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Stereoselective Photodimerization of (*E*)-Stilbenes in Crystalline γ-Cyclodextrin Inclusion Complexes

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Solid-state irradiation of the crystalline inclusion complex of (*E*)-stilbene in γ-cyclodextrin (γ-CD) yields a single isomer of *syn*-tetraphenylcyclobutane stereoselectively in high yield. In contrast, the photodimerization of stilbene in solution is very inefficient and unselective, and no photodimer is observed even upon prolonged irradiation of pure crystals. The monosubstituted stilbenes form a pair of photodimers stereoselectively, viz. the syn head-to-head and syn head-to-tail isomers, in comparable yields. The photodimer yields of about 70% and the biphasic decay kinetics of the excited stilbene (as established by picosecond time-resolved diffuse-reflectance spectroscopy) indicate that the stilbene guests are located in at least two distinct sites in the γ-CD crystal lattice, i.e., a *dimerization site* where excited stilbene is in close reach of another stilbene guest molecule and an *isomerization site* where excited stilbene does not find a close neighbor for dimerization and thus undergoes trans → cis isomerization only.

Introduction

Cyclodextrins (CDs) form cage-type or channel-type crystal lattices depending on whether they crystallize from water as hydrates or in the presence of excess guest molecules as inclusion complexes.[1] As a result, CD crystal structures exhibit well-defined cavities of varying sizes and shapes that can be occupied by a variety of organic and inorganic guest molecules[2,3] and are thus utilized as rigid microvessels for thermal as well as photochemical reactions.[4] Crystalline cyclodextrins are typical examples of highly organized and constrained reaction media that are frequently exploited to improve the efficiency and selectivity of photoreactions.[4−6] However, only a few studies on bimolecular photoreactions in solid CD inclusion complexes have been reported that clearly demonstrate improved stereo- and/or regioselectivity (including cycloadditions and photoreductions)[7−9] as compared to the corresponding reactions carried out in solution.

In this study, we report the effects of the crystalline γ-cyclodextrin environment (see Figure 1) on the efficiency and stereoselectivity of the photodimerization of stilbene and its derivatives. Stilbenes are excellent candidates to demonstrate the modulation of photochemical reactivity by solid-state host/guest interactions for the following reasons: (i) Stilbenes exhibit a diverse photochemical behavior in solution that includes reversible trans → cis isomerization, cyclization to dihydrophenanthrene, and dimerization to yield tetraphenylcyclobutane products.[10,11] The latter pathway is extremely inefficient in solution;[12] it leads to a mixture of stereoisomers of tetraphenylcyclobutanes in low yields[12−14] and is thus a good proving ground to test enhanced efficiency and selectivity in the solid state. (ii) Stilbenes form readily inclusion complexes with cyclodextrins,[15,16] which can be isolated in crystalline form as shown in this study. (iii) Irradiation of diammonium-substituted stilbene in aque-

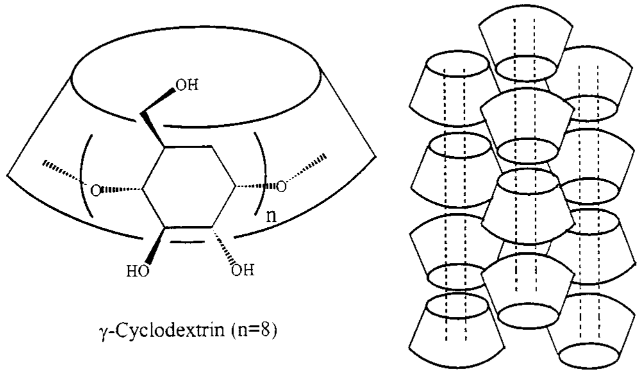

Figure 1. Schematic presentation of (left) the toroidally shaped structure of γ-cyclodextrin and (right) the channel-type crystal lattice of its inclusion complexes.

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(12) (a) Even at concentrations as high as 0.5 M, irradiations of (*E*)-stilbene in benzene for 2 months yielded only 27% conversion into cyclobutane products.[13] (b) Note that somewhat better dimerization efficiencies have been achieved in water[16a] and in other hydroxylic solvents such as methanol[14] due to the hydrophobic effect.[12c] (c) Tanford, C. *The Hydrophobic Effect*; Wiley: New York, 1980.

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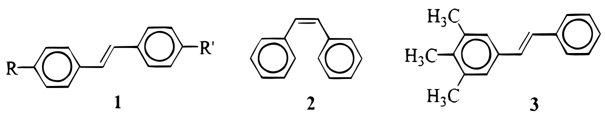
Chart 1



1a. R = H, R' = H; **1b.** R = OCH_3, R' = OCH_3

1c. R = CH_3, R' = H; **1d.** R = Cl, R' = H

1e. R = OCH_3, R' = H; **1f.** R = CN, R = H

Table 1. Isolation of γ-CD/Stilbene Inclusion Complexes and Host/Guest Ratios[a]

	host/guest molar ratio		
stilbene[b]	method A[c]	method B[d]	mass balance[e] (%)
1a	1:1.75	1:1.60	92
1b	1:1.70	1:1.65	91
1c	1:1.80	1:1.70	94
1d	1:1.95	1:1.85	83
1e	1:1.77	1:1.70	90
1f	1:1.80	1:1.70	88
2	1:0.90	1:0.95	48
3	1:0.85	1:0.86	43

[a] Inclusion complexes were prepared by the addition of γ-CD and stilbene in a molar ratio of 1:2.3. [b] Identified in Chart 1. [c] Ratios determined from the ^1H NMR spectra of the inclusion complexes. [d] Ratios obtained from the relative masses of γ-CD and stilbene in the inclusion complex. [e] Mass balance of the precipitated inclusion complex: % mass balance = 100 × (mg inclusion complex/mg γ-CD + mg stilbene).

