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Structural studies of supramolecular β-cyclodextrin complexes with butyrophenone and valerophenone: an explanation for photochemical reaction modification†‡

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X-Ray crystallographic studies of β-cyclodextrin (β-CD) inclusion complexes with butyrophenone and valerophenone characterize these complexes as 2:2 β-CD/guest systems with the alkyl chains of the included guest molecules conformationally restricted; the structures explain the reported observation of the modification of the Norrish type II photoreaction for the included aryl alkyl ketones in crystalline β-CD complexes.

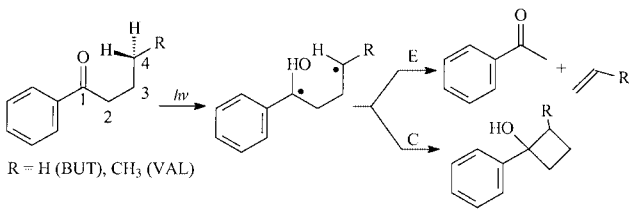
The use of controlling media to modify the outcome of photochemical reactions has been an active area of research since the late 1970s.[1] Understanding how the controlling media changes the outcome of a reaction is important for designing future experiments in which a specific outcome is desired. X-Ray crystallography represents a powerful tool for observing these influences at a molecular level.

β-Cyclodextin (β-CD), a cyclic oligomer composed of seven D-glucose units, is an example of one such host system in which the outcome of photochemical reactions, *e.g.* the photoreaction of aryl alkyl ketones, can be modified.[2] This Norrish Type II photochemical process involves photoexcitation of the carbonyl group and has been rigorously examined for aryl alkyl ketones.[3–5] They undergo γ-hydrogen abstraction exclusively from the $(n\pi^*)^3$ state yielding a triplet 1,4-diradical as the primary intermediate (Scheme 1). Once the 1,4-diradical is formed, intersystem crossing produces the singlet diradical which then reacts *via* one of two pathways. Overlap of radical orbitals leads to cyclization (C), producing cyclobutanols. The elimination pathway (E) involves cleavage of the central 2,3 σ bond producing acetophenone and alkenes.

The use of β-CD as a controlling media for modifying the outcome of the Norrish Type II photoreaction of aryl alkyl ketones in the solid state has been reported.[6] In these studies, crystalline powder samples of β-CD complexes with various aryl alkyl ketones were prepared and their photochemical reactions analyzed. The general observation was that inclusion in β-CD lead to an increase in cyclization products (as compared to solution phase studies), and this trend became more pronounced as the alkyl chain became longer. In an effort to determine how the β-CD environment influences the outcome of the photoreaction of the included aryl alkyl ketones,[7] crystallographic studies were pursued. This report presents the structures of the β-CD/butyrophenone inclusion complex and the β-CD/valerophenone inclusion complex.

The two crystal structures are very similar.[8] Both are composed of face-to-face β-CD dimers containing two included aryl alkyl ketone molecules with the β-CD dimers packing in a channel[9] (Fig. 1). The guest molecules are packed with their phenyl rings face-to-face located in the center of the β-CD dimer. This leaves the alkyl chains of the ketones extending to the primary hydroxy ends of the β-CD dimer.

Examination of the structures reveals the influence the β-CD dimer environment has on the observed reaction outcomes. Although defined conformations for the included guest molecules could not be unequivocally obtained because of disorder,



Scheme 1 Reaction scheme of the Norrish Type II reaction for butyrophenone (BUT) and valerophenone (VAL). Atom numbering shown pertains to text discussion.

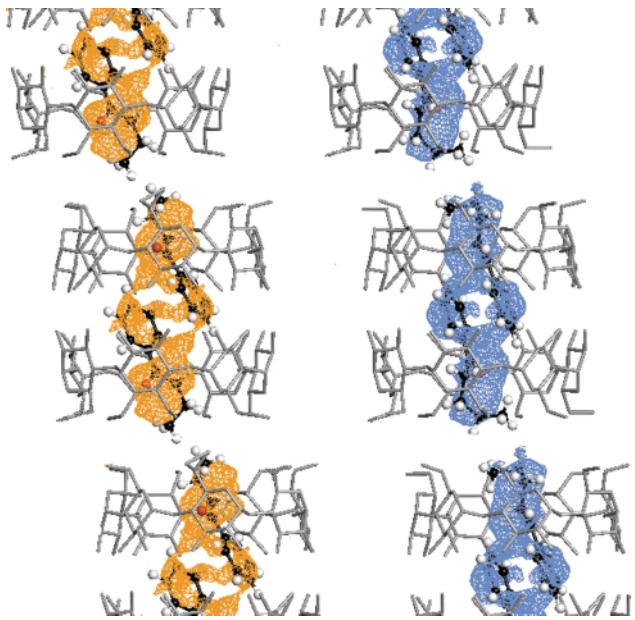


Fig. 1 Structures of the β-CD/butyrophenone (left) and β-CD/valerophenone (right) inclusion complexes. β-CD is shown as gray sticks while the guest molecules are shown in ball and stick with coloring as follows: red = oxygen; white = hydrogen; black = carbon. The difference electron density ($F_o - F_c$) the disordered guest molecules were fit to is shown in orange (β-CD/butyrophenone) and blue (β-CD/valerophenone).

† Electronic supplementary information (ESI) available: full experimental details. See http://www.rsc.org/suppdata/cc/b0/b00282m/

‡ Chemical Insight from Crystallographic Disorder–Structural Studies of Supramolecular Photochemical Systems, Part 4; Part 3, T. J. Brett, J. M. Alexander and J. J. Stezowski, *J. Chem. Soc., Perkin Trans. 2*, 2000, in press.

