Journal of Photochemistry and Photobiology A: Chemistry 207 (2009) 144–152

Contents lists available at ScienceDirect

Journal of Photochemistry and Photobiology A: Chemistry

journal homepage: www.elsevier.com/locate/jphotochem

Chiral photochemistry within natural and functionalized cyclodextrins: Chiral induction in photocyclization products from carbonyl compounds

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ARTICLE INFO

Article history:
Available online 18 March 2009

Dedicated to dear friend and colleague Professor Harou Inoue on the occasion of his 60th birthday.

Keywords:
Chiral induction
Hydrogen abstraction
Cyclodextrin
Functionalized cyclodextrin
Supramolecular chemistry

ABSTRACT

Chiral induction in products resulting from hydrogen abstraction upon excitation of carbonyl compounds included in four cyclodextrin related host systems has been examined. The chiral induction obtained in photoproducts is moderate. Results suggest that there is potential to improve the asymmetric interaction between the reactant molecules and the supramolecular host cyclodextrins. However, no models that would help us to predict the outcome of chiral induction in a photochemical reaction have resulted from this investigation. Given the use of cyclodextrins as chiral stationary phases in HPLC and GC separations we are optimistic that there is considerable potential for cyclodextrins as chiral hosts in photoreactions.

1. Introduction

Supramolecular chiral photochemistry has attracted considerable attention as a unique methodology for inducing molecular chirality in photoproducts [1,2]. Several chiral organic hosts such as cyclodextrins [3–5], Toda's diols [6,7], and cholic acid [8] and inorganic host such as chirally modified zeolites [9,10] have been used to achieve chiral induction in photoproducts during photochemical reactions. In this study we have used β-cyclodextrin (β-CD) and functionalized β-CD (monofuncionalized at the 6-position with chirally pure amine, amino alcohol and amino acid; **1**–**4**) as hosts to carry out the photochemical reactions (Scheme 1). In general, chiral induction obtained with cyclodextrin host–guest complexes in photochemical reactions of achiral substrates that yield chiral photoproducts has been low to moderate [11–13]. Further, in most cases, photolysis was carried out either in solid state or at low temperatures using mixed solvents. Due to poor solubility of the complexes in aqueous solutions, there are only very few reports of the chiral induction using cyclodextrin complexes [14,15]. Our current focus is on investigating the chiral induction obtained on cyclization products resulting from photoinduced γ- and δ-hydrogen abstractions using natural and functionalized cyclodextrins as hosts in water. The photochemical hydrogen abstractions we have explored are listed in Schemes 2–4. We have chosen two classes of carbonyl compounds for investigation: (a) achiral ketones (**5a**–**9a**) yielding enantiomeric chiral products [16–21] and (b) chiral ketones (**10a**–**14a**) [22,23] yielding diastereomeric products. Our interest in examining the use of functionalized cyclodextrins came from the belief that specific interaction between chiral attachments and reactant molecules would enhance the chiral induction process. Although CD as such is chiral thus far it has not been able to provide significant chiral induction in most photoreactions. We believed that CD would serve as a confined vessel and bring the reactant and the chiral substituent closer and facilitate chiral induction in photoproducts.

The achiral α-adamantyl acetophenone derivatives **5a**–**7a** (Scheme 2) upon irradiation undergo γ-hydrogen abstraction to afford chiral cyclobutanols (both *cis* and *trans* isomers) [16]. The major cyclization photoproduct in isotropic medium (hexane) as well as organized media like Faujsite zeolites and crystalline state is *trans* cyclobutanol [17–19]. The photocyclization of achiral α-mesitylacetophenone **8a** and **9a** (Scheme 3) leads to the corresponding 2-phenyl-2-hydroxy-4,6-dimethylindan via δ-hydrogen atom abstraction [20,21]. Irradiation of the substrates in isotropic medium (hexane) results in racemic photoproducts. The photochemistry of chiral α-oxoamides **10a**–**14a** (Scheme 4) involves γ-hydrogen abstraction to form diastereomeric azetidinones (β-lactams, **10b**–**14b**) and oxazolidinones photoproducts (**10c**–**14c**), the ratio being dependent on the medium used [22,23]. The net hydrogen transfer by the photoexcited carbonyl can occur either by direct hydrogen abstraction or in two steps: electron transfer followed by proton transfer [24–26].

