆₀ with approximately 0.3Å for all the systems. It was also found that for the most stable geometries of (NABs-Li@ C_{60})^{0,+}, NABs locate on the side close to the Li. In spite of small variation around 0.1-0.2 Å for the distances as compared to those in the gas phase, the solvent effects on the binding strength between NABs and Li@C₆₀ are dramatic. The CPCM predicted binding energies are added in Tables 1 and 3. According to Table 1, the bindings in aqueous solution are weakened by approximately 2–3 kcal/mol. The solvation of nucleobases and $Li@C_{60}$ decrease their binding to different extent, depending on the degree of solvation. Because of different polarity of nucleobases, evidenced by the dipole moments of C (6.45 Debye)~G(6.43)>T(4.20)>A(2.44)>Li@C₆₀(0.91) at the M06-2X/6-311G** level, it can be expected that G and C are more strongly solvated than T and A, which decreases the binding to Li@C₆₀ by 3.33, 3.08, 2.11 and 1.86 for C, G, T and A, respectively. The M06-2X predicted binding sequence changes to G>A>T>C with respective binding energy of -8.65, -8.00, -7.30 and -6.84 kcal/mol, from the sequence G>C>A>T in the gas phase. The sequence in aqueous solution is the same as the binding of NABs to (5,5) SWCNT.⁴¹

Table 2 shows the COSMO+PM6-DH2 predicted binding energies for NABs-Li@ C_{60} also follow the same trend as CPCM+M06-2X, and they are just lower than the latter by 0.4–1.3

kcal/mol. The PM6-DH2 again yields acceptable results for the π - π stacking systems. For the binding of NABs to $(\mathbf{Li}@\mathbf{C_{60}})^+$ in aqueous solution, Figure 11 indicates that the parallel conformation for cytosine was also located, which was instable in the gas phase. This may be due to the fact that in aqueous solution van der Waals interaction via π - π interaction becomes a dominant role in stabilizing (NABs- $\mathbf{Li}@\mathbf{C_{60}})^+$ after considerable decrease of electrostatic attraction. According to Table 3, the bindings of NABs to $(\mathbf{Li}@\mathbf{C_{60}})^+$ are dramatically weakened by approximately 2.9–8.6 kcal/mol as compared to those in the gas phase, which is more significant than that in the case of NABs- $\mathbf{Li}@\mathbf{C_{60}}$. Similar to NABs- $\mathbf{Li}@\mathbf{C_{60}}$, the binding of G and C decreases much more than T and A. As a result of stronger polarity (dipole moments of $(\mathrm{Li}@\mathbf{C_{60}})^+$ and $\mathrm{Li}@\mathbf{C_{60}}$, 2.14 and 0.91 Debye), the higher degree of solvation of $(\mathrm{Li}@\mathbf{C_{60}})^+$ further decreases its binding to NABs. Strong solvation almost eliminates the binding difference to $(\mathrm{Li}@\mathbf{C_{60}})^+$ and $\mathrm{Li}@\mathbf{C_{60}}$, e.g., for the given NAB, the binding to $(\mathrm{Li}@\mathbf{C_{60}})^+$ is only slightly stronger by 0.4–0.7 kcal/mol than that to $\mathrm{Li}@\mathbf{C_{60}}$. The binding sequence of (NABs- $\mathrm{Li}@\mathbf{C_{60}})^+$ in aqueous solution is the same as that of NABs- $\mathrm{Li}@\mathbf{C_{60}}$, G>A>T>C.

Table 4, summarizing HOMO, LUMO, and IP for NABs, $\text{Li}@C_{60}$, and NABs- $\text{Li}@C_{60}$ in the gas phase and aqueous solution, shows that solvent effects increase their frontier orbitals and consequently decrease IPs. In the aqueous solution, $\text{Li}@C_{60}$ has much lower IP than guanine that possesses the lowest IP among the four NABs (3.70 vs. 5.50 eV). The identical IPs of complexes NABs- $\text{Li}@C_{60}$ and $\text{Li}@C_{60}$ also indicate that ionization process would occur on $\text{Li}@C_{60}$ rather than NABs. Figure S3 shows that, for all these complexes in aqueous solution the SOMOs localize exclusively on the surface of C_{60} , further confirming that the ionization process would occur in the metallofullerene due to its much lower ionization potential. In spite of variation in binding and electronic structure, the most interesting is that in aqueous solution $\text{Li}@C_{60}$ is also able to well protect NABs from radiation.

