JOC Article

Pressure and Temperature-Controlled Enantiodifferentiating [4+4] Photocyclodimerization of 2-Anthracenecarboxylate Mediated by Secondary Face- and Skeleton-Modified γ-Cyclodextrins

Cheng Yang,[†] Asao Nakamura,[†] Gaku Fukuhara,[‡] Yumi Origane,[†] Tadashi Mori,[‡] Takehiko Wada,[‡] and Yoshihisa Inoue*,[†,‡]

ICORP Entropy Control Project, JST, 4-6-3 Kamishinden, Toyonaka 560-0085, Japan, and Department of Applied Chemistry, Osaka University, 2-1 Yamada-oka, Suita 565-0871, Japan

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

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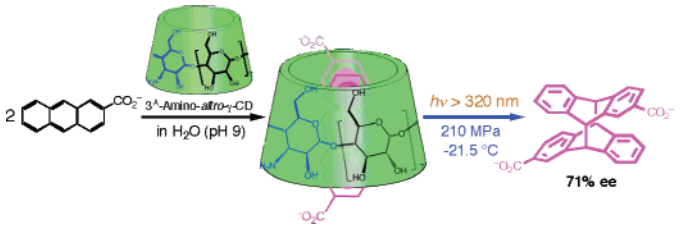

A series of secondary-face-substituted and skeleton-modified γ-cyclodextrins (γ-CDs) were prepared as chiral hosts for enantiodifferentiating [4+4] photocyclodimerization reactions of 2-anthracenecarboxylic acid (AC). These γ-CD derivatives form stable ternary complexes with ACs, with altroside-bearing γ-CDs undergoing induced-fit conformational changes upon complexation, and the photocyclodimerization of AC was, thus, dramatically accelerated. The enantiomeric excess (ee) of *anti-head-to-head* cyclodimer **3** was greatly enhanced in general with altroside-bearing γ-CDs **7**−**9**. Although mono-*altro*-γ-CD **9** and 3^A-azido-3^A-deoxy-*altro*-γ-CD **7** gave **2** in ee's smaller than those obtained with native γ-CD, 3^A-amino-3^A-deoxy-*altro*-γ-CD **8** yielded **2** in much higher ee's, which is likely to be ascribed to the combined effects of the less-symmetric cavity and the electrostatic interactions. The influence of temperature and high pressure on the supramolecular photochirogenic reaction has been investigated in depth. An ee as high as 71% was obtained for cyclodimer **2** in the photocyclodimerization of AC mediated by **8** at 210 MPa and −21.5 °C.

Introduction

Achieving a high level of stereocontrol in solution-phase photochirogenesis is still a great challenge,[1−3] with several strategies having been proposed to achieve chirality control in solution-phase photochemistry.[2,3] The diastereomeric approach using a chiral auxiliary introduced to a substrate has been well-studied and proven to be the most effective strategy in controlling the stereoselectivity of photoreactions, despite the inherently low chiral-source efficiency.[1,4] Enantiodifferentiating photosensitization provides a unique tool for transferring the chiral information from an optically active sensitizer to a prochiral substrate via noncovalent interactions in the excited state.[5−11] By carefully designing the energetic and stereochemical features of the relevant sensitizer and substrate, only a

* Corresponding author. Permanent address: Department of Applied Chemistry, Osaka University, 2-1 Yamada-oka, Suita 565-0871, Japan. Tel.: +81-6-6879-7920. Fax: +81-6-6879-7923.
[†] ICORP Entropy Control Project.
[‡] Osaka University.

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catalytic amount of chiral compound can result in efficient chirality amplification. In the rather short history of photochirogenesis, studies on enantiodifferentiating photosensitizations have mostly dealt with unimolecular reactions, while only a limited amount of effort has been devoted to sensitized bimolecular photochirogenesis, examples of which include photochemical cyclodimerization and polar addition reactions.[8−11] More recently, a new and potentially promising alternative, that is, supramolecular photochirogenesis, has been developed in the interdisciplinary region comprised of supramolecular, asymmetric, and photochemistry. In this strategy, an optically active host molecule provides the chiral environment for photochemically transferring chirality to the complexed guest molecule through weak ground-state interactions, such as hydrogen bonding, van der Waals, $\pi-\pi$, and hydrophobic interactions. The orientation of the substrate can be strictly regulated with respect to the chiral host by multiple supramolecular interactions so as to guarantee the subsequent effective stereospecific photoreaction.

To secure highly effective stereocontrol in a supramolecular photochirogenesis system, two requisite characteristics are desired for a chiral host. First, the prochiral substrate should be strongly bound to the chiral host, and more preferably, the host binding accelerates the subsequent photoreaction to minimize the concurrent photoreaction of free substrate in the bulk solution. Catalytic turnover caused by a lower binding constant for the photoproduct is desirable. Otherwise, a large excess of chiral host is required. Second, a chiral environment of the binding site is essential for executing a highly stereospecific transformation of the prochiral substrate bound at the chiral site. Several successful methodologies have been developed in supramolecular photochirogeneses exploiting natural and synthetic chiral hosts and templates.[12−19] Ramamurthy et al. reported a series of supramolecular photochirogenic reactions in chirally modified supercages of zeolites.[13−15] Bach et al. took advantage of intermolecular dual hydrogen bonding interactions of Kemp's chiral triacid derivatives with prochiral substrates to achieve a high diastereo- or enantioselectivity.[17−21] We have also reported enantiodifferentiating photoreactions employing protein,[22] DNA,[23] and nanoporous material,[24] as well as native and modified cyclodextrins (CDs),[25−31] as chiral hosts.

Possessing inherently chiral cavities, CDs have attracted tremendous interest as molecular reaction vessels to improve the efficiency as well as selectivity of thermal and photochemical reactions.[32−37] CD-mediated asymmetric photoreactions were investigated for the first time in the solid-state photolysis of a benzaldehyde−β-CD complex by Rao and Turro.[38] Since then, a variety of CD-mediated or -sensitized asymmetric photoreactions, including photoisomerizations of cyclooctenes[25−28] and diphenylcyclopropanes,[39] photocyclodimerizations of anthracene derivatives,[29−31,40−42] stilbenes [43−45] and coumarin derivatives,[46−48] photocyclizations of tropolones,[49] and *N*-alkyl pyridones,[50] as well as photocycloadditions of phenoxyalkenes,[51] have been investigated by employing native and primary-face-modified CDs as chiral hosts in the solution and in the solid states. However, the optical purities hitherto obtained from CD-mediated photochirogenic reactions are low or even not reported.

The γ-CD-mediated enantiodifferentiating [4+4] photocyclodimerization of 2-anthracenecarboxylic acid (AC) has recently attracted extensive interest.[22,29−31,42] Photoirradiation of AC affords four configurational isomers **1**−**4**, among which *syn-head-to-tail* (*syn*-HT) cyclodimer **2** and *anti-head-to-head* (*anti*-HH) cyclodimer **3** are chiral, while *anti*-HT cyclodimer **1** and *syn*-HH cyclodimer **4** are achiral (Scheme 1). Native γ-CD has been known to form a very stable 1:2 host−guest complex with AC in aqueous solution, from which the photocyclodimerization is dramatically accelerated.[40,41] The enantiodifferentiating photocyclodimerization of AC and the separation of the photoproducts **1**−**4** were first carried out only recently,[29] with native γ-CD

