PERKIN 2

Chemical insight from crystallographic disorder-structural studies of supramolecular photochemical systems. Part 3.[1] The β-cyclodextrin–7-hydroxy-4-methylcoumarin inclusion complex: direct observation of photodimerization by X-ray crystallography

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As part of an ongoing structural study of supramolecular photochemical β-cyclodextrin(β-CD)–coumarin derivatives systems the crystal structure of the β-CD–7-hydroxy-4-methylcoumarin complex has been determined for the unreacted crystal and for a crystal exposed to UV light for 6 days. The 7-hydroxy-4-methylcoumarin molecules form a crystalline 2:2 host–guest (H–G) complex with β-CD. The guest molecules are disordered, with pairs of guest molecules similarly oriented with respect to each other distributed over three sites. The guest molecules are oriented with their reactive double bonds separated by about 3.5–3.7 Å and oriented parallel to each other. Crystallographic analysis of the photoreacted crystal shows the reaction proceeds within the crystal to produce the topochemically predicted *anti*-HT photodimer. The system is appropriately described as a "reaction nano-vessel", where the inter-molecular interactions of import to the outcome of the reaction are confined to a single β-CD dimer cavity. *Ab initio* molecular orbital calculations of the conformation of the *anti*-HT 7-hydroxy-4-methylcoumarin photodimer show that the preferred gas-phase geometry for the cyclobutyl ring is planar, the same as that observed in the β-CD complex. This provides further evidence for classifying the β-CD dimer environment as non-constraining.

Introduction

An undoubtedly attractive feature of solid-state photochemical reactions is their ability to produce stereoselective products. Photodimerizations are among the best-studied photochemical reactions in crystals and also among the potentially most useful because of the prevalence of stereospecific four-membered rings in biologically relevant molecules.[2] The pioneering studies by Schmidt and his co-workers focussed on the photodimerization of cinnamic acids.[3–5] From these studies the topochemical postulate was formulated which states that a solid-state reaction proceeds with minimum movement of the atoms or molecular groups involved. These studies were based on correlations of structures for unreacted crystals and the determined structures of the recrystallized photoproducts. Stress in the photolysed crystal caused by atomic motions involved in the reaction usually destroyed the crystal.

The most insightful structural studies of solid-state photodimerizations are those in which the reaction proceeds without destroying the crystal. In these cases, the atomic motions that occur during the photochemical transformations can directly be tracked. Few examples of crystal-to-crystal (homogeneous) photodimerizations were known before the early 1990's.[6–10] Technological advancements in X-ray diffraction instrumentation and computer graphics allowed for the direct observation of photodimerizations at low conversion in crystals where the reaction was inhomogeneous.[11,12] In the early 1990's, studies by Wegner and his colleagues provided examples of photodimerizations which were made to be homogeneous by irradiating the crystal on the red tail of the absorption spectrum, thus producing a uniform transformation throughout the crystal allowing for crystallographic study at various points of photochemical conversion.[13–16]

Supramolecular photochemical systems consisting of a photoreactive guest contained within a host lattice should be less restrictive in allowing crystal-to-crystal transformations in that the host structure usually exists regardless of the presence of guest molecules (*e.g.* zeolites, ureas, dianin's compound). β-Cyclodextrin (β-CD), however, is an example of a host molecule which exhibits different crystal structures for different included guests. β-CD alone (and with some small guests) crystallizes from water as a herring-bone packed monomer. With most moderate-to-large size guests β-CD crystallizes as a face-to-face dimer held together by an extensive network of hydrogen bonds between secondary hydroxyls. Furthermore, the packing arrangement of the β-CD dimers is influenced by the nature of the included guest.[1] Even so, the nature of the β-CD dimer environment has been classified as non-constraining, because it allows included molecules to take on conformations observed in the gas phase but not in neat crystals[17] and allows necessary migrations for photochemical transformations to occur.[18]

This paper describes our continuing study of supramolecular photochemical β-CD complexes with selected coumarins. The photochemistry of coumarin and several derivatives has been well studied. Upon photolysis, coumarin and its derivatives can give four structural isomers (Scheme 1), the product ratio of which in solution is strongly influenced by the solvent polarity and the multiplicity of the excited state involved.[19] Photodimerizations of coumarins in neat and co-crystals have generally been found to proceed topochemically.[20,21] In this study, the photodimerization of 7-hydroxy-4-methylcoumarin

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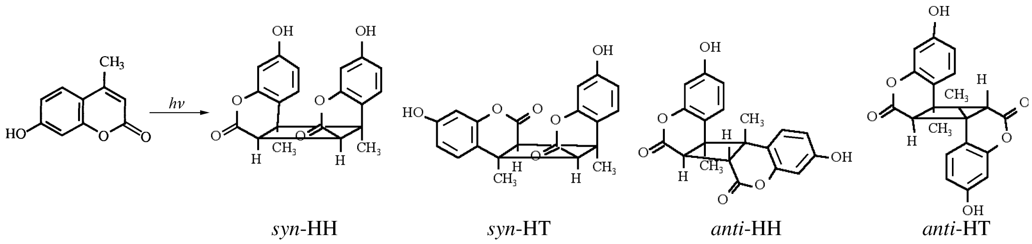

Scheme 1 Possible [2 + 2] photodimers produced in 7-hydroxy-4-methylcoumarin photodimerization.

within β-CD was directly observed by X-ray crystallography. In addition, theoretical calculations of the geometry of the photoproduct were pursued in order to examine further the effects of the β-CD dimer environment.

