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CONFORMATIONAL CHANGE OF PHOTORESPONSIVE CAPPED CYCLODEXTRIN DETECTED BY CIRCULAR DICHROISM

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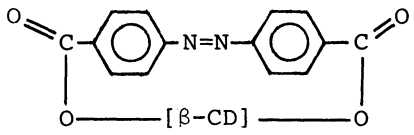
The circular dichroism spectrum of azobenzene-capped β-cyclodextrin (I) was found, in some cases, to show an abrupt change on addition of guest molecules with ionic nature. This nonstoichiometric behavior was regarded as evidence for a conformational transition of the cyclodextrin moiety caused by outside binding of the guest molecules.

Cyclodextrins bind a variety of substances into their cavity in aqueous solution. Furthermore, they exert catalytic activity on suitable included substrate molecules mimicking the action of enzymes.[1] Although a great deal of effort has been invested to improve their catalytic activity by chemical modifications,[1] the force driving complex formation and the mechanism of inclusion are still unclear and a matter of speculation. Saenger et al. proposed that α-cyclodextrin·substrate complex formation is mainly due to a change in conformation of α-cyclodextrin itself.[2] Although there exist some arguments against the suggestion as the mechanism solely responsible for clathration,[3,4] the conformational change of cyclodextrins itself seems to be involved in complex formation as evidenced by optical rotation[5] and circular dichroism[6,7] data. Chemical modification of cyclodextrins by probe moiety might be a promising method to examine their structural changes. We have, in fact, recently demonstrated stoichiometrical changes in the circular dichroism spectrum of azobenzene-capped β-cyclodextrin (I)[8] induced by substrate addition, which might be due to a conformational change of the cyclodextrin moiety. In this report, we wish to report non-stoichiometric changes in the circular dichroism spectrum of I which are somewhat similar to those observed for helix-coil transition of polypeptides.



I

Capped cyclodextrin I exhibits an induced dichroism in the n-π* region of the cap azobenzene.[6] After irradiation appears an additional induced band in the π-π* region of the cap. Both dichroism bands decrease in intensity on addition of guest molecules. The analysis of these phenomena indicates that I forms complexes of 1:1 or 1:2 host/guest stoichiometry. However among the substrates shown in Table 1, nonstoichiometric behaviors have been observed for L-α-methylbenzylamine, L-mandelic acid and N-acetyl-L-phenylalanine with trans-I as a host (Figure 1), that is, the circular dichroism of I is almost unaffected by substrate addition until an abrupt change takes place at high guest concentrations.

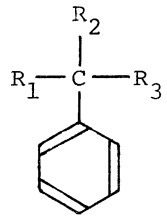


Table 1. Complex formation and conformational transition of I

	Guest[a]				Formation constants[b]	
	R_1	R_2	R_3	Host	$K_1(M^{-1})$	$K_2(M^{-1})$
(A)	H	CH_3	NH_2	trans-I	transition	
				cis-I	c)	122
(B)	H	CH_3	NHAc	trans-I	c)	27.5
				cis-I	c)	2090
(C)	H	CH_3	OH	trans-I	c)	16.1
				cis-I	c)	145
(D)	CH_3	COOH	OH	trans-I	transition	
				cis-I	c)	68
(E)	H	H	$CH(NH_2)COOH$	trans-I	c)	1.2
				cis-I	1920	45
(F)	H	H	CH(NHAc)COOH	trans-I	transition	
				cis-I	c)	94

a) All guests are in L-configuration. b) Formation constants were obtained based on the 1:2 host/guest stoichiometry previously reported[7] (25°, Tris buffer, pH 7.2). K_1 and K_2 are formation constants for the first and the second inclusion steps respectively. c) Values are too large to be determined definitly.

This phenomenon is somewhat analogous to the helix-coil transition of polypeptides, confirming two different structures for I. The nonstoichiometric behavior demonstrates the presence of interactions between I and guest molecules which are different from those of inclusion complex formation. One possible explanation is that I has the guest molecules aggregated around its cyclodextrin moiety and undergoes a conformational change when the guest concentration reaches a limit. It is not clear if the effect is created simply by substrate binding to the outer side of cyclodextrin wall or additionally by disruption of the interglucosidic, intramolecular hydrogen bonds between O(2) and O(3).

