The Potential Energy Surface of Guanine Is Not Flat: An *ab Initio* Study with Large Basis Sets and Higher Order Electron Correlation Contributions

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An investigation of the potential energy surface (PES) of guanine was performed. The (nonplanar) molecular geometries of seven different forms of guanine were studied using the ab initio LCAO-MO method at the MP2 level with valence double-ζ basis sets augmented by d- and p-polarization functions (6-31G(d,p)). Among the studied forms are the four lowest energy tautomers, one rotamer, and two transition state forms for proton transfer between oxo and hydroxo tautomers of guanine N(7)H and N(9)H tautomers. Our best estimation of the relative stabilities of the tautomers includes electron correlation contributions calculated at the MP2/6-31G(d,p) reference geometries at the MP4(SDTQ)/6-31G(d,p), MP4(SDQ)/6-311G(d,p), and MP2/6-311++G-(df,pd) levels. Three tautomers (and one rotamer) are located within 10 kJ mol^{-1} on the MP2 level PES of guanine. The calculated energy barriers for the proton transfer are larger than 150 kJ mol^{-1} and do not change by more than a few kJ mol^{-1} upon application of the SCRF model based on the Onsager approximation.

Introduction

Among the crucial factors governing the three-dimensional structure of DNA are two types of DNA base interactions: hydrogen bonding and stacking interactions.[1] All the conformational variability of DNA is strongly effected by base−base interactions. Hydrogen bonding (pairing) between DNA bases connects together two DNA strands, and stacking interactions link vertically separated neighboring base-pairs within one strand and across the double helix. The hydrogen-bonding pattern between bases is controlled by the complementarity of their forms. Since all of the nucleic acid bases (NAB) contain nitrogen atoms incorporated into six- and/or five-member rings and oxygens and/or nitrogens from the amino groups connected to these rings, hydrogens could migrate from one heteroatom to another. Such a process creates the possibility for the existence of a number of different tautomeric forms.

The formation of rare tautomers might be responsible for the development of substitution mutation at the DNA-synthesis level. For example, guanine (Gua), which in DNA is mostly in the canonical keto form and is paired with cytosine, could adopt the rare enol tautomeric form and, as a consequence, form hydrogen bonds with thymine (uracil in RNA). Such a molecular mechanism of point mutation was postulated in the early 1950s by Watson and Crick.[2] An experimental support for this mechanism is extremely difficult, mainly due to problems with detections of relative low concentration of the rare tautomeric forms responsible for such mutations. On the other hand, high-level theoretical calculations could furnish information on both structures and the relative energies of the minor forms. In addition, the transition states structures connecting the minimum energy conformations and the transition barriers between the normal and rare tautomers could be characterized by quantum mechanical calculations.

Guanine, one of the most important nucleic acid bases occurring in both DNA and RNA, is also the most intriguing species in the class of NABs. Its importance has been demonstrated by a numerous experimental[1] and theoretical investigations[3] including calculations of its thio- and seleno-derivatives.[4] In addition to being the largest NAB, it also has the most complex tautomeric equilibria. At least three different tautomers are observed in the IR isolated matrix experiments.[5] Furthermore, amino tautomers of guanine exhibit the most pronounced nonplanarity among NABs.[6]

The function of guanine in DNA is complex. However, before one is able to evaluate the properties of NABs in biological systems, its gas-phase equilibria have to be understood in detail. Until now, the large size of guanine had prohibited the use of accurate theoretical techniques to study its potential energy surface (PES). On the other hand, the fact that three of the most stable guanine tautomers lie within 5 kJ mol^{-1} on its potential energy surface requires reliable methods to describe their relative energies. Such reliability is achieved when ab initio correlated calculations are carried out with inclusion of electron correlation up to higher order terms and the contributions from triplet excitation. The last obstacle in the accurate theoretical study of guanine is its nonplanarity. Recent investigations proved that the nonplanarity of the amino group of guanine is the largest one in the NAB series. Such pronounced nonplanarity of guanine tautomers prevents application of molecular symmetry which facilitates MP4(SDTQ) level calculations for uracil.[3g,7]

Not only the small energetic differences among guanine tautomers but also the way in which these minimum energy points on the guanine PES are connected are of importance for the understanding of biologically important relationships among these species. The reliable predicted geometry is a prerequisite for accurate calculation of other properties. To our knowledge, such studies incorporating both minimum energy and transition forms have not yet been performed.