3.6. The Electron Density Difference and Visualization Noncovalent Interactions

It could be imagined that during the course of the formation of these complexes, electron density transfer occurs and the variation can be made clearly by subtracting electron density of NAB, Li and C₆₀ in standalone state from the entire system. Neutral and cationic $Li@C_{60}$, G- $Li@C_{60}$ and C- $Li@C_{60}$ complexes were chosen to plot the electron density differences. As shown in Figure 12, the green and purple represent the region in which electron density is decreased and increased upon the combination, respectively. It is obvious that for the neutral Li@C₆₀ (a) the electron density is shifted from Li atom to its neighboring carbon atoms in the cage. Meanwhile, it could be observed that there is also electron density increasing in the regions far from the Li atom. This phenomenon could be explained by the change of electronegativity of carbon atoms. For the neighboring carbon atoms, the electronegativity is deceased due to the increasing of electron shielding, which was corresponding to the increasing of electron density. In this sense, the electron density would transfer continuously in order to balance the electronegative. For the neutral complexes (b and c), the plots are similar to the Li@C₆₀. It should be noted that the electron density differences of NAB fragments are insignificant within this isovalue setting. This phenomenon supports the conclusion that the charge transfer from NAB to $Li@C_{60}$ is insignificant in the neutral state. For the cationic Li@C60 complex, the increasing and decreasing regions distributed on the inner and outer surface of cage, respectively. This could be explained by the electrostatic attractive and repulsive which were caused by the Li⁺. Plots within smaller isovalue (s=±0.0004 au) were shown in Supporting informations. The cationic complex $(G-Li@C_{60})^+$ was similar to $(Li@C_{60})^+$, but $(C-Li@C_{60})^+$ was quite different, at which there was an obvious region between O/N atoms in cytosine and cage due to the unpaired electrons.

From Yang's approach, we could utilize the sign of λ_2 to distinguish bonded ($\lambda_2 < 0$) from nonbonded ($\lambda_2 > 0$) interactions. The gradient isosurfaces are colored according to the corresponding values of sign(λ_2) ρ , which is found to be a good indicator of interaction strength. Large negative values of sign(λ_2) ρ are indicative of attractive interactions (such as dipole-dipole or hydrogen bonding); while if sign(λ_2) ρ is large and positive, the interaction is nonbonding.³¹ Values near zero indicate very weak, van der Waals interactions. The gradient isosurfaces provide a rich visualization of noncovalent interaction as broad regions of real space, rather than simple pairwise contacts between atoms. We first consider the neutral and cationic Li@C₆₀ molecule. As shown in Figure 13, there are areas of nonbonded overlap located at the center of the hexagonal and pentagonal rings. Meanwhile, there is another lower density surface between Li and cage. Comparing a and d in Figure 13, it could be detected that there are more orange splashes in d, where the stronger repulsion is expected. The stronger repulsion also agrees with the judgment based on charge population. As for the NAB-Li@ C_{60} systems (b-c, and e-f), there are lower density surfaces between the overlapping portions of NAB and cage, where either π - π stacking or σ - π is expected. It should be noted that graph e has the largest percent of blue region, indicating the largest noncovalent interaction among the four complexes. This trend also agrees with the above binding energies. Figure shows that the sign(λ_2) ρ can be employed to visualize noncovalent interaction.

