

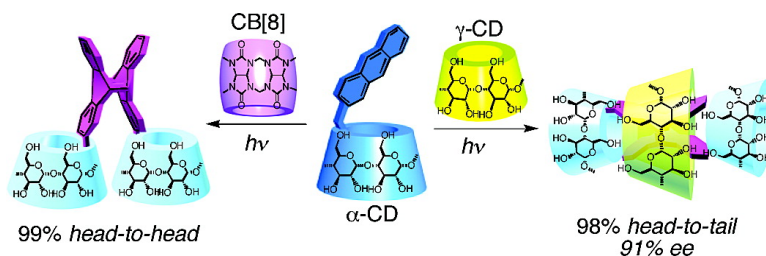
Communication

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# Highly Stereoselective Photocyclodimerization of $\alpha$ -Cyclodextrin-Appended Anthracene Mediated by $\gamma$ -Cyclodextrin and Cucurbit[8]uril: A Dramatic Steric Effect Operating Outside the Binding Site

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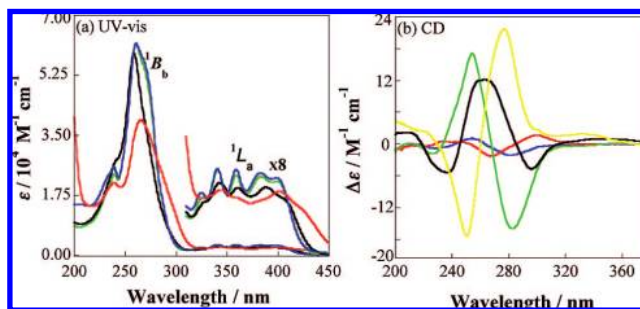
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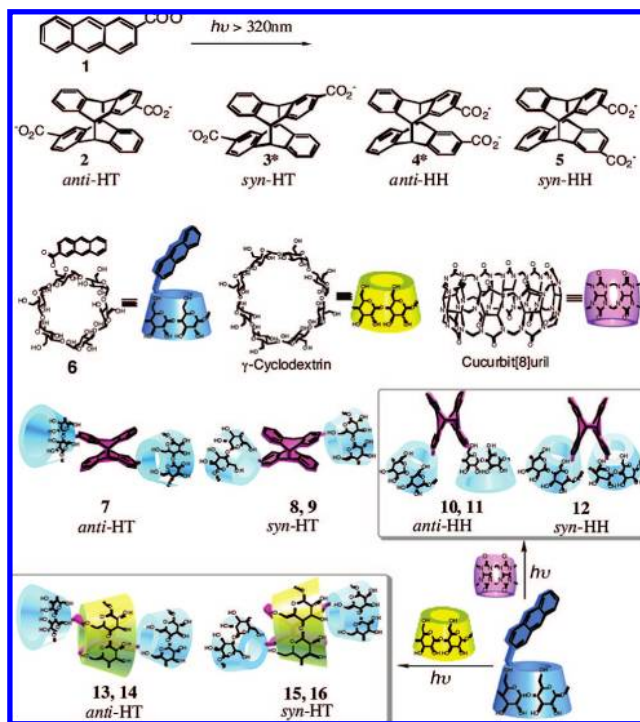
Stereochemical control through substrate encapsulation by natural and synthetic hosts is now a standard technique in both thermochemical and photochemical reactions. It is widely accepted that precise size/shape matching of guest substrate with the interior of the host cavity is pivotal for the critical control of reactivity and selectivity,<sup>1</sup> as emphasized in currently accepted molecular recognition theories.<sup>2</sup> Then, a question arises: Is it feasible to affect a reaction not by altering the matching elements of the host interior but through interactions occurring outside the cavity? In this paper, we will demonstrate that a bulky group of guest substrate located outside the host cavity can critically manipulate the stereoselectivity of photoreaction occurring inside the cavity.