A comprehensive study of the properties of guanine has to address a number of issues. Among them are effects of basis sets, electron correlation contributions, reference geometries, and zero-point energies (ZPE) on the calculated tautomeric equilibria. In this paper we present the results of high-level ab initio investigations carried out for major tautomers of guanine

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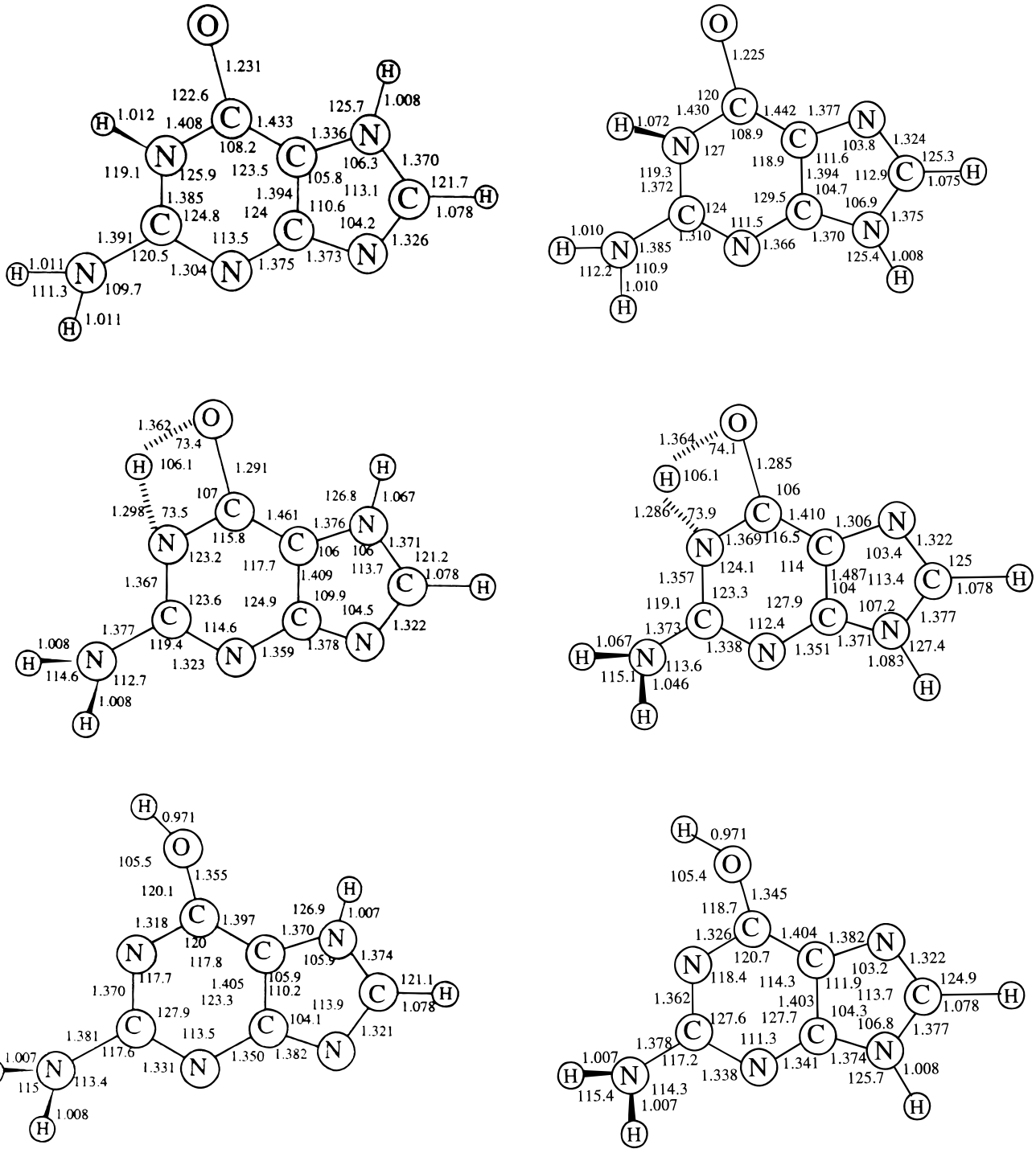

Figure 1. (a) Molecular parameters of Gua-7 minimum energy and transition state forms (bond distances in angstroms, bond angles in degrees). (b) Molecular parameters of Gua-9 minimum energy and transition state forms (bond distances in angstroms, bond angles in degrees).

and in addition to the two transition energy species connecting the oxo- and hydroxo- forms. Though a number of lower level theoretical studies of guanine have been reported,[3] transition state forms have not been investigated yet.

