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DFT Investigation on Oxidation and Hydration Effect for Double Hydrogen-Bonded System

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Abstract

The trust worthy B3LYP/6-311+G* method is employed to investigate the double hydrogen-bonded system with a special emphasis on oxidation and hydration effect. Proton transfer occurs spontaneously upon oxidation from amido group to adjacent imidazole fragment. The larger the pH value of the environment is, the significant the influence to the geometry structure is. The electron population on the HOMO orbital determines the IR vibrational frequency of the H-bond being blue-shift or red-shift. The complex prefers to be oxidized under the basic condition. The weak acidic environment is recommended to prevent the DNA mutation.

1. Introduction

DNA damage and corresponding structural variations of the base pairs have attracted a lot of experimental and theoretical efforts. Generally, the DNA damage may originate from radiations, chemical reactions, and electron attachment /detachment. These ways are interrelated and coupled with each other, which makes the damage mechanism more complicated. Single-electron reduction/oxidation, caused *by* electron attachment/detachment, is ubiquitous in physical, chemical, and biological systems. The appropriate redox reaction provides the driving force for the chemical process, photosynthesis and respiration, and operation of living things. While the improper process causes the DNA mutation, resulting in various diseases, such as cancer. When electron transfer is coupled with the proton shift, the mechanism becomes more enigmatic. The coupling of proton chemistry with redox reactions is important in many

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enzymes and is central to energy transfer in biology.

DNA triplexes have received considerable attention because of their potential both for control of gene expression and as therapeutic agents [1-5]. Although the triplex is affected by numerous contributions such as stacking, hydration, counterions, phosphate environment, backbone restrictions, H-bond is the predominant interaction that determines the structure and dynamics of DNA triplexes. A special work carrying out with the density functional theory method was focused on the H-bonds of DNA triplexes recently [6]. The imidazole ring (ImH) is an essential constituent of many biological compounds such as adenine, guanine, histamine, and the histidine residues of proteins. The unique ring structure of ImH permits it as the H-bridge because one proton can be picked up by the bare N atom and the other one can be released from the other N atom. This action has been employed to explain the proton conductivity properties [7-8] of solid ImH material and also in the actual biological surrounding where a long H-bonded chain is present, many investigations have been carried out in both experimental [9-12] and theoretical [13-19] fields.

Adenine, an elementary chemical component of DNA, RNA, and Adenosine triphosphate (ATP), playing an essential role in replication in all known living systems, is significant in many other aspects of biochemistry including celluar respiration and protein synthesis [20-29]. The dehydrogenation of adenine and the H-atom loss in pyrimidine DNA bases induced by low-energy electrons have been explored [30-31]. The relatively high activity of adenine N9 site has been suggested in previous experimental and theoretical studies [32-36]. The dehydrogenated adenine (DA) has been observed in these investigations, while no related discussions can be found yet. Recently the noncovalent interaction between adenine and ImH has been reported [37]. The investigation on triplex ImH-adenine-ImH (HIAIH), which has been taken as the prototype model in our previous work [38], should furnish some significant and detailed information about the structure and the properties of the biomolecular systems.

As is known that the coupling of base pairs is through multi-hydrogen bonds, therefore, only the matrixes involving double H-bonds between **DA** and ImHs are considered here. In present work, the coupling characteristic, the corresponding IR frequency shifts, the frontier molecular orbitals and charge populations, as well as the energy changes are investigated based on double hydrogen-bonded ImH-dehydrogenat -ed adenine-ImH trimer (**HIDAIH**). In this section, the hydration and the oxidation effects are represented. The conclusions are deduced in the last part. In the following chapter, a brief introduction on computational details is shown.

2. Computational Details

Hybrid density functional (DFT) methods have proven to be successful in describing nucleic base dimers [39] and DNA triplex [6]. Especially, the B3LYP hybrid functional is found to be reliable for geometry optimizations and property explorations [22, 40-44]. Therefore, all of the calculations including the geometry optimization, IR frequency, and the related energies were performed employing the B3LYP functional equipped with 6-311+G(d) basis set, implemented with the Gaussian 03 program [45]. To clarify whether the optimized structures correspond to the genuine local minima on the global potential energy surface or not, the vibrational frequency analyses were carried out at the same level. The related energy calculations were all corrected with the zero-point energy, which was obtained during the IR frequency

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calculation. The oxidation occurs when the electron is detached from the highest-occupied molecular orbital (HOMO), and the corresponding energy changes is defined as the ionization potential (IP). Any bond length variations should reflect the electron density pattern of the HOMO orbital. Those in bonding regions should be weakened and lengthened, while those locate in anti-bonding regions should be strengthened and therefore shortened. For the selected model, HIDAIH, odd electron occupies the HOMO, therefore, the lowest-unoccupied molecular orbital (LUMO) of the oxidized system correspond to the HOMO of HIDAIH. Thus, the HOMO and LUMO orbitals are all explored for the inspection of the oxidation and hydration effect. The spin density analyses were also performed to investigate the charge population on oxidation and hydration.

