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Dual Chiral, Dual Supramolecular Diastereodifferentiating Photocyclodimerization of 2-Anthracenecarboxylate Tethered to Amylose Scaffold

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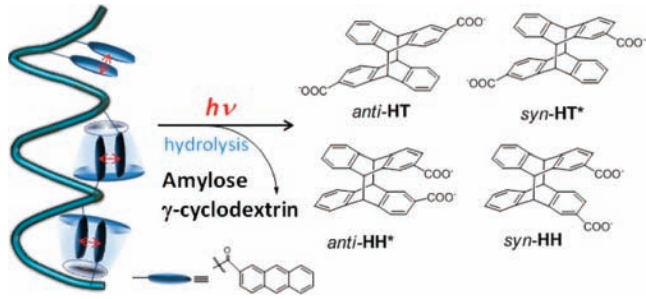
ABSTRACT



Newly synthesized 6-*O*-(2-anthroyl)amylose (AC-Am; 51% substitution) was photolyzed in (aqueous) DMSO solutions to give HH dimers as major products (after saponification), with modest enantiomeric excesses (ee) of 12−15% and 1−2% for *syn*-HT and *anti*-HH dimers, respectively. Addition of γ-cyclodextrin switched the product selectivity to HT and enhanced the ee of *syn*-HT up to 37%, while the chiral sense of *anti*-HH was inverted by changing the irradiation temperature, demonstrating usefulness of the dual-supramolecular approach to photochirogenesis.

Photochirogenesis,[1] providing unique, versatile routes to optically active compounds, is one of the most attractive and challenging topics in current photochemistry as an alternative to conventional catalytic and enzymatic asymmetric syntheses.[2] Supramolecular approach to photochirogenesis is of particular interest from the entropic point of view, as the stereodifferentiation in the excited state occurs in inherently low-entropic (well-organized) environment.[1b,c,3] In their pioneering work, Tamaki et al. reported the significant acceleration of photocyclodimerization of anthracenecarboxylates and -sulfonates as well as the formation of optically active cyclodimers in the presence of cyclodextrin (CDx), although their enantiomeric excesses (ee) were not determined.[4]

We examined the enantiodifferentiating photocyclodimerization of 2-anthracenecarboxylate (AC) mediated by chiral

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(3) For representative papers, see: (a) Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982. (b) Albrecht, D.; Vogt, F.; Bach, T. *Chem.—Eur. J.* **2010**, *16*, 4284.

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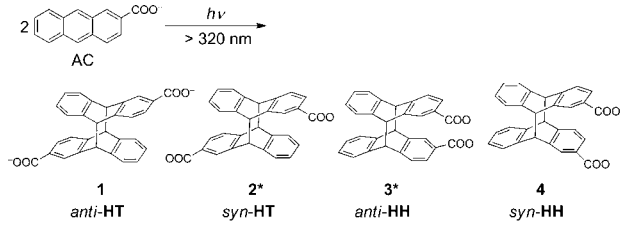
Scheme 1. Photocyclodimerization of 2-Anthracenecarboxylate

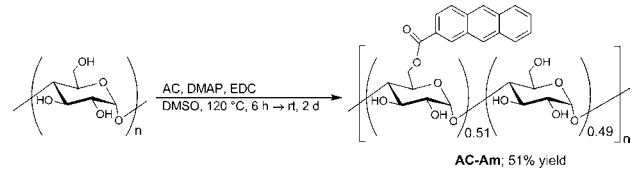


(The absolute configurations of **2*** and **3*** are arbitrary)

supramolecular hosts, such as CDxs[5] and biomolecules,[6] to obtain chiral *syn-head-to-tail* (*syn*-HT) and *anti-head-to-head* (*anti*-HH) cyclodimers **2*** and **3*** in good ee's (Scheme 1). Recently, we have demonstrated that the diastereodifferentiating photocyclodimerization of AC tethered to a cellulose scaffold, followed by saponification of the photolyzate, affords cyclodimers **1**−**4** in HH:HT ratios of up to 9:1 and **2*** and **3*** in up to 20−22% ee. The HH/HT ratio and ee were critical functions of the degree of substitution (DS) and the conversion, for which the conformational changes of flexible 2,3-di-*O*-methylcellulose backbone upon cross-linking photocyclodimerization are likely to be responsible.[7]

In this study, we propose a novel "dual-supramolecular" approach to photochirogenesis, where inherently helical amylose was used as chiral scaffold and γ-CDx as chiral host. Amylose is essentially a linear polysaccharide composed of α-1,4-glucose units, that is, unbranched portion of starch, which is known to form left-handed single helices in DMSO.[8] AC moieties to function as chromophore/guest/substrate were introduced to the 6-position of amylose through an ester linkage for easier retrieval of the photocyclodimers from the scaffold by saponification. The esterification of amylose was carried out under the condition similar to that employed for modifying celluloses.[8i] Thus, amylose was first swollen in DMSO at 120 °C for 6 h to give a homogeneous solution, and then reacted to AC with DMAP and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMSO at room temperature to afford 6-*O*-(2-anthroyl)amylose (**AC-Am**) in 51% yield (Scheme 2). The