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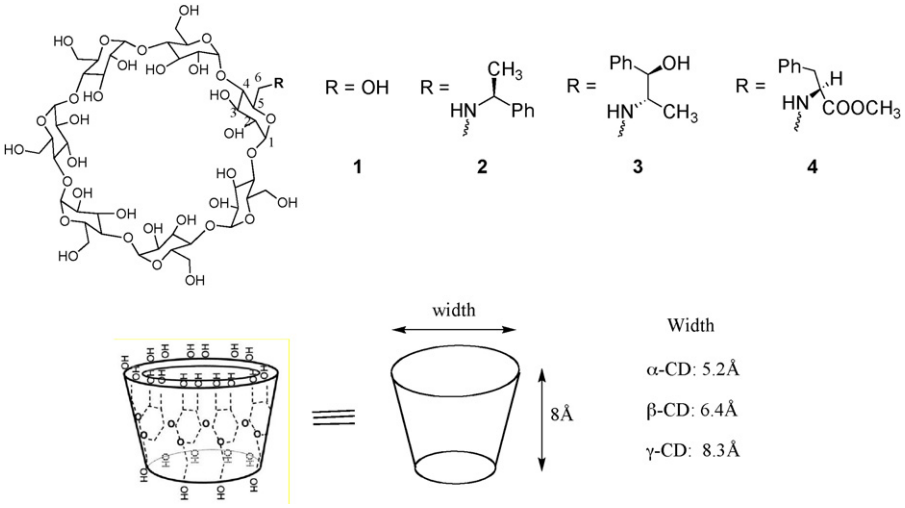
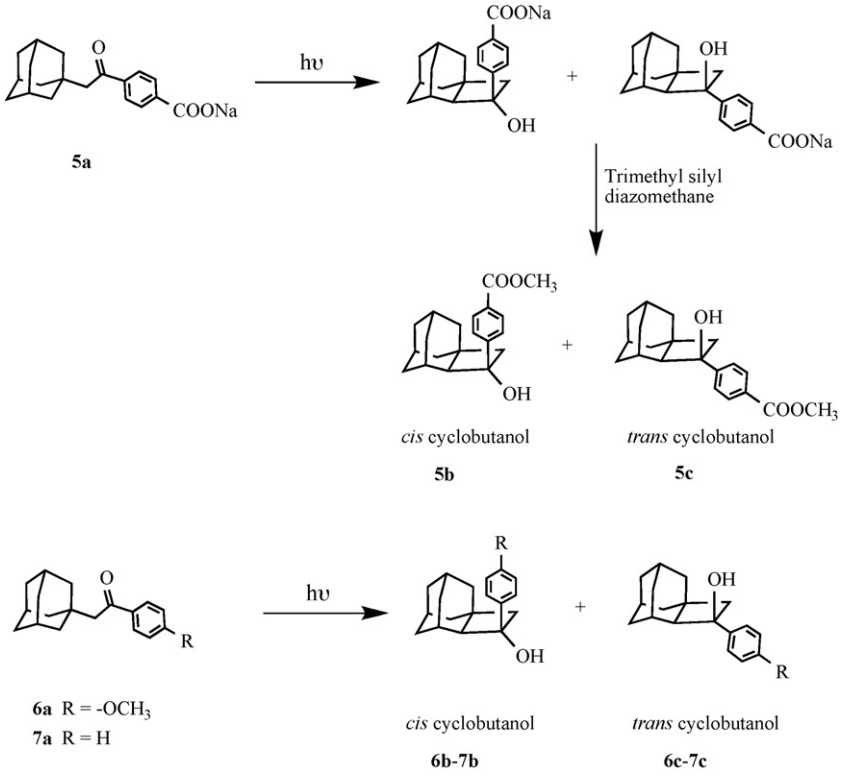
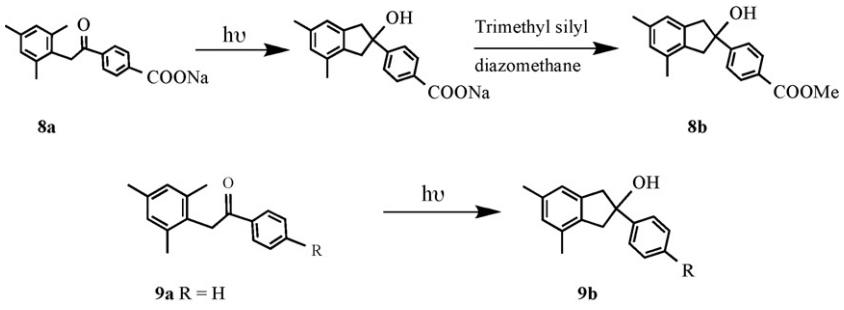
doi:10.1016/j.jphotochem.2009.03.004



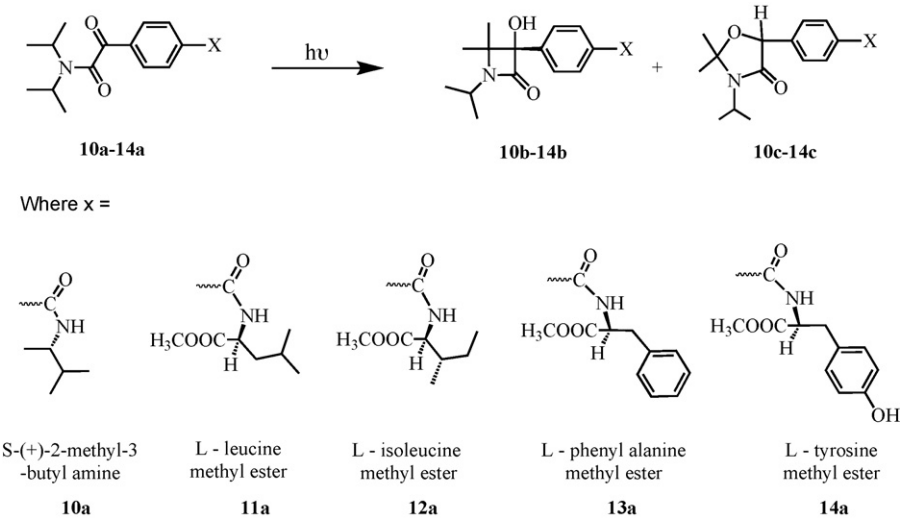
Scheme 1. Structures of natural and chirally modified β-CD.



Scheme 2. Structures of adamantyl acetophenones (**5a–7a**) and their respective photoproducts.



Scheme 3. Structures of mesityl acetophenones (**8a** and **9a**) and their respective photoproducts.



Scheme 4. Structures of α-oxoamides (**10a–14a**) and their respective photoproducts.

To any one seeking chiral induction through a supramolecular strategy CDs offers a great potential. Their ready availability and inherent chiral nature encourage one to pursue photochemical studies in this medium. Furthermore, successful use of CD as a stationary phase in GC and HPLC columns to separate chiral molecules provides strong incentive to explore the use of CD as a reaction medium. In the past we have explored the use of CD as a chiral medium for photoreactions, but the limited success was of concern [27,28]. Recent successful observations in zeolite media [29,30] prompted us to reinvestigate CDs as chiral reaction media. Our goal in this study is to explore the potentials and limitations of cyclodextrins as hosts to induce chiral induction in photoreactions that have been investigated in zeolites and crystals. The systems presented in Schemes 2–4 have been investigated in crystalline state and zeolites and in these media high enantioselectivities or diastereselectivities have been obtained.

2. Results and discussion

The studies conducted consist of three parts: (a) host–guest complexation; (b) characterization of host–guest complexes by one- and two-dimensional NMR experiments and (c) photochemistry of host–guest complexes. Experimental observations and their interpretations are presented in this section. β-CD was monofunctionalized with chirally pure amine such as *S*-(−)-methyl benzyl amine, aminoacid such as L-(−)-phenyl alanine methyl ester and amino alcohol such as (1*R*, 2*S*)-(−)-norephedrine on the primary side (Scheme 1). Synthetic procedures adopted to functionalize CD and characterizations (FAB-MS analysis and ^{1}H NMR) of functionalized CD are presented in Section 4.