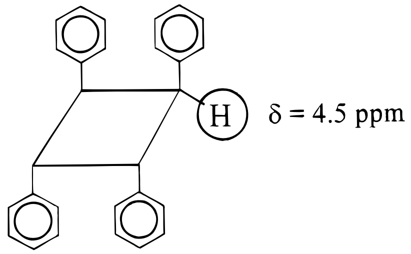
ous γ-CD solution yields two stereoisomeric cyclobutane products in good yields.[15] (iv) All stilbenes in this study do not undergo photodimerizations in the neat crystalline state (see the Discussion).[28] Thus, a series of crystalline γ-CD inclusion complexes with the substituted stilbenes in Chart 1 are irradiated by steady-state and time-resolved (diffuse-reflectance) techniques to explore the stereo- and regioselectivity in the formation of the cyclobutane photoproducts as well as the reaction dynamics of excited stilbene in the solid-state inclusion complexes.

Results

I. Formation and Characterization of the Crystalline Stilbene/γ-Cyclodextrin (γ-CD) Inclusion Complexes. When a concentrated solution of (*E*)-stilbene (**1a**, 1.6 mmol) in ethanol (10 mL) was added to a saturated solution of γ-cyclodextrin (γ-CD, 0.7 mmol) in water and stirred for 12 h, a fine white microcrystalline precipitate formed, which was isolated after thorough washing with ether and cold water. This white precipitate was considered to be the stilbene/γ-CD inclusion complex since (i) the stilbene/γ-CD molar ratio was highly reproducible from batch to batch (vide infra) and (ii) the stilbene component could not be removed by extensive washing with ether. The mass balance between the starting material and the isolated precipitate revealed the inclusion complex of stilbene (**1a**) in γ-CD to be formed in 92% yield (see Table 1).

The molar ratio between the γ-CD host and the stilbene guest was determined by both the ^1H NMR spectroscopic analysis (method A)[16,17] and from the mass of the (*E*)-stilbene in the precipitate as determined by decomplexation (method B, see the Experimental Section). For example, the characteristic NMR signals (doublets at δ 4.9 ppm)[17] of the C_1H protons of the glucose units in the γ-CD were quantitatively compared with the signals of the aromatic protons of stilbene **1a,** which led to a host/guest ratio of 1:1.75. This host/guest ratio was in reasonable agreement with the ratio of 1:1.60 obtained from the mass analysis of the (*E*)-stilbene extracted from the pure complex. Similar procedures were applied for the preparation and analysis of the γ-CD inclusion complexes of the other (substituted) stilbenes in Chart 1, and the molar host/guest ratios and yields of the inclusion complexes are given in Table 1. In all cases, the γ-cyclodextrin and stilbene solutions were mixed together in a molar ratio of 1:2.3. Slightly lower host/guest ratios were obtained when the stilbene and the γ-CD were added in a precise 2:1 molar ratio. On the other hand, addition of stilbene in a higher excess than a factor of 2.3 did not increase the host/guest ratios in Table 1. Interestingly, the host/guest ratios obtained for the stilbenes **2** and **3** in Chart 1 did not exceed 1:0.90 and 1:0.85, respectively.

Chart 2



II. Photodimerization of Stilbene in the γ-CD Inclusion Complexes and Characterization of the Cyclobutane Photoproducts. The microcrystalline γ-CD complex of (*E*)-stilbene (**1a**, 770 mg) was irradiated in a Rayonet photochemical reactor at λ = 330 nm. After 24 h of photolysis, the complex was dissolved in 30 mL of distilled water saturated with NaCl at 50 °C, and the organic contents were extracted into chloroform. Analysis of the crude reaction mixture by GC and ^1H NMR (vide infra) indicated the formation of the photodimer 1,2,3,4-tetraphenylcyclobutane and (*Z*)-stilbene. Separation of the crude reaction mixture by column chromatography yielded the photodimer and (*Z*)-stilbene in 48% and 10% yield, respectively. Prolonged irradiation (up to 72 h) of the stilbene/γ-CD complex did not further improve the yields. Most importantly, only one (out of four possible) tetraphenylcyclobutane isomer was found as photoproduct, and it was identified as the syn isomer (see Chart 2) by ^1H NMR spectroscopy and X-ray crystallography. Thus, the NMR spectrum showed a singlet at δ 4.5 ppm, which was characteristic of cyclobutane protons,[13a] and the syn stereochemistry was unambiguously determined by X-ray structural analysis of a single crystal (see the Experimental Section).[18] Similarly, photolysis of the microcrystalline complexes of γ-CD with stilbene **1b** and the monosubstituted (*E*)-stilbenes (**1c**−**f**) afforded photodimers as the major products in addition to small amounts (<10%) of the corresponding (*Z*)-stilbenes, which were also isolated (see Table 2). On the basis of the chemical shift of the cyclobutane protons in the NMR spectra, the syn configuration was assigned to all photodimer products (see the Experimental Section).[13,14,19,20]

