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Reversible encapsulation of guests in modified cyclodextrins: studies with the β-cyclodextrin percinnamate·1,7-dioxaspiro[5,5]undecane system

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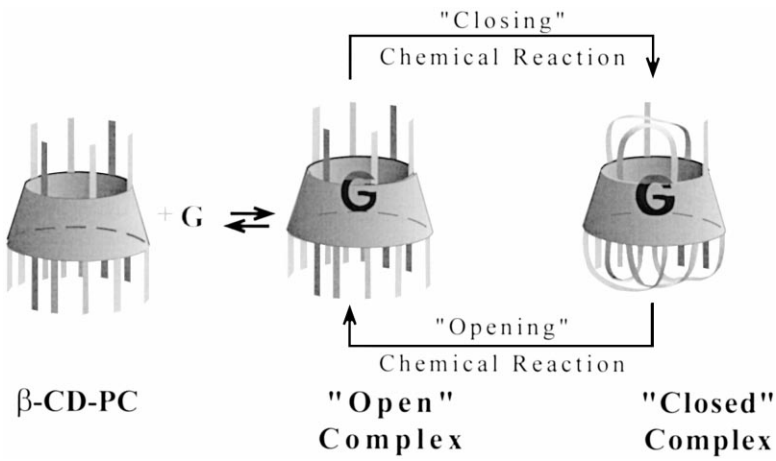
Abstract—UV irradiation of a solution of the pheromone 1,7-dioxaspiro[5,5]undecane (DU) and β-cyclodextrin percinnamate (β-CD-PC) induces the formation of intramolecular cyclobutane bridges that trap the pheromone within the cyclodextrin cavity. Release of the pheromone can be achieved by bond-breaking chemical reactions, suggesting that such systems may be used for the controlled release of this or other pheromones under field conditions. © 2001 Elsevier Science Ltd. All rights reserved.

The notion of trapping guest molecules within the cavities of host molecules has attracted much attention.[1] Hosts that can be closed, trapping a guest, and then opened, to release the guest, have also been proposed and demonstrated.[2]

A simple technique for controlling the binding and release of guest molecules involves modified cyclodextrins having substituents capable of bond-forming chemical reactions. Bridges are formed, closing the open ends of the cavity and thereby trapping guest molecules present in the solution in which the modified cyclodextrin is dissolved. Subsequent bond-breaking reactions release the guest. This approach (depicted in Scheme 1) has been demonstrated with α- and β-cyclodextrin percinnamate and a variety of guests.



Scheme 1. The reversible inclusion and imprisonment of guest molecule G by α-cyclodextrin (CD) derivative through intramolecular bond-forming chemical reaction of the CD substituents in the 'open complex'. A different chemical reaction opens the 'closed complex' and releases the guest.

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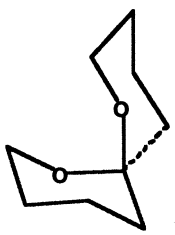
Intramolecular photo-cycloaddition (λ>300 nm radiation) achieved trapping while photo-cleavage (λ=254 nm radiation) reversed the reaction.[2] Chemical reaction of the entrapped guest within these closed cavities has also been described.[3]

The study of one system, β-cyclodextrin percinnamate (β-CD-PC) host with the pheromone 1,7-dioxaspiro[5,5]undecane (DU), is described here. This spiroacetal pheromone is the main component of the sex pheromone of the olive fruit fly *Dacus oleae*, which is widely distributed throughout the Mediterranean basin and parts of North Africa. It is a major pest in countries where olives are principal domestic and export agricultural products. It was anticipated that this easily prepared pheromone could be widely used in trapping systems to control the olive fly. However, the fact that DU is a volatile liquid at room temperature has led to a number of approaches to construct slow-release systems for effective field use.

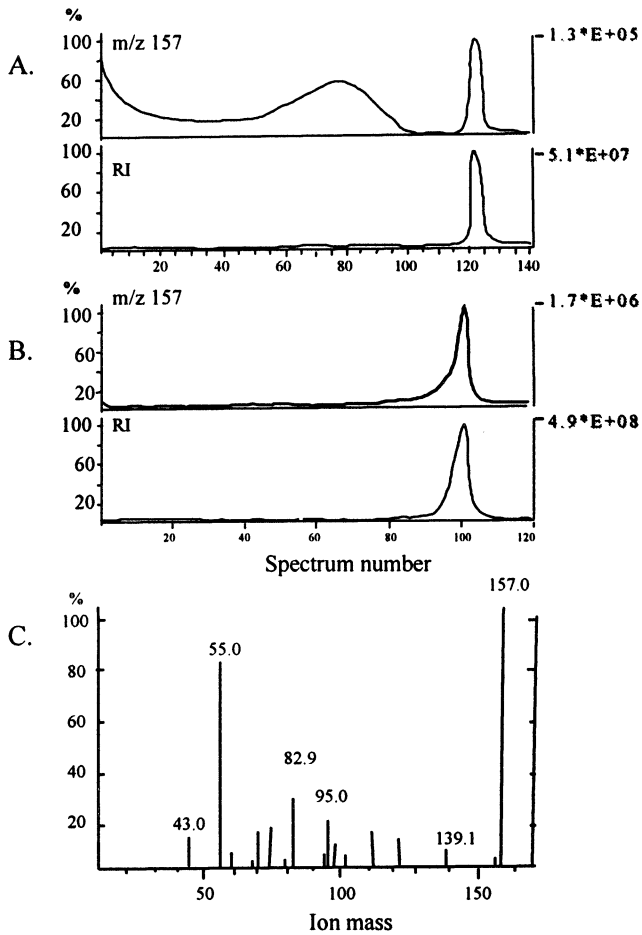
β-Cyclodextrin percinnamate (β-CD-PC) might be an ideal initial system to test the practical effectiveness of the approach depicted in Scheme 1 for the controlled release of DU. It had previously been shown that various cyclodextrin derivatives form inclusion complexes with DU[4] and X-ray structures established that the DU molecule lies within the CD cavity.[5]



