Strikingly Different Effects of Hydrogen Bonding on the Photodynamics of Individual Nucleobases in DNA: Comparison of Guanine and Cytosine

Tomáš Zelený,[†] Matthias Ruckenbauer,[‡,#] Adelia J.A. Aquino,[‡,§,∥] Thomas Müller,[⊥] Filip Lankaš,[⊗] Tomáš Dršata,[⊗] William L. Hase,[§] Dana Nachtigallova,*,[⊗] and Hans Lischka*,[‡,§]

[†]Regional Centre of Advanced Technologies and Materials, Department of Physical Chemistry, Faculty of Science, Palacky University Olomouc, 17. listopadu 1192/12, 771 46 Olomouc, Czech Republic

[‡]Institute of Theoretical Chemistry, University of Vienna, Währingerstraße 17, A-1090 Vienna, Austria

[§]Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79409-1061, United States

[∥]Institute of Soil Research, University of Natural Resources and Life Sciences, Peter-Jordan-Straße 82, A-1190 Vienna, Austria

[⊥]Institute of Advanced Simulation, Jülich Supercomuter Centre, Forschungszentrum Jülich, D-52425 Jülich, Germany

[⊗]Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Flemingovo nam. 2, 166 10 Prague, Czech Republic

Ⓢ *Supporting Information*

ABSTRACT: Ab initio surface hopping dynamics calculations were performed to study the photophysical behavior of cytosine and guanine embedded in DNA using a quantum mechanical/molecular mechanics (QM/MM) approach. It was found that the decay rates of photo excited cytosine and guanine were affected in a completely different way by the hydrogen bonding to the DNA environment. In case of cytosine, the geometrical restrictions exerted by the hydrogen bonds did not influence the relaxation time of cytosine significantly due to the generally small cytosine ring puckering required to access the crossing region between excited and ground state. On the contrary, the presence of hydrogen bonds significantly altered the photodynamics of guanine. The analysis of the dynamics indicates that the major contribution to the lifetime changes comes from the interstrand hydrogen bonds. These bonds considerably restricted the out-of-plane motions of the NH_2 group of guanine which are necessary for the ultrafast decay to the ground state. As a result, only a negligible amount of trajectories decayed into the ground state for guanine embedded in DNA within the simulation time of 0.5 ps, while for comparison, the isolated guanine relaxed to the ground state with a lifetime of about 0.22 ps. These examples show that, in addition to phenomena related to electronic interactions between nucleobases, there also exist relatively simple mechanisms in DNA by which the lifetime of a nucleobase is significantly enhanced as compared to the gas phase.
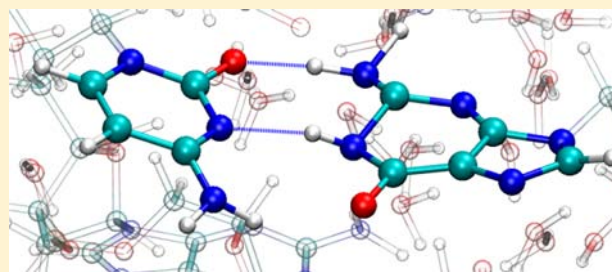
INTRODUCTION

In the last decades, impressive progress has been achieved in the understanding of the photodynamics of nucleic acids. The experimentally observed ultrafast excited state relaxation of all five naturally occurring nucleobases[1−6] has been explained by internal conversion via conical intersections.[7−18] The excited state behavior of nucleobases embedded within the DNA or RNA structure is, however, much less understood. The complex behavior of their excited state decay made it difficult to resolve the relaxation mechanisms in molecular detail. It has been shown in several experimental studies that the decay properties of nucleic acids in DNA depend on the base sequence and the conformation.[4,19−28] In contrast to isolated nucleic acid bases in gas phase and water, where conversion to the ground state occurs on picosecond or subpicosecond time scale, the relaxation of nucleobases in DNA ranges in the picosecond

and up to hundreds of picoseconds time scale. On the basis of the experimental observations, it has been suggested that in addition to excited states localized on single nucleobases also delocalized exciton and excimer/exciplex complexes are responsible for nonradiative relaxation of nucleic acids.[19,21,23,29−38] Static quantum chemical calculations which can provide information about the character of excimer/exciplex complexes and the influence of both, inter- and intrastrand interactions within the DNA helix[39−48] support these suggestions. The relaxation mediated by a proton-transfer within base-pairs was suggested also.[49] The role of the second strand, and consequently this type of relaxation mechanism, was, however, lately questioned by Crespo-Hernandez et al.[19]

Static calculations as discussed above cannot, however, give the final decision about the relaxation mechanisms and their time scales. For that purpose, photodynamical simulations need to be performed.[24,48,50−56] Despite the relatively large number of theoretical investigations devoted to the study of interactions of nucleic acid bases in their excited states, a comprehensive understanding of these phenomena is still lacking.

The formation of excitons and excimers/exciplexes described above results from the electronic interaction between nucleobases. In addition, the surrounding DNA environment can influence the mobility of a nucleobase also by steric and Coulombic effects. Hydrogen bonding plays a major role in this respect as well. This environmental effect has been investigated recently in our group by means of quantum mechanical/ molecular mechanical (QM/MM) nonadiabatic surface-hopping simulations of the adenine model 4-aminopyrimidine (4AP) as QM part using a complete active space self-consistent field (CASSCF) approach. 4AP was embedded into a nearest-neighbor nucleobase environment (MM) in order to study interactions occurring in single and double stranded B-DNA, respectively.[57,58] Only a small overall elongation of the total relaxation time was observed as compared to the photo-dynamics of the isolated 4AP. The excited state relaxation was found to proceed mainly via a conical intersection characterized by a puckering of a ring CH group,[59] which had no direct involvement in hydrogen bonding. The photodynamics of a single adenine embedded in $(dA)_{10}$ and $(dA)_{10}\cdot(dT)_{10}$ oligonucleotides has been investigated also by means of the semiempirical orthogonalization model (OM2) method.[60] An increase of the decay time by about an order of magnitude as compared to adenine relaxation in vacuo or in water was found. In this case, the decay is characterized by out-of-plane motion of the adenine NH_2 group. Besides the methodological differences in the two dynamics simulations leading to different reaction pathways, these examples show that the photo-dynamics of individual nucleobases may be quite differently influenced by the DNA environment. The effect of DNA structure on the relaxation pathways of adenine was also investigated by Conti et al. who suggested that the sterical hindrances create a barrier on the paths toward the conical intersection.[48]