Method

The ab initio LCAO-MO method[8] was used for the study of the title species. The calculations were carried out with the GAUSSIAN90, GAUSSIAN92, and GAUSSIAN94 series of programs.[9] All geometries were optimized by the gradient procedure[10] at the C_1 symmetry (all molecular parameters optimized). Following the HF/6-31G(d,p) level optimizations, the MP2(full) level was applied to find the minimum energy points on the PESs of guanine while the molecular geometries of the two transition state structures were optimized at the MP2-(frozen core) level using the standard 6-31G(d,p) Pople's valence double-ζ basis set augmented by d- and p-polarization functions. At the Hartree−Fock (HF) level, all optimized structures were checked by an analysis of the harmonic vibrational frequencies obtained from diagonalization of the force constant matrixes to find the order of the stationary points.

The molecular geometries of the three lowest energy tautomers were additionally optimized using the DFT(B3-LYP) method[11] in conjunction with the 6-311++G(df,pd) basis set.

TABLE 1: Relative Energies and Dipole Moments of the Seven Tautomers Calculated at MP2 Level of Theory with Different Basis Sets Using Geometries Optimized at MP2/6-31G(d,p) Level[a]

basis set	GUA 7-H	GUA 7-OH	GUA 9-H	GUA 9-OH	GUA 9-OH$_{(trans)}$	GUA 7-TS	GUA 9-TS
6-31G(d,p)	0.00	18.64	0.25	4.72	7.46	169.62	155.71
6-31++G(d,p)	0.00	16.63	2.03	3.98	6.64	171.2	159.0
6-311G(d,p)	0.00	16.09	−0.84	1.59	4.03	168.57	153.76
6-311G(2d,2p)	0.00	15.59	1.29	2.26	3.90	168.11	155.42
6-311++G(2d,2p)	0.00	15.12	2.76	3.36	4.34	169.17	158.42
6-311++G(df,pd)	0.00	9.79	0.81	−3.46	−1.26	161.88	149.00
(μ) MP2/6-311++G(2d,2p)	1.78	4.26	6.30	3.05	3.90	1.98	5.36

[a] Relative energies in kJ/mol and dipole moments in debye.

Also their harmonic vibrational frequencies were calculated at the same level.

To improve the calculated energies, electron-correlation contributions were determined by using the Møller−Plesset perturbation theory[12] through single-point second-order (MP2) frozen core calculations using a series of basis sets of increasing quality (6-31++G(d,p), 6−311G(d,p), 6−311G(2d,2p), 6-311++G(2d,2p), and 6-311++G(df,pd)). Higher order electron contributions were accounted for at the MP4(SDTQ)/6-31G(d,p), the MP4 (SDQ)/6-31++G(d,p), and the MP4(SDQ)/6-311G(d,p) levels, at the appropriate MP2/6-31G(d,p) geometries.

Results and Discussion

Nonplanarity of the NABs has attracted recently a lot of attention.[6] It is obvious from the previous HF level calculations with basis sets augmented by at least d-polarization functions on heavy elements that the amino groups in guanine tautomers exhibit notable nonplanarity. In addition, the pyramidal structure of the amino group in guanine does also influence the configuration of the hydrogen attached to the N1 atom, and a strong hydrogen−hydrogen repulsion between this hydrogen and the one from the amino group causes significant nonplanarity measured by the value of the dihedral angle (ca. 6°) between H−N(1) and the guanine ring. The results of geometry optimization of two guanine tautomers at the MP2/6-31G(d,p) levels have been already published by Sponer and Hobza (partial optimization)[3f] and Stewart et al.[3i]

We have restricted our study to the four lowest energy tautomers: two oxo-amino forms N7−H and N9−H and two hydroxo-amino forms N7−OH and N9−OH (Figure 1). Since in the case of the N9−OH two closed energy rotamers (defined by the directions of the OH groups) of which comparable energy could exist, an occurrence which is prohibited for the N7−OH tautomer due to the strong repulsion between the N7 hydrogen and the one from the hydroxo group, both rotamers (N9−OH and N9−OHt) were included in our study. Also two transition forms responsible for the energy barriers for conversion from the oxo to the hydroxo tautomers were investigated.

