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## PHYSICS AND CHEMISTRY

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# The Nitron (Anti-cancer drug) Interaction with Carbon Nanotubes (Delivery): The Semi-Empirical Approach

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Samera F. Resan  
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**ABSTRACT.** Modeling of the quantum interaction properties of nitron radicals on the surface walls of the single-walled carbon nanotubes is investigated by PM3 calculations. It is found that the interaction potential of the nitron radical (2) with the tubes results in stable complexes when it reacts with the nitron (2) and metastable conformations with nitron (1). We have studied the effect of the diameter, length, position, and rotation characteristics of the CNT on binding the nitron. Our results suggest that the binding energy is lower as the CNT diameter increases, while as the CNT length increases the binding energy initially increases and then slightly increases.

**KEYWORDS.** anti-cancer, drug delivery, CNT, nitron, semi-empirical calculation, binding energy

### INTRODUCTION

The characteristics and behavior of nanomaterials is a new field for science, being limited to nanoscale dimensions (1–100 nm). The nanostructures have a quantum nature due to their

atomic and molecular size. Thus, the prediction and understanding of these nanomaterials must be based on experimental and theoretical research. The method in which experiments can approach the atomic level for nanomeasurements is a question that needs answering.

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Carbon nanotubes (CNT), which were discovered by Iijima,<sup>[1]</sup> are sheets of graphite wrapped around a cylindrical form. CNT can be synthesized by the techniques of electric arc discharge, laser ablation, and catalytic decomposition of hydrocarbons.<sup>[2–8]</sup> Because the CNT have special high surface areas, high mechanical strengths, unique electronic properties, excellent chemical and thermal stability, and the ability to be applied at atomic levels, it makes them promising structures for working in a wide field of application. Several applications, due to their unique properties, are in drug delivery, biosensors, antigen recognition, and DNA hybridization. Many of these applications are in biology and medicine. The ability of CNT to penetrate into cells offers the potential use of CNT as vehicles for the delivery of drug and antibiotic molecules without toxic effects.<sup>[9–20]</sup> Bianco et al. developed a new strategy for the multiple functionalization of CNT with amphotericin B (AmB) and fluorescein.<sup>[21]</sup> Ammonium functionalized CNT for the ability to form supra-molecular complexes with nucleic acid by electrostatic interactions. This CNT-DNA complex acts as a non-viral vector to deliver plasmid DNA into the cell.<sup>[22]</sup> Azamian and colleagues used a simple non-covalent route to attach a reactive molecule to the sidewall of SWNT. This reactive molecule could then be used to attach to the wall of the tubes. This related work is of interest to the development of biosensors based on nanotubes.<sup>[23]</sup> Lieber's group has shown that SWNT are ideal probe tips for AFM due to their small diameter.<sup>[24]</sup> CNTs also sustain the osteoblast growth and bond formation, and thus represent a potential technological advance in bone bio-engineering.<sup>[25]</sup> In spite of the wide applications for CNT, theoretical studies of the interaction mechanism between the carbon nanotubes and biomolecules are few.<sup>[20,26,27]</sup> Only Mavrandonakis et al. have studied the interaction of an amino acid with CNT.<sup>[27]</sup>

In this work, we explore the ability of the CNT to become vehicles for the delivery of the anti-cancer drug (nitron) by examining the interaction of the nitron radicals on the surface of single-walled CNT, which is defined as bond-alternation patterns of an armchair.<sup>[28]</sup> Then, we examine this interaction as a function of CNT

length and diameter. Also, we investigated the effect of position modifications of the nitron-CNT bond on the interaction energy. Lastly, we examined the effect of nitron radical rotation about the bond, which produces on the surface of CNT on the interaction energy.