The present investigation is dedicated to the study of the influence of the DNA environment on the photodecay dynamics of nucleobases using an extended structural model of a DNA dodecamer (Figure 1). The DNA fragment chosen in this study is a frequently used standard DNA model, which has been selected as a representative example to investigate the environmental effects on the ultrafast photodynamics in DNA. As target compounds for the photexcitation, the nucleobases cytosine and guanine of a Watson−Crick pair have been chosen where, similar to the above-mentioned cases of 4AP and adenine, only one of the two components is treated quantum mechanically at a time. On-the-fly surface hopping dynamics simulations are performed combining a flexible ab initio description of the QM part with an efficient MM representation of the DNA and the water environment.[18,50,54] Since in the present approach the electronic excitations are confined to a single base of cytosine or guanine, processes such as exciton or excimer/exciplex formation or charge transfer will not be included in our dynamics setup. However, it can still provide an interesting view on the influence of the DNA environment on the photophysics of individual nucleobases.
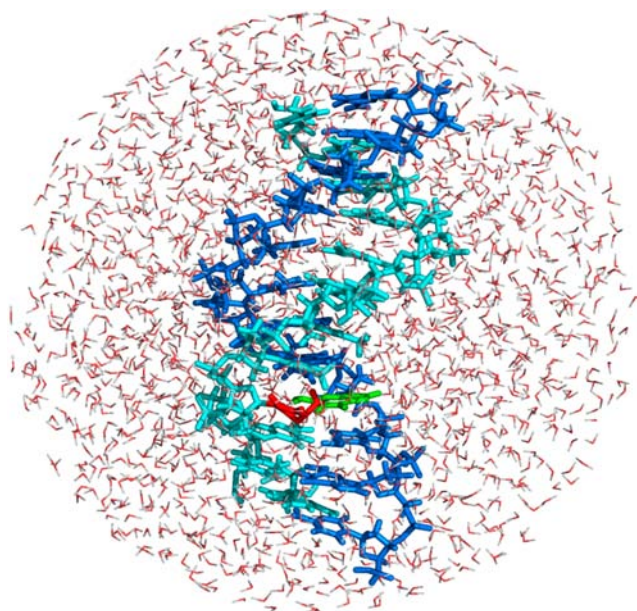

Figure 1. The d(CpGpCpGpApApTpTpCpGpCpG) DNA dodeca-mer solvated with water molecules and neutralized by K^+ ions. Cytosine (in red) or guanine (in green) is treated at ab initio level (QM part).

■ COMPUTATIONAL DETAILS

On-the-fly surface hopping nonadiabatic dynamics simulations were performed to study the photophysics of guanine and cytosine embedded in the solvated DNA dodecamer using a combined quantum mechanical/molecular mechanical (QM/MM) approach as described in refs 61−63. The entire system consists of the d(CpGpCpGpApApTpTpCpGpCpG) dodecamer (see Figure 1), a standard model of DNA, solvated by water molecules and neutralized by K^+ ions with additional K^+ and Cl^- ions included to mimic physiological conditions. The QM part was confined to a single base, guanine and cytosine, respectively, while the remaining system was treated at the MM level. The QM methods were identical to those used in the previous studies on isolated guanine and cytosine,[64,65] that is, the complete active space self-consistent field (CASSCF) and the multireference configuration interaction level including single excitations (MR-CIS) for cytosine and guanine, respectively. The choice of the methods was based on a detailed investigation of the reliability of methods for the description of potential energy surfaces (PESs) for excited states by comparison with more advanced methods and experiments of isolated species (see refs 64, 65) In the case of guanine, higher correlation effects need to be included to obtain a correct ordering of states. Details are given in the section SI.1. of the Supporting Information. Analytic gradients and nonadiabatic coupling vectors necessary for the dynamics were calculated as described in refs 66−69. The 6-31G* basis set[70,71] was used throughout the calculations. The MM part was treated at the empirical Amber Parm99 level.[72,73] Details about the electrostatic embedding scheme[61] are given in Supporting Information.

The initial conditions for dynamics simulations were generated according to the scheme given in the ref 61. Its purpose is to generate a Wigner distribution for the QM part as in the gas phase calculations and to combine it with sampling a classical dynamics for the MM environment. The procedure is described in detail in section SI.1. of the Supporting Information.

The distribution of electronic states in which the trajectories were initiated followed closely the procedures adopted for isolated guanine[65] and cytosine.[64] The selection of initial conditions based on the energies and oscillator strengths was applied to isolated guanine and cytosine, that is, QM part only. For guanine, the trajectories were initiated in the energy window around the calculated band maximum

$(5.62 \pm 0.25$ eV) with a propagation time of 0.5 ps. The dynamics was performed with 38 and 15 trajectories starting in the S_1 $(\pi\pi^*)$ and S_2 $(\pi\pi^*)$ states, respectively. The cytosine dynamics (propagation time 1.2 ps) was initiated in the excitation energy window 5.25 ± 0.25 eV, with 12, 30, and 6 trajectories started in S_1, S_2, and S_3 states, respectively. Concerning resulting changes of the energy distribution due to the embedding into the DNA environment see the histograms of the initial state energies (Figure S1 of the Supporting Information) and the discussion below. On-the-fly ab initio surface hopping dynamics simulations were performed using Tully's surface hopping approach.[55,74] Details of the dynamics simulation setup are given in Supporting Information.

The structures found in the course of the dynamics were analyzed in terms of the Cremer-Pople parameters[75] using Boeyen's classification scheme.[76] Following this analysis, the degree (Q) of puckering is a measure of the deviation from planarity, in particular $Q = 0$ Å indicates planar structures. During the dynamics, the formation and breaking of intra- and interstrand hydrogen bonds, respectively, were monitored. For this purpose, we identified interstrand hydrogen bonds by $O(N)\cdots H$ distances with up to 2.5 Å.

The QM/MM surface hopping dynamics calculations were performed with the program package NEWTON-X[62,63] using a module including the QM/MM approach[61] extended by a link atom procedure. For the QM calculations, the COLUMBUS program system[77–79] was employed.