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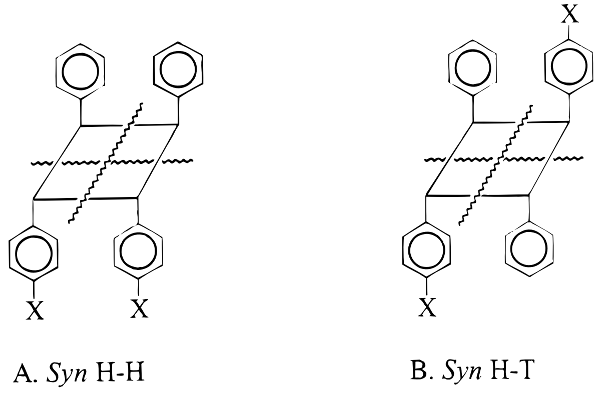
Table 2. Steady-State Photolysis of Stilbene/γ-CD Inclusion Complexes[a]

	isolated yield[c] (%)				photo-
stilbene[b]	(*E*)-stilbene	(*Z*)-stilbene	syn photodimer	H–T:H–H[d]	dimer yield[e] (%)
1a	22	10	48	*f*	61
1b	40	9	42	*f*	70
1c	38	6	46	57:43	72
1d	36	(trace)	52	55:45	79
1e	29	10	42	60:40	59
1f	22	9	60	54:46	76
2	23	64	0	*g*	0
3	66	18	0	*g*	0

[a] Photolysis ($\lambda = 330$ nm) of the inclusion complexes was carried out for 24 h at room temparature. [b] Identified in Chart 1. [c] Based on the amount of stilbene present in the inclusion complex prior to irradiation. [d] Molar ratio between head-to-tail and head-to-head isomers as determined by gas chromatography using *p*-methylanisole as internal standard. [e] Based on the conversion of stilbene in the photoreaction. [f] No distinction between H–H and H–T isomers. [g] No photodimers obtained.

Chart 3



A. *Syn* H-H B. *Syn* H-T

GC analysis revealed that monosubstituted stilbenes formed two distinct *syn*-cyclobutane isomers in about equal amounts. These two photodimers were identified as the syn head-to-head (H–H) and the syn head-to-tail (H–T) isomers (see Chart 3) by a careful analysis of the fragmentation pattern of their mass spectra as follows: The H–H isomers showed three major components in their mass spectra that were assigned to the unsubstituted, monosubstituted, and disubstituted stilbene as the result of fragmentation of the cyclobutane isomer **A** along the wavy lines in Chart 3. In contrast, isomer **B** (see Chart 3) could only form one (monosubstituted) stilbene fragment regardless of the fragmentation mode.

In the case of the *p*-cyanostilbene/γ-CD complex, the two isomers (syn H–H and syn H–T) could be separated by column chromatography (see the Experimental Section). In addition to the mass-spectral fragmentation pattern, ^{1}H NMR spectroscopy was utilized to identify the isomers. Thus, the cyclobutane protons of the syn H–T dimer appeared as a singlet at δ 4.55 ppm, whereas those of the syn H–H dimer exhibited an A_2B_2 pattern with two doublets centered at δ 4.40 and 4.60 ppm in good agreement with the spectra reported in the literature.[14] In all cases, the two syn photodimers (H–H and H–T) were formed in comparable yields (see Table 2). In addition, the ratio of syn (H–H) and syn (H–T) isomers did not change with time over prolonged irradiation periods as established for the *p*-methylstilbene/γ-CD complex.

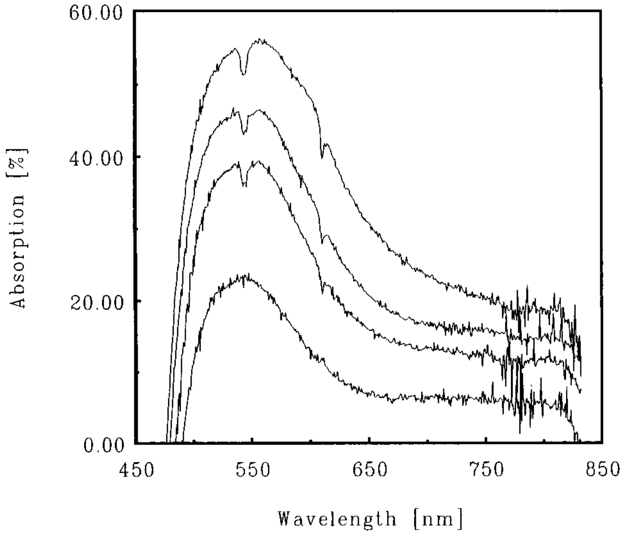


Figure 2. Transient absorption spectra recorded at (top-to-bottom) 50, 350, 1000, and 4000 ps following the 25-ps laser excitation (at 355 nm) of crystalline stilbene**1a**/γ-CD inclusion complex showing the decay of stilbene excited singlet state.

In contrast, photolysis of (*Z*)-stilbene (**2**) and the trimethyl-substituted stilbene (**3**) as crystalline γ-CD complexes resulted in the formation of isomerization products only, and no photodimers were found in the reaction mixture even after prolonged irradiation periods. Note that in these complexes the host/guest molar ratio was about H:G $\approx$ 1:1 as opposed to that of the other stilbenes (H:G $\approx$ 1:2, see Table 1). All stilbenes in Table 2 were also irradiated under the same conditions as (i) neat crystals and (ii) dissolved in benzene solution (0.3 M). However, no photoproducts were obtained in the solid state, and inefficient, unselective photoreactions were observed in solution.[12,13]

III. Picosecond Time-Resolved Laser Flash Photolysis. The crystalline inclusion complex of stilbene (**1a**) in γ-CD was exposed to the third-harmonic (355 nm) laser pulse of a mode-locked Nd:YAG laser (25-ps pulse width). At this wavelength, only stilbene absorbed the laser light. The transient absorption spectra were recorded in the diffuse-reflectance mode (see the Experimental Section) at various times after the laser excitation. As shown in Figure 2, the transient spectra showed a broad absorption band with maximum at 570 nm and a tail reaching far into the red wavelength region beyond 700 nm. At shorter wavelengths (below 480 nm), a strong emission was detected, which appeared to extend beyond the blue edge of the detection system (at 400 nm). On the basis of the similarity with the transient absorption spectra of excited (*E*)-stilbene recorded in dichloromethane solution ($\lambda_{max} = 590$ nm, see Table 3), in heptane solution ($\lambda_{max} = 580$ nm),[21] and in acetonitrile solution ($\lambda_{max} = 575$ nm),[22] we assign the absorption signals to the excited singlet state of (*E*)-stilbene (**1a**). Interestingly, no emission was observed in dichloromethane solution. Instead, a second (weaker) absorption band at 480 nm was observed.[22] Whether a similar 480-nm absorption band was or was

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(21) Shkurinov, A. P.; Koroteev, N. I.; Jonusauskas, G.; Rulliere, C. *Chem. Phys. Lett.* **1994**, *223*, 573.