2.1. Structure of functionalized β-CDs

One of the important questions that needed to be addressed at the early stage of this investigation was whether the chiral group in the functionalized CD host is inside or outside the cavity of β-CD? This was important because if the appendix chiral auxiliary tended to stay within the CD cavity, the reactant guest may fail to get included. 2D-ROESY analyses of **2**, as evidenced by the correlation peaks between the phenyl protons of the chiral group with the inner protons of β-CD ($H_3/H_5/H_6$) (Fig. 1), suggested that the phenyl part of the chiral group was inside the cavity of β-CD. However, it is not clear at this stage whether the phenyl encapsulation is intermolecular or intramolecular in nature (Scheme 5). Similar 2D-ROESY NMR analyses of **3** and **4** indicated that they are also undergoing phenyl encapsulation in water.

2.2. Host–guest complexation studies

Complexation behaviors of CDs were probed by proton, 2D-ROESY and DOSY NMR experiments. The benzene carboxylate substrates **5a** and **8a** formed water-soluble complexes with CD and monofunctionalized CD while the other substrates were partially soluble only at pD > 10. The ^{1}H NMR spectra of adamantyl acetophenone derivative **5a** in D_2O and in the presence of CDs are presented in Fig. 2. The adamantane proton signals of the guest are downfield shifted by ∼0.2 ppm in the CD complexes of **5a**. The downfield shift is possibly due to the inclusion and change in polarity experienced by the guest within CD cavity compared to water. However the change in the chemical shift of the phenyl proton signals was <0.1 ppm (∼0.02 and 0.06 ppm upfield shift of H_a and H_b signals, respectively) suggesting the exposure of the more hydrophilic benzene carboxylate part to aqueous outside. The 2D-ROESY NMR spectra of **5a**@β-CD and **5a@2** are presented in Figs. 3 and 4. In both cases, strong correlation peaks were observed for the adamantane protons of the guest with the inner protons of the β-CD ($H_3/H_5/H_6$)

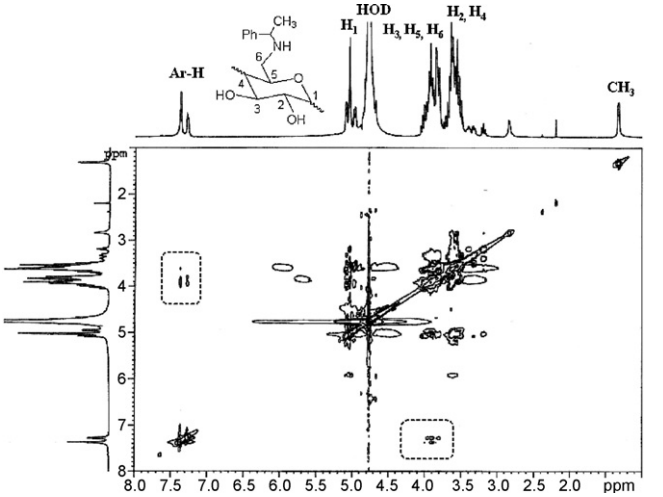
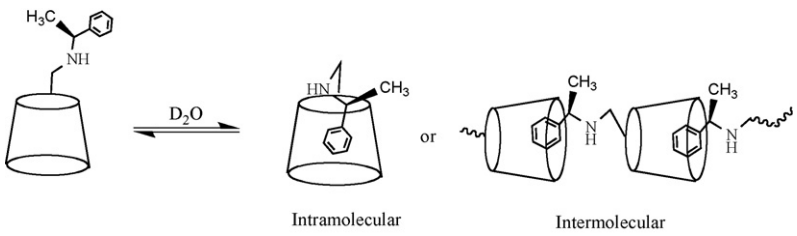
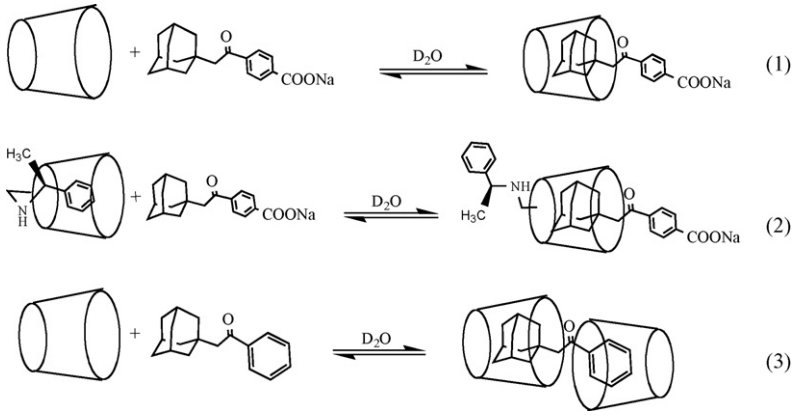


Fig. 1. 2D-ROESY NMR spectrum of **2** in D_2O (correlation peaks are highlighted in rectangular boxes).



Scheme 5. Schematic representation depicting the intermolecular and intramolecular self-complexation of **2** in water.



Scheme 6. Schematic representation of the complexes of **5a**@β-CD and **5a@2** in water.

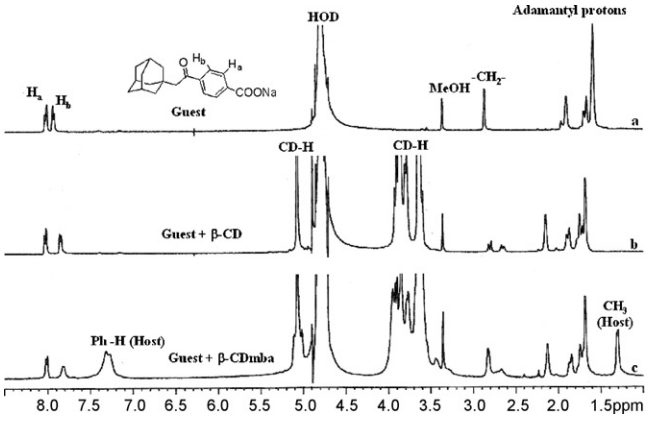


Fig. 2. ^{1}H NMR spectra of the CD complexes of **5a** in D_2O. (a) **5a** only, (b) **5a**@β-CD (1:2) and (c) **5a@2** (1:2).