In all studied tautomers noticeable deviations of the amino groups from the planes of the molecular rings are observed. The dihedral angles specified by the three rings' atoms and N(amino) deviate from the plane by ca. 2°, and as a consequence, the amino nitrogens lay less than 0.05 Å above the molecular planes. Relatively large deviations of the amino hydrogens from the molecular planes are observed (up to over 30° or 0.4 Å).

The calculated MP2/6-31G(d,p) molecular parameters of guanine furnish accurate geometries for further studies of the basis set and electron correlation effects on the relative energies of the tautomers and the energetic barriers involving transformations of the oxo- and hydroxo-forms (Table 1). At the MP2 level, the most pronounced effect of the basis set extension is

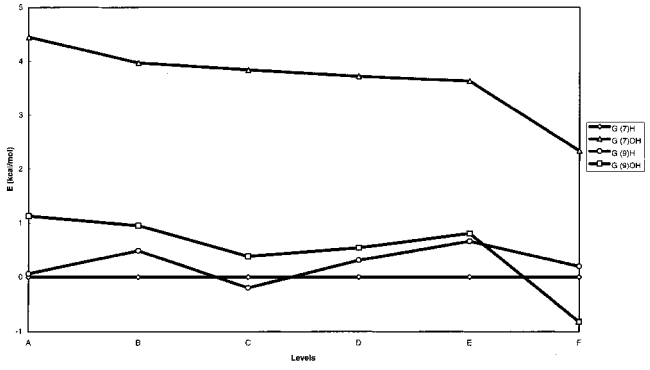

Figure 2. Relative energies of guanine tautomers estimated at MP2 level with differnt basis sets: (A) 6-31G(d,p), (B) 6-31++G(d,p), (C) 6-311(d,p), (D) 6-311G(2d,2p), (E) 6-311++G(2d,2p), and (F) 6-311++G(df,pd).

noticed for the hydroxo-forms (Figure 2). For the 7-OH tautomer, enlargement of the basis set from 6-31G(d,p) to 6-311++G(df,pd) stabilize this form by ca. 9 kJ/mol with the f-polarization functions of the heavy elements and the d-functions of hydrogens being the most important factors of its stabilization. A similar effect is also observed for both 9-OH forms. The relatively large energies of both transition forms are not drastically affected by the increase of the basis set, so we did not perform calculations of their energies using an expensive 6-311++G(df, pd) basis set.

Effects of the higher level correlation contributions on the tautomeric properties of guanine were studied up to the MP4-(SDTQ) level with the 6-31G(d,p) basis set and up to the MP4-(SDQ) level with two larger basis sets: 6-31++G(d,p) and 6-311G(d,p) (Table 2, Figure 3). These effects are the most striking for the Gua 9 tautomers. At the MP4(DQ)/6-31G(d,p) level the Gua 9-H form has the lowest energy; however, inclusion of higher contributions destabilize this tautomer over the Gua7-H form, and the latter becomes the lowest energy tautomer at the MP4(SDTQ)/6-31G(d,p) level. The effect of the higher electron correlation contribution is even more visible with the triple-valence 6-311G(d,p) basis set. With this basis set, in going from the MP4(SD) to MP4(SDQ) level, the relative energy of the Gua 9-H form increases by 5.6 kJ/mol while the corresponding increase for the Gua 9-OH forms amounts to ca. 10 kJ/mol. Also the oxo form of Gua 7-H is significantly destabilized at the MP4 level in comparison to the MP2 values. The changes of relative stabilities with the increase of the basis sets are opposite for the MP2 levels where an increase of the basis set sizes stabilize the studied forms relative to Gua 7-H and the MP4 levels where Gua 7-H is stabilized by inclusion of the higher electron correlation contributions and an enlarging of the basis sets. The only undetermined factor in the variation of relative energies is the role of the higher angular momentum polarization functions in conjunction with the MP4 level predictions (especially f-orbitals on heavy elements) since these