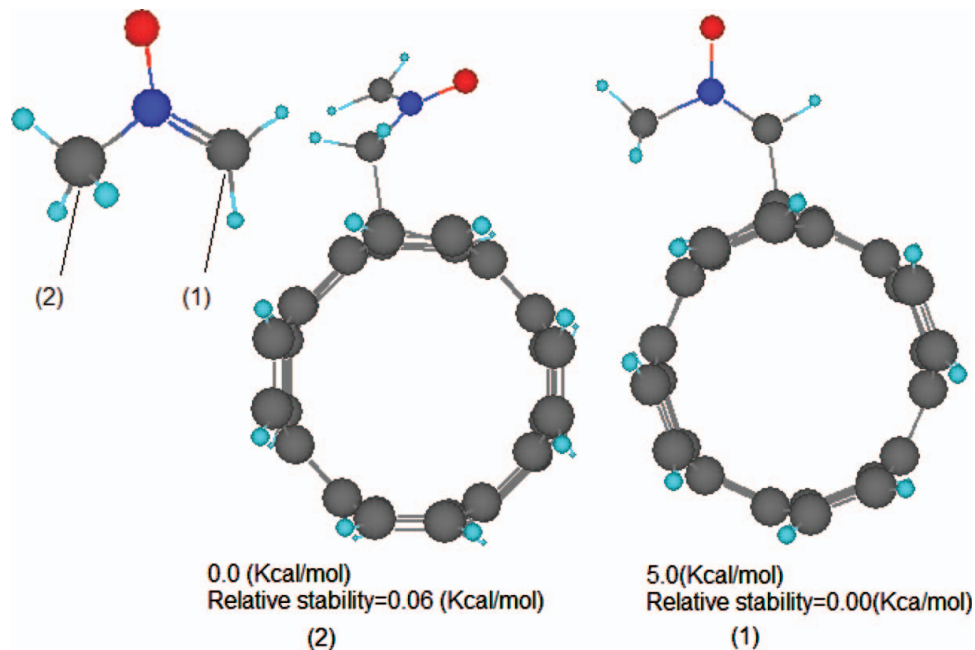
## COMPUTATIONAL DETAILS

The theoretical calculations of molecular quantum mechanics can be used to investigate properties beyond the scope of current crystallographic methods and to bridge gaps in understanding experimental results. In many cases, the results of the experimental methods are unable to accurately describe small complex systems, or it can be used to further investigations and to predict the physical nature of hydrogen bonding interactions. Molecular quantum mechanics provides the interaction energies that are not provided by x-ray and NMR experiments. To investigate the structural and electronic properties of CNTs decorated with the nitron radicals, we used the PM3 method. PM3 is a reparameterization of AM1, which is based on the neglect of diatomic differential overlap (NDDO) approximation. PM3 differs from AM1 only in the values of the parameters. The parameters for PM3 were derived by comparing a much larger number and wider variety of experimental versus computed molecular properties. PM3 is primarily used for organic molecules, but is also parameterized for many main group elements. The problem in quantum computational that arises is how to perform an accurate calculation for a nano-sized system without ending in a prohibitively large computation. The dangling bonds at the ends of the tubes were saturated by hydrogen atoms. The resolution of PM3, as implemented in the HyperChem Release 7.52 for Windows Molecular Modeling System program package,<sup>[29]</sup> was employed for the geometry optimizations.

## RESULTS AND DISCUSSION

For our investigation, it was important to determine the most stable isomers of the nitron

FIGURE 1. Geometry optimized structures of two isomer of nitron radicals with CNT and their relative stability using PM3 method. (Color figure available online.)



radical as a complex with CNT. We calculated the interaction, binding energy BE, of the nitron radicals with the CNT,  $BE = E_{\text{nitron+CNT}} - (E_{\text{nitron}} + E_{\text{CNT}})$ ; where  $E_{\text{nitron+CNT}}$  is the energy of the complex of nitron and CNT. We find that upon reaction with the single-tube wall, the nitron radical forms stable complexes when the CNT reacts with the nitron radical (2) and comparable with the nitron radical (1), as shown in Figure 1 along with their relative binding energies and relative stabilities. Thus, we further studied only the interaction of the nitron radical (2) with CNT. The first important factor is the interaction of nitron with CNT as a function of the CNT diameter. The effect of increases in the CNT diameter on the BE of the nitron radicals with CNT (for constant length equal  $7.35\text{\AA}$ ) are shown in Figure 2. An increase in diameter of the CNT leads to a decrease in the binding energy of the nitron radicals with CNT. This case shows the mechanism of lower binding between the nitron with CNT as the CNT diameter increases. In the nitron binding, a single covalent nitron-CNT bond is formed with CNT. The nitron-CNT bond becomes longer as the diameter of the CNT increases (Figure 3). The increases of the CNT

diameter shown exponential increase of the covalent bond length and decrease the binding energy, see Figure 2. This suggests there is a relationship between the covalent bond length increase and the decrease in the binding energy. The second important factor is the interaction of nitron with different lengths of CNT evaluated

FIGURE 2. The binding energy between the nitron with CNT as a function of the CNT diameter using PM3 method. (Color figure available online.)

