JOC Article

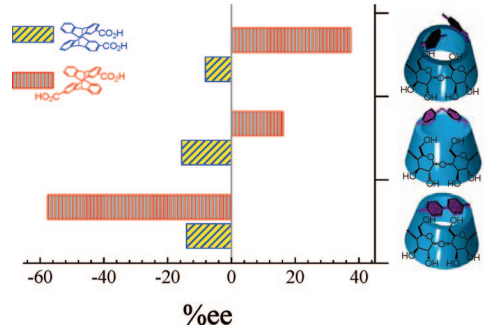
Supramolecular Enantiodifferentiating Photocyclodimerization of 2-Anthracenecarboxylate Mediated by Capped γ-Cyclodextrins: Critical Control of Enantioselectivity by Cap Rigidity

Cheng Yang, Tadashi Mori, and Yoshihisa Inoue*

Department of Applied Chemistry, Osaka University, Suita 565-0871, Japan

inoue@chem.eng.osaka-u.ac.jp

Received March 8, 2008



A series of γ-cyclodextrins (CDs) modified with capping and noncapping aromatic group(s) were synthesized to mediate the enantiodifferentiating [4 + 4] photocyclodimerization of 2-anthracenecarboxylic acid (AC). The complexation behavior of these γ-CDs with AC was studied by circular dichroism, UV−vis, and NMR spectroscopy to reveal the formation of stable 1:2 host−guest complexes in all cases. The capped γ-CD with a biphenyl group bridging the A and D glucose units was shown to confine the included AC molecules most strictly among the capped and noncapped γ-CDs examined. Photocyclodimerization of AC mediated by capped γ-CDs considerably improved the yield and enantiomeric excess (ee) of the *head-to-head* photodimer **3**. The ee and the absolute configuration of *syn-head-to-tail* photodimer **2** critically depended on the rigidity of capping. Thus, the flexibly capped and rim-substituted γ-CDs afforded **2** in moderate ee's of around 40%, whereas γ-CD with a rigid biphenyl cap gave the antipodal **2** in −58% ee. Interestingly, the ee of **2** mediated by flexibly capped γ-CDs was highly sensitive to the temperature variation as a consequence of large differential entropy changes in the enantiodifferentiation process. In contrast, the entropy effect does not appear to play a significant role in the photocyclodimerization of AC with rigidly capped γ-CDs. The differential enthalpy and entropy changes obtained for the enantiodifferentiating photocyclodimerization mediated by native and most of the modified γ-CDs gave an excellent enthalpy−entropy compensation plot with an exception of the biphenyl-capped γ-CD, indicating the operation of significantly different enantiodifferentiation mechanism within the rigidly capped cyclodextrin cavity.

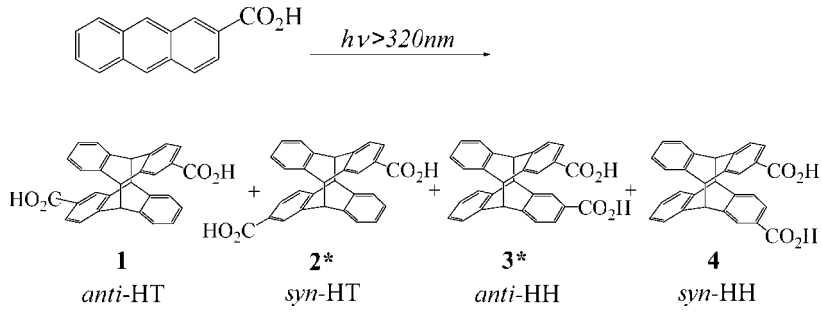
Introduction

Supramolecular photochirogenesis has recently received considerable attention as a promising approach for controlling the enantiodifferentiating process occurring in the excited state.[1,2] In contrast to the conventional photosensitization in which weak short-lived interactions within an exciplex intermediate have to be controlled, chiral hosts are able to intimately interact with the substrate both in the ground and excited states for a sufficient period of time by virtue of multiple supramolecular interactions such as hydrogen bonding, hydrophobic, van der Waals, and electrostatic interactions. Consequently, the use of chiral hosts is a potentially very attractive strategy to efficiently transfer the host's chiral information to the interacting guest substrate. In the past decade, a variety of chiral hosts,

(1) (a) Inoue, Y.; Ramamurthy, V. *Chiral Photochemistry*; Marcel Dekker: New York, 2004. (b) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025. (c) Griesbeck, A. G.; Meierhenrich, U. J. *Angew Chem., Int. Ed.* **2002**, *41*, 3147. (d) Turro, N. J *Pure Appl. Chem.* **1995**, *67*, 199. (e) McClenaghan, N. D.; Absalon, C.; Bassani, D. M. *J. Am. Chem. Soc.* **2003**, *125*, 13004.

10.1021/jo800533y CCC: $40.75
Published on Web 07/08/2008

SCHEME 1. Enantiodifferentiating [4 + 4] Photocyclodimerization of 2-Anthracenecarboxylic Acid



including cyclodextrin,[3] biomolecule,[4] chirally modified zeolite,[5] and chiral template,[6] have been employed as molecular containers for mediating chiral photoreactions.

α-, *β*-, and *γ*-Cyclodextrins (CDs) are truncated cone-shaped macrocyclic molecules composed of 6−8 glucose residues, respectively. Their hydrophobic cavities of varying sizes (4.5−8.5 Å) are capable of encapsulating a wide range of organic guests in aqueous solutions through the hydrophobic interaction.[7] Since CDs are soluble in water, readily available, inherently chiral, and transparent in most UV−vis regions, they have been extensively used in CD-mediated chiral photoreactions.[8] We have recently reported the enantiodifferentiating [4 + 4] photocyclodimerization of 2-anthracenecarboxylic acid (AC) with native and modified *γ*-CDs (Scheme 1).[9] Photocyclodimerization of AC in the presence of native *γ*-CD gives *head-to-tail* (HT) photodimer **2** in up to 41% ee but *head-to-head* (HH) photodimer **3** in poor ee of <5%. We have endeavored to improve the stereochemical outcomes of the supramolecular photocyclodimerization of AC by introducing functional group(s) into the *γ*-CD rim, modifying the framework of the *γ*-CD, and manipulating entropy-related factors.[9b–e]

An intriguing issue concerning the CD-mediated photochirogenesis is the vital role of entropy, whose degree of commitment varies significantly depending on the structure of CD employed. The enantiodifferentiating photoisomerization of (*Z*)-cyclooctene to chiral (*E*)-isomer included and sensitized by *β*-CD benzenecarboxylates was found to be almost independent of the reaction temperature, indicating a trivial contribution of the entropy term.[8b] However, the entropy factor was demonstrated to play an important role in the enantiodifferentiating photoisomerization of (*Z,Z*)-1,3-cyclooctadiene sensitized by *γ*-CD-naphthoxylacetate.[8j] As far as the photocyclodimerization of AC is concerned, the entropy-related factors such as temperature, solvent, and pressure appear to be pivotal in determining the product chirality for all *γ*-CD derivatives hitherto examined. These results indicate that *β*- and *γ*-CD cavities possess much different characters in particular from the entropic point of view. In this context, it is interesting to mention that the inherently low-entropic environment of *β*-CD's rigid cavity can be made flexible by permethylating the hydroxyl groups of *β*-CD.[8d]

As a natural consequence of the above discussion, we became interested in examining the chiral photoreaction mediated by capped CDs, which possess more rigid skeletons and are expected to behave differently from their parent CD.[10] The photocyclodimerization of AC mediated by *γ*-CD with a rigid bridging cap was found to give the photoproduct antipodal to that obtained by using native and modified *γ*-CDs without a bridging cap.[9e] In the present study, we expanded the variation of CD hosts with capping modification and further examined in detail the AC photocyclodimerization mediated by a series of *γ*-CD derivatives with flexible and rigid caps, as well as the relevant noncapping substituent(s), to elucidate the critical dependence of this supramolecular photochirogenic reaction upon capping modification and rigidity of the cap.