The target system chosen is the [4 + 4] photocyclodimerization of 2-anthracene carboxylate (**1**) to **2–5**.<sup>3</sup> We previously reported that photoirradiation of **1** mediated by native  $\gamma$ -cyclodextrin (CD) gives *syn-head-to-tail* (*syn*-HT) dimer **3\*** as a major product (46% yield) in 41% enantiomeric excess (ee) but minor *anti-head-to-head* (*anti*-HH) dimer **4\*** in <5% ee,<sup>3a</sup> and also that the modification of  $\gamma$ -CD with a rigid cap or a cationic side arm can improve the ee of **3\*** and **4\*** to 58 and 41%, respectively.<sup>3b,c</sup> In this study to explore the possibility of external control of photoreaction inside a host, we employed 6-*O*-(2-anthracenecarbonyl)- $\alpha$ -CD (**6**) as a guest substrate that carries anthracene as a chromophoric/photoreactive moiety and  $\alpha$ -CD as a bulky hydrophilic substituent to be located outside the host cavity upon inclusion of the anthracene moiety by  $\gamma$ -CD or cucurbit[8]uril (CB[8]) host.

Addition of  $\gamma$ -CD (1 mM) to an aqueous solution of **6** (0.25 mM)<sup>4</sup> led to a hypsochromic shift of the <sup>1</sup>B<sub>b</sub> band (Figure 1a), implying formation of an H aggregate in the cavity. In the circular dichroism spectra, the original negative couplet was dramatically switched to a negative–positive–negative couplet with crossover points at 245 and 285 nm (Figure 1b), which appears to be a sum of two oppositely signed couplets centered at slightly different wavelengths. This may be rationalized by the coexistence of two dominant stereoisomeric precursor complexes to **2** and **3\***. Interestingly, inclusion of two molecules of **1** in a  $\gamma$ -CD cavity led to a circular dichroism spectrum with a positive couplet (Figure 1b), demonstrating that the bulky  $\alpha$ -CD moiety critically alters the arrangement of anthracenes in the  $\gamma$ -CD cavity. In contrast, complexation of **6** with CB[8] induced a significant bathochromic shift and a weak oppositely signed Cotton effect (Figure 1). The stepwise 1:1 and 1:2 association constants were determined from the spectral changes as  $270 \pm 20$  and  $21700 \pm 600 \text{ M}^{-1}$  for  $\gamma$ -CD, and  $24300 \pm 700$  and  $13700 \pm 500 \text{ M}^{-1}$  for CB[8].



**Figure 1.** (a) UV-vis spectra of 0.25 mM **6** with (black) and without (green) 1.0 mM  $\gamma$ -CD and of 0.05 mM **6** with (red) and without (blue) 0.05 mM CB[8] in water at 25 °C. (b) Circular dichroism spectra of 0.5 mM **6** with (black) and without (green) 1.5 mM  $\gamma$ -CD, of 0.05 mM **6** with (red) and without (blue) 0.05 mM CB[8], and of 0.4 mM **1** with 1.0 mM  $\gamma$ -CD (yellow) in water at 25 °C.



Photoirradiation of **6** was performed at  $\lambda > 320 \text{ nm}$  in the presence and absence of  $\gamma$ -CD or CB[8] in aqueous solutions at 25 °C or at  $-20 \text{ }^\circ\text{C}$  under a pressure of 210 MPa. Photocyclodimerization of **6** gave stereoisomeric dimers **7–12** (for the structures of **2–16** and their stereochemical relationship, see Chart S1 in Supporting Information),<sup>4</sup> relative yield of which was

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**Table 1.** Product Distribution and Enantiomeric Excess of Cyclodimers **2–5** Obtained in the Photocyclodimerization of Anthracene Guests **1** and **6** in the Presence/Absence of  $\gamma$ -CD or CB[8] Host<sup>a</sup>

guest	host	temp/°C	product distribution/%				HT:HH <sup>b</sup>	% ee <sup>c</sup>	
			2	3*	4*	5		3*	4*
<b>1</b>	none	25	41	37	13	9	78:22	0	0
	$\gamma$ -CD <sup>d</sup>	25	43	44	7	6	87:13	32	-3
	CB[8]	25	40	37	14	9	77:23	0	0
<b>6<sup>e</sup></b>	none	25	34	42	17	7	76:24	5	-16
	$\gamma$ -CD	25	35	60	3	2	95:5	81	-3
		-20 <sup>f</sup>	30	68	1	1	98:2	91	-2
	CB[8]	25	1.4	1.4	77	20	3:97	17	-10
		-20 <sup>f</sup>	0.5	0.7	82	17	1:99	18	-8