4. Conclusions

In order to discuss the protection mechanism of DNA from radiation, the interaction of four nucleic acid bases (NABs) such as adenine (A), cytosine (C), guanine (G), and thymine (T), with the endohedral metallofullerene (Li@ C_{60}) was extensively investigated with the-stateof-art theoretical methods for describing non-covalent systems, like M06-2x, PBE-D, and PM6-DH2 methods. In the gas phase, the M06-2x predicted binding strength of NABs to $Li@C_{60}$ decreases in the sequence G>C>A>T. As dispersion was explicitly included, PBE-D relatively enhances the binding of A and T and brings about the sequence G>A>C~T. The performance of the new emerging dispersion corrected empirical method, PM6-DH2, is rather acceptable on the non-covalent systems, NABs-Li@C₆₀. PM6-DH2 predicted similar binding energies to those from PBE-D within 0.5kcal/mol. The PM6-DH2 is a very promising method to nanoscale systems. In the aqueous solution, binding of NABs-Li@ C_{60} is considerably decreased, and the M06-2X and PM6-D methods yield the different sequence from the gas phase, G>A>T>C. The encapsulation of Li atom so significantly decreases the IP of C_{60} that the IP of $Li@C_{60}$ is lower than those of NABs. Together with the low IP, the dominant localization of SOMO on Li@C60 moiety of the complexes NABs-Li@C₆₀ indicates that an electron would be ejected from Li@C₆₀ upon radiation and $Li@C_{60}$ is therefore able to protect DNA bases from radiation. In addition, it was revealed that Li prefers coordination with the hexagonal ring at $Li@C_{60}$, which clarifies the existing controversy in this respect. Finally, Yang's reduced density gradient approach clearly shows that the weak and strong noncovalent interaction regions in the complexes, NABs-Li@ C_{60} and (NABs-Li@C₆₀)⁺. The method will be extended to visualize the noncovalent interactions for other bio-nano systems. 41

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work at Shandong University (Sun and Bu) is supported by NSFC (20633060, 20973101), NCET, and the Independent Innovation Foundation (2009JC020) of Shandong University. The project described here was also supported in part by the National Institute of General Medical of the National Institute of Health (SC3GM082324),

the American Recovery and Reinvestment Act (3SC3GM082324-02S1) and ACS PRF (47286-GB5) in terms of scholarly development (Wang at Albany State University). A part of the calculations were carried out at Shanghai Supercomputer Center, High-Performance Super-Computer Center at SDU, and High-Performance Computational Platform at SDU Chem School.