(2) (a) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741. (b) Rau, H. *Chem. Rev.* **1983**, *83*, 535.

(3) (a) YangC.; Inoue, Y. In *Cyclodextrin Materials Photochemistry, Photophysics and Photobiology*; Douhal, A., Ed.;Elsevier: New York, 2006; pp241−265. (b) Breslow, R.; Dong, S. D. *Chem. Rev.* **1998**, *98*, 1997. (c) Takahashi, K *Chem. Rev.* **1998**, *98*, 2013. (d) Rao, V. P.; Turro, N. J. *Tetrahedron Lett.* **1989**, *30*, 4641. (e) Shailaja, J.; Karthikeyan, S.; Ramamurthy, V. *Tetrahedron Lett.* **2002**, *43*, 9335. (f) Pattabiraman, M.; Natarajan, A.; Kaanumalle, L. S.; Ramamurthy, V. *Org. Lett.* **2005**, *7*, 529. (g) Inoue, Y.; Dong, F.; Yamamoto, K.; Tong, L.-H.; Tsuneishi, H.; Hakushi, T.; Tai, A. *J. Am. Chem. Soc.* **1995**, *117*, 11033. (h) Fleck, M.; Yang, C.; Wada, T.; Inoue, Y.; Bach, T. *Chem. Commun.* **2007**, 822.

(4) (a) Sugahara, N.; Kawano, M.; Wada, T.; Inoue, Y. *Nucleic Acids Symp. Ser.* **2000**, 115. (b) Wada, T.; Nishijima, M.; Fujisawa, T.; Sugahara, N.; Mori, T.; Nakamura, A.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 7492. (c) Nishijima, M.; Pace, T. C. S.; Nakamura, A.; Mori, T.; Wada, T.; Bohne, C.; Inoue, Y. *J. Org. Chem.* **2007**, *72*, 2707. (d) Nishijima, M.; Wada, T.; Mori, T.; Pace, T. C. S.; Bohne, C.; Inoue, Y. *J. Am. Chem. Soc.* **2007**, *129*, 3478. (e) Lhiaubet-Vallet, V.; Encinas, S.; Miranda, M. A. *J. Am. Chem. Soc.* **2005**, *127*, 12774.

(5) (a) Joy, A.; Ramamurthy, V. *Chemistry* **2000**, *6*, 1287. (b) Sivaguru, J.; Natarajan, A.; Kaanumalle, L. S.; Shailaja, J.; Uppili, S.; Joy, A.; Ramamurthy, V. *Acc. Chem. Res.* **2003**, *36*, 509. (c) Sivaguru, J.; Poon, T.; Franz, R.; Jockusch, S.; Adam, W.; Turro, N. J. *J. Am. Chem. Soc.* **2004**, *126*, 10816.

(6) (a) Aechtner, T.; Dressel, M.; Bach, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5849. (b) Bauer, A.; Weskamper, F.; Grimme, S.; Bach, T. *Nature* **2005**, 1139. (c) Inoue, Y. *Nature* **2005**, 1099. (d) Mizoguchi, J.-i.; Kawanami, Y.; Wada, T.; Kodama, K.; Anzai, K.; Yanagi, T.; Inoue, Y. *Org. Lett.* **2006**, *8* (26), 6051.

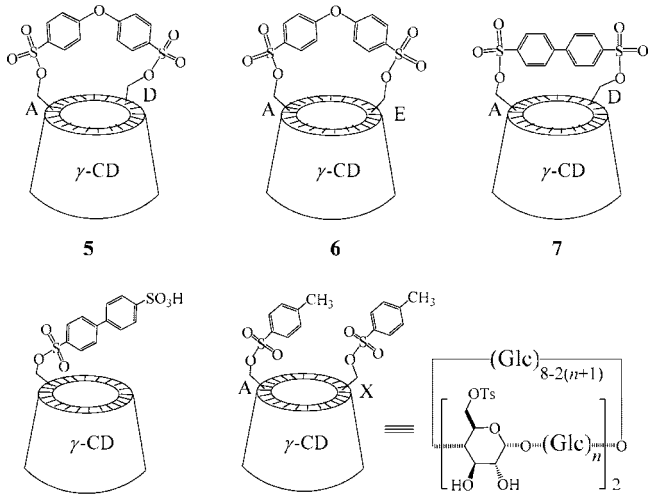
(7) (a) Rekharsky, M. V.; Inoue, Y *Chem. Rev.* **1998**, *98*, 1875. (b) Nelson, A.; Belitsky, J. M.; Vidal, S.; Joiner, C. S.; Baum, L. G.; Stoddart, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 11914. (d) Liu, Y.; Yu, H. M.; Chen, Y.; Zhao, Y. L. *Chem. Eur. J.* **2006**, 3858. (e) Tomatsu, I.; Hashidzume, A.; Harada, A. *J. Am. Chem. Soc.* **2006**, *128*, 2226. (f) Jeon, W. S.; Moon, K.; Park, S. H.; Chun, H.; Ko, Y. H.; Lee, J. Y.; Lee, E. S.; Samal, S.; Selvapalam, N.; Rekharsky, M. V.; Sindelar, V.; Sobransingh, D.; Inoue, Y; Kaifer, A. E.; Kim, K. *J. Am. Chem. Soc.* **2005**, *127*, 12984.

(8) (a) V. P., Rao; N. J., Turro *Tetrahedron Lett.* **1989**, *30*, 4641. (b) Inoue, Y.; Wada, T.; Sugahara, N.; Yamamoto, K.; Kimura, K.; Tong, L.-H.; Gao, X.-M.; Hou, Z.-J.; Liul, Y. *J. Org. Chem.* **2000**, *65*, 8041. (c) Inoue, Y.; Dong, S. F.; Yamamoto, K.; Tong, L.-H.; Tsuneishi, H.; Hakushi, T.; Tai, A. *J. Am. Chem. Soc.* **1995**, *113*, 2793. (d) Fukuhara, G.; Mori, T.; Wada, T.; Inoue, Y. *Chem. Commun.* **2005**, 4199. (e) Koodanjeri, S.; Ramamurthy, V. *Tetrahedron Lett.* **2002**, *43*, 9229. (f) Shailaja, J.; Karthikeyan, S.; Ramamurthy, V *Tetrahedron Lett.* **2002**, *43*, 9335. (g) Koodanjeri, S.; Joy, A.; Ramamurthy, V. *Tetrahedron* **2000**, *56*, 7003. (h) Vizvardi, K.; Desmet, K.; Luyten, I.; Sandra, P.; Hoornaert, G.; Van der Eycken, E. *Org. Lett.* **2001**, *3*, 1173. (i) Mori, T.; Weiss, R. G.; Inoue, Y. *J. Am. Chem. Soc.* **2004**, *126*, 8961. (j) Yang, C.; Mori, T.; Wada, T.; Inoue, Y. *New J. Chem.* **2007**, *31*, 697.

