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Direct Observation of a Photoinduced Nonstabilized Nitrile Imine Structure in the Solid State

Shao-Liang Zheng, Yizhong Wang, Zhipeng Yu, Qing Lin,* and Philip Coppens*

Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14260

Received September 22, 2009; E-mail: qinglin@buffalo.edu; coppens@buffalo.edu

The photoinduced ring opening of 2,5-diphenyltetrazole with the generation of N_2 and a nitrile imine was first reported by Huisgen and co-workers in 1967.[1] As a highly reactive dipole, nitrile imine reacts readily with a variety of dipolarophiles[2] to form five-membered-ring heterocycles.[3] Recently, we employed photogenerated nitrile imines for functionalization of an alkene-containing protein in living cells.[4] Whereas crystal structures of stabilized nitrile imines have been reported,[5] nonstabilized *N*-arylnitrile imines have only been spectroscopically observed as transient intermediates in low-temperature matrices.[6]

Four alternative structures have been postulated for nonstabilized nitrile imines: propargylic, allenic, 1,3-dipolar, and carbenic (Scheme 1). To date, theoretical calculations of nitrile imine structures have

Scheme 1
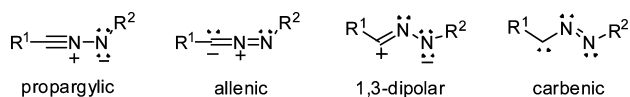
generated conflicting results in the literature. For example, in 1993, a high-level computational study using configuration interaction (QCISD) and a large basis set concluded that the stable nitrile imine structure has a nonplanar, allenic geometry and that the propargylic structure does not correspond to a local minimum on the potential energy surface.[7] More recent density functional theory calculations in combination with natural resonance theory indicated that all four resonance structures are necessary for a full description and that the carbenic form dominates for $F-CNN-F$ and $H_2N-CNN-NH_2$.[8] In contrast, a spin-coupled valence bond calculation using the geometry from a CASSCF calculation suggested that the stable electronic structure of $H-CNN-H$ is predominantly propargylic.[9] To provide direct evidence, herein we report the use of photocrystallography[10] to observe for the first time the structure of a nonstabilized nitrile imine photochemically generated in situ in the solid state.

In our initial study, a crystal of 2-(4′-methoxyphenyl)-5-(2″-isopropoxy-4″-methoxyphenyl)tetrazole[2b] was photoirradiated with a 325 nm He–Cd laser (45 mW/cm²) at 280 K for 12 h. While the crystal showed a darkening of its color, no products could be detected in the X-ray photodifference map, defined as the difference in electron densities after and before laser exposure. A closer examination revealed that the tetrazole molecules are tightly packed in the crystal lattice with the distance between the dissociating N^3-N^4 atoms and an adjacent methyl group on the neighboring tetrazole equal to 2.65 Å, resulting in a very small void for N_2 to escape (Figure S1 in the Supporting Information). To overcome this problem, we envisioned that the void next to N^3-N^4 could be enlarged by the use of rigid supramolecular frameworks formed by complexation of carboxylates with Zn.[11] To test this, we prepared a small panel of *N*-aryl tetrazoles **1–6** carrying carboxyl groups and potential H-bond donors such as NH_2 and OH (Figure 1). Crystals of the Zn–tetrazole complexes Zn-**1**
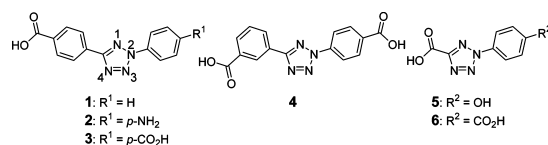
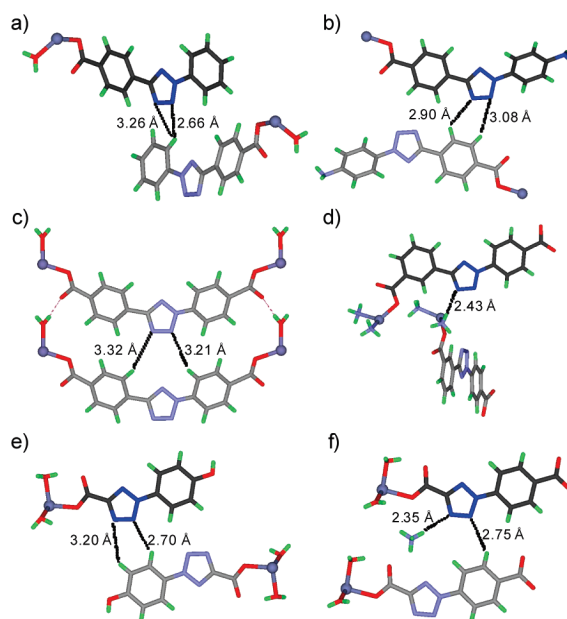**Figure 1.** Structures of the tetrazole compounds used in this study.