TABLE 2: Relative Energies of the Seven Tautomers Calculated at MP4 Level of Theory with Different Basis Sets Using Geometries Optimized at MP2/6-31G(d,p) Level[a]

basis set		GUA 7-H	GUA 7-OH	GUA 9-H	GUA 9-OH	GUA 9-OH$_{(trans)}$	GUA 7-TS	GUA 9-TS
6-31G(d,p)	MP4(DQ)	0.00	19.13	−2.43	2.04	5.47	190.06	172.45
	MP4(SDQ)	0.00	22.96	−1.53	6.95	10.27	184.60	168.43
	MP4(SDTQ)	0.00	21.59	0.38	8.15			
6-31++G(d,p)	MP4(DQ)	0.00	17.93	−0.68	2.14	5.54		
	MP4(SDQ)	0.00	21.59	0.29	6.66	9.97		
6-311G(d,p)	MP4(DQ)	0.00	17.03	−3.47	−0.57	2.67		
	MP4(SDQ)	0.00	25.69	2.15	9.16	12.31		

[a] Relative energies in kJ/mol.

TABLE 3: Relative Energies of the Three Guanine Tautomers Calculated at Different Levels of Theory at the HF, DFT, and MP2 Optimized Geometries[a]

level	GUA 7-H	GUA 9-H	GUA 9-OH
DFT/6-311++G(df,pd)//HF/6-31G(d,p)	0	1.34	5.78
MP2/6-311++G(df,pd)//HF/6-31G(d,p)	0	1.98	−2.25
DFT/6-311++G(df,pd)//DFT/6-311++G(df,pd)	0	1.57	10.32
MP2/6-311++G(df,pd)//DFT/6-311++G(df,pd)	0	1.14	−2.52
DFT/6-311++G(df,pd)//MP2/6-31G(d,p)	0	1.78	6.47
MP2/6-311++G(df,pd)//MP2/6-31G(d,p)	0	0.81	−3.46

[a] Relative energies in kJ/mol.

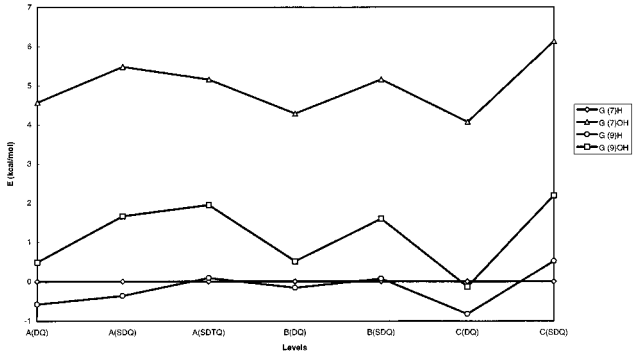

Figure 3. Relative energies of guanine tautomers estimated at MP4 level with different basis sets: (A) 6-31G(d,p), (B) 6-31++G(d,p) and (C) 6-311G(d,p).

functions significantly lower the energy of the Gua 9-OH form at the MP2 level. However, such calculations are still beyond the power of our computational facilities.

The energy differences among the three lowest energy tautomers of guanine are very small. Such a phenomenon calls for careful investigation of all factors contributing to the total energies of these forms. We started with an investigation of the effects of the calculated geometries on the tautomeric properties. The three lowest energy tautomers of guanine were additionally studied at different reference geometries: HF/6-31G(d,p), DFT/6-311++G(df,pd), and MP2/6-31G(d,p) using two levels of theory, DFT and MP2, in conjunction with the largest (6-311++G(df,pd)) basis set feasible for us (Table 3). The total MP2/6-311++G(df,pd) energies of all tautomers decrease from the HF, DFT, to MP2 reference geometries indicating that the last set of the geometries is the closest to the minimum energy structures at the MP2/6-311++G(df,pd) potential energy surface. Single-point MP2 calculations resulted in an insignificant difference (by ca. 1 kJ/mol) of the relative tautomeric stabilities in going from the HF/6-31G(d,p) to the MP2/6-31G(d,p) geometries. The DFT level of theory is much more sensitive of the reference geometry, and although the DFT relative energies for the HF and MP2 optimized geometries are similar, DFT reference geometries destabilize the energies of Gua 9-OH tautomers by over 4 kJ/mol. Also, the relative energies and even order of stabilities predicted for different reference geometries of Gua9-OH by the single-point MP2 and DFT calculations differ significantly. At the MP2 level this tautomer is predicted to have the lowest energy, stabilized by over 2 kJ/mol compared to that of Gua 7-H. For the same reference geometries its relative stability at the DFT level ranges from ca. 6 kJ/mol (HF and MP2 geometries) to 10.3 kJ/mol (DFT geometries). However, it is interesting to notice that the DFT//MP2 relative energies of these three tautomers are very close in the magnitude and orders to the values predicted at the MP4(SDTQ)/6-31G(d,p)//MP2, MP4(SDQ)6-31++G(d,p)//MP2, and MP4(SDQ)/6-311G(d,p)//MP2 levels of theory. A very similar trends was noticed recently in our studies of cytosine.[13]