(9) (a) Nakamura, A.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 966. (b) Yang, C.; Fukuhara, G.; Nakamura, A.; Origane, Y.; Fujita, K.; Yuan, D.-Q.; Mori, T.; Wada, T.; Inoue, Y. *J. Photochem. Photobiol. A: Chem.* **2005**, *173*, 375. (c) Nakamura, A.; Inoue, Y. *J. Am. Chem. Soc.* **2005**, *127*, 5338. (d) Yang, C.; Nakamura, A.; Fukuhara, G.; Origane, Y.; Mori, T.; Wada, T.; Inoue, Y. *J. Org. Chem.* **2006**, *71*, 3126. (e) Yang, C.; Nakamura, A.; Wada, T.; Inoue, Y. *Org. Lett.* **2006**, *8*, 3005.

(10) (a) Engeldinger, E.; Armspach, D.; Matt, D. *Chem. Rev.* **2003**, *103*, 4147. (b) Rudzinski, C. M.; Young, A. M.; Nocera, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 1723. (c) Tabushi, I.; Shimokawa, K.; Shimizu, N.; Shirakata, H.; Fujita, K. *J. Am. Chem. Soc.* **1976**, *98*, 7855. (d) Fujita, K.; Shinoda, A.; Imoto, T. *J. Am. Chem. Soc.* **1980**, *102*, 1161. (e) Breslow, R.; Canary, J. W.; Varney, M.; Waddell, S. T.; Yang, D. *J. Am. Chem. Soc.* **1990**, *112*, 5212.

SCHEME 2. Flexibly Capped (5, 6), Rigidly Capped (7), and Rim-Substituted γ-Cyclodextrins (8, 9a−d) Employed as Modified Chiral Hosts



9a: X = B (*n* = 0)
9b: X = C (*n* = 1)
9c: X = D (*n* = 2)
9d: X = E (*n* = 3)

Result and Discussion

Synthesis. Capped γ-CDs **5**−**9** (Scheme 2) were synthesized by reacting native γ-CD with relevant aryl(di)sulfonyl (di)chlorides. The obtained γ-CD derivatives **5**−**7** were converted to the corresponding diazido-γ-CDs, the regiochemistry of which was determined through the HPLC comparison of the resulted diazido-γ-CDs with the authentic samples reported earlier.[9b]

Complexation of AC with Capped γ-CDs. Each aromatic group in **8** and **9a**−**d** is attached to one of the glucose units and therefore retains considerable flexibility, whereas that in **5**, **6**, and **7** is bridging two transannular glucose units to function as a rigid cap. As exemplified for **5** in Figure 1, most of the capped γ-CDs exhibit a positive induced circular dichroism (ICD) signals at the ^1L_a band around 230 nm and a negative ICD signals at the ^1L_b band around 260 nm, suggesting that the aromatic group perching on the primary rim of γ-CD is considerably tilted.[12] The only exception is **9a**, whose two tosyl groups are close to each other and the possible ICD signals at the ^1L_a band were overwhelmed by the intense exciton coupling signals. Two tosyl groups in **9a** are deduced to be arranged in a right-handed screw, according to the first-positive, second-negative sign of the apparently exciton-coupling ^1L_a band.

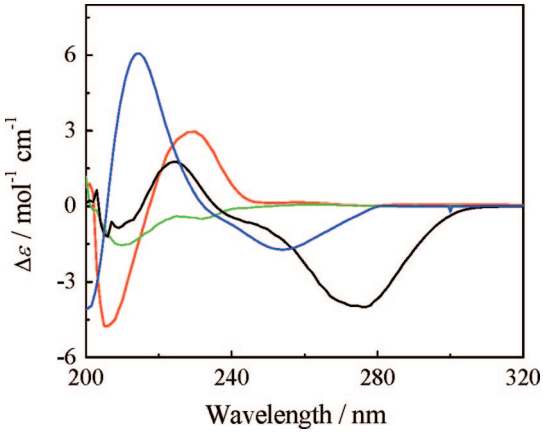


FIGURE 1. Circular dichroism spectra of **5** (blue), **7** (black), **9a** (red), and **9c** (green) in aqueous solution at 25 °C.

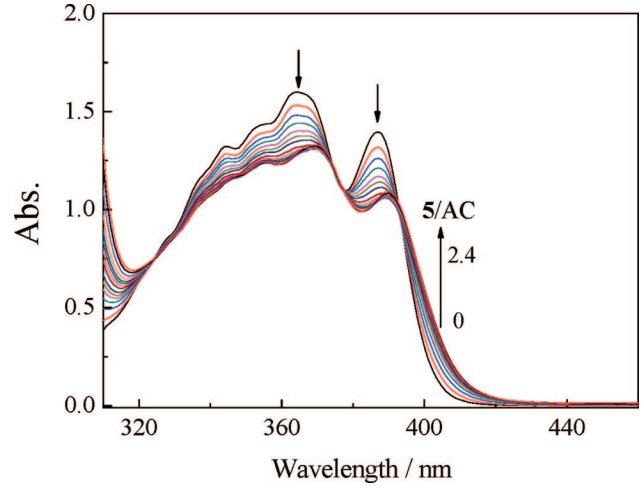


FIGURE 2. UV−vis spectral changes of 2-anthracenecarboxylic acid ([AC] = 0.5 mM) in aqueous solution upon gradual addition of **5** from 0 to 1.2 mM.

TABLE 1. Stepwise 1:1 and 1:2 Association Constants (K_1 and K_2) for Complexation of 2-Anthracenecarbolate with Native, Capped, or Primary Rim-Substituted γ-Cyclodextrins (γ-CDs) in Aqueous Solution at 20 °C

host	K_1 (M^{-1})	K_2 (M^{-1})	K_2/K_1	K_1K_2 (× 10^6 M^{-2})
γ-CD[a]	182	56700	312	10.3
5	1580	16400	10	25.9
6	1390	16200	12	22.5
7	1280	12500	10	16.0
8	6870	3130	0.46	21.5
9a	280	10800	39	3.0
9b	350	7450	21	2.6
9c	320	7620	24	2.4
9d	270	8320	31	2.2

[a] Reference 9a.

To elucidate the influence of the capping modifications of γ-CD on the complexation behavior with AC, we carried out the UV−vis and NMR spectral studies. As can be seen from Figure 2, the addition of capped γ-CD to an aqueous solution of AC resulted in a pronounced bathochromic shift of the AC's ^1L_a transition, suggesting an imitate stacking of two AC molecules in a γ-CD cavity.

Possessing a large hydrophobic cavity, native γ-CD forms 1:1 and 1:2 host−guest complexes in a sequential manner with a small 1:1 association constant (K_1 = 182 M^{-1} at 20 °C) and a much larger 1:2 association constant (K_2 = 56700 M^{-1} at 20 °C).[9a]

$$\text{AC} + \gamma\text{-CD} \overset{K_1}{\rightleftharpoons} \text{AC}\subset\gamma\text{-CD}$$

$$\text{AC} + \text{AC}\subset\gamma\text{-CD} \overset{K_2}{\rightleftharpoons} 2\text{AC}\subset\gamma\text{-CD}$$

The association constants for stepwise 1:1 and 1:2 complexation of capped γ-CD with AC were determined by UV−vis spectral titration. As listed in Table 1, the K_1 values obtained with capped γ-CDs **5**−**7** are consistently higher by a factor of

(11) See Supporting Information.
(12) Kodaka, M. *J. Am. Chem. Soc.* **1993**, *115*, 3702.

