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Enhancement of Diastereoselectivity in Photodimerization of Alkyl 2-Naphthoates with Chiral Auxiliaries via Inclusion within γ-Cyclodextrin Cavities

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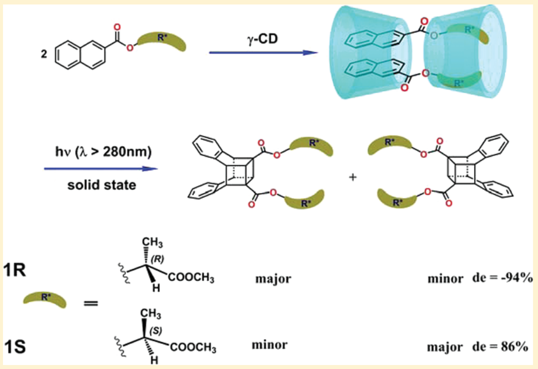
Ⓢ *Supporting Information*



ABSTRACT: Irradiations of alkyl 2-naphthoates are known to result in four isomeric "cubane-like" photodimers: *anti*^{HH}-**2**, *syn*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2** where the *anti*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2** consist of pairs of diastereomers. Here, chiral auxiliary and chiral microreactor strategies have been combined to achieve high diastereoselectivity in photodimerizations of an enantiomeric pair of 2-naphthoates with (*R*)- and (*S*)-1-methoxycarbonylethyl esters as chiral auxiliaries (**1R** and **1S**). Thus, irradiations of their γ-cyclodextrin (γ-CD) complexes have been conducted. Fluorescence, IR, and NMR spectra of both enantiomers of **1** demonstrate that their γ-CD complexes are mainly 2:2 with the molecules of **1** in head-to-head orientations. Irradiation of the complexes in the solid state mainly resulted in *anti*^{HH}-**2**. The absolute configuration of each diastereomer of *anti*^{HH}-**2** has been established for the first time here. The diastereomeric excesses (de's) of *anti*^{HH}-**2** from **1R** and **1S** were 94% and 86%, respectively. These de's are much higher than those found from irradiations in solution (55% for **1R** and **1S**), where the opposite diastereomeric form is in excess! Calculations of the energies of various conformations of the head-to-head 2:2 inclusion complexes were performed using the PM3 approach. The predicted major diastereomers based on the calculation are consistent with those found experimentally.

■ INTRODUCTION

Enantioselectivity in organic transformations continues to be a topic major interest in organic photochemistry.[1−4] Of the various approaches attempted to achieve high chiral inductions, those employing chiral auxiliaries[5−10] and chiral microreactors[11−15] have shown considerable promise. In the former, a removable auxiliary is connected to a prochiral substrate by a covalent or ionic (electrostatic)[10] bond. The chiral auxiliary can influence the manner in which the prochiral reactant is transformed to its diastereomeric photoproducts. The diastereomers can be separated usually, even when asymmetric induction is small. Then, removal of the auxiliary yields the enantiomerically pure products. Several very successful examples of this approach have been reported for reactions conducted in solution.[5−9] Furthermore, a large number of chiral auxiliaries that are inexpensive, readily added to a prochiral reactant, inert under the conditions of irradiation, and readily removed from the photoproducts, have been developed.[5] In the second strategy, inherently chiral hosts[15−29] or chirally modified confining media[12,13] are used as microreactors to provide chiral cavities and/or surfaces which bias the course of the photochemical reaction to proceed enantioselectively.

Among the chiral microreactors explored,[11−13] the most popular have been chirally modified zeolites[12,13] and cyclodextrins.[15−32] Both types are readily available, inexpensive, and capable of including a wide variety of organic molecules. Because γ-cyclodextrin (γ-CD), an octa-D-glucopyranose, can accommodate two aromatic molecules (with appropriate substituents) into its cavity, it can enhance photodimerization reactions, such as those involving cycloadditions, while promoting enantiodifferentiation. For example, Inoue et al.[18−28] have employed γ-CD to achieve enantioselectivity in the photodimerization of 2-anthracenecarboxylate. Venkatesan[29] and Hubig[30] and their coworkers obtained high stereoselectivity in photodimerization of coumarins and (*E*)-stilbenes, respectively, in solid γ-CD inclusion complexes. Recently, we achieved 48% enantiomeric excess (ee) during the photodimerization of methyl 3-methoxy-2-naphthoate in aqueous solutions of γ-CD[31,32] and irradiation of the solid

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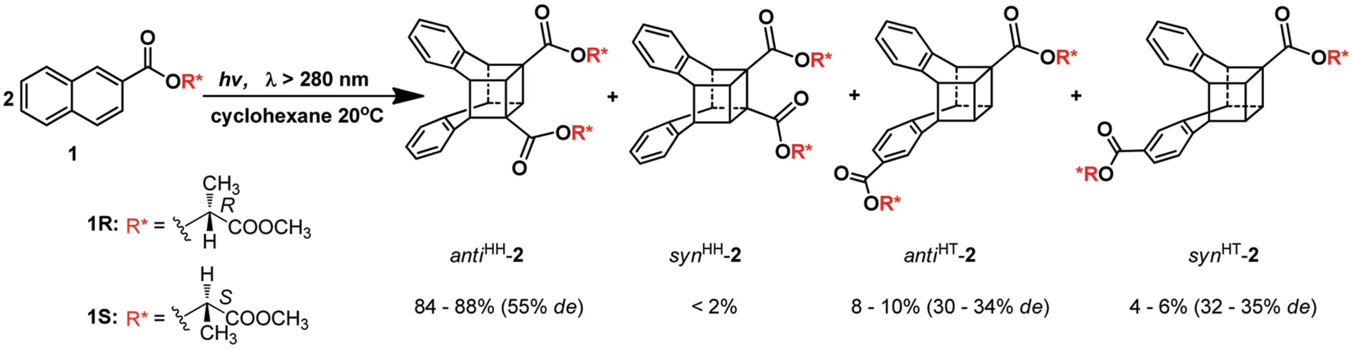
Scheme 1. Chiral Auxiliary Strategy for Diastereoselective Photodimerizations of Alkyl 2-Naphthoate Enantiomers



complex gave similar results: 23% and 34% ee at 25 and 0.5 °C, respectively.[33]