Scheme 2. Synthesis of 6-*O*-(2-Anthroyl)amylose **AC-Am**



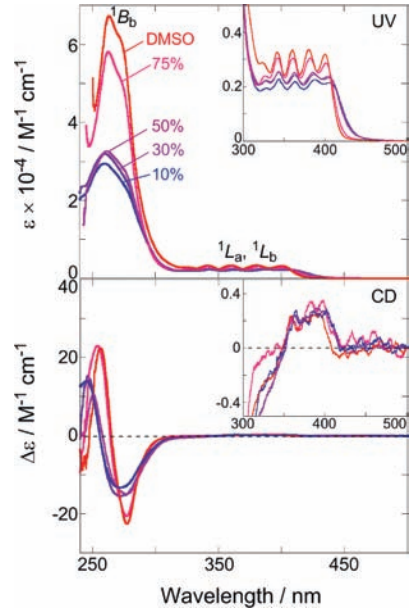


Figure 1. UV/vis (top) and CD (bottom) spectra of a 150 μM (in chromophore unit) solution of **AC-Am** in DMSO, a 110 μM solution in 3:1 (v/v) DMSO-H_2O, both measured in a 2-mm cell, a 75 μM solution in 1:1 DMSO-H_2O, a 45 μM solution in 3:7 DMSO-H_2O, and 23 μM solution in 1:9 DMSO-H_2O, measured in a 1-cm cell at room temperature; insets: magnification of the *L* band region (300−500 nm).

DS of **AC-Am** obtained was determined as 0.51 by UV/vis spectroscopy; see the Supporting Information (SI).

The chiroptical properties of **AC-Am** were examined in DMSO-H_2O by using UV/vis and circular dichroism (CD) spectroscopies. As shown in Figure 1, a pronounced hypochromic effect[9] with appreciable band-broadening and a hypsochromic shift was observed for the ^1B_b band but a hypochromic effect with a bathochromic shift for the ^1L_b band particularly in aqueous solutions of low DMSO contents (≤50%). Since methyl 2-anthracenecarboxylate (**5**), a reference compound, showed much smaller hypochromic effect in water-rich solvent (Figure S4 in SI), **AC-Am** is likely to aggregate and include AC pendants in the hydrophobic amylose cavity in water-rich solvents, due to the hydrophobic nature of AC and the more flexible amylose backbone in water than in DMSO.[8a]

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(8) For examples, see:(a) Fujii, M.; Honda, K.; Fujita, H. *Biopolymers* **1973**, *12*, 1177. (b) Kadokawa, J.; Kaneko, Y.; Nagase, S.; Takahashi, T.; Tagaya, H. *Chem.—Eur. J.* **2002**, *8*, 3321. (c) Star, A.; Steuerman, D. W.; Heath, J. R.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2002**, *41*, 2508. (d) Sanji, T.; Kato, N.; Tanaka, M. *Org. Lett.* **2006**, *8*, 235. (e) Ikeda, M.; Frusho, Y.; Okoshi, K.; Tanahara, S.; Maeda, K.; Nishino, S.; Mori, T.; Yashima, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 6491. (f) Kim, O.-K.; Melinger, J.; Chung, S.-J.; Pepitone, M. *Org. Lett.* **2008**, *10*, 1625. (g) Frampton, M. J.; Claridge, T. D. W.; Latini, G.; Brovelli, S.; Cacialli, F.; Anderson, H. L. *Chem. Commun.* **2008**, 2797. (h) Numata, M.; Shinkai, S. *Adv. Polym. Sci.* **2008**, *220*, 65. (i) Ikai, T.; Okamoto, Y. *Chem. Rev.* **2009**, *109*, 6077.

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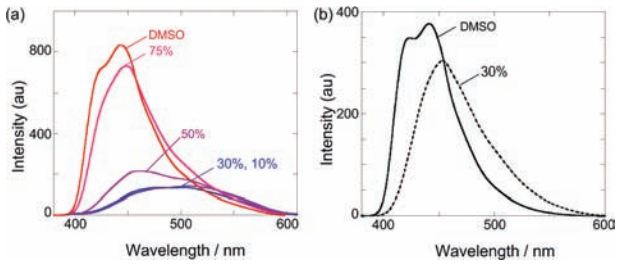

Figure 2. Fluorescence spectra at room temperature of (a) **AC-Am** (15 μM in chromophore unit) in 100%−10% DMSO solution excited at 315 nm and (b) **5** (7.4 μM) in 100% (solid line) and 30% DMSO solution (dashed line) excited at 338 nm; for all examined solutions, comparable absorbances were attained at each excitation wavelength.