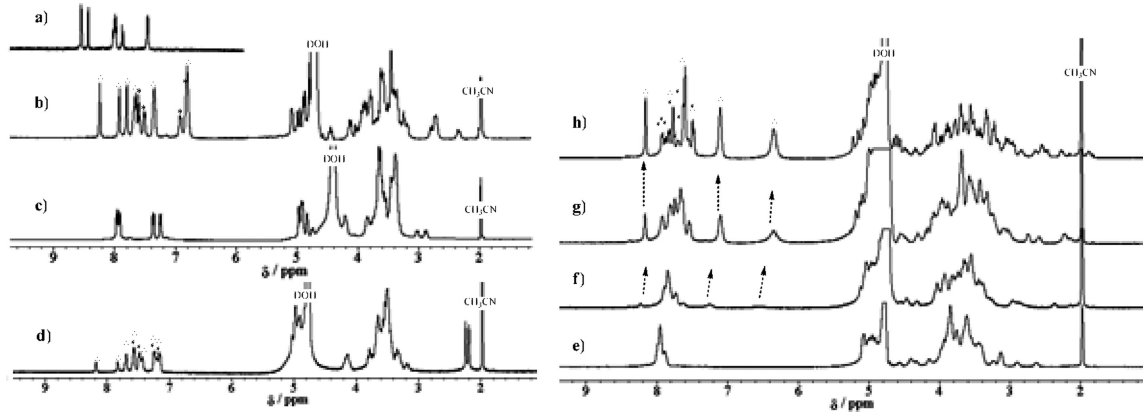


FIGURE 3. ^{1}H NMR spectra of (a) AC (1.0 mM), (b) AC (4.0 mM) + **5** (3.0 mM), (c) **5** (4.0 mM), (d) **9c** (3.0 mM) + AC (3.0 mM), and **7** (3.0 mM) in the absence of AC (e) and presence of (f) 0.5 mM, (g) 2.0 mM, and (h) 4.0 mM AC in D_2O buffer solutions (pD 9.5) at ambient temperatures. The signals marked by asterisk and triangle are assigned to the aromatic protons of capped γ-CDs and AC, respectively.

7−9 than that of native γ-CD. The enhanced K_1 values may be accounted for in terms of the reduced surface of AC molecule exposed to aqueous solution as well as the increased van der Waals interaction with the bridging aromatic moiety. The primary rim of capped γ-CD should be more hydrophobic than that of native γ-CD due to the aromatic capping, and the first included AC molecule is likely to orient its hydrophilic carboxylate group to the secondary rim of γ-CD with the aromatic moiety being hidden beneath the cap.

In general, the first binding of AC is enhanced but the second is retarded by primary-rim modification, regardless of capping (**5**−**7**) or substitution (**8**, **9a**−**d**). A series of A,X-ditosylated γ-CDs **9a**−**d** show only modest improvement of K_1 by a factor of 1.5−1.9. This is possibly due to the partial self-inclusion of the tosyl group that hinders to some extent the inclusion of AC. In contrast, biphenylsulfonated γ-CD **8** gives the largest K_1 value as high as 6870 M^{-1} (a 38-fold enhancement), implying that the biphenyl moiety functions as a spacer that efficiently fills the space remaining upon inclusion of the first AC. However, the K_2 value for **8** is 2.4−3.5 or 18-fold smaller than those for other capped CDs **9a**−**d** or native γ-CD, respectively. As a result of the enhanced K_1 and reduced K_2, biphenyl-substituted **8** gives an unusual K_2/K_1 ratio of 0.46, which is inverted from those for native, rim-substituted, and other capped CDs. Interestingly, the overall association constants (K_1K_2) for capped **5**−**7** and biphenyl-substituted **8** are 1 order of magnitude larger than those for the relevant rim-substituted **9a**−**d**, most probably due to the generally increased hydrophobicity of the cavity.

The K_2 values for capped γ-CDs are roughly 10-fold higher than the relevant K_1 values, which is attributable to the more efficient van der Waals and π−π interactions upon inclusion of the second AC molecule.[9a] However, the K_2 values for capped CDs are significantly (3.5- to 4.5-fold) smaller than the K_2 for native γ-CD, in sharp contrast to the large enhancement in K_1. This may be rationalized in terms of the relatively limited positional and rotational freedoms for the second AC molecule due to the presence of capping moiety and/or the hydrophobic nature of the bridging cap that hinders the inclusion in favorable *head-to-tail* fashion.

The NMR spectral study clearly revealed the restricted motions of ACs included in the cavity of rigidly capped γ-CDs. As shown in Figure 3, addition of AC into a D_2O solution of **5** resulted in large upfield shifts of the proton signals of both diphenyl ether moiety and AC. The nonanomeric proton signals of free **5** are packed in a narrow region of 3.3−3.9 ppm with two protons located at 2.91 and 3.02 ppm. Upon inclusion of AC, these signals are distributed over a much wider range of 2.2−4.1 ppm. These anisotropic NMR shifts indicate that AC molecules cannot freely rotate within the cavity of rigidly capped γ-CD, unevenly shielding/deshielding the individual glucose units. This is reasonable because the aromatic group transannularly bridging two glucose units will significantly decrease the primary opening of γ-CD and obstruct the motion of AC molecule inserted in the narrowed window. For the simply (di)tosylated γ-CDs, the substituent introduced still holds considerable freedoms and the guests are less confined, which is supported by the fact that the nonanomeric signals of **9c** appear in a narrow range of 3.2−3.8 ppm even after complexation with AC (Figure 3d).

The restricted motion of AC is more evident for rigidly capped γ-CD **7**. As shown in Figure 3e−h, the proton signals of AC immediately shift to much higher field at 0.5 mM concentration. Further increasing concentration of AC only leads to slight upfield shifts of AC protons. This indicates that ACs exist primarily as 1:2 host−guest complexes even at the low concentration, for which the large K_2 value is responsible. On the other hand, the signals of CD moiety gradually dispersed to a much wider range upon addition of AC to show a chemical shift of up to 1.81 ppm in the presence of 4 mM AC (Figure 3h). This substantial anisotropic effect indicates that the biphenyl capping induces *higher rigidity* to CD than the diphenyl ether bridge does and thus more severely restricts the motion of the included AC molecules. This idea is further supported by the fact that **5** shows four aromatic proton signals while **7** gives eight, revealing that the free rotation of the benzene rings is allowed in **5** but prohibited in **7** in the NMR time scale. On the basis of these results, we conclude that the degree of host rigidification induced by capping increases in the order **8**, **9a**−**d** < **5**, **6** < **7**.

Photocyclodimerization of AC with Capped γ-CDs: Critical Control of Enantioselectivity by Cap Rigidity. Photolyses of AC mediated by these capped γ-CDs were carried out under argon atmosphere, using a high pressure mercury lamp fitted with a glass filter (UV-35). The photoproducts were analyzed by chiral reversed-phase HPLC to give the chemical yields, product ratios, and ee values shown in Table 2. In water at 0 °C, photocyclodimerization of AC in the presence of native γ-CD affords the HH photodimers **3** and **4** in a low combined yield of 12%. In contrast, the use of capped γ-CDs considerably

