

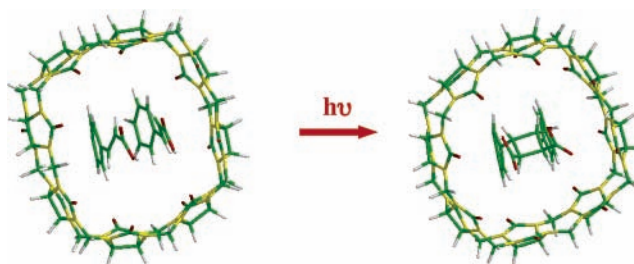
Templating Photodimerization of *trans*-Cinnamic Acids with Cucurbit[8]uril and γ -Cyclodextrin

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ABSTRACT



Cucurbit[8]uril and γ -cyclodextrin are able to align two olefin molecules in a head–head fashion within their large cavities. Excitation of such templated olefins results in *syn* head–head cyclobutanes in nearly quantitative yields. The methodology revealed here works with *trans*-cinnamic acids that do not dimerize either in solution or in the solid state and with the ones that yield only *anti* head–tail dimer in the solid state.

The reactions of *trans*-cinnamic acids are examples of [2 + 2] photodimerization that have been investigated extensively since 1889.¹ Some of these acids exhibit a dual behavior on photolysis dependent on the reaction medium. While in solution *trans*–*cis* isomerization occurs exclusively, on photolysis of the crystal these acids react to give dimeric products under conditions where the two reactive C=C bonds are within the topochemically stipulated distance (<4.2 Å) and parallel (Scheme 1).^{2,3} Most of the current efforts in solid-state photochemistry are devoted to establishing reliable strategies that would steer molecules so as to obtain a crystal structure that would favor photodimerization.⁴ In this paper, we establish the utility of cucurbit[8]uril (CB[8])⁵ and γ -cyclodextrin (γ -CD) in templating photodimerization of a variety of *trans*-cinnamic acids to a single isomer (*syn* head–head dimer) both in solution and the solid state. Remarkably,

the methodology reported here with CB[8] and γ -CD is general and works with a number of cinnamic acids that do not dimerize (γ -packing) and also with the ones that give *anti* head–tail dimers (α -packing) in solid state. Since CB[8] is known to include mostly cationic guest molecules, until now its scope as a reaction medium has been limited.

Photodimerization of C_2 -symmetric *trans*-diaminostilbene hydrochloride within CB[8] has recently been reported.⁶ As far as we are aware, neither neutral olefins nor olefins with different substituents have been included and aligned within CB[8]. We show in this report that CB[8] can include neutral

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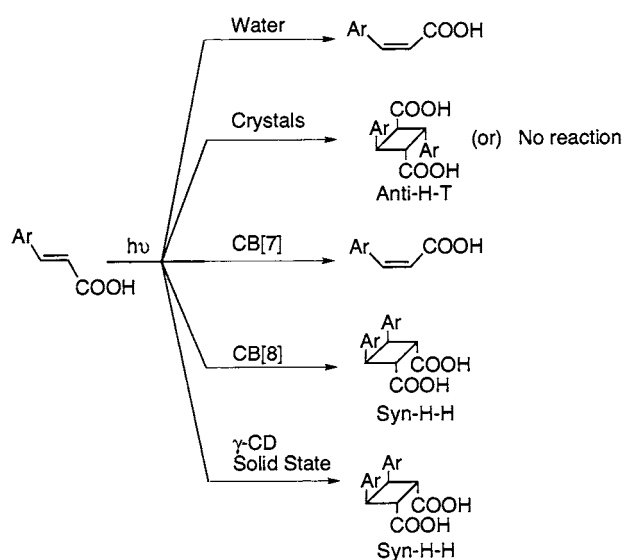
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Scheme 1



Ar = (1a) 3-MeO-C₆H₄; (1b) 3-Me-C₆H₄; (1c) 4-MeO-C₆H₄;
(1d) 4-Me-C₆H₄; (1e) H-C₆H₄; (1f) 4-HO-C₆H₄; (1g) 4-NH₃⁺-C₆H₄ Cl⁻

guest molecules such as cinnamic acids and that the resulting host–guest complexes are soluble enough in water to conduct photochemical studies (Tables 1 and 2). We further provide