■ RESULTS AND DISCUSSION

Conical Intersections and Hopping Structures. All sets of experimental investigations agree that in the gas phase the cytosine relaxation takes place within 1−3 ps.[1,2,5,80] Guanine has been reported to decay significantly faster within less than 0.5 ps.[1] In the theoretical studies of the photophysics of isolated cytosine, three different types of conical intersections between the S_1 and S_0 states were reported.[15,16,49,81–91] Following the notation of ref 64, they are characterized as *semiplanar*, *oop-NH$_2$* with a strong out-of-plane deformation of the amino group and *C6-puckered*. Nonadiabatic dynamics simulations show[64] that 68% of trajectories decay via semiplanar conical intersections (Figure 2a), and about 7% and 8% decay via *oop-NH$_2$* and *C6-puckered* structures, respectively. The remaining 17% of trajectories did not relax within the 1.2 ps simulation time.

For guanine, two types of conical intersection structures were found, possessing either a strong puckering at the C2 atom (for atomic numbering see Scheme 1) connected with out-of-plane displacement of the amino group[13,92–95] (*ethylenic*[65] conical intersection) or a puckering at the C6 atom and out-of-plane displacement of the oxygen atom[13,92,93] (*oop-O*).[65] In surface hopping dynamics simulations,[65] the majority of hopping structures (95%) were found to be of *ethylenic* character (Figure 2b).

The extent of ring puckering is quantified in Table 1 where the Q values of the Cremer-Pople puckering parametrization are collected. The data demonstrate that the relaxation process in the gas phase requires strongly puckered structures for guanine, while relatively small distortions from ring planarity were observed during the dynamics of cytosine. About 20% of trajectories of isolated photoexcited cytosine relaxed to the ground state at structures with Q parameter smaller than 0.15 Å and the majority of hopping structures were characterized by Q parameter smaller than 0.3 Å. In contrast thereto, much larger puckering was required for guanine to relax to the ground state. About 60% of hopping structures have a Q value larger than 0.6 Å.[65]
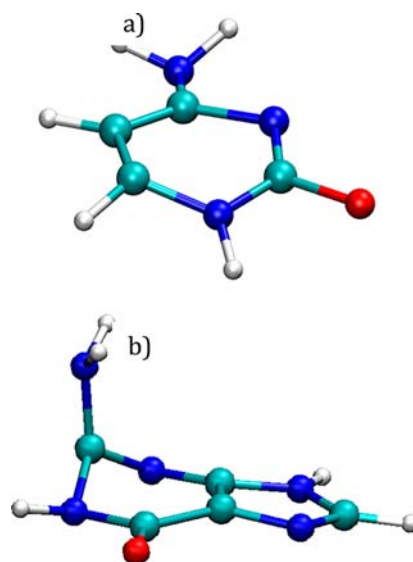

Figure 2. Dominant conical intersection structures: The *semiplanar* conical intersection of cytosine (a) and the *ethylenic* conical intersection of guanine (b).

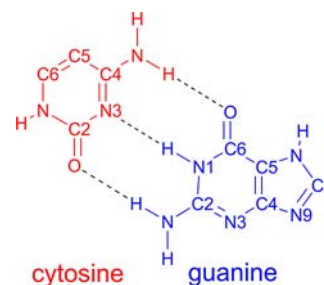**Scheme 1. Numbering Scheme of the Cytosine−Guanine Base Pair**

Table 1. Q Values for Ring Puckering Computed for the S_1/S_0 Hopping Structures of the Deactivation Dynamics of Cytosine and Guanine in the Gas Phase and Embedded in DNA

	Q (Å)			
	cytosine		guanine	
	$Q < 0.15$	$Q < 0.30$	$Q < 0.3$	$Q < 0.6$
Isolated[a]	20%	84%	0%	40%
Embedded	60%	94%	N/A	N/A

[a]Refs 64, 65.

A similar situation is found in the QM/MM dynamics. When cytosine is photoexcited within the DNA structure, the hopping structures show a large variety of conformations, but all characterized by a low degree of ring puckering with Q values not larger than 0.3 Å. About 60% even have values smaller than 0.15 Å. Only 3 trajectories (6%) show hopping structures with puckering larger than 0.3 Å.

In case of guanine, significant ring puckering was observed during the QM/MM dynamics. However, only few conformations with above-mentioned NH$_2$ out-of-plane displacement of the ethylenic conical intersection were found. The structures which occurred at the few (four) hoppings observed in total during the entire simulation time are characterized by a puckering at the C6 atom.

Hydrogen Bond Dynamics in the Excited State. The importance of the intra- and interstrand hydrogen bond dynamics for the photodynamics of DNA has already been discussed in the Introduction. Formation of intrastrand hydrogen bonds of the electronically excited nucleobase with nearest neighboring stacked base and breaking interstrand hydrogen bonds in a Watson−Crick base pair has been shown for 4-aminopyrimidine (used as model for 9H-adenine) to be an important theme during the photodynamical relaxation process.[57,58] The distribution of intra- and interstrand hydrogen bonds sampled over all trajectories of the present simulations with full DNA environment is shown in Figure 3 for embedded cytosine and in Figure 4 for embedded guanine, respectively.

In the case of the photodynamics of cytosine (Figure 3b), the interstrand hydrogen bonds are those expected from the Watson−Crick base pair. Those involving the proton acceptor atoms N3 and O (Scheme 1) show a narrow distribution of bond lengths with maxima around 2 Å. On the other hand, the interstrand bond formed by the NH_2 group displays a broad distribution indicating a larger flexibility of this group. In the ground state (Figure 3c), the NH_2 interstrand bond is much less flexible with a maximum bond length of ∼2.4 Å. The intrastrand hydrogen bonding was monitored between the hydrogen atoms of the NH_2 group of cytosine and the O atoms of the carbonyl group of adjacent thymines. Their distribution is broad with maxima at ∼3.5 Å and larger. The same types of intrastrand hydrogen bonds are observed also in the ground state dynamics, although their distributions are somewhat narrower than those for the excited state. Analyzing the hopping structures with respect to hydrogen bonding shows that in 11% interstrand bonds are broken and in 13% intrastrand bonds are formed. As expected, the breaking of the interstrand hydrogen bonds occurs almost exclusively between the amino group of cytosine and oxygen of guanine.

For embedded guanine, Figure 4 shows narrow distributions of all three intermolecular (Watson−Crick) hydrogen bonds both in ground and excited states. Two intrastrand hydrogen bonds were formed both resulting from interaction of H atoms of the guanine amino group (distribution maxima at 3.0 and 3.5 Å, respectively) with one nitrogen of the adenine above. This interaction is noteworthy since exactly this NH_2 group is required to make out-of-plane torsions for guanine accessing a conical intersection. Two out of five trajectories which relax to the ground state have one interstrand hydrogen bond broken. The consequences of the rigidity of the hydrogen bonding for the cytosine and guanine dynamics will be discussed below.