TABLE 2. Photocyclodimerization of 2-Anthracenecarboxylate in the Presence/Absence of Native, Capped, or Primary Rim-Substituted γ-CDs in Water and 50% Aqueous Methanol[a]

			relative yield (%)[b]				ee (%)[b,c]		
host	solvent	temp (°C)	**1**	**2**	**3**	**4**	**2**	**3**	HH/HT[d]
γ-CD	H_2O	0	42.9	45.5	6.9	4.7	37.1	−0.8	0.13
	50% MeOH	−45	46.4	33.2	13.3	7.1	28.8	−8.7	0.26
5	H_2O	40	35.9	36.8	15.3	12.0	13.7	−15.1	0.38
		25	35.7	36.4	15.7	12.2	14.1	−15.4	0.39
		15	35.1	33.4	16.1	15.9	15.2	−15.6	0.47
		0	34.2	31.1	16.8	17.9	16.2	−15.6	0.53
6	H_2O	40	34.3	21.8	22.7	21.2	9.3	−21.9	0.78
		25	35.0	21.6	22.4	20.9	9.6	−23.0	0.77
		15	37.4	20.8	21.2	20.6	9.5	−23.3	0.72
		0	38.8	20.6	20.5	20.0	9.5	−24.0	0.68
7	H_2O	30	39.1	22.8	24.9	13.2	−53.0	−16.1	0.62
		15	39.0	24.4	22.9	13.7	−55.8	−15.4	0.58
		0	39.2	28.0	20.1	12.7	−57.6	−14.1	0.49
	50% MeOH	0	40.1	26.8	24.2	8.9	−33.6	−33.1	0.49
		−30	38.4	25.9	25.0	10.7	−37.6	−35.4	0.56
		−45	37.3	23.0	28.5	11.1	−40.4	−35.9	0.66
8	H_2O	30	40.3	39.3	11.8	8.5	27.7	−11.4	0.26
		15	40.0	40.2	10.9	8.9	32.5	−10.6	0.25
		0	39.6	38.6	11.7	10.1	37.4	−8.2	0.28
	50% MeOH	0	42.0	37.1	14.6	6.2	14.1	−26.6	0.26
		−30	46.3	33.0	13.3	7.4	17.4	−30.8	0.26
		−45	51.3	26.8	14.3	7.6	20.4	−35.1	0.28
9a	H_2O	30	40.3	40.7	10.1	8.9	27.3	−3.8	0.23
		15	40.5	38.0	11.7	9.7	32.1	−5.6	0.27
		0	43.0	36.5	10.6	9.9	39.1	−7.5	0.26
	50% MeOH	0	42.2	35.4	15.0	7.3	8.4	−17.7	0.29
		−30	46.4	32.9	13.5	7.2	18.4	−21.4	0.26
		−45	49.9	28.5	14.5	7.0	22.3	−25.4	0.28
9b	H_2O	30	40.1	38.5	12.1	9.3	25.9	−10.9	0.27
		15	38.4	38.6	12.6	10.4	27.5	−11.4	0.30
		0	37.8	38.7	12.3	11.2	33.0	−11.7	0.31
	50% MeOH	0	41.0	35.6	16.2	7.2	9.7	−25.9	0.31
		−30	43.9	34.3	14.1	7.7	17.4	−22.9	0.28
		−45	44.4	31.0	16.3	8.3	21.7	−20.2	0.33
9c	H_2O	30	40.1	36.9	13.4	9.5	25.2	−9.7	0.30
		15	38.2	36.5	14.0	11.4	30.9	−9.1	0.34
		0	39.6	38.6	11.7	10.1	37.4	−8.2	0.28
	50% MeOH	0	39.3	32.6	20.4	7.7	13.1	−27.5	0.39
		−30	41.2	29.8	19.3	9.7	21.6	−31.0	0.41
		−45	41.1	24.7	23.7	10.5	24.3	−35.0	0.52
9d	H_2O	30	42.6	38.5	11.7	7.3	24. 7	−5.3	0.23
		15	42.1	40.2	10.4	7.3	29.9	−4.1	0.22
		0	41.9	42.7	9.1	6.3	36.9	−2.4	0.17
	50% MeOH	0	43.7	34.9	15.2	6.3	17.9	−21.5	0.27
		−30	44.6	32.2	15.5	7.7	28.8	−21.1	0.30
		−45	42.7	28.7	19.2	9.3	34.4	−21.6	0.40

[a] Aqueous buffer solution (pH 9) containing 0.8 mM AC and 2 mM γ-CD irradiated at 366 nm under argon atmosphere using a high-pressure mercury lamp equipped with a glass filter (Toshiba UV-35). [b] Relative yield and ee determined by using a tandem column of Intersil ODS-2 (GL Science) and Chiralcel OJ-R (Daicel). [c] Positive/negative ee sign corresponds to the excess of the first-/second-eluted enantiomers, respectively. [d] HH/HT = ([**3**] + [**4**])/([**1**] + [**2**]).

enhances the HH yield in general to 33−41% under the same condition. This result seems reasonable, as the increased hydrophobicity around the capped primary rim of **5**−**7** hinders penetration of AC's anionic carboxylate moiety into the primary side and destabilizes the HT orientation to enhance the HH/HT ratio. This conclusion is reinforced by the fact that primary rim-substituted γ-CDs **8**, **9a**−**d** also give the HH dimers in 15−24% combined yield in water at 0 °C, which is appreciably higher than that (11%) obtained with native γ-CD. Certainly, the transannularly capped γ-CDs **5**−**7** is more effective in improving the HH yield than the substituted γ-CDs.

Photocyclodimerization of AC mediated by rim-substituted γ-CDs **8**, **9a**−**d** in water at 0 °C gave HT dimer **2** in 33−39% ee, which is comparable to that (37% ee) obtained with native γ-CD. However, the ee of **2** is significantly reduced to 16.2% and 9.5% upon photocyclodimerization with diphenyl ether-capped γ-CDs **5** and **6**. Intriguingly, the use of biphenyl-capped γ-CD **7** resulted in the formation of antipodal **2** in a much higher 58% ee. These results clearly indicate that the original diastereoselectivity upon HT complex formation with native γ-CD, or the enantioselectivity of **2** derived therefrom, is not significantly affected by simple primary-rim substitution (**8**, **9a**−**d**) but appreciably altered (reduced) by flexible capping (**5**, **6**) and even inverted by rigid capping to give a better ee for the antipodal product (**7**). It is particularly interesting to mention that the structural difference between **5** and **7** is only one oxygen atom, which however leads to the strikingly different stereochemical outcomes.

Energetic considerations allow us to quantitatively evaluate the stability difference between the diastereomeric HT com-

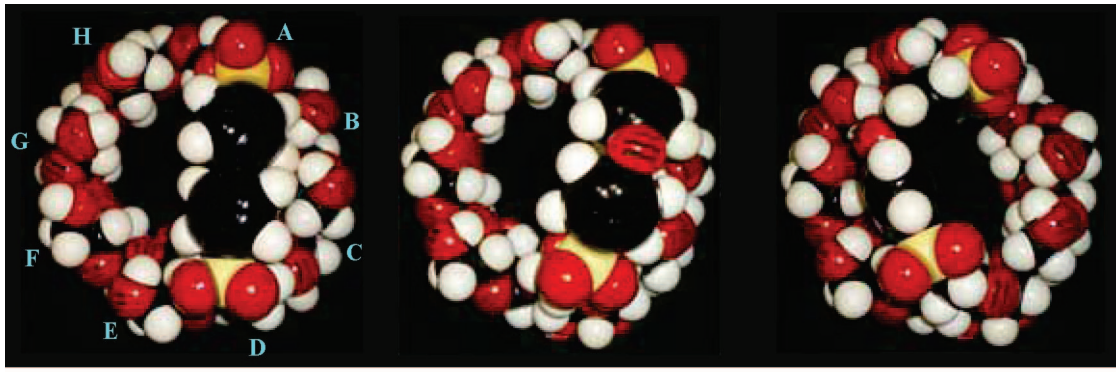


FIGURE 4. CPK models of rigidly A,D-capped **7** (a) and flexibly A,D-capped **5** in different conformations (b and c).

plexes precursor to enantiomeric **2**, by using the relationship between the differential free energy and the enantiomer ratio: $\Delta\Delta G^\circ = -RT \ln[(100 + \%\text{ ee})/(100 - \%\text{ ee})]$. In this evaluation, we use biphenylsulfonyl- or A,D-ditosyl-substituted **8** and **9c** as noncapped references structurally related to **7** and also diphenyl ether-bridged **5** as a reference with a flexible cap. Both of the noncapped hosts afford photodimer **2** in 37.4% ee, and native γ-CD gives almost the same result (37.1% ee) in water at 0 °C (Table 2). This means that one of the diastereomeric HT complexes, precursor to the first-eluted (on chiral HPLC) enantiomer of **2**, is favored by 1.8 kJ mol^{-1} over the antipodal complex. The flexible capping in **5** reduces the ee to 16.2%, which is equivalent to the free energy difference of 0.7 kJ mol^{-1} in favor of the same precursor complex. In contrast, rigidly capped **7** affords antipodal **2** in 57.6% ee, indicating that the precursor complex to the second-eluted enantiomer of **2** is favored by 3.0 kJ mol^{-1}. Thus, the free energy change induced by rigid capping amounts to 4.8 kJ mol^{-1}, which is much greater than that (1.1 kJ mol^{-1}) caused by flexible capping.

