Gas phase photoisomerization of urocanic acid – a theoretical study

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Abstract

The photochemistry of urocanic acid is investigated theoretically by means of time-dependent density functional theory. The topology of the potential energy surface along the isomerization pathway and close to the Franck–Condon region is investigated and consequences for the photoisomerization reactions are outlined. A recently published supersonic jet spectroscopy study is reinterpreted in the light of these and earlier theoretical results to give a clear picture of the gas phase photochemistry. It is found that the photochemistry of the two isomers is fundamentally different, in contrast to the situation in solution.

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1. Introduction

Urocanic acid (4-imidazoleacrylic acid), see Fig. 1, is an epidermal chromophore normally present in human skin [1]. Since the absorption spectrum of urocanic acid in aqueous solution strongly overlaps with that of DNA in the UVB region it was thought that it has a UV protective role [2].

However, as De Fabo [3] have demonstrated the cis isomer of urocanic acid is a potent immunosuppressor. Photoisomerization of urocanic acid occurs in the UV range [4], and the immunosuppressive effect has also been linked to UV-induced skin cancer [5].

These findings sparked a large interest in understanding the photochemistry of this chromophore, and a large number of spectroscopic studies have been reported. See a recent review [6] for many references. Soon it turned out that the photochemistry is quite complex and dependent on both wavelength [7] and protonation state [8,9].

Recently, supersonic jet spectroscopy was used to investigate the gas phase photochemistry of the neutral form of trans-urocanic acid [10]. They concluded that the lowest lying excited state resulted from a quite strongly absorbing $\pi \to \pi^*$ transition that was close to the band origin which was placed at 4.04 eV, and that the population of this state led to photoisomerization provided that an excess energy of about 4 kcal mol$^{-1}$ was added. When this energy was available, the system exhibited double emission, indicating that some of the population had photoisomerized, and conse-
quently this energy was interpreted as the isomerization barrier.

In the gas phase spectra a second, very broad feature with maximum absorption at 4.54 eV appears. This is indicative of a state with a large difference between ground and excited state geometry, and therefore a large relaxation. No dual emission was observed from this state. The authors concluded that this was due to absorption to the S2 state, which was also assumed to be of $\pi \rightarrow \pi^*$ based on the large oscillator strength.

There have also been two recent high-level quantum chemistry investigations of the low-lying states of urocanic acid in the neutral form [11,12]. Although quite reliable methods were used, complete active space with second order perturbation (CASPT2) and time-dependent density functional theory (TD-DFT) [13], the theoretical predictions were in very poor agreement with the subsequently published supersonic jet experiment, at least in the current interpretation. The CASSCF/CASPT2 S1 band origin of trans-UCA was placed at 4.66 eV, (vertical excitation energy 4.93 eV) and the vertical excitation energy of the second $\pi \rightarrow \pi^*$ transition was calculated to be 5.40 eV. This is a surprising large discrepancy, since CASPT2 is claimed to have an accuracy of $\approx 0.1$ eV. Independent calculations using TD-DFT [12] gave the corresponding vertical excitation energies of 4.54 and 5.50 eV, again in poor agreement with experiment. These results were very disappointing from the theoreticians perspective.

However, somewhat curiously, the calculated vertical excitation energy to the S1 state of the cis form of UCA is in almost perfect agreement with the measured band origin, 4.16 using CASPT2 and 4.05 using TD-DFT. At the same time the calculated vertical excitations to the S1 state of the trans form is much closer to the maximum absorption of the second, broad feature.

Furthermore, the experiment provided an estimate of the S1 band origin in the cis form of UCA to be about 3.4 kcal mol$^{-1}$ above that of the trans form. It was surprising that they did not observe any isomerization upon populating the broad feature, since the density of states is often quite high in the region of S2 and the internal energy should be well above the isomerization threshold once the S1 state is reached.

Also this anomaly would be explained if we assumed that the first region was due to the cis isomer and the second to the trans isomer. To test our hypothesis we have investigated the potential energy surface along the photoisomerization coordinate and in the planar conformations (The Franck–Condon regions).

2. Computational details

In order to explore the potential energy surface of urocanic acid we have used a combination of the configuration interaction method using single excitations (CIS) and TD-DFT. The former have been used to approximate the initial relaxation on the excited state surface including the important bond stretch coordinates, while the latter has been used to calculate more accurately the single point energies.
The calculations were carried out in the following manner: starting from the planar ground state geometry, we performed geometry optimizations using the CIS method to mimic the initial fast relaxation mostly related to bond stretching (and also some angular relaxation). This geometry was then used to calculate the band origin (energy difference between the ground state at the ground state geometry and the excited state at the excited state geometry) and fluorescence maximum (energy difference between the ground state and the excited state at the excited state geometry). These can be directly compared with earlier theoretical work where they were calculated with the CASPT2 method on CASSCF geometries. For the published CASSCF geometries, we have also done single point TD-DFT calculations for comparison.