1,7-dioxaspiro[5,5]
undecane (DU)

The irradiation of β-CD-PC to form 'closed' complexes with DU was carried out in both dilute solutions and in the neat pheromone. An acetonitrile solution of DU (1 mM) was irradiated (λ>300 nm; Rayonette Reactor) and the reaction monitored by IR (1636 and 1719 cm^{-1} decrease; 1750 cm^{-1} increase) and UV (λ_{max} 276 nm) spectroscopy, both of which indicated that cinnamate photo-cycloaddition takes place. The complex was isolated (60–80% recovery) by precipitation with methanol; unreacted pheromone is left in solution while the precipitate contains β-CD-PC, both complexed and uncomplexed, reacted and unreacted. Characteristic infrared bands at ca. 2935 and 2871 cm^{-1} indicate the presence of the pheromone. A similar irradiation of β-CD-PC (~15 mM) dissolved in neat pheromone was performed. In order to ensure complete removal of excess pheromone, the irradiated solution was evacuated at 80°C at low pressure; the residue was then triturated consecutively three times with methanol and each time the residue was evacuated under high vacuum. The infrared spectrum of the resulting complex displayed the characteristic pheromone bands. Control experiments without irradiation, in solution and in neat pheromone, showed either no pheromone or only difficult-to-characterize traces. The mass spectra of the isolated complexes were taken as described in Scheme 2.

When the sample was irradiated (150 h) until no free double bonds were observed in the IR spectrum, only one sharp, large peak at ca. 380–400°C (spectra 95–105) was obtained (Scheme 2B). In accord with previous results with the β-CD-PC host and other guests,[2] the complex disintegrates at this temperature and the pheromone is released. When only partial photo-chemical reaction has taken place (50 h irradiation) the IR



Scheme 2. Characterization of the β-CD-PC pheromone complex, obtained by irradiation of acetonitrile solutions of the components by mass spectroscopy, as a function of temperature. FAB/MS of the photo-product was performed by warming a sample in the probe of a PGS-70B Finnigan-Mat instrument up to 400°C (at 10^{-6} mmHg) and monitoring the m/z=157 signal (MW of the pheromone 156.23 au). The approximate temperatures given in the text were correlated with spectrum number (x-axes) in separate calibration experiments. (A) Short irradiation time (50 h). Total ion current (bottom); ions with m/z 157 (top). (B) Long irradiation time (150 h). Total ion current (bottom), ions with m/z mass 157 (top). (C) The full mass spectrum of the pure pheromone. The same CI mass spectra were obtained for the species in spectra 68–92 of the short irradiation experiment (A) and in spectra 95–105 of the long irradiation experiment (B).

spectrum of the reaction product indicates that there are still unreacted double bonds of the cinnamate residues.

The broad peak at 100–200°C (spectra 68–92, Scheme 2A) is ascribed to free pheromone molecules, which are loosely held in partially closed cavities. The sharper peaks at 380–400°C (spectra 118–130, Scheme 2A and spectra 90–110, Scheme 2B) are ascribed to the cage-trapped material, which is only released by thermal disintegration of the host. The short irradiation results (Scheme 2A) indicate that even partial closing of the cavities suffices to trap DU and high vacuum at 100°C is required for its release.

Our findings raise a number of questions and suggest further experiments. One important question is the minimum number of cyclobutane rings needed to close-off the cyclodextrin cavity and prevent release of the spiroketal DU. Molecular graphics (data not shown) suggests that even the formation of a single cyclobutane ring may already provide sufficient steric interference to achieve an appreciable degree of closure of one face of the CD cavity. We conclude that β-CD-PC and related systems may provide essential components for novel devices with 'tunable' binding and release capabilities for a variety of applications. Preparation of large samples of the β-CD-PC pheromone complex and use under field conditions, in comparison with other slow-release methods, is being planned.

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