Ternary Complexes and Diels–Alder Reaction of Cyclopentadiene in Crystalline Cyclodextrins

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Ternary complexes of cyclodextrins with cyclopentadiene and a dienophile undergo solid-state Diels–Alder cycloadditions.

Most reported catalytic reactions of cyclodextrins (CDs) involve a binary complex of the CD with a single organic substrate.[1] In a few reports, two dissimilar organic reactants have been contacted within a ternary CD complex in solution.[2] In the solid state, contacts between reactive guest molecules seem more probable than in solution because of the proximity of neighbouring CD binding sites. We now report the formation of ternary CD complexes in the solid state and Diels–Alder reactions between the guests in such complexes.

(3)

(5)   (6)

(7)   (8)

a; R = PhCH₂
b; R = Ph
c; R = Me[CH₂]₇
d; R = Buᵗ
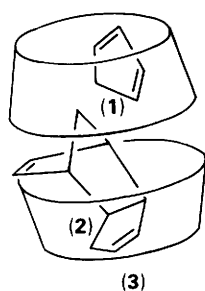
Formation of solid ternary complexes was demonstrated in a model system consisting of the CD, cyclopentadiene (1), and *endo*-dicyclopentadiene (2).

Thus, α-cyclodextrin (α) was precipitated from water by addition of (1) containing 1—5% of (2). The resulting solid had stoicheiometry (α)₂·(1)·(2), and was identified as a crystalline inclusion complex by powder X-ray diffraction and by FTIR spectroscopy.[3] Space-filling models, as well as comparison with known structures of α complexes,[4,5] suggested the geometry (3), where one of the α cavities (5 Å free diameter) is filled by the methylene bridge of (2) plus a molecule of (1). An isomorphic complex (α)₂·(2) was obtained in the absence of (1). A complex of α with pure (1) did not crystallize, however.

β-Cyclodextrin (6 Å cavity, β) did not give a ternary complex with these guests. Instead, a binary complex β·(2) crystallized even when (1) was present in great excess.

A ternary γ-cyclodextrin (γ) complex was prepared by an indirect route involving absorption of guest from the vapour phase.[6] Thus, γ·(1) was obtained by the precipitation method and was extensively washed with chloroform to remove >99% of the guest. The resulting 'empty' γ (4) rapidly and reversibly absorbed both (1) and (2) from the vapour phase. On exposure of (4) to the mixed vapours of (1) and (2) at room temperature for 4 h, a ternary complex γ·(1)₂·(2) was obtained.

Space-filling models indicate that (1) and (2) fit loosely in the large (8 Å) γ cavity. Diffusion within solid γ and the binding of multiple guest molecules are thus reasonable.

Native α, β, and γ (crystallized from water in the absence of organic guests) absorbed (1) from the vapour phase more slowly than (4), giving α·(1)₀.₀₅, β·(1)₀.₀₄, and γ·(1)₀.₃ after comparable times. The differing behaviour of (4) and native γ can be attributed to differences in crystal packing, as noted previously.[6]

Diels–Alder reactions of (1) within solid CD complexes were investigated by the following typical procedure. The binary complex β·(5a)₀.₃ was prepared by cocrystallization of β with the maleimide. On exposure to vapours of (1) (43 °C; 1 h), this was converted to a binary complex with the Diels–Alder adduct, β·(6a)₀.₃. The reaction was monitored *via* the shift in the carbonyl absorption in the solid-state FTIR spectrum (from 1707 to 1701 cm⁻¹) and by dissolution of the complex in hot water and isolation of (6a) (>96%).

Similar reactions with (1) were observed for α, β, and γ complexes with (5a) and (5b) and for β complexes with (5c) and (5d), giving (6a—d). Complexes of β with (7a) and (7c) likewise reacted, giving (8a) and (8c) in 64 and 91% yield, respectively; the corresponding α complexes did not react. Adduct (8a) was enantiomerically enriched ([α]D −17°, CHCl₃), owing to asymmetric induction by the chiral CD environment.[7]
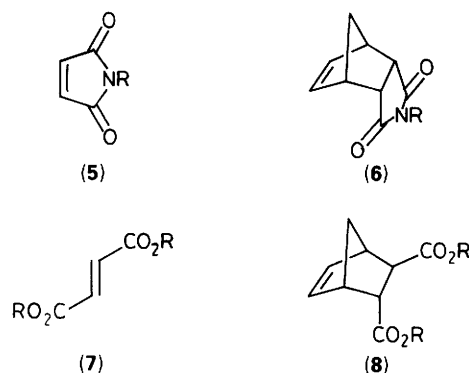
In all cases examined [(5a,b) and (6a,c)] the reaction proceeded faster and more completely in the order γ > β > α. Probably, the larger cavities of γ and β present reduced steric barriers for diffusion of (1) into the solid and for subsequent reaction.

A transient intermediate in the solid state reaction must be a ternary complex CD·(1)ₓ·(5 or 7)ᵧ, which is analogous to the stable ternary complexes formed between CD, (1), and (2). To our knowledge, this is the first demonstration of ternary complexation of nonidentical organic guests in a solid CD phase and of a bimolecular reaction within such a phase.[8]

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