Experimental

Preparation and crystallization of β-CD inclusion complexes

7-Hydroxy-4-methylcoumarin was purchased from Aldrich and recrystallized once before using. In a typical inclusion complex preparation, about 180 mg of the solid guest compound were suspended in 40 ml of a saturated aqueous solution of β-CD. The mole ratio of guest : β-CD was in slight excess of 3 : 2. This solution was heated until either the solid melted or dissolved, at which point the 7-hydroxy-4-methylcoumarin would interact and complex with the β-CD in the aqueous phase. Cooling of this solution produced an aqueous solution saturated in the inclusion complex. Slow evaporation of the water at room temperature from the filtered aqueous solution typically produced crystals after 2–3 weeks.

Crystallographic studies

For structure determination of the unreacted β-CD–7-hydroxy-4-methylcoumarin complex a colorless crystal of dimensions 0.9 × 0.8 × 0.2 mm was sealed in a thin-walled glass capillary. Care was taken to make sure the capillary was sealed to ensure that the crystal would not dehydrate, which destroys the crystal. Diffraction data were collected at room temperature by the oscillation method using a Bruker AXS molybdenum target rotating anode X-ray source and an 18 cm MARResearch imaging plate detector. The program MARXDS[22] was used for indexing and integration of the data set. In all, 20912 reflections (12422 unique, $R_{\mathrm{int}} = 0.0252$) were recorded to a resolution of 0.81 Å. The overall completeness of the data set was 86.3%. The phase problem was solved by isostructural replacement of the β-CD dimer coordinates from an isomorphous structure. Waters of hydration and guest 7-hydroxy-4-methylcoumarin sites were located in difference electron density maps ($F_o - F_c$). Analysis of these maps revealed three separate sites in each half of the β-CD dimer for guest 7-hydroxy-4-methylcoumarin molecules. Due to high correlation between the site population and atomic displacement parameters, refinement of the site populations was meaningless. Site populations were then determined by iterative fixing of occupancy factors, refinement, and examination of results. This was done for the reacted crystal also and the occupancies determined were the best compromise between the two. Occupancies of the three sites were fixed at 40, 35 and 25%, respectively. Least-squares refinement on F^2 of 1698 parameters was carried out using SHELXL97[23] and converged to a final $R_1 = 0.0741$, $wR_2 = 0.1954$, and GOF = 1.090 for 11538 reflections with $F_o > 4\sigma(F_o)$. For the β-CD and waters, all non-hydrogen atoms were treated anisotropically. 7-Hydroxy-4-methylcoumarin molecules were refined as rigid bodies with restrained individual isotropic displacement parameters. Hydrogen atoms on carbon atoms were generated geometrically and fixed in a riding model. A final difference electron density map showed no distinct features with $\rho_{\max} = 0.647$ and $\rho_{\min} = -0.371$ e Å^{-3}.

For structure determination of the photoreacted β-CD–7-hydroxy-4-methylcoumarin complex a colorless crystal of dimensions 1.0 × 1.0 × 0.2 mm was sealed in a thin-walled glass capillary. The capillary and crystal were then placed inside a Pyrex test tube and irradiated with a Hanovia 450 W medium pressure Hg arc lamp for 7 days. Diffraction data were then collected at room temperature as described above. In all, 22467 reflections (12548 unique, $R_{\mathrm{int}} = 0.0238$) were recorded to a resolution of 0.81 Å. The overall completeness of the data set was 85.9%. The phase problem was solved by isomorphous replacement of the β-CD dimer coordinates from the unreacted crystal. Waters of hydration were located in difference electron density maps ($F_o - F_c$). The water positions in the unreacted and reacted crystal were nearly identical. Comparison of difference electron density maps in the β-CD dimer torus for the unreacted and photoreacted crystal revealed that a large shift in atomic positions inside the torus had occurred. The four-membered cyclobutyl rings could easily be distinguished, and were obviously planar in conformation. The photodimer produced was easily identified as the *anti*-HT dimer. Three *anti*-HT dimers were built into the difference electron density. Their occupancies were determined as explained above and fixed at 40, 35 and 25%, respectively. Least-squares refinement on F^2 of 1903 parameters was carried out using SHELXL97[23] and converged to a final $R_1 = 0.0718$, $wR_2 = 0.1901$, and GOF = 1.078 for 11455 reflections with $F_o > 4\sigma(F_o)$. For the β-CD and full occupancy waters, all non-hydrogen atoms were treated anisotropically. 7-Hydroxy-4-methylcoumarin *anti*-HT photodimers were refined subject to geometric restraints with restrained refinement of isotropic displacement parameters. Hydrogen atoms on carbon atoms were generated geometrically and were fixed in a riding model. A final difference electron density map showed no distinct features with $\rho_{\max} = 0.619$ and $\rho_{\min} = -0.360$ e Å^{-3}. From this crystallographic analysis the crystal appeared to be 100% photoreacted. Crystal data and refinement details for both the unreacted and photoreacted crystal are summarized in Table 1. CCDC reference number 188/241. See http://www.rsc.org/suppdata/p2/a9/a906042a for crystallographic files in .cif format.