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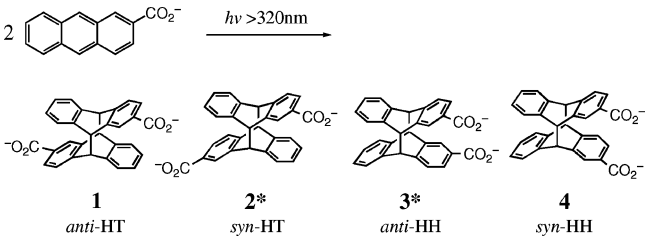
SCHEME 1



being proven to afford *syn*-HT cyclodimer **2** in an enantiomeric excess (ee) of up to 41% and *anti*-HH cyclodimer **3** in low ee's of <5%. Endeavors have been devoted to the improvement of both the chemical and the optical yields of **3** by introducing two cationic groups to the primary face of γ-CD,[30,31,42] indeed the chemical and optical yields of cyclodimer **3** were increased by 1.8 and 10 times, respectively, by using regioisomers of dipyridinio-appended γ-CDs.[42] Also, γ-CD derivatives having two amino groups on the primary rim of γ-CD significantly improved the yield and ee of HH cyclodimers **3** and **4**.[30] The chemo- and enantioselectivities of the HH cyclodimers could be precisely regulated by manipulating the multiple controlling factors that affect them, including the distance between the two amino groups, the reaction temperature, and the solvent composition.[30] Interestingly, a single flexible diamino sidearm introduced to the primary face of γ-CD was shown to be more effective than the two cationic groups on the primary rim in improving the chemical yield and ee of the *syn*-HH cyclodimers, giving **3** in 42% yield and 41% ee under the optimized conditions.[31]

These successful results obtained by using native and primary-face-modified γ-CDs prompted us to develop a new methodology for manipulating the chiral host−guest interactions in the ground and excited states in this supramolecular photochirogenic system via the exploitation of more sophisticated CD derivatives, as well as multiple external controlling factors. In this study, we synthesized a series of secondary-face-modified γ-CDs **5**−**9** (Scheme 2) as chiral hosts for the supramolecular photochirogenic cyclodimerization of AC. Native CDs are composed of several α-(1 → 4)-linked glucopyranose units, with the intramolecular hydrogen-bonding network formed between the adjacent 2-OH and 3-OH group of the secondary face accounting for the rigid nature of its hydrophobic cavity. Consequently, chemical modification on the secondary face of CDs will partly break the network to give a more flexible hydrophobic cavity.[52] On the other hand, the nucleophilic ring opening of 2,3-mannoepoxide **6** will generate 2,3-inverted CD mutants with an altroside residue,[53−58] which possess an inherently chiral cavity of significantly altered size, shape, and hydrophobicity. Accordingly, we expect that the chemo- and stereoselectivity of the photocyclodimerization mediated by these secondary-face-modified γ-CDs will be entirely different from those obtained by native and primary-face-modified γ-CDs. We further manipulated the supramolecular photochirogenic reaction by external factors such as temperature and pressure, which were demonstrated in recent studies to be crucial in controlling the stereochemical outcomes of photochirogenesis.[5,6]

Results and Discussion

Complexation Studies. The binding behavior (stoichiometry and stability) of AC with native γ-CD has been studied previously to show the formation of a very stable 1:2 host−guest ternary complex through a 1:1 complex in aqueous solution.[29,40,41] To elucidate the complexation behavior of AC with the modified CDs, NMR, UV−vis, and CD spectral studies were performed.

NMR Spectral Examinations. ^{1}H NMR spectra of the modified γ-CDs in the presence and absence of AC were recorded in D_2O solutions at 35 °C. The modified γ-CDs gave much more complicated NMR spectra than the native γ-CD as a consequence of the loss of the C_8 symmetry. As exemplified in Figure 1, the altroside signals are readily identified because of their substantial deviations from the glucoside signals. Thus, the glucoside's H2−H6 protons appear in narrow ranges of δ 3.47−3.59 ppm (H2, H4) and 3.70−3.92 ppm (H3, H5, H6), while the altroside's protons are spread over a wider range, exhibiting a great upfield shift for H1^A and significant downfield shifts for H2^A, H4^A, and H5^A. The altroside unit of a mono-*altro*-CD derivative is considered to be in a dynamic equilibrium of three conformers: $^1C_4$, $^0S_2$, and $^4C_1$ (Scheme 3).[55,57−59] We measured the vicinal ^{1}H−^{1}H coupling constant $J_{1,2}$ of the altroside's H1 and H2 protons to assess the conformational properties of the altroside in **7**−**9** (Table 1). As judged from the large $J_{1,2}$ values observed, the $^1C_4$ and $^0S_2$ conformers are thought to be dominant for the altroside residue incorporated in derivatives **7**−**9**. The $J_{1,2}$ values of **8** and **9** (6.0 and 5.6 Hz, respectively) are appreciably larger than that of **7** (4.4 Hz), suggesting that the conformational equilibrium is strongly dependent on the substituent at the 3^A-position.

The addition of mono-*altro*-γ-CD **9** to an aqueous solution of AC led to significant upfield shifts of the aromatic signals of AC (Figure 1), which are readily explained by the mutual ring current effects of two face-to-face stacked AC molecules accommodated within one CD cavity. Interestingly, the inclusion of AC molecules gives rise to an allosteric change of these altroside-bearing hosts. Thus, the altroside's $J_{1,2}$ of both **7** and **9** decreased to 3.6 Hz upon complexation with AC. This means that the conformational equilibrium of altroside is shifted to the $^4C_1$ form to satisfy the steric requirements arising from the inclusion of two AC molecules and further demonstrates that these altroside-bearing γ-CDs display enzyme-like behavior to bind guests through a substrate-induced-fit mechanism. Upon complexation with AC, the CD component signals disperse more widely over the range of δ 3.36−3.93 ppm rather than undergo equivalent unidirectional shifts, indicating that the protons of different sugar units are subjected to nonequivalent shielding and deshielding effects. This anisotropic effect is very similar to that observed upon complexation of naphthalene derivatives and mono-*altro*-β-CD[57] and implies that the bound AC molecules are not able to freely rotate as a result of the distortion of the altroside-bearing γ-CD cavity.

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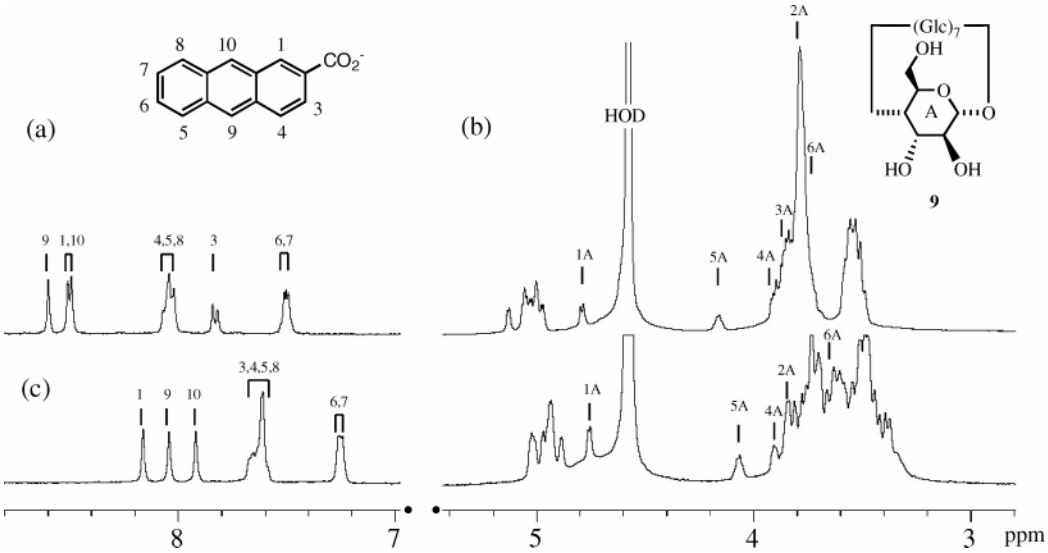
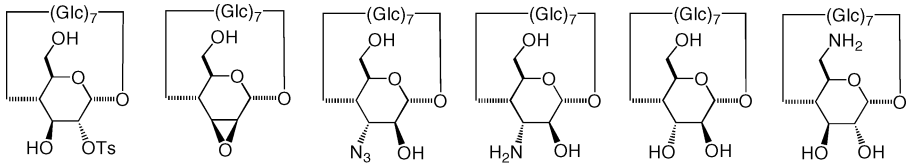


FIGURE 1. ^{1}H NMR spectra of (a) AC (2 mM), (b) **9** (4 mM), and (c) a mixture of AC (4 mM) and **9** (4 mM) in a pD 9.0 D_2O buffer solution at 35 °C.

