Cavity-Directed, Highly Stereoselective [2+2] Photodimerization of Olefins within Self-Assembled Coordination Cages**

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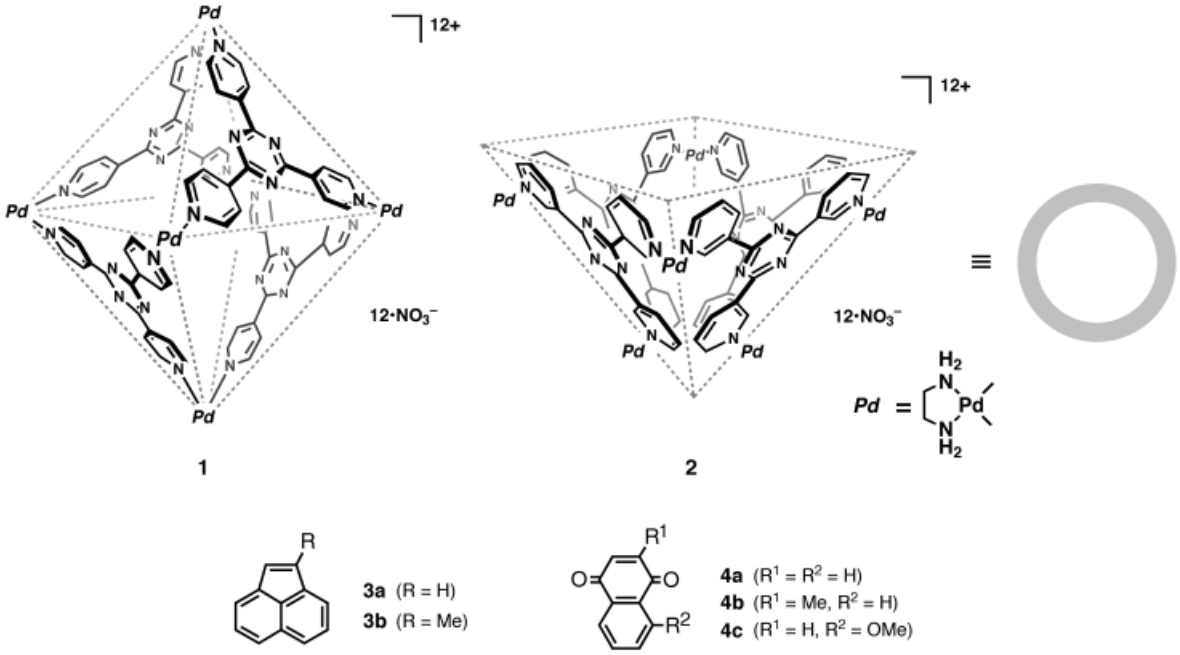
Selective encapsulation and isolation of molecules are one of the most attractive features of cagelike molecules.[1] Intermolecular chemical reactions of two or more substrates encapsulated in a molecular cage can be remarkably accelerated and suitably controlled as a result of the dramatically increased concentration and the strictly regulated orientation of the substrates in the cavity.[2] Such systems provide artificial mimics of the sophisticated active site of enzymes.[3] Recently we reported that structurally well-defined coordination cages (**1** and **2**), which self-assemble from six metal ions and four tridentate ligands, selectively encapsulate large organic molecules at the fixed position of the nanosized cavity.[4, 5] Thus, they are expected to facilitate intermolecular [2+2] photochemical reactions and control the stereo- and regiochemistry in stringent geometrical environment. The photodimerization has been studied extensively in some media such as micelles, zeolites, organic hosts (for example, cyclodextrins and cucurbiturils),[6] and crystals.[7] However, a high degree of stereo- and regiochemical control is still desired. Here we report remarkably accelerated, highly stereoregulated [2+2] photodimerization of acenaphthylenes (**3**)[8] and naphthoquinones (**4**)[9] within the coordination cages (**1** and **2**) in an aqueous medium that give rise to only *syn* and head-to-tail isomers.