Table 1. Fluorescence Lifetimes of 6-*O*-(2-Anthroyl)amylose (**AC-Am**) and Methyl 2-Anthracenecarboxylate (**5**)[a]

compd	λ_{em}/nm	n[b]	τ_1	A_1	τ_2	A_2	τ_3	A_3	χ^2
AC-Am	443[c]	2	2.7	0.72	9.7	0.28			1.2
	476	3	0.9	0.74	4.6	0.19	18.3	0.07	0.9
	560	3	0.9[d]	0.77	4.6[d]	0.11	21.4	0.12	1.4
5	453	1	22.9						1.1
	520	1	23.0						1.0

[a] Fluorescence lifetime (τ_i) and relative abundance (A_i) of each component determined by single photon counting method in aqueous solution containing 30% DMSO at room temperature, unless stated otherwise. [b] Number of components. [c] In 100% DMSO. [d] Fixed to the values determined at 476 nm.

The CD spectra of **AC-Am** also behaved differently in DMSO-rich versus water-rich solvents (Figure 1, bottom), exhibiting a sharp negative couplet at the major ^1B_b band in 100 and 75% DMSO solutions, but a broader, blue-shifted negative couplet for the major band but an appreciable red shift in the ^1L_b band in 50−10% DMSO solutions. According to the exciton chirality theory,[10] these results indicate that the AC chromophores in **AC-Am** align homogeneously along the left-handed helical amylose backbone in DMSO-rich solutions but become less regularly in water-rich solvents, where ACs are included in the amylose cavity and difficult to be homogeneously aligned, yet keeping the left-handed helical arrangement on the average.

Fluorescence spectral studies supported the above view and revealed interesting behavior of AC in the excited state. As was the case with the UV/vis and CD spectra, the fluorescence intensity of **AC-Am** abruptly dropped when the DMSO content was decreased from 75 to 50%, whereas that of reference compound **5** showed only a small decrease even in 30% DMSO solution (Figure 2). Although both compounds showed moderate red shifts and band-broadening in water-rich solvents, the fluorescence spectrum of **AC-Am** was very different in shape from that of **5** accompanying a new band at 500−600 nm (Figure 2), which may be assigned to excimer emission.

The fluorescence decay profile measured at 476 nm in aqueous solution containing 30% DMSO was obviously of multiple components and reasonably fitted to a sum of three exponential functions to give the lifetimes of 0.9, 4.6, and 18.3 ns (Table 1). These values are significantly shorter than that for reference compound **5** (22.9 ns) determined under comparable conditions and appreciably shorter than those (2.7 and 9.7 ns) for **AC-Am** in DMSO. The observation of multiple lifetimes indicates that the environment around the AC moieties in **AC-Am** is not uniform, while the shorter lifetimes are attributable to the accelerated photocyclodimerization as a consequence of the high local AC concentration particularly in the hydrophobic amylose cavity of **AC-Am** in water-rich solvent. The long-lived species would be assigned to an excimer, as the lifetime measurement at 560 nm, with fixed τ_1 and τ_2, led to an appreciably larger abundance of the third component at the expense of the second one.

Photoirradiation of **AC-Am** was performed at 360 nm in DMSO and in 1:9 DMSO-H_2O at 25 to −15 °C. The photolyzed **AC-Am** was saponificated to retrieve AC dimers **1**−**4**, which were subjected to chiral HPLC analysis to give the results shown Table 2. In DMSO, where the amylose backbone forms left-handed helix, the sterically more hindered HH dimers were consistently favored (71−64%) at 15 and 81% conversions, indicating that neighboring AC pendants were preferentially photocyclodimerized in HH fashion, similar to the photobehavior of AC-cellulose.[7] The somewhat lower HH selectivity at 81% conversion may be attributed to the cross-linking HT photocyclodimerization of ACs located at more distant positions in later stages after the consumption of neighboring ACs. In contrast, the use of aqueous DMSO solution lowered the HH selectivity to 65% even at 14% conversion and further to 50% at 48% conversion, indicating increased contribution of the remote photocyclodimerization due to the more flexible amylose backbone in aqueous solution.

The enantioselectivity obtained (Table 2) distinctly differed for **2*** (12−15% ee) and **3*** (≤2% ee), supporting the discrete mechanistic origins of these two chiral cyclodimers. The consistently higher ee's for **2*** than for **3*** indicate that the enantioface of AC pendant located at a distant position is better recognized upon photocyclodimerization, while that of neighboring AC is poorly differentiated, possibly due to the originally random orientation and/or the very fast, and hence less discriminating, photocyclodimerization.