Quantum-chemical calculations

To gain a better understanding of the nature of the β-CD dimer environment, *ab initio* molecular orbital geometry optimizations were carried out to examine the preferred conformation of the cyclobutyl ring in the 7-hydroxy-4-methylcoumarin *anti*-HT photodimer. All calculations were performed at the Hartree–Fock level of theory with the 6-31G(d) basis set using the program Gaussian98.[24] One of the representative 7-hydroxy-4-methylcoumarin *anti*-HT dimers from the photoreacted crystal was used as a starting model. Its geometry was optimized, which produced a planar conformation for the cyclobutyl ring [C–C–C–C torsion angle for the cyclobutyl ring (τ) = 0.49°]. From this model the 4-methyl groups were removed and replaced with hydrogen atoms. The geometry of this molecule was then optimized, which produced a puckered conformation for the cyclobutyl ring ($\tau = 14.16°$). Then the 4-methyl groups were reintroduced on the cyclobutyl ring of this structure. The geometry of this molecule was optimized,

Table 1 Crystal data and structure refinement statistics for the unreacted and photoreacted β-CD–7-hydroxy-4-methylcoumarin complex

	Unreacted	Photoreacted
Empirical formula	$(C_{42}H_{70}O_{35})_2(C_{10}H_8O_3)_2(H_2O)_{22.5}$	$(C_{42}H_{70}O_{35})_2(C_{20}H_{16}O_6)(H_2O)_{22.5}$
Formula weight	3018.64	3018.64
T/K	298(2)	298(2)
Crystal system	Triclinic	Triclinic
Space group	$P1$	$P1$
a/Å	18.01(6)	18.13(6)
b/Å	15.53(6)	15.48(6)
c/Å	15.37(6)	15.40(6)
α/°	103.35(6)	102.90(6)
β/°	113.22(3)	113.35(3)
γ/°	99.46(6)	99.53(6)
V/Å^3	3709(23)	3682(23)
Z	1	1
D_c/g cm^{-3}	1.361	1.351
Reflections (unique)	20912 (12422, $R_{int} = 0.0252$)	22467 (12548, $R_{int} = 0.0238$)
Goodness-of-fit on F^2	1.090	1.078
R_1, $wR(F^2)$ indices $[F_o > 4\sigma(F_o)]$	0.0741, 0.1954	0.0718, 0.1901

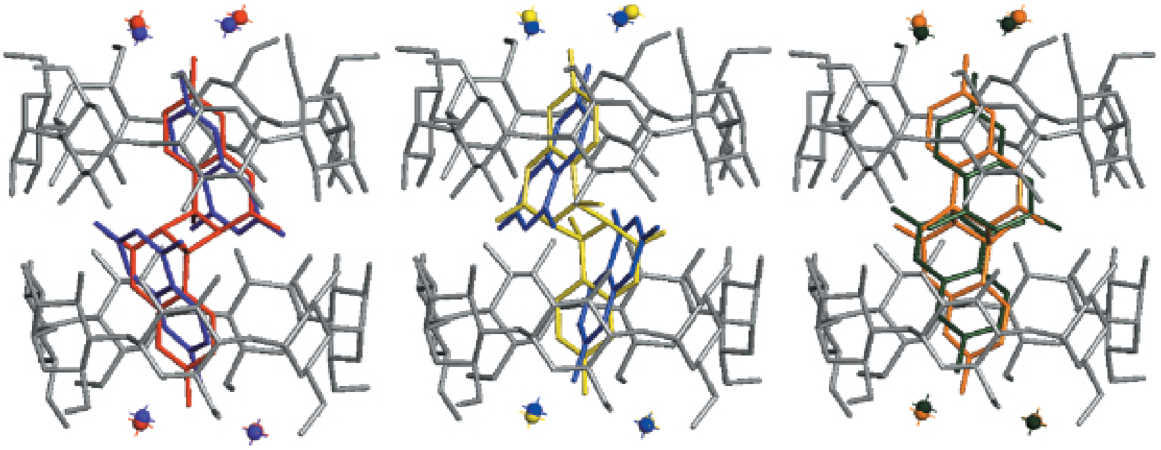

Fig. 1 Crystal structure of the unreacted and photoreacted β-CD–7-hydroxy-4-methylcoumarin complex. Water molecules in close proximity to the 7-hydroxy group of the guest molecules are also included. All hydrogens and other water oxygens have been omitted for clarity. The β-CD dimer contains three pairs of guest molecules (in the unreacted structure), and three photodimers (in the reacted structure). The corresponding photodimers are overlayed on the corresponding unreacted pairs. The orientation of the β-CD dimer is identical in each of the pictures. Color scheme is as follows: pair 1 = purple; dimer 1 = red; pair 2 = blue; dimer 2 = yellow; pair 3 = green; dimer 3 = orange; β-CD = grey.

producing a planar conformation for the cyclobutyl ring ($\tau = 0.50°$).

