

Interaction of size expanded DNA bases with small neutral gold nanoclusters

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Microscopic understanding of the interaction between biological (or organic) molecules and metal nanoparticles is an important aspect in the emerging area of nanobiomaterials.¹ Gold nanoparticles, being nontoxic and highly biocompatible, are attractive candidates for therapeutic applications such as drug delivery vehicles. Conjugated gold nanoparticles are of fundamental importance in the development of potential miniature devices. Such systems find applications in catalysis, molecular electronics, DNA sequencing as well as in microscopy markers.² It has been realized that the optical, electronic and catalytic properties of such systems depend characteristically on the conjugating molecule that forms complex with the gold nanoparticles. This has directed research efforts towards developing different protocols for synthesizing conjugated gold nanoparticles of various sizes and shapes with a variety of conjugated molecules.

DNA-gold interactions play an important role in nanobiotechnology. Recent experimental and theoretical studies have focused on understanding the nature of DNA-gold interactions. Modified DNA analogs, in which natural DNA base are replaced by size-expanded bases (x-bases³ and y-bases⁴) have recently been prepared. Enhanced conducting and fluorescent properties of size expanded bases in contrast to natural DNA bases, as well as expanded dimensions of the resulting modified helices makes xDNA and yDNA attractive candidates for development of nano scale molecular devices. We have recently studied the nature of intermolecular interactions between gold clusters and x-bases (and natural DNA bases).⁵

To understand the exact nature of yDNA-metal interactions, we have performed quantum chemical calculations on (y-base)-Au₃ and (y-base)-Au₆ systems. We investigate the interaction of y-bases with and gold clusters employing density functional theory with hybrid B3LYP exchange correlation functional using Gaussian03 suite of programs. Two equilateral gold triangles were placed on each side of the y-bases in their optimized geometry in order to model the first layer of the FCC bulk gold crystal. In order to investigate the basis set effects, three methods were used in this research: (a) LANL2MB was applied to all atoms (b) LANL2DZ basis set was used for all atoms and (c) Los Alamos RECP (LANL2DZ) pseudopotential was used for gold atoms, while 6-31G+(d) basis set was used for all atoms of the y-bases. All geometry optimizations were performed using GDIIS method with tight convergence criteria. Vibrational analysis has been carried out in all cases in order to characterize the computed stationary points as absolute minimum structures, and also to evaluate the thermodynamic parameters. Nucleus independent chemical shift (NICS) values show enhanced aromaticity of the ring [π] systems in the complexed y-bases. Natural bond order (NBO) analysis has been carried out in order to characterize noncovalent interactions between gold clusters and conjugated molecules.