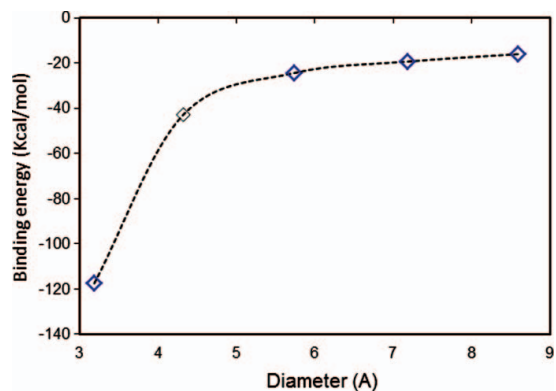


FIGURE 3. The length of nitron-CNT bond as a function of the CNT diameter using PM3 method.

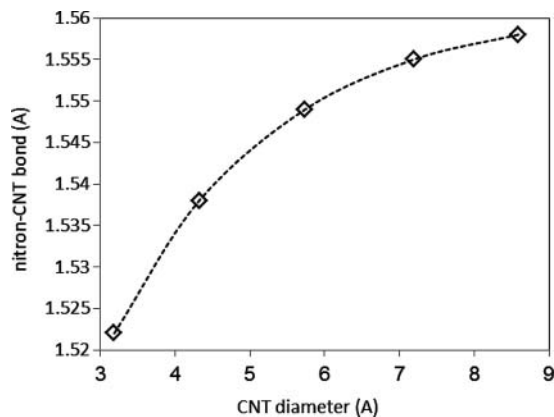
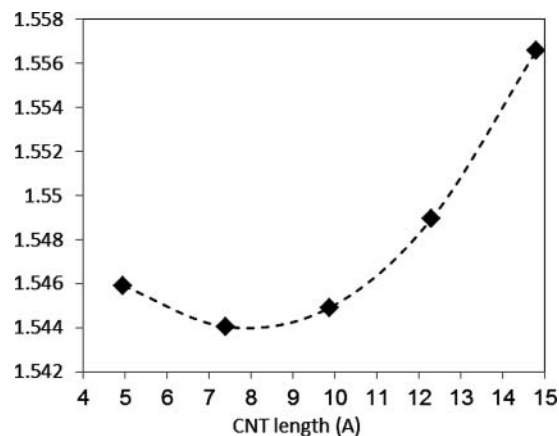


FIGURE 5. The length of nitron-CNT bond as a function of CNT length using PM3 method.



(for constant diameter equal  $5.45\text{\AA}$ ). The CNT length during their synthesis is a very important property. The binding energy of the nitron radicals with CNT depends on the length of CNT, as shown in Figure 4. As the length of the CNTs increase, the binding energy between the nitron radicals and CNT also increases. Note that in each case we put the nitron-CNT bond in the middle of the CNT. Beyond a few Angstroms of length,  $\sim 10\text{\AA}$ , the binding energy essentially did not change. Thus, we concluded that the binding between the nitron and CNT depends on the diameters of CNT more than their lengths. The nitron-CNT bond length as a function of CNT length is shown in Figure 5. Initially, there

is a nominal decrease for a few angstrom of CNT length, and then it increases as the CNT length increases. However, the nitron-CNT bond increases as the length of CNT increases. This behavior for interaction of nitron radical with CNT is opposite to the interaction of glycine radical with CNT.<sup>[30]</sup> The relative stability of the nitron radicals with CNT increases as a function of the nitron-CNT bond position on the cylindrical surface of CNT, as this position changes from the middle of the CNT toward one of the

FIGURE 4. The binding energy of the nitron radicals with the CNT as a function of CNT length using PM3 method.

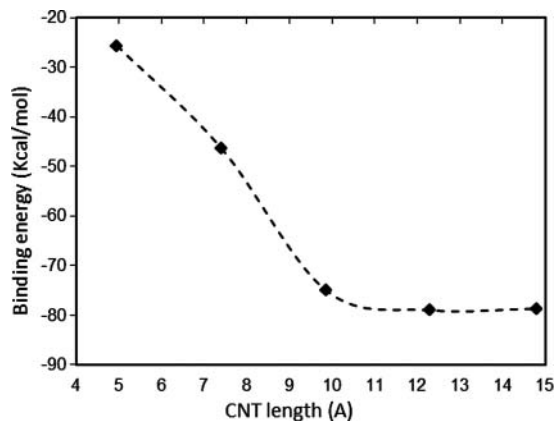


FIGURE 6. The relative stability of the nitron radicals with CNT as a function of the position of the single covalent nitron-CNT bond that formed, from the middle of the CNT toward one of their two ends using PM3 method. (Color figure available online.)

