

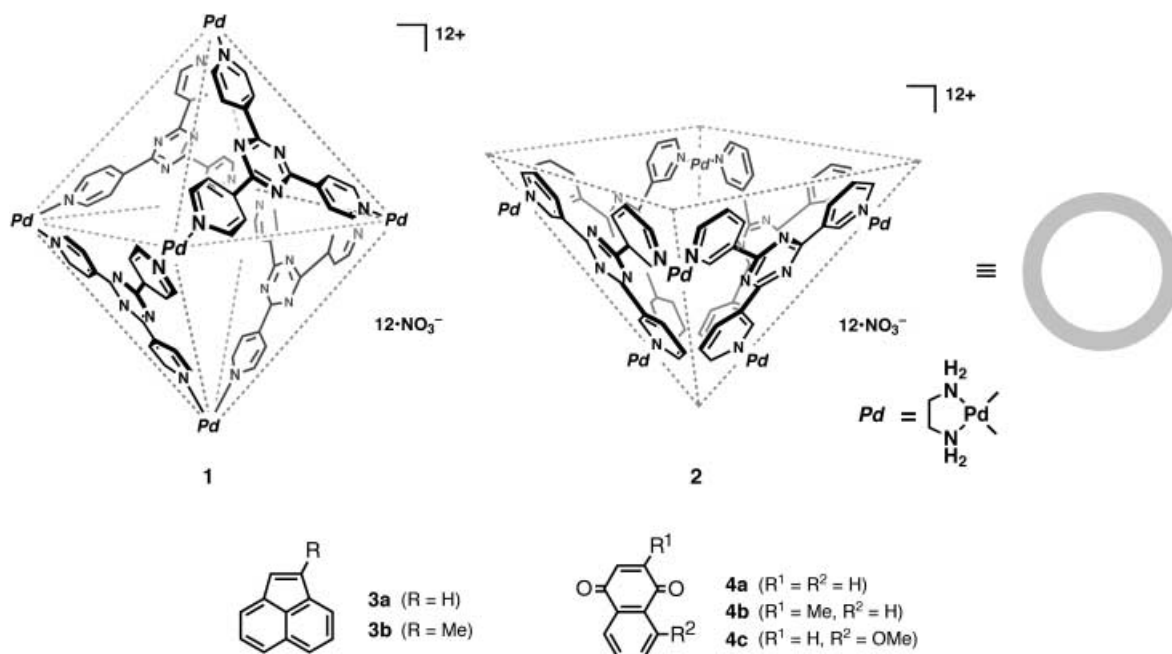
Cavity-Directed, Highly Stereoselective [2+2] Photodimerization of Olefins within Self-Assembled Coordination Cages**

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Selective encapsulation and isolation of molecules are one of the most attractive features of cage-like 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 D₂O (2.0 mM) for 10 min at 80 °C. Analysis of the D₂O solution after filtration of free **3a** by ¹H NMR spectroscopy showed formation of the encapsulation complex **1**·(**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 δ = 5.84, 5.61, 3.39, and 2.87 (Figure 1b). The signals of **1**



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(δ = 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 CDCl₃, 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-methylenacenaphthylene (**3b**) [Eq. (1)] was also

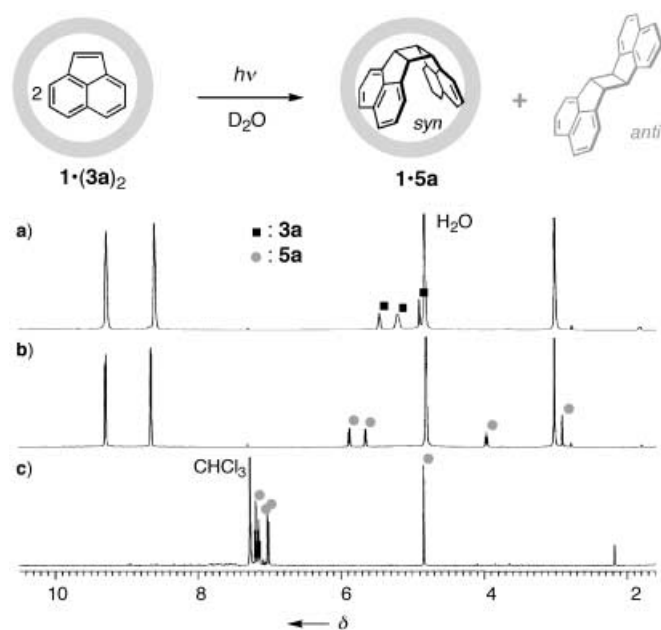


Figure 1. ^1H NMR spectroscopic analysis (500 MHz, D_2O , 27°C) of the photodimerization of **3a** within cage **1**: a) before irradiation ($1 \cdot (3a)_2$) in D_2O ; b) after irradiation (400 W) for 0.5 h; c) after extraction with CDCl_3 .

highly controlled by the cage. The irradiation of the $1 \cdot (3b)_n$ ($n = \text{ca. } 2$) 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).