(22) As a possible assignment for this absorption band, the stilbene excimer has been considered, but no unambiguous experimental proof could be provided. See: Peters, K. S.; Freilich, S. C.; Lee, J. *J. Phys. Chem.* **1993**, *97*, 5482.

Table 3. Spectral Data and Decay Kinetics of the Stilbene (Singlet) Excited States inDichloromethane (DCM) and in γ-CD Inclusion Complexes[a]

	transient absorption maximum (nm)		decay rate constants (s^{-1})			
				γ-cyclodextrin		
stilbene[b]	γ-CD	DCM	DCM	k_1[c,f]	k_2[d,f]	R[e,f]
1a	565	590	$\geq 4.0 \times 10^{10}$	2.9×10^9	1.8×10^8	20:80
				(3.0×10^9)	(2.0×10^8)	(57:43)
1b	580	*g*	*g*	4.6×10^9	4.1×10^8	26:74
1c	600	590	$\geq 4.0 \times 10^{10}$	6.8×10^9	1.8×10^8	21:79
1d	565	600	2.4×10^{10}	6.2×10^9	5.9×10^8	52:48
				(5.5×10^9)	(3.1×10^8)	(80:20)
1e	580	560	1.6×10^{10}	1.5×10^9	1.3×10^8	45:55
				(1.5×10^9)	(−)	(100:0)
1f	580	550	$\geq 4.0 \times 10^{10}$	3.3×10^9	2.9×10^8	40:60
				(5.3×10^9)	(7.0×10^8)	(67:33)
3	576	*g*	*g*	1.4×10^9	1.7×10^8	69:31

[a] Measured by time-resolved (ps) spectroscopy upon 25-ps laser excitation at 355 nm. [b] Identified in Chart 1. [c] First-order rate constant for fast decay component. [d] First-order rate constant for slow decay component. [e] Ratio of fast and slow component as determined by their initial relative absorbance (A_0) at time $t = 0$ ps ($R = A_{0,\text{fast}}$ (%):$A_{0,\text{slow}}$ (%)). [f] Values for preirradiated samples in parentheses (see text). [g] Not measured in DCM.

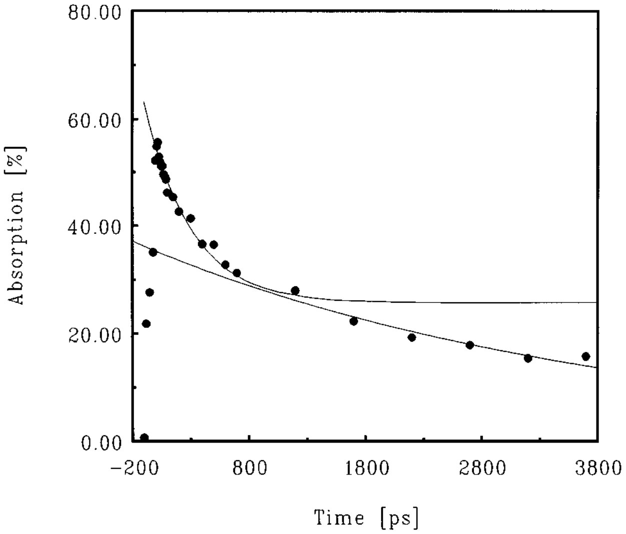

Figure 3. Biphasic decay of stilbene excited singlet state in the crystalline stilbene/γ-CD inclusion complex. The solid lines represent the best exponential fits of the data points for the fast and slow decay component.

not present in the transient diffuse-reflectance spectrum of the solid-state stilbene/γ-CD complex could not be examined owing to the strong emission that interfered with the detection of transient absorption signals below 490 nm (see Figure 2).

The transient spectra of excited stilbene in the γ-CD inclusion complex decayed completely to the spectral baseline on the picosecond and early nanosecond time scale in a biphasic manner (see Figure 3), and the biexponential fit of the data points yielded two first-order rate constants of $k_{\text{fast}} = 2.9 \times 10^9$ s^{-1} and $k_{\text{slow}} = 1.8 \times 10^8$ s^{-1}. In contrast, the transient absorption spectra of excited stilbene in dichloromethane decayed very rapidly with a rate constant exceeding the time resolution of the laser spectrometer ($k > 4 \times 10^{10}$ s^{-1}). Similar transient spectra were obtained for the substituted stilbenes (**1b**–**f**) in γ-CD, and they closely resembled the corresponding spectra in dichloromethane solution (see Table 3). A comparison of the decay patterns of the transient spectra in crystalline γ-CD and in dichloromethane solution again revealed characteristic differences in the kinetics. For example, stilbenes **1d** and **1e** in dichloromethane solution decayed following first-order kinetics, and rate constants of 1.6×10^{10} and 2.4×10^{10} s^{-1} were determined, respectively. In contrast, the decay traces in the γ-CD samples exhibited a biphasic behavior as observed for unsubstituted stilbene in Figure 3, and the rate constants for the fast and the slow decay components differed by about 1 order of magnitude (see Table 3). Also shown in Table 3 are the ratios R between the absorbance of the fast component and that of the slow component, which varied substantially for the various stilbenes. In general, the lifetimes of the excited stilbenes in dichloromethane solution were within or close to the time resolution of the kinetic spectrometer (25 ps), and the rate constants determined in the crystalline γ-CD samples were at least 1 order of magnitude slower than those measured in dichloromethane solution (see Table 3). In both media, the rate constants varied somewhat with the stilbene substituents, but did not reveal any perceptible trend. In no case did the transient absorption signals persist beyond 5 ns.