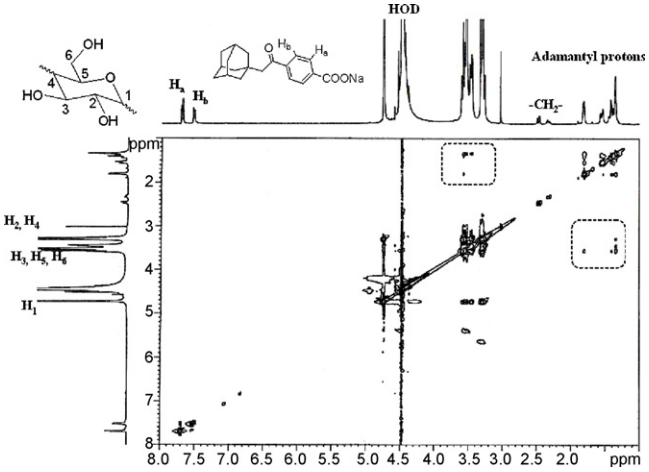


Fig. 3. 2D-ROESY NMR spectra of the complex of **5a**@β-CD (1:1). Correlation peaks are highlighted in rectangular boxes.

suggesting the inclusion of the adamantane part of the guest within the CD cavity. No correlation peaks were observed for the phenyl protons of the guest with the CD inner protons suggesting that benzene carboxylate group being outside the cavity. These observations suggested that adamantane part of the guest alone is included within the cavity of β-CD and **2** (Scheme 6). It is important to note that at high pH the guest–CD complexes become soluble because of the deprotonation of the hydroxyl groups of CD. While deprotonation is likely to favor decomplexation, in our case such is not happening. This is evident from the 2D-ROESY analysis of the complexes at pD > 10. Observed correlation peaks of the guest signals with the host signals confirms that the guest is indeed complexed at pD > 10.

Adamantyl acetophenone substrates **6a** and **7a** formed water insoluble complexes with the CDs. However, they were partially soluble at pD > 10 in the presence of excess β-CD. This suggested to us that the host:guest ratio may be higher than 1:1. The DOSY NMR

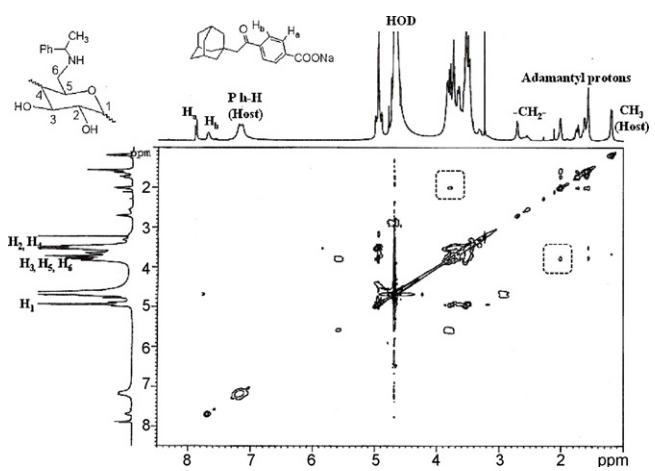


Fig. 4. 2D-ROESY NMR spectra of the complex of **5a@2** (1:1). Correlation peaks are highlighted in rectangular boxes.

experiments suggested that the CD host and the guest **7a** were diffusing at the same rate. This is consistent with complex formation between **7a** and β-CD. The 2D-ROESY analysis of **7a**@β-CD and ^{1}H NMR studies suggested that both phenyl and adamantane parts of the guest are encapsulated in the CD cavity. This is possible only if **7a** formed a 1:2 (G:H) complex. Based on the above NMR results we propose a structure for the complex of **7a** with CD as shown in Scheme 6 (Eq. (3)). Similar results were obtained with **6a**.

Similar to that of the adamantyl acetophenone **5a**, the benzene carboxylate mesityl acetophenone substrate **8a** formed a water-soluble complex while substrate **9a** formed a water insoluble complex. Addition of two equivalents of β-CD or the functionalized CD (**2**) resulted in the downfield shift of methyl proton signals (0.1–0.15 ppm), the chemical shift difference in the phenyl proton signals of the guest was less than 0.1 ppm as anticipated. 2D-ROESY NMR analyses were carried out to further elucidate the nature of the complex, however due to poor complexation behavior of **8a**, no correlation peaks were seen between the guest and the host. α-Oxoamides **10a**–**14a** formed water insoluble complexes and the complexes were not soluble even at pD > 10 and hence detailed NMR studies of the CD complexes could not be carried out. Because of lack of reliable NMR data we are unable to predict the structure of the above complexes.

2.3. Photochemical studies

We have employed three different strategies to induce chirality in the photoproducts. The first strategy involved the use of chiral natural β-CD as host on achiral guests **5a**–**9a** (adamantyl and mesityl acetophenones). The second strategy involved the use of chirally functionalized β-CD (**2**–**4**) as hosts on achiral reactants **5a–9a**. The third strategy employed the use of chiral hosts **1**–**4** on chiral reactants **10a**–**14a** (α-oxoamides). Results obtained are presented in Tables 1 and 2 and discussed in this section.

2.4. Adamantyl acetophenones and mesityl acetophenones

Irradiation of adamantyl acetophenone derivative **5a** in water resulted in racemic *cis* and *trans* cyclobutanols (Scheme 2) [16]. The photoproducts present as sodium salt were converted to their corresponding methyl esters (**5b** and **5c**) by treatment with aq. HCl and trimethyl silyl diazomethane and ee was estimated by HPLC analysis of methyl esters. Similarly the CD complexes were irradiated and analyzed under identical conditions. No appreciable ee was obtained with the natural β-CD as the host. However, aqueous solution irradiation of **5a@2** resulted in 20% ee in *cis* cyclobutanol and 9% ee in *trans* cyclobutanol. This observation suggested that the extra chiral group in **2** is playing a role in the chiral induction process. However, 2D-ROESY NMR data suggested that there are no correlation peaks between the apendant methyl benzyl amine group of the host and the encapsulated guest, at least in the NMR time scale. Observation of correlation peaks between the adamantane protons of the guest and the inner protons ($H_3/H_5/H_6$) of the host suggested that the enantiomeric excess observed is indeed an effect of complexation. However, at this stage we are unable to visualize how the chiral auxiliary methyl benzyl amine is able to provide chiral induction in the photoproduct.