Time Constants. The time evolution of the ground state and excited state population of cytosine embedded in DNA is shown in Figure 5. The same fitting procedure was used as for the isolated cytosine before.[64] The ground state population was fitted biexponentially with a three-parameter function

$$f(t) = 1 - a \exp(-t/\tau_1) - (1 - a)\exp(-t/\tau_2) \qquad (1)$$

where t is the simulation time and τ_1 and τ_2 are time constants, a is the fraction of population which decays with time τ_1 and $(1 - a)$ is the fraction following the path with the decay constant τ_2. The nonrelaxed trajectories were assumed to deactivate within the exponential decay τ_2. While in case of isolated cytosine 17% of the trajectories did not relax to the ground state within the simulation time 1.2 ps, only 7% of trajectories stayed in the excited state within the same simulation time in case of embedded cytosine.
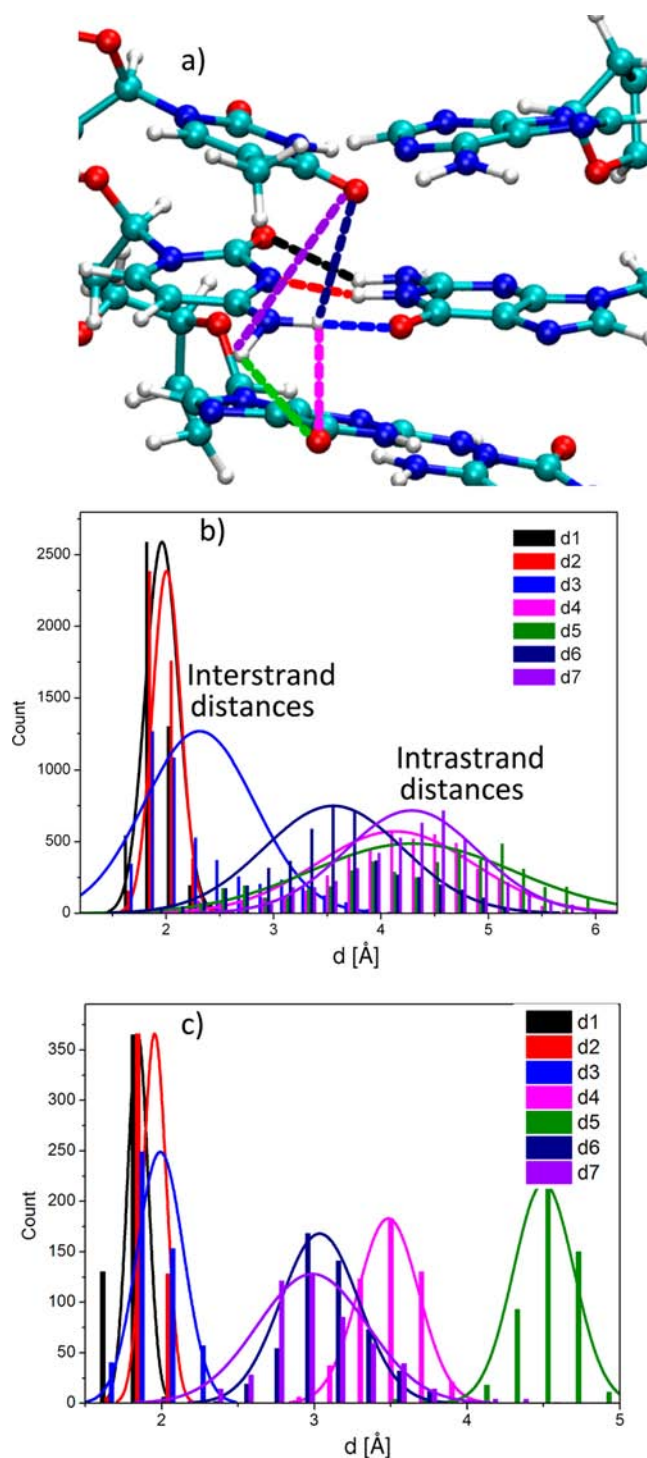

Figure 3. Structure of embedded cytosine with definitions of interstrand (d1−d3) and intrastrand (d4−d7) hydrogen bonds (a). Distribution of hydrogen bond distances during the cytosine dynamics in (b) the excited and (c) the ground state.

Applying this fitting procedure also for embedded cytosine (Table 2), 21% of the population decays with a time constant τ_1 of 12 fs and 79% of the population decays with a constant of 0.48 ps. Similar results were obtained for isolated cytosine (see Table 2) with the slower decay component being by about 0.2 ps larger than for embedded cytosine. The lifetime averaged over the initial populations is 0.38 ps in the present case, somewhat smaller as compared to the 0.58 ps obtained for
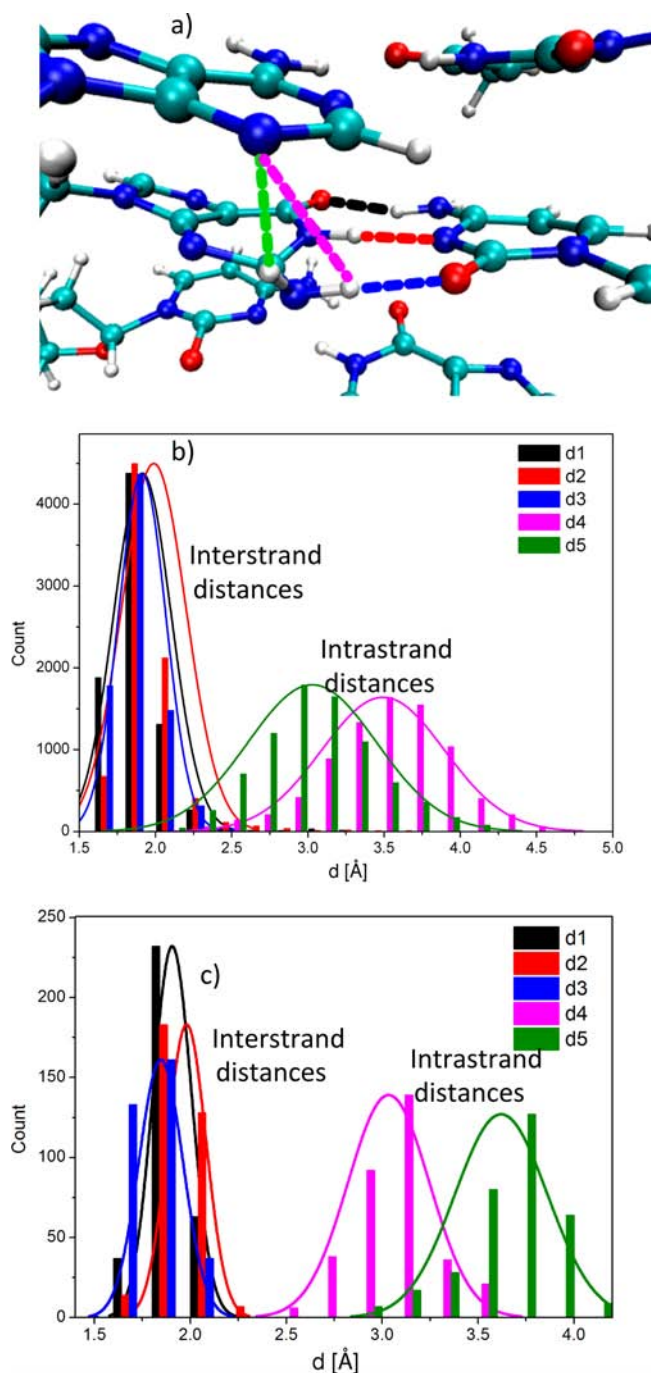
Figure 5. The time evolution of the population of the S_0, S_1, S_2 and S_3 states of cytosine.