Quantitative formation of a *syn* dimer of acenaphthylene (**3a**) within cage **1** was clearly observed in the following experiment: An excess amount of **3a** was suspended in a solution of **1** in D_2O (2.0 mM) for 10 min at 80 °C. Analysis of the D_2O solution after filtration of free **3a** by ^1H NMR spectroscopy showed formation of the encapsulation complex $\mathbf{1}\cdot(\mathbf{3a})_2$ had occurred (Figure 1a). The signals of **3a** were highly upfield-shifted as a result of the efficient encapsulation in the cavity. After the clear solution was irradiated (400 W) for 0.5 h at room temperature, the signals derived from **3a** completely disappeared and one set of new signals appeared at $\delta = 5.84$, 5.61, 3.39, and 2.87 (Figure 1b). The signals of **1** ($\delta = 9.28$, 8.52, and 2.99; Figure 1a) remained unchanged, which suggests that no decomposition of cage **1** occurred during the irradiation. The product was identified as *syn* dimer **5a** after extraction with $CDCl_3$, and the yield was estimated to be >98% based on **3a** (Figure 1c).[8, 10]



The following experiments revealed that the cavity of cage **1** dramatically accelerated the reaction and strictly controlled the stereochemistry of the product. No reaction took place in benzene (2.0 mM) after 0.5 h in the absence of cage **1**.[11] At higher concentrations (150 mM, 3 h, in benzene), adducts were formed in low yield with poor stereoselectivity (*syn*: 19%, *anti*: 17%).

The regiochemistry of the [2+2] addition of asymmetrically substituted 1-methylacenaphthylene (**3b**) [Eq. (1)] was also

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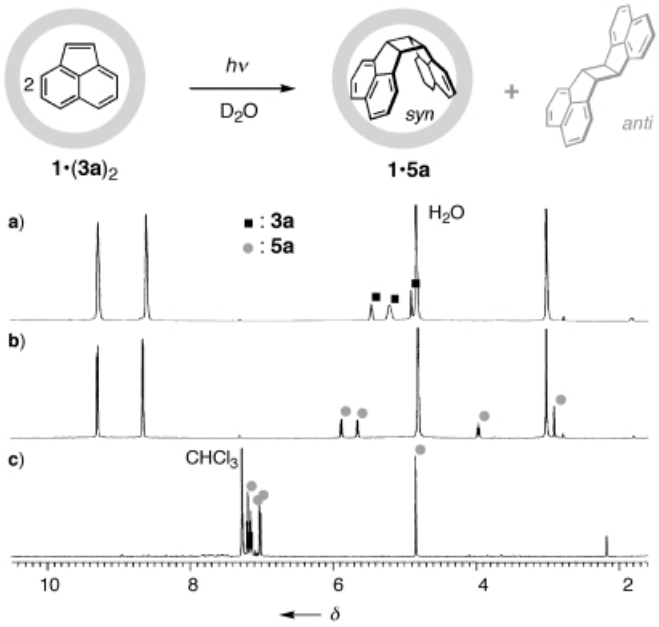

Figure 1. ^{1}H NMR spectroscopic analysis (500 MHz, D_2O, 27 °C) of the photodimerization of **3a** within cage **1:** a) before irradiation (**1**·(**3a**)$_2$) in D_2O; b) after irradiation (400 W) for 0.5 h; c) after extraction with $CDCl_3$.