The basicity varies upon both proton dissociation and hydration with H-bond formation, which can be reflected by the pH value in solution experimentally. Thus, in order to provide some useful information to the experimentalist, the deprotonated ImH and the hydrated ImH are all explored to investigate the influence of basic variation.

3. Results and Discussions

The atomic numbering of dehydrogenated adenine (**DA**) is shown in Figure 1. The optimized geometry parameters of **DA**, reduced **DA**, and oxidized **DA** are all collected in Table 1. The primary bond lengths of the optimized model system (**HIDAIH**), triplex deprotonated imidazole-dehydrogenated adenine-imidazole (**IDAIH**$^-$), the hydrated **HIDAIH** (**HIDAIHW**), and the hydroxyl-**HIDAIH** (**HIDAIHOH**$^-$) as well as the corresponding oxidized complexes are all represented in Figure 2. IR frequencies of these trimers are described in Figure 3 and the assignment of the H-bonds with distinct IR intensity is performed. The charge populations of the optimized complexes are delineated in Figure 4. Figure 5 represents the HOMO, LUMO, and the spin densities of these trimers.

According to our experience on **HIAIH** [38], it is significant to explore the electronic effect on **DA**. Table 1 demonstrates that the bond length variations upon electron attachment are in reverse with those on oxidation. This phenomenon is different with our findings on adenine, as declare that the effect introduced by adenine hydrogen-loss is distinguished. Similar to that of adenine, the C_6-N_6 reduces upon oxidation while it lengthens upon electron capture. The positive charge population of **DA** shown in Figure 1 illustrates that N_6-Hs prefer to participate in H-bond formation with the ImH fragments. The oxidation of **DA** is endothermic (194.6kcal/mol), which stands between adenine (186.8kcal/mol) and ImH (201.1kcal/mol), while its reduction is an exothermic process (-74.3kcal/mol), in reverse with adenine (8.6kcal/mol) and ImH (19.7kcal/mol). As indicate that **DA** prefers to capture an electron and not easy to be oxidized. While oxidative damage to DNA plays a key role in mutagenesis and carcinogenesis, which has attracts considerable interest recently [46-52]. Therefore, only the oxidation effect on trimer is investigated following.

3.1 Geometry Characters

The primary H-bond parameters and the optimized triplex structures are all represented in Figure 2. As shown in the figure, two H-bonds, N…H-C and N_6-H…N, are generated between adenine and every ImH fragments of **HIDAIH**. Although the H atom has been detached from N_9 site of adenine, the influence to these four H-bonds is very weak and no change is found as

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compared to those of **HIAIH** [38]. Thus, it is presumed that the variation of H dissociation from N_9 on charge population of adenine is feeble. Upon oxidation, the proton transfers spontaneously from N_6 to the bare N of right ImH. Such phenomenon has been observed in **HIAIH** and ImH dimer [19] systems. The reduction of two central N-H…N bonds and the lengthening of two peripheral C-H…N bonds upon oxidation are also illustrated by Figure 2, as suggests that the electron density on adenine framework decreases upon oxidation. The double bond characteristic of C_6N_6 increases, which is represented with the reduced bond length.

The pH value enhances when the proton is detached from the bonded N of left ImH, **IDAIH**$^-$. The influence on geometry structure of this proton detachment is significant as displayed in Figure 2. First of all, the proton is pulled by left ImH fragment from N_6 owing to its strong basicity. This proton transfer results in the basic enhancement of adenine coupled with the decreasing of proton donor capability and the increasing of the proton accept ability. Second, the right ImH rolls and rotates, resulting in the breaking of original double H-bonds and the formation of novel N_7…H-N bond with the right ImH fragment which is perpendicular to adenine. For the oxidized triplex, **HIDAIH**$^+$, when the proton is peeled off from the left ImH fragment, **IDAIH**, the transferred proton locates back to N_6 and the other proton on N_6 can be transferred spontaneously to left ImH fragment where the proton detachment occurs, following with the lengthening of all H-bonds. During this process, there is no distinct variation for C_6N_6 bond, which still carries typical double bond characteristics.

