Hydrogen atom transfer in the photochemical isomerization of hydrazones of 1,2,4-oxadiazole derivatives

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Abstract

DFT calculations on the photoisomerization of hydrazones of 1,2,4-oxadiazole derivatives to 1,2,5-triazoles have been performed showing that the reaction occurred through the first excited singlet state. The *Z* isomer gave the reaction through a hydrogen atom transfer of the hydrazonic nitrogen atom to the nitrogen atom in four position on the oxadiazole ring. In this case, the isomerization was a concerted reaction. The *E* isomer could undergo the same reaction. However, it could not be a concerted reaction but required the presence of a ring opening intermediate.

Keywords 1,2,4-Oxadiazole · 1,2,5-Triazole · Photoisomerization · DFT calculation · Hydrogen atom transfer

1 Introduction

The photoisomerization of pentatomic heterocyclic compounds is one of the most studied photochemical reaction allowing to obtain some significant synthetic processes [1–3].

Some years ago, the photochemical isomerization of 1,2,4-oxadiazole derivatives **1** has been reported to give the corresponding triazoles **2** (Scheme 1) [4]. When the reaction was performed in the presence of $\text{Ry}(\text{bpy})_2\text{Cl}_2$, a new photoisomerization to the triazole **3** was observed (Scheme 1) [5]. While a theoretical explanation of the reaction **1** → **3** has been reported [6], no hypothesis is available on the possible mechanism of the photochemical reaction **1** → **2**. The described reaction is the photochemical version of the thermal Boulton–Katritzky rearrangement (Scheme 2) [7, 8].

The Boulton–Katritzky reaction can occur in acid catalyzed, base catalyzed and uncatalyzed conditions and seems to involve a S_{Ni} process requiring a quasi-aromatic transition state depicted in the Fig. 1 [9, 10]. In the proposed scheme the hydrazonic nitrogen atom attacks the oxadiazole ring inducing the observed ring cleavage. It could be interesting to verify if the same type of mechanism works when the reaction is photochemically performed. However,

recently we found that, in the photochemical isomerization of 2-furylidenetetalone (Scheme 3), where a quasi-aromatic transition state similar to that proposed for the Boulton–Katritzky rearrangement could be considered, this type of transition state was not present [11]. Furthermore, the reaction occurred through the attack of the oxygen atom of the carbonyl group on the furan ring, showing a behavior quite similar to that described for the Boulton–Katritzky rearrangement.

It is difficult to use the mechanism proposed for the Boulton–Katritzky rearrangement for the photochemical version of this reaction: both *Z* and *E* isomers are reactive in the photochemical reaction while the transition state calculated in the thermal reaction can be obtained only using the *Z* isomer. Furthermore, *Z,E* photoisomerization did not occur in the tested substrates, and, finally, the yields of the 1,2,4-triazole derivative are higher when the *E* isomer is used in the photochemical reaction (Scheme 4) [4].

On the basis of these results, we decided to perform a DFT study on *E* and *Z* isomer of **1** to identify the mechanism of the described reaction and to verify two hypotheses, a. if a quasi-aromatic transition state is involved in the reaction as in thermal Boulton–Katritzky reaction, b. if the reaction occurs through the attack of the hydrazonic nitrogen atom to the oxadiazole ring.

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Scheme 1 Photochemical isomerizations of 1,2,4-oxadiazole derivatives

Scheme 2 Boulton-Katritzky rearrangement

Fig. 1 Proposed transition state in the Boulton-Katritzky rearrangement

Scheme 3 Photochemical isomerization of 2-furylidene tetralone

2 Results and discussion

In this study the photochemical behavior of **1** has been studied. The computational work has been conducted at DFT level of theory using B3LYP/6-311G* (d,p) on Gaussian09. The *Z* isomer of the 1,2,4-oxadiazole derivative **1** showed a calculated absorption at $\lambda = 410$ nm (in dioxane *Z-1* showed an absorption at $\lambda = 366$ nm ($\log \epsilon = 4.22$) [12]), corresponding to an electronic transition from orbital 89 (NHOMO) to

orbital 91 (LUMO). This way, an excited singlet state with an energy of 291 kJ mol^{-1} was obtained. The *E* isomer did not show a stability comparable to that of the *Z* isomer. It showed an energy higher for 20 kJ mol^{-1} . This difference is due to the fact that one of the phenyl groups present on the molecule cannot be planar and conjugated with the rest of the molecule. The structure of the *E* isomer of **1** is reported in Fig. 2.

The *E* isomer of **1** showed a calculated absorption at $\lambda = 401$ nm (*E-1* showed an absorption in dioxane at 335 nm ($\log \epsilon = 4.31$) [12]). Also, in this case, the observed absorption corresponds to an electronic transition from the NHOMO to the LUMO orbital of the molecule and allowed to obtain an excited singlet state at 318 kJ mol^{-1} (Fig. 3). The above-described situation does not allow the *Z* $\rightarrow$ *E* isomerization while the *E* $\rightarrow$ *Z* isomerization is possible.

Both *E* and *Z* isomers of **1** allowed the formation of the same triplet state because the geometry of the double bond is lost (Fig. 4). The energy of this triplet state was determined at 177 kJ mol^{-1} (Fig. 3). The triplet state cannot be responsible of the observed reaction (see below) and can be deactivated to give the starting materials.

