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Manipulating Photochemical Reactivity of Coumarins within Cucurbituril Nanocavities

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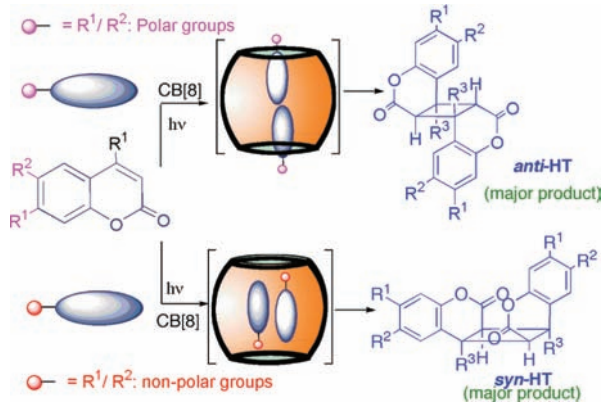
ABSTRACT



Coumarin derivatives that are either cationic (7-ammonium) or neutral (7-hydroxy, 7-methoxy, 6-methyl) form a 1:2 host−guest complex with cucurbit[8]uril (CB[8]). Direct irradiation of these coumarin@CB[8] complexes in water gives head-to-tail (HT) adduct as the major product. The nature of the functional group (polar or nonpolar) at the 6 or 7 position on the coumarin dictates the type of HT adduct (*syn-* or *anti-*). It is postulated that the available free volume and the hydrophobic confined environment are responsible for the observed selectivity.

Construction of new *nano* environments and their use as *nano*-reactors[1,2] has drawn the attention of chemists and photochemists[3–15] in this decade of *nano* revolution. Some of key factors that have to be considered before employing organized assemblies[3] to control photoreactivity within supramolecular environments are (a) available free space, (b) structural rigidity, and (c) type of nonbonding interaction that develops between the host and the guest. In our opinion cucurbiturils[6–13] not only satisfy the above requirements, but

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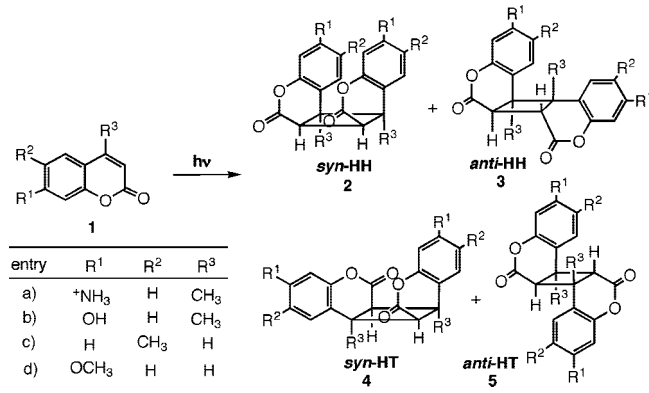
are also water-soluble making them appealing from an environmental perspective.

Cucurbiturils[6–13] have well-defined *nano*-cavities similar to those of cyclodextrins,[10,12] but have not been investigated to the same extent. Recent efforts by various groups, most notably those of Kim,[9,10] Day,[11] Isaacs,[8,12] and Kaifer[13] among others, have opened up new opportunities for using cucurbiturils as "*nano*-reaction vessels" to carry out various transformations.[16–19] Cucurbiturils (CBs) have been shown to be effective in manipulating photochemical reactivity of cationic stilbenes,[16,17] azastilbenes,[18] and cinnamic acid derivatives.[19] This prompted us to investigate the use of cucurbiturils to manipulate photochemical reactivity of both cationic and neutral coumarin derivatives.[20–28] It is well-established in literature that γ-CD forms a 1:2 host−guest complex with coumarins.[25] We reasoned that CB[8] with similar cavity volume[8,9] (479 Å^3) as that of γ-CD (cavity volume 427 Å^3), will be an ideal candidate and will most likely form a 1:2 host−guest complex with various coumarin derivatives. Understanding the supramolecular photochemical behavior of coumarin derivatives is critical in comprehending their use in biological systems[29] and as photocross-linking motifs for alignment in liquid crystal displays.[30]