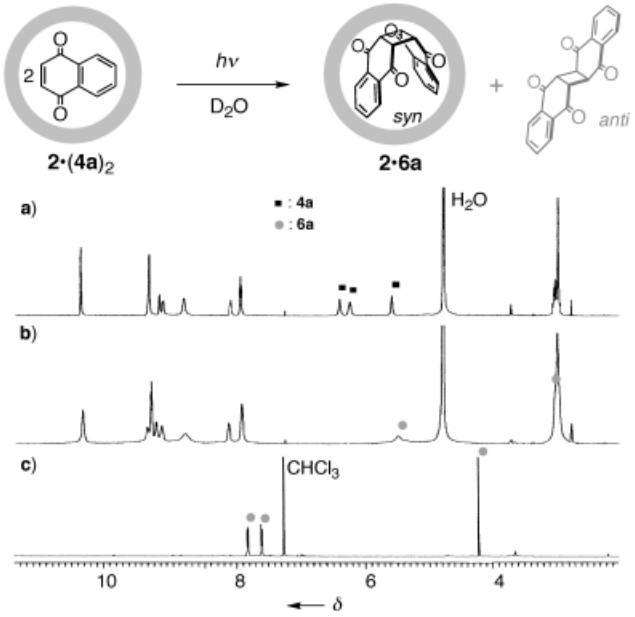

Figure 2. ^{1}H NMR spectroscopic analysis (500 MHz, D_2O, 27 °C) of the photodimerization of **4a** within bowl **2**: a) before reaction (**2**·(**4a**)$_2$) in D_2O; b) after irradiation (400 W) for 3 h; c) after extraction with $CDCl_3$.

highly controlled by the cage. The irradiation of the **1**·(**3b**)$_n$ (n = ca. 2) complex for 3 h at 0.5 mM gave head-to-tail *syn* isomer **5b** in >98% yield without any other regio- and stereoisomers.[8, 12, 13] The photoirradiation of the sterically demanding substrate **3b** without the cage in benzene no longer gave the adducts, even at a very high concentration (150 mM).

The photodimerization of naphthoquinones (**4**) was most effectively controlled by the bowl-shaped coordination host **2**.[5] Thus, naphthoquinone (**4a**; 5.0×10^{-2} mmol) was added to an aqueous solution (3.0 mL) of **2** (15.0×10^{-3} mmol, 5.0 mM) and the mixture was stirred for 10 min at 80 °C to give encapsulation complex **2**·(**4a**)$_n$ (n = ca. 2; Figure 2a). After filtration of excess **4a**, the resulting solution was irradiated for 3 h at room temperature. The ^{1}H NMR spectrum of the solution showed very broad signals (Figure 2b) which suggested the conformation of the host's framework was restricted by strong interactions between the host and the guest.[2g] The ^{1}H NMR spectrum of the product obtained after extraction with $CDCl_3$ clearly showed the formation of *syn* dimer **6a** in >98% yield (Figure 2c).[9, 10] This result strikingly contrasts to that obtained in benzene where the *anti* dimer (21%) was predominantly formed over the *syn* dimer (2%) at a high concentration (50 mM).

The structure of **2**·**6a** was confirmed by X-ray crystallographic analysis. A single crystal suitable for X-ray analysis was obtained by diffusing acetone into an aqueous solution of **2**·**6a** at room temperature for 10 days. As expected, the crystal structure showed the dimer **6a** in the *syn* configuration in the cavity (Figure 3). The framework of **2** adopted a box-shaped conformation to nicely accommodate **6a** in the cavity through aromatic interactions ($\pi-\pi$ and CH$-\pi$ interactions of around 3.5 Å).[2g] Two aromatic rings of **6a** were pinched by the host and significantly distorted to maximize the host–guest interactions.

The regioselectivity in the photodimerization of 2-metylnaphthoquinone (**4b**) within the cage **1** was very high (96% head-to-tail), while moderate within the bowl **2** (78% head-to-tail).[9b, 13] Interestingly, the regioselectivity was remote-controlled by a substituent on the naphthalene ring: 5-methoxynaphthoquinone (**4c**) was photodimerized in the bowl **2** with 79% head-to-tail selectivity. The irradiation of **4b** without the cages (50 mM, 3 h, in benzene) did not afford any dimerized products, while that of **4c** gave the *anti* dimer in 21% yield.

The present study has shown that the self-assembled nanocages act as molecular flasks to promote intermolecular [2+2] photodimerization of large olefins in a surprisingly efficient fashion. The cages are readily available and their cavities are extraordinarily large, which makes possible the creation of new chemistry within the localized microspace of discrete molecules.