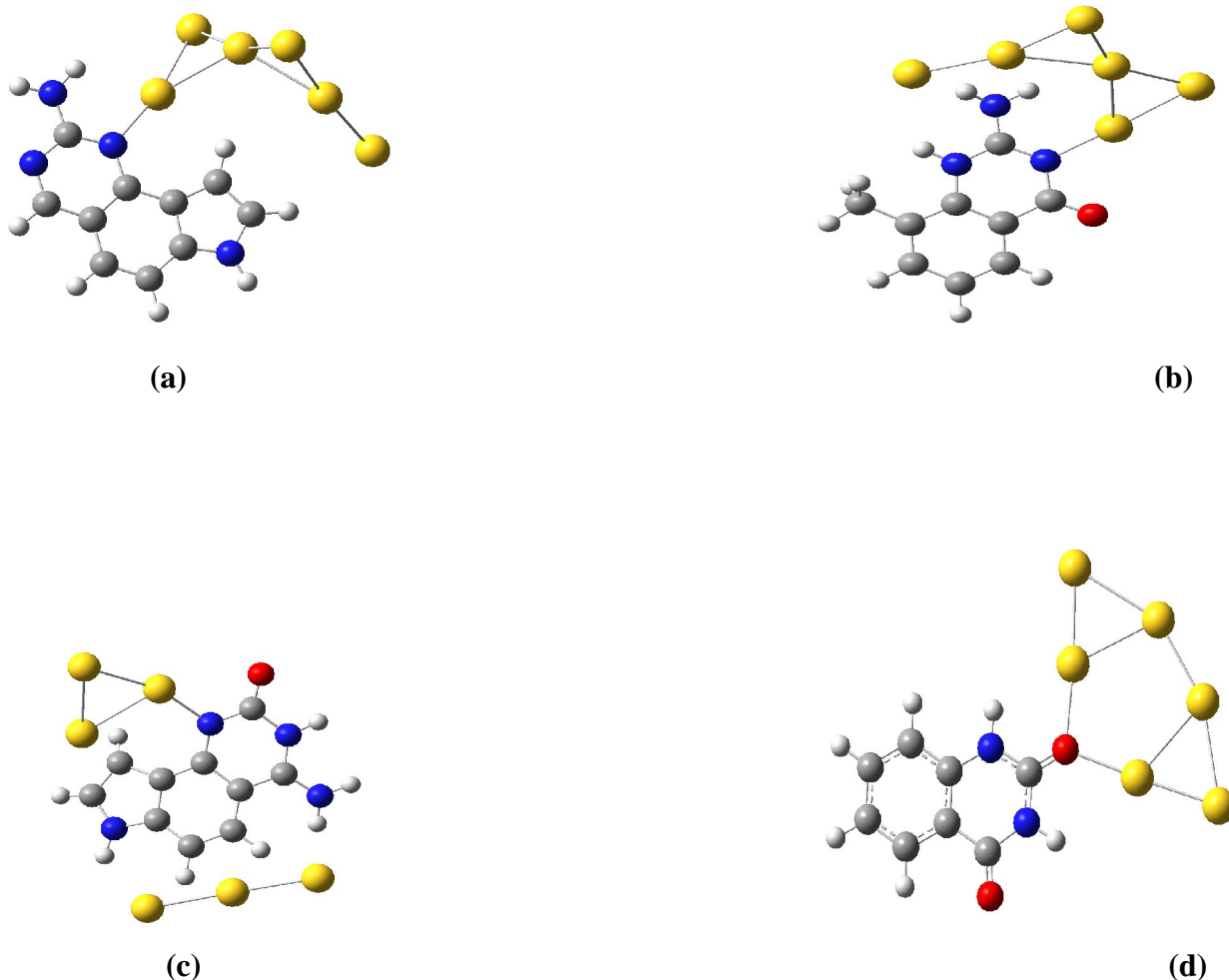


Fig. 1. Optimized structures of (y-base)-Au₆ complexes obtained at B3LYP/RECP(gold)6-31+G(d,p) level of theory. (a) yA-Au₆ (b) yC-Au₆ (c) yG-Au₆ (d) yT-Au₆

In Fig. 1, the optimized structures of complexes of y-bases with gold clusters are shown. It is clear from the diagram that the y-bases interact asymmetrically with gold clusters. No other local minima are seen in the neighborhood of these geometries. The Au₆ complexed geometries of y-Adenine (yA), y-Cytosine (yC) and y-Guanine (yG) show that gold atoms prefer to bind the bare nitrogen atoms of the y-bases instead of the oxygen atoms. The absence of bare nitrogen in y-Thymine (yT) forces the gold atoms to bind the oxygen atoms. The binding of gold atoms to high electronegative elements (N and O) suggests a Lewis acid (Au) -Lewis base (N or O) type of interaction between metal clusters and y-bases.

The binding energies, enthalpies of formation and free energies of formation of (y-base)-Au₆ complexes. The binding energies of these complexes are influenced by charge transfer from y-base atoms to Au atoms. The binding energy follows the order: yG-Au₆ > yC-Au₆ > yA-Au₆ > yT-Au₆, whereas the amount of charge transfer (from y-base to gold atoms) follow the order: yG-Au₆ > yA-Au₆ > yC-Au₆ > yT-Au₆. This implies that the binding is also influenced by factors other than charge transfer interactions. Apart from direct N-Au and O-Au coordinate

binding, the interaction between gold atoms and y-bases in these complexes is also reinforced by N-H...Au of hydrogen bonds. The presence of more hydrogen bonds between H atoms of y-base and Au atoms in yC-Au₆ and yG-Au₆ explains the relatively greater binding energy in both these complexes. The greater number of Au-H hydrogen bonds in yC-Au₆ explains the relatively greater binding energy than yA-Au₆ complex, inspite of relatively greater charge transfer in the later.

An important structural change which takes place in y-bases on gold complexation is an increase in bondlengths of all the atoms of y-bases leading to their expansion in volume. In spite of bondlength and volume expansion, these complexes seem to be quite stable as reflected from their binding energy values. The reason of such a large volume expansion may possibly be some form of an electrostatic cavity driven by gold clusters and massive charge transfer to the gold cluster resulting in electronic redistribution within the y-base itself. The decrease in HOMO-LUMO gap on gold complexation in all these cases indicates possibly greater conducting properties of gold complexed y-DNA.

In short, we have computationally described the interaction of yDNA bases with small gold clusters through a variety of aspects including geometrical, spectroscopic and energetic ones. To get insights into essential elements of interaction, the contribution of typical energy interaction components have been investigated. Further studies exploring the robustness of these findings with respect to variation in cluster sizes as well as geometrical constraints are in progress.

References

1. Ratner, M.; Ratner, D. *Nanotechnology: A Gentle Introduction to the Next Big Idea*; Prentice Hall: Upper Saddle River, NJ, **2002**.
2. (a) Jin, R.; Cao, Y.; Mirkin, C. A.; Kelly, K. L.; Schatz, G. C.; Zheng, J. G. *Science* **2001**, 294, 1901. (b) Mirkin, C. A.; Letsinger, R. L.; Mucic, R. C.; Storhoff, J. J. *Nature (London)* **1996**, 382, 607.
3. (a) Liu, H.; Gao, J.; Maynard, L.; Saito, D.Y.; Kool, E.T. *J. Am. Chem. Soc.* **2004**, 126, 1102. (b) Liu, H.; Gao, J.; Lynch, S.R.; Saito, D.Y.; Maynard, L.; Kool, E.T. *Science* **2003**, 302, 868. (c) Liu, H.; Gao, J.; Lynch, S.R.; Kool, E.T. *J. Am. Chem. Soc.* **2004**, 126, 6900. (d) Gao, J.; Liu, H.; Kool, E.T. *J. Am. Chem. Soc.* **2004**, 126, 11826. (e) Liu, H.; Gao, J.; Kool, E.T. *J. Am. Chem. Soc.* **2005**, 127, 1396. (f) Liu, H.; Gao, J.; Kool, E.T. *J. Org. Chem.* **2005**, 70, 639. (g) Lee, A.H.F.; Kool, E.T. *J. Am. Chem. Soc.* **2005**, 127, 3332. (h) Gao, J.; Liu, H.; Kool, E.T. *Angew. Chem., Int. Ed.* **2005**, 44, 3118.
4. (a) Liu, H.; He, K.; Kool, E.T. *Angew. Chem., Int. Ed.* **2004**, 43, 5834. (b) Lee, A.H.F.; Kool, E.T. *J. Org. Chem.* **2005**, 70, 132.
5. Sharma, P.; Singh, H.; Sharma, S.; Singh, S.; *J. Chem. Theory Comput.* (in press).