A magnitude of zero-point energy (ZPE) contributions depends on the level of theory applied. Calculations of the harmonic vibrational frequencies for guanine tautomers at the electron correlated levels are still not feasible for us; but from the combined experimental and theoretical studies on the number of nucleid acid bases and their derivatives, it is obvious that the DFT/B3LYP level calculations, with even medium sizes of basis sets, are in impressive agreement with the isolated-matrix IR experimental data [for a recent review see ref 14]. Having this in mind, we investigated the impact of the DFT/6-311++G-(df,pd) calculated ZPE contributions on the total energies of the most stable tautomers of guanine. The relative change of the ZPE energy differences in going from the HF/6-31G(d,p) to the DFT/6-31++G(df,pd) level is tremendous (by over 100%), but since these contributions are smaller than 0.5 kJ/mol, the effect on the total relative energies (destabilization of Gua 9-H and Gua 9-OH) is insignificant.

To evaluate the effect of the core electron energies on the tautomeric properties, MP2/6-31G(d,p)(full) and MP2/6-31G-(d,p)(frozen core) calculations were carried out for the Gua 7-H, Gua 9-H and Gua 9-OH tautomers. This effect stabilizes the Gua 7-H form over the Gua 9-H form by 1 kJ/mol and is negligible in the case of Gua 9-OH.

The fact that all studied minimum energy forms of guanine lie very close on the PES does not necessarily mean that the transformation among these forms are low energy processes. Since such phenomena are of a crucial importance from the biological viewpoint, energetic provisions of the oxo-hydroxo equilibrium for both series of tautomers Gua-9 and Gua-7 were

studied in detail. As was expected, the molecular parameters of the transition states for both Gua-9 and Gua-7 systems are intermediate between those of the related oxo and hydroxo tautomers. Transferring protons are located 1.364(1.362) Å from the oxygens and 1.286(1.298) Å from the nitrogens for the Gua-9 (Gua-7) tautomers. Both transition states are characterized by large imaginary frequencies (2300 Gua-9 and 2291 Gua-7 at the HF/6-31G(d,p) level) which indicate sizable energy barriers for such processes. This is in accord with the calculated relative energies of the transition state forms which amount to 185 (169) kJ/mol for Gua-9 and 168 (158) kJ/mol for Gua-7 tautomers at the MP4(SDQ)/6-31G(d,p) (MP2/6-311++G(2d,2p)) levels. In DNA moiety these barriers could be significantly decreased by interactions with a polar environment. However, the simple self-consistent reaction field approach applied to account for the interaction with a polar solvent (SCRF/6-31G(d,p) level geometry optimization followed by the MP2/6-31G(d,p)//SCRF/6-31G(d,p) single-point calculations) changed the energy barriers by only few kJ/mol. It supports the theory that such reactions are carried out by direct involvement of water molecules,[15] and such studies are in progress in our laboratory.[16]

The magnitudes of dipole moments of all tautomers calculated with the MP2/6-311++G(2d,2p) wave functions at the MP2/6-31G(d,p) reference geometries are presented in Table 1. The dipole moment for Gua 9-H are being approximately 3-fold larger than those predicted for Gua 7-H, and they are responsible for the stabilization of Gua 9-H in polar solvents. For example, although Gua 7-H seems to be the predominant form in a gas phase as concluded from the photoelectron spectral investigations in the gas phase[17] and IR matrix-isolation experiments,[18] while in the polar solutions guanine is found only as Gua 9-H.[19] A similar effect is predicted from our data for the 6-thioguanine and 6-selenoguanine species.[4,20]

