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Efficient Excited-State Deactivation of the Gly-Phe-Ala Tripeptide via an Electron-Driven Proton-Transfer Process

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The secondary structures of proteins (α-helices, β-sheets, etc.) are determined to a large extent by hydrogen bonds involving the CO and NH groups of the backbone. The biological function of proteins depends decisively on their three-dimensional structure. The enzymatic activity of proteins is highly specific and involves hydrogen-bond interactions between the enzyme and the substrate. Life on earth thus depends strongly on the functionality of hydrogen bonds in biological molecules.[1]

The role of hydrogen bonds for the structure and function of proteins in the electronic ground-state is nowadays well understood.[2] The role of hydrogen bonds in the UV-induced photochemistry of biological macromolecules, on the other hand, is less clear. UV exposure of peptides or proteins results in a complex photochemistry which eventually leads to structural changes and the loss of functionality. Mechanisms which suppress undesired photoinduced reactions in proteins are therefore of fundamental importance.

Very recently, the electronic and vibrational spectra of various conformers of several tripeptides with an aromatic chromophore, such as Trp-Gly-Gly, Phe-Gly-Gly, and Gly-Phe-Ala, have been obtained by double-resonance spectroscopy in supersonic jets.[3−6] The assignment of the spectra to specific conformers has become possible by comparison with accurate ab initio calculations.[3−6] Unexpectedly, the conformers with the lowest energy (according to the ab initio calculations) were not observed in the resonant two-photon ionization (R2PI) spectra. Similar observations have recently been made for isolated DNA bases[7] and DNA base pairs.[8] The absence of certain tautomers could be explained by the identification of particularly efficient radiationless decay processes which render the lifetime of the excited states too short to allow the detection of the R2PI signal.[9−11] Herein, we report the preliminary results of excited-state ab initio calculations which provide evidence for an efficient excited-state deactivation mechanism in one of the low-energy conformers of Gly-Phe-Ala (named GFA_06[$\gamma_L(g^-)$] in ref 3); see Figure 1. This is the conformer of lowest free energy in the family of γ structures which exhibit at least one intramolecular hydrogen bond; see Figure 4 of ref 3. The most essential feature of this mechanism is an electron-driven proton-transfer reaction along a pre-existing C═O···N—H hydrogen bond in a charge-transfer (CT) excited state of the tripeptide.

The ground-state equilibrium geometry of Gly-Phe-Ala has been determined with the second-order Møller−Plesset (MP2) method. The excited-state potential-energy surfaces have been explored with the CC2 method, which is a simplified and computationally efficient modification of the coupled-cluster method with singles and doubles. Coordinate-driven minimum-energy paths (so-called relaxed scans) in the excited states were obtained with the CC2 method. All calculations were carried out with the TURBOMOLE program package. A more detailed description of the computational methods can be found in the Supporting Information.

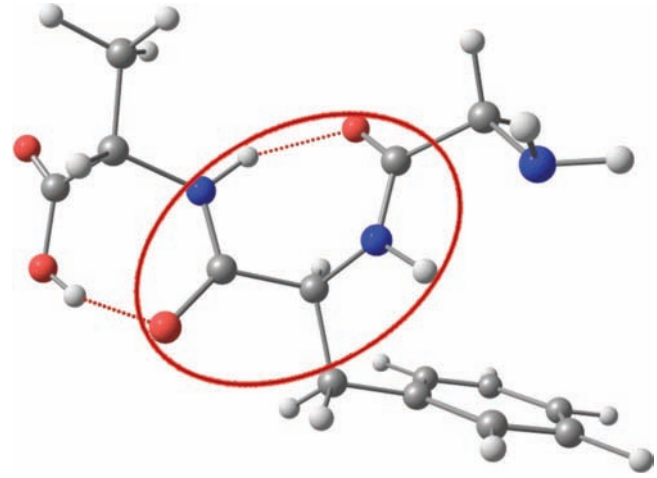

Figure 1. Ground-state equilibrium geometry of Gly-Phe-Ala. The ellipse encircles a hydrogen-bond motif named γ turn, which is commonly found in the backbone of peptides.