As shown in Scheme 1, photoexcitation of coumarin derivatives leads to four different adduct,s[20–28] viz., *syn*-head-to-head (*syn*-HH, **2**), *anti*-head-to-head (*anti*-HH, **3**), *syn*-head-to-tail (*syn*-HT, **4**), and *anti*-head-to-tail (*anti*-HT, **5**). Pioneering studies done by various groups in the last four decades[20–28] have led to an understanding of the photoreactivity of coumarin derivatives that can be summarized as follows ($R^1 = R^2 = R^3 = H$):[20–28] (a) *syn*-HH adduct **2** is formed upon direct irradiation in polar solvents perhaps via a singlet excited state. (b) In nonpolar solvents, nonreactive self-quenching widely suppresses formation of any of the adducts. However, *syn*-HT adduct **4** is formed in detectable amounts. (c) *anti*-HH adduct **3** is formed in higher yield after triplet sensitized irradiation with benzophenone in both polar and nonpolar solvents. Trace amounts of the *anti*-HT adduct **5** are also formed.

Scheme 1. Photochemical Dimerization of Coumarin Derivatives



1

entry	R^1	R^2	R^3
a)	$^+NH_3$	H	CH_3
b)	OH	H	CH_3
c)	H	CH_3	H
d)	OCH_3	H	H

The above observations prompted the suggestion of a reactive spin state dependent selective formation of *anti* adducts from the triplet state (sensitized irradiation) and *syn* adducts from the singlet state (direct irradiation).[20–28] Due to the competing nonreactive self-quenching process, the dimerization quantum yield of coumarins is comparatively poor in most cases requiring long irradiation times (>24 h).[20–28] A variety of coumarin derivatives have been investigated in solution[20–23,27,28] as well as in constrained media, viz., crystalline environments,[24,31,32] cyclodextrins,[25,26] micelles,[33] and gold surfaces.[34] Extensive study of topochemical reactivity of coumarins in crystals has led to the structural characterization of coumarin adducts **2**−**5**.[24] All four adducts **2**−**5** of various coumarin derivatives have been characterized by X-ray crystallography.[20–28,32]

Preliminary results from our laboratory indicate that both neutral and cationic coumarins form a stable 1:2 host−guest complex with CB[8]. The coumarin@CB[8] host−guest complexes (**1**@CB[8]) were characterized by ^{1}H NMR spectroscopy (Figure 1) and by absorbance measuments (Job plot).[35] The observed upfield shift of olefinic as well as aromatic protons upon inclusion of **1a**@CB[8] were found to be consistent with the upfield shift of protons of CB[8] complexes with stilbenes and cinnamic acid derivatives reported in the literature.[16–19]

Irradiation of an aqueous solution of a coumarin@CB[8] host−guest complex (**1**@CB[8]) with UV light (>300 nm) produced *head-to-tail* (HT) adduct as the major product (Table 1). The photoproducts were characterized by NMR spectroscopy and were consistent with literature reports.[20–28,36] For 4-methyl-substituted coumarin derivatives

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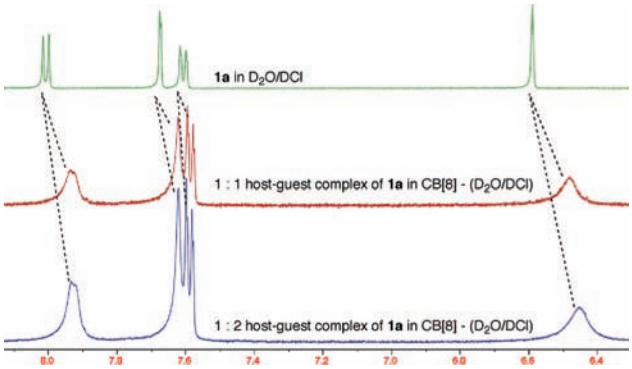

Figure 1. Complexation of **1a** with CB[8] characterized by ^{1}H NMR spectroscopy. Comparison of aromatic resonances. The methyl resonance shows comparable shift.[35]

($R^3 = CH_3$, Scheme 1) as in **1a** and **1b**,[24,25,32] it is well-established in literature that cyclobutyl protons for *anti* coumarin adducts resonate near δ 3.4 ppm with the corresponding methyl singlet resonance between δ 1.2 and 1.35 ppm, and for the *syn* adduct the cyclobutyl protons resonate near δ 3.6 ppm with the corresponding methyl singlet resonance between δ 1.6 and 1.7 ppm. As expected,[20,21] in the case of **1b**, direct irradiation in methanol gave *syn*-HH adduct **2b** with its characteristic methyl singlet resonance at δ 1.66 ppm.[35] As reported,[20,21] triplet-sensitized irradiation in methanol gave increased amounts of *anti*-HH adduct **3b** with its characteristic methyl singlet resonance at δ 1.24 ppm.[35] Irradiation of the inclusion complex of **1b**@CB[8] gave *anti*-HT adduct **5b** as the major product with its characteristic methyl singlet resonance at δ 1.33 ppm.[35] In the case of adducts from **1c** and **1d**, ^{1}H NMR signals of cyclobutyl protons[35] were compared with previously reported literature[27] values that clearly established the formation of *syn*-HT **4c** and **4d** as the major photoproduct, respectively. Product distribution was not dependent on the time of irradiation (Table 1).