Conclusions

The principal conclusions from this theoretical study on molecular structures and properties of guanine are 1. Three tautomers (and one rotamer) are located within 10 kJ mol^{-1} on the MP2 level PESs of guanine. The energy difference between Gua 7-H and Gua 9-H is only 0.38 kJ mol^{-1} at the (MP4(SDTQ)/6-31G(d,p)//MP2/6-31G(d,p)) and −3.36 kJ mol^{-1} at the (MP2/6-311++G(df,pd)//MP2/6-31G(d,p)) levels. MP2/6-311++G(df,pd) calculations at different reference geometries stabilize the latter form, while higher correlation energy contributions and basis functions with lower angular momentum stabilize Gua 7-H.

2. Energy barriers calculated for the proton transfers form oxo to hydroxo forms are larger than 150 kJ mol^{-1} (gas phase). These numbers are virtually unchanged for the predictions including continuum polar solvents (SCRF approximations). To account for equilibria in biological environments, a supermolecule approach with explicit interactions with water molecules should be applied.

3. Due to a large difference in dipole moments, Gua 9-H is predicted to be stabilized in the polar solvents.

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Supporting Information Available: Tables of total energies (au) of the considered guanine tautomers calculated at different levels of theory (3 pages). See any current masthead page for ordering information.

References and Notes

(1) (a) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1984. (b) Jeffrey, G. A.; Saender, W. *Hydrogen Bonding in Biological Structure*; Springer-Verlag: New York, 1991.

(2) Watson, J. D.; Crick, F. H. C. *Nature* **1953**, *171*, 737.

(3) (a) Kwiatkowski, J. S.; Zelinski, T. J.; Rein, R. *Adv. Quantum. Chem.* **1986**, *18*, 85. (b) Person, W. B.; Szczepaniak, K.; Szczepaniak, M.; Kwiatkowski, J. S.; Czerminski, R. J. *J. Mol. Struct.* **1989**, *194*, 239. (d) Leszczynski, J. *Int. J. Quantum Chem.* **1992**, *19*, 43. (e) Sponer, J.; Leszczynski, J.; Hobza, P. *J. Biol. Struct. Dyn.* **1996**, *14* (1), 117. (g) Gould, I. R.; Burton, N. A.; Hall, R. J.; Hiller, I. H. *J. Mol. Struct. (THEOCHEM)* **1995**, *331*, 147. (f) Sponer, J.; Hobza, P. *J. Phys. Chem.* **1994**, *98*, 3161. (h) Colominas, C.; Luque, F. J.; Orozco, M. *J. Am. Chem. Soc.* **1996**, *118*, 6811. (i) Stewart, E. L.; Foley, C. K.; Allinger, N. L.; Bowen, J. P. *J. Am. Chem. Soc.* **1994**, *116*, 7282.

(4) (a) Szczepaniak, K.; Person, W. B.; Leszczynski, J.; Kwiatkowski, J. S. *Adv. Biochem.* **1995**, *41*, 1995. (b) Leszczynski, J. *J. Mol. Struct. (THEOCHEM)* **1994**, *311*, 37. (c) Bugg, C. E.; Thewalt, U. J. *J. Am. Chem. Soc.* **1970**, *92*, 3520. (d) Stewart, M. J.; Leszczynski, J.; Rubin, Y. V.; Blagoi, Y. P. *J. Phys. Chem.* **1997**, *101*, 4753. (e) Alhambra, C.; Luque, F.; Estelrich, J.; Orozco, M. *J. Org. Chem.* **1995**, *60*, 969.

(5) (a) Szczepaniak, K.; Szczepaniak, M.; Szajda, W.; Person, W. B.; Leszczynski, J. *J. Can. Chem.* **1991**, *69*, 1718. (b) Szczepaniak, K.; Szczepaniak, M. *J. Mol. Struct.* **1987**, *156*, 29. (c) Radchenko, E. D.; Plohotnichenko, A. M.; Sheina, G. G.; Blagoi, Yu. P. *Biophysics* **1983**, *28*, 559 (English edition). (d) Stepanian, S. G.; Sheina, G. G.; Radchenko, E. D.; Blagoi, Yu. P. *J. Mol. Struct.* **1985**, *131*, 333. (e) Graindourze, M.; Smets, Y.; Zeegers-Huyskens, Th.; Maes, G. *J. Mol. Struct.* **1990**, *222*, 345.