The potential energy profiles for proton transfer along the C═O···H—N hydrogen bond are shown in Figure 2a. The UV absorbing state in the R2PI experiments is the lowest $^1\pi\pi^*$ state of the phenyl ring (▽); see also Table S1 in the Supporting Information. The singlet excited states on the amino acid backbone involve the excitation of an electron from a nonbonding orbital (n) of the backbone (see Figure S1a in the Supporting Information) to an unoccupied orbital which is localized on the same branch of the backbone (see Figure S1b in the Supporting Information). It is designated as the locally excited (^{1}LE) state in the following. At its optimized geometry the lowest ^{1}LE state lies below the spectroscopic $^1\pi\pi^*$ state (□ in Figure 2a). In addition, there exists a low-lying singlet state which involves the excitation of an electron from an orbital located in the region of the hydrogen-bonded NH group (see Figure S1c in the Supporting Information) to an unoccupied orbital located in the region of the hydrogen-bonded CO group (see Figure S1d in the Supporting Information). This state can be classified as a charge-transfer (^{1}CT) state. The top-up triangles in Figure 2a show the energy of this state along its minimum energy path

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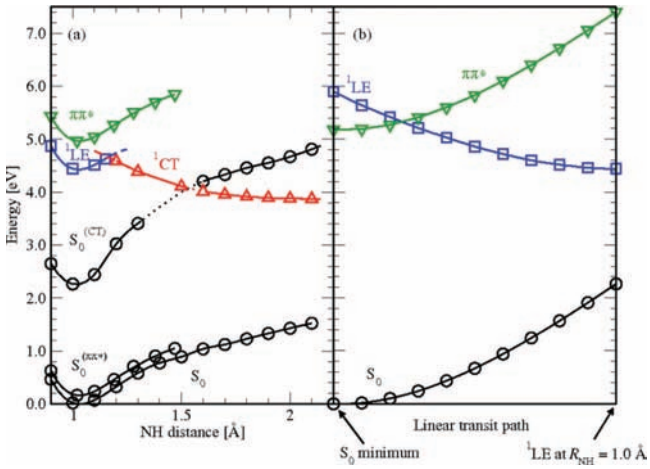

Figure 2. (a) Minimum-energy profiles of the $^1\pi\pi^*$ state (▽), the locally excited state, ^{1}LE (□), and the charge-transfer state, ^{1}CT (△), of Gly-Phe-Ala along the proton-transfer coordinate. The $^1\pi\pi^*$, ^{1}LE, and ^{1}CT energies have been determined at the minimum-energy geometries of the respective state. The ground-state energies designated as S_0 have been calculated at the minimum-energy geometries of the S_0 state, while the S_0 energies designated as $S_0^{(CT)}$ have been determined at the minimum-energy geometries of the ^{1}CT state. (b) Potential-energy profiles of the $^1\pi\pi^*$, ^{1}LE, and S_0 states along the linearly interpolated transit path between the S_0 minimum-energy geometry and the ^{1}LE minimum-energy geometry at $R_{NH} = 1.0$ Å.

(relaxed scan). The potential energy function designated as $S_0^{(CT)}$ in Figure 2a represents the energy of the S_0 state calculated at the geometries of the minimum-energy path in the ^{1}CT state. The crossing of the ^{1}CT and $S_0^{(CT)}$ curves is a true crossing (conical intersection). The crossing of the ^{1}LE and ^{1}CT curves, on the other hand, is an apparent crossing, since these two reaction paths have individually been optimized.

To reveal the mechanism for the internal conversion from the $^1\pi\pi^*$ state to the ^{1}LE state, we have calculated the energies of the $^1\pi\pi^*$, ^{1}LE, and ^{1}CT states along the linearly interpolated transit path (LITP) (see computational methods in the Supporting Information) from the S_0 minimum to the ^{1}LE minimum (at a fixed NH distance of 1.0 Å). These PE profiles are shown in Figure 2b. It is seen that there exists a crossing (conical intersection) only slightly above the minimum of the $^1\pi\pi^*$ surface.

The overall mechanistic picture suggested by these ab initio electronic-structure data is as follows. Absorption of a UV photon populates the $^1\pi\pi^*$ state. The $^1\pi\pi^*$ population relaxes to the ^{1}LE state via a low-lying conical intersection (see Figure 2b). The ^{1}LE surface is, in turn, intersected by the ^{1}CT surface (see Figure 2a). Population of the ^{1}CT state corresponds to the transfer of an electron from the NH group to the CO group along the intramolecular hydrogen bond (see Figure 1). The proton then follows the electron, which leads to a pronounced stabilization of the CT state and thus to a conical intersection with the S_0 state (see Figure 2a). In this way, the electronic excitation energy is converted, via three conical intersections, into comparatively harmless vibrational energy in the closed-shell ground state.

In summary, the present ab into electronic-structure calculations suggest a detailed mechanism which can explain that the excited-state lifetime of one of the intramolecularly hydrogen-bonded conformers of Gly-Phe-Ala is too short to allow the detection of an R2PI signal. The radiationless decay mechanism is an electron-driven excited-state proton-transfer process, which has been identified previously in various hydrogen-bonded systems.[11−13]

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Supporting Information Available: The computational methods used in this work are described. Figure S1 shows the most relevant frontier orbitals of Gly-Phe-Ala. Table S1 shows the vertical excitation energies at the optimized ground state. Cartesian geometries of the optimized ground and first excited-state are given. This material is available free of charge via the Internet at http://pubs.acs.org.

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