Results and discussion

Structure of the unreacted β-CD–7-hydroxy-4-methylcoumarin complex

The β-CD–7-hydroxy-4-methylcoumarin complex crystallizes as a face-to-face β-CD dimer containing two included 7-hydroxy-4-methylcoumarin molecules (Fig. 1). The mode of inclusion of the 7-hydroxy-4-methylcoumarin molecules is similar to that observed in the β-CD complex with 4,7-dimethylcoumarin,[1] with guest molecules packing in an aromatic face-to-face fashion within the β-CD dimer cavity with the carbonyl ends of the molecules pointing into the dimer center. The 7-hydroxy-4-methylcoumarin molecule pairs are disordered over three sites. The occupancy of each of the three pairs is 40, 35 and 25% for P1, P2, and P3, respectively.† All three sites are quite similar in that the molecules are aligned roughly identical with respect to each other and the protruding 7-hydroxy groups are in nearly the same position.

The β-CD dimers pack in what has been termed the intermediate type (IM).[25] In IM structures, the β-CD dimers are essentially arranged as close packed layers with the layers stacking one on top of another with a significant shift. This shift places the sevenfold axis of a dimer near the rim of a dimer below in a nearly cage-like environment for the guest molecules where interaction with guest molecules in neighboring β-CD dimers is unlikely. However, this environment does allow for considerable interaction of the guest with surrounding waters of crystallization and primary hydroxys of adjacent β-CD dimers. As can be seen in Fig. 2, this is definitely the case in the β-CD–7-hydroxy-4-methylcoumarin complex. Each of the 7-hydroxy groups of the pair of guest molecules that extend to the primary hydroxy ends of the β-CD dimer is involved in hydrogen bonds with two waters. Waters O(25) and O(28) hydrogen bond with OHA of P1, P2, and P3, while waters O(26) and O(24) hydrogen bond with OHB of P1 and P2. The geometry of interaction of these waters with OHB(P3) is not optimal for a strong hydrogen bond with the distances of the OHB(P3) to both O(24) and O(26) greater than 3.5 Å. However, upon photoreaction this hydroxy group is brought into a position where it does likely hydrogen bond with these two waters. These features are discussed further in the following section. These interactions are illustrated in Fig. 2 for P1 and listed in Table 2.

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† Atom naming throughout is as follows. For the cyclodextrins, A*n*(G*mo*), where element symbol A, atom number *n* of glucose residue *m* of cyclodextrin *o*. For the guest 7-hydroxy-4-methylcoumarin molecules and the corresponding photodimers, atom names are shown in Fig. 3 and explained in the caption, and followed in the text by either (P*n*) or (D*n*), where P*n* stands for (unreacted) Pair *n* and D*n* for the corresponding photodimer *n*. Water oxygens are simply O followed by a residue number in parentheses.

Table 2 Possible hydrogen bond interactions in the interdimer region for the unreacted, photoreacted β-CD–7-hydroxy-4-methylcoumarin docosahydrate crystal

Atoms	Distance/Å	Angle/°
β-CD to water		
O6(G62)···O(25)	2.75(1), 2.72(2)	C6(G62)–O6(G62)···O(25) 127.9(7), 133.4(6)
O6(G51)$^{\mathrm{I}}$···O(25)	2.89(1), 2.79(1)	C6(G51)$^{\mathrm{I}}$–O6(G51)$^{\mathrm{I}}$···O6(G2)$^{\mathrm{I}}$ 101.3(4), 105.7(8)
O6(G51)$^{\mathrm{I}}$···O(26)$^{\mathrm{I}}$	2.90(1), 2.877(8)	C6(G51)$^{\mathrm{I}}$–O6(G51)$^{\mathrm{I}}$···O(26)$^{\mathrm{I}}$ 121.6(5), 127.8(4)
O6(G12)$^{\mathrm{II}}$···O(24)$^{\mathrm{I}}$	2.76(1), 2.753(7)	C6(G12)$^{\mathrm{II}}$–O6(G12)$^{\mathrm{II}}$···O(24)$^{\mathrm{I}}$ 106.0(3), 104.9(3)
Water to water		
O(16)···O(26)$^{\mathrm{I}}$	2.95(2), 2.85(2)	
Guest to water (for P1, D1)		
OHA···O(25)	2.54(3), 2.52(2)	C7A–OHA···O(25) 125.0(8),131(1)
OHA···O(28)	2.80(3), 2.71(2)	C7A–OHA···O(28) 109.5(7), 114(1)
OHB···O(24)	2.68(2), 2.90(2)	C7B–OHB···O(24) 141(1), 117(1)
OHB···O(26)	2.70(4), 2.82(2)	C7B–OHB···O(26) 133.3(8), 110.6(9)
Guest to water (for P2, D2)		
OHA···O(25)	2.55(2), 2.79(3)	C7A–OHA···O(25) 128.9(4), 115(1)
OHA···O(28)	2.73(2), 2.48(3)	C7A–OHA···O(28) 111.3(4), 127(1)
OHB···O(24)	3.33(2), 2.66(2)	C7B–OHB···O(24) 101.5(4), 117(1)
OHB···O(26)	2.76(2), 2.67(2)	C7B–OHB···O(26) 118.1(4), 108.1(9)
Guest to water (for P3, D3)		
OHA···O(25)	2.91(2), 2.50(3)	C7A–OHA···O(25) 111.1(4), 131(1)
OHA···O(28)	2.63(2), 2.89(3)	C7A–OHA···O(28) 126.6(5), 111(1)
OHB···O(24)	N.I., 3.15(3)	C7B–OHB···O(24) N.I., 99(1)
OHB···O(26)	N.I., 2.66(3)	C7B–OHB···O(26) N.I., 115(1)