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the interpretation of this disorder does reveal some relevant conformational restrictions. With the molecules included in the β-CD dimer with the phenyl rings packing face-to-face in the center, the alkyl chains must take on a cisoid conformation about the 2,3-bond. This helps bring a γ-hydrogen into close proximity with the carbonyl oxygen, as would be required for its abstraction.[10]

Once a γ-hydrogen is abstracted, the resultant 1,4-diradical is most surely conformationaly restricted by the β-CD dimer environment. It is well established that efficient cleavage requires a 1,4-diradical conformation in which the radical p orbitals can overlap significantly with the central σ bond being cleaved. If this does not happen, cyclization occurs from a conformation involving minimal orbital overlap.[11,12] Given these requirements, cyclization can only occur from a cisoid conformation of the 1,4-diradical while elimination can occur from either cisoid or transoid forms. With the phenyl rings of the molecules packed tightly in the center of the β-CD dimer, any such rotation must occur at the alkyl chain end of the molecule. Given the boundaries imposed by the β-CD dimer, the alkyl chains are not be able to undergo free rotations to transoid geometries.

The fashion in which the β-CD dimers pack also plays a role in the reaction modification. The observed channel type packing brings the alkyl chains of included molecules in adjacent β-CD dimer cavities within close proximity. Extension of the alkyl chain by one methyl group, *i.e.* going from butyrophenone to valerophenone, effectively stuffs the channel more tightly, limiting the allowed motion of the alkyl chain even more. This hindered motion accounts for the observed increase in cyclization products with increasing alkyl chain length.

The β-CD complexes with butyrophenone and valerophenone can be considered as 'reaction nanotubes' much akin to the β-CD/coumarin complex.[13] The mode of inclusion of the guest molecules produces conformational restrictions for the alkyl chains imposed by the surrounding β-CD dimer walls and intratube packing. Said restrictions produce cisoid conformations about the central 2,3-bond which will allow for the γ-hydrogen abstraction. The 1,4-diradical produced is also conformationally hindered in this manner and additionally restricted because of interactions between molecules in adjacent dimer cavities in the channel. This effect becomes more pronounced as the alkyl chain length is increased and is a contributing factor in the observed increase in cyclization products with increasing alkyl chain length. Further studies of inclusion complexes with aryl alkyl ketones possessing longer alkyl chains (*e.g.* hexanophenone, heptanophenone and ocatanophenone) will shed more light on this affect and are in progress.

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Notes and references

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7 Since the study in ref. 6 was conducted on powder crystalline samples, it was necessary to verify that the elimination and cyclization processes occurred in our crystals. This was done as follows: photolyzed inclusion complex crystals were dissolved in water and the included compounds (unreacted ketones and photoproducts) were extracted with CH_2Cl_2. Analysis of the extraction mixtures by GC–MS and TLC revealed three components: the unreacted ketones, a cyclobutanol (C product) and acetophenone (E product). Full details are available as ESI.†
8 For both complexes, the methods of X-ray diffraction data collection and structure determination and refinement were similar and will be summarized here. Full details are available in the .cif file. Data were collected at room temperature on crystals sealed in glass capillaries using an automated Siemens P4 diffractometer with a sealed tube Mo target source. For the β-CD/butyrophenone complex, 6708 unique reflections (R_{int} = 0.0306) were collected to $2\theta_{max}$ = 50°. For the β-CD/valerophenone complex, 11163 unique reflections (R_{int} = 0.0241) were collected to $2\theta_{max}$ = 60°. For both structures, the phase problem was solved by molecular replacement of the β-CD coordinates from the isomorphous β-CD/coumarin complex (ref. 13). Difference electron density maps revealed the guest molecules were very disordered in both cases. The disorder was interpreted as phenyl ring face-to-face packing of the guest molecules with identically packing pairs distributed over multiple sites. Least-squares refinement on F^2 was carried out using SHELXL97 (G. M. Sheldrick, SHELXL97. Program for the Refinement of Crystal Structures. University of Göttingen, Germany, 1997). *Crystal data*: for $C_{42}H_{70}O_{35}{\cdot}C_{10}H_{12}O{\cdot}11.5H_2O$, M_r = 1490.36, monoclinic, space group *C*2 (no. 5), a = 19.352(2), b = 24.599(2), c = 15.916(2) Å, β = 109.378(7)°, Z = 4, D_c = 1.385 g cm^{-3}, crystal size 0.7 × 0.5 × 0.4 mm. Final refinement details: 923 parameters, R_1 = 0.0668, wR_2 = 0.1748 and GOF = 1.052 for 5202 reflections with $F_o > 4\sigma(F_o)$. For $C_{42}H_{70}O_{35}{\cdot}C_{11}H_{14}O{\cdot}11H_2O$, M_r = 1495.38, monoclinic, space group *C*2 (no. 5), a = 19.339(2), b = 25.581(1), c = 16.010(2) Å, β = 109.080(7)°, Z = 4, D_c = 1.327 g cm^{-3}, crystal size 0.6 × 0.4 × 0.4 mm. Final refinement details: 907 parameters, R_1 = 0.0915, wR_2 = 0.2504 and GOF = 1.020 for 6425 reflections with $F_o > 4\sigma(F_o)$. CCDC 182/1595. See http://www.rsc.org/suppdata/cc/b0/b002828m/ for crystallographic files in .cif format.
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