Table 1. Photochemistry of *trans*-Cinnamic Acids That Are Photoinactive in the Solid State

| host/guest | guest/host ^a | syn H–H ^b (%) | cis ^b (%) |
|---|-------------------------|--------------------------|----------------------|
| 3-MeO-<i>t</i>-CA (1a)^c | | | |
| CB[8] solution | 2:1 | 72 | 28 |
| CB[8] solid state | 1:1 | 78 | 22 |
| γ-CD solid state | 2:1 | 96 | 4 |
| 3-Me-<i>t</i>-CA (1b)^c | | | |
| CB[8] solution | 2:1 | 83 | 17 |
| CB[8] solid state | 1:1 | 45 | 55 |
| γ-CD solid state | 2:1 | 99 | 1 |
| 4-MeO-<i>t</i>-CA (1c)^c | | | |
| CB[8] solution | 2:1 | 72 | 28 |
| CB[8] solid state | 1:1 | 48 | 52 |
| γ-CD solid state | 2:1 | 100 | |

^a Mixing ratios of the host and the guest; stoichiometry of the complexes are unknown at this time. ^b Yields reported are based on NMR integration at 100% conversion; ¹H NMR spectra of the irradiated samples are provided in the Supporting Information. ^c Irradiation in the crystalline state leads to no photoreaction.

a simple technique to include even water-insoluble neutral guests within CB[8] to pursue photochemistry in the solid state. *trans*-4-Aminocinnamic acid hydrochloride **1g** is a highly water-soluble cationic olefin. A comparison of ¹H NMR spectra of this compound in D₂O, D₂O–CB[7], and D₂O–CB[8] presented in Figure 1 suggests the inclusion of this olefin into the cavities of host CB[7] and CB[8]. Observed upfield shifts of olefinic as well as aromatic protons of *trans*-4-aminocinnamic acid hydrochloride upon inclusion

Table 2. Photochemistry of *trans*-Cinnamic Acids That Yield *Anti* H–T Dimer upon Irradiation in the Solid State

| host/guest | guest/host ^a | <i>anti</i> H–T ^b (%) | <i>syn</i> H–H ^b (%) | <i>cis</i> ^b (%) |
|--|-------------------------|----------------------------------|---------------------------------|-----------------------------|
| 4-Me-<i>t</i>-CA (1d) | | | | |
| crystals | | 100 | | |
| CB[8] solid state | 1:1 | 66 | 15 | 19 |
| | 1:3 | 46 | 26 | 28 |
| | 1:5 | 32 | 39 | 29 |
| CB[7] solid state | 1:1 | 80 | | 20 |
| γ-CD solid state | | | | |
| 2:1 | | | 100 | |
| <i>t</i>-CA (1e) | | | | |
| crystals | | 100 | | |
| CB[8] solution | 2:1 | | 54 | 46 |
| | 1:5 | 19 | 29 | 52 |
| CB[7] solid state | 1:1 | 68 | | 32 |
| γ-CD solid state | 2:1 | | 99 | 1 |
| 4-HO-<i>t</i>-CA (1f) | | | | |
| crystals | | 100 | | |
| CB[8] solution | 2:1 | | 38 | 62 |
| | 1:3 | 24 | 48 | 28 |
| γ-CD solid state | 2:1 | | 99 | 1 |
| 4-NH₃⁺-C₆H₄ Cl⁻ (1g) | | | | |
| crystals | | 100 | | |
| CB[8] solution | 1:2 | | 88 | 12 |
| | 1:1 | 68 | 14 | 18 |

^a Mixing ratios of host and guest; stoichiometry of the complexes are unknown at this time. ^b Yields reported are based on NMR integration at 100% conversion; ¹H NMR spectra of the irradiated samples are provided in the Supporting Information.

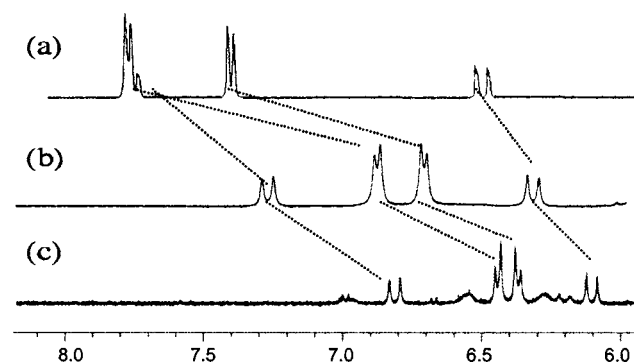


Figure 1. ¹H NMR spectrum of **1g**: (a) in D₂O; (b) in the presence of 2 equiv of CB[7]; (c) in the presence of 1.5 equiv of CB[8].