The time-resolved diffuse-reflectance measurements were also carried out with preirradiated samples of crystalline stilbene/γ-CD inclusion complexes.[23] For a complete comparison, new batches of stilbene/γ-CD complexes were prepared and divided into three samples. The first sample was used to determine the host/guest ratios which were in close agreement with those determined earlier (see Table 1). The second sample was irradiated for 72 h prior to time-resolved diffuse-reflectance measurements, and the photodimer yields were determined by quantitative NMR measurements. The third sample was examined by laser flash photolysis without preirradiation. A careful comparison of the biphasic decays observed upon laser photolysis of preirradiated and unirradiated samples revealed that the relative amounts of the slow component decreased at least by 50% upon preirradiation, whereas the decay rate constants remained more or less the same (see Table 3). In fact, in the case of methoxystilbene (**1e**) the slow component disappeared completely in the decay kinetics of the preirradiated sample, and a monoexponential decay was observed with a rate constant of $k = 1.5 \times 10^9$ s^{-1}, which was identical to that of the fast component in the biphasic decay of the corresponding unirradiated sample.

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[23] We thank one of the reviewers for suggesting this experiment.

Discussion

Photodimerization of (E)-stilbene to yield tetraphenylcyclobutane dimers can be achieved in good yields and with excellent (syn) stereoselectivity by prior incorporation of the substrates into crystalline γ-cyclodextrin matrixes as inclusion complexes with a host/guest ratio of about 1:2.

I. Synthetic Relevance. A. Photodimerization in Solution. The photodimerization of stilbene in organic solvents is an extremely inefficient and unselective process which results in a variety of stereo- and regioisomeric photoproducts in very low yields.[12,13] Thus, even at stilbene concentrations as high as 0.5 M, this bimolecular photoreaction cannot compete with the (unimolecular) trans → cis photoisomerization and subsequent cyclization of the stilbene, which results in (Z)-stilbene and phenanthrene formation, respectively.[13] Since both reaction pathways originate from the excited singlet state of stilbene as the common precursor,[10,11] the predominance of the photoisomerization is solely due to its rapid rate[24] as compared to that of the diffusion-limited photodimerization. In fact, the excited singlet state of all stilbene derivatives decayed with rate constants $k > 10^{10}\ \mathrm{s}^{-1}$ in dichloromethane solution (see Table 3). Thus, even in the best case of diffusion-limited dimerization (i.e., $k_{\mathrm{dim}} \approx 10^{10}\ \mathrm{M}^{-1}\ \mathrm{s}^{-1}$),[25] this pathway can only effectively compete with the other fast decay routes of excited stilbene if stilbene concentrations $[\mathrm{S}] \gg 1$ M are applied.

B. The Solid-State Approach. In general, rate-limiting diffusional processes prior to reaction are readily obviated in organized and constrained media in which the reactants are permanently positioned at close distance. Such a pre-assembly of the reaction partners not only improves the efficiency of a bimolecular photoreaction that must compete with rapid unimolecular pathways but also generally enhances its stereo- and/or regioselectivity (as compared to the corresponding reaction in solution) owing to the fixed relative orientation of the substrates in a rigid microenvironment. Accordingly, numerous photochemical reactions have been carried out in the solid crystalline state to improve efficiency and selectivity.[26] In fact, there are even reports of bimolecular photoreactions that exclusively occur in the crystalline state and not in solution.[27]

However, the photodimerization of stilbenes is generally suppressed in the crystalline solid-state.[28] X-ray crystallographic studies on various stilbenes uniformly reveal that the lack of dimerization reactivity is due to the large distance ($d > 5$ Å) and frequently nonparallel orientation of the olefinic double bonds of the stilbenes in crystal lattices.[29] Thus, in accord with the topochemical postulates established by Schmidt and co-workers,[30] a [2 + 2] cycloaddition to yield tetraphenylcyclobutane would require too large a movement of atoms in the stilbene crystal lattices.[31]

C. Efficient Photodimerization in Crystalline γ-Cyclodextrin Inclusion Complexes. As demonstrated in this study, the incorporation of stilbene molecules into the rigid cavities of crystalline γ-cyclodextrin is the method of choice to overcome the above-described problems in solution as well as in neat crystals. Thus, stilbene photodimer yields as high as 79% (see Table 2) are obtained, and most importantly, absolute syn- stereoselectivity is achieved whereas stilbene photodimerizations in organic solvents[12−14] or aqueous γ-CD solution[15] result in *syn*- and *anti*-cyclobutane products. We conclude that in the crystalline inclusion complexes with host/guest ratio of 1:2 most stilbene molecules are positioned in close distance and fixed orientation to each other and thus readily dimerize upon photoexcitation to yield stereoselectively *syn*-tetraphenylcyclobutane.[33] Interestingly, the monosubstituted stilbenes **1c**−**f** form two regioisomeric cyclobutane photoproducts in comparable yields (see Table 2, column 5). We conclude that there is no preferred (H−H or H−T) orientation of these stilbene molecules in the cyclodextrin cavities prior to photodimerization, and thus, the H−H/H−T ratios in Table 2 are close to a statistical distribution of 50:50.

