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Host-Guest Complexation of Oligosaccharides: Interaction of Maltodextrins with Hydrophobic Fluorescence Probes in Water

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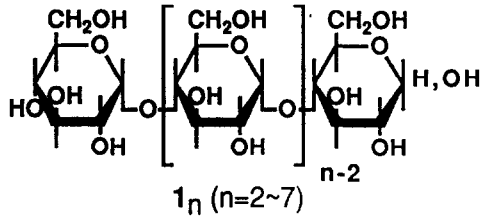
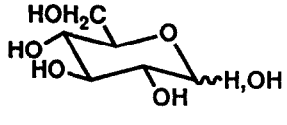
Key Words: host-guest complexation; oligosaccharide; maltodextrin; ANS (TNS); hydrophobic effect

Abstract: *Fluorimetric titration studies indicate that higher homologs of maltodextrin, i.e., β-1,4-linked linear glucose oligomers, bind fluorescence probes 1,8-ANS and 2,6-TNS in a 1:1 stoichiometry in water at pH 6.8 and 25 °C. Although the binding constants even for heptaose (5.7 M^{-1} for ANS and 27 M^{-1} for TNS) are significantly smaller than those for the cyclic counterpart, β-cyclodextrin (93 M^{-1} for ANS and 1700 M^{-1} for TNS), the micropolarities of the probe-binding sites of linear and cyclic hosts are rather similar to each other.*

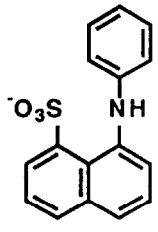
Cell-surface oligosaccharides play important roles in the intercellular recognition. Hakomori, et. al., have recently demonstrated that the cell-cell adhesion is initiated by direct oligosaccharide-oligosaccharide interactions, and suggested the importance of hydrophobic effects therein.[2] The present work is concerned with the hydrophobic guest-binding properties of linear oligosaccharides. We report here on the interaction of maltodextrins $\mathbf{1}_n$ (n = 2~7) and parent glucose ($\mathbf{1}_1$) with hydrophobic fluorecence probes in water.[3]



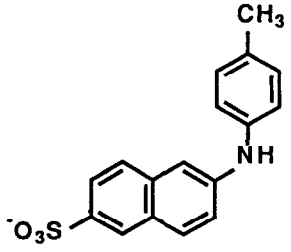
$\mathbf{1}_n$ (n=2~7)



$\mathbf{1}_1$



1,8-ANS



2,6-TNS

Cyclodextrin (β-CD), a cyclic heptamer of D-glucose having an α-1,4-glycoside linkage, forms a 1:1 complex with 8-anilino-1-naphthalenesulfonate (1,8-ANS, 1.0 x 10^{-4} M) in water at pH 6.8. It also forms both 1:1 and 2:1 (β-CD to guest) complexes with 6-toluidino-2-naphthalenesulfonate (2,6-TNS, 5.0 x 10^{-5} M). Fluorimetric titration at 25 °C gave the binding constants K_{11} = 93 M^{-1} for 1,8-ANS and K_{11} = 1700 M^{-1} and K_{21} = 240 M^{-2}, in reasonable agreement with literature values.[4] Steric effects of the substituents are primarily responsible for the different behaviors of the two probes. Intracavity complexation of the naphthalene ring is allowed for 2,6-TNS, while *not* for 1,8-ANS.[4c,4d]

Maltodextrins $\mathbf{1}_n$ (n = 2~7) are linear glucose oligomers having an α-1,4-glycoside linkage. These as well as parent glucose ($\mathbf{1}_1$) were also found to enhance the fluorescence intensities (I) of 1,8-ANS and 2,6-TNS, in a similar manner as β-CD. The correlations of I for 1,8-ANS and $[\mathbf{1}_n]$ are shown in Figure 1. The efficiencies in enhancing I increase dramatically with increasing n of $\mathbf{1}_n$ as a result of intramolecular cooperativity of the glucose residues in higher homologs.[3] This point becomes clearer when I vs $n\cdot[\mathbf{1}_n]$ plots (Figure 2) are compared; the term $n\cdot[\mathbf{1}_n]$ represents the total concentration of the glucose units. Thus, the effects of *one* glucose unit are the more pronounced for the higher homologs.

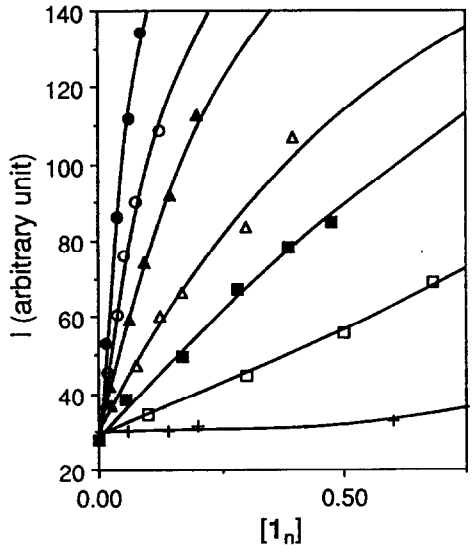


Figure 1. Correlations between I and $[\mathbf{1}_n]$ for $\mathbf{1}_1$ (+), $\mathbf{1}_2$ (□), $\mathbf{1}_3$ (■), $\mathbf{1}_4$ (▲), $\mathbf{1}_5$ (▲), $\mathbf{1}_6$ (○), and $\mathbf{1}_7$ (●) under conditions of [ANS] = 0.1mM at pH 6.8 and 25 °C.