within the cavities of cucurbiturils are consistent with the literature reports on cucurbituril complexes of viologens⁷ and *trans*-diaminostilbene hydrochloride.⁶ Irradiation of *trans*-

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4-aminocinnamic acid hydrochloride in aqueous solution yields the corresponding *cis* isomer, and upon irradiation as crystals the only product obtained was the *anti* head–tail dimer (Table 2). Remarkably, irradiation of *trans*-4-aminocinnamic acid hydrochloride (0.02 M) included in CB[8] (0.01 M) in aqueous solution gave the *syn* head–head dimer along with the corresponding *cis* isomer of the olefin. It is thus clear that the larger cavity of CB[8] accommodates two molecules of *trans* 4-aminocinnamic acid hydrochloride and aligns them in a geometry favorable for formation of the *syn* head–head dimer. As expected, irradiation of *trans*-4-aminocinnamic acid hydrochloride–CB[7] complex, a host with a smaller cavity (similar to that of β -cyclodextrin), produced only the corresponding *cis* isomer.

Computed structures at the AM1 level for complexes of *trans*-4-aminocinnamic acid hydrochloride (and dimers) with CB[7] and CB[8] are provided in Figures 2 and 3.⁸

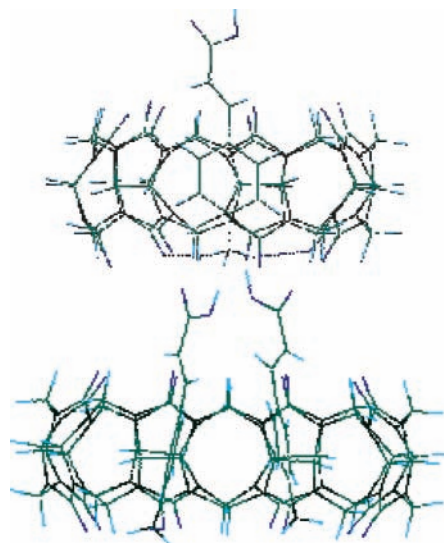


Figure 2. Computed structures at the AM1 level for complexes of *trans*-4-aminocinnamic acid hydrochloride with (top) CB[7] and (bottom) CB[8]. Note that only one molecule fits within CB[7] and two molecules in a head–head geometry within CB[8].

These structures are revealing in terms of what can be accomplished with CB[7] and CB[8]: (a) CB[7] is able to

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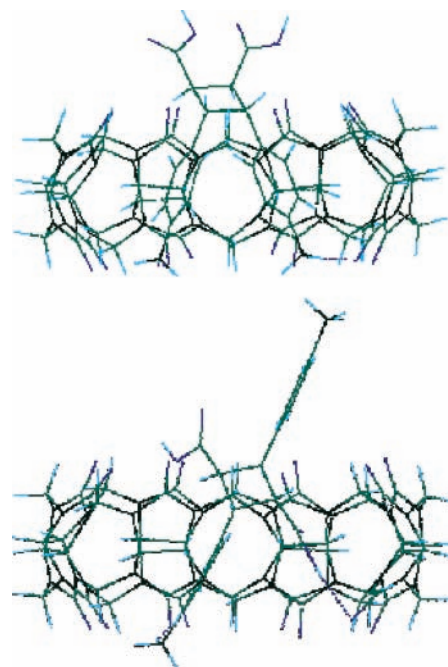


Figure 3. Computed structures (at the AM1 level) of complexes of (top) *syn* head–head and (bottom) *anti* head–tail dimers of *trans*-4-aminocinnamic acid hydrochloride within CB[8]. Note that while the *syn* head–head dimer fits nicely within CB[8], in the case of the *anti* head–tail dimer half the molecule projects outside the cavity.

include only one molecule whereas CB[8] accommodates two (Figure 2). (b) As per computations, alignment of two olefins in a head–head fashion is favored within a CB[8] cavity. (c) When a structure with head–tail arrangement was minimized, one of the olefins tended to stay at the rim of CB[8] suggesting that host–guest complexes do not prefer head–tail arrangement of cinnamic acids. (d) While the *syn* head–head dimer easily fits within CB[8], the *anti* head–tail dimer does not (Figure 3). Qualitative reasoning based on AM1 calculations is consistent with the model that CB[8] can template cinnamic acids to form *syn* head–head dimers.