The relatively low yields (<18%) of (Z)-stilbene formation from the (E)-stilbenes **1a**−**f** and **3** in Table 2 reveal that the rigid cyclodextrin matrix strongly impedes the

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[28] Note that 1,2,3,4,5-pentafluorostilbene, which crystallizes in tightly packed π-stacks with an intermolecular distance of about 3.5 Å, is the only stilbene derivative that photodimerizes in the crystalline state (in a head-to-tail configuration). See: Coates, G. W.; Dunn, A. R.; Henling, L. M.; Ziller, J. W.; Lobkowsky, E. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1998**, *120*, 3641.

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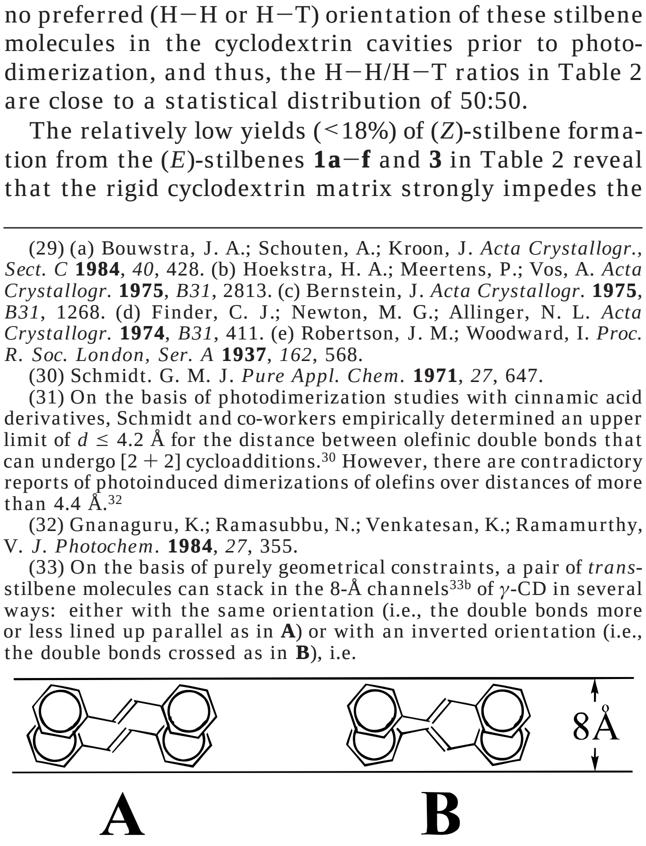
[31] On the basis of photodimerization studies with cinnamic acid derivatives, Schmidt and co-workers empirically determined an upper limit of $d \leq 4.2$ Å for the distance between olefinic double bonds that can undergo [2 + 2] cycloadditions.[30] However, there are contradictory reports of photoinduced dimerizations of olefins over distances of more than 4.4 Å.[32]

[32] Gnanaguru, K.; Ramasubbu, N.; Venkatesan, K.; Ramamurthy, V. *J. Photochem.* **1984**, *27*, 355.

[33] On the basis of purely geometrical constraints, a pair of *trans*-stilbene molecules can stack in the 8-Å channels[33b] of γ-CD in several ways: either with the same orientation (i.e., the double bonds more or less lined up parallel as in **A**) or with an inverted orientation (i.e., the double bonds crossed as in **B**), i.e.



Concerted [2 + 2] cycloaddition of *trans*-stilbene with preorientation **A** will lead to the formation of the *syn*-cyclobutane.[28,33c,d] On the other hand, if preorientation **B** is photoactive (it may not undergo photocycloaddition due to insufficient π-orbital overlap between the crossed double bonds), it will result in the formation of the *anti*-cyclobutane. Thus, the fact that *syn*-cyclobutanes are obtained stereoselectively in good yields suggests that the stilbene guests in the γ-CD channels preferentially stack with parallel orientation (**A**). (b) Ding, J.; Steiner, T.; Saenger, W. *Acta Crystallogr. Sect. B* **1991**, *47*, 731. (c) Fleming, S. A.; Ward, S. C. *Tetrahedron Lett.* **1992**, *33*, 1013. (d) Inokuma, S.; Yamamoto, T.; Nishimura, J. *Tetrahedron Lett.* **1990**, *31*, 97.

trans → cis isomerization. This is particularly true for the cases where the CD cavities are "stuffed" with approximately two stilbenes per host molecules (see **1a**–**f** in Table 1). Importantly, stilbenes **2** and **3** do not undergo photodimerization if irradiated as γ-CD inclusion complexes. In both cases, a host/guest ratio of approximately 1:1 was determined for the inclusion complexes (see Table 1) even when the stilbene guests were applied in more than 2-fold excess as compared to the CD host. Obviously, both stilbenes are too bulky to be packed more tightly in the γ-CD cavities. As a result, the two substrates **2** and **3** lack a stilbene neighbor in close reach to undergo cycloaddition, and thus no photodimers are found. Instead, photoisomerization is the only reaction route available for these stilbenes, and moderate yields of 23% and 18% are obtained for stilbenes **2** and **3**, respectively.