References

- 1. Loft S, Poulsen HE. J Mol Med. 1996; 74:297. [PubMed: 8862511]
- Mecocci P, Fanó G, Fulle S, MacGarvey U, Shinobu L, Polidori MC, Cherubini A, Vecchiet J, Senin U, Beal MF. Free Radical Bio Med. 1999; 26:303. [PubMed: 9895220]
- 3. Burrows CJ, Muller JG. Chem Rev. 1998; 98:1109. [PubMed: 11848927]
- 4. Sun W, Bu Y, Wang Y. J Phys Chem C. 2011; 115:3220.
- 5. Yamada M, Akasaka T, Nagase S. Accounts Chem Res. 2009; 43:92.
- 6. Cagle DW, Kennel SJ, Mirzadeh S, Alford JM, Wilson LJ. P Nat Acad Sci USA. 1999; 96:5182.
- 7. Zeng XH, Bi Q, Guo GC, Ruda HE. Phys Lett A. 2003; 313:21.
- 8. Belash IT, Bronnikov AD, Zharikov OV, Palnichenko AV. Synthetic Met. 1990; 36:283.
- 9. Guha S, Nakamoto K. Coordin Chem Rev. 2005; 249:1111.
- 10. Bethune DS, Johnson RD, Salem JR, de Vries MS, Yannoni CS. Nature. 1993; 366:123.
- 11. Broclawik E, Eilmes A. J Chem Phys. 1998; 108:3498.
- 12. Chang CM, Jalbout AF. J Comput Theor Nanosci. 2009; 6:1487.
- 13. Dunlap BI, Ballester JL, Schmidt PP. J Phys Chem. 1992; 96:9781.
- 14. Chang CM, Jalbout AF. Thin Solid Films. 2010; 518:2070.
- 15. Jalbout AF. J Organomet Chem. 2008; 693:1143.
- 16. Jalbout AF. J Phys Chem C. 2009; 113:504.
- 17. Zhang M, Harding LB, Gray SK, Rice SA. J Phys Chem A. 2008; 112:5478. [PubMed: 18491877]
- 18. Zhao Y, Schultz NE, Truhlar DG. J Chem Theory Comput. 2006; 2:364.
- 19. Boys SF, Bernardi F. Mol Phys. 1970; 19:553.
- Frisch, MJ.; Trucks, GW.; Schlegel, HB.; Scuseria, GE.; Robb, MA.; Cheeseman, JR.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, GA., et al. Gaussian 09, Revision A.02. Gaussian, Inc; Wallingford CT: 2009.
- 21. Barone V, Cossi M. J Phys Chem A. 1998; 102:1995.
- 22. Grimme S. J Comput Chem. 2004; 25:1463. [PubMed: 15224390]
- 23. Grimme S. J Comput Chem. 2006; 27:1787. [PubMed: 16955487]
- 24. Perdew JP, Burke K, Ernzerhof M. Phys Rev Lett. 1996; 77:3865. [PubMed: 10062328]
- 25. Neese, F. ORCA—an ab initio, density functional and semiempirical program package, Ver. 2.8.0, Max-Planck-Institut fur Bioanorganische Chemie, Mulheim an der Ruhr. 2010.
- 26. Rezác J, Fanfrlík Ji, Salahub D, Hobza P. Journal of Chemical Theory and Computation. 2009; 5:1749.
- 27. Korth M, Pitonák M, Rezác J, Hobza P. Journal of Chemical Theory and Computation. 2009; 6:344.
- 28. Riley KE, Pitonák M, Jurecka P, Hobza P. Chem Rev. 2010; 110:5023. [PubMed: 20486691]
- 29. Stewart, JJP. MOPAC2009, Stewart Computational Chemistry, Version 11.052W. web: HTTP:// OpenMOPAC.net
- 30. Klamt A, Schüümann G. J Chem Soc Perkin Transactions. 1993; 2:799.
- Johnson ER, Keinan S, Mori-Sánchez P, Contreras-García J, Cohen AJ, Yang W. J Am Chem Soc. 2010; 132:6498. [PubMed: 20394428]
- 32. Lu, T. "Multiwfn: A multifunctional wavefunction analyzer", Version 1.5. 2010. http:// Multiwfn.codeplex.com
- 33. Humphrey W, Dalke A, Schulten K. J Mol Graph. 1996; 14:33. [PubMed: 8744570]
- Slanina Z, Uhlik F, Lee SL, Adamowicz L, Nagase S. Int J Mol Sci. 2008; 9:1841. [PubMed: 19325833]
- 35. Maheshwari S, Chakraborty D, Sathyamurthy N. Chem Phys Lett. 1999; 315:181.

- Mpourmpakis G, Tylianakis E, Papanikolaou D, Froudakis GE. J Nanosci Nanotechnol. 2006; 6:3731. [PubMed: 17256322]
- 37. Mpourmpakis G, Froudakis G. J Chem Phys. 2006; 125:204707. [PubMed: 17144723]
- 38. Mpourmpakis G, Froudakis G, Andriotis AN, Menon M. J Phys Chem C. 2007; 111:6593.
- 39. Cox SR, Williams DE. J Comput Chem. 1981; 2:304.
- 40. Wiberg KB, Rablen PR. J Comput Chem. 1993; 14:1504.
- 41. Wang Y. J Phys Chem C. 2008; 112:14297.
- 42. Stewart J. J Mol Model. 2007; 13:1173. [PubMed: 17828561]



Figure 1.

The top and side views of the optimized η^5 -Li@C₆₀ (top) and η^6 -Li@C₆₀ (bottom) with M06-2x/6-311G**. The small purple ball stands for a Li atom, and the stick is C₆₀.



Figure 2.

The ground state interaction potential for the Li atom approaching the center of C_{60} through a center of the pentagon. The interaction potential variation in the 0~2.0 Å is shown enlarged in the inserted graph.



Figure 3.