In Tables 1 and 2 are presented the results of seven cinnamic acids based on their solid-state reactivity. The first group of cinnamic acids, 3-methoxy-, 3-methyl-, and 4-methoxycinnamic acids, do not dimerize or isomerize in the solid state. They only isomerize in solution (Table 1). However, irradiation of the host–guest complexes of cinnamic acids (6×10^{-5} M) in CB[8] (3×10^{-5} M) both in solution and in the solid state resulted in a single dimer (*syn* head–head) (>70%). Although minor amounts (30%) of *cis* isomer were also formed no other dimers were detected by ^1H NMR. The host–guest complex was obtained by sonication (30 min) of the water-insoluble CB[8] in an aqueous solution of the above cinnamic acids. The clear solution obtained indicated the complexation of the water-soluble neutral guests with the water insoluble host. Consistent with the model that larger cavities of CB[8] is critical to inclusion and alignment of

two molecules, use of CB[7] as the host gave only the *cis* isomer. To establish the generality of CB[8] as a templating agent we explored the use of solid complexes. The complex was prepared by mechanically grinding of the host CB[8] (80 mg; 6×10^{-4} mol) and the guest cinnamic acids (10 mg; 1.5×10^{-5} mol) together with an agate pestle and mortar.⁹ Irradiation of these solid complexes gave only the *syn* head–head dimer with minor amounts (15%) of the *cis* olefin. Irradiation of complexes of these cinnamic acids in CB[7] accomplished by a similar grinding method gave the *cis* olefins only. The absence of any product on irradiation of pure olefin crystals and the *syn* head–head dimers and *cis* olefins obtained as complexes of CB[8] and CB[7] clearly indicate inclusion of the cinnamic acids within these hosts through the solid-state grinding technique.

The second group of olefins consists of 4-methyl- and 4-hydroxycinnamic acid derivatives that yield the *anti* head–tail dimer in the crystalline state (Table 2). Of these, the host–guest complex of 4-methylcinnamic acid that is not soluble in water could only be prepared by the “grinding” technique. Consistent with the above observations, irradiation of CB[8] complexes of cinnamic acid and 4-hydroxycinnamic acid in water and as solid complexes gave the corresponding *syn* head–head dimer along with the *cis* isomer of the olefin (Table 2). Since the uncomplexed crystals gave *anti* head–tail dimer, to avoid complication from photoreactions from pure crystals that produce *anti* head–tail dimer use of excess host that would eliminate any uncomplexed crystalline guest was attempted. Although the yields of *syn* head–head dimer depend on the amount of the host, even the 5-fold excess of the host failed to eliminate completely formation of the *anti* head–tail dimers (Table 2, CB[8] solid-state entries). The fact that the amount of *syn* head–head dimer increased with the host amount we believe that CB[8] is orienting even these olefins in a head–head fashion. Only crystal structure determination of the complexes would unequivocally solve this problem. Irradiation of CB[7] complexes with all seven cinnamic acids listed in Tables 1 and 2 resulted in the *cis* isomer only reinforcing the requirement of a larger cavity for dimerization.

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From the presentation above it is clear that the CB[8] cavity dimension similar to that of γ -CD has the ability to include two molecules of cinnamic acids and align them in such a way to yield only a *syn* head–head dimer. Now the question arises whether γ -CD itself can behave like CB[8]. All six neutral cinnamic acids investigated here formed complexes with γ -CD but these were not soluble in water. Therefore, irradiation of these as solids gave the *syn* head–head dimer in very high yield (>95%). Unlike in the case of CB[8] geometric isomerization was only a very minor pathway (<5%; Tables 1 and 2). Cyclodextrin complexes could not be formed by grinding cinnamic acids with γ -CD although they are readily prepared by stirring aqueous solutions of γ -CD with saturated ethyl acetate solution of the guest. Cavities of CB[8] and γ -CD can preorganize cinnamic acids toward a single dimer, and this approach compliments the novel methods reported recently for pre-organizing C_2 -symmetric olefins.⁴ The method reported here for templating nonsymmetric olefins is superior to the ones reported previously where only partial success has been achieved.¹⁰

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Supporting Information Available: Experimental details, NMR spectral data for photodimers, molecular structures of the hosts and details of AM1 computation are provided in the Supporting Information. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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