Photoreactions

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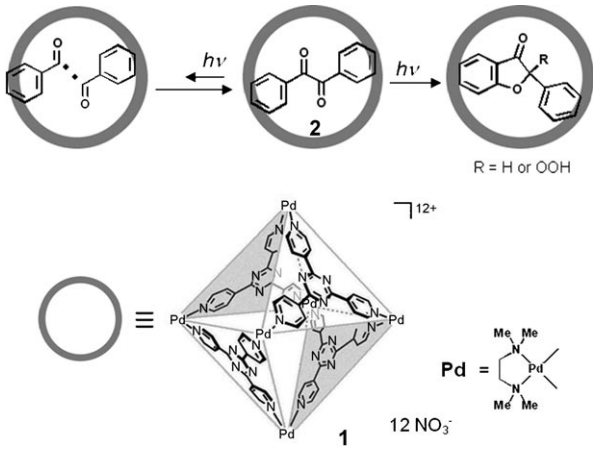
The Confined Cavity of a Coordination Cage Suppresses the Photocleavage of α-Diketones To Give Cyclization Products through Kinetically Unfavorable Pathways**

*Takahito Furusawa, Masaki Kawano, and Makoto Fujita**

In contrast with the rich photochemistry of ketones,[1] the photochemical reactions of α-diketones have been largely unexplored, mainly because the major reaction pathways from α-diketones are initiated by homolytic cleavage into acyl radicals that subsequently give a mixture of many degradation products.[2,3] By analogy with ketones, α-diketones should potentially have photochemical pathways leading to synthetically useful species. However, the formation of such compounds is normally dominated by homolytic cleavage. If α-diketones are confined in a restricted cavity of cages, the acyl radicals formed by the homolytic cleavage are immediately recombined to give the starting α-diketones.[4] As a result, the cleavage pathway is negligible and otherwise unfavorable reaction pathways can be major reaction courses. Expecting the formation of kinetically unfavorable photochemical products from α-diketones, we examined the enclathration of an α-diketone by a cage compound and studied subsequent photochemical reactions in the cage. We employed the self-assembled M_6L_4 cage (**1**), which has a well-established binding ability for neutral organic molecules.[5] We found that the unprecedented intramolecular photocyclization of the α-diketone (**2**) can lead to cyclized products without cleavage of the α-diketone framework (Scheme 1).

Diphenylethanedione (**2**) was employed as a guest molecule. When an excess amount (approximately 5 equivalents) of **2** was suspended in an aqueous solution of **1** (8 mM) at 100 °C for 1 h, water-insoluble **2** was partially dissolved and the colorless solution turned pale yellow. After the filtration of excess **2**, ^{1}H NMR spectroscopy indicated that the guest signals were significantly shifted upfield ($\Delta\delta \approx -2.1$–$-3.5$), which was diagnostic of the formation of an inclusion complex (Figure 1). From the integral ratio, we estimated that approximately two guest molecules were encapsulated per cage, giving the complex **1**⊃(**2**)$_2$. Single crystals suitable for X-ray crystal structure analysis were obtained from water by the slow evaporation of water over a week. The crystallographic analysis confirmed the structure of the **1**⊃(**2**)$_2$ complex. The single-crystal X-ray diffraction analysis revealed that the two guest molecules were orthogonally packed in the cavity of **1**, wherein each of them adopted a twisted conformation with a dihedral angle of 82° between the two carbonyl groups (Figure 2).

Upon photoirradiation, we obtained rather unusual products from **2** accommodated in the cage. An aqueous



Scheme 1. The photoreaction of **2** in the cavity of **1**.

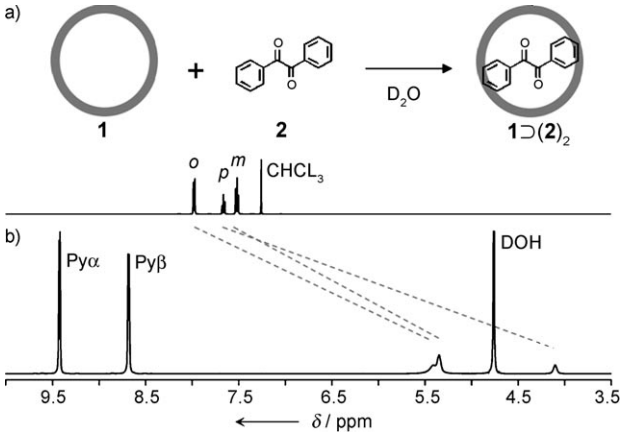


Figure 1. ^{1}H NMR spectra (500 MHz, RT, TMS as the internal standard) of a) **2** in $CDCl_3$ and b) the **1**⊃(**2**)$_2$ complex in D_2O. Pyα and Pyβ represent the pyridine α and β protons of the ligand.