I = $x + 1, y, z$; II = $x, y, z - 1$. N.I. = No interaction.

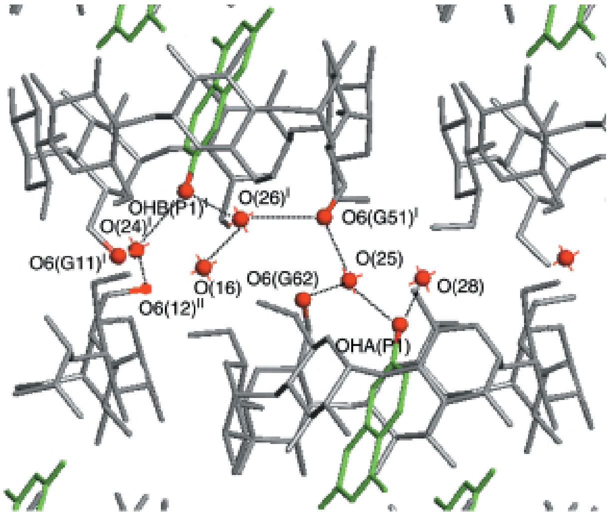

Fig. 2 Possible hydrogen bond interactions in the interdimer region. All cyclodextrin atoms are colored grey except for the +*gauche* conformer primary hydroxy oxygens (red). Water oxygens are red also. For clarity, only one pair (pair 1) of guest 7-hydroxy-4-methylcoumarin molecules is shown. Possible hydrogen bonds are designated with dashed lines. See Table 2 for geometric information. Hydrogens have been omitted for clarity.

The waters involved in hydrogen bonds with the guest molecules are also hydrogen bonded to β-CD primary hydroxys and other waters. Of the 14 primary hydroxys in the β-CD dimer, 11 take on the common −*gauche* conformation,[26] with the C6–O6 bond pointing away from the cavity. The other three primary hydroxys, those of G11, G51, and G62, are +*gauche* conformers, with the C6–O6 bond pointing in toward the cavity. Two of these, the primary hydroxys of G51 and G62, are involved in direct hydrogen bond interactions with two of the water molecules involved in direct interactions with the guest molecules (see Fig. 2). O6(G62) hydrogen bonds with O(25) while O6(G51) actually hydrogen bonds with two of these waters, O(25) and O(26). These interactions and others extend from dimer to dimer throughout the crystal producing a crystal highly stabilized by a plethora of hydrogen bonds. This environment effectively creates a "reaction nano-vessel" where the interactions of import to the reaction are limited to a single β-CD dimer container. As discussed in the following section, this becomes even more evident in the analysis of the structure of the photoreacted crystal.

As mentioned above, the three pairs of 7-hydroxy-4-methylcoumarin molecules display nearly identical arrangements with respect to one another. This arrangement is shown in Fig. 3 for pair 1. Examination of the orientation of the guest molecules within the β-CD dimer reveals that the reactive double bonds are ideally placed to produce the observed *anti*-HT dimer. According to topochemical stipulations,[3–5] reactive double bonds which undergo dimerization should lie within 4.2 Å of each other and lie parallel to one another. As can be seen in Table 3, the relative orientations are ideal to support the observed photodimerization.

Structure of the photoreacted β-CD–7-hydroxy-4-methylcoumarin complex

A crystal of the β-CD–7-hydroxy-4-methylcoumarin complex was exposed to photolysing radiation for 6 days to ensure (nearly) complete conversion to photoproduct and then used in single crystal structure determination. This observation alone indicated that the environment experienced by the reacting molecules was non-constraining, as the atomic movements required for the photoreaction to occur took place without destroying the crystal. Analysis of the structure reveals that the photodimer formed is the *anti*-HT photodimer, the topochemically predicted product from the analysis of the unreacted crystal. To the limits of the crystallographic analysis, it appears as though the conversion to the *anti*-HT product is 100%.