SCHEME 2



SCHEME 3

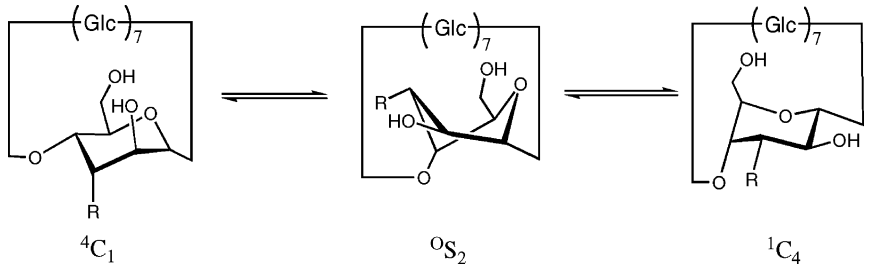


TABLE 1. Vicinal ^{1}H−^{1}H Coupling Constants ($J_{1,2}$) of the α-D-Altropyranoid Ring in Mono-*altro*-γ-CD Derivatives 7, 8, and 9[a]

	$J_{1,2}$ (Hz)		
additive	**7**	**8**	**9**
none	4.4	6.0	5.6
AC	3.6	n.d.[b]	3.6

[a] γ-CDs (4 mM) and AC (4 mM) in pD 9.0 D_2O buffer solution at 35 °C. [b] Not determined.

UV−Vis and Circular Dichroism Spectral Examinations. The addition of γ-CD derivatives to an aqueous solution of AC induced notable changes in the UV−vis spectrum from which a 1:2 stoichiometry of the host−guest complexation was determined by the Job plot analysis.[60] This result reveals that the more-or-less irregular cavities of mono-*altro*-γ-CDs are still capable of accommodating two AC molecules, as is the case with native γ-CD, and hence, the conversion of a glucoside to an altroside does not greatly alter the size of the CD cavity.

Further evidence in support of the 1:2 stoichiometry was obtained through the circular dichroism spectral studies of the complexation of AC with modified γ-CDs. A clear bisignate Cotton effect was observed (with its maxima and minima split by up to 30 nm) at wavelengths corresponding to the major absorption band of AC′ (centered at 262 nm) upon the addition of AC to an aqueous solution of **8**,[60] verifying that two AC molecules are indeed closely packed in the same CD cavity. According to the exciton chirality theory,[61] the positive first Cotton effect observed indicates that the dominant orientation of the ^1B_b transition moments of two stacked AC molecules form a right-handed screw in the CD cavity, as illustrated in Scheme 4 (top), and hence, the cyclodimer **2** derived therefrom is considered to be the major enantiomer.

From CD spectral titration data, the association constants for stepwise 1:1 (K_1) and 1:2 complexations (K_2) were determined by the nonlinear least-squares method. Table 2 summarizes the

(60) See Supporting Information for UV−vis and CD spectral analysis.

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SCHEME 4

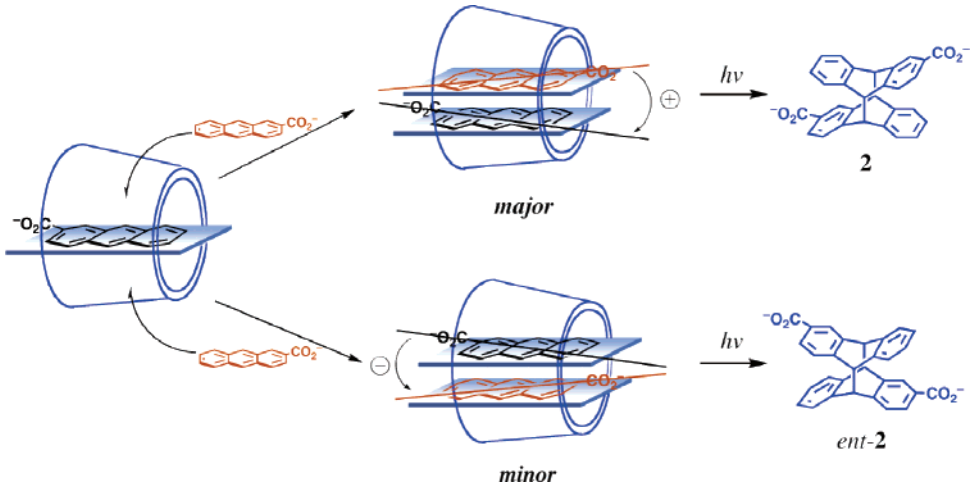

TABLE 2. Association Constants for the Complexation of AC with Native and Modified γ-CDs and Calculated Populations of Free and Complexed AC Species in Solutions under the Conditions of Photoirradiation

	association constant[a]				% population of AC[b]		
host	K_1 (M^{-1})	K_2 (M^{-1})	K_1K_2 ($10^6\ M^{-2}$)	K_2/K_1	free	1:1 complex	1:2 complex
γ-CD[c]	182 (≡ 1)[d]	56 700 (≡ 1)[e]	10.3 (≡ 1)[f]	310	16.9	5.1	78.0
5	174 (0.96)[d]	17 300 (0.31)[e]	3.01 (0.29)[f]	100	28.1	8.2	63.7
6	162 (0.89)[d]	21 500 (0.38)[e]	3.48 (0.34)[f]	130	26.6	7.2	66.2
7	119 (0.65)[d]	9620 (0.17)[e]	1.14 (0.11)[f]	81	40.3	8.3	51.4
8	291 (1.6)[d]	14 600 (0.26)[e]	4.25 (0.41)[f]	50	24.0	11.5	64.5
9	137 (0.75)[d]	8630 (0.15)[e]	1.18 (0.11)[f]	63	39.6	9.3	51.1

[a] Association constants for the stepwise 1:1 and 1:2 inclusion complexations obtained at 20 °C. [b] Populations calculated for the photolysis solutions at 20 °C, assuming [AC] = 0.8 mM and [host] = 2.0 mM. [c] Reference 29. [d] Relative to K_1 for native γ-CD. [e] Relative to K_2 for native γ-CD. [f] Relative to K_1K_2 for native γ-CD.