II. The Microenvironment of Excited Stilbene in the γ-CD Crystal Lattice. A revealing result of this investigation is the fact that we are unable to achieve quantitative yields of photodimerization even after prolonged irradiation. Instead, the photodimer yields average around 70%, which is more or less reproducible from batch to batch (see Table 2). Thus, we conclude that most but not all stilbene molecules are located at sites within the γ-CD channels where a neighbor stilbene molecule is in close reach. In other words, part of the excited stilbene guests are unable to dimerize and thus decay by either isomerization or other (radiative or nonradiative) deactivation routes.[34] The concept of (at least) two different environments for the excited stilbene molecules in the crystal lattice, i.e., with or without a stilbene neighbor, is confirmed by the fact that, in all time-resolved experiments, the excited stilbene decays in first approximation[35] with biphasic kinetics. Since the slow component in the biphasic decays is substantially reduced or even disappears in the preirradiated samples (see Table 3), we propose to assign the slow decay to that of excited stilbenes with a neighbor in close reach. These excited stilbene molecules dimerize or decay by radiative or nonradiative deactivation, but they cannot easily isomerize to the (*Z*)-stilbene as revealed by the low isomerization yields.[36] On the other hand, the fast decay is tentatively assigned to excited stilbenes without close neighbors, which cannot dimerize but readily undergo trans → cis isomerization with relatively fast rates. Despite the fact that excited stilbene **3** does not dimerize in crystalline γ-CD channels, its biphasic decay suggests two environments in the γ-CD channels, one where it can isomerize (fast component) and one where isomerization is inhibited and merely radiative and nonradiative deactivation of the excited stilbene state is observed.

In summary, the microenvironment of the γ-CD crystal lattice has the following effects on the predominant reaction pathway of photoexcited stilbene: (i) There are (at least) two sites for stilbene guests in the γ-CD channels, which cause the excited stilbene to decay at two (independent) rates. (ii) Isolated stilbene molecules can isomerize with rates of $k_{\mathrm{fast}} \approx 10^9\ \mathrm{s}^{-1}$, which are about 1 order of magnitude slower as compared to those in solution. (iii) Isomerization is suppressed wherever a stilbene neighbor is in close reach and dimerization occurs instead leading to cyclobutane photoproducts in high yields and with absolute syn stereoselectivity.

Experimental Section

I. Materials and Methods. (*E*)-Stilbenes (**1a**, and **1b**) and (*Z*)-stilbene (**2**) were used as received from Aldrich. The stilbenes **1c**–**f** were prepared following literature procedures[37] and recrystallized from ethanol. γ-Cyclodextrin was obtained as a gift from Cerestar Co. and used as received. Dichloromethane was purified by standard procedures.[38] ^{1}H NMR spectra were recorded in $CDCl_3$ on a General Electric QE-300 spectrometer, and the chemical shifts are reported in ppm units downfield from internal standard tetramethylsilane. GC–MS analyses were carried out on a HP 5890 gas chromatograph interfaced to a HP 5970 mass spectrometer (EI, 70 eV). Melting points were measured on a Mel-Temp (Laboratory Devices) apparatus and are uncorrected.

II. Preparation of the Stilbene/γ-CD Inclusion Complexes and Determination of the Host/Guest Ratios. Solid-state γ-CD complexes of the stilbenes **1a**–**f**, **2**, and **3** were prepared following the reported procedure.[39] In a typical experiment, 1.5 mmol (0.280 g) of the (*E*)-stilbene (**1a**) dissolved in ethanol was added to an aqueous solution of 0.77 mmol (1.00 g) of γ-CD. The solution turned cloudy immediately, and subsequently, a white precipitate formed over a period of 12–16 h while the suspension was stirred. The precipitate was filtered, washed with ether followed by cold water, and dried at 50 °C for 10 h. Part of the microcrystalline powder was subsequently dissolved in deuterated DMSO, and the molar ratio (1:1.75) between host (γ-CD) and guest (stilbene) was determined by ^{1}H NMR spectroscopy. The ratio of the relative masses of γ-CD and (*E*)-stilbene were determined as follows: 0.250 g of the inclusion complex was subjected to the decomplexation by dissolving it in a saturated solution of NaCl in water. (*E*)-Stilbene was extracted from the aqueous solution with chloroform, the solvent was evaporated under reduced pressure, and the mass of the (*E*)-stilbene was determined after drying for 10 h at 80 °C. The mass of γ-CD was taken as the difference between the mass of stilbene and that of the inclusion complex (0.250 g), and a molar ratio of 1:1.6 was calculated that was in good agreement with that obtained from the ^{1}H NMR spectrum of the inclusion complex.

III. Steady-State Photolysis of the Inclusion Complexes and Characterization of the Products. A 700 mg portion of finely ground solid-state γ-CD inclusion complex of the (*E*)-stilbene (**1a**) was irradiated in a Rayonnet photochemical reactor with UV light at $\lambda = 330$ nm. The sample was occasionally agitated to ensure uniform exposure to light. After irradiation of the complex for 24 h, the sample was suspended in 50 mL of distilled water saturated with sodium chloride. After warming of the solution at 50 °C for 1 h, the organic contents were extracted into chloroform. The chloroform extracts were dried over anhydrous sodium sulfate, concentrated in vacuo, and purified by column chromatography. The photodimer was isolated in 48% yield by elution with 10% chloroform in hexane on silica gel. The ^{1}H NMR and GC/MS spectral data[13] are as follows: mp 164–165 °C (lit.[13] mp 165 °C); ^{1}H NMR ($CDCl_3$) δ 4.45 (s, 4H), 7.10–7.20 (m, 12 H), 7.30–7.50 (m, 8H); GC/MS *m*/*z* (relative intensity) 180.25 (100). X-ray crystallographic examination of a single crystal yielded cell parameters identical with those previously published.[18] Similar irradiation procedures were applied to the inclusion complexes with the other stilbenes (**1b**–**f**), and the photo-

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[34] Owing to the channel-type arrangement of γ-CD inclusion complexes in the crystalline state (see Figure 1), we avoid the misleading picture of separated 1:1 and 2:1 complexes of stilbene with cyclodextrin in the crystal lattice and prefer the simple distinction between stilbene guests with and without a close neighbor.