The reaction within the β-CD dimer cavity proceeds topochemically with minimal movement of atoms to form the *anti*-HT photodimer. These displacements are shown in Fig. 4 and listed in Table 4. As would be expected, the largest

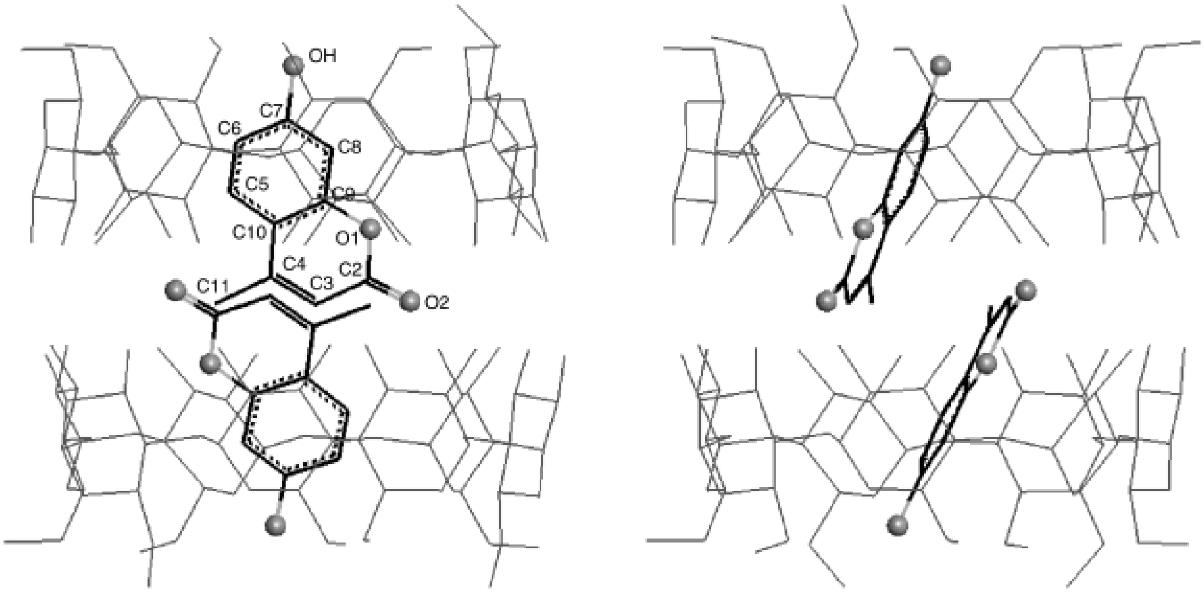

Fig. 3 Two views of the arrangement of the 7-hydroxy-4-methylcoumarin molecules (pair 1) in the β-CD dimer cavity. β-CD is shown as grey lines. Guest 7-hydroxy-4-methylcoumarin molecules are shown as black lines with grey filled circles for the oxygen atoms. Atom naming is shown for one of the 7-hydroxy-4-methylcoumarin molecules. Atom naming in the text is shown in the figure with an "A" or "B" appended to designate molecule A or B of a given pair (*e.g.* C4A). Hydrogens are omitted for clarity.

Table 3 Geometric parameters describing the orientation of the photoreactive guests

Atoms involved	Distance/Å
Separation distances	
C3A(P1) · · · C4B(P1)	3.59(4)
C4A(P1) · · · C3B(P1)	3.58(4)
C3A(P2) · · · C4B(P2)	3.65(2)
C4A(P2) · · · C3B(P2)	3.52(2)
C3A(P3) · · · C4B(P3)	3.66(2)
C4A(P3) · · · C3B(P3)	3.74(2)
Molecule pair	**Angle/°**
Angles between reacting double bonds	
P1	3.7(9)
P2	9.8(6)
P3	7.1(9)

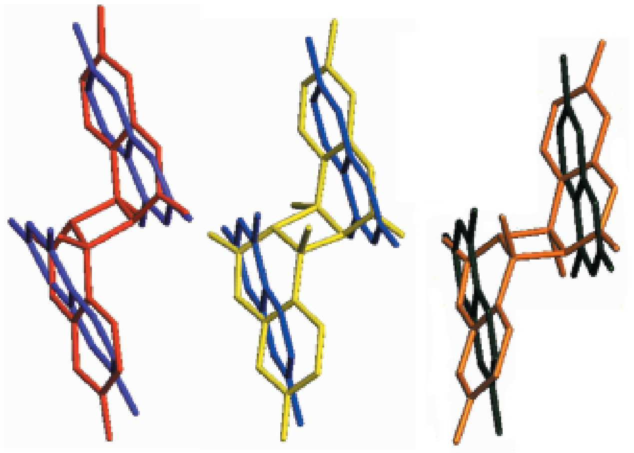

Fig. 4 Unreacted 7-hydroxy-4-methylcoumarin pairs and their corresponding photodimers shown to view the displacement the individual atoms undergo upon photoreaction. Atom displacements are given in Table 4. Color scheme is as in Fig. 1.

atom displacements are those for the atoms directly involved in the reaction, C3A, C4A, C3B, and C4B. The average displacements in the three reacting pairs for these atoms are 1.08, 1.15, 1.14 and 1.20 Å, for C3A, C4A, C3B, and C4B, respectively.