[*] T. Furusawa, Dr. M. Kawano, Prof. Dr. M. Fujita
Department of Applied Chemistry
School of Engineering
The University of Tokyo
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656 (Japan)
Fax: (+81) 3-5841-7257
E-mail: mfujita@appchem.t.u-tokyo.ac.jp

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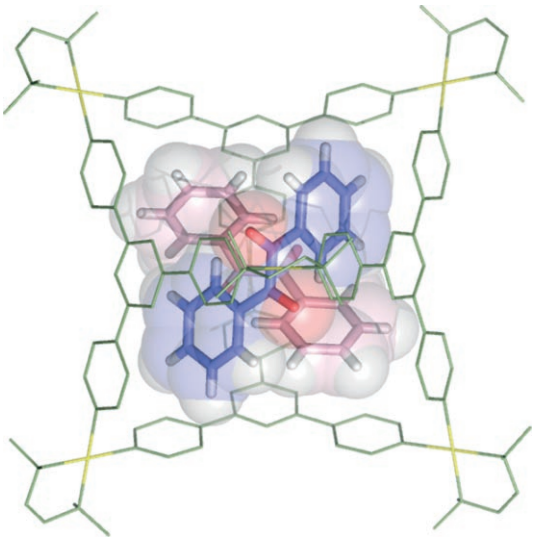


Figure 2. Crystal structure of the $\mathbf{1}\supset(\mathbf{2})_2$ complex.

solution of the clathrate $\mathbf{1}\supset(\mathbf{2})_2$ was irradiated for 6 h by using a high-pressure mercury lamp. The ^{1}H NMR spectrum recorded after irradiation showed that the signals that were assigned to guest **2** completely disappeared along with the apparition of new signals. Although the ^{1}H NMR spectrum after extraction with chloroform was very complex (Figure 3a), we were able to isolate three major products by using silica-gel column chromatography and gel-permeation chromatography. For the major product, we noticed a singlet signal appearing at $\delta = 5.02$ ppm, which was tentatively assigned as a benzylic proton (Figure 3b). For the two other products, hydroxy protons observed at $\delta = 8.79$ ppm and 11.39 ppm were seen to be characteristic (Figure 3c,d). All the products were shown to incorporate aromatic rings: a monosubstituted as well as an *o*-disubstituted benzene ring. From the information given above, coupled with the detailed analysis of the 2D NMR data, we assigned the structures of three main products (**3**–**5**) as shown in Figure 3b–d. The yields of **3**–**5** were estimated to be 31, 7, and 14%, respectively, by integration of the ^{1}H NMR spectra.

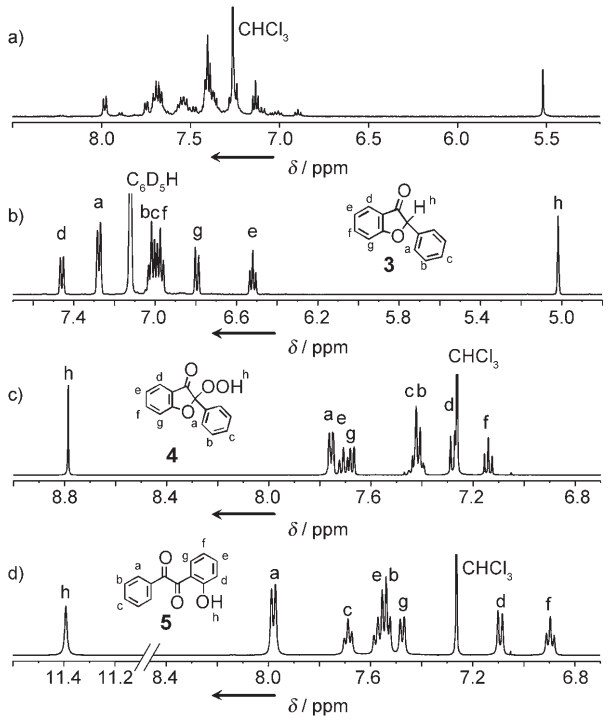


Figure 3. ^{1}H NMR spectra (500 MHz, $CDCl_3$, RT, TMS as the internal standard) of a) reaction mixture after extraction, b) **3** (in C_6D_6), c) **4**, and d) **5**.