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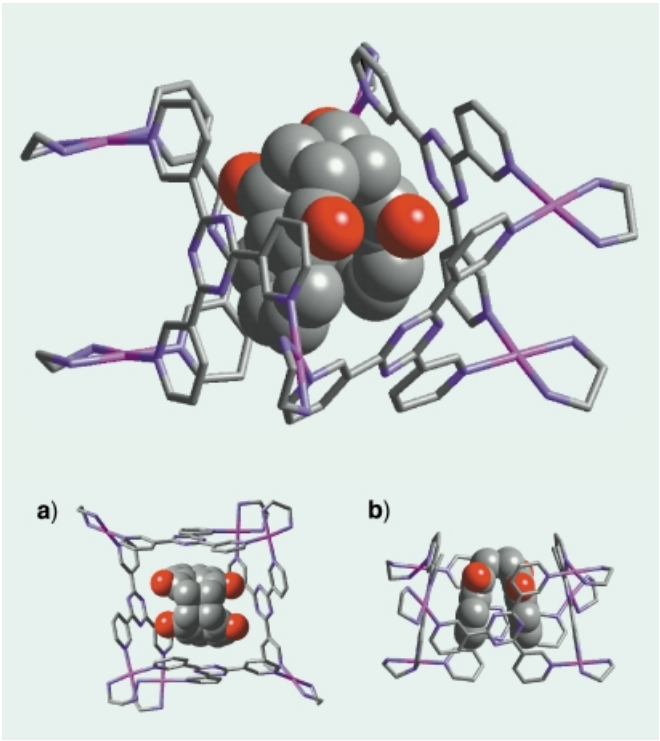

Figure 3. The crystal structure of **2**·**6a**: a) top view; b) side view.

Experimental Section

Photodimerization of **3a** within coordination cage **1**: Acenaphthylene (**3a**; 6.0 mg, 39.5×10^{-3} mmol) was suspended in a solution (3.2 mL) of **1** (19.3 mg; 6.5×10^{-3} mmol, 2.0 mM) in D_2O and the mixture was stirred for 10 min at 80 °C. After any free **3a** had been filtered off, the clear solution was placed in quartz or Pyrex cells and irradiated with 400 W high-pressure mercury lamp (SEN LIGHTS CORP. HB400X-15) for 0.5 h at room temperature. The solution was extracted with $CDCl_3$ and the product identified as *syn* dimer **5a** in a yield of >98% (by ^{1}H NMR spectroscopy). The crude product was purified by column chromatography (silica gel) to give **5a** as a colorless solid (1.8 mg, 92% yield).[8] Satisfactory spectroscopic data were obtained for **5a**, **1**·**5a**, and for all the compounds described in this paper (see Supporting Information).

X-ray crystal structure of **2**·**6a**: Single crystals suitable for X-ray analysis were obtained by diffusing acetone into an aqueous solution of **2**·**6a** (15.0 mM, 0.5 mL) at room temperature for 10 days. Crystal data for **2**·**6a**: $C_{104}H_{108}N_{48}O_{40}Pd_6$, $M_r = 3308.78$, crystal dimensions $0.25 \times 0.20 \times 0.20$ mm^3, tetragonal space group $P4_32_12$ (no. 96), $a = b = 25.013(3)$, $c = 25.063(5)$ Å, $V = 15680(4)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.402$ g cm^{-3}, $F(000) = 6656$, radiation, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $T = 113(2)$ K, reflections collected/unique 101179/18140 ($R_{int} = 0.2097$). The structure was solved by direct methods (SHELXL-97) and refined by full-matrix least-squares methods on F^2 with 814 parameters. $R_1 = 0.1061$ ($I > 2\sigma(I)$), $wR_2 = 0.2724$, GOF = 1.046; max/min. residual density 1.652/ − 1.694 e Å^{-3}. Further refinement was unsuccessful because of the high degree of disorder of the counterions and water molecules. CCDC-174264 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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