Calculated frontier orbitals and spin density (SP) of $Li@C_{60}$ complex. (a) SOMO of $Li@C_{60}$ neutral complex; b) the spin density of $Li@C_{60}$ neutral complex; c) and d) HOMO and LUMO of cationic complex ($Li@C_{60}$)⁺. The isovalue of frontier orbitals and SP are 0.02 and 0.004 au, respectively.



Figure 4.

Charge population of carbon atoms for the neutral complexe, $Li@C_{60}$ (blue line); vertical ionized complex ($Li@C_{60}$)⁺ (black line) and adiabatic ionized (red line). The label of each carbon atom is shown in the left graph.



Figure 5.

Side and top views of NAB-Li@ C_{60} neutral complexes obtained at M06-2x(red) and PBE-D(black) methods.



Figure 6.

Plots of the SOMO and spin density (SP) of the neutral complexes, NAB-Li@C₆₀. The isovalue of SOMO and SP are 0.02 and 0.0004 a.u., respectively.





Side and top views of NAB-Li@C₆₀ neutral complexes obtained at PM6 (black) and PM6-DH2 (red) methods.









Figure 9. Side and top views of NAB-Li@ C_{60} cationic complexes obtained at PBE-D method.

	[A-Li@C60] ⁺	[T-Li@C60] ⁺	[G-Li@C60] ⁺	[C-Li@C60] ⁺
	ა ემემ იცია	<u>္ အဆ</u> မ္နဲ	* % %	
LUMO				
		395 5		
номо	6.03 2.0 2.0 2.0 2.0 2.0 2.0 2.0 2.0			10 10 10 10 10 10 10 10 10 10 10 10 10 10 10

Figure 10.

Plots of the frontier orbital of NAB-Li@ C_{60} neutral complexes. The isovalue is 0.02



Figure 11.

Side and top views of (NAB-Li@C₆₀) (black) and cationic complexes (NAB-Li@C₆₀)⁺ (red) obtained with the CPCM+M06-2X/6-311G**.



Figure 12.

Fragmental electron density isosurfaces (s= ± 0.0012 au) for neutral and cationic Li@C₆₀ (a,d), G-Li@C₆₀ (b,e), and C-Li@C₆₀ (e, f)complexes. The purple and blue isosurface represent the region in which electron density is increased and decreased after combination.

Sun et al.



Figure 13.

Gradient isosurfaces (s=0.5 au) for neutral and cationic $Li@C_{60}$ (a,d), C-Li@C₆₀ (b,e), and G-Li@C₆₀ (e, f) complexes. The surfaces are colored on a blue-green-red(BGR) scale according to values of sign(λ_2) ρ , ranging from -0.04 to 0.02 au. Blue indicates strong attractive interactions, and red indicates strong nonbonded overlap.

The binding energies (E_0 , kcal/mol) and ESP charge (e) for neutral complexes, NABs-Li@ C_{60} . Data in parentheses include BSSE correction.

		$E_{ m b}{}^{a}$			ESP c	harge ^b	
	AC JUIN		AC JOIN MUDD	M06	-2X	CPCM+N	I06-2X
	V7-0010	rbe-D	CFCIMH:M00-2A	NAB	Li	NAB	Li
$Li@C_{60}$					0.840		1.521
A-Li@C ₆₀	-9.86(-6.95)	-11.41(-8.29)	-8.00	-0.013	0.745	-0.010	1.423
T-Li@C ₆₀	-9.41(-6.62)	-9.99(-7.17)	-7.30	-0.010	0.758	-0.012	1.422
G- Li@C ₆₀	-11.73(-8.27)	-13.40(-9.72)	-8.65	-0.007	0.741	-0.010	1.422
C- Li $@C_{60}$	-10.17(-7.36)	-10.48(-7.28)	-6.84	-0.009	0.757	-0.0121	1.432

^aM06-2X/6-311++G**//M06-2X/6-311G**; CPCM+M06-2X/6-311++G**//CPCM+M06-2X/6-311G**; PBE-D/6-311G**

 $b_{M06-2X/6-311++G^{**//6-311G^{**}}}$

The binding energies (E_b , kcal/mol) for the complexes, (NABs-Li@C₆₀) calculated with PM6-DH2//PM6 and PM6-DH2//PM6-DH2.