The dual-supramolecular approach was applied to this scaffold-based photochirogenic system by using γ-CDx as a chiral host for better manipulation of the original orientation of AC pendants in **AC-Am**. The complexation behavior of AC pendants with γ-CDx was examined in aqueous (10% DMSO) solution by CD spectroscopy to give the results shown in Figure 3.

As shown in Figure 3a, the couplet amplitude was reduced upon addition of γ-CDx to reach a plateau at the highest

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Table 2. Dual-Supramolecular Photocyclodimerization of 6-*O*-(2-Anthroyl)amylose (**AC-Am**) in DMSO and 1:9 DMSO-H_2O in the Presence and Absence of γ-Cyclodextrin (γ-CDx)[a]

solvent (DMSO content)	**AC-Am**/μM[b]	γ-CDx/mM	temp/°C	irrad time/min	convn/%	relative yield (ee)[c]/% **1**	**2***	**3***	**4**	HT:HH[d]
100%	120	0	25	0.5	15	18	11 (*12*)	37 (*1*)	34	29:71
				60	81	23	13 (*13*)	32 (*−2*)	32	36:64
10%	23	0	25	3	14	21	14 (*13*)	34 (*2*)	31	35:65
				60	48	33	17 (*15*)	35 (*1*)	15	50:50
	31	9.2	25	3	25	39	17 (*21*)	32 (*−6*)	12	56:44
		37	25	3	26	43	17 (*24*)	28 (*−10*)	12	60:40
			−5	3	13	33	15 (*32*)	37 (*1*)	15	48:52
			−15[e]	3	13	54	22 (*37*)	15 (*10*)	9	76:24

[a] Irradiated at 360 ± 10 nm under N_2 with a 300-w Xe lamp through a band-pass filter. [b] Concentration of appended AC unit. [c] Enantiomeric excess; the first-eluted enantiomer on an ODS + OJ-RH tandem column was given a positive sign; error in ee ≤2%. [d] Product ratio, (**1**+**2**):(**3**+**4**). [e] NaCl (17%) was added to the aqueous solution.

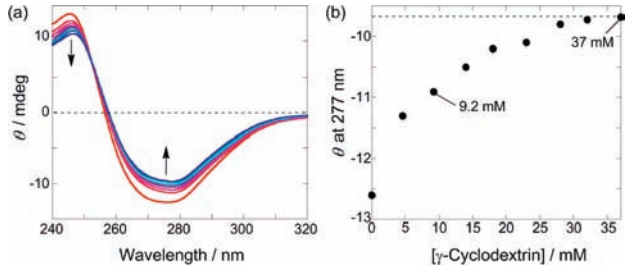

Figure 3. (a) CD spectral changes of an aqueous (10% DMSO) solution of **AC-Am** (31 μM in AC unit) upon gradual addition of γ-cyclodextrin (γ-CDx) of 0−37 mM (from red to blue) at room temperature, measured in a 1-cm cell. (b) Plot of θ at 277 nm as a function of the concentration of γ-CDx.

concentrations of up to 37 mM (1200-fold excess) (Figure 3b). Based on this result, we performed the dual-supramolecular photocyclodimerization of **AC-Am** at two γ-CDx concentrations of 9.2 and 37 mM, where the CD spectral change was half and fully saturated, respectively. As can be seen from Table 2, the addition of γ-CDx not only accelerates the photocyclodimerization but also affects the product distribution and ee. Thus, the conversion upon 3 min irradiation was almost doubled (from 14% to 25−26%), while the HT dimers was more favored (56−60% versus 35% obtained without γ-CDx) and the ee's of **2*** and **3*** were enhanced from 13−15 to 24% and from ≤2 to −10%, respectively. These results indicate that the HT complexation of two distant AC pendants and the subsequent photocyclodimerization are more accelerated than the HH complexation and photocyclodimerization of neighboring ACs, for which the steric hindrance upon HH complexation of neighboring ACs with γ-CDx would be responsible.

Significant temperature effects were observed on both product distribution and ee (Table 2). By lowering the irradiation temperature to −15 °C, the HT preference was further augmented to 76% and the enantioselectivity of **2*** reached the highest value of 37% ee, due to the increased energetic barrier for less favored complexation, while antipodal **3*** was given in 10% ee.

In conclusion, our dual-chiral, dual-supramolecular approach to photochirogenesis was successfully applied to the scaffold-based supramolecular photochirogenic system by using amylose as chiral scaffold and γ-CDx as chiral host in aqueous solution. Thus, the HT content was switched from 29% to 76% upon addition of γ-CDx. Furthermore, the added host not only accelerated the photocyclodimerization but also critically manipulated the ee and chiral sense of photoproducts to give the much enhanced ee's at low temperatures. Similar dual-supramolecular strategy should be effective in related photochirogenic systems based on poly- and oligosaccharides.

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Supporting Information Available: General experimental methods and the spectroscopic data for **AC-Am** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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