The basicity of the right ImH increases when a water molecule binds on it with H-bond. Accordingly, as compared with those of **HIDAIH**, the N_6-H…N bond length between adenine and the right ImH of **HIDAIHW** reduces, while the C-H…N bond increases owing to the strengthening of C-H coupling. It can also be concluded that the variation of basicity owing to water binding is less significant as compared to that upon proton detachment. Similar to **HIDAIH**, the proton transfers spontaneously to right ImH as an electron is eliminated from **HIDAIHW**.

For the hydroxyl bonded ImH, the pH value is stronger than the hydrated ImH while weaker as compared to deprotonated ImH. Therefore, the geometry variations of the triplex, **HIDAIHOH**$^-$, should be larger as compared to the alterations of **HIDAIHW** and less than the changes of **IDAIH**$^-$, as is illustrated distinctly in Figure 2 that the proton on N_6 transfers spontaneously to the right ImH fragment whose basicity is enhanced. The N_6-H…N bond between adenine and the other ImH is broken with the rolling of ImH around C-H…N bond. Although the left ImH is still in the same plane with adenine, there is only C-H…N bond and the electrostatic interaction between electronegative N(ImH) and electropositive H(N_6). The other spontaneous proton transfer is observed between ImH and hydroxyl group, as demonstrates that OH is a strong base. Upon oxidation, the double bond characteristic of C_6N_6 increases and the N_6-H…N is regenerated with the rolling back of the left ImH.

By extrapolation, the proton transfer occurs spontaneously under strong basic environment or upon oxidation. If the base is strong enough, the rolling, or even the rotating of the other ImH fragment occurs easily.

3.2 IR Frequencies

IR spectroscopy is one of the standard methods to investigate molecular structures, providing the information about the structural

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details including the H-bonds and protonation status of chemical groups at the active site. The IR vibrational frequency analyses are performed to get related structural information as well as to validate the triplexes corresponding to the local minima on the global potential energy surface.

Figure 3 collects the harmonic vibrational IR spectra of all optimized triplexes. The IR spectra of the H-bonds involving the N_6H group carry significant intensity, and they are assigned in the figure. Two N_6H…N stretching vibrational modes of **HIDAIH** combined together, generating the symmetry N-H…N and anti-symmetry N-H…N stretching modes at 3207.8 and 3314.6 cm^{-1}, respectively. After oxidation, these two stretching modes are red-shifted in different degree. The N_6-H…N stretching, is assigned at 3036.9 cm^{-1}, while the vibration at 2766.7 cm^{-1} is assigned as the N_6…H-N mode, which is red-shifted by more than 500 cm^{-1} owing to its electron density reduction. The spectra variation of N_6…H-N stretching mode is small although the proton transfers upon proton detachment on left ImH, as illustrates the similar electron environment before and after proton dissociation. The other N_6-H…N stretching disappears for the rotation of right ImH fragment and another mode with strong intensity at 3113.8 cm^{-1} is assigned to the N_7…H-N stretching. For the oxidized system, **IDAIH**, the assignments are performed for N_6…H-N and N_6-H…N stretching modes at 3457.3 and 3193.2 cm^{-1}, respectively. As compared with the IR spectra in **IDAIH**$^-$, distinct blue-shift can be observed for N_6…H-N stretching when the system is oxidized. The blue-shift of H-bond upon oxidation has attracts extensive attentions [19, 53-54]. The vibrational stretching of two N_6-H…N modes are red-shifted slightly (3167.1 and 3302.8 cm^{-1}) upon hydration owing to the weakening of two H-bonds originated from the basic enhancement of right ImH. These two modes are red-shifted distinctly in the oxidized system, **HIDAIHW**$^+$, although it is not as significant as that in **HIDAIH**, the phenomenon is similar. Only one N_6…H-N bond stretching with strong intensity can be found at 3135.8 cm^{-1} in the hydroxyl bonded system, **HIDAIHOH**$^-$. The other one with strong intensity corresponds to the N…H-O stretching, which can be found in both hydrated and hydroxyl bonded systems. After the electron detachment, the N_6…H-N stretching is blue-shifted by 300 cm^{-1}, which originates from the electron density decreasing on **DA** fragment. Another N_6-H…N stretching is assigned at 3181.2 cm^{-1}.