K_1 and K_2 values thus obtained, as well as the population of free and bound AC species in each solution used for photoirradiation. As expected from the large cavity size of γ-CD, which is capable of accommodating two AC molecules, K_2 is significantly larger than K_1 for all hosts investigated. It is noted, however, that the K_2 values for modified γ-CDs are significantly smaller by a factor of 0.15−0.38 than that for native γ-CD, while the K_1 values are only moderately reduced or even enhanced by a factor of 0.65−1.6, affording more exaggerated variations in the overall binding constants (K_1K_2). As judged from the K_2/K_1 ratio (Table 2), the modified CDs **5**−**9** show 3−6 times reduced preference for the 1:2 over the 1:1 complexation, in comparison to native γ-CD. In particular, the altroside-bearing γ-CDs **7**−**9** show the smallest K_2 values and K_2/K_1 ratios. This seems reasonable, because these *altro*-CDs possess deformed, more-flexible cavities, which may lead to smaller enthalpic gains and/or larger entropic losses upon guest inclusion.[56] The electrostatic interactions between the amino group of **8** and the carboxylic group of AC can account for the specifically high K_1 value of **8**. By using these association constants, the population of free and complexed AC species was calculated for aqueous solutions for photolysis, each of which contains 0.8 mM AC and 2 mM host. As can be seen from Table 2, the majority (50−80%) of AC in the solution forms the 1:2 complex, while only 5−10% forms the 1:1 complex, and the remaining 20−40% exist in the bulk solution. These populations, particularly that in the bulk water, may seem insufficient for the selective formation of the photoproducts from the 1:2 complex. However, the quantum efficiency of the photodimerization of AC in aqueous solution is known to be 8 times smaller than that for the 1:2 complex of AC within native γ-CD,[40] and the AC molecule accommodated in the 1:1 complex is further protected from external attack of another AC and could be effectively unreactive. Assuming similar situations for the modified γ-CDs, we may tentatively conclude that the 1:2 complexes of **5**−**9** account for 91−95% of the photoproducts obtained under the conditions employed.

Kinetic Study of the Photocyclodimerization of AC in the Presence of 5−9. To further elucidate the influence of these modified γ-CDs on the photoreaction of AC, we first investigated the kinetic behavior of the photocyclodimerization in the presence of these hosts. Degassed aqueous buffer solutions containing 0.8 mM AC and 2 mM γ-CD derivatives were irradiated at 20 °C and >320 nm, by using a high-pressure mercury lamp equipped with a uranium filter. A merry-go-round apparatus was used to ensure the equal light exposures for all reaction solutions. The NMR and TLC analyses of the sample solutions before and after irradiation clearly showed that no structural change of the chiral hosts occured during the photoirradiation. At least at the initial stages of photolysis where the incident light was fully absorbed by AC in the solution, the photocyclodimerization of AC followed first-order kinetics, and the plot of the logarithm of AC concentration against the irradiation time gave a good straight line in each case. The first-order rate constants (k_1), determined by monitoring the consumption of AC by UV−vis spectrometry, are summarized in Table 3. It is clear that the γ-CDs dramatically accelerate the photocyclodimerization of AC in aqueous solution by a factor of 6.4−10.5. Because the order of acceleration, that is, native γ-CD > **8** ∼ **5** ∼ **6** > **9** ∼ **7** (Table 3), nicely correlates with the order of AC population of the 1:2 complex (Table 2), we attribute this acceleration to the confinement of two AC

TABLE 3. First-Order Rate Constants for the Photocyclodimerization of AC in the Presence and Absence of γ-CD Derivatives[a]

host	k_1 ($10^{-3}s^{-1}$)	host	k_1 ($10^{-3}s^{-1}$)
none	0.60 (≡ 1)[b]	**7**	3.84 (6.4)[b]
γ-CD	6.31 (10.5)[b]	**8**	5.40 (9.0)[b]
5	5.12 (8.5)[b]	**9**	3.91 (6.5)[b]
6	5.33 (8.9)[b]		

[a] Borate buffer solutions (25 mM, pH 9), containing AC (0.8 mM) and native or modified γ-CD (2 mM), were simultaneously irradiated at >320 nm in a temperature-controlled water bath at 20 °C, using a merry-go-around apparatus. [b] Relative rate.

molecules in one CD cavity, which greatly enhances the local concentration and induces the face-to-face orientation favorable for photodimerization. Intriguingly, this result is in marked contrast to that obtained with bispyridinio-γ-CDs,[42] where a deceleration effect was observed, as a result of the unsuitable relative orientation of two AC molecules enforced by the ion-pairing interaction.

Enantiodifferentiation Mechanism of the CD-Mediated Photocyclodimerization of AC. Obviously, the 1:2 complex of γ-CD with AC is not a single species but a mixture of at least four orientational isomers, which are the precursors to photoproducts **1**−**4**. Thus, two AC molecules in the γ-CD cavity are longitudinally stacked with each other in the head/tail, as well as syn/anti, fashion with respect to the carboxyl group. The original orientational distribution in the ground state will be secured in the cyclodimers produced upon photoirradiation, as the tightly packed complex structures and the short lifetime of AC do not allow the rotation or the positional exchange of AC in the cavity.[29] Consequently, the product distribution of four isomeric cyclodimers generated in the presence of a γ-CD derivative intrinsically depends on the distribution of the corresponding precursor complexes between the CD and AC in the ground state, although the product distribution is not exactly the same as that of the precursor complexes because the photodimerization efficiency will be different for each complex.

The formation of the ternary complex is essential for the enantioselective production of chiral cyclodimers.[29,30] When an AC molecule is brought into the inherently chiral γ-CD cavity, as shown in Scheme 4, its two enantiotopic faces become diastereotopic, and the inclusion of a second AC molecule to the upper or lower face of the first one leads to a diastereomeric pair of 1:2 complexes, from which an enantiomeric pair of photocyclodimers is produced. Therefore, the stereochemical outcomes of photoproducts, that is, product ratios and ee's, are critical functions of the distribution of the precursor complexes, which are determined by their relative stability under the conditions employed. In this context, we may claim that the photoreaction provides us with a practical tool for estimating the population of these orientational and diastereomeric 1:2 inclusion complexes, which are effectively inaccessible by conventional methods.

Multidimensional Control of the Product Distribution and Enantiomeric Excess of Cyclodimers. We investigated the effects of temperature, pressure, and various hosts on the photocyclodimerization of AC. In a typical run, a Pyrex tube containing an aqueous buffer solution (3 mL) of AC (0.8 mM) and a host (2 mM) was irradiated at >320 nm in a temperature-controlled water/ethylene glycol bath at a given temperature. Irradiations under high hydrostatic pressure of up to 450 MPa were performed in a thermostated high-pressure vessel equipped with sapphire windows for external irradiation. The relative yields and ee's of the photocyclodimers were determined by chiral HPLC analysis on tandem columns of Inertsil ODS-2 and Chiralcel OJ-R; the positive or negative sign of the reported ee corresponds to the excess of the first- or second-eluted enantiomer, respectively. The product distribution and ee obtained under a variety of conditions are listed in Table 4.

Host Dependence. Somewhat unexpectedly, the relative yields of cyclodimers **1**−**4** were very insensitive to the modification of the γ-CD host under comparable conditions. All of the employed hosts consistently gave HT cyclodimers **1** and **2** as the major products (83−93%), while the combined yield of HH cyclodimers **3** and **4** stayed low (7−17%). Hence, the HT/HH ratio is kept high at 4.5−13.3 over the entire temperature (−22 to 50 °C) and pressure (0.1 to 210 MPa) ranges examined (the high HT/HH ratios obtained at low temperature and high pressure). This is not surprising in view of the different degrees of electrostatic repulsion between the AC molecules' anionic carboxylate moieties of the ternary complex in the HH and HT conformations.

In contrast, the product's ee is more sensitive to the skeletal and peripheral modifications of γ-CD, exhibiting moderate variations. Thus, the ee obtained at 0 °C and 0.1 MPa varied from +26 to +53% for **2** and from +7 to −16% for **3**, depending on the stereochemistry and substituents introduced at the 2-, 3-, or 6-positions of γ-CD. For comparison purposes, we first examine the product distribution and ee obtained under common conditions (i.e., 0 °C and 0.1 MPa) to assess the effects of host modification on the photocyclodimerization. It is rather surprising that native γ-CD, 2-tosyl- (**5**), and 2,3-mannoepoxy-CDs (**6**) give exactly the same ee's of 40% for **2** and 2% for **3**. The similarity in enantioselectivity for **5**, **6**, and native γ-CD may indicate that the simple substitution of the 2-OH as well as the mannoepoxidation does not greatly alter the chiral environment of the γ-CD cavity.