The fact that the supramolecular complexation/photocyclodimerization process is extremely sensitive to the cap rigidity not only reveals a critical correlation between the host structure and its function but also provides us with a practical tool for modifying the host structure to critically control the supramolecular complexation and the subsequent photochirogenesis.

CPK model examinations show that the biphenyl bridge in **7** is tightly fixed over the space surrounded by the A, B, C, and D glucose units (Figure 4a). AC molecule can penetrate only through the narrowed window formed by the biphenyl and the E, F, G, and H glucose units. The existence of an oxygen atom in the bridge of **5** makes the cap moiety flexible enough to lean against the A−D glucose rim (Figure 4b), allowing AC molecules to penetrate through the opening surrounded by E−H glucose units or to occupy the CD cavity near the A−D glucose units (Figure 4c). In comparison to **7**,[9e] **5** and **6** allow a wider variety of conformationally different diastereomeric precursor complexes, which most probably leads to the formation of **2** in lower ee.

The ee of HH dimer **3** is susceptible not only to capping modification but also to simple substitution, but no product chirality inversion occurs, both of which are very different from the behavior of the ee of HT dimer **2**. Thus, native γ-CD gives almost racemic **3** (−0.8% ee) in water at 0 °C, while rim-substituted **8**, **9a**−**d** afford **3** in better ee's (−8.2%, −7.5%, −11.7%, −8.2%, and −2.4%, respectively) and capped **5**−**7** in much higher ee's (−15.6%, −24.0%, and −14.1%, respectively) under the same conditions. By performing the photoreaction with **7** in 50% aqueous methanol at −45 °C, the chemical and optical yields of **3** can be optimized to 28.5% and −35.9% ee, respectively. The noncapped reference hosts **8** and **9c** also afford **3** in similar ee values (−35.1% and −35.0%, respectively). We may conclude therefore that the diastereoselectivity of HH precursor complex is more critically controlled by substitution and capping modification.

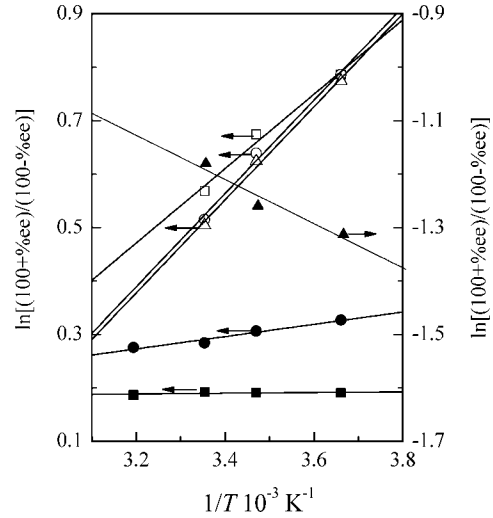


FIGURE 5. Representative temperature-dependence (differential Eyring) plots of the enantiomeric excesses (ee's) of **2** obtained in the photocyclodimerization of AC mediated by flexibly capped **5** (●) and **6** (■); rigidly capped **7** (▲); and rim-substituted **8** (□), **9c** (○), and **9d** (△) in aqueous solution.

Temperature Effects: Opposite Behavior of Capped versus Substituted γ-CDs. The photocyclodimerization of AC mediated by γ-CD derivatives **5**−**9** was carried out over the temperature ranges from +45 to 0 °C in water and from 0 to −45 °C in 50% aqueous methanol to give the results shown in Table 2.

Lowering temperature does not appear to greatly alter the product distribution but consistently enhances the enantioselectivities of **2** and **3**. It is to note that photocyclodimerization of AC with rim-substituted γ-CDs **8**, **9a**−**d** is more sensitive to the temperature change than that with capped γ-CDs **5**−**7**. Interestingly, the ee of **2** almost increases in common from 25−28% at 30 °C to 33−39% at 0 °C in the photocyclodimerization of AC mediated by rim-substituted CDs **8**, **9a**−**d**, while the ee of **3** is kept low (mostly <12%). Over the same temperature range, the ee values of both **2** and **3** obtained with capped γ-CDs **5**−**7** exhibit only slight changes of 0−5%. We

TABLE 3. Differential Entropy ($\Delta\Delta S$) and Enthalpy ($\Delta\Delta H$) Changes for the Formation of Enantiomeric 2 in the Photocyclodimerization of 2-Anthracenecarboxylate Mediated by Capped (5−7) and Substituted γ-Cyclodextrins (8, 9a−d)

		2		3	
solvent	host	$\Delta\Delta H$ (kJ mol^{-1})	$\Delta\Delta S$ (J mol^{-1} K^{-1})	$\Delta\Delta H$ (kJ mol^{-1})	$\Delta\Delta S$ (J mol^{-1} K^{-1})
H_2O	**5**	−1.0	−0.8	0.2	−2.0
	6	−0.1	1.4	0.9	−0.8
	7	3.0	0.2	−0.9	−5.8
	8	−6.2	−16.3	0.8	−3.0
	9a	−6.1	−15.6	−1.5	−6.9
	9b	−3.6	−7.6	2.1	3.3
	9c	−5.0	−11.7	1.7	5.0
	9d	−6.2	−16.3	1.8	3.7
50% MeOH	**7**	1.8	0.8	0.4	−0.6
	8	−1.5	−3.1	−1.4	−9.4
	9a	−3.3	−10.7	−0.7	−3.9
	9b	−2.8	−8.8	1.9	2.2
	9c	−2.7	−7.8	−1.3	−5.3
	9d	−4.1	−12.0	0.0	−3.6

plotted the logarithm of the enantiomer ratio of **2** as a function of reciprocal temperature to quantitatively analyze the enanatiodifferentiating process and thus to elucidate the origin of this contrasting temperature-dependence behavior. As illustrated in Figure 5, all of the data obtained for each capped γ-CD (**5**−**7**) fall on a good straight line, indicating that a single enantiodifferentiation mechanism operates in the temperature range employed. By using the Eyring equation, the differential enthalpy change ($\Delta\Delta H$) and entropy change ($\Delta\Delta S$) for the formation of antipodal products are calculated from the slope and intercept, respectively.[13] The $\Delta\Delta H$ and $\Delta\Delta S$ values obtained for capped CDs **5**−**7** and substituted CDs **8**, **9a**−**d** in water and 50% aqueous methanol are summarized in Table 3.