Figure 2. Crystal structures of Zn–tetrazole complexes Zn-**1** to Zn-**6**: (a) Zn(**1**)₂(H₂O)₂; (b) Zn(**2**)₂; (c) Zn(**3**)(H₂O); (d) Zn(**4**)(NH₃)₂; (e) Zn(**5**)₂(H₂O)₄(CH₃OH)₂; (f) Zn(**6**)₂(H₂O)₄(NH₄)₂. Zn is shown in silver. The distances between N^3-N^4 and the nearest surrounding atoms are marked on the structures.

to Zn-**6** were obtained by allowing ∼17 mM tetrazole solutions [dissolved in 2:1 MeOH/H₂O and mixed with Zn(NO₃)₂ and NH₄OH] to stand in air at room temperature for 2 weeks (Figure 2; also see Table S1 for crystal data and structural refinement). Structural analyses indicated the Zn to be tetracoordinated with two carboxylates and two water molecules in all structures except that of Zn–tetrazole **4**, in which two NH₃ molecules serve as the ligands (Figure 2d). A close examination of the tetrazole packing revealed that the empty spaces (voids) varied significantly, with the distances between N^3-N^4 and the nearest surrounding atoms being 2.66, 2.90, 3.21, 2.43, 2.70, and 2.35 Å, respectively (Figure 2).

To test the photoreactivity, all six crystals were exposed to the 325 nm He–Cd laser beam. Whereas the crystals of Zn-**2**–**5** showed slow decay indicated by color darkening (Figure 3a), only the Zn-**3** crystal afforded a discrete photodifference map after 2 min of photoirradiation at 90 K (Figure 3b). This is consistent with the fact that crystal Zn-**3** has the largest void around N^3-N^4 (3.21 Å in Figure 2c). Subsequent
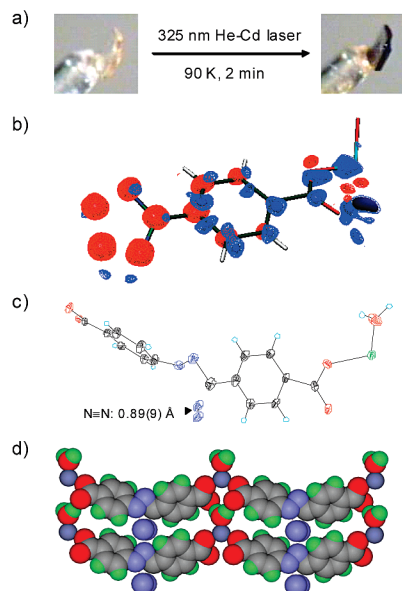
Figure 3. Photocrystallography of complex Zn-**3**. (a) Color change of the crystal upon laser exposure. (b) Photodifference map based on F_o(after) − F_o(before): blue, 2.0; light-blue, 1.0; orange, −1.0; red, −2.0 e/Å³. Only half of the map is shown because of the twofold symmetry. (c) ORTEP representation of the geometry-refined nitrile imine structure. (d) Packing of the nitrile imines and molecular N_2 in the crystal lattice. The N≡N bonds are perpendicular to the plane of view.