After that, we explored the potential energy along the coordinate defined by the dihedral angle around which the isomerization takes place. This was done by starting from the CIS-optimized excited state planar geometry, incrementing the dihedral angle by $15^\circ$, and performing a TD-DFT calculation at that geometry. By only performing the geometry optimization at the planar geometry (where it will stay planar due to the symmetry) this scheme will be biased towards these geometries. In other words, the calculated barriers along the dihedral coordinate should provide overestimates of the minimum barriers.

For all density functional theory calculations, we have used Becke's three parameter hybrid functional [14] for exchange combined with the correlation functional due to Lee et al. [15] (B3LYP). The excitation energies were calculated using the 6-311+G(d,p) basis set, including both polarization functions and diffuse basis functions. For excitation energies we used the GAUSSIAN implementation of TD-DFT [16], which only allowed us to do single point calculations, since gradients were not available.

For the CIS geometry optimization we chose a somewhat smaller basis set, the 6-31G base set which contains polarization functions on heavy atoms but no diffuse functions. Normally, in neutral systems, this gives quite good geometries while sometimes diffuse functions are required to get more accurate energies.

All calculations were carried out with the Gaussian 98 [17] suite of programs.

3. Results and discussion

To start with, we compare vertical excitation energies calculated at the Hartree–Fock, B3LYP, and CASSCF geometries using the TD-DFT/B3LYP method. Obviously, the lowest energy for the ground state is obtained with B3LYP. The HF and CASSCF geometries are close in energy ($<1.0$ kcal mol$^{-1}$ difference) for both isomers. Consequently, the TD-DFT excitation energies are also very similar for CIS and CASSCF geometries ($<0.1$ eV difference for the three excitations). In general these excitation energies are overestimated by $\approx 0.2$ eV compared to the B3LYP geometry. This places them between or close to the previously published TD-DFT and CASPT2 results [11,12].

We now turn to the results after letting the system relax on the $S_1$ potential energy surface and compare the results from our single point TD-DFT calculations on CIS geometries with both previously published single point CASPT2 calculations on CASSCF geometries and our TD-DFT calculations on the same CASSCF geometries. Looking first at the trans isomer, the results from both the CIS and CASSCF geometries are close to the CASPT2 ones (4.17/3.94 eV compared with 4.17 eV for fluorescence maximum and 4.37/4.55 eV vs. 4.66 eV for band origins). The discrepancy is much larger between CASPT2 and TD-DFT for the cis isomer with the band origin lying $\approx 0.6$ eV lower than both the TD-DFT/CASSCF and TD-DFT/CIS values (3.37 compared with 3.95/3.95 eV). However, we note that the experiments put the band origin of the first transition at 4.04 eV with a presumably small shift from the ground state, which is perfectly consistent with our TD-DFT results of the cis isomer (band origin 3.95 eV and vertical excitation 4.04 eV). In terms of absolute energies it turns out that the CIS geometry is closer to the TD-DFT minimum for the trans isomer while the energy is virtually the same between the two geometries for the cis isomer. Therefore we choose the CIS geometry for sub-
sequent calculation of the energy profile along the dihedral coordinate.

Similar calculations were carried out for the S2 state which is of n → π* character with a very small oscillator strength, therefore hardly visible in spectroscopic experiments. Here the results are more dependent on the geometry, but the trends from the CASSCF/CASPT2 calculations are preserved, with the S2 minimum substantially lower than the S1 minimum in the case of the trans isomer while still above for the cis. So excitation to the S1 surface of the trans isomer is likely to populate the dark n → π* state with substantial relaxation as a consequence, while in the cis case the system will probably remain and emit from the S1 state. This corresponds to our interpretation of the experiment. In the experiment, a large relaxation took place, and it was thought that it was due to internal conversion from the S2 state to the S1 state, but without any detectable isomerization taking place. In our interpretation the situation would be reversed, with absorption taking place on the S1 (π → π*) surface, and then internal conversion to the S2 (n → π*) surface.

Finally, we also calculated the band origin and fluorescence maxima for the second π → π* transition, which both TD-DFT and CASPT2 calculated to be absorbing at 5.4–5.5 eV for the trans isomer, while the current interpretation of the gas phase spectra places is at 4.5 eV. The band origin is predicted to be quite close to the vertical excitation energy (5.43 eV compared two 5.72 eV at the HF geometry) in the trans case while the cis isomer shows considerably larger relaxation (4.78 eV is the band origin). These results cast very little new light over the experimental spectra and will not be further discussed, we only conclude that it seems unlikely that this is the state responsible for the absorption around 4.5 eV.

Note that there is a difference in protonation state between the two isomers, since the most stable protomer of the cis isomer allows for an intramolecular hydrogen bond while keeping the carboxylic hydrogen in its preferred position. This turns out to have dramatic consequences for the potential energy surfaces.