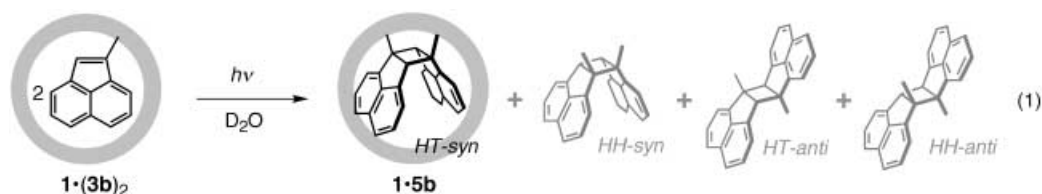


Figure 2. ^1H NMR spectroscopic analysis (500 MHz, D_2O , 27°C) of the photodimerization of **4a** within bowl **2**: a) before reaction ($2 \cdot (4a)_2$) in D_2O ; b) after irradiation (400 W) for 3 h; c) after extraction with CDCl_3 .

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 $\text{CH}-\pi$ interactions of around $3.5 \text{ \AA}$).^[2g] Two aromatic rings of **6a** were pinched by the host and significantly distorted to maximize the host–guest interactions.

The photodimerization of naphthoquinones (**4**) was most effectively controlled by the bowl-shaped coordination host **2**.^[5] Thus, naphthoquinone (**4a**; $5.0 \times 10^{-2} \text{ mmol}$) was added to an aqueous solution (3.0 mL) of **2** ($15.0 \times 10^{-3} \text{ mmol}$, 5.0 mM) and the mixture was stirred for 10 min at 80°C to give encapsulation complex $2 \cdot (4a)_n$ ($n = \text{ca. } 2$; Figure 2a). After filtration of excess **4a**, the resulting solution was irradiated for 3 h at room temperature. The ^1H 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 ^1H 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 regioselectivity in the photodimerization of 2-methylnaphthoquinone (**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.

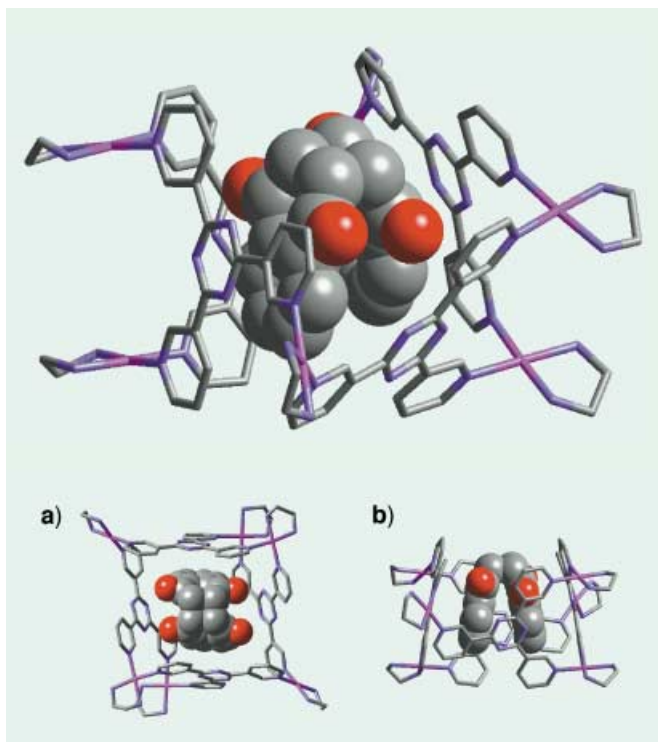


Figure 3. The crystal structure of **2·6a**: a) top view; b) side view.

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 $80^\circ C$. 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 1H 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 $0.25 \times 0.20 \times 0.20$ mm³, tetragonal space group $P4_32_12$ (no. 96), $a = b = 25.013(3)$, $c = 25.063(5)$ Å, $V = 15680(4)$ Å³, $Z = 4$, $\rho_{calcd} = 1.402$ g cm⁻³, $F(000) = 6656$, radiation, $\lambda(MoK\alpha) = 0.71073$ 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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