It can be observed that the IR spectroscopy may support some complementary information for geometry structure, especially for the H-bond. Furthermore, the calculated IR information can be compared with the experimental data to verify the reliability of the selected theoretical method. Thus, the IR spectroscopy is a very useful tool for both experimentalist and theoretician.

3.3 Charge Populations

The nature of the variation reflected by the geometry structure and the IR frequency can be traced from the charge populations. Figure 4 represents the charge populations on every fragment of the optimized complexes. With the analyses on the charge population and the bonding mode, it is supposed to furnish some underlying information to explain the geometry structure changes and the IR frequency alterations. Upon oxidation, the electron detachment occurs usually on the highest occupied molecular orbital (HOMO), from which some significant information about the geometry variation and the IR spectra shift upon oxidation can be obtained. After oxidation, the HOMO corresponds to the lowest unoccupied molecular

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orbital (LUMO) of the oxidized system when there is only one electron on this HOMO. It is effective especially in analysis on the H-bond variation [18, 41]. The HOMO, LUMO, and the spin densities of the investigated complexes are collected in Figure 5.

There is no charge on every fragment of the neutral triplex system, **HIDAIH**, as shown in Figure 4. The single electron occupies the HOMO orbital and populates on **DA** (Figure 5). The N_6H group is involved in HOMO region. Upon oxidation by electron detachment, the system carries one positive charge, almost all of which locates on the right ImH fragment (Figure 4). Thus, it is the proton not hydrogen transferred from N_6 to the right ImH. The HOMO populates on left ImH now and the N_6H coupling is weakened. Therefore, the IR spectra red-shifts of two H-bonds are observed. When a proton is detached from left ImH of **HIDAIH**, a negative charge should left on left ImH. While Figure 4 tells us that almost all negative charges populate on the middle **DA** fragment. Therefore, it is the proton not the H atom transferred from N_6 to the left ImH and the single electron is still left on **DA**. The HOMO located on **DA** attracts the ImH H(N) and reduces the NH coupling, leading to the red-shifts of two H-bonds. The oxidation of **IDAIH**$^-$ generates a neutral system and there is no charge on every fragment (Figure 4). The HOMO populated on left ImH attracts the H in N-H…N_6, leads to the strengthening of NH coupling and blue-shift of this H-bond. Three fragments of the hydrated triplex, **HIDAIHW**, possess near zero charges, similar to those of **HIDAIH**. The frontier orbitals are similar to those of **HIDAIH**. After oxidation, one positive charge is left on the right ImH fragment of the system and no odd electron remains. Here, it still should be the proton transfer from N_6 to right ImH. The hydroxyl bonded system, **HIDAIHOH**$^-$, bears one negative charge on **DA** fragment. Therefore, we can say definitely that they are consecutive proton transfers from N_6 to hydroxyl group through the right ImH. For the oxidized system, no significant charge can be found on each fragment. The detached electron should be the odd one populates on **DA**. The HOMO of **HIDAIHOH** located on right ImH fragment attracts the H in N_6…H-N bond, leading to the strengthening of NH coupling and blue-shift of this H-bond.

The spin density demonstrates the single electron population. Here, the spin density populations of all complexes with single electron indicate that the single electron locates on **DA** fragment, supporting the results obtained from HOMO analyses.

3.4 Ionization Potential

The adiabatic ionization potentials (IPs) are determined at B3LYP/6-311+G(d) level. It has been reported that the IP of **HIAIH** is 161.5 kcal/mol [38]. For the dehydrogenated system, **HIDAIH**, the IP is 163.3 kcal/mol, which is almost equal to that of **HIAIH**. Therefore, the influence of hydrogen detachment from N_9 site on the IP is weak. If the proton on N of left ImH fragment is detached, the IP can be reduced significantly to 98.6 kcal/mol. It indicates that the proton separation is helpful for oxidation. The binding of **HIDAIH** with water molecule through N-H…O bond is an exothermic reaction, 7.0 kcal/mol energy is released. For the oxidized system, **HIDAIH**$^+$, the hydration process is more exothermic. The binding energy of **HIDAIH**$^+$ with water is 14.2 kcal/mol. Upon proton detachment from water, it is more convenient to detach one electron from the system. The corresponding IP is 89.2 kcal/mol, about half of that of **HIDAIH**.