As could be expected, the profile for the ground state energies is for both protomers dominated by a large barrier (69.3 and 66.8 kcal mol⁻¹) peaking at 90° for both protomers. However, the two curves behave differently in the region around 0° (cis conformation) due to the different protonation states, which in the cis protomer allows hydrogen bonding, while for the trans protomer electrostatic interaction between the nitrogen and oxygen makes the energy curve repulsive in this area.

For the S1 and S2 states of the trans protomer the corresponding curves are seen in Fig. 2. It is clear that the topology of the potential energy surfaces is quite different in the excited state. For the S2 state, which is almost degenerate with the S1 state at the planar trans structure a barrier of more than 20 kcal mol⁻¹ has to be overcome to reach the cis structure on this section of the potential energy surface. Although this should be an overestimate, it seems unlikely that the observed isomerization takes place in this state. For the S1 state, the barrier to pass towards a twisted structure is merely 1.1 kcal mol⁻¹, which is considerably lower than the estimate from experiment, which was 4 kcal mol⁻¹. Since our methodology provides an upper bound for the barrier within the chosen formalism, this provides further support that the observed photoisomerization does not originate from the trans isomer. It should be noted that the results close to the fully twisted conformation (90°) is probably not very reliable since the S0/S1 gap is vanishing and a conical intersection in
this region seems likely, which could only be described properly with a multireference method. An $S_2/S_1$ crossing is predicted as the dihedral angle approaches zero, so that the lowest lying singlet is of $n \rightarrow \pi^*$ character. This is due to that this excitation reduces the total density of the oxygen involved in the unfavorable electrostatic interaction with the unprotonated nitrogen.

Turning to the cis protomer, the curves can be studied in Fig. 3. Again, for the $S_2$ state, a considerable barrier of more than 10 kcal $\cdot$ mol$^{-1}$ is predicted. As before, we note that it is likely that the TD-DFT method does not give a satisfactory description close to the twisted geometry, and therefore the local minimum seen at 90° is possibly an artifact. The fact that we are probably overestimating the barrier implies that the experimental estimate could very well be compatible with this barrier, but since the $S_2$ state is well separated from the $S_1$ in the cis conformation and has a very small oscillator strength we believe that isomerization in the $S_2$ state is not observed experimentally. For the $S_1$ potential energy surface, we can see that the overall topology from the trans protomer is preserved, with a minimum at 90°. However, the breaking of the intramolecular hydrogen bond raises the barrier between the planar and twisted form to around 5 kcal mol$^{-1}$ in our calculations. Recalling that the experimental estimate was 4 kcal mol$^{-1}$ this seems like a quite reasonable estimate, and is in line with our hypothesis. From the graph it seems that the overall barrier to reach the trans conformation is $\approx$12 kcal mol$^{-1}$, but this is in part an effect of the lack of geometric relaxation, the starting geometry is somewhat strained to optimize the intramolecular hydrogen bond. To investigate the magnitude of this effect we recalculated the energy including nuclear relaxation in the planar trans conformation. This lowered the energy at 180° by 4 kcal mol$^{-1}$, giving a total barrier of 8 kcal mol$^{-1}$, which is more in the regime of the experiment.

In the experiment it could be seen that the origin emission after isomerization was blueshifted 1200 cm$^{-1}$ or 3.4 kcal mol$^{-1}$ relative to the origin of the absorbing species. We calculated the band origin of the $S_1$ state for the cis protomer in the trans conformation, which would give rise to the observed emission after isomerization according to our hypothesis. The resulting band origin is calculated to be 4.1 kcal mol$^{-1}$ (1450 cm$^{-1}$) above that of the cis conformation of the same protomer, in fair agreement with experiment.

We also note that the topology of the potential energy surface for both isomers is consistent with the one suggested in a recent paper [18], where isomerization is believed to take place via a twisted intermediate. In both the cis and trans case, we predict that the minimum is reached at a twisted geometry.

4. Conclusions

In conclusion, the following picture of the gas phase photochemistry of urocanic acid has emerged. For the trans form, excitation to the $S_1$ ($\pi \rightarrow \pi^*$) surface leads to internal conversion to the ($n \rightarrow \pi^*$) state in which substantial geometric relaxation takes place before emission. This does not lead to isomerization and is observed as the broad feature in the spectrum. In the cis form, excitation to the $S_1$ state leads to photoisomerization if sufficient energy is provided, and otherwise it emits from the $S_1$ surface after only minor geometric relaxation. The barrier has its origin in the breaking of the intramolecular hydrogen bond formed for the cis isomer, while for the trans isomer there is
only a very small barrier, which would lead to ef-
ficient isomerization if there had not been the
competing process of internal conversion.

Finally, we note that our hypothesis is critically
dependent on the assumption that the vapour on
which the experiment is performed contains a
mixture of trans and cis isomers, and we ac-
knowledge the fact that this should be tested. But
the very encouraging correspondence between
theory and experiment, and clear understanding
that our interpretation provides, gives us confi-
dence to suggest that the experiment should be re-
examined in the light of this hypothesis.

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