<sup>a</sup> Aqueous solutions of **6** (0.4 mM) +  $\gamma$ -CD (4 mM) or **6** (0.05 mM) + CB[8] (0.05 mM) were irradiated at  $\lambda > 320$  nm under Ar for 1 h; conversion >95%. <sup>b</sup> HT/HH = ([**2**] + [**3**\*])/([**4**\*] + [**5**]). <sup>c</sup> First-eluted enantiomer is given a positive sign; error <0.5% ee. <sup>d</sup> Reference 3a. <sup>e</sup> Reaction mixture was hydrolyzed in aqueous KOH (2 M) for 2 days and neutralized with 2 M HCl before HPLC analysis. <sup>f</sup> Run under a pressure of 210 MPa.

determined by HPLC after hydrolyzing the products in an alkaline solution to give **2–5**.

As shown in Table 1, photodimerization of free **6** gave **2–5** in an HT/HH ratio (76:24) comparable to that (78:22) for **1**. Photodimerization of **6** in the presence of  $\gamma$ -CD afforded  $\alpha$ -CD-stopped rotaxanes **13–16** in a high combined yield of 95%, providing an efficient route to  $\gamma$ -CD-wheeled rotaxanes, which are least accessible among the homologous CDs.<sup>5</sup> The formation of HH dimers **4\*** and **5** is markedly suppressed to 5% yield, probably due to the steric repulsion of two  $\alpha$ -CDs in HH-stacked precursor complexes. Thus, the use of  $\gamma$ -CD not only increases the relative yield of **3\*** from 42 to 60% but also greatly enhances the ee from 5 to 81%, which is much higher than that (32% ee) obtained in the photodimerization of **1** mediated by  $\gamma$ -CD.<sup>3a</sup> This reveals that bulky  $\alpha$ -CD, being located away from the stereogenic centers to be formed, vitally affects the stereochemical outcomes of the photochirogenic reaction occurring inside the cavity. We ascribe this significant stereoselectivity enhancement to the more confined orientation of anthracenes in the pseudorotaxane stoppered by  $\alpha$ -CDs.

Interestingly, this supramolecular photochirogenesis turned out to be sensitive to pressure and temperature to considerably improve the HT dimers in 98% selectivity, in particular, **3\*** in 68% yield and in an ee as high as 91%, in water at -20 °C under a pressure of 210 MPa.

To our surprise, the use of CB[8] as a host totally inverted the product selectivity from 98% HT (for  $\gamma$ -CD) to 99% HH (Table 1). It is intriguing that the steric repulsion between the two  $\alpha$ -CDs does not appear to play an important role in determining the product's HT/HH ratio but significantly affects the anti/syn ratio of HH dimers, favoring the less hindered *anti*-dimer **4\*** (77% yield at 25 °C and 82% at -20 °C and 210 MPa) rather than *syn*-dimer **5**, revealing a dual role of the bulky  $\alpha$ -CD in the critical stereodifferentiation step of the supramolecular photodimerization. Even with achiral CB[8],  $\alpha$ -CD located outside can transfer its chiral information to give **3** and **4** in 17 and -10% ee, respectively.

CB[8]<sup>6</sup> and  $\gamma$ -CD<sup>7</sup> possess similarly large cavities (480 and 430 Å<sup>3</sup>, respectively) enough to accommodate two anthracene guests. However, the cavities of barrel-shaped CB[8] and truncated cone-shaped  $\gamma$ -CD are different in depth (9.1 versus 7.9 Å) and portal

diameter (6.9 versus 7.5–8.3 Å), both of which appear to play decisive roles in determining the efficiency of subsequent photocyclodimerization of HT-oriented 1:2 host-**6** complex. Possessing a short cavity with wide openings,  $\gamma$ -CD allows deep penetration of HT-oriented anthracene moieties to facilitate the photocyclodimerization at the 9,10-positions. In contrast, CB's cavity with narrow portals hinders deep penetration and mutual overlap of two anthracenes to almost completely suppress the subsequent photodimerization, allowing only the photodimerization of HH-oriented complex in low ee.