Table 2. Fitting Parameters for Cytosine and Guanine Relaxation after UV Excitation in the Gas Phase and Embedded within DNA Structure

	cytosine				guanine
	τ_1 (ps)	a	τ_2 (ps)	$1-a$	τ_1 (ps)
Isolated[a]	0.013	0.16	0.688	0.84	0.224
Embedded	0.012	0.21	0.480	0.79	>0.5[b]

[a]Ref 64, 65. [b]Less than 9% of the trajectories relaxed to the ground state within the 0.5 ps.

Figure 4. Structure of embedded guanine with definitions of interstrand (d1−d3) and intrastrand (d4,d5) hydrogen bonds (a). Distribution of hydrogen bond distances during the guanine dynamics in (a) the excited and (b) the ground state.

isolated cytosine. This decrease is likely to be the consequence of a shift of excited states to somewhat higher energies in embedded cytosine (see Figure S1 in the Supporting Material).

In the gas phase dynamics simulations previously performed for guanine,[65] the S_2 state was depopulated within 20 fs. The following relaxation from S_1 to the ground state occurred in about 0.22 ps. In the dynamics of guanine embedded in the DNA double strand, a fast depopulation of the S_2 state and a corresponding increase of the population of S_1 state are observed also. However, in strong contrast to the gas phase results, the relaxation from S_1 to S_0 becomes very slow in the
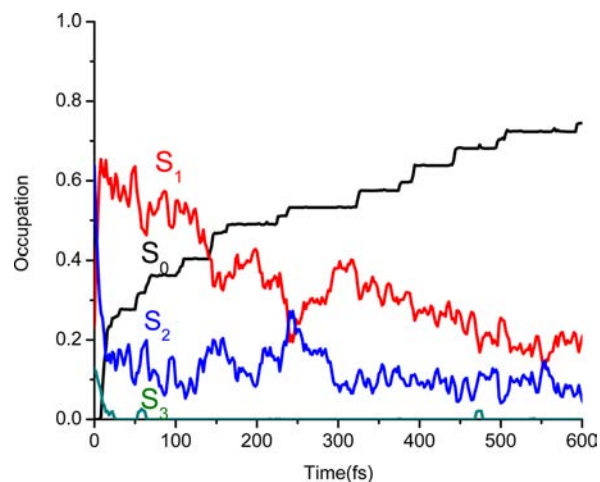
embedded case. In fact, only 9% of trajectories relax into the ground state within the simulation time of 0.5 ps despite the fact that in case of embedding the initial excitation energies were even found to be larger than for the isolated system.

Hydrogen Bond Restraints and the Decay Dynamics. What is the reason for the completely different behavior of photoexcited guanine embedded in DNA as compared to the gas phase whereas cytosine shows the same behavior in both cases? The explanation lies in the different structural characteristics of the decay pathways. As has been discussed above, in case of cytosine, the nonadiabatic deactivation proceeds via relatively modest ring puckering. Even though the interstrand hydrogen bonds, with one exception, do not show any significant flexibility during the course of the dynamics, this fact does not restrict the rather indiscriminate decay mechanism of cytosine. As a result, a similar dynamics behavior in gas phase and in DNA is observed. It has been shown previously that the populations of deactivation channels strongly depend on the details of the computational level used for simulation studies.[64,90,91] Although studies performed at CASSCF level using a larger active space show the semiplanar conical intersection as the most frequently used,[64,96] the other channels of $\pi\pi^*$ character are predicted to become important when higher correlation effects are included in the calculations.[64] Thus, other conical intersections, including the *oop-NH₂* conical intersection could become more important. As shown in Figure 3a, the hydrogen bond to the NH₂ group of cytosine is quite flexible during the excited state dynamics. Thus, this reaction channel will not be affected significantly by embedding of cytosine within DNA. The two other conical intersections discussed (*C6-puckered* and *oop-O*)[64] are not expected to have a significant effect either. In case

of the *C6-puckered* MXS, the largest structure deformation on the C6 atom is not directly involved in interstrand hydrogen bonding, and the *oop-O* MXS is relatively high in energy even if higher correlation effects are included.

The situation is quite different for guanine where the out-of-plane bending of the amino group (*ethylenic* conical intersection) plays an important role for the photodeactivation. The even more pronounced rigidity of the hydrogen bonds in this case, in particular the interstrand bonds, significantly restrict the out-of-plane motion of the NH_2 group and thus block the deactivation path to the ground state. Sobolewski and Domcke[49] investigated the reaction paths of excited state proton transfer for cytosine−guanine base pair and predicted the same effect of interstrand hydrogen bonds. A similar situation concerning the out-of-plane bending of the NH_2 group has been found also in the OM2 dynamics of embedded adenine.[60] This situation can be compared with simulations performed for isolated 4AP and 4AP embedded in a single strand.[57] For the isolated 4AP, 20% of trajectories decay via this channel and only 11% in case of the single-strand embedded 4AP. This indicates that the stacking forces also contribute to the steric hindrance of the motion of this group, but probably to a smaller extent than the interstrand hydrogen bonds as the narrow distributions of interstrand hydrogen bonds for guanine (Figure 4a) show. In view of these detailed mechanistic findings relating to the photoactivity of a single nucleobase within DNA, it should be noted, however, that these results were obtained under neglect of electronic coupling between different nucleobases. To explain the mechanism of the formation of long-lived excited states observed experimentally for single- and double-stranded DNA, these interactions need to be included in the computational model.