The conversion of **1** to **2** is a photoisomerization of a pentaatomic heterocyclic compound. The photoisomerization of this type of compounds has been the object of an intense research work in the past [1–3]. Most of pentaatomic heterocyclic compounds gave the corresponding isomers through the formation of a ring opening process, or through the formation of a Dewar isomer. The possible scheme of these reaction is described in Scheme 5.

We tested the possible formation of ring opening biradical of **1**, such as the biradical **4** reported in the reaction A of the Scheme 5, the formation of the ring contracted intermediate, such as **5** reported in the reaction A of the Scheme 5, and the formation of the Dewar isomer of **1**, as **6** in the reaction B of the Scheme 5. All those species showed a very high energy and cannot be obtained starting from the excited states of **1**. However, testing the possible reactivity of the *Z* isomer of **1**, we found that a simple 1,5-HAT (hydrogen atom transfer) process can allow the transformation [13]. The excited singlet state of *Z-1*, if we impose the transfer of the hydrogen atom on the hydrazone to the nitrogen atom in four position on the 1,2,4-oxadiazole ring, allowed the direct transformation of *Z-1* into **2** (Fig. 3). The reaction occurred through the formation of a transition state at 185 kJ mol^{-1} (Fig. 5). It is a late transition state where the triazole ring is formed and the O–N bond in the oxadiazole ring is broken. The hydrogen atom is bridged between the nitrogen atom in the oxadiazole and that in the final triazole.

The *E*-isomer can give the same reaction via a photochemical *trans*–*cis* isomerization reaction to give the corresponding reactive *Z* isomer. However, the singlet excited state of *E-1* can be converted directly into the triazole

Scheme 4 Some photochemical isomerization of 1,2,4-oxadiazole derivatives **Fig. 2** The *E* isomer of compound **1** **Fig. 4** The triplet state of compound **1** **Fig. 3** Possible paths for the photochemical conversion of **1** into **2**

derivative though the same reaction reported above. A hydrogen atom transfer can allow the formation of a ring opening product **4**, where the shift of the hydrogen atom induced the ring opening of the oxadiazole (Figs. 4 and 6, Scheme 6).

The intermediate **4** can be converted, through a transition state at 159 kJ mol^{-1} (ST2, Figs. 4 and 7), into the triazole (Scheme 6).

Scheme 5 Possible invoked mechanisms for the photoisomerization of pentatomic heterocycles

The observed higher yields obtained when the *E* isomer is used could be explained considering that i. the *Z* isomer of **1** has only one way to react because the *Z*→*E* isomerization cannot be present (the excited singlet state of the *E* isomer is higher in energy than the *Z* isomer); ii. the singlet excited state of the *E* isomer of **1**, on the contrary, can interconvert into the triazole through the formation of the intermediate **4**, and can give the *Z* isomer through the photoisomerization and

Fig. 5 The structure of ST1

Fig. 7 Transition state in the conversion 4 → 2

Fig. 6 The product obtained through a hydrogen atom transfer from the singlet excited state of *E*-1

then, follows the isomerization route of the *Z* isomer; iii. The intersystem crossing quantum yields of the conversion of the excited singlet states of *Z* and *E* isomer of **1** is not known and it can determine the efficiency of the isomerization processes.

The triplet state of **1** cannot give the same reaction. The triplet state of **1** can give two hydrogen atom transfer

processes. The first was a 1,3-HAT process to give the diazocompound **5** (Scheme 7) [14, 15], while the second was a 1,5-HAT process to give the oxadiazole derivative **6** (Scheme 7). Both **5** and **6** showed an energy higher than that of the triplet state (at 203 kJ mol^{−1} for **5** and at 255 kJ mol^{−1} for **6**) showing that these processes cannot be present in the photoisomerization.

In conclusion, the described photoisomerization of *E*- and *Z* isomers of **1** can occur in two different processes involving the first excited singlet state. In the case of the *Z* isomer, the process is concerted, and the 1,5-HAT process allowed the formation of the triazole without the formation of intermediates, while, in the case of the *E* isomer, the isomerization occurs also in this case through a 1,5-HAT process but with the formation of an open intermediate species.

Furthermore, we have shown that the photochemical version of the Boulton–Katritzky rearrangement does not occur through the formation of a quasi-aromatic transition state, and that the reaction does not require the attack of hydrazonic nitrogen atom to the oxadiazole ring to occur, while the driving force of the reaction is a hydrogen shift process from the hydrazone to the oxadiazole ring.

Scheme 6 Reaction mechanism for the photochemical isomerization of *E*-1

Scheme 7 Hydrogen atom transfer in triplet Z-1

3 Materials and methods

Gaussian09 has been used for the discussions about the computed geometries [16]. All the computations were based on the Density Functional Theory (DFT) [17] and Time-Dependent DFT (TD-DFT) [18, 19] using the B3LYP hybrid xc functional [20]. Geometry optimizations and TD-DFT results from the Gaussian09 program have been obtained at the B3LYP/6-311G+(d,p) level of approximation. Geometry optimizations were performed with default settings on geometry convergence (gradients and displacements), integration grid and electronic density (SCF) convergence. Redundant coordinates were used for the geometry optimization as produced by the Gaussian09 program. Analytical evaluation of the energy second derivative matrix w.r.t. Cartesian coordinates (Hessian matrix) at the B3LYP/6-311G+(d,p) level of approximation confirmed the nature of minima on the energy surface points associated to the optimized structures. The transition states were calculated in S_0 state.

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Availability of data and material All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Declarations

Conflict of interest The author has no relevant financial or non-financial interests to declare.

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