[35] The possibility of more than two distinct locations for the stilbene cannot be excluded since the kinetic traces can also be fitted with more than two exponentials.

[36] In fact, (*E*)-stilbene does not photoisomerize at all as 2:1 complex with γ-CD in aqueous solution.[15]

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dimers were purified by column chromatography. The spectral data of the photodimers are as follows. **Photodimer of 1b:**[16a] ^{1}H NMR (CDCl$_3$) δ 3.65 (m, 12H), 4.30 (s, 4H), 7.20−7.30 (m, 8H), 7.40−7.50 (m, 8H); GC/MS *m*/*z* (relative intensity) 240.15 (100). In the case of **1c**−**e**, the syn H−H and syn H−T isomers were obtained as a mixture, which could not be separated either by column chromatography or by preparative TLC. **Photodimers of 1c:**[16a] ^{1}H NMR (CDCl$_3$) δ 1.85 (s, 6H), 4.30 (s, 4H), 7.10−7.20 (m, 10H), 7.55−7.75 (m, 8H); GC/MS of syn H−H photodimer *m*/*z* (relative intensity) 208 (55), 194 (100), 180 (50); GC/MS of syn H−T photodimer *m*/*z* (relative intensity) 194 (100). **Photodimers of 1d:**[16a] ^{1}H NMR (CDCl$_3$) δ 4.40 (s, 4H), 7.15−7.25 (m, 10H), 7.50−7.70 (m, 8H); GC/MS of syn H−H photodimer *m*/*z* (relative intensity) 249.5 (62), 214.5 (100), 180 (45); GC/MS of syn H−T photodimer *m*/*z* (relative intensity) 214.5 (100). **Photodimers of 1e:**[16a] ^{1}H NMR (CDCl$_3$) δ 3.60 (s, 6H), 4.35 (s, 4H), 7.10−7.20 (m, 10H), 7.55−7.75 (m, 8H); GC/MS of syn H−H photodimer *m*/*z* (relative intensity) 240 (63), 210 (100), 180 (50); GC/MS of syn H−T photodimer *m*/*z* (relative intensity) 210 (100). **Photodimers of 1f.**[14] In the case of **1f**, the H−H and the H−T isomers could be readily separated by column chromatography using CHCl$_3$/hexanes (25:75) as eluent on 200 mesh silica gel, and the spectral data are as follows: **Syn H−H photodimer of 1f:** ^{1}H NMR (CDCl$_3$) δ 4.45−4.46 and 4.55−4.60 (A$_2$B$_2$, 4H), 7.10−7.20 (m, 14H), 7.45−7.55 (m, 4H); GC/MS *m*/*z* (relative intensity) 230 (34) 205 (100), 180 (23). **Syn H−T photodimer of 1f:** ^{1}H NMR (CDCl$_3$) δ 4.50 (s, 4H), 7.10−7.20 (m, 14H), 7.50−7.55 (m, 4H); GC/MS *m*/*z* (relative intensity) 205 (100).

IV. Laser Flash Photolysis. The diffuse-reflectance laser photolysis setup has been described previously in detail.[40] Briefly, the third-harmonic output (355 nm, 25 ps) of a mode-locked Nd:YAG laser (QUANTEL, YG 501-C) was used as the excitation source. The fundamental laser pulse (1064 nm) was focused into a 10-cm cuvette containing a 1:1 mixture of H$_2$O and D$_2$O to generate a white continuum pulse of 25-ps duration, which was utilized as the analyzing light pulse. The continuum light was split into two beams, which were used as reference light and probe light for the crystalline sample stored in a 1-mm cuvette. The diffuse-reflected probe light was collected by fiber optics and detected by an unintensified dual-diode-array detector (Princeton Instruments) attached to a flat-field spectrograph (Instrument S.A.). The diffuse-reflectance transient absorption spectra, which represent the average over 100−300 laser shots, are presented as percentage absorption: % ABS = $100 \times (1 - R/R_0)$, with R and R_0 representing the diffuse-reflected sample light and the reference light, respectively.

V. X-ray Diffraction Studies. To determine the mode of stilbene stacking within γ-CD channels, single crystals (suitable for X-ray structural analysis) of various stilbene/γ-CD inclusion complexes were obtained as follows.

General Procedure. For example, a solution of (*E*)-stilbene (17 mmol) in diethyl ether (10 mL) was mixed with a saturated aqueous solution of γ-CD (7.7 mmol in 10 mL) and the mixture deposited a well-formed crop of transparent crystals during 48 h (at 22 °C). These crystals were dissolved in DMSO-d_6, and ^{1}H NMR spectroscopy established the molar ratio of 1:1.80 between host (γ-CD) and guest (stilbene).

The X-ray data collected from several well-faced transparent single crystals at −150 °C showed poor diffracting ability, and no high-angle reflections above sin $\theta/\lambda > 0.3$ were obtained. However, a comparison of several single crystals (with different stilbenes) indicated that all crystals exhibited tetragonal symmetry and were isomorphous with γ-CD dodecahydrate and other related complexes.[33b,41] On the basis of the observed isomorphism, the coordinates of the γ-CD atoms were taken from an earlier study[33b] to perform data refinement that converged at $R \sim 0.25$. This result indicates that the γ-CD host structure of the stilbene inclusion complex is very similar to that of γ-CD clatherates.[33b,41] However, attempts to localize the stilbene guests within the more or less ordered γ-CD lattice failed due to total disorder even with the heavy-atom derivative 4,4′-dibromo (*E*)-stilbene. Such a massive disorder, which is not observed in γ-CD crystals of tetragonal symmetry containing other guest molecules such as water or alcohol, as well as the poor diffracting ability of these crystals, indicates that the stilbene molecules populate the γ-CD channels in a highly irregular manner.[34,35]

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