CONCLUSIONS

The photophysical behavior of cytosine and guanine embedded in DNA has been investigated by nonadiabatic dynamics simulations at the multiconfigurational ab initio level. A state-averaged CASSCF(14,10) approach including four electronic states and MR-CIS calculations including four electronic states were used for describing the dynamics of cytosine and guanine, respectively. The QM/MM approach used in this study accounts for sterical constraints, Coulomb interactions and effects of hydrogen bonding of the DNA environment on the excited state relaxation of an individual nucleobase species.

The dynamics simulations show remarkable differences in the influence of the hydrogen bonded interactions of the DNA environment on the decay rates of photoexcited cytosine and guanine, respectively. In case of photoexcited cytosine, already the isolated molecule shows relatively small puckering of the hopping structures to the ground state, and thus, the geometrical restrictions exerted by the hydrogen bonds of the DNA environment do not inhibit the photodeactivation of cytosine

A significantly different influence of the hydrogen bonded environment of DNA was observed in the photodynamics of guanine. While the isolated guanine relaxed to the ground state with a lifetime of about 0.22 ps, only a negligible amount of trajectories decayed into the ground state for guanine embedded in DNA within the simulation time of 0.5 ps, although the observed ring puckering was large. This fact can be explained by the restraining conditions of the hydrogen bonded interactions in this case, which does not allow the necessary out-of-plane motions of the NH_2 group of guanine to

reach the conical intersection with the ground state. As was shown in the dynamics simulations of isolated and embedded 4-aminopyrimidine,[57] the intrastrand hydrogen bonds influence the NH_2 out-of-plane relaxation path to certain smaller extent. However, the narrow distribution of the interstrand hydrogen bonds of guanine largely excludes the above-mentioned relaxation channel here showing the primary responsibility of the latter for the drastic excited state lifetime prolongation.

The photodynamics of guanine embedded in DNA demonstrates that there are also relatively simple mechanisms available by which the lifetime of a nucleobase in DNA is significantly enhanced and can be used to explain the lifetimes of 4−6 ps observed by Crespo-Hernnadez et al.[19] in their investigations on the $d(GC)_9 \cdot d(GC)_9$ duplex. Analysis of the types of conical intersections occurring for the other nucleobases leads to the expectation that they should not be influenced by surrounding DNA environment to the same extent as guanine. In the case of adenine, this prediction is based on the fact that the mechanism of CH out-of-plane distortion found in the ab initio dynamics is mainly responsible for the decay. However, any fraction of decay pathways via out-of-plane motion of the amino group will show similar retardation in the decay lifetime as has been found for guanine. The complexity of the photodynamics of thymine and uracil—similar to the one of cytosine[12]—makes predictions difficult but gives also rise to expectations that the variability of the structures observed at the hopping events of the isolated species will lead to rather small effects of hydrogen bonded restraints on the dynamics in DNA.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text describing details of the Computational Details, total energies and Cartesian coordinates of cytosine and guanine, figure with the histogram of initial energies and additional references. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
hans.lischka@ttu.edu; dana.nachtigallova@uochb.cas.cz
Present Address
[#]Goethe Universitaet Frankfurt/Main, Senckenberganlage 31, D-60325 Frankfurt am Main, Germany
Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) Canuel, C.; Mons, M.; Piuzzi, F.; Tardivel, B.; Dimicoli, I.; Elhanine, M. *J. Chem. Phys.* **2005**, *122*, 074316.

(2) Kang, H.; Lee, K. T.; Jung, B.; Ko, Y. J.; Kim, S. K. *J. Am. Chem. Soc.* **2002**, *124*, 12958.

(3) Kang, H.; Jung, B.; Kim, S. K. *J. Chem. Phys.* **2003**, *118*, 6717.

(4) Crespo-Hernandez, C. E.; Cohen, B.; Hare, P. M.; Kohler, B. *Chem. Rev.* **2004**, *104*, 1977.

(5) Ullrich, S.; Schultz, T.; Zgierski, M. Z.; Stollow, A. *Phys. Chem. Chem. Phys.* **2004**, *6*, 2796.

(6) Saigusa, H. *J. Photochem. Photobiol., C* **2006**, *7*, 197.

(7) Blancafort, L. *J. Am. Chem. Soc.* **2006**, *128*, 210.

(8) Chen, H.; Lis, S. *J. Phys. Chem. A* **2005**, *109*, 8443.

(9) Chung, W. C.; Lan, Z. G.; Ohtsuki, Y.; Shimakura, N.; Domcke, W.; Fujimura, Y. *Phys. Chem. Chem. Phys.* **2007**, *9*, 2075.

(10) Perun, S.; Sobolewski, A. L.; Domcke, W. *J. Phys. Chem. A* **2006**, *110*, 13238.

(11) Gustavsson, T.; Banyasz, A.; Lazzarotto, E.; Markovitsi, D.; Scalmani, G.; Frisch, M. J.; Barone, V.; Improta, R. *J. Am. Chem. Soc.* **2006**, *128*, 607.

(12) Barbatti, M.; Aquino, A. J. A.; Szymczak, J. J.; Nachtigallova, D.; Hobza, P.; Lischka, H. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 21453.

(13) Marian, C. M. *J. Phys. Chem. A* **2007**, *111*, 1545.

(14) Matsika, S. *J. Phys. Chem. A* **2004**, *108*, 7584.

(15) Ismail, N.; Blancafort, L.; Olivucci, M.; Kohler, B.; Robb, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 6818.

(16) Zgierski, M. Z.; Patchkovskii, S.; Fujiwara, T.; Lim, E. C. *J. Phys. Chem. A* **2005**, *109*, 9384.

(17) Serrano-Andres, L.; Merchan, M.; Borin, A. C. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 8691.

(18) Lan, Z. G.; Lu, Y.; Fabiano, E.; Thiel, W. *ChemPhysChem* **2011**, *12*, 1989.