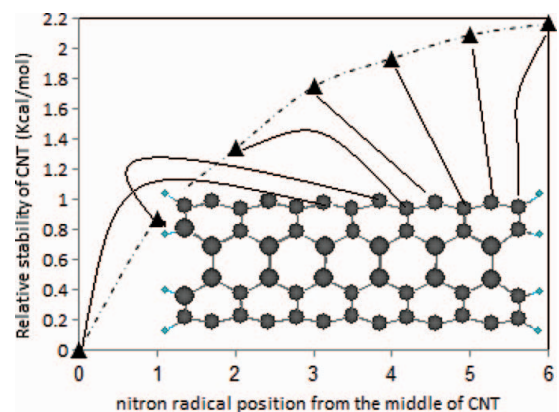
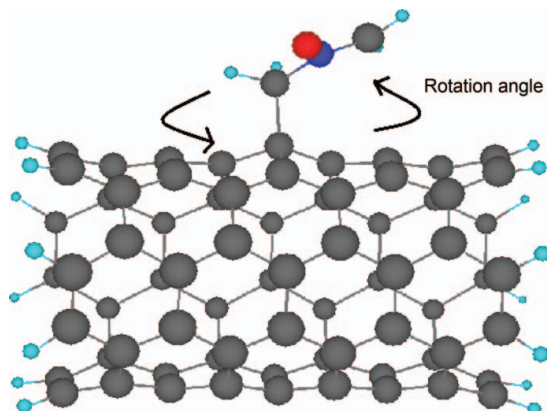
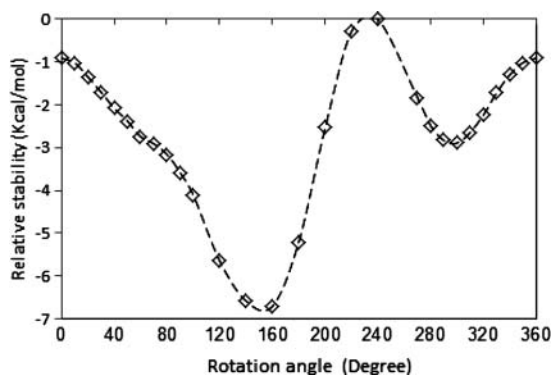


FIGURE 7. The angle of rotation processes. (Color figure available online.)



two ends (Figure 6). The complexes formed by the nitron radical and the single tube wall are more stable when the reaction occurs far from the middle of the CNT. Also, this behavior is opposite to the stability of the glycine radical on the surface of CNT.<sup>[30]</sup> Figure 7 shows the direction of the rotation process of the nitron radical around the nitron-CNT covalent bond on the surface of CNT (for constant distance equal  $5.71\text{\AA}$  and length equal  $9.82\text{\AA}$ ). Figure 8 shows the relative stability as a function of rotation of the nitron radical about the nitron-CNT bond. In the optimized case, at  $0^\circ$ , we rotated the nitron in an angle from  $0^\circ$  to  $360^\circ$ . The relative stability decreased until the angle was  $160^\circ$ , then it increased. From the rotation angles of  $210^\circ$  to  $250^\circ$ , the stability became more than the opti-

FIGURE 8. The relative stability as a function of the rotation angle using PM3 method.



mized case. Figure 8 shows two potential wells, but with different depths. The nearest distance for the oxygen atom from the surface of CNT was at a rotation angle of  $250^\circ$ , which may increase the related stability. The relative stability due to the rotation between the nitron and CNT may relate to the overlap of the molecular orbitals between them.

## CONCLUSIONS

We have performed PM3 calculations on the structural properties of CNT upon adsorption of various nitron radicals. Among these two isomers, nitron radical (2) forms stable complexes with CNT. The results of the diameter and length of the CNT on the binding energies with nitron showed a decrease as the CNT diameter increased, while the binding energies increased with a CNT length increase. The nitron radicals are shown to prefer to bond and situate far from the middle of the CNT cylindrical surface. The stereo geometry (curvature of CNT surface) between the nitron radicals and CNT may limit the binding energies behavior. The rotation of nitron around the nitron-CNT bond showed a new optimized point.

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