(6) (a) Leszczynski, J. *Chem. Phys. Lett.* **1990**, *174*, 347. (b) Kwiatkowski, J. S.; Lesyng, B.; Palmer, M. H.; Saenger, W. *Z. Naturforsch.* **1982**, *37c*, 937. (c) Palmer, M. H.; Kwiatkowski, J. S.; Lesyng, B. *J. Mol. Struct. (THEOCHEM)* **1983**, *92*, 283. (d) Riggs, N. V. *Chem. Phys. Lett.* **1991**, *177*, 447. (e) Gould, I. R.; Hiller, I. H. *Chem. Phys. Lett.* **1989**, *161*, 185. (e) Nowak, M. J.; Lapinski, L.; Fulara, J.; Les, A.; Adamowicz, L. *J. Phys. Chem.* **1992**, *96*, 1562. (f) Sponer, J.; Florian, J.; Hobza, P.; Leszczynski, J. *J. Biomol. Struct. Dyn.* **1996**, *13*, 827. (g) Bludski, O.; Sponer, J.; Leszczynski, J.; Spirko, V.; Hobza, P. *J. Chem. Phys.* **1996**, *105*, 11042.

(7) Leszczynski, J. *J. Phys. Chem.* **1992**, *96*, 1649.

(8) For example, see: Hehre, W. H.; Radom, L.; v. Schleyer, P.; Pople, J. A. *Ab initio Molecular Orbital Theory*; Wiley: New York, 1986.

(9) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L. Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. GAUSSIAN94, Revision D.3; Gaussian, Inc.: Pittsburgh, PA, 1995.

(10) Schlegel H. B. *J. Comput. Chem.* **1982,** 3, 314.

(11) (a) Kohn, W.; Sham, L. J. *Phys. Rev. A* **1965**, *140*, 1133. (b) Parr, R. G.; Tang, W. In *Density Functional Theory of Atoms and Molecules*; Oxford University: New York, 1989. (c) Perdew, J. P.; Wang, Y. *Phys. Rev. B* **1986**, *33*, 8822. (d) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8800. (c) Bescke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (e) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Phys.* **1980**, *58*, 1200. (f) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (g) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1993**, *37*, 785.

(12) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(13) Kwiatkowski, J. S.; Leszczynski, J. *J. Phys. Chem.* **1996**, *100*, 941.

(14) Nowak, M. J.; Lapinski, L.; Kwiatkowski, J. S.; Leszczynski, J. In *Current Trend in Computational Chemistry*; Leszczynski, J., Ed.; World Scientific Publishing Co. Pte. Ltd.: New York, 1997; Vol. 2, p 140.

(15) Cox, J. R.; Woodcock, S.; Hiller, I. H.; Vincent, M. A. *J. Phys. Chem.* **1990**, *94*, 5499−5501. Luque, F. J. Orozco, M. *J. Chem. Soc., Perkin Trans. 2*, **1993**, 683−690. Parchment, O. G.; Hillier, I. H.; Green, V. S. *J. Chem. Soc., Perkin Trans. 2* **1991**, 799−802. Alagona, G.; Ghio, C. *Chem. Phys. Lett.* **1996**, *204*, 239−249. Craw, J. S.; Guest, J. M.; Cooper, M. D.; Burton, N. A.; Hillier, I. H. *J. Phys. Chem.* **1996**, *100*, 6304−6309. Wong, M. W.; Wiber, K. B.; Frisch, M. J. *JACS* **1992**, *114*, 1645−1652.

(16) Gorb, L.; Leszczynski, J. *J. Am. Chem. Soc.* **1997**, submitted for publication.

(17) Lin, J.; Yu, C.; Peng, S.; Aklyama, I.; Li, K.; Lee, K.; LeBreton, P. *J. Phys. Chem.* **1980**, *84*, 1006.

(18) Szczesniak, M.; Leszczynski, J.; Szajda, W.; Szczepaniak, K.; Hernandez, L.; Person, W. B., to be published.

(19) Shugar, D.; Psoda, A. In *Landolt-Bornstein's New Biophysics. Part I. Nucleic Acids*; Springer: Berlin, 1990.

(20) Venkateswarlu, D.; Leszczynski, J. *J. Phys. Chem.* **1997**, submitted for publication.