The combined use of the chiral auxiliary and chiral microreactor strategies in diastereoselective photochemical reactions has also been reported. For example, Ramamurthy and coworkers[13,34,35] have examined the unimolecular photocyclization of tropolone ethers with chiral auxiliaries in Y-type zeolites. The diastereomeric excess (de) of the photoproduct from irradiation of tropolone-2-methylbutyl ether increased from 53% in unmodified NaY to 90% in chirally modified Y-type zeolite.[34] However, the de's of several other tropolone derivatives, >80% in NaY, were not increased when irradiated within chirally modified Y zeolites.[13] Thus, the degree to which a chiral microreactor and chiral auxiliary will affect stereoselectivity is still somewhat unpredictable, and additional investigations are needed to discover the underlying factors that are necessary to design a successful stereoselective system based upon chiral auxiliaries or chiral microreactors.

In previous work,[36] we used a chiral auxiliary strategy to achieve asymmetric induction in the photodimerization of alkyl 2-naphthoates, **1R** and **1S** (Scheme 1). Irradiation of these substrates in organic solutions yielded four "cubane-like" photodimers: *syn* or *anti* and head-to-head (HH) or head-to-tail (HT) isomers: *anti*^{HH}-**2**, *syn*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2**. The major product, *anti*^{HH}-**2**, accounted for >84% of the total, while the yield of *syn*^{HH}-**2** was less than 2%. Photodimers *anti*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2** each consist of a pair of diastereomers; de's of 55% were achieved in the formation of *anit*^{HH}-**2**. The chiral auxiliaries in these photodimers are readily removed by hydrolysis so that the enantiomers of the photodimers can be obtained.[37]

Here, we report the photodimerizaions of **1R** and **1S** within the cavity of γ-CD in the solid state. By combined use of a chiral auxiliary and a chiral microreactor, de's as high as 94% in the *anti*^{HH}-**2** photodimer have been obtained. Furthermore, the major diastereomer of *anti*^{HH}-**2** is different from the one obtained from irradiations of **1R** and **1S** in cyclohexane solutions! This is the first example, to the best of our knowledge, in which the effect of diastereomeric interactions of a chiral auxiliary and a γ-CD host on the pathways for photodimerizations of the guest molecules have been investigated. The results indicate that the subtle differences in the environments experienced by the naphthyl groups in the **1R** and **1S** complexes with CD can cause very large changes in their photochemical courses.

RESULTS

Preparation of Samples for Irradiation. Samples were prepared by stirring an aqueous solution of γ-CD and a concentrated solution of **1R** or **1S** in dichloromethane overnight at ambient temperature. Details are provided in the Experimental Section. The isolated white solid complexes were characterized by X-ray powder diffraction, IR spectroscopy (Figures S1 and S2, Supporting Information), and fluorescence spectroscopy. The X-ray powder pattern of the complexes differed from the sum of that of pure γ-CD and the enantiomer of **1**, indicating that the samples were true complexes rather than mechanical mixtures. The IR absorption spectra of the complexes were also different from those of the sum of the components. The absorption corresponding to the carbonyl chromophore in the alkyl group of pure **1** was shifted from 1757 to 1747 cm^{-1} in the complex, again indicating inclusion within the cavity of γ-CD. The fluorescence spectra of the substrate and the complex, both in the solid state, are shown in Figure 1. The substrate alone exhibits the structured fluorescence characteristic of naphthoate monomer, with maxima at 370 and 386 nm and a shoulder at 405 nm; the complex shows a structureless excimer-like emission with a maximum at 407 nm. Because the guest/host ratios in the

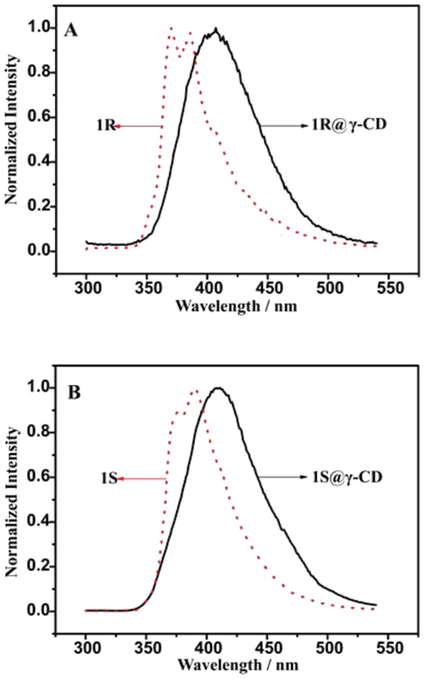


Figure 1. Fluorescence spectra of the enantiomers of solid **1** and their solid inclusion complexes with γ-CD: (A) **1R** and **1R**@γ-CD; (B) **1S** and **1S**@γ-CD.