However, the altroside-bearing CD derivatives **7**−**9** exhibited distinctly different photoenantiodifferentiating behavior compared to native γ-CD. The ee of cyclodimer **3** was appreciably enhanced to −10.2% by using **8** as a chiral host and up to −15.9% in the case of **9**, which is 1 order of magnitude larger than that obtained with native γ-CD. Interestingly, host **7** showed the opposite enantiomeric preference to give antipodal cyclodimer **3** in +6.6% ee. Although **7** and **9** as chiral hosts gave cyclodimer **2** in moderate 26−29% ee, the ee of **2** was doubled to 53% by using 3-amino-*altro*-γ-CD **8**. It is thus demonstrated that replacing one of CD's glucosides with an altroside can be used as a versatile tool for manipulating the chiral environment of the original CD cavity, which in turn enables us to obtain unique stereochemical outcomes upon supramolecular photochirogenesis. It is noted that hosts **7**−**9**, possessing the identical mono-*altro*-γ-CD framework, afford significantly different ee's for both **2** and **3**, with the highest ee at 0 °C and 0.1 MPa obtained with 3^A-amino-*altro*-γ-CD **8**, for which the electrostatic interaction between the 3-amino group of **8** and the AC's carboxylate are believed to play an important role. To further elucidate the role of the amino substitution on the secondary rim of CD, the results obtained with host **8** are compared with those with host **10**, in which one amino group is introduced on the primary face of γ-CD and all the sugar units remain intact, that is, as glucosides. As can be seen from Table 4, photocyclodimerization of AC mediated by **10** yields **2** and **3** in 39 and

TABLE 4. Photocyclodimerization of AC in the Presence of Native and Modified γ-CDs[a]

			relative yield (%)[b]				% ee[b,c]		ratio		
										anti/syn	
host	pressure (MPa)	temp. (°C)	**1**	**2**	**3**	**4**	**2**	**3**	HT/HH[d]	**1/2**	**3/4**
γ-CD	0.1	0	42.7	45.9	6.8	4.6	39.2	−1.4	7.77	0.93	1.48
	210	−10	34.6	54.5	5.4	5.5	45.4	−3.2	8.17	0.63	0.98
		0	34.8	54.2	5.2	5.8	42.1	−3.8	8.09	0.64	0.90
		20	34.6	52.4	6.5	6.5	36.8	−3.5	6.69	0.66	1.00
		40	33.9	49.7	8.6	7.8	31.1	−2.5	5.10	0.68	1.10
5	0.1	0	43.3	44.2	7.0	5.6	39.1	−1.5	6.94	0.98	1.25
		10	42.6	44.8	7.6	5.0	35.4	−1.1	6.94	0.95	1.52
		20	42.7	43.9	8.0	5.4	32.4	−1.9	6.46	0.97	1.48
		30	42.5	43.3	8.6	5.6	28.5	−3.3	6.04	0.98	1.54
		40	42.6	41.5	9.2	6.7	25.6	−3.3	5.29	1.03	1.37
		50	42.4	40.4	10.8	6.4	22.7	−3.9	4.81	1.05	1.69
	210	−8	33.9	55.1	5.7	5.3	44.8	−1.8	8.09	0.62	1.08
		0	33.7	55.2	5.8	5.3	43.3	−2.7	8.01	0.61	1.09
		20	33.5	52.9	7.0	6.7	38.1	−3.1	6.31	0.63	1.04
		40	33.9	50.2	8.4	7.5	32.5	−3.6	5.29	0.68	1.12
6	0.1	0	42.4	45.9	6.8	4.9	39.8	1.5	7.55	0.92	1.39
		10	42.4	45.0	7.5	5.1	36.1	−1.1	6.94	0.94	1.47
		20	43.3	43.4	8.0	5.3	32.7	−2.8	6.52	1.00	1.51
		30	42.6	42.9	8.9	5.6	28.7	−4.1	5.90	0.99	1.59
		40	42.8	41.4	9.8	5.9	24.9	−5.9	5.36	1.03	1.66
		50	42.8	40.1	10.9	6.1	20.1	−6.9	4.88	1.07	1.79
	210	−8	40.3	51.1	4.8	3.8	47.2	−2.9	10.63	0.79	1.26
		0	40.5	50.7	4.8	3.9	45.0	−3.1	10.48	0.80	1.23
		20	40.7	48.5	5.9	4.8	39.1	−3.6	8.34	0.84	1.23
		40	37.4	47.1	8.0	7.5	31.9	−6.1	5.45	0.79	1.07
7	0.1	0	42.0	44.8	8.3	4.9	28.6	6.6	6.58	0.94	1.69
		10	41.9	44.2	8.8	5.1	25.8	5.9	6.19	0.95	1.73
		20	41.9	43.3	9.3	5.4	23.0	4.5	5.80	0.97	1.72
		30	42.0	42.2	10.1	5.7	20.0	2.0	5.33	1.00	1.77
		40	42.3	40.9	10.8	6.0	16.6	1.3	4.95	1.03	1.80
		50	42.6	39.3	11.9	6.2	12.9	−0.3	4.52	1.08	1.92
	210	−12	34.7	54.8	5.2	5.3	38.2	1.4	8.52	0.63	0.98
		0	34.0	54.8	5.6	5.5	34.7	1.2	8.00	0.62	1.02
		20	33.9	52.6	7.0	6.5	29.9	0.8	6.41	0.64	1.08
		40	33.2	49.3	9.5	8.0	24.7	0.1	4.71	0.67	1.19
8	0.1	0	42.9	46.6	5.6	4.8	52.8	−10.2	8.61	0.92	1.17
		10	42.7	46.0	6.3	5.0	48.0	−9.8	7.85	0.93	1.26
		20	42.6	45.2	6.9	5.2	42.4	−9.7	7.26	0.94	1.33
		30	42.7	44.2	7.7	5.4	37.4	−9.5	6.63	0.97	1.43
		40	42.8	43.1	8.5	5.6	32.8	−8.5	6.09	0.99	1.52
		50	43.1	41.2	9.9	5.8	27.4	−7.0	5.37	1.05	1.71
		55	43.3	40.6	10.3	5.8	23.8	−6.2	5.21	1.07	1.78
	210	−21.5	40.0	52.9	3.6	3.4	71.0	−13.9	13.27	0.76	1.06
		−8	39.6	52.5	4.0	3.9	63.5	−11.0	11.66	0.75	1.03
		0	39.3	52.0	4.4	4.3	59.2	−10.5	10.49	0.76	1.02
		20	35.6	51.8	6.5	6.1	50.8	−9.7	6.94	0.69	1.07
		40	34.5	51.3	7.0	7.3	41.3	−8.8	6.00	0.67	0.96
9	0.1	0	45.2	42.1	7.6	5.0	25.6	−15.9	6.93	1.07	1.52
		10	44.8	42.1	8.1	5.0	22.9	−15.5	6.63	1.06	1.62
		20	44.5	41.1	8.7	5.4	20.2	−13.9	6.07	1.08	1.61
		30	44.0	40.9	9.5	5.6	17.9	−12.5	5.62	1.08	1.70
		40	43.6	39.7	10.3	6.3	15.0	−11.7	5.02	1.10	1.63
		50	43.8	38.9	11.2	6.0	12.4	−9.6	4.81	1.13	1.87
	210	−8	37.2	52.2	5.4	5.2	36.8	−27.0	8.43	0.71	1.04
		0	37.0	51.7	5.6	5.7	33.9	−26.1	7.85	0.72	0.98
		20	36.4	50.4	6.7	6.5	29.0	−21.6	6.58	0.72	1.03
		40	35.1	47.8	9.2	7.8	23.1	−16.7	4.88	0.73	1.18
10	0.1	0	35.3	49.5	7.5	7.7	38.7	−1.6	5.58	0.71	0.97