Table 1. Photodimerization of Coumarin Derivatives **1a**−**d**

				product distribution[b]				
				HH		HT		
entry	compd	medium	time[a] (h)	**2**	**3**	**4**	**5**	HT/HH
1	**1a**	DCl-D_2O	36	70		19	11	0.43
2		CB[8]/DCl-D_2O	36	27		20	53	2.70
3	**1b**	CH_3OH	36	98	2			
4		CH_3OH/sens* [3]	36	75	25			
		H_2O	24		trace			
5		CB[8]/H_2O	36	32			68	2.13
6		CB[8]/H_2O	72	28			72	2.57
7	**1c**	$CDCl_3$	36	2	98			
		C_6H_6	36	2	98			
8		H_2O	24	trace	trace			
9		CB[8]/H_2O	24	31		69		2.22
10	**1d**	C_6H_6	36	trace				
11		H_2O	18	trace				
12		CB[8]/H_2O	18	30		70		2.33

[a] All irradiations were performed with a 450 W medium pressure Hg -lamp with <300 nm cut off filter. [b] Based on relative integration of ^{1}H NMR signals of the photoproducts. Reported values are based on an average of minimum 3 runs with ±5% error. Product yields were between 30% and 60% depending on the time of irradiation. The assignments of the dimer were based on previous literature reports. Photoreactions of coumarin in water were carried out under conditions similar to those of coumarin@CB[8] complex in water.

Irrespective of the coumarin derivative, within CB[8], the *head-to-tail* (HT) adduct was preferred as the major product. The type of HT adduct (*syn*- or *anti*-) formed within the cavity of CB[8] depended on the nature of coumarin substituents (Table 1). Coumarins with polar substituents (OH, H_3N^+) at the 7-position, as in **1a**,**b**, gave *anti*-HT **5** as the major photoproduct, and *syn*-HH **2** as the minor photoproduct (Table 1), while coumarins with nonpolar substituents (CH_3, OCH_3) at the 6- or 7-position, as in **1c**,**d**, gave *syn*-HT **4** as the major photoproduct, and *syn*-HH **2** as the minor photoproduct (Table 1). It should be emphasized that the photoproduct preferred within CB[8] was generally not preferred upon direct irradiation of coumarin in solution. This raises an interesting question regarding the preferential formation of *anti*-HT **5** with **1a**,**b** and *syn*-HT **4** with **1c**,**d** within CB[8].

To answer the question about the formation of *anti*-HT **5** as the major photoproduct in the case of **1a**,**b**, we looked at crystal structures of cyclobutane adducts **2**−**5** of different coumarin derivatives that have been reported in the literature.[24–27,32,36] Based on the available crystal structure as reference, different cyclobutane adducts corresponding to the **1b** derivative, i.e., **2b**−**5b**, were optimized at the RB3LYP/6-31G(d,p) level by using the Gaussian 03 package (Table 2).[37] The effective volume of each of the cyclobutane adducts **2b**−**5b** was computed from the corresponding optimized structure[35] and compared with the available volume in CB[8] (volume from X-ray structure is 479 Å^3).[8,9] It must be emphasized that the computed volume is expected to be higher than the volume calculated from the X-ray crystal structure as the optimization is done in the gas phase.[38] Upon comparison of available free volume within CB[8] and the volume of the adducts **2b**−**5b**, it is quite tempting to speculate that formation of *anti*-HT adduct **5b** will be preferred within the CB[8] cavity. As *syn*-HH **2b** is observed as the minor photoproduct, we believe that its effective

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Table 2. Computed Volume[a] for Coumarin Adducts **2**−**5**

compd	computed volume (Å^3)			
	syn-HH **2**	*anti*-HH **3**	*syn*-HT **4**	*anti*-HT **5**
adducts from **1b**	536	521	537	471 [430 [b]]
adducts from **1c**	254 [220 [b]]	274	265	307

[a] All optimizations were performed with the Gaussian 03 package (ref 37) at the RB3LYP/6-31G(d,p) level. The optimized structural coordinates are provided in the Supporting Information. [b] The values within parentheses have been computed from X-ray crystal structures available in the literature (ref 26 for *anti*-HT **5b**, ref 27 for *syn*-HT**2c**).

volume (Table 2) is comparable to the volume of CB[8]. Further, under direct irradiation within CBs, hindrance to the required orthogonal orientation[20–28] of coumarin monomers will prevent the formation of *anti*-HH **3b**.