(19) Crespo-Hernandez, C. E.; Cohen, B.; Kohler, B. *Nature* **2005**, *436*, 1141.

(20) Crespo-Hernandez, C. E.; Kohler, B. *J. Phys. Chem. B* **2004**, *108*, 11182.

(21) Markovitsi, D.; Gustavsson, T.; Talbot, F. *Photochem. Photobiol. Sci.* **2007**, *6*, 717.

(22) Miannay, F.-A.; Bányász, Á.; Gustavsson, T.; Markovitsi, D. *J. Am. Chem. Soc.* **2007**, *129*, 14574.

(23) Onidas, D.; Gustavsson, T.; Lazzarotto, E.; Markovitsi, D. *J. Phys. Chem. B* **2007**, *111*, 9644.

(24) Bouvier, B.; Dognon, J. P.; Lavery, R.; Markovitsi, D.; Millie, P.; Onidas, D.; Zakrzewska, K. *J. Phys. Chem. B* **2003**, *107*, 13512.

(25) Kononov, A. I.; Bakulev, V. M.; Rapoport, V. L. *J. Photochem. Photobiol., B* **1993**, *19*, 139.

(26) Plessow, R.; Brockhinke, A.; Eimer, W.; Kohse-Hoinghaus. *J. Phys. Chem. B* **2000**, *104*, 3695.

(27) Ge, G.; Georghiou, S. *Photochem. Photobiol.* **1991**, *54*, 301.

(28) Abo-Riziq, A.; Grace, L.; Nir, E.; Kabelac, M.; Hobza, P.; de Vries, M. S. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 20.

(29) Emanuele, E.; Zakrzewska, K.; Markovitsi, D.; Lavery, R.; Millie, P. *J. Phys. Chem. B* **2005**, *109*, 16109.

(30) Onidas, D.; Gustavsson, T.; Lazzarotto, E.; Markovitsi, D. *Phys. Chem. Chem. Phys.* **2007**, *9*, 5143.

(31) Takaya, T.; Su, C.; de La Harpe, K.; Crespo-Hernandez, C. E.; Kohler, B. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 10285.

(32) Middleton, C. T.; de La Harpe, K.; Su, C.; Law, Y. K.; Crespo-Hernandez, C. E.; Kohler, B. *Annu. Rev. Phys. Chem.* **2009**, *60*, 217.

(33) Buchvarov, I.; Wang, Q.; Raytchev, M.; Trifonov, A.; Fiebig, T. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 4794.

(34) Markovitsi, D.; Sharonov, A.; Onidas, D.; Gustavsson, T. *ChemPhysChem* **2003**, *4*, 303.

(35) Markovitsi, D.; Gustavsson, T.; Vaya, I. *J. Phys. Chem. Lett.* **2010**, *1*, 3271.

(36) Kohler, B. *J. Phys. Chem. Lett.* **2010**, *1*, 2047.

(37) Kwok, W. M.; Ma, C. S.; Phillips, D. L. *J. Am. Chem. Soc.* **2006**, *128*, 11894.

(38) Schwalb, N. K.; Temps, F. *Science* **2008**, *322*, 243.

(39) Santoro, F.; Barone, V.; Improta, R. *J. Am. Chem. Soc.* **2009**, *131*, 15232.

(40) Lange, A. W.; Herbert, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 3913.

(41) Roca-Sanjuan, D.; Olaso-Gonzalez, G.; Gonzalez-Ramirez, I.; Serrano-Andres, L.; Merchan, M. *J. Am. Chem. Soc.* **2008**, *130*, 10768.

(42) Schultz, T.; Samoylova, E.; Radloff, W.; Hertel, I. V.; Sobolewski, A. L.; Domcke, W. *Science* **2004**, *306*, 1765.

(43) Sobolewski, A. L.; Domcke, W.; Hattig, C. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 17903.

(44) Improta, R. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2656.

(45) Santoro, F.; Barone, V.; Lami, A.; Improta, R. *Phys. Chem. Chem. Phys.* **2010**, *12*, 4934.

(46) Hu, L. H.; Zhao, Y.; Wang, F.; Chen, G. H.; Ma, C. S.; Kwok, W. M.; Phillips, D. L. *J. Phys. Chem. B* **2007**, *111*, 11812.

(47) Starikov, E. B.; Cuniberti, G.; Tanaka, S. *J. Phys. Chem. B* **2009**, *113*, 10428.

(48) Conti, I.; Altoe, P.; Stenta, M.; Garavelli, M.; Orlandi, G. *Phys. Chem. Chem. Phys.* **2010**, *12*, 5016.

(49) Sobolewski, A. L.; Domcke, W. *Phys. Chem. Chem. Phys.* **2004**, *6*, 2763.

(50) Groenhof, G.; Schafer, L. V.; Boggio-Pasqua, M.; Goette, M.; Grubmuller, H.; Robb, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 6812.

(51) Tonzani, S.; Schatz, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 7607.

(52) Bittner, E. R. *J. Photochem. Photobiol., A* **2007**, *190*, 328.

(53) Bouvier, B.; Gustavsson, T.; Markovitsi, D.; Millie, P. *Chem. Phys.* **2002**, *275*, 75.

(54) Lu, Y.; Lan, Z. G.; Thiel, W. *Angew. Chem., Int. Ed.* **2011**, *50*, 6864.

(55) Alexandrova, A. N.; Tully, J. C.; Granucci, G. *J. Phys. Chem. B* **2010**, *114*, 12116.

(56) Markwick, P. R. L.; Doltsinis, N. L. *J. Chem. Phys.* **2007**, *126*, 175102.

(57) Nachtigallova, D.; Zeleny, T.; Ruckenbauer, M.; Muller, T.; Barbatti, M.; Hobza, P.; Lischka, H. *J. Am. Chem. Soc.* **2010**, *132*, 8261.

(58) Zeleny, T.; Hobza, P.; Nachtigallova, D.; Ruckenbauer, M.; Lischka, H. *Collect. Czech. Chem. Commun.* **2011**, *76*, 631.

(59) Barbatti, M.; Lischka, H. *J. Am. Chem. Soc.* **2008**, *130*, 6831.

(60) Fabiano, E.; Thiel, W. *J. Phys. Chem. A* **2008**, *112*, 6859.

(61) Ruckenbauer, M.; Barbatti, M.; Muller, T.; Lischka, H. *J. Phys. Chem. A* **2010**, *114*, 6757.