Irradiation of the water-soluble CD complexes of mesityl acetophenone derivative **8a** resulted in very low enantiomeric excess of the photoproducts (Scheme 3). This is consistent with the 2D-ROESY analysis of the complex that suggested a weaker complex between **8a** and CD. The hydrophilic benzene carboxylate group is expected to face aqueous outside, while the hydrophobic mesityl part of the guest to be present within the CD cavity.

Substrates **6a**, **7a** and **9a** formed water insoluble complexes with natural and functionalized CDs and hence irradiations were carried out in solid state. Irradiation of **6a** and **7a** in hexane and as solid host–guest complexes with CDs **1**–**4** resulted in *cis* and *trans* cyclobutanols (Scheme 2). The ee was considerably small (5%) for the cyclobutanols from **6a** within both β-CD and **2**. However, ee on the cyclobutanol photoproducts of substrate **7a** were 16% within β-CD and 21% within host **2**. The only difference between substrates **6a** and **7a** is the presence of $-OCH_3$ group on the *para* position of the phenyl moiety in **6a**. Based on correlation peaks of the guest proton signals with the inner protons of CD (2D-ROESY) we are confident that **6a** and **7a** form host–guest complexes with β-CD and **2**. The ee obtained in the indanol product upon irradiation of **9a**–host complexes was in the order of ∼10% (Table 1).

2.5. α-Oxoamides

Since natural and functionalized CDs were capable of inducing only moderate chiral induction in the photoproducts we decided to employ the third strategy, where a remote chiral auxiliary was linked covalently to the reactant. Presence of a chiral auxiliary would generate diastereomerically related biradical intermediates during photoexcitation. We envisioned that these biradical intermediates would react at slightly different rates, leading to enhanced stereoselectivity in the photoproducts. The reaction chosen for the study was the photochemical conversion of α-oxoamide to β-lactam (Scheme 4). The *para* substituted α-oxoamide upon irradiation as cyclodextrin complexes resulted in chiral β-lactams and oxazolidinones. The % de obtained on the β-lactams of the α-oxoamides is summarized in Table 2.

The % de was dependent on the chiral auxiliary. For example, when comparing substrates **13a** and **14a**, irradiation of substrate **13a** resulted in 17% de (B isomer, the second diastereomer eluting from the HPLC column) within β-CD, while substrate **14a** resulted in 47% de (B isomer) within β-CD. The only difference between these two oxoamides is that substrate **14a** has a hydroxyl group

Table 1
% ee[a] obtained for photoproducts[b] of **5a–9a**[c,d] within hosts **1**–**4** (Scheme 1).

Medium	**5b** (*cis* cyclobutanol)	**5c** (*trans* cyclobutanol)	**6c** (*trans* cyclobutanol)	**7c** (*trans* cyclobutanol)	**8b** indanol	**9b** indanol
Solution[e]	0	0	5 A	5 A	0	2 A
1	0	0	5 A	16 A	4 B	12 B
2	9 B	20 B	0	21 A	4 B	11 A
3	[f]	[f]	7 A	7 B	[f]	10 A
4	[f]	[f]	0	0	[f]	0

[a] A, B represents the first and second enantiomer, respectively eluting from the HPLC/GC.
[b] The % conversions were typically 25–40%.
[c] Enantiomers of photoproducts **6B** and **7B** could not be separated in HPLC/GC and therefore not included in the table.
[d] Complexes of substrates **5a** and **8a** were irradiated as aqueous solutions. Substrates **6a**, **7a** and **9a** were irradiated in the solid state.
[e] Substrates **5a** and **8a** were irradiated in water and the other substrates were irradiated in hexane.
[f] The experiments with these hosts were not carried out.

Table 2
Percentage diasteromeric excess (de)[a] obtained for β-lactam photoproducts[b] **10b**–**14b** within CD hosts.

Medium	10b	11b	12b	13b	14b
CH_3CN	2 A	1 B	0	5 B	3 B
1	25 A	11 A	4 A	17 B	47 B
2	8 A	13 A	8 A	23 A	43 B
3	10 A	6 B	0	8 A	22 B
4	16 A	5 B	0	8 A	38 B

[a] A, B represents the first and second diastereomer, respectively eluting from the HPLC.
[b] The % conversions were typically 25–40%.

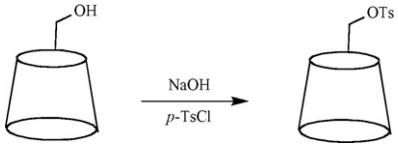
in the *para* position of the chiral tyrosine part. The hydroxyl group in the *para* position of the phenyl moiety of **14a** might be involved in hydrogen bonding with the hydroxyl groups in the rim of the host, thereby restricting the mobility of the guest. This might be the probable reason for the relatively high %de observed in **14a** compared to that of **13a**. Furthermore, irradiation of oxoamide **13a** within the functionalized **2** resulted in 23% de (A isomer). By tethering an extra chiral group to the primary face of CD (methyl benzyl amine in this case) we were able to switch the isomer from 17% de of B isomer to 23% de of A isomer. The other oxoamides **10a**–**12a** upon photolysis resulted in only 10–15% de of the corresponding β-lactam photoproduct probably due to poor binding characteristics. Due to the poor solubility of the complexes in water (even at pD > 10), complexation studies using NMR could not be carried out.

3. Conclusion

Chiral induction in chemical reactions has fascinated chemists for several decades. While chiral induction of thermal reactions is pursued with synthetic goals, chiral induction of photoreactions is attempted with the goal of understanding intermolecular interactions in the excited state. The chiral induction of photoreactions in solution under ambient conditions continues to be fairly low [31,32] and this has forced photochemists to seek newer strategies. Of the various approaches, photochemistry of supramolecular assemblies has shown promise [1–7,33]. We have explored in recent years the use of crystals and zeolites as reaction media with considerable success [29,30]. Our attempts to use cyclodextrin as chiral host have been met with mixed results [14,27,28]. Given that cyclodextrin and functionalized cyclodextrins are routinely used as column materials in HPLC and GC to separate chiral products, we believed that these would lead to reasonably high chiral induction in photoreactions. Results of the current as well as previous studies have shown that the above analogy does not hold good since the chiral separation is based on 'multiple events' while chiral induction is dependent on a 'single event'. We are still hopeful that relatively inexpensive cyclodextrins could be used as a supramolecular host to conduct chiral photochemistry and we will continue to look for right examples.