[a] Photoirradiation was carried out under an argon atmosphere in Pyrex tubes (1-cm i.d.) or in a 0.15-mL quartz cuvette (0.2-cm light path) for high-pressure experiments, with a 300-W high-pressure mercury lamp fitted with a uranium filter or an optical glass filter (Toshiba UV-35). AC (0.8 mM) and the γ-CD derivative (2 mM) were dissolved in 25 mM borate buffer (pH 9.0). [b] Relative yields and ee's were determined by chiral HPLC, using tandem columns of Intersil ODS-2 (GL Science) and Chiralcel OJ-R (Daicel). [c] The absolute configuration of cyclodimers has not been determined and the positive/negative ee sign corresponds to the excess of the first/second-eluted enantiomer, respectively. Errors in the values of % ee are ±0.5% for isomer **2** and ±3% for isomer **3**. [d] [**3** + **4**]/[**1** + **2**].

−2%, respectively, which are the same as those obtained with native γ-CD. This is not very surprising, because the chiral environment as well as the C_8 symmetric structure of the γ-CD cavity is not greatly changed upon replacing a hydroxyl group on the primary face with an amino group. However, the situation is completely different for mono-*altro*-γ-CD hosts **7**−**9**, possessing an unsymmetrically distorted cavity. The effects of altroside modification are clearly revealed by examining the

results obtained with native γ-CD and unsubstituted mono-*altro*-γ-CD **9**. Thus, *altro*-γ-CD **9** as a chiral host affords **2** in 26% ee and **3** in −16% ee, both of which are significantly deviated from the original ee's of 39 and −1.4% obtained with native γ-CD. It is of particular interest that the ee of the *anti*-HH cyclodimer **3**, which is consistently low (1−2% ee) upon photochirogenesis with native and substituted γ-CDs **6**, **7**, and **10**, is significantly improved, up to 16%, by using the skeleton-modified, but unsubstituted, *altro*-γ-CD **9**. This shows strong evidence for the important contribution that the unsymmetrically distorted cavity plays in enhancing the product's ee. However, the unsymmetrical skeleton and van der Waals interactions with the *altro*-CD walls are not sufficient to effectively differentiate the diastereomeric ternary complex precursor to **2**, and the introduction of an amino group at the 3-position of *altro*-CD dramatically enhances, up to 53%, the ee of *syn*-HT cyclodimer **2**. The amino group, attached to the altroside residue in **8**, controls electrostatically the orientation and particularly the stacking of included AC molecules in collaboration with the deformed *altro*-CD cavity, exhibiting distinctive differentiation behavior.

It is concluded that the deformed chiral CD cavity and the electrostatic interactions with included guests can be jointly used as versatile tools for enhancing the enantioselectivity of the initial molecular recognition upon inclusion and the subsequent photoreaction upon irradiation. Both of these factors contribute to developing a desirable low-entropy environment designed for specific chiral recognition and photoreactions by shaping the chiral cavity and restricting the stacking orientation suitable for a particular guest inclusion and photoreaction.

Pressure Effects on Photocyclodimerization. The effects of high pressure on photophysical and photochemical processes have been studied in considerable detail.[62−67] Recently, we demonstrated the critical role of pressure in enantiodifferentiating and diastereodifferentiating photoreactions. Thus, the product chirality of the asymmetric photosensitizations can be manipulated simply by changing the applied pressure, unless the differential activation volume ($\Delta\Delta V^{\ddagger}$) is equal to zero for the formation of the enantiomeric or diastereomeric pair.[6,68−70] As far as CDs are concerned, the pressure effects have been investigated on the excimer formation in CD−bichromophoric systems,[71] the regulation of the association equilibrium of CD inclusion complex,[72] and in the improvement of binding kinetics.[73] For an asymmetric reaction mediated by CD, a pronounced pressure effect on the stereoselectivity is expected, because a more compact complex and, hence, deeper/tighter inclusion is favored under high pressure, which certainly causes more intimate host−guest interactions, thereby enhancing the chiral recognition ability of a given CD cavity. To the best of our knowledge, however, there have been no reports on the study of the pressure effect on CD-mediated chiral photoreactions.

We investigated the photocyclodimerization of AC in the presence of various CD hosts at 0.1 MPa (atmospheric pressure) and at 210 MPa to elucidate the role of pressure in this supramolecular photochirogenesis. The results, summarized in Table 4, clearly demonstrate that the use of high pressure is a powerful tool for manipulating the product distribution and chirality. In all cases examined, the yield of cyclodimer **2** is significantly enhanced, becoming the dominant product (>50% relative yield) at 210 MPa at the expense of cyclodimers **1** and **3**, while the yield of **4** is less affected. The anti/syn ratios of both HH and HT cyclodimers obtained at 210 MPa are consistently lower than those obtained at atmospheric pressure, being independent of the hosts employed. This indicates that the differential reaction volumes ($\Delta\Delta V°$) for the diastereomeric complex precursor pairs to the syn isomers **2** and **4** are smaller than those for anti **1** and **3**.

Fortunately, by applying a pressure of 210 MPa, both of the chemical and optical yields of cyclodimer **2** are substantially increased in all examined cases including native γ-CD. For example, the ee of **2** obtained at 0 °C in the photocyclodimerization mediated by *altro*-γ-CD **9** is dramatically enhanced from 25.6% at 0.1 MPa to 33.9% at 210 MPa. The degree of pressure enhancement at 0 °C is appreciably higher for altroside-bearing γ-CDs **7**−**9** (showing a 6−8% increase) than for native and substituted γ-CDs **5**, **6**, and **10** (3−5% increase). The same is true for the ee of minor product **3**, that is, a 1−2% increase for native γ-CD, **5**, and **6** versus a 4−10% increase for **7**−**9**. These results indicate that the altroside-bearing γ-CDs provide diastereomeric precursor complex pairs to **2** and **3**, which differ in volume and are, thus, highly sensitive to pressure. This seems reasonable, because the introduction of irregular altroside into the glucoside sequence of CD disturbs the hydrogen-bond network on the secondary rim and makes the CD skeleton flexible. This apparently small change not only facilitates a closer induced-fit to the preferred guest (and a poorer fit for the unfavorable), amplifying the guest discrimination, but also enables us to dynamically control the complexation and subsequent photochemical behavior by entropy-related factors such as temperature, pressure, and solvation. The pressure dependence of the ee can be interpreted in terms of the nonzero differential reaction volume ($\Delta\Delta V°$) between the diastereomeric complex pair. Although it is difficult to seriously discuss the $\Delta\Delta V°$ value from the ee data at only two pressures, the reaction volume ($\Delta V°$) is thought to be smaller for the formation of the first-eluted enantiomer of **2** (to which a positive ee sign is tentatively assigned) than the second-eluted one, because the ee is enhanced by applying pressure. A good ee of 59.2% was achieved by carrying out the photoreaction in the presence of **8** at 210 MPa and 0 °C. Although usually not emphasized, or even recognized, the use of high pressure is particularly interesting and advantageous in the photochirogenesis performed in aqueous solutions because the freezing point of water goes down to −22 °C at 210 MPa. This allows us to examine the temperature effect on the photoreaction far beyond the normal freezing point of water (0 °C). Eventually, photoirradiation of AC with 3-amino-*altro*-γ-CD **8** in water under an ultimate

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condition of −21.5 °C and 210 MPa gave cyclodimer **2** as the major product (53% yield) in an ee as high as 71%, which is the best ee value ever reported for a bimolecular photochirogenic reaction in the solution phase.