Thus, the basic environment is in favor of the ionization, while the influence of the neutral

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condition is indistinctive. To prevent the DNA mutation, it is better to provide the weak acidic environment.

4. Conclusions

The trustworthy B3LYP/6-311+G* method is employed to investigate the imidazole-dehydrogenated adenine-imidazole system in terms of the geometry structure, IR spectroscopy, electron population, and the adiabatic ionization potential.

Proton transfer occurs spontaneously upon oxidation from amido group to adjacent imidazole fragment. The larger the pH value of the environment is, the significant the influence to the geometry structure is. The electron population on the HOMO orbital determines the IR vibrational frequency of the H-bond being blue-shift or red-shift upon oxidation. The complex prefers to be oxidized under the basic condition. The weak acidic environment is recommended to prevent the DNA mutation.

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References and Notes

[1] Best, G. C.; Dervan, P. B. *J. Am. Chem. Soc.* **1995**, *117*, 1184.
[2] Pundlik, S. S.; Gadre, S. R. *J. Phys. Chem. B* **1997**, *101*, 9657.
[3] Shields, G. C.; Laughton, C. A.; Orozco, M. *J. Am. Chem. Soc.* **1997**, *119*, 7463.
[4] Robles, J.; Grandas, A.; Pedroso, E.; Luque, F. J.; Eritja, R.; Orozco, M.; *Curr. Org. Chem.* **2002**, *6*, 1333.
[5] Wang, J.; Sun, L. Bu, Y. *J. Phys. Chem. B* **2010**, *114*, 1144.
[6] Peters, M.; Rozas, I.; Alkorta, I.; Elguero, J. *J. Phys. Chem. B* **2003**, *107*, 323.
[7] Daycock, J. T.; Jones, G. P.; Evans, J. R. N.; Thomas, J. M. *Nature* **1968**, *218*, 672.
[8] Kawada, A.; McGhie, A. R.; Labes, M. M. *J. Chem. Phys.* **1970**, *52*, 3121.
[9] Colombo, L.; Bleckmann, P.; Schrader, B.; Schneider, R.; Plesser, Th. *J. Chem. Phys.* **1974**, *61*, 3270.
[10] Loeffen, P. W.; Pettifer, R. F.; Fillaux, F.; Kearley, G. J. *J. Chem. Phys.* **1995**, *103*, 8444.
[11] B. S. Hickman, M. J. J. Mascal, Titman, I. G. Wood, J. Am. Chem. Soc. 121 (1999) 11486.
[12] Su, C. C.; Chang, H. C.; Jiang, J. C.; Wei, P. Y.; Lu, L. C.; Lin, S. H. *J. Chem. Phys.* **2003**, *119*, 10753.
[13] Basch, H.; Krauss, M.; Stevens, W. J.; *J. Am. Chem. Soc.* **1985**, *107*, 7267.
[14] Nagy, P. I.; Durant, G. J.; Smith, D. A. *J. Am. Chem. Soc.* **1993**, *115*, 2912.
[15] Scheiner, S.; Yi, M. Y. *J. Phys. Chem.* **1996**, *100*, 9235.
[16] Münch, W.; Kreuer, K. D.; Silvestri, W.; Maier, J.; Seifert, G. *Solid State Ionics.* **2001**, *145*, 437.
[17] Tatara, W.; Wójcik, M. J.; Lindgren, J.; Probst, M. *J. Phys. Chem. A* **2003**, *107*, 7827.
[18] Yan, S.; Bu, Y. *J. Phys. Chem. B* **2004**, *108*, 13874.
[19] Yan, S.; Bu, Y.; Cao, Z.; Li, P. *J. Phys. Chem. A* **2004**, *108*, 7038.
[20] Holmen, A. *J. Phys. Chem. A* **1997**, *101*, 4361.
[21] Russo, N.; Toscano, M.; Grand, A.; Jolibois, F. *J. Comp. Chem.* **1998**, *19*, 989.
[22] Liu, B. P.; Ding, Y. J.; Yuan, X. A. *J. Mol. Struct.: Theochem.* **2008**, *848* 47.
[23] Conti, I.; Garavelli, M.; Orlandi, G. *J. Am. Chem. Soc.* **2009**, *131*, 16108.
[24] Vogt, N.; Dorofeeva, O. V.; Sipachev, V. A.;

2011 © The American Computational Science Society. All rights reserved.