4. Experimental

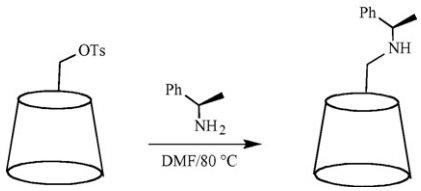
4.1. Synthesis of mono-6-deoxy-6-(p-tolylsulfonyl)-β-cyclodextrin [34]



To a stirred suspension of 12 g of **β-CD** in 100 mL of water, was added a solution of NaOH (1.3 g in 4 mL water) in drops over 6 min. A clear solution was obtained to which was added slowly a solution of *p*-tolylsulfonyl chloride (2 g in 6 mL of MeCN) over 8 min. The resulting suspension was stirred for 3 h at RT and filtered. The filtrate was kept in the refrigerator overnight. The precipitated solids were filtered, washed with cooled water (5 °C) followed by acetone. The ditosylated product and the sulfonic acid impurity were separated by recrystallization of the crude product from hot water. The product was dried at room temperature under reduced pressure and analyzed by ^{1}H NMR.

^{1}H NMR: (DMSO, 400 MHz): δ 7.72 (d, 2H), 7.39 (d, 2H), δ 5.71 (m, 14H), δ 4.68 (m, 7H), δ 3.2–3.36 (m, 48H), δ 2.4 (d, 3H).

4.2. Functionalization of β-CD with S-(−)-methyl benzyl amine [35]

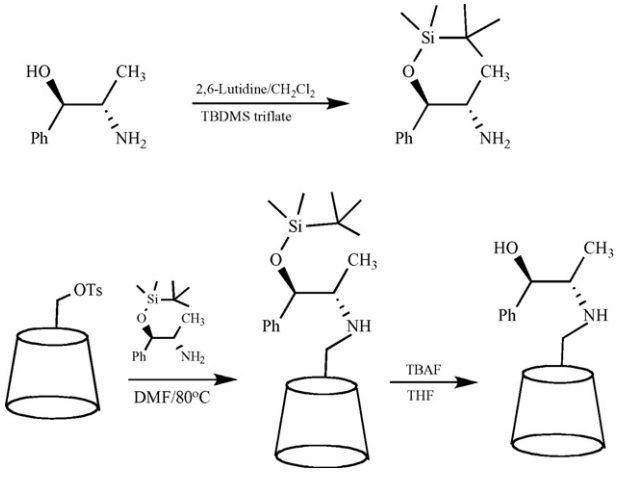


To 400 mg of the mono tosyl β-CD dissolved in 15 mL of DMF was added 3 mL of *S*-(−)-methyl benzyl amine under nitrogen atmosphere. The solution was then heated to 80 °C and the reaction was continued further for 24 h. The reaction mass was then cooled to room temperature. The DMF was then distilled off under reduced pressure and the yellow solids were suspended in acetone, sonicated for 10 min. The slurry was filtered and washed with acetone. The crude product thus obtained was purified by recrystallization using water–acetone (30:70) twice. The product formation was confirmed by ^{1}H NMR.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.10–7.27 (m, 5H), δ 5.56 (m, 14H), δ 4.68 (m, 7H), δ 3.45 (m, 27H), δ 3.13 (m, 23H), δ 1.0 (m, 3H).

FAB-MS *m*/*z* 1238.

4.3. Functionalization of β-CD with (1R,2S)-(−)-norephedrine [35]



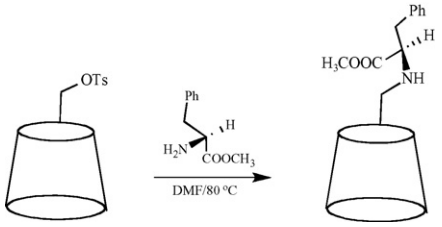
To 400 mg of the mono tosyl β-CD dissolved in 15 mL of DMF was added 1.7 g of (1*R*,2*S*)-(−)-norephedrine (–OH group protected with TBDMS) under nitrogen atmosphere. The solution was then heated to 80 °C and the reaction was continued further for 24 h. The reaction mass was then cooled to room temperature. The DMF was then distilled off under reduced pressure and the yel-

low solids were suspended in acetone, sonicated for 10 min. The slurry was filtered and washed with acetone. The product was then suspended in dry THF and a gram of TBAF was added and stirred under nitrogen atmosphere. The product was then precipitated out by adding water/methanol mixture and filtered. The crude product thus obtained was purified by recrystallization using water–acetone (70:30) twice. The product formation was confirmed by ^{1}H NMR.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.1–7.4 (m, 5H), δ 5.6–5.78 (m, 14H), δ 4.8 (m, 7H), δ 3.45–3.65 (m, 23H), δ 3.13 (m, 24H), δ 0.8 (m, 3H).

FAB-MS m/z 1268.

4.4. Functionalization of β-CD with L-(−)-phenyl alanine methyl ester [35]



To 400 mg of the mono tosyl β-CD dissolved in 15 mL of DMF was added 3 mL of L-(−)-phenyl alanine methyl ester under nitrogen atmosphere. The solution was then heated to 80 °C and the reaction was continued further for 24 h. The reaction mass was then cooled to room temperature. The DMF was then distilled off under reduced pressure and the yellow solids were suspended in acetone, sonicated for 10 min. The slurry was filtered and washed with acetone. The crude product thus obtained was purified by recrystallization using water–acetone (30:70) twice. The product formation was confirmed by ^{1}H NMR.

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.10–7.3 (m, 5H), δ 5.56 (m, 13H), δ 4.78 (m, 7H), δ 3.45–3.65 (m, 25H), δ 3.13 (m, 30H).

