Fully Collaborative Guest Binding by a Double Cyclodextrin Host

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A double cyclodextrin host (**3b**) shows the largest association constant reported for a modified cyclodextrin ($K_{ass.}$ = 2 030 000 mol^{-1} dm^3; with ethyl orange); the greater (×224) degree of association of this guest with (**3b**) as compared with β-cyclodextrin, demonstrates the full collaboration of the two binding sites.

Cyclodextrin exhibits unique enzyme-like recognition and catalytic properties, but its guest-binding ability is weaker than some enzymes. In order to enhance the binding ability, additional binding sites have been introduced onto cyclodextrins, successfully in some cases.[1] Host molecules, (**1**)[2] and (**2**),[3] which have a second cyclodextrin as an additional site, have also been constructed, but they showed at most a fourfold enhancement of binding ability using appropriate guests, suggesting that the additional cyclodextrin was inefficient as a second binding site. In this report, we describe that (**3b**) shows the largest association constant ($K_{ass.}$ = 2 030 000 mol^{-1} dm^3 for ethyl orange) for the reported modified cyclodextrins demonstrating an effective collaboration of the two cyclodextrin moieties in guest-binding.

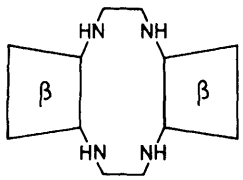
The disulphides, (**3a**) and (**3b**), were prepared by air oxidation of 6-deoxy-6-mercaptocyclodextrins[4] and purified using Sephadex G-15- and reversed phase-column chromatography. Their structures were confirmed by ^{1}H n.m.r. and u.v. spectra, elemental analyses, and reduction to the starting material with dithiothreitol. Association constants for the formation of adducts between (**3a**), (**3b**), α-, or β-cyclodextrins and some guests were computed by the Scatchard treatment[5] of electronic and fluorescence spectral data. Strong and weak association constants, K_1 and K_2, respectively, for α- or β-cyclodextrins with methyl or ethyl orange were computed by Klotz's method.[3,6] Job's plot[7] of the association between (**3a**) or (**3b**) and methyl or ethyl orange confirmed the 1 : 1 host–guest binding. These results are summarized in Table 1.

The intensity and wavelength of the fluorescence of 2-*p*-toluidinonaphthalene-6-sulphonate (TNS) are well known to reflect the hydrophobicity of the environments of the TNS.

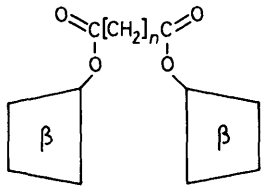
Table 1. Association constants (mol^{-1} dm^3) between cyclodextrins and some guests.[a]

	α-CD		(**3a**)		β-CD		(**3b**)	
	K_1	K_2	K	K/K_1	K_1	K_2	K	K/K_1
ANS[b]					110		695	6.3
TNS[c]					1 800		87 000	48
MO[d]	7 840	40	26 000	3.5	2 970	606	583 000	196
EO[e]	15 300	256	18 700	1.2	9 030	388	2 030 000	224

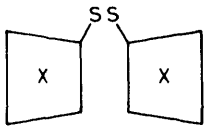
[a] In carbonate buffer (pH 10.60, I = 0.05 M) at 25 °C. [b] 1-Anilinonaphthalene-8-sulphonate. [c] 2-*p*-Toluidinonaphthalene-6-sulphonate. [d] Methyl orange. [e] Ethyl orange.



(1)



(2)



(3a) X = α

(3b) X = β

While the (2)–TNS complex showed *ca.* tenfold enhancement of the intensity shown by TNS in water,[3] the (3b)–TNS complex demonstrated an even greater enhancement (50-fold). The wavelength of the fluorescence maximum of TNS, the (1)–TNS complex, or the (2)–TNS complex was 480, 444,[2] or 447[3] nm, respectively, whereas the (3b)–TNS complex showed a maximum at a shorter wavelength, 436 nm. Moreover, (3b) could bind TNS more strongly (48 times) than β-cyclodextrin.

These results suggest that the two β-cyclodextrins of (3b) can include the two aromatic parts of the guest more efficiently than those of (1) or (2). Also, for alkyl orange dyes, (3b) showed quite large association constants up to 2 030 000 mol^{-1} dm^3 and great enhancement of K/K_1 up to 224 times, demonstrating that the additional β-cyclodextrin could work fully as a second binding site. The observation that ethyl orange was more strongly bound by (3b) than methyl orange indicates that the dialkyl amino group of the dye was accommodated in the cyclodextrin cavity.

The collaboration of two binding sites may be attributable to the short bridge (a disulphide bond) between the two binding sites. However, far smaller (3.5 times) or negligible (1.2 times) enhancements of K/K_1 in the binding of alkyl orange dyes were observed for the double α-cyclodextrin (3a). This means that it is difficult to link the collaborative effect with strong guest-binding.

We are indebted to Dr. Nobuaki Nakamura (Japan Maise Products Co. Ltd.) for a generous gift of α- and β-cyclodextrins.

Received, 5th June 1984: Com. 776

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