The pressure-dependence behavior of the ee of **3** is somewhat different. Thus, the second-eluted enantiomer (assigned with negative ee) is preferred at high pressures, irrespective of the host employed, although the *altro*-CDs show much better performance. In an extreme case, the ee of **3** obtained with host **9** at 0 °C is significantly increased from 16% at 0.1 MPa to 26% at 210 MPa. On the other hand, the positive ee values of 1.5 and 6.6% obtained with **6** and **7** at 0 °C are inverted to a negative ee of −3.1% or reduced to 1.2% ee at 210 MPa. It is concluded, therefore, that the diastereomeric complex precursor to the second-eluted enantiomer of **3** has a smaller volume than the antipodal precursor complex and is thus favored at higher pressures.

Temperature Effects: Entropy-Controlled Enantiodifferentiation. The photocyclodimerizations catalyzed by γ-CD derivatives were performed over a temperature range of +55 to −21.5 °C and at pressures of 0.1 and 210 MPa to give the results shown in Table 4. Although the yield of cyclodimer **1** was insensitive to the temperature change for all hosts examined, the yield of cyclodimer **2** increased at the expense of **3** and **4** on lowering the reaction temperature. As a result, the HT/HH ratio was greatly enhanced from a moderate 4−6 at 40−50 °C to a highly selective 7−13 at 0 to −22 °C, irrespective of the host employed. Thus, the HT complex precursors to **1** and **2** are enthalpically stabilized at low temperatures.

In most cases the ee's of both **2** and **3** display highly temperature-dependent behaviors. Lowering the temperature leads to a continuous increase of the ee of **2** over the temperature range examined, regardless of the hosts and pressures applied. To more quantitatively evaluate the temperature-dependent behavior of product chirality, the natural logarithm of the relative enantiomer ratio of **2** is plotted against the reciprocal temperature.[11,29,74,75] Figure 2 illustrates some such plots for the formation of **2** mediated by γ-CD and **5**−**9** at 0.1 MPa and by **8** at 210 MPa, all of which afford excellent straight lines over the temperature range examined. Because the stereochemical outcome of the photoreaction is determined almost exclusively by the relative stability of the ground-state complexes (with an assumption that the photocyclodimerization efficiencies are comparable among the complexes), these plots are considered to be the differential van't Hoff plots, representing the difference in stability of a diastereomeric ternary complex pair of AC with γ-CD. From the intercept and slope of the plot, the differential activation enthalpy ($\Delta\Delta H^{\ddagger}$) and entropy changes ($\Delta\Delta S^{\ddagger}$) were calculated as summarized in Table 5.

The differential activation parameters shown in Table 2 reveal that the enantioselectivity of **2** rests on a critical counterbalance of the gain in differential enthalpy ($\Delta\Delta H^{\ddagger}<0$; in favor of the first-eluted enantiomer of **2**) and a loss in the differential entropy ($\Delta\Delta S^{\ddagger}<0$; favoring the antipode) upon formation of the relevant precursor complex. The total balance, that is, the free energy change ($\Delta\Delta G^{\ddagger} = \Delta\Delta H^{\ddagger} - T\Delta\Delta S^{\ddagger}$) is, however, for the first-eluted enantiomer of **2** in the examined temperature range of −21.5 °C to +50 °C (and even to +100 °C). This means that the precursor complex of the first-eluted enantiomer is more tightly packed in the cavity and, hence, enthalpically stabilized through stronger van der Waals interactions with the CD walls, while the overall difference in entropic loss arising from the termolecular association itself and the reduced freedom derived therefrom does not greatly differ between the diastereomeric precursor complex pair.

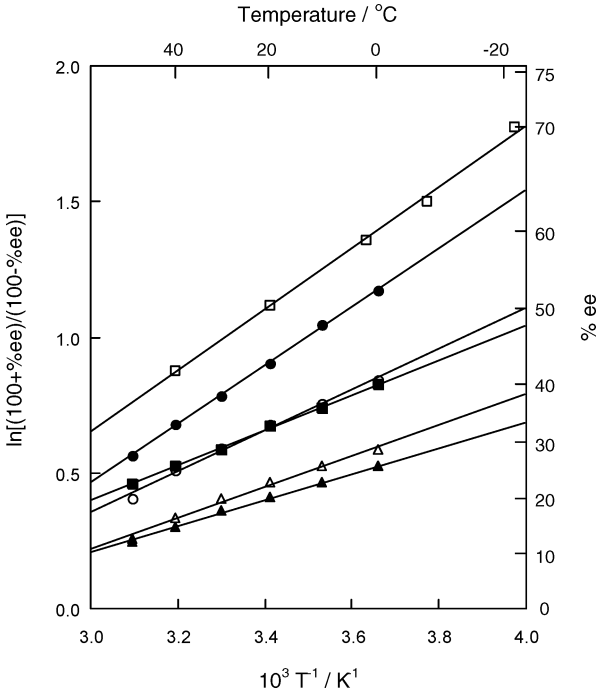

FIGURE 2. Plots of the natural logarithm of the relative yield of first- and second-eluted enantiomers of **2** against the reciprocal temperature upon photocyclodimerization of AC catalyzed by **5** (■), **6** (○), **7** (△), **8** (●), and **9** (▲) at 0.1 MPa and **8** (□) at 210 MPa.

TABLE 5. Differential Activation Parameters Determined from the Temperature Dependence of the ee of Cyclodimer 2 in the Photocyclodimerization of AC Catalyzed by Native and Modified γ-CDs

host	pressure (MPa)	$\Delta\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta\Delta S^{\ddagger}$ (J mol^{-1} K^{-1})
γ-CD[a]	0.1	−5.80	−14.1
	210	−4.55	−9.2
5	0.1	−5.36	−12.8
	210	−4.21	−8.3
6	0.1	−6.29	−15.1
	210	−5.21	−11.1
7	0.1	−4.78	−12.5
	210	−3.88	−8.2
8	0.1	−9.39	−22.7
	210	−8.97	−23.0
9	0.1	−4.00	−10.3
	210	−4.23	−9.6

[a] Reference 29.

The ee of cyclodimer **3** also varies appreciably with the reaction temperature, but the temperature-dependence profile is highly dependent on the host's structure, which is in sharp contrast to the steady enhancement of ee observed for cyclodimer **2**. Thus, by lowering the temperature, the ee of **3** shows only a slight increase for native γ-CD, a slow decrease followed by a sign-inversion for **5** and **6**, and a moderate increase for *altro*-CDs **7**−**10**. It is emphasized that, as was the case with cyclodimer **2**, the highest ee of −27% was achieved for **3**

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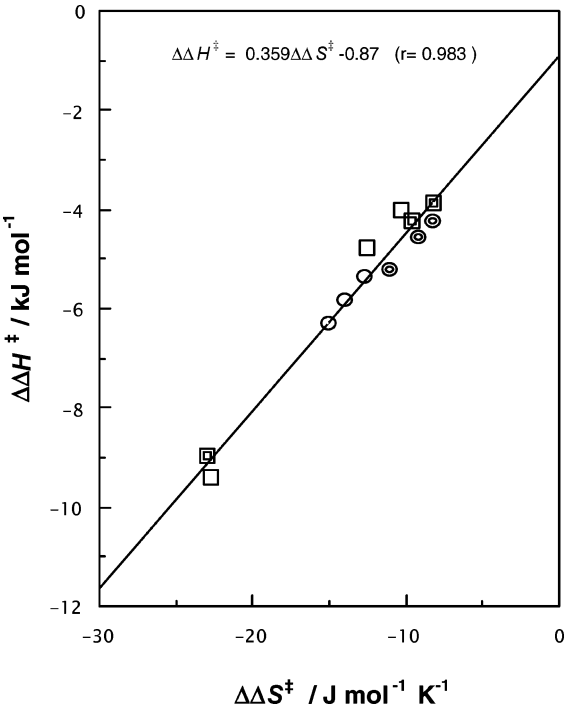

FIGURE 3. Enthalpy−entropy compensation plot for the differential activation parameters obtained in the enantiodifferentiating photocyclodimerization of AC mediated by native and substituted γ-CDs **5** and **6** (circle) and *altro*-γ-CDs **7**−**9** (square) at 0.1 MPa (open symbols) and at 210 MPa (double-lined symbols).

through the joint use of the entropy-related factors, that is, temperature and pressure.