Before analyzing the $\Delta\Delta H$ and $\Delta\Delta S$ values obtained, it is better to discuss the essential enantiodifferentiating step in this supramolecular photocyclodimerization and the nature of the differential parameters obtained from the temperature-dependence studies. The size of γ-CD cavity is not large enough to allow swapping of two AC molecules included in the cavity, and therefore the equilibrium between two diastereomeric complexes is established only through consecutive dethreading and rethreading of AC. It is accepted in general that the association rate constant (k_a) for a guest molecule to penetrate into the cavity of a supramolecular host like CD is normally in a range of 10^7-10^8 M^{-1} s^{-1}.[14] Since the second association constants K_2 determined experimentally for this capped γ-CD−AC system are in a range of 3000−16000 M^{-1}, the dissociation rate constants (k_d) for the 1:2 host−guest complex are estimated to be 10^4-10^5 s^{-1}. Therefore the residence time of AC in the 1:2 host−guest complex is much longer than the lifetime of an excited AC molecule (the fluorescence lifetime of AC is ca. 16 ns). On the basis of this estimation and the fact that the quantum efficiency of photocyclodimerization within the γ-CD cavity is high ($\Phi = 0.4-0.5$),[15] we may safely conclude that the product's ee is determined essentially by the stability difference of two diastereomeric complexes formed upon enantioface-selective inclusion of the second AC molecule into a 1:1 γ-CD−AC complex in the ground state and therefore the obtained differential parameters are thermodynamic in nature.

As can be seen from Table 3, rim-substituted γ-CDs **8**, **9a**−**d** afford in general much larger $\Delta\Delta H$ and $\Delta\Delta S$ values than capped γ-CDs **5**−**7** in both water and aqueous methanol solutions. In view of the flexible skeleton of γ-CD, it is reasonable that these substituted γ-CDs form two diastereomeric complexes with substantially different enthalpic changes (arising from the van der Waals contacts within the cavity) and entropic changes (from the conformational alteration and desolvation upon complexation). Indeed, the entropy term is known to play an important role in the enantiodifferentiating photoreactions conducted in the cavity of γ-CD,[8j,9d] but not in the cavity of β-CD.[8b] Therefore, the results obtained with the rim-substituted γ-CDs are in line with our previous observations, suggesting that they bind substrates in an induced-fit manner.[16]

In this context, it is unusual that capped γ-CDs **5**−**7** afford only negligible differential entropies of 0.2−1.4 J mol^{-1} K^{-1}, which are 1−2 orders of magnitude smaller than those for noncapped γ-CDs **8**, **9a**−**d**. This result is compatible with the idea that the capped CD skeleton is restricted in motion and hence does not greatly alter its original conformation upon diastereodifferentiating complexation with ACs. This is the first experimental demonstration of the reaction control by the low-entropy environment existing in capped γ-CD cavity.

Synchronized with the much reduced $\Delta\Delta S$ values, the $\Delta\Delta H$ values for **5** and **6** are also decreased significantly to 0.1−1.0 kJ mol^{-1}, leading to the modest enantioselectivities for **2** (9.5−16.2% ee). Despite the similarly low $\Delta\Delta S$ of 0.2−0.8 kJ mol^{-1}, much larger $\Delta\Delta H$ values of 1.8 and 3.0 kJ mol^{-1} are observed for rigidly capped **7**, indicating that the significant enantioselectivity (57.6% ee) obtained with **7** is absolutely enthalpic in origin. This observation indicates that without causing major conformational changes in **7**, one of the diastereomeric AC pairs, precursor to the dominant enantiomer of **2**, fits more nicely into the rigidly capped γ-CD cavity than its antipodal one does. We may say therefore that the complementarity of the preferred diastereomeric AC pair with the cavity of **7** is close to that in a classical lock-and-key model.[17]

In a previous paper,[8d] we demonstrated that the inherently low-entropy environment of the native β-CD cavity can be modified to a highly entropy-susceptive one by breaking the hydrogen-bonding network on the secondary rim through permethylation of β-CD's hydroxyl groups. Thus, the present work demonstrates that the opposite process to build up a low-entropy cavity from a highly flexible, conformationally diverse one is also feasible through sophisticated modification and that the resulting low-entropy environment contributes to the development of efficient chiral supramolecular (photo)reactions.

Rare Deviation from the Enthalpy−entropy Compensation Observed for Rigidly Capped γ-CD 7. The enthalpy−entropy compensation is an intriguing phenomenon that is widely observed for essentially all chemical and biological reactions and equilibria.[18,19] It provides a powerful tool for analyzing, understanding, and even predicting the thermodynamic behavior based on the existing experimental data.[20] We have demon-

(13) (a) Inoue, Y.; Yokoyama, T.; Yamasaki, N.; Tai, A. *J. Am. Chem. Soc.* **1989**, *111*, 6480. (b) Hoffmann, R.; Inoue, Y. *J. Am. Chem. Soc.* **1999**, *121*, 10702.

(14) (a) Zhang, X.; Gramlich, G.; Wang, X.; Nau, W. M. *J. Am. Chem. Soc.* **2002**, *124*, 254. (b) Dyck, A. S. M.; Kisiel, U.; Bohne, C. *J. Phys. Chem. B* **2003**, *107*, 11652.

(15) Tamaki, T.; Kokubu, T.; Ichimura, K. *Tetrahedron* **1987**, *43*, 1485.

(16) (a) Corbett, P. T.; Tong, L. H.; Sanders, J. K. M.; Otto, S. *J. Am. Chem. Soc.* **2005**, *127*, 8902. (b) Kasai, K.; Aoyagi, M.; Fujita, M. *J. Am. Chem. Soc.* **2000**, *122*, 2140.

(17) Bender, M. L.; Van Etten, R. L.; Clowes, G. A.; Sebastian, J. F. *J. Am. Chem. Soc.* **1966**, *88*, 2318.

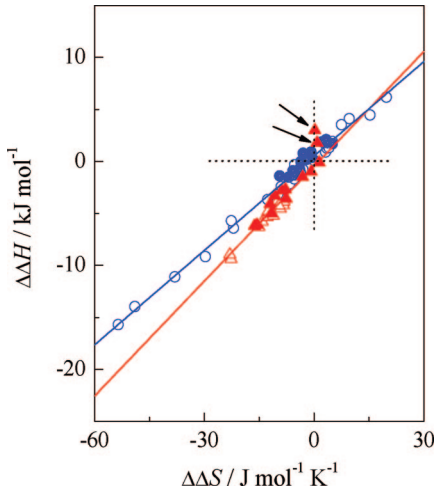


FIGURE 6. Entropy−enthalpy compensation plots of the differential thermodynamic parameters obtained for dimer **2** in this work (▲) and in ref 9b (△), and for dimer **3** in this work (●) and in ref 9b (○). The data points for **2** obtained with rigidly capped **7** are indicated by an arrow. The red and blue regression lines are for **2** (excluding the data obtained with **7**) and **3**, respectively.

strated that the enantiodifferentiation mechanism of the photocyclodimerization of AC with native and modified γ-CDs is essentially unchanged even when one of the glucose units is converted to an altrose on the basis of the nice compensatory entropy−enthalpy relationship observed.[9d]

To examine the validity of global entropy−enthalpy compensation, we plotted the $\Delta\Delta H$ values against the $\Delta\Delta S$ values for the formation of dimers **2** and **3** mediated by primary rim-modified **5**−**8** and **9a**−**d** in water and 50% aqueous methanol and also those reported for the same photoreaction mediated by secondary rim- and skeleton-modified γ-CDs.[9d] As can be seen from Figure 6, the $\Delta\Delta H$ and $\Delta\Delta S$ values for the formation of **2** (red symbols), excepting the data obtained with **7** (indicated by an arrow), are nicely fitted to a single regression line that satisfies the equation $\Delta\Delta H = 0.37\Delta\Delta S - 0.4$ ($r = 0.97$), while those for **3** (blue symbols) fall on a different regression line: $\Delta\Delta H = 0.30\Delta\Delta S - 0.6$ ($r = 0.98$), indicating that the equipodal temperatures for the formation of **2** and **3** are 370 and 300 K, respectively. This seems reasonable since the HT and HH dimers are formed from different diastereomeric precursor complexes.