Table 1. Photodimerizations of **1R** and **1S** in Cyclohexane Solutions and in the Complexes with γ-CD and Effect of Temperature on Product Distribution and Diastereoselectivity

			relative yield[a] (%)			de[a] (%)		
substrate	sample	temp (°C)	*anti*^{HH}-**2**	*anti*^{HT}-**2**	*syn*^{HT}-**2**	*anti*^{HH}-**2**	*anti*^{HT}-**2**	*syn*^{HT}-**2**
1R	cyclohexane	20	84	10	6	55	34	−35
1R	γ-CD complex	20	74	9	17	−84	54	−85
1R	γ-CD complex	0	71	12	17	−88	29	−81
1R	γ-CD complex	−20	80	6	14	−90	28	−85
1R	γ-CD complex	−35	75	3	22	−94	20	−88
1S	cyclohexane	20	88	8	4	−54	−30	32
1S	γ-CD complex	20	94	1	5	70	30	82
1S	γ-CD complex	0	98	0.5	1.5	72	32	87
1S	γ-CD complex	−20	97	0.5	2.5	83	47	91
1S	γ-CD complex	−35	98	0.5	1.5	86	46	92

[a] Relative yield and de were determined by HPLC using an ODS-3 column and a Daicel Chiral IA column, respectively; the error in relative yield and de < 2%; the first peak of each diastereomeric pair on the HPLC trace is termed **A**, and the second peak **B**; de (%) = (A − B)/(A + B).

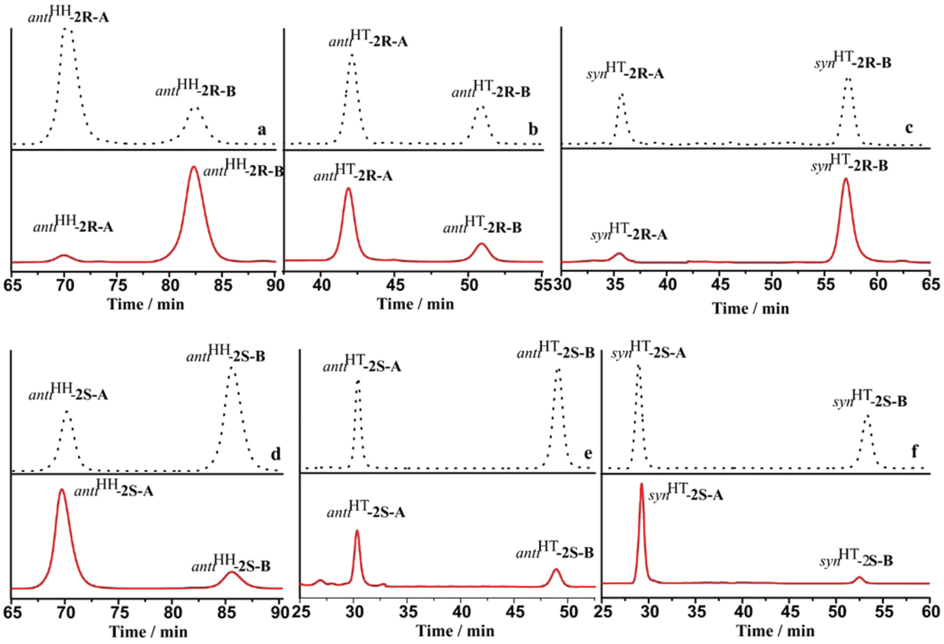


Figure 2. Typical HPLC chromatograms (Daicel chiral IA column) of the photodimers from irradiations at 20 °C of **1R** and **1S**: photodimerization in cyclohexane solutions (black dots) and in γ-CD complexes as powders (red lines): (a) *anti*^{HH}-**2R**; (b) *anti*^{HT}-**2R**; (c) *syn*^{HT}-**2R**; (d) *anti*^{HH}-**2S**; (e) *anti*^{HT}-**2S**; (f) *syn*^{HT}-**2S**. For each diastereomeric pair, the first eluting peak is termed **A** and the second **B**. The elution solvents are: (a) 95/5 hexane/isopropyl alcohol; (b) 8/2 hexane/ethanol; (c) 8/2 hexane/isopropyl alcohol; (d) 95/5 hexane/ethanol; (e) 6/4 hexane/ethanol; (f) 6/4 hexane/isopropyl alcohol.

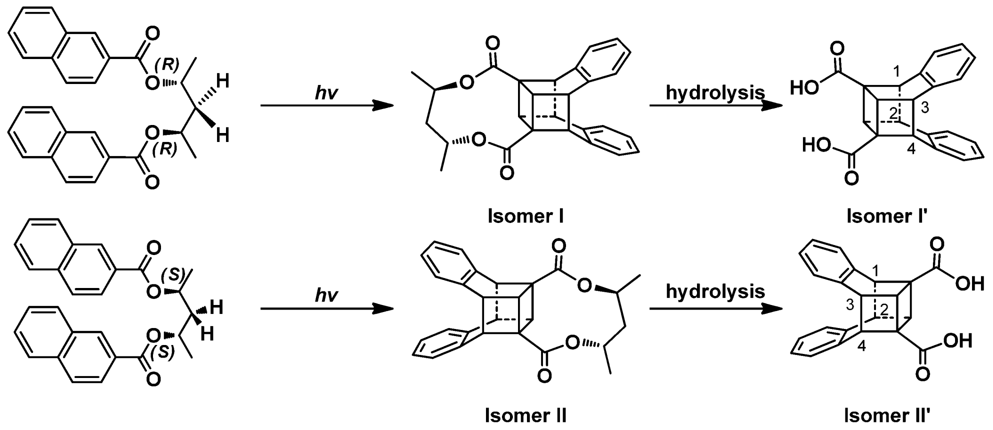
complexes were found to be 0.93/1.0 for **1R** and that of 0.95/1.0 for **1S** by integration of ^{1}H NMR spectra (Figure S3, Supporting Information; a technique for which the probable experimental error is at least ±5%), the excimeric emissions in the complexes are attributed to the coinclusion of two naphthoate moieties in two host cavities; the complexes are 2:2.