least-squares refinement gave a 13% yield of the corresponding nitrile imine product. The dissociated N_2 was visible in the photodifference map with a bond length of 0.89(9) Å (Figure 3c), which is within experimental error of its value in molecular N_2 (1.09 Å). The occupancy of N_2 in the crystal lattice was 8%, less than the value of 13% for the nitrile imine, suggesting that some of the N_2 escaped from the crystal lattice. Since apart from the CNN center the structure of tetrazole **3** is symmetric, the photodifference map showed twofold symmetry (Figure 3b). Using a free geometry refinement model,[12] we fit the electron density to two symmetry-related nitrile imine geometries (only one is shown in Figure 3c).[13] Evidently, in the solid state, the nitrile imine adopted a bent geometry with an increased twisting of the flanking phenyl rings (dihedral angle = 62.1° for the nitrile imine vs 38.8° for **3**; compare Figure 3c to Figure 2c), to allow the trapping of the escaping N_2 in the intrastrand space (Figure 3d). The photoreactivity of **3** is not due to the electronic effect of the carboxylic groups, as photoirradiation of the Zn-free crystal of **3**, which has smaller voids around N^3−N^4 in the crystal (Figure S2), did not yield a recognizable photodifference map.

The bent geometry of the nitrile imine can be ascribed to either the 1,3-dipolar or carbenic structure (Scheme 1). These two could be distinguished by a water-quenching experiment: it was expected that the dipolar structure would undergo 1,3-addition to generate a hydrazonic acid intermediate, which would tautomerize to afford the stable hydrazide, while the carbenic structure would undergo 3,3-addition[14] to generate a metastable α-hydroxyazobenzene, which would decompose slowly to produce benzaldehyde and phenyldiazene[15] (Scheme 2). When tetrazole **3** was irradiated with a handheld UV lamp (UVP, 302 nm, 0.16 A) in 1:1 acetonitrile/water, the 1,3-addition product was found to be the major product in the product mixture on the basis of ¹H NMR analysis (Figure S3). Moreover, water quenching of the nitrile imine derived from reactive 2-phenyl-5-*p*-methoxyphenyl tetrazole[4b] yielded exclusively the 1,3-addition product with no traces of benzaldehyde (Figure S4), thereby excluding the existence of the carbenic structure. To ensure that there is no crossover between the 1,3- and 3,3-addition pathways, we prepared α-hydroxyazobenzene separately from α-azohydroperoxide and

Scheme 2
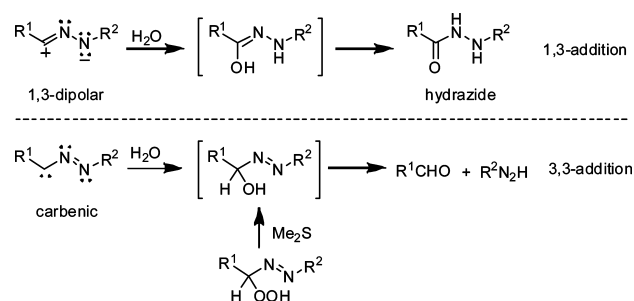
followed its decay in the NMR tube in 1:1 CD_3CN/D_2O. We found the major product to be benzaldehyde with no traces of hydrazide (Figure S5). Hence, we propose that the 1,3-dipolar structure represents the major electronic structure of the photogenerated nitrile imine. The bent geometry in the 1,3-dipolar structure can explain the high reactivity of the photogenerated nitrile imines in cycloaddition reactions in aqueous media[4] because of the lower activation barriers that result from dipole structural preorganization.[16]

In summary, we have reported the direct observation of a photogenerated, bent nitrile imine structure in a Zn coordination crystal. The efficiency of tetrazole ring rupture in the solid state appears to depend on the size of the void around the N^3−N^4 bond. A water-quenching study suggested that the bent geometry represents the 1,3-dipolar form, a major electronic structure involved in the photoinduced 1,3-dipolar cycloaddition in aqueous media.

Supporting Information Available: Experimental procedures, characterization data, structural information, and CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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