Rykov, A. N. *J. Phys. Chem. A* **2009**, *113*, 13816.
[25] Dolgounitcheva, O.; Zakrzewski, V. G.; Ortiz, J. V. *J. Phys. Chem. A* **2009**, *113*, 14630.
[26] Conti, I.; Donato, E. D.; Negri, F.; Orlandi, G.; *J. Phys. Chem. A* **2009**, *113*, 15265.
[27] Improta, R.; Santoro, F.; Barone, V.; Lami, A. *J. Phys. Chem. A* **2009**, *113*, 15346.
[28] Verma, S.; Mishra, A. K.; Kumar, J. *Acc. Chem. Res.* **2010**, *43*, 79.
[29] Acocella, A.; Jones, G. A.; Zerbetto, F. *J. Phys. Chem. B* **2010**, *114*, 4101.
[30] Gohlke, S.; Abdoul-Carime, H.; Illenberger, E. *Chem. Phys. Lett.* **2003**, *380*, 595.
[31] Li, X.; Sevilla, M. D.; Sanche, L. *J. Phys. Chem. B* **2004**, *108*, 19013.
[32] Li, X.; Sanche, L.; Sevilla, M. D. *J. Phys. Chem. B* **2004**, *108*, 5472.
[33] Bera, P. P.; Schaefer, H. F.; *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 6698.
[34] Lind, M. C.; Bera, P. P.; Richardson, N. A.; Wheeler, S. E.; Schaefer, H. F. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 7554.
[35] Xie, H.; Cao, Z. *Int. J. Quantum Chem.* **2007**, *107*, 1261.
[36] Xie, H.; Xia, F.; Cao, Z. *J. Phys. Chem. A* **2007**, *111*, 4384.
[37] Churchill, C. D. M.; Wetmore, S. D. *J. Phys. Chem. B* **2009**, *113*, 16046.
[38] Cui, P. Y.; Meng, L. Q.; Liu, B. P. *Struct. Chem.* **2010**, *21*, 873.
[39] Nir, E.; Janzen, C.; Imhof, P.; Kleinermanns, K.; de Vries, M. S. *Phys. Chem. Chem. Phys.* **2002**, *4*, 740.
[40] Plützer, C.; Hünig, I.; Kleinermanns, K. *Phys. Chem. Chem. Pys.* **2003**, *5*, 1158.
[41] Wang, Y.; Kong, F. Z.; Fu, A. P.; Wang, Z. *J. Comput. Sci. Eng.* **2011**, *1*, 1.
[42] Sun, W. *J. Comput. Sci. Eng.* **2011**, *1*, 54.
[43] Yan, S.; Bu, Y.; Cukier, R. I. *J. Chem. Phys.* **2006**, *124*, 124314.
[44] Yan, S.; Zhang, L.; Cukier, R. I.; Bu, Y.; *ChemPhysChem* **2007**, *8*, 944.
[45] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*; Gaussian, Inc.: Wallingford CT, **2004**.
[46] Schumm, S.; Prévost, M.; García-Fresnadillo, D.; Lentzen, O.; Moucheron, C.; Kirsch-De Mesmaeker, A.; *J. Phys. Chem. B* **2002**, *106*, 2763.
[47] Pogozelski, W. K.; Tullius, T. D. *Chem. Rev.* **1998**, *98*, 1089.
[48] Burrows, J. C.; Muller, J. G. *Chem. Rev.* **1998**, *98*, 1109.
[49] Armitage, B. *Chem. Rev.* **1998**, *98*, 1171.
[50] Russo, N.; Toscano, M.; Grand, A. *J. Comput. Chem.* **2000**, *21*, 1243.
[51] Saito, I.; Nakamura, T.; Nakatami, K. *J. Am. Chem. Soc.* **2000**, *122*, 3001.

2011 © The American Computational Science Society. All rights reserved.

[52] Wieczorek, R.; Dannenberg, J. J. *J. Am. Chem. Soc.* **2003**, *125*, 14065.
[53] Hobza, P.; Havlas, Z.; *Chem. Rev.* **2000**, *100*, 4253.
[54] Joseph, J.; Jemmis, E. D. *J. Am. Chem. Soc.* **2007**, *129*, 4620.

2011 © The American Computational Science Society. All rights reserved.