In this study, we have demonstrated that the supramolecular interactions outside the binding site can critically affect the stereochemical outcomes of chiral photoreaction occurring inside the binding site by manipulating not only the ground-state complexation selectivity but also the excited-state reactivity. This enabled us to achieve a dramatic inversion of the HT/HH ratio from 98:2 to 1:99 by just switching the host from  $\gamma$ -CD to CB[8] in the photodimerization of **6** at -20 °C and 210 MPa. This finding provides us with a novel strategy for designing supramolecular reaction systems to more critically manipulate the stereochemical outcomes.

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**Supporting Information Available:** UV-vis, CD, and NMR spectra of **6** with and without a host, and the details of photoreaction and photodimer structure. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- (a) Breslow, R.; Schmuck, C. *J. Am. Chem. Soc.* **1996**, *118*, 6601. (b) Kang, J.; Rebek, J., Jr *Nature* **1997**, *385*, 50. (c) Yoshizawa, M.; Tamura, M.; Fujita, M. *Science* **2006**, *312*, 251. (d) Pluth, M. D.; Bergman, R. G.; Raymond, K. N. *Science* **2007**, *316*, 85. (e) Kaanumalle, L. S.; Gibb, C. L. D.; Gibb, B. C.; Ramamurthy, V. *J. Am. Chem. Soc.* **2005**, *127*, 3674. (f) Jon, S. Y.; Ko, Y. H.; Park, S. H.; Kim, H.-J.; Kim, K. *Chem. Commun.* **2001**, 1938. (g) Inoue, Y.; Ramamurthy, V. *Chiral Photochemistry*; Marcel Dekker: New York, 2004. (h) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741. (i) Griesbeck, A. G.; Meierhenrich, U. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3147. (j) Turro, N. J. *Acc. Chem. Res.* **2000**, *33*, 637. (k) Smit, B.; Maesen, T. L. M. *Nature* **2008**, *451*, 671.
- (a) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, Germany, 1995. (b) Steed, J. W.; Atwood, J. L., Eds.; *Encyclopedia of Supramolecular Chemistry*; Marcel Dekker: New York, 2004. (c) Behr, J.-P., Ed.; *The Lock-and-Key Principle: The State of the Art 100 Years on*; John Wiley & Sons, Ltd.: Chichester, UK, 1995.
- (a) Nakamura, A.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 966. (b) Nakamura, A.; Inoue, Y. *J. Am. Chem. Soc.* **2005**, *127*, 5338. (c) Yang, C.; Nakamura, A.; Wada, T.; Inoue, Y. *Org. Lett.* **2006**, *8*, 3005. (d) Nishijima, M.; Wada, T.; Mori, T.; Pace, T. C. S.; Bohne, C.; Inoue, Y. *J. Am. Chem. Soc.* **2007**, *129*, 3478.
- For details of the analysis of self-association and complexation of **6**, and structural relationship between photodimers **2–16**, see Supporting Information.
- (a) Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1959. (b) Wenz, G.; Han, B. H.; Muller, A. *Chem. Rev.* **2006**, *106*, 782. (c) Klota, E. J. F.; Claridge, T. D. W.; Anderson, H. L. *J. Am. Chem. Soc.* **2006**, *128*, 15374. (d) Okada, M.; Takashima, Y.; Harada, A. *Macromolecules* **2004**, *37*, 7075.
- (a) Lee, J. W.; Samal, S.; Selvapalam, N.; Kim, H.-J.; Kim, K. *Acc. Chem. Res.* **2003**, *36*, 621. (b) Lagona, J.; Mukhopadhyay, P.; Chakrabarti, S.; Isaacs, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 4844. (c) Kim, K.; Selvapalam, N.; Ko, Y. H.; Park, K. M.; Kim, D.; Kim, J. *Chem. Soc. Rev.* **2007**, *36*, 267. (d) Ko, Y. H.; Kim, E.; Hwang, I.; Kim, K. *Chem. Commun.* **2007**, 1305.
- (a) Rekharsky, M. V.; Inoue, Y. *Chem. Rev.* **1998**, *98*, 1875. (b) Breslow, R.; Dong, S. D. *Chem. Rev.* **1998**, *98*, 1997.

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