Single crystals of **3**–**5** that were suitable for X-ray diffraction were obtained by recrystallization from appropriate solvents. This confirmed our proposed structure for the products **3**–**5** (Figure 4). For **3**, the intramolecularly cyclized

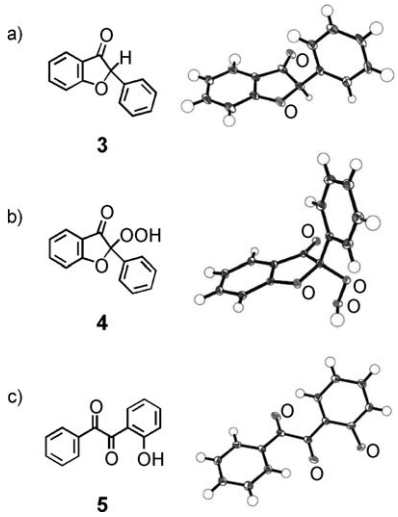
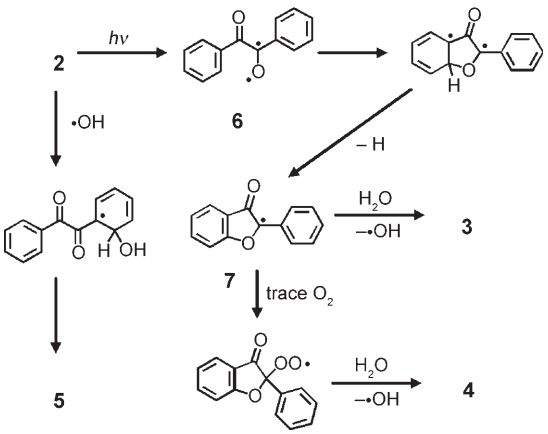


Figure 4. Thermal-ellipsoid plots (50% probability level) of the molecular structures of a) **3**, b) **4**, and c) **5**.

structure with a magnetically isolated benzylic proton was confirmed (Figure 4a). Product **4** has an analogous structure with a HOO group at the benzylic position (Figure 4b). Product **5** was shown to have the same diketone framework as the starting material **2** and a hydroxy group was introduced at the *ortho* position of the benzene ring (Figure 4c).

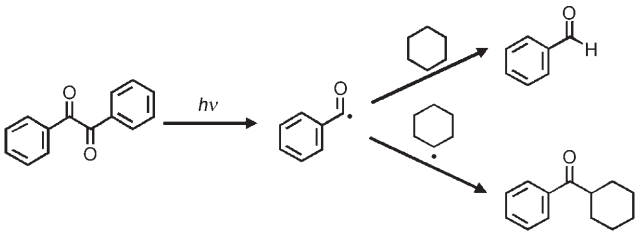
The proposed reaction mechanisms for the formation of these three products are shown in Scheme 2. First, the biradical **6** was generated by the photoexcitation of the carbonyl n–π* transition. Subsequently, the nucleophilic radical center on the oxygen atom attacked the terminal of the α,β-unsaturated carbonyl moiety of the adjacent benzoyl moiety to give cyclized structure **7** through a radical addition–elimination reaction. The resulting carbon radical abstracted the hydrogen radical either directly or after being trapped by molecular oxygen to give the cyclized products **3** and **4**, respectively. Even under the anaerobic conditions used, it is likely that a trace amount of oxygen remained and the formation of **4** could not be completely avoided. The product **5** was presumably formed through the direct conjugate addition of a hydroxyl radical to the benzene ring while the diketone framework remained intact. The hydroxyl radical



Scheme 2. Proposed reaction mechanisms for the formation of **3**, **4**, and **5**.

can be formed from water through hydrogen radical abstraction. Several products (such as, for example, more oxidation products of **3**–**5**) were probably involved in the complex reaction mixture, however, none have been isolated thus far.

To study how cage **1** affected the photoreaction of **2**, a control experiment without cage **1** under anaerobic conditions was examined. The degassed cyclohexane solution of **2** was irradiated for 3 h to give benzaldehyde (5%) and cyclohexyl phenyl ketone (10%) as major products. These were formed through the benzoyl radical route as a result of the homolytic cleavage of the α-diketone unit (Scheme 3).



Scheme 3. Photoreaction of **2** in cyclohexane.

Benzoic acid was also formed (10%), although we could not determine the reaction pathway. More importantly, we could not detect any trace amounts of **3**–**5**, which form in the absence of homolytic cleavage. When this reaction was examined under aqueous conditions (H_2O/methanol = 6:4), only a trace amount (< 1%) of the product **3** was detected in the reaction mixture. Each of the additional products formed was found in less than 5% yield by ^1H NMR spectroscopy and were not further analyzed. The presence of traces of **3** in the resulting aqueous solution indicates that the reaction pathway leading to this product is possible under these conditions, but is overwhelmingly dominated by the competing diketone cleavage pathway. We emphasize herein that the diketone homolytic cleavage is completely suppressed within cage **1** and that kinetically unfavorable pathways without homolytic cleavage became major pathways thanks to the remarkable cage effect of **1**.

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