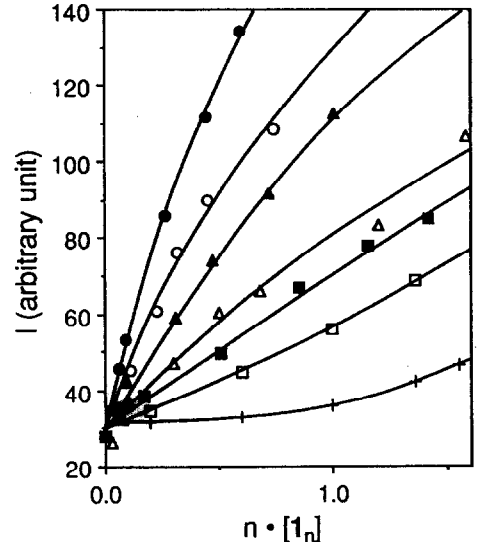


Figure 2. Correlations between I and $n\cdot[\mathbf{1}_n]$ for $\mathbf{1}_1$ (+), $\mathbf{1}_2$ (□), $\mathbf{1}_3$ (■), $\mathbf{1}_4$ (▲), $\mathbf{1}_5$ (▲), $\mathbf{1}_6$ (○), and $\mathbf{1}_7$ (●) under conditions of [ANS] = 0.1mM at pH 6.8 and 25 °C.

The I-[1_n] (Figure 1) or I-n·[1_n] correlations (Figure 2) for higher homologs (1_n, $n \geq 4$) exhibit a saturation behavior in a similar manner as for β-CD. This is indicative of an ANS-1_n complexation ($n \geq 4$) with a well-defined stoichiometry being taking place. In fact, the titration data were analyzed according to the Benesi-Hildebrand equation based on a 1:1 stoichiometry. Thus, plots of $1/(I - I_0)$ vs $1/[1_n]$ ($n \geq 4$) gave a straight line (correlation coefficient, ≥ 0.99); the binding constant K and I_∞ were obtained from the slope and intercept, where I_0 (= 27 in an arbitrary unit) and I_∞ are respectively the fluorescence intensities of free 1,8-ANS and 1,8-ANS·1_n complex and I is the observed intensity in the presence of 1_n. The titration data for 2,6-TNS were analyzed similarly. For every 1_n ($n \geq 5$), double reciprocal plots gave a *single* straight line, indicating that formation of 2:1 complex was not taking place in this case. The K and I_∞ values for 1_n and β-CD are summarized in **Table I**.

Table I. Binding constants (K) and Fluorescence intensities (I_∞) for 1,8-ANS and 2,6-TNS complexes.[a]

host	ANS complex		TNS complex		K_{TNS}/K_{ANS}
	K (M^{-1})	I_∞	K (M^{-1})	I_∞	
1_1 (glucose)	-	-	-	-	-
1_2 (maltose)	-	-	-	-	-
1_3 (maltotriose)	-	-	-	-	-
1_4 (maltotetraose)	1.8	200	-	-	-
1_5 (maltopentaose)	1.8	350	1.9	560	1.1
1_6 (maltohexaose)	3.4	320	8.8	360	2.6
1_7 (maltoheptaose)	5.7	390	27	500	4.7
β-cyclodextrin	93	430	1700	540	18

[a] At pH 6.8 and 25 °C. For ANS complexes, excitation at 348 nm and emission at 520nm. For TNS complexes, excitation at 317nm and emission at 450 nm.

The following observations are noteworthy. (1) The binding constants for both 1,8-ANS and 2,6-TNS increase *gradually* on going from tetraose or pentaose through hexaose to heptaose, in marked contrast to a *sharp* β-CD/ α-CD selectivity.[4] (2) There is a big difference in K's for cyclic and acyclic heptamers, β-CD and 1_7. (3) Acyclic hosts still show a preference for a *naphthyl guest* 2,6-TNS over a *phenyl guest* 1,8-ANS, but not in such a pronounced manner as cyclic host β-CD; the selectivity K_{TNS}/K_{ANS} decreases sharply on going from the higher to lower homologs of 1_n (**Table I**). (4) The I_∞ values of 1,8-ANS and 2,6-TNS for acyclic hosts 1_5~1_7 are similar to each other and are rather close to those for β-CD. These results suggest that the ANS- and TNS-binding with flexible linear oligosaccharides is generally weak and less selective, but

pentaose and higher homologs are capable of undergoing an *induced-fit* type adjustment to the present hydrophobic guests so as to provide a hydrophobic "cavity" which may be compared with β-CD.[4a,5a]

The well-known nature of ANS and TNS suggests that their binding to the present oligosaccharides in water is promoted by a hydrophobic effect.[6] This was further evidenced by examining the effects of added salts. The hydrophobic effect is known to be either strengthened by nonchaotropic and salting-out salts such as NaCl or weakened by chaotropic and salting-in salts such as NaSCN.[7] In accord with this, the binding constants (K) of pentaose $\mathbf{1}_5$ for 1,8-ANS decrease with respect to added salts (2 M in unbuffered water) in the order, NaCl (5.8) ≈ LiCl (5.2) > none (2.5) > LiSCN (1.9) ≈ NaSCN (1.8 M^{-1}). The hydrophobic nature of sugars, especially oligosaccharides, is well documented.[5]

This work reveals a potentially hydrophobic character of linear oligosaccharides. The hydrophobic effect is itself important, but more than that. Polar host-guest interaction may also be promoted in a relatively hydrophobic area. Further work is now under way along this line.

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