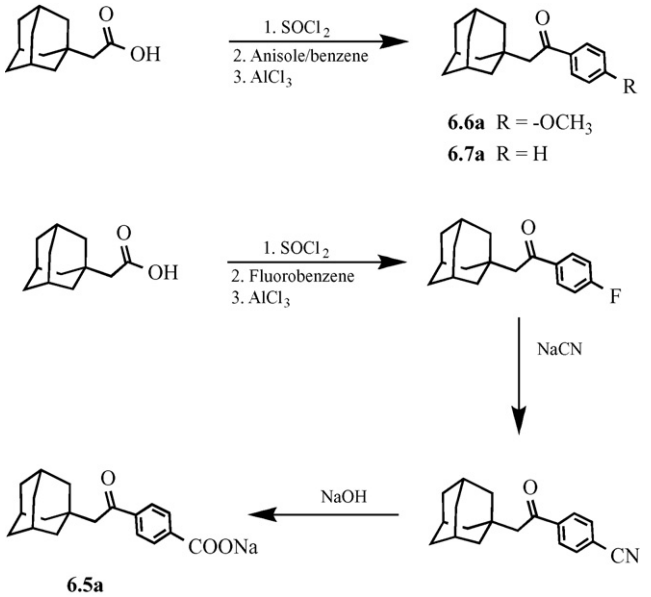
FAB-MS m/z 1296.

4.5. NMR analysis

The 2D-ROESY NMR of CDs and CD complexes in D_2O was carried out using the standard pulse sequence ROESYPHSW in Bruker 500 MHz NMR.

4.6. Synthesis of adamantyl acetophenones

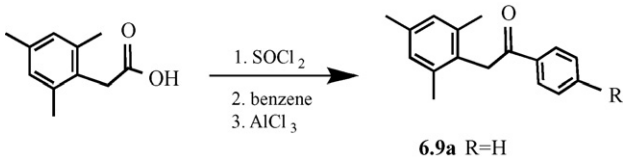
The adamantyl acetophenones **5a**–**7a** were synthesized by following literature procedures [17–19] as per the following scheme.



6.5a: ^{1}H NMR (400 MHz, D_2O): δ 1.5–2.1 (m, 15H), 2.85 (s, 2H), 7.8–8.2 (m, 4H).

4.7. Synthesis of mesityl acetophenones

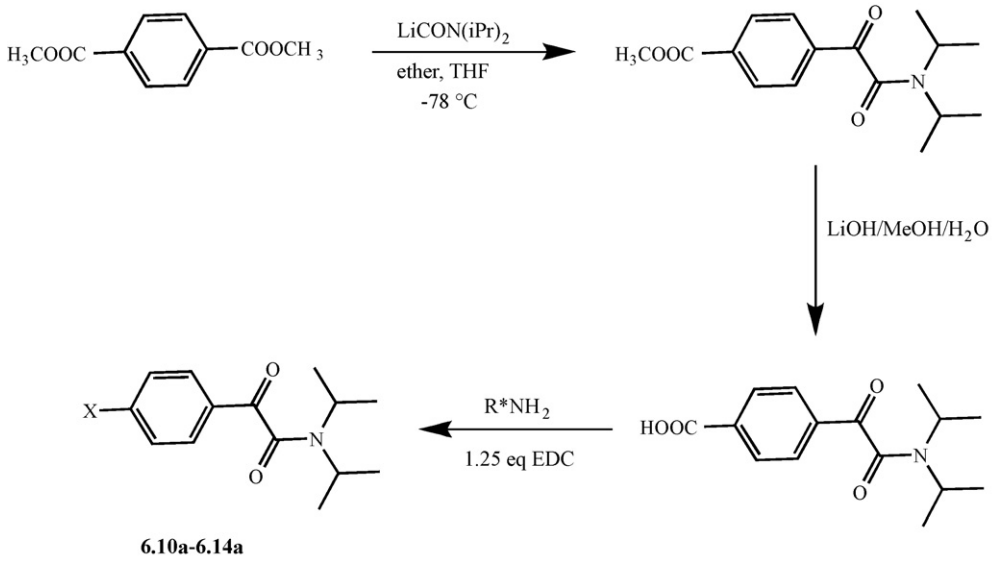
The mesityl acetophenones **8a**–**9a** were synthesized by following literature procedures [36] as per the following scheme. Substrate **8a** was prepared by following the procedure adapted for substrate **5a**, excepting that mesityl acetyl chloride was used instead of adamantyl acetyl chloride.



8a: ^{1}H NMR (400 MHz, D_2O): δ 1.9–2.4 (m, 11H), 7.04 (m, 2H), 8.0–8.35 (m, 4H).
9a: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16 (s, 6H), 2.26 (s, 3H), 4.32 (s, 2H), 6.87 (s, 2H), 7.46–7.50 (m, 2H), 7.56–7.61 (m, 1H), 8.01–8.07 (m, 2H).

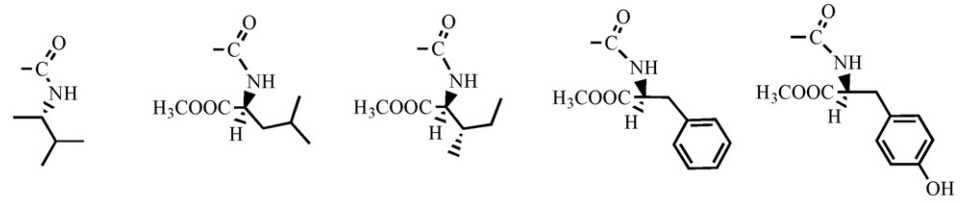
4.8. Synthesis of α-oxoamides

The α-oxoamides **10a**–**14a** were synthesized by following literature procedures [37] as per the following scheme.