(62) Barbatti, M.; Granucci, G.; Lischka, H.; Ruckenbauer, M.; Persico, M. *NEWTON-X: A Package for Newtonian Dynamics Close to the Crossing Seam*; 0.14b ed., 2007; www.univie.ac.at/newtonx.

(63) Barbatti, M.; Granucci, G.; Persico, M.; Ruckenbauer, M.; Vazdar, M.; Eckert-Maksic, M.; Lischka, H. *J. Photochem. Photobiol., A* **2007**, *190*, 228.

(64) Barbatti, M.; Aquino, A. J. A.; Szymczak, J. J.; Nachtigallova, D.; Lischka, H. *Phys. Chem. Chem. Phys.* **2010**, *13*, 6145.

(65) Barbatti, M.; Szymczak, J. J.; Aquino, A. J. A.; Nachtigallova, D.; Lischka, H. *J. Chem. Phys.* **2011**, *134*, 014304.

(66) Shepard, R.; In *Modern Electronic Structure Theory*, Yarkony, D. R., ed.; World Scientific: Singapore, 1995, 345.

(67) Shepard, R.; Lischka, H.; Szalay, P. G.; Kovar, T.; Ernzerhof, M. *J. Chem. Phys.* **1992**, *96*, 2085.

(68) Lischka, H.; Dallos, M.; Szalay, P. G.; Yarkony, D. R.; Shepard, R. *J. Chem. Phys.* **2004**, *120*, 7322.

(69) Dallos, M.; Lischka, H.; Shepard, R.; Yarkony, D. R.; Szalay, P. G. *J. Chem. Phys.* **2004**, *120*, 7330.

(70) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(71) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257.

13668

dx.doi.org/10.1021/ja3028845 | *J. Am. Chem. Soc.* 2012, 134, 13662–13669

(72) Cornell, W. D.; Cieplak, P.; Bayly, C. I.; Gould, I. R.; Merz, K. M.; Ferguson, D. M.; Spellmeyer, D. C.; Fox, T.; Caldwell, J. W.; Kollman, P. A. *J. Am. Chem. Soc.* **1995**, *117*, 5179.

(73) Wang, J. M.; Cieplak, P.; Kollman, P. A. *J. Comput. Chem.* **2000**, *21*, 1049.

(74) Tully, J. C. *J. Chem. Phys.* **1990**, *93*, 1061.

(75) Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1354.

(76) Boeyens, J. C. A. *J. Chem. Crystallogr.* **1978**, *8*, 317.

(77) Lischka, H.; Shepard, R.; Brown, F. B.; Shavitt, I. *Int. J. Quantum Chem.* **1981**, *S15*, 91.

(78) Lischka, H.; Shepard, R.; Pitzer, R. M.; Shavitt, I.; Dallos, M.; Muller, T.; Szalay, P. G.; Seth, M.; Kedziora, G. S.; Yabushita, S.; Zhang, Z. Y. *Phys. Chem. Chem. Phys.* **2001**, *3*, 664.

(79) Lischka, H.; Shepard, R.; Shavitt, I.; Pitzer, R. M.; Dallos, M.; Mueller, T.; Szalay, P. G.; Brown, F. B.; Ahlrichs, R.; Boehm, J. G.; Chang, A.; Comeau, D. C.; Gdanitz, R.; Dachsel, H.; Ehrhardt, C.; Ernzerhof, M.; Hoechtl, P.; Irle, S.; Kedziora, G.; Kovar, T.; Parasuk, V.; Pepper, M. J. M.; Scharf, P.; Schiffer, H.; Schindler, M.; Schueler, M.; Seth, M.; Stahlberg, E. A.; Zhao, J.-G.; Yabushita, S.; Zhang, C. L.; Barbatti, M.; Matsika, S.; Schuurmann, M.; Yarkony, D. R.; Brozell, S. R.; Beck, E. V.; Blaudeau, J.-P.; Ruckenbauer, M.; Sellner, B.; Plasser, F.; Szymczak, J. J. *COLUMBUS, An ab Initio Electronic Structure Program*; release 5.9.2, 2008; www.univie.ac.at/columbus.

(80) Kosma, K.; Schroter, C.; Samoylova, E.; Hertel, I. V.; Schultz, T. *J. Am. Chem. Soc.* **2009**, *131*, 16939.

(81) Blancafort, L.; Cohen, B.; Hare, P. M.; Kohler, B.; Robb, M. A. *J. Phys. Chem. A* **2005**, *109*, 4431.

(82) Zgierski, M. Z.; Fujiwara, T.; Lim, E. C. *Chem. Phys. Lett.* **2008**, *463*, 289.

(83) Tomic, K.; Tatchen, J.; Marian, C. M. *J. Phys. Chem. A* **2005**, *109*, 8410.

(84) Merchan, M.; Gonzalez-Luque, R.; Climent, T.; Serrano-Andres, L.; Rodriuguez, E.; Reguero, M.; Pelaez, D. *J. Phys. Chem. B* **2006**, *110*, 26471.

(85) Merchan, M.; Serrano-Andres, L. *J. Am. Chem. Soc.* **2003**, *125*, 8108.

(86) Kistler, K. A.; Matsika, S. *J. Chem. Phys.* **2008**, *128*, 215102.

(87) Kistler, K. A.; Matsika, S. *J. Phys. Chem. A* **2007**, *111*, 2650.

(88) Blancafort, L.; Robb, M. A. *J. Phys. Chem. A* **2004**, *108*, 10609.

(89) Blancafort, L. *Photochem. Photobiol.* **2007**, *83*, 603.

(90) Lan, Z. G.; Fabiano, E.; Thiel, W. *J. Phys. Chem. B* **2009**, *113*, 3548.

(91) Hudock, H. R.; Martinez, T. J. *ChemPhysChem* **2008**, *9*, 2486.

(92) Serrano-Andres, L.; Merchan, M.; Borin, A. C. *J. Am. Chem. Soc.* **2008**, *130*, 2473.

(93) Lan, Z. G.; Fabiano, E.; Thiel, W. *ChemPhysChem* **2009**, *10*, 1225.

(94) Yamazaki, S.; Domcke, W.; Sobolewski, A. L. *J. Phys. Chem. A* **2008**, *112*, 11965.

(95) Chen, H.; Li, S. H. *J. Chem. Phys.* **2006**, *124*, 154315.

(96) Gonzalez-Vazquez, J.; Gonzalez, L. *ChemPhysChem* **2010**, *11*, 3617.