Enthalpy−Entropy Compensation. The global examinations and rationalization of the entropy−enthalpy compensation phenomena, which are found for a wide variety of host−guest complexation systems have been well-documented.[76−79] All of these examinations have been done using the activation parameters obtained at atmospheric pressure, with the effect of pressure on the compensation effect remaining unanswered. In this context, it is of great interest to test the general validity of the enthalpy−entropy compensation effect for host−guest complexations under high pressure. All of the $\Delta\Delta H^{\ddagger}$ values obtained for **2** in this and previous[29] studies are plotted against the relevant $\Delta\Delta S^{\ddagger}$ values to give the enthalpy−entropy compensation plot illustrated in Figure 3. It is noted that the differential activation parameters obtained at 0.1 and 210 MPa fall on a single straight line, affording the following compensatory relationship: $\Delta\Delta H^{\ddagger} = 0.359\Delta\Delta S^{\ddagger} - 0.87$ (correlation coefficient 0.983). From the slope of the line, the equipodal temperature is determined to be 359 K (86 °C), at which the diastereomeric complex pair for the formation of enantiomeric **2** should be of identical stability and, thus, give racemic **2**. The excellent compensatory relationship reveals for the first time that changing either the host skeleton or the pressure does not alter the enantiodifferentiating mechanism in the supramolecular photochirogenesis.

Conclusions

In this study, we have gained new insights into the ternary complex formation and expanded the scope of supramolecular photochirogenesis by using a series of secondary-face- and skeleton-modified γ-CD derivatives **5**−**9** as chiral hosts for the enantiodifferentiating [4+4] photocyclodimerization of AC, as well as probing its limitations. Crucially, we have learned about the critical factors and mechanisms that govern the supramolecular and photochirogenic interactions in the ground and excited states and obtained some useful, generally applicable guidelines for controlling and enhancing the stereochemical outcomes of supramolecular photochirogenesis.

In the present supramolecular photochirogenic reaction of AC in the presence of modified γ-CDs, it was revealed that both the secondary-face substitution and the glucoside-to-altroside mutation of native γ-CD greatly affect the complexation and photochirogenic behavior. *Altro*-γ-CDs, possessing a more flexible skeleton as a result of the reduced hydrogen-bonding network around the secondary rim, suffer considerable skeletal conformational changes upon the inclusion of two AC molecules in the cavity. This, however, enables us to more dynamically and effectively control the initial enantioface-selective stacking of the two ACs in the cavity and, thus, the subsequent enantiodifferentiating photocyclodimerization by utilizing several entropy-related factors.

As expected, all modified γ-CDs form stable 1:2 host−guest complexes with AC and greatly accelerate the photocyclodimerization reaction, compared to that in bulk solution. The chemo- and enantioselectivity of the photoreaction are also significantly influenced by host modification. The skeleton-modified *altro*-γ-CDs, in particular unsubstituted **9** and 3-amino derivative **8**, are more susceptible to environmental variants, affording the highest HT/HH ratios and best ee's under the optimized conditions.

The use of high pressure in the CD-mediated photochirogenesis in water is particularly interesting and potentially advantageous in two respects: (1) the inherently large volume change anticipated for the supramolecular complexation and (2) the expanded temperature range (down to −22 °C) applicable to aqueous systems. Both may drive the supramolecular photochirogenesis to higher enantiodifferentiation. By applying pressure, the yield of cyclodimer **2** is consistently increased at the expense of cyclodimer **1** and **3** in all cases examined. More importantly, the ee's of **2** and **3** are also enhanced greatly at high pressure without exception.

Temperature also functions as a vital factor for further improving the chemical and optical yields of the photochirogenesis, particularly with the flexible *altro*-CDs. Thus, at 210 MPa, the ee's of **2** and **3** obtained for the photocyclodimerization of AC mediated by **8** reach their best values of 71% at −21.5 °C and −27% at −8 °C, respectively. These are tremendous enhancements in ee from the corresponding values of 39 and −1.4% obtained with native γ-CD at 0 °C under atmospheric pressure.

Finally, we wish to emphasize that all of these impressive changes and enhancements of ee do not involve any mechanistic changes, as supported by the excellent enthalpy−entropy compensation, but are driven exclusively by entropy-related factors, such as the flexible *altro*-CD skeleton, pressure, and temperature. Exploiting the entropy-related factors for critically controlling the fate of the reaction rate or equilibrium has not been very popular until recently,[5,6] but our methodology or the

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joint use of multiple entropy-related factors should not be restricted to this particular supramolecular photochirogenic reaction. Indeed, its principals should be widely applicable to a variety of other systems where the weak interactions dominate the reaction kinetics and thermodynamics. The present findings certainly help us to more comprehensively understand the mechanistic details of supramolecular photochirogenesis and are also very encouraging in the pursuit of more sophisticated stereochemical control by applying this versatile and powerful strategy.

Experimental Section

Photolyses. Photoirradiations under atmospheric pressure were carried out in a temperature-controlled water/ethylene glycol bath. Sample solutions, sealed under an argon atmosphere in Pyrex tubes, were placed near the lamp surface or in a merry-go-round apparatus and irradiated at wavelengths longer than 320 nm, using a 300-W high-pressure mercury lamp fitted with a uranium glass filter. Irradiations under high pressure were conducted in a pressure vessel fitted with sapphire windows and connected to a pump. A 0.15-mL quartz cuvette (light path, 0.2 cm) filled with a sample solution was placed in the high-pressure vessel, which was thermostated by circulating a 1:1 mixture of water and ethylene glycol through the reactor body. The pressure was applied with a plunger pump, and its magnitude was measured by a pressure gauge. The sample solution was photoirradiated through the sapphire window at 366 nm using a high-pressure mercury lamp equipped with an optical glass filter (Toshiba UV-35).

Syntheses of γ-CD Derivatives. One of the 2-hydroxyl groups of γ-CD was selectively tosylated to give 2^A-tosyl-γ-CD **5** by using NaH as a base and anhydrous DMF as a solvent.[80,81] The treatment of **5** with $Ba(OH)_2$ in aqueous solution at 4 °C afforded $2^A,3^A$-epoxy-*manno*-γ-CD **6** in good yield.[82,83] 3^A-Azido-3^A-deoxy-*altro*-γ-CD **7** was prepared by reacting **6** with NaN_3, which was then transformed to 3^A-amino-3^A-deoxy-*altro*-γ-CD **8** by a reduction with triphenylphosphine.[58] Mono-*altro*-γ-CD **9** was prepared in 64% yield by refluxing the aqueous solution of **6** for 5 d.[84] For comparison purposes, 6^A-amino-6^A-deoxy-γ-CD **10** was synthesized by the reduction of 6^A-azido-6^A-deoxy-γ-CD with triphenylphosphine.[85]

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Supporting Information Available: The UV−vis and CD spectral study for the complexation of AC and γ-CD derivatives and the synthesis and characterization of compounds **7**, **8**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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