6.10a-6.14a

Where x =



S-(+)-2-methyl-3 -butyl amine	L - Leucine methyl ester	L - Isoleucine methyl ester	L - phenyl alanine methyl ester	L - tyrosine methyl ester
6.10a	**6.11a**	**6.12a**	**6.13a**	**6.14a**

10a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.945–0.973 (dd, 6H, J = 6.8, 4.4 Hz), 1.146–1.167 (dd, 6H, J = 6.8, 2 Hz), 1.18–1.152 (d, 3H, J = 6.8 Hz), 1.56 (d, 6H, J = 6.8 Hz), 1.7 (m, 1H), 3.56–3.68 (m, 2H), 4.04–4.12 (m, 1H), 6.02 (d, 1H), 7.84 (d, 2H), 7.96 (d, 2H).
11a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92–1.0 (m, 6H), 1.12–1.16 (dd, 6H, J = 6.8, 2 Hz), 1.52–1.56 (d, 6H, J = 6.8, 2.0 Hz), 1.65–1.80 (m, 3H), 3.5–3.68 (m, 2H), 3.8 (s, 3H), 4.8–4.9 (m, 1H), 6.6 (d, 1H), 7.9 (d, 2H), 8.0 (d, 2H).
12a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92–0.98 (m, 6H), 1.14–1.18 (dd, 6H, J = 6.8, 2.4 Hz), 1.56–1.59 (d, 6H, J = 6.8), 1.6–1.8 (m, 3H), 3.55–3.7 (m, 2H), 3.74 (s, 3H), 4.5–4.7 (m, 1H), 6.75 (d, 1H), 7.8 (d, 2H), 7.99 (d, 2H).
13a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.14–1.18 (dd, 6H, J = 6.8, 2.0 Hz), 1.55 (d, 6H), 3.2–3.34 (m, 2H), 3.56–3.68 (2H, m), 3.78 (3H, s), 5.08 (m, 1H), 6.67 (d, 1H), 7.0–7.3 (m, 5H), 7.8 (d, 2H), 7.9 (d, 2H).
14a: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16–1.2 (dd, 6H, J = 6.8, 2.0 Hz), 1.56 (d, 6H, J = 6.8 Hz), 3.085–3.223 (m, 2H), 3.577–3.653 (2H, m), 3.76 (3H, s), 4.98–5.2 (m, 1H), 6.75 (d, 1H), 6.86 (d, 2H), 7.8 (d, 2H), 7.94 (d, 2H).

4.9. Complexation, irradiation, extraction and analysis procedures

Complexes of substrates **5a** and **8a** were irradiated as aqueous solution as these substrates formed water-soluble complexes. The complexes of other substrates were irradiated as hexane slurry or in the solid state as these substrates formed water insoluble complexes.

4.9.1. Water-soluble complexes

To 0.6 mL a 5.6 mM solution of the guest in D_2O was added four equivalents of the corresponding host and the solution was sonicated for 10 min. The ^{1}H NMR spectra of the complex was recorded to confirm the inclusion of the guest. The complex solu-

tion was then irradiated for the required time and the solution was treated with D_2SO_4 until the pH of the solution was <2. The precipitated guest was then extracted into $CDCl_3$ and the organic layer was concentrated and the residue was dissolved in isopropanol. The enantiomeric excess was determined by HPLC analysis of the corresponding methyl ester derivatives.

4.9.2. Water insoluble complexes

To a solution of 2 mg of the guest dissolved in ~1 mL of diethyl ether, was added a saturated solution of the corresponding host (120 mg in ~3–5 mL water) and stirred overnight. The resulting precipitate was filtered, washed with water and diethyl ether. The solids were then dried in air and then irradiated as hexane slurry or in the solid state for the required time. The irradiated sample was then suspended in water (the solids were filtered in the case of hexane slurry) and the photoproducts were extracted using ethyl acetate. The organic layer was then concentrated and the residue dissolved in isopropanol and the enantiomeric/diastereomeric excess was analyzed by HPLC.

4.10. Analysis conditions

HPLC and GC conditions for photoproducts of substrates are given below. All the samples were monitored at 240 or 254 nm. The solvent composition of the eluent and the retention times for individual diastereomers are listed below:

5b: HPLC-chiralcel-OD, mobile phase: 98:02 hexane to isopropanol; flow rate = 0.3 mL/min; λ_{max} = 240 nm; retention time of enantiomers: 121.2 and 132.3 min.
5c: HPLC-chiralcel-OD, mobile phase: 98:02 hexane to isopropanol; flow rate = 0.3 mL/min; λ_{max} = 240 nm; retention time of enantiomers: 71.2 and 79.3 min.
6c: HPLC-chiralcel-OD, mobile phase: 98:02 hexane to isopropanol; flow rate = 0.6 mL/min; λ_{max} = 254 nm; retention time of enantiomers: 20.1 and 22.5 min.
7c: GC-βdex 350, Initial temperature = 100 °C; initial time = 1 min; rate = 5 °C/min; final temperature = 158 °C; final time = 30 min; rate A = 20 °C/min; final temperature = 250 °C; final time = 5 min; retention time of enantiomers: 24.0 and 24.9 min.
8b: HPLC-chiralcel-OD, mobile phase: 90:10 hexane to isopropanol; flow rate = 0.7 mL/min; λ_{max} = 254 nm; retention time of enantiomers: 21.0 and 32.3 min.
9b: HPLC-chiralcel-OD, mobile phase: 90:10 hexane to isopropanol; flow rate = 0.7 mL/min; λ_{max} = 254 nm; retention time of enantiomers: 17.5 and 21.0 min.
10b: HPLC-chiralcel-OJ, mobile phase: 95:5 hexane to isopropanol; flow rate = 0.7 mL/min; retention time of diastereomers: 28.3 and 37 min.
11b: HPLC-chiralcel-AD, mobile phase: 85:15 hexane to isopropanol; flow rate = 0.5 mL/min; retention time of diastereomers: 46.0 and 53.0 min.
12b: HPLC-chiralcel-AD, mobile phase: 90:10 hexane to isopropanol; flow rate = 0.8 mL/min; retention time of diastereomers: 60.0 and 71.0 min.
13b: HPLC-chiralcel-OD, mobile phase: 80:20 hexane to isopropanol; flow rate = 0.5 mL/min; retention time of diastereomers: 24.3 and 30.0 min.
14b: HPLC-chiralpak-AD, mobile phase: 80:20 hexane to isopropanol; flow rate = 0.6 mL/min; retention time of diastereomers: 34.0 and 56.0 min.

Acknowledgments

We thank the National Science Foundation, USA for financial support (CHE-0213042 and CHE-0531802).

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