Chemical insight from crystallographic disorder: structural studies of a supramolecular β-cyclodextrin/coumarin photochemical system

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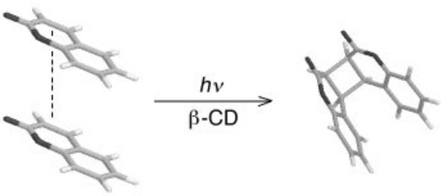
From a combination of X-ray crystallography, solid-state NMR, and theoretical calculations, a model of a β-cyclodextrin (β-CD)–coumarin inclusion complex has been developed which characterizes the complex as a 2 : 3 β-CD–coumarin system with the coumarin molecules located in β-CD dimer 'reaction nano-tubes'; the model explains the reported yield for the coumarin photodimerization reaction carried out in powdered solids.

Several important contributions have been made to determine the mechanistic and controlling factors that produce given reaction outcomes in solid-state photochemical reactions.[1] Most such studies have focused on reactions carried out in neat crystals; however, co-crystallizing or 'host' media have been used to produce reaction outcomes not observed in neat crystals,[2] thus expanding the arsenal of the solid-state photochemist to produce a desired result. Detailed studies of such important systems at the molecular level are much less common.

β-Cyclodextrin (β-CD), a cyclic oligomer made of seven D-glucose units, is an example of one such host system in which the outcome of photochemical reactions can be modified.[3] An example system is the photodimerization of coumarin and coumarin derivatives. Upon photolysis, coumarin and its derivatives can give four structural isomers, the product ratio of which in solution is strongly influenced by the solvent polarity and the multiplicity of the excited state involved.[4] Product distributions in neat crystals and co-crystals have been found to correspond to the pre-irradiation disposition of the molecules in the crystal.[5,6] A study of the photodimerization of coumarin and coumarin derivatives in crystalline powder β-CD complexes has been reported.[7] However, these complexes were not subjected to detailed structural studies. The β-CD–coumarin complex presents an especially interesting model system for the study of intermolecular solid-state photochemical reactions in supramolecular systems. Scheme 1 illustrates the photochemical reaction in the supramolecular complex.

Not unexpectedly, room temperature X-ray crystallographic studies of the β-CD–coumarin complex[8] present a feature common to crystallographic studies of β-CD complexes: disorder. Although there is disorder of the guests at room temperature, difference Fourier maps ($F_o - F_c$) clearly reveal three general sites for coumarin molecules per cyclodextrin dimer (Fig. 1). Solid-state ^{13}C magic angle spinning NMR experiments with decoupling verified the 2 : 3 host:guest (H : G) ratio.[9] This finding corrects the previous characterization of this system as a 2 : 2 H:G system, and, as will be described below, helps to explain the previously reported 64% yield in the photodimerization reaction.[7] The disorder present was such that the coumarin orientations could not be determined unambiguously from conventional difference electron density maps. The shape of the difference electron density plots corresponding to the guest coumarins is flat and elliptical (like naphthalene), hence the general layout of the coumarins is definable.



Scheme 1

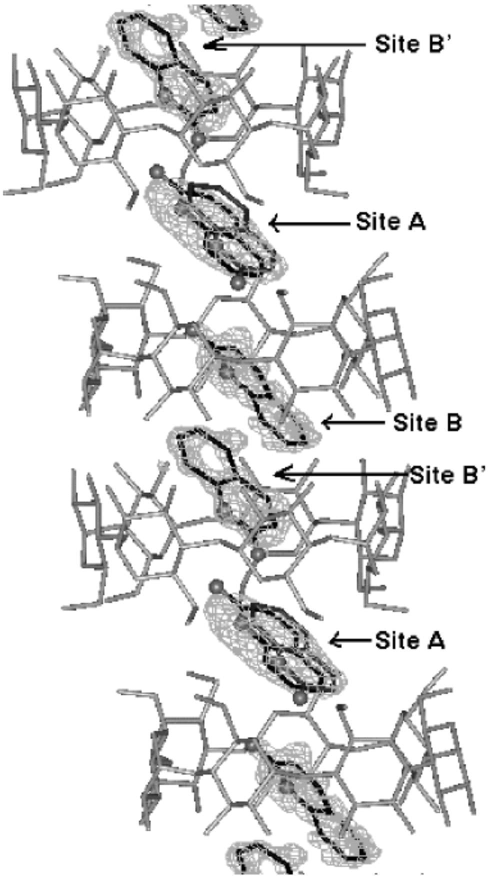


Fig. 1 Structure of the β-CD–coumarin 'reaction nano-tube' with the difference electron density ($F_o - F_c$) in the CD overlaid. CDs are in grey while coumarin molecules are shaded as follows: carbon = black; oxgen = light grey balls. Coumarin molecules at crystallographically disordered site A are shaded with black carbons for one orientation and grey carbons for the other ortientation. Waters of crystallization are omitted for clarity. The β-CD dimer stacks are roughly parallel to the crystallographic *c*-axis. See text for details. See: http://www.rsc.org/suppdata/cc/1999/1275/ for a colour version of this figure.