Photodimerization of the Complexes in their Solid State. The complexes were irradiated at >280 nm, and the photoproducts were isolated as described in the Experimental Section. Three photodimers, *anti*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2** (Scheme 1), were isolated from the irradiation of both **1R** and **1S**, and the material balances were greater than 95%. On this basis, other possible photodimer, *syn*^{HH}-**2** (observed from solution irradiations), could have been present in no more than trace amounts. Generally, 6 h of irradiation was required to reach ca. 10% conversion, and the yields increased only slightly upon additional irradiation.

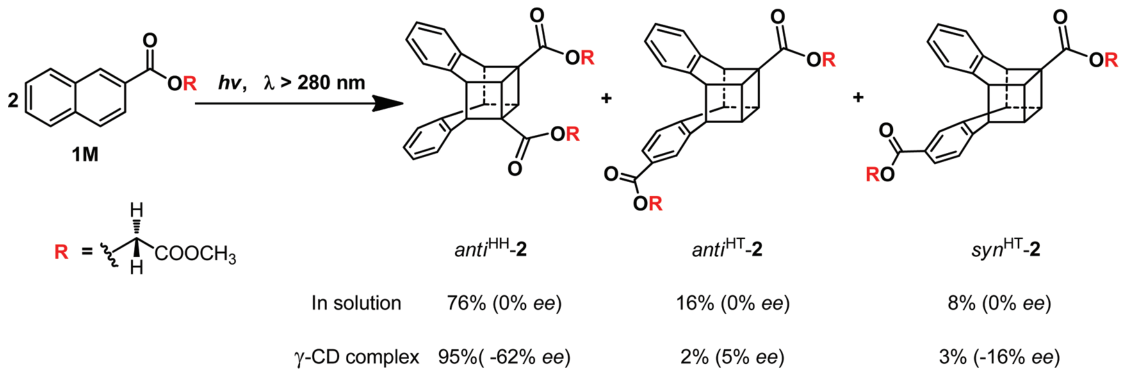
The product distributions from the solid-state irradiations of the complexes, as well as for irradiations of **1** in cyclohexane solutions, are collected in Table 1. At each temperature, the regioselectivity of the photocycloadditions, in terms of both the HH/HT and *anti*^{HT}/*syn*^{HT} ratios, is different for the complex and solution irradiations. For example, at 20 °C, the ratio of HH/HT photodimer from **1R**, 84/16 in solution, is decreased to 74/26 in the γ-CD complex. By contrast, the HH/HT ratio from **1S** increases from 88/12 in solution to 94/6 in its γ-CD complex. Also, although the yield of *syn*^{HT}-**2** is higher than that of *anti*^{HT}-**2** from complexes of both **1R** and **1S**, the yield of *anti*^{HT}-**2** is ca. twice of that of *syn*^{HT}-**2** in cyclohexane solutions.

The diastereomeric mixtures of the above three photodimers were separated by HPLC using either a chiral or an achiral column. Figure 2 shows a typical HPLC chromatogram of the photodimers of **1R** and **1S** using a chiral column, produced in the photodimerization both in organic solutions and in γ-CD

Scheme 2. Photodimerization of 2,4-Pentanediyl-*bis*-2-Naphthoate



Scheme 3. Photodimerization of Methoxycarbonylmethyl 2-Naphthotate in Cyclohexane Solution and γ-CD Complex as Powders



complexes at 20 °C. The diastereomers are designated in terms of their elution sequence: the first peak of each diastereomeric pair is **A** and the second is **B**. The ^{1}H NMR and circular dichroism spectra of each optically pure diastereomer have been reported previously.[36] The de's for all of the diastereomer pairs are listed in Table 1. The chiral induction for the photodimerization in the γ-CD cavities is enhanced significantly over what was found from irradiations in cyclohexane. Thus, the de's for solution and complex irradiations of **1R** at 20 °C are 55% and 84%, respectively, for *anti*$^{\mathrm{HH}}$-**2**, and 35% and 85%, respectively, for *syn*$^{\mathrm{HT}}$-**2**. Enhancement of the product chirality from **1S** is also significant: the *de* for *anti*$^{\mathrm{HH}}$-**2** increases from 54% in cyclohexane to 70% in the complex at 20 °C, and for *syn*$^{\mathrm{HT}}$-**2** from 32% to 82%. Also, by inclusion in the cavity of γ-CD, the major diastereomer of *anti*$^{\mathrm{HH}}$-**2** from **1R** and **1S** as well as *anti*$^{\mathrm{HT}}$-**2** from **1S**, is different from the one obtained from the solution phase irradiations. For example, although more of **A** of *anti*$^{\mathrm{HH}}$-**2** is isolated from irradiation of **1R** in solution, more **B** is obtained from irradiations of the solid complex.

The influence of temperature on the regio- and diastereoselectivities in the photodimerization of the enantiomers of **1** in their γ-CD complexes was also investigated in the range between 20 and −35 °C (Table 1). Lowering the temperature did not appreciably affect the regioselectivity: the HH/HT ratios are almost constant (75/25 for **1R** and 97/3 for **1S** on average) throughout the temperature range. However, *syn*$^{\mathrm{HT}}$-**2**/*anti*$^{\mathrm{HT}}$-**2** ratio increases with decreasing temperature and the diastereoselectivities of *anti*$^{\mathrm{HH}}$-**2** and *syn*$^{\mathrm{HT}}$-**2** increase significantly as temperature is decreased.