Another issue to be addressed about the photoreactivity of coumarins within CB[8] is the preferential formation of *anti*-HT **5** with polar substituents as in **1a**,**b** and *syn*-HT **4** with nonpolar substituents **1c**,**d**. It is well established in literature[9,12] that guests molecules can be effectively templated when they interact with the carbonyl portals of CBs. We conjecture that the polar functional group (OH or H_3N^+) with the ability to form hydrogen bonds as in **1a**,**b** interacts with the carbonyl portal of CB[8] templating the preferential formation of *anti*-HT **5**. Coumarins with nonpolar functional groups (CH_3 or OCH_3) as in **1c**,**d** are expected not to have sufficient interaction with the carbonyl portal of CB[8] due to their hydrophobic nature (Figure 2). The hydrophobic interaction between coumarins **1c**,**d** and the CB[8] cavity results in the coumarin completely residing inside the nanocavity. In case of **1c**, based on the computed volume (Table 2), all four adducts **2c**−**5c** will be able to fit inside the CB[8] nanocavity. We believe that the hydrophobic interaction forces the coumarin monomers of **1c** to adopt a conformation that leads to the preferential formation of *syn*-HT **4** (Figure 2).

The ratio of the adducts HT/HH is ∼2 for all coumarin derivatives (Table 1, entries 2, 5, 6, 9, and 12) which indicates similar interactions determining product ratio within CB[8]. Our results indicate that both available volume and preorientation based on noncovalent interaction of coumarin monomers within the CB[8] cavity determine the nature of the coumarin adduct formed in the photoreaction. It is important to highlight the fact that the enhanced coumarin adduct within CB[8] is generally not observed in isotropic media under identical conditions. For example, in **1b** the *anti*-adduct in isotropic media is postulated to be formed via the triplet state, and is observed only under triplet-sensitized

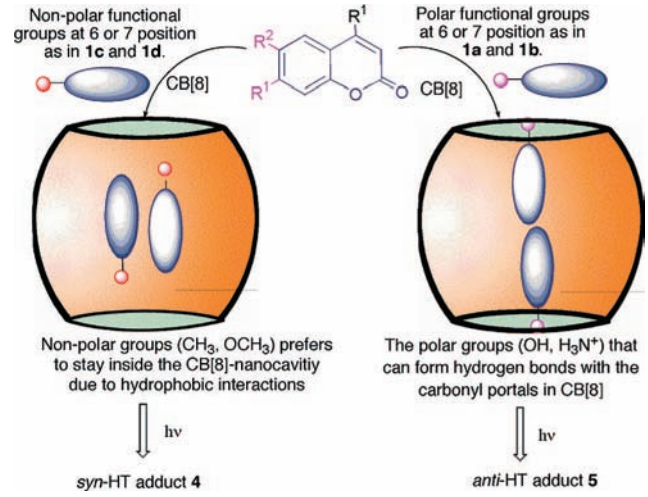

Figure 2. Cartoon representing the templating effect of CB[8] in the case of polar coumarin derivatives **1a**,**b** (right) and nonpolar coumarin derivatives **1c**,**d** (left).

irradiation conditions. As *anti*-HT **5b** is observed as the major product upon direct excitation of the **1b**@CB[8] complex, questions about teh nature of the reactive spin state arise.[20–28] Utilizing various photophysical techniques we are investigating the nature of the reactive spin state.

Modifying reaction pathways via supramolecular interactions to alter/improve existing reactivity and/or selectivity has inspired chemists for decades. In this regard, employing CBs to modify the photoreactivity of coumarin derivatives leading to preferential formation of HT adducts has opened up new opportunities for studying the role of the supramolecular environment in detail. To understand the nature of supramolecular interactions, inherent properties of coumarin@CB host−guest complexes are being explored by using various spectroscopic techniques (photophysical studies, NMR, etc.).

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Supporting Information Available: Experimental procedures, NMR spectra of photoproducts, and optimized geometric parameters. This material is available free of charge via the Internet at http://pubs.acs.org.

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