Table 1 indicates the important role of amino and carboxylic groups in inducing the conformational transition. Hydroxy group itself is not a factor to cause the transition. There exists a discrepancy, however, in the case of phenylalanine which does not exhibit the transition in spite of the presence of both amino and carboxylic groups in it. In the aqueous solution of pH 7.2, amino and carboxylic groups should exist as ammonium cation and carboxylate anion respectively. If the total ionic nature of one substrate is important for the transition, the discrepancy might be interpreted by the fact that phenylalanine is ionically neutral as one molecule. It is thus another problem how the ionic nature is related to the conformational tran-

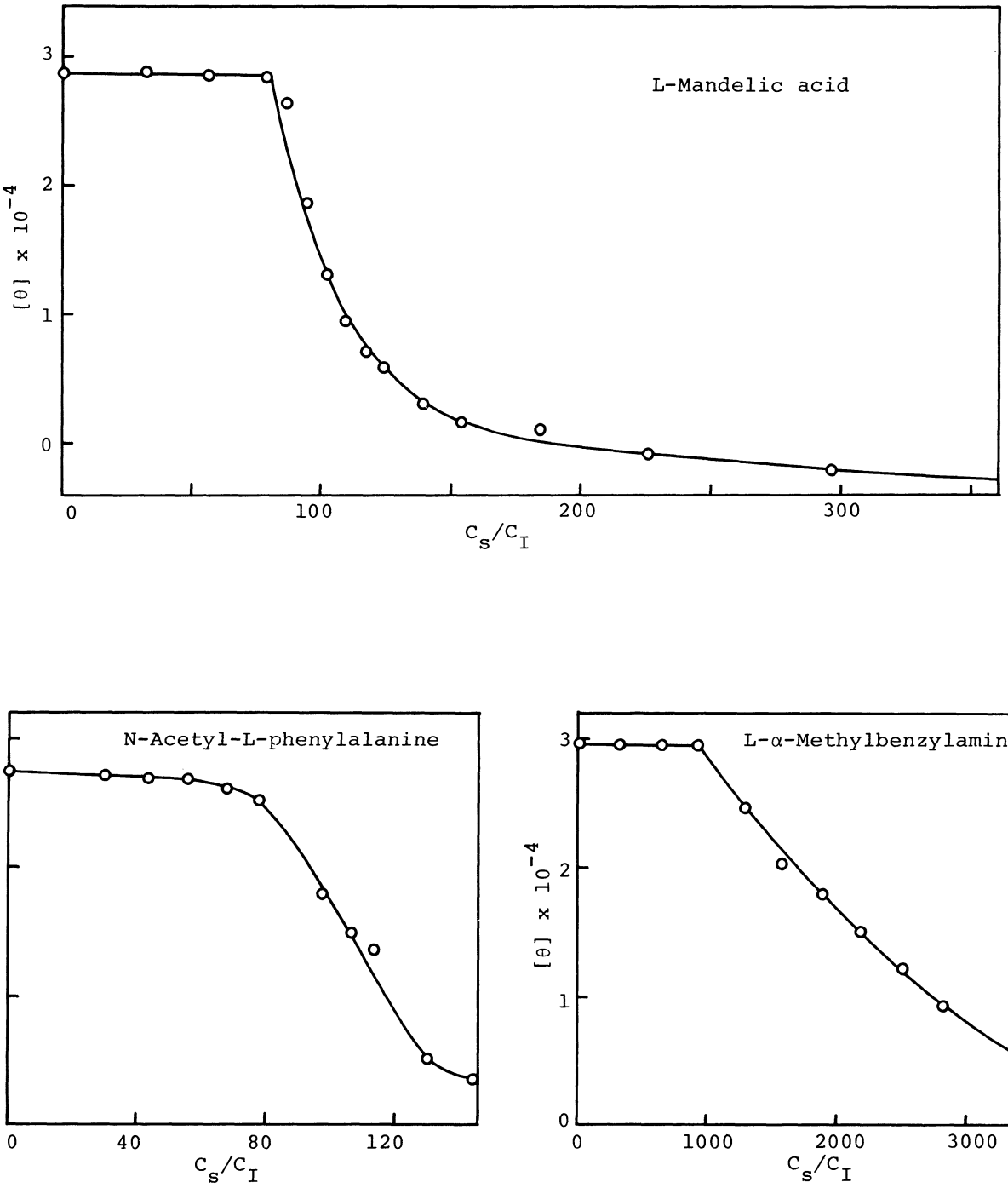


Fig. 1 Plots of the molecular ellipticity at 355 nm of trans-I as a function of substrate/I molar ratio (C_S/C_I).

sition.

Contrast to the case for trans-I, these substrates form complexes with cis-I of 1:2 host/guest stoichiometry (Table 1). It implies that cis-I can involve guest molecules without regard to their ionic character, and that trans-I can involve only non-ionic guest molecules. The result of the stoichiometry indicates that the guest molecule included first is bound to I much more strongly than the second one. The behavior of these guest molecules is similar to that of amino acids reported previously.[7)]

Further work is needed to clarify the actual scheme of these phenomena.

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8) 6,6',O,O'-(4,4'-azobenzenedicarbonyl)cycloheptaamylose. Synthesis, purification and analysis of this compound were described in ref. 6.

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