Determination of the Absolute Configuration of the Diastereomers of *anti*$^{\mathrm{HH}}$-2. In other work, we investigated the intramolecular photodimerization of 2,4-pentanediyl-*bis*-2-naphthoate.[38] Irradiation of (2*R*,4*R*)-(−)-2,4-pentanediyl-*bis*-2-naphthoate in cyclohexane yielded its *anti*$^{\mathrm{HH}}$-**2** intramolecular photodimer as the sole product, and ^{1}H NMR spectra and HPLC chromatograms demonstrated that it consisted of one diastereomer only (de > 98%; Scheme 2). The absolute configuration of this diastereomer was established by X-ray crystallography analysis of a single crystal to be **isomer I** (Figure S4, Supporting Information). Also, irradiation of (2*S*,4*S*)-(+)-2,4-pentanediyl-*bis*-2-naphthoate, under the same conditions, produced only one diastereomer of the *anti*$^{\mathrm{HH}}$-**2** intramolecular photodimer that was shown to be **isomer II** (evidently, **isomer I** and **II** are pair of enantiomers; Scheme 2). While **isomer I** exhibits one negative band in its CD spectrum around 220 nm, **isomer II** shows a positive peak in the same wavelength region. Hydrolysis of each of these isomers gave one carboxyl-substituted cubane-like dimer[37] (**isomer I′** or **II′**, respectively; Scheme 2) that have the same ^{1}H NMR spectra, but mirror image CD spectra: **isomer I′** exhibits a positive band and **isomer II′** a negative band, demonstrating that they are enantiomers. The carboxyl-substituted cubane-like photodimers obtained upon hydrolysis of *anti*$^{\mathrm{HH}}$-**2R-A** and *anti*$^{\mathrm{HH}}$-**2S-A** from irradiations of **1** exhibit CD spectra that are the same as that of **isomer I′**; those from the hydrolyzed *anti*$^{\mathrm{HH}}$-**2R-B** and *anti*$^{\mathrm{HH}}$-**2S-B** photodimers have the same CD spectra as that of **isomer II′**. Thus, the absolute configurations of the cubane-like frameworks in diastereomers **A** and **B** of *anti*$^{\mathrm{HH}}$-**2** are established unambiguously. Inspection of the structures of

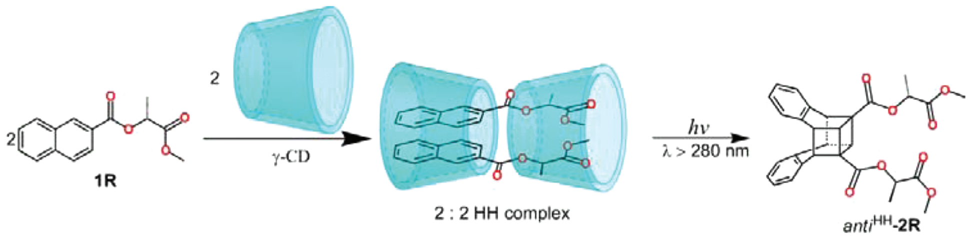


Figure 3. Proposed 2:2 HH complex.

isomers I′ and **II′** reveals that they each contain four stereogenic carbons (atoms 1, 2, 3 and 4). In **isomer I′**, all four atoms are in the *R* configuration, while those in **isomer II′** in S-configuration.

Photodimerization of Methoxycarbonylmethyl 2-Naphthoate. To obtain more information about the factors that control the diastereoselectivity in the photodimerization of **1R** and **1S** within γ-CD cavities, the photodimerization of an achiral substrate, methoxycarbonylmethyl 2-naphthoate (**1M**, Figure S5, Supporting Information), in solid γ-CD complex was performed (Scheme 3). The samples for irradiation were prepared with the method described above. As in the case of **1R** and **1S**, while **1M** alone in solid state exhibits naphthoate monomer fluorescence, the solid-state complex shows excimer-like emission (Figure S6, Supporting Information). In the IR absorption spectra, the absorptions corresponding to both the carbonyl chromophore in the alkyl group and that immediately connected to the naphthyl are shifted from 1751 and 1720 cm^{-1}, respectively, in pure **1M** to 1766 and 1728 cm^{-1}, respectively, in the complex (Figure S7, Supporting Information). The ratio of guest/host in the complex was found to be near to 1:1 by integration of ^{1}H NMR spectrum. All the above observations suggest that **1M** with γ-CD form 2:2 inclusion complex.

The sample was irradiated in the same conditions as **1R** and **1S** at 20 °C. Photoirradiation of **1M** both in cyclohexane solution and in γ-CD complex resulted in *anti*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2**, with *anti*^{HH}-**2** as the main product (Scheme 3). The products were isolated and analyzed by HPLC and ^{1}H NMR (Figures S8 and S9, Supporting Information). The ee values measured by HPLC for each photodimer are shown in Scheme 3. Although in solution photodimerization no stereoselectivity was observed for any photodimer, photodimerization with γ-CD complex gave significant enantioselectivity. The ee value was as high as 62% for *anti*^{HH}-**2**. Analysis of the CD spectra of the pair of *anti*^{HH}-**2** enantiomers reveals that the absolute configuration of the major enantiomer is the same as that for **isomer II′** and that of the minor enantiomer the same as **isomer I′** (Scheme 2).