NABs-Li@C ₆₀		E _b	
	PM6-DH2/PM6	PM6-DH2/PM6-DH2	COSMO+PM6-DH2
А	-8.50	-8.19	-7.14
Т	-7.94	-7.90	-6.92
G	-9.47	-10.12	-7.23
С	-8.10	-7.76	-5.60

The binding energies (E_0 , kcal/mol) and ESP charge (e) for cationic complexes, (NABs-Li@C₆₀)⁺. Data in parentheses include BSSE correction.

		$E_{ m b}{}^{a}$			ESP c	harge ^b	
	AC 2014		AC JOINT MUUC	M06	-2X	CPCM+I	M06-2X
	V7-00141	rbe-D	CF CM+M00-2A	NAB	Li	NAB	Li
(Li@C ₆₀) +					0.529		1.362
A-(Li@C ₆₀) ⁺	-12.89(-9.72)	-17.15(-13.68)	-8.42	-0.005	0.490	-0.008	1.283
$T-(Li@C_{60})^+$	-10.97(-8.05)	-12.17(-9.38)	-8.05	-0.049	0.462	-0.010	1.271
$G-(Li @C_{60})^+$	-15.26(-11.70)	-19.90(-15.99)	-9.11	-0.016	0.470	-0.008	1.272
C-(Li@C ₆₀) ⁺	-16.92(-14.51)	-20.69 (-16.99)	-7.28	-0.009	0.500	-0.010	1.283

"M06-2X/6-311++G**//M06-2X/6-311G**; CPCM+M06-2X/6-311++G**//CPCM+M06-2X/6-311G**; PBE-D/6-311G**

b M06-2X/6-311++G**//M06-2X/6-311G**

Frontier orbitals energies for NAB-Li@C₆₀ complexes and their ingredients. All energies are in eV.

HOMO (SOMO) I C ₆₀ -7.60 A -7.45 T -8.17 G -7.20 G -7.20 Li@C60 -5.39 A-Li@C60 -5.24 T-Li@C60 -5.34 G-Li@C60 -5.34	A06-2X/6-311G**		CPCM+M06-2	X/6-311G*	*
C ₆₀ -7.60 A -7.45 T -8.17 G -7.20 C -7.20 C -7.20 Li@C60 -5.24 A-Li@C60 -5.24 T-Li@C60 -5.35 G-Li@C60 -5.34	SOMO) LUMO	Π	(OMOS) OMOH	DMU	Π
A -7.45 T -8.17 G -7.20 C -7.20 Li@C60 -5.39 A-Li@C60 -5.24 T-Li@C60 -5.34 G-Li@C60 -5.34	60 –3.12	8.02	I		
T	45 -0.23	8.19	-7.36	0.40	5.90
G -7.20 C -7.85 Li@C60 -5.39 A-Li@C60 -5.24 T-Li@C60 -5.35 G-Li@C60 -5.34	17 –0.45	8.87	-7.83	0.16	6.27
C -7.85 Li@C60 -5.39 A-Li@C60 -5.24 T-Li@C60 -5.35 G-Li@C60 -5.34	20 –0.53	7.73	-7.02	0.83	5.50
Li@C60 -5.39 A-Li@C60 -5.24 T-Li@C60 -5.35 G-Li@C60 -5.34	85 –0.45	8.76	-7.78	0.31	6.06
A-Li@C60 -5.24 T-Li@C60 -5.35 G-Li@C60 -5.34	39 –3.29	5.98	-4.57	-2.59	3.70
T-Li@C60 -5.35 G-Li@C60 -5.34	24 –3.16	5.70	-4.56	-2.53	3.69
G-Li@C60 -5.34	35 –3.27	5.81	-4.57	-2.54	3.68
	34 –3.25	5.74	-4.55	-2.53	3.68
C-Li@C60 –5.24	24 –3.16	5.60	-4.56	-2.53	3.69