Unprecedentedly, the thermodynamic parameters for **2** obtained with rigidly capped **7** in water and aqueous methanol appreciably deviate upward from the regression line obtained without including these two points; see Figure 6. Interestingly, the parameters obtained for **2** by using flexibly capped CDs **5** and **6** do not show any deviation. This obvious difference in thermodynamic behavior between the rigidly and flexibly capped CDs indicates that there exists a critical cap rigidity to switch the mechanism of enantiodifferentiation in this supramolecular photochirogenesis system. The exemption of rigidly capped CD **7** is in line with the above observation that the photodimerization with **7** gives the same enantiomer of **3** in ee's comparable to those obtained by using flexibly capped γ-CDs rather than leads to the chirality inversion of product **2**, and also with the conclusion that the tight bridging in **7** significantly limits the conformational freedoms as compared with the flexibly capped **5**, **6** and rim-substituted **8**, **9a**−**d**.

The contrasting behavior observed reveals a distinct role of the rigid capping in the formation of **2** and **3**, which can be rationalized in terms of the structures of diastereomeric complexes which are precursor to the corresponding photodimers. The HH-oriented AC pairs, precursor to **3**, are deduced to orient their carboxylate moiety to the secondary rim due to the increased hydrophobicity and narrowed opening of the primary rim of rigidly capped **7**. It is energetically favorable for the aromatic moiety of AC to hide beneath the cap than to protrude into bulk water through the narrow window, a conformation that the HT AC pairs are forced to take. Therefore, the HH AC pairs will not be significantly restricted even in the cavity of rigidly capped γ-CD **7**, and the same enantiodifferentiation mechanism operates for the formation of **3** is followed with all modified γ-CDs. The above results demonstrate that the entropy effect on the supramolecular photochirogenesis system is not a simple function of the rigidity of CD frame, but also critically correlated with the host−guest complexation models.

Conclusions

In this study, we have synthesized a series of capped and rim-substituted γ-CDs as chiral hosts for mediating the enantiodifferentiating photocyclodimerization of AC. All of the γ-CDs form stable 1:2 host−guest complexes with AC. The HH/HT ratio is significantly improved by using substituted and in particular capped γ-CDs. The ee of chiral HT dimer **2** is unusually insensitive to the rim substitution but is significantly affected by the capping modification; the flexibly capped CDs give the same enantiomer in smaller ee's, whereas the rigidly capped CD affords the antipodal product in a greatly enhanced ee of 58%. In contrast, the ee of chiral HH dimer **3** is much more sensitive to the modification and is greatly enhanced to 35% by rim-substitution and to 36% by rigid capping.

A clear deviation from the compensatory enthalpy−entropy relationship is found for the thermodynamic parameters obtained in the photocyclodimerization with rigidly capped CD **7**, indicating a switching of the enantiodifferentiation mechanism. Such structural fine-tuning may be used for critically manipulating the stereochemical outcomes of supramolecular photochirogenesis.

Experimental Section

General. FAB-MS spectra were measured on a JEOL JMS-DX303 mass spectrometer. NMR spectra were recorded on a JEOL JNM-EX 400 spectrometer; all chemical shifts are reported against the acetonitrile signal used as an internal standard. UV−vis absorption spectra were recorded on a JASCO V-550 spectrophotometer. Circular dichroism spectra were measured on a JASCO J-810 spectropolarimeter.

Materials. 4,4′-Oxydibenzene-1-sulfonyl chloride, biphenyl-4,4′-disulfonyl dichloride and γ-CD were purchased from Tokyo Kasei. 6^A,6^X-Ditosyl-γ-CDs **9a**−**d**, the capped γ-CD **7**, and the rim-

(18) (a) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963; reprint version from Dover, New York, 1989. (b) Grunwald, E.; Steel, C. *J. Am. Chem. Soc.* **1995**, *117*, 5687. (c) Exner, O. *Correlation Analysis of Chemical Data*; Plenum: New York, 1988.

(19) Very recently, the only exceptions from the compensatory enthalpy−entropy relationship have been reported for a cucurbit[7]uril−ferrocene system: Rekharsky, M. V.; Mori, T.; Yang, C.; Ko, Y. H.; Selvapalam, N.; Kim, H.; Sobransingh, D.; Kaifer, A. E.; Liu, S.; Isaacs, L.; Chen, W.; Moghaddam, S.; Gilson, M. K.; Kim, K.; Inoue, Y. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 20737.

(20) For earlier examples and analyses of the compensatory enthalpy-entropy relationship in various supramolecuar systems, see: Inoue, Y.; Wada, T. *Advances in Supramolecular Chemistry*; Gokel, G. W., Ed.; JAI Press: Greenwich, CT, 1997; Vol. 4, pp 55−96.

substituted γ-CD **8** were synthesized according to the procedures described in the literature.[21,9e]

Synthesis of Capped γ-CDs 5 and 6. 4,4′-Oxydibenzene-1-sulfonyl chloride (1.47 g, 4 mmol) was added to a solution of γ-CD (2.6 g, 2 mmol) in dry pyridine (100 mL). The reaction mixture was stirred for 2 h at room temperature. To the resulting mixture was added ethanol (10 mL) to quench the reaction, and the solvent was removed in vacuo. The residue obtained was dissolved in distilled water and subjected to reversed-phase HPLC to give **5** as white solid (292 mg, 9.2%). HR-MS (FAB): *m*/*z* calcd for $C_{60}H_{86}NaO_{45}S_2$ $[M + Na]^+$, 1613.38, found 1613.38. ^{1}H NMR (D_2O/DMSO-d_6 = 2:3 v/v): δ 7.97−7.95 (d, 2H, *J* = 8 Hz), 7.93−7.91 (d, 2H, *J* = 8.4 Hz), 7.38−7.35 (d, 2H, *J* = 8.4 Hz), 7.26−7.24 (d, 2H, *J* = 8.4 Hz), 4.97−4.93 (m, 6H), 4.84 (m, 2H), 4.74 (m, 1H), 4.22 (m, 2H), 3.84 (m, 3H), 3.81−3.50(m, 21H), 3.48−3.35(m, 19H), 3.04−3.00 (d, 1H, *J* = 12.4 Hz), 2.90−2.87(d, 1H, *J* = 12.0 Hz). **Data for 6.** Yield 98.6 mg, 3.1%. HR-MS (FAB): *m*/*z* calcd for $C_{60}H_{86}NaO_{45}S_2$ $[M + Na]^+$, 1613.38, found 1613.38. ^{1}H NMR (D_2O/CD_3OD = 1:1 v/v): 7.95−7.93 (d, 4H, *J* = 8.8 Hz), 7.26−7.24 (d, 4H, *J* = 8.4 Hz), 5.08−4.94(m, 8H), 4.53−4.50 (d, 2H, *J* = 10.4 Hz), 3.36−3.31 (dd, 2H, *J* = 9.6, 10.4 Hz), 3.84−3.68 (m, 20H), 3.64−3.45 (m, 20H), 3.41−3.23 (m, 4H).

(21) Fujita, K.; Yamamura, H.; Imoto, T.; Fujioka, T.; Mihashi, K. *J. Org. Chem.* **1988**, *53*, 1943.

Supporting Information Available: The NMR and MS spectra of capped γ-CDs. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800533Y