■ DISCUSSION

Photodimers of alkyl 2-naphthoates have been known for several decades.[36−43] For example, photoirradiation of the simplest ester of 2-naphthoic acid, methyl 2-naphthoate, resulted in a cubane-like *anti*^{HH} photodimer as the unique product that results from a two-photon process.[31,32,43] The first photon produces an excited singlet state of the 2-naphthoate ester that undergoes a photodimerization to yield an open-cage [4 + 4] cycloaddition product. Absorption of the second photon allows the cage to close into the cubane-like photodimer. More recently, we reported that photodimerization of 2-naphthoate with a bulky alkyl ester group also leads to *syn*^{HH}, *anti*^{HT}, and *syn*^{HT} photodimers (Scheme 1) in addition to *anti*^{HH} photodimers (as in the case of **1R** and **1S**).[36] In the past, we have used chiral microreactor and chiral auxiliary strategies separately to achieve high stereoselectivity in the photodimerization of alkyl 2-naphthoates. In the former strategy, photodimerization of achiral methyl 3-methoxy-2-naphthoate was carried out in aqueous solutions within cavities of γ-CD.[31,32] Upon irradiation at ambient temperatures, γ-CD inclusion complexes of the naphthoate ester produced the *anti*^{HH} photodimer with 48% ee in >95% yield. In the latter strategy, a chiral auxiliary ester group was appended to the naphthoate and irradiations were conducted in organic solutions.[36] All four of the photodimers in Scheme 1 were produced, and up to 55% de's were found in the formation of the *anti*^{HH} photodimers. By combination of the above two strategies in the present study, significantly higher diastereoselectivity has been achieved.

Fluorescence and IR spectra of the **1**−γ-CD complexes have been analyzed to probe the mechanism responsible for enhancement of the regioselectivity. As shown in Figure 1, **1** in its neat solid state exhibits monomer fluorescence and the **1**−γ-CD complexes show excimer-like emission. The latter requires that two naphthoate moieties reside in the cavities. Furthermore, the frequencies of the IR absorptions corresponding to the carbonyl of the ester group of neat **1** and within the complexes differ by 10 cm^{-1}, indicating that the ester group is also within the γ-CD cavity. Finally, the observation based on ^{1}H NMR spectra that the molar ratio of **1** to γ-CD in the complexes is near 1:1 requires that they are, in fact, 2:2. Because the main photodimer is head-to-head (the HH/HT photodimer ratio was 74/26 for **1R** and 94/6 for **1S**), we propose that the vast majority of the complexes has two naphthoate moieties held in a "head-to-head" orientation by two γ-CD molecules which constitute a cavity (Figure 3). The presence of some head-to-tail photodimers in the product mixture suggests that a small fraction of the pairs of γ-CD hosts may accommodate their two guest molecules in a head-to-tail orientation.[44] In this argument, we assume reasonably that photodimerization of the HH complex yields only the HH photodimer (*anti*^{HH}-**2**) and that of the HT complex produces only the HT photodimers (either *anti*^{HT}-**2** or *syn*^{HT}-**2**) because the limited free volume in the HH and HT complexes precludes their interconversion in the solid phase. Thus, the HH and HT complexes, once formed and precipitated, are in locked orientations.

To gain additional insights into the source of the stereoselectivity in the formation of photodimer *anti*^{HH}-**2**, geometric structures of the 2:2 inclusion complex were optimized using the PM3 method implemented in the Gaussian 03 program package.[45−47] Three possible orientations were considered for two CD units to form a CD dimer (CD$_2$) (Figure S10, Supporting Information): the wide-to-wide (WW; wide is the wider rim of CD), the wide-to-small (WS, small is