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However, the direction of orientation (defined by which direction the carbonyl points) is not obvious. Consequently, lattice energy calculations[10] were employed to probe the most energetically favorable arrangement of coumarin orientations. The calculations indicate that an antiparallel pair of coumarin molecules in the center of the β-CD dimer (sites B and B′) is favored, while the orientation at site A must be aligned parallel with one of these two molecules. Because of space group symmetry, the orientation at site A is necessarily disordered; this coumarin sits on a crystallographic two-fold axis, but does not itself posses two-fold symmetry. The consequence is that site A's orientation is such that it could react with either site B or site B′. Either case requires some migration of the guest coumarins to bring the molecular orbitals involved closer to each other, which should be allowed in the CD's non-constraining environment.[11]

Analysis of these experiments produces an intriguing model that provides insight into the photochemical behavior of the system. The β-CD dimers pack in the crystal in a 'channel packing' motif,[12] in which the dimers stack one on top of another producing channels parallel to the *c* axis throughout the crystal allowing for interaction between guests in adjacent CD dimer cavities. The coumarin molecule at site A actually resides at the dimer-stacking interface. Even though the pair of molecules at site B is only separated by about 3.65 Å, they are antiparallel and cannot react without reorientation to give the observed *syn*-HH dimer.[13] Thus, the photodimerization likely happens between a coumarin molecule at site A and one either at site B or site B′ (depending on their respective orientations). On average, this leaves one of the three coumarin molecules per β-CD dimer unreacted, making the maximum theoretical yield 67%.

We conclude that the β-CD environment described here behaves not as a 'reaction nano-vessel', an environment where the interactions of import occur only within a single β-CD dimer, but rather as a 'reaction nano-tube', an environment where there is a considerable amount of interaction between molecules in adjacent β-CD dimers. This 'reaction nano-tube' allows for a 2:3 H:G ratio and limits the theoretical yield to 67%. In addition, the study nicely illustrates that important chemical information can be determined for complex, disordered systems by structural studies using complementary methods.

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Notes and references

1 For example see: V. Ramamurthy and K. Venkatesan, *Chem. Rev.*, 1987, **87**, 433 and references therein.

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8 *Crystal data* for $(C_{42}H_{70}O_{35})\cdot(C_9H_6O_2)_{1.5}\cdot 12H_2O$: M_r = 1570.38, monoclinic, space group *C*2 (no. 5), a = 19.322(2), b = 24.641(3), c = 16.050(2) Å, β = 108.759(8)°, Z = 4, D_c = 1.442 g cm^{-3}, crystal size 0.5 × 0.4 × 0.1 mm, λ = Mo-Kα, T = 293(2) K. Data were collected on an automated Siemens P4 diffractometer with a sealed tube source. 6778 unique reflections (R_{int} = 0.0403) were collected to $2\theta_{max}$ = 50°. The structure was solved by molecular replacement of the β-CD coordinates from an isomorphous structure. Coumarin sites were located in difference electron density maps ($F_o - F_c$). Coumarin molecules in orientations determined from the lattice energy calculations were refined as rigid bodies. Least-squares refinement on F^2 of 835 parameters was carried out using SHELXL97 (G. M. Sheldrick, *SHELXL97, Program for the Refinement of Crystal Structures.* University of Göttingen, Germany, 1997) and converged to a final R_1 = 0.0893, wR_2 = 0.2037 and GOF = 1.239 for 3369 reflections with $F_o > 4\sigma(F_o)$. All non-hydrogen atoms were treated anisotropically except those of the coumarin molecules and low occupancy waters. Hydrogens on carbon atoms were generated geometrically and were fixed in a riding model. A final difference electron density map showed no distinct features with ρ_{max} = 0.46 and ρ_{min} = −0.33 e Å^{-3}. CCDC 182/1260. See http://www.rsc.org/suppdata/cc/1999/1275/ for crystallographic data in .cif format.

9 ^{13}C MAS spectra were obtained at 7.1 T with a standard Bloch decay pulse sequence on a sample of about 200 mg of hydrated crystalline complex. The dynamics of the guest made cross-polarization ineffective. 2048 transients were averaged, with an 80 s delay between acquisitions to allow spin relaxation. The spinning speed used was 4 kHz; at this speed, no rotational sidebands were observed. Assignments for coumarin resonances were deduced by comparison with a reference solution NMR spectrum (Aldrich). Assignments for β-CD resonances were deduced by comparison with previously published results (M. J. Gidley and S. M. Bociek, *J. Chem. Soc., Chem. Commun.*, 1986, 1223). Overlapping peaks were deconvolved to obtain integrated spectral intensities. Spectral shifts were referenced to the high frequency resonance of adamantane, and converted to a TMS scale by adding 38.56 ppm. The shifts obtained (relative to TMS), along with intensities, are as follows: δ_C 160 (3C), 154 (3C), 143 (3C), 131 (3C), 128 (3C), 124 (3C), 119 (3C), 117 (3C), 116 (3C), 104 (14C), 81 (14C), 73 (42C), 60 (14C).

10 Lattice energy calculations were performed using the CrystalPacker module in Cerius^2 (Molecular Simulations). Calculations performed were single point energy calculations with coumarin molecules located at positions from the crystallographic model. For the calculations, the orientations at site B and B′ were fixed as: an antiparallel pair, a parallel pair pointing in the +*c* direction, and a parallel pair pointing in the −*c* direction. With each of the fixed arrangements at site B, the orientation at site A was varied to each of the four orientations possible, and each time the energy was calculated. The low energy arrangements displayed an antiparallel pair at site B and B′ with site A aligned parallel to either of the molecules at site B or B′.

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13 The *syn*-HH dimer was the reported product of the study in ref. 7. We verified formation of this product in our crystals as follows: the reaction product was extracted with CH_2Cl_2 and the crystal structure of the isolated photoproduct verified that it was the *syn*-HH dimer. The coordinates of this structure have also been deposited.

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