The displacements for the 7-hydroxy groups are equally as large. The average displacements for these atoms in the three reacting pairs are 1.16 and 1.13 Å for OHA and OHB, respectively. This is a bit surprising given the strong hydrogen bond interactions with the water molecules discussed above. Despite the relatively large movement of these hydroxy groups upon photoreaction, the water molecules they interact with remain relatively stationary, with the largest displacement being for water O(25), which moves 0.50 Å. This observation provides solid evidence for classifying the environment experienced by the guest 7-hydroxy-4-methylcoumarin molecules as a "reaction-nano vessel". Even though the interactions of the waters with the guest are obviously strong and significant (as gauged by geometric parameters), the interactions of these waters with other surrounding structural waters and β-CD hydroxys are sufficiently strong to minimize their allowed movement. These (guest to water) hydrogen bond interactions are actually strengthened upon photoreaction, as can be seen in the geometric parameters given in Table 2. One of the hydroxys, OHB(P3), which is not in a position favorably to interact with O(24) and (26), moves into a position where it can form hydrogen bond interactions with these waters upon photoreaction.

Conformational analysis of the guest 7-hydroxy-4-methylcoumarin *anti*-HT photodimer

To gain more insight into the nature of the β-CD dimer cavity, conformational analysis of the cyclobutyl ring of the 7-hydroxy-4-methylcoumarin *anti*-HT photodimer was carried out. Cyclobutyl rings are classical strained ring systems that can display puckered and planar conformations. Puckered conformations reduce steric interactions by staggering substituents on adjacent carbons. Planar conformations are often favored, however, in order to produce an energy favorable structure for the entire molecule. The structure determination of the photoreacted β-CD–7-hydroxy-4-methylcoumarin complex clearly revealed that the cyclobutyl ring of the photodimer contained in the β-CD dimer cavity was planar.

An examination of the conformations for other structurally characterized coumarin photodimers revealed only four examples characterized by X-ray crystallography (Table 5). All

Table 4 Displacements (Å) for individual atoms of the molecules involved in photodimerization

Atom	P1–D1	P2–D2	P3–D3
O1A	0.26	0.47	0.55
O2A	0.40	0.69	0.69
C2A	0.41	0.45	0.62
C3A	1.04	0.95	1.26
C4A	0.87	1.21	1.37
C5A	0.56	0.83	0.84
C6A	0.35	0.55	0.62
C7A	0.59	0.62	0.91
C8A	0.72	0.75	0.92
C9A	0.42	0.47	0.57
C10A	0.50	0.69	0.81
C11A	0.35	1.92	0.84
OHA	1.01	1.01	1.45
O1B	0.48	0.87	0.91
O2B	0.76	1.14	0.65
C2B	0.75	0.73	0.58
C3B	1.35	1.05	1.03
C4B	1.08	1.43	1.08
C5B	0.61	1.32	0.92
C6B	0.44	0.94	0.69
C7B	0.85	0.58	0.90
C8B	0.96	0.89	1.11
C9B	0.50	0.61	0.71
C10B	0.55	0.96	0.75
C11B	0.47	1.60	0.46
OHB	1.28	0.79	1.31

Displacements for water atoms involved in hydrogen bonds with guest atoms

O(24)	0.11
O(25)	0.50
O(26)	0.22
O(28)	0.38

Table 5 Cyclobutyl ring conformations for coumarin photodimers

Coumarin dimer	τ/°	Ref.
syn-HH coumarin	20.5^a	18
syn-HH 6-methylcoumarin	12.3^a	31
syn-HT 7-methoxycoumarin	19.3^a	32
anti-HH coumarin	23.0^a	33
anti-HT 7-hydroxy-4-methylcoumarin	0.5^b	This paper
anti-HT 7-hydroxycoumarin	14.16^b	This paper

^{a} From crystal structure. ^{b} From theoretical calculations.