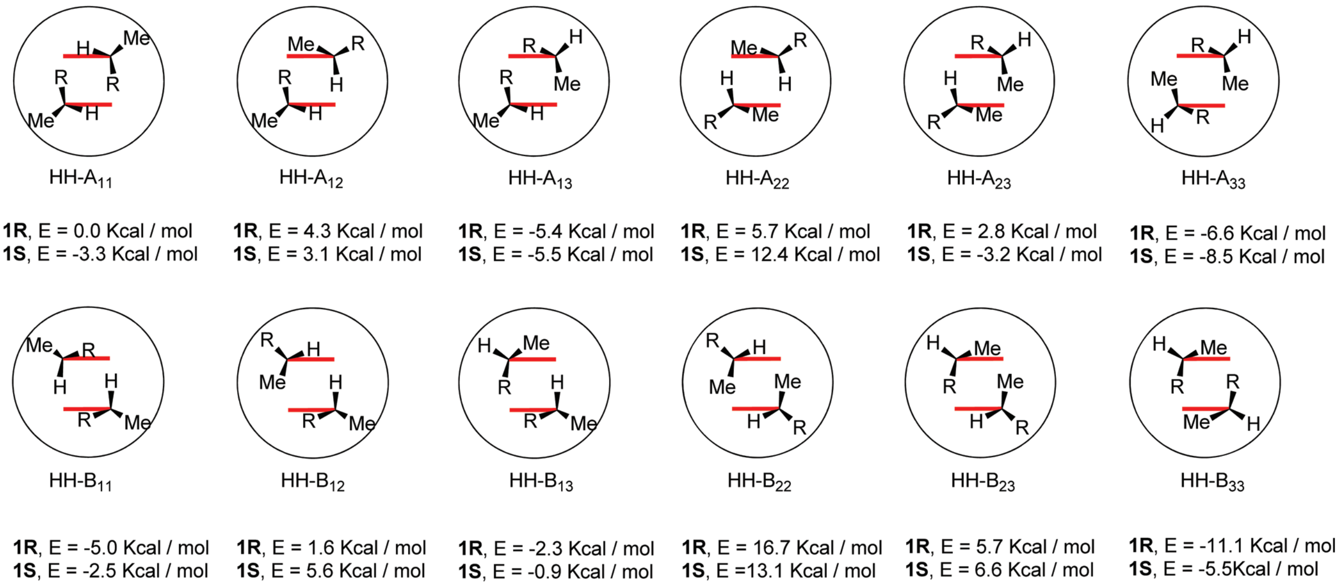


Figure 4. Schematic representation of the minimum energy conformers of the head-to-head 2:2 complex of the substrate and γ-CD; A- and B-type conformers are predicted to produce *anti*^{HH}-**2-A** and *anti*^{HH}-**2-B**, respectively. R = −COOMe; red bar = 2-naphthoate.

the smaller rim of CD), and the small-to-small (SS). The energies of 24 minimum energy conformers have been calculated. All conformers with WW CD_2 and WS CD_2 were found to have much higher energies than those with the SS CD_2 packing (Table S1, Supporting Information). This observation is consistent with the MD results reported by Jaime et al.[48,49] that the WS CD_2 is more favorable for α-CD and the SS CD_2 is more stable for β- or γ-CD. Figure 4 shows the optimized 12 conformers in which the pair of CDs are in SS orientations and the two naphthoates are in head-to-head orientations. Their energies are also shown in Figure 4. In all conformers, the two naphthoates are parallel and can form an *anti*^{HH} photodimer upon irradiation. Depending on the orientation of the two naphthoates, the conformers can be divided into A-type (HH-A) and B-type (HH-B) that would generate the A and B diastereomer of the *anti*^{HH} photodimer, respectively. According to the calculations for **1R**, the energy of conformer HH-B_{33} (−11.1 kcal/mol) is lower than the other conformers examined by at least 4.5 kcal/mol. At room temperature, where the complexes were prepared, the vast majority of the complexes should be HH-B_{33}. Of course, the roles of solvent, entropy, and reversibility in solution are not taken into account by the calculations. Regardless, *anti*^{HH}-**2R-B** is predicted to be produced preferentially by the complexes with **1R**.

HH-A_{33} with **1S** is calculated to have the lowest energy (−8.5 kcal/mol) among the conformers examined (lower than others by at least by 3.0 kcal/mol). Thus, the calculations predict (subject to the caveats mentioned above) that irradiation of the complexes with **1S** should yield mostly the *anti*^{HH}-**2S-A** diastereomer. The predictions for both **1R** and **1S** are borne out by the experimental results presented above.

The temperature effect on the diastereoselectivity is not understood fully at this time. It is possible that the two naphthoate groups within the head-to-head 2:2 inclusion complex must adjust their lowest energy orientations somewhat in order to undergo photodimerization. Such an adjustment would become increasingly more difficult as temperature is lowered. The activation energy for such an adjustment in A-type and B-type conformers may be different, resulting in the observed temperature dependence of the diastereoselectivity as well as affecting differently the relative quantum efficiencies for photodimerization. The above proposal also explains the low conversion of the photodimerization. Since such an adjustment is difficult in solid state, it needs long time irradiation to reach high conversion. These are interesting phenomena that will require additional experimentation to probe.

The substrate **1M** that has similar structure with **1R** and **1S** but lacks a chiral auxiliary also can form 2:2 guest/host head-to-head inclusion complex with γ-CD. Photoirradiation of the solid complex at ambient temperature mainly resulted in *anti*^{HH}-**2** photodimer (with 95% yield). The ee value of this photodimer was 62%, and the absolute configuration of the major enantiomer is the same as that for **isomer II′**. It is noted that the effect of γ-CD on the stereoselectivity in the photodimerization of an achiral alkyl 2-naphthoate is similar to that of a chiral auxiliary in the *S*-configuration in solution photodimerization. For example, photodimerization of **1S** in solution gave *anti*^{HH}-**2** in 55% ee, and the major diastereomer also has the absolute configuration of **isomer II′**. The stereoselectivity of *anti*^{HH}-**2** both from irradiation of **1M** in γ-CD complex and **1S** or **1R** in solution is evidently lower than that of **1S** or **1R** in γ-CD complex. These results demonstrate that the high diastereoselectivity for **1S** or **1R** in γ-CD complex irradiation originates the combination of the effects of chiral auxiliary and chiral cavity of γ-CD.

■ CONCLUSIONS

For the first time, the consequences of diastereomeric interactions on the photodimerization of a chiral substrate within a chiral γ-cyclodextrin host have been explored. The results demonstrate that combination of chiral auxiliary and chiral microreactor strategies can enhance induction of chirality in a photochemical dimerization such as the one here involving an enantiomeric pair of naphthoic esters (**1**). Furthermore, the diastereomeric interactions created by complexation of **1R** and **1S** (separately) within the cavity of the γ-CD hosts have a very large influence on the courses of the photodimerizations. The differences between the interactions of the enantiomers of the chiral groups attached to the naphthyl groups of **1** and the cyclodextrin hosts lead to subtle changes in the orientations of the aromatic moieties and, therefore, the photodimers they produce.