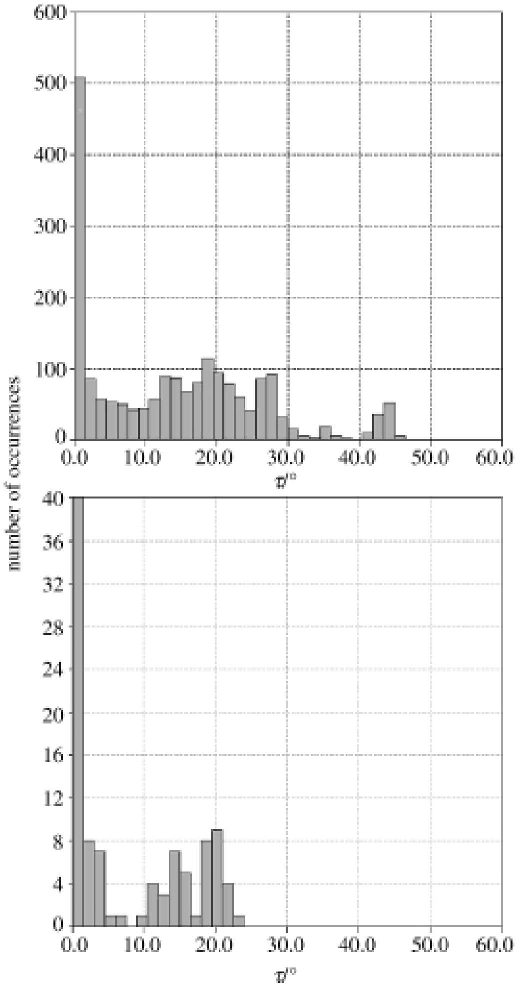

Fig. 5 Distributions of cyclobutyl ring conformations (given by the cyclobutyl CCCC dihedral, τ) found in organic crystal structures in the CSD (excluding cubanes and cyclobutanones). The histogram at the top shows the distribution for cyclobutyl rings, while the bottom is for cyclobutyl rings with methyl groups in non-adjacent carbon atoms.

four exhibit puckered cyclobutyl rings. However, none of these contains substituents on the cyclobutyl ring like the 7-hydroxy-4-methylcoumarin *anti*-HT photodimer. Hence, a more extensive study was carried out.

A search of the Cambridge Structural Database (CSD) (version 5.16, October 1998) was conducted to examine the distribution of cyclobutyl ring conformations in organic crystal structures. First, a search was conducted for cyclobutyl rings (excluding cubanes and cyclobutanones) of which 1980 occurrences were found in 1391 structures. Then a search of cyclobutyl rings with methyl groups on non-adjacent carbons was conducted (again excluding cubanes or cyclobutanones), revealing 101 occurrences in 44 different structures. The cyclobutyl ring pucker can be characterized by the cyclobutyl C–C–C–C dihedral angle (τ), which was tabulated for both searches. The distributions are shown in Fig. 5. Both searches displayed a high occurrence of the planar conformation for cyclobutyl rings in organic crystal structures. The peak for puckered conformations occurs at around 19–20° in both cases. Cyclobutane itself has long been known to exhibit a puckered structure in the ground state.[27–29] The C–C–C–C torsion angle τ in the gas phase has been determined by analysis of gas-phase IR and Raman spectra and determined to be 21(1)° at the equilibrium geometry.[27] Additionally, the energy difference between the puckered and planar conformers was determined as 513 cm^{-1}. Because the analysis of structural data left no clear answer as to the preferred conformation of the cyclobutyl ring, theoretical calculations were carried out.

A recent theoretical study on the conformation of cyclobutane stressed the importance of basis set effects on the predicted conformations of the cyclobutane ring.[30] In the study, Hartree–Fock (HF), density functional B3LYP, and electron correlation MP2 methods were all employed using various basis sets, from minimal (STO-3G) to extensive [6-31G(d,p)]. In general it was observed that more minimal basis sets produced less puckered geometries. The inclusion of polarization functions for carbon atoms produced puckered geometries quite close to that experimentally measured. The level of theory invoked (HF, B3LYP, or MP2) was not as important for producing the experimentally observed geometry as long as polarization functions were included for the carbon atoms. In light of these findings, we chose to carry out HF calculations using the 6-31G(d) basis set for geometry optimizations of the *anti*-HT photodimer.

Optimization of the geometry of *anti*-HT photodimer D1 from the crystal structure of the photoreacted β-CD–7-hydroxy-4-methylcoumarin complex produced a molecule with a planar cyclobutyl ring (τ = 0.50°). From this optimized structure the 4-methyl groups were removed from the cyclobutyl ring, producing the *anti*-HT 7-hydroxycoumarin dimer. This structure was then optimized, producing a puckered conformation for the cyclobutyl ring ($\tau = 14.16°$). To this model the 4-methyl groups were again added to the cyclobutyl ring and another optimization was carried out. This calculation again yielded a planar conformation for the cyclobutyl ring. Thus it seems the preferred gas-phase geometry for the *anti*-HT 7-hydroxy-4-methylcoumarin dimer contains a planar cyclobutyl ring. The environment of the β-CD dimer cavity allows this conformation to be adopted, further supporting its characterization as non-constraining.

Conclusions

Analysis of the structures of the unreacted and photoreacted β-CD–7-hydroxy-4-methylcoumarin complex shows that the system can be described as a collection of isolated reaction nano-vessels within a framework composed of an extensive network of non-covalent interactions. Even though the guest 7-hydroxy-4-methylcoumarin molecules interact directly with this network through hydrogen bonds and are responsible for the observed β-CD dimer packing motif, this interaction does nothing to prevent the photodimerization from proceeding in a predictable manner. Likewise, the photodimerization does not disrupt this framework. Furthermore, the cyclobutyl ring in the photoproduct is observed to take on a planar conformation within the β-CD dimer cavity, the same conformation that is predicted from theoretical molecular orbital calculations for the gas-phase molecule, further extending the argument that the β-CD dimer cavity is non-constraining.

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