Analyses of the data by several techniques show that the molecules of **1** and γ-CD form 2:2 HH guest/host inclusion complexes. Of the three photodimers made from solid-state irradiations, *anti*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2**, the absolute configurations of the major product, the *anti*^{HH}-**2** diastereomers, could be established. While the de's of *anti*^{HH}-**2** from **1R** and **1S** were 55% in cyclohexane solution photoreactions (in which the chiral microreactor, γ-cyclodextrin, was absent) and that from **1M** (in which the chiral auxiliary was absent) was 62% in solid γ-CD complex irradiations, the photoirradiation of **1R** and **1S** in solid γ-CD complexes gave the de's of *anti*^{HH}-**2** up to 84% and 70%, respectively. The de's could be enhanced further to 94% for *anti*^{HH}-**2R** and 86% for *anti*^{HH}-**2S** by lowering the temperature to −35 °C. Rather unexpectedly, the major and minor diastereomers of *anti*^{HH}-**2R** and *anti*^{HH}-**2S** from the solution reactions are inverted in the solid-state complex (microreactor) irradiations.

The exact reasons why different major diastereomers of the photodimers are produced upon irradiation of **1R** and **1S** in the γ-CD complexes and in solution remain to be determined. However, it is clear that the stereochemistry of *anti*^{HH}-**2** of **1R** and **1S** from irradiations in solution must be controlled only by the chiral auxiliaries and that of **1M** from irradiation in γ-CD complex must be controlled only by the chiral cavity of γ-CD. For the 2:2 HH **1R** (or **1S**)/γ-CD complexes, a balance of steric and electronic factors in the cavities of the 2 γ-CD and the two chiral auxiliaries of the two complexed molecules of **1** leads to the eventual dimer stereochemistry. The calculations provide some valuable insights about the photochemistry within the solid state complexes. For **1R**, the energy of conformer HH-B_{33} is lower than the other conformers by at least 4.5 kcal/mol. For **1S**, the energy of conformer HH-A_{33} is lower than that of the other conformers by 3.0 kcal/mol. Thus, the relative population of HH-B_{33} for **1R** is predicted to be higher than that of HH-A_{33} for **1S**. Assuming that ground-state orientations determine primarily the modes of dimerization of the pairs of **1** in their excited states in the complexes, the de's of the photodimers from **1R** should be (and are) higher than those of the photodimers from **1S**. In solution, pairs of molecules of **1** have much more orientational lability and may change their relative positions to a larger extent within their excited states before undergoing dimerization.

Although many questions persist concerning what controls the specific pathways leading to these photodimerizations, the results presented here (and their analyses) provide clear opportunities for gaining deeper insights into the basic factors controlling chiral induction by auxiliaries, chiral hosts, and their interactions. Future work will explore those factors.

■ EXPERIMENTAL SECTION

Materials. **1R**, **1S**, and **1M** were synthesized according to the literature method.[36] γ-Cyclodextrin was used as received. HPLC-grade dichloromethane, cyclohexane, and dimethyl sulfoxide were used without further purification. Doubly distilled water was used throughout this work.

Instrumentation. X-ray powder diffractograms were recorded on a X-ray diffractometer (Cu Kα (λ = 1.54059 Å); operating current 40 mA) with a one-dimensional LYNXEYE detector. IR spectra of KBr pellets were obtained on a FT-IR spectrometer. Fluorescence spectra of the solid substrates and the guest/host complexes were recorded on a fluorescence spectrophotometer in the front-face mode. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer.

Preparation and Characterization of the Solid Complexes of 1 and γ-Cyclodextrin. In a typical procedure, a solution of γ-CD (0.04 mmol) in 5 mL of water was added to a concentrated solution of **1R**, **1S**, or **1M** (0.09 mmol in 0.1 mL dichloromethane), and the mixture was stirred overnight at ambient temperature. The precipitate was filtered, and the solid was washed several times with diethyl ether to remove any uncomplexed **1** and then dried overnight in a vacuum oven (10^{-2} Torr) at 50 °C.

Irradiation Procedures and Product Analyses. A dried complex was powdered finely, spread, and sandwiched between two Pyrex plates. The sample was then irradiated with a 500-W high-pressure mercury lamp for ca. 6 h, unless stated otherwise, with frequent shaking of the sample to place different parts of the powder directly at the surface being irradiated. After irradiation, the sample was dissolved in 1 mL of DMSO, and then dichloromethane was added. The solution was washed several times with saturated brine solution to remove DMSO and γ-CD and then dried over anhydrous magnesium sulfate. After evaporation of the solvent, the residue (products) was separated by HPLC on a chromatograph (UV detection at 220 nm) with an Intersil ODS-3 semipreparative column (5 μm, 250 × 10 mm) and acetonitrile/water (6:4, v/v) as the eluting solvent, for *anti*^{HH}-**2**, *anti*^{HT}-**2**, and *syn*^{HT}-**2**, and with a Daicel Chiral IA semipreparative column (5 μm, 250 × 10 mm) and hexane/ethanol (or isopropyl alcohol) as eluting solvent (see caption of Figure 2 and Figure S8, Supporting Information) for the diastereomers. The separated products were characterized by ^{1}H NMR spectroscopy (see Figure S9, Supporting Information, and ref 36).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray powder diffractograms and IR absorption spectra of the substrates and complexes, measurements of substrate/γ-CD ratios of the complexes, NMR of **1M**, fluorescence spectra of **1M** and its complex with γ-CD, HPLC chromatograms of photodimers of **1M**, ^{1}H NMR of photodimers of **1M**, CIF and absolute configuration of the intramolecular photodimer of (2*R*,4*R*)-(−)-2,4-pentanediyl-bis-2-naphthoate, and calculation of energies and coordinates of the optimized conformers for the HH 2:2 complex. This material is available free of charge via the Internet at http://pubs.acs.org.

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