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Cyclodextrins (α-, β-, and γ -) as Guests to Calcichrome (Calcion) in Water

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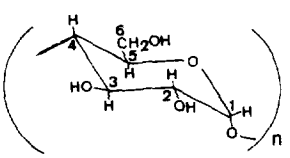
Abstract: The three cyclodextrins (α-, β-, and γ-) formed inclusion complexes with calcichrome (calcion), a non-cyclic tetramer, as host in water. The stability constants K (570, 380 and 430 M^{-1} respectively) of the 1:1 host to guest complexes formed were determined by proton nmr spectroscopy at 25°C.

In a previous paper[1], we have reported the first case of cyclodextrins **1**(α-, β-, and γ-) acting as guest molecules instead of as host. The host molecule was cyclotetrachromotropylene **2**. Since the non-macrocycle calcichrome (also known as calcion, with the structure shown in **3** assigned by us[2]) was found to adopt a folded conformation resembling that of **2**[2], we were interested to find out if it would also act as a host to the three cyclodextrins in water. This paper reports, to the best of our knowledge, the first case of the three cyclodextrins acting as guest molecules to a non-macrocyclic host.

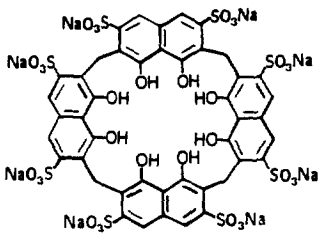


1

n = 6, α-cyclodextrin

n = 7, β-cyclodextrin

n = 8, γ-cyclodextrin



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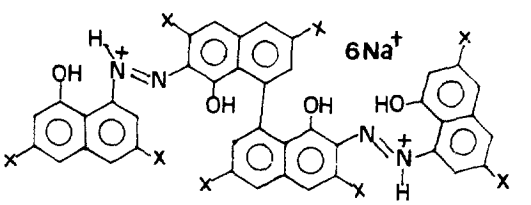


3

X=SO_3^-

RESULTS AND DISCUSSION

That there is complexation between cyclodextrins and calcichrome in water is shown by the observed

changes in the proton nmr spectra of cyclodextrins and calcichrome (Figures 1 and 2). The proton chemical shifts of cyclodextrins in D_2O are shifted upfield whereas those of calcichrome are shifted downfield . Since H_3, the proton in the inner wall of the cyclodextrin cavity is the least shielded (Table 1), the cyclodextrin molecule sits partially inside the hydrophobic cavity of the folded conformation of calcichrome, similar to the case of **2** as host[1], as shown in **4**. If cyclodextrins acted as host molecules (CPK molecular models indicate that calcichrome is able to enter partially into the cavities of the three cyclodextrins), the H_3 proton would have been the most shielded.

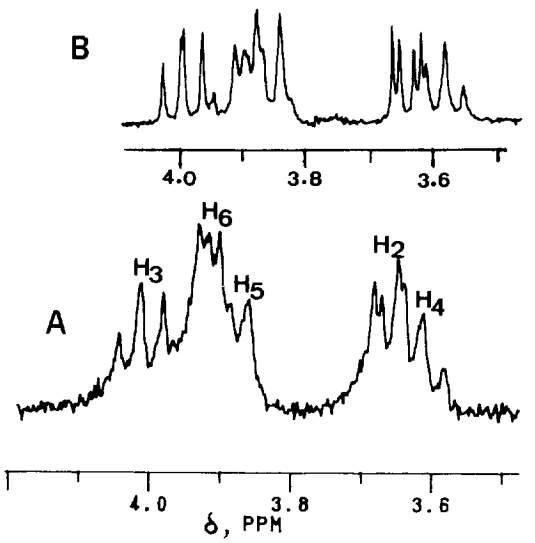


Figure 1. 300 MHz proton nmr spectra in D_2O at 25 ^{0}C of 0.0025 M of α-cyclodextrin (solvent peak at 4.80 ppm, not shown, as internal reference); (A) no host, (B) in the presence of 0.0037 M of calcichrome.

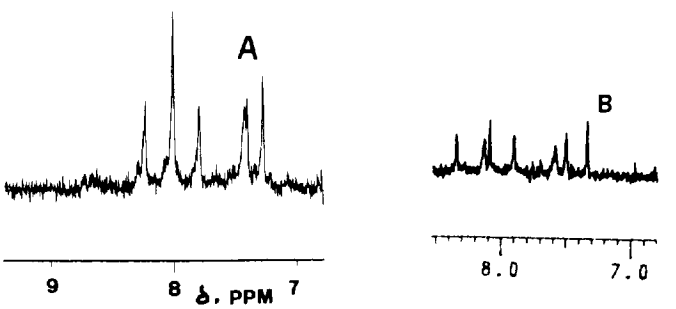


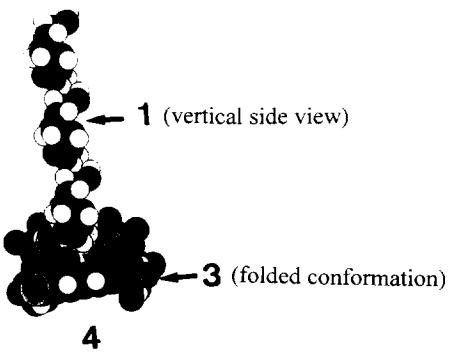
Figure 2. 300 MHz proton nmr spectra in D_2O at 25 ^{0}C of (A) 0.0087 M of calcichrome and (B) 0.0037 M of calcichrome in the presence of 0.0025 M of β-cyclodextrin.

Table 1. Proton nmr chemical shifts of cyclodextrins in D_2O at 25°C

Cyclodextrin		H_1	H_2	H_3	H_4	H_5	H_6
α	δ_u [a]	5.08	3.65	4.00	3.61	3.86	3.92
	$\Delta\delta$ [b]	0.05(0.05)[c]	0.03	0.02	0.06	0.01	0.04 (0.04)[c]
β	δ_u [a]	5.10	3.67	3.99	3.60	d	3.90
	$\Delta\delta$ [b]	0.05(0.07)[c]	0.05	0.03	0.02	d	0.07 (0.09)[c]
γ	δ_u [a]	5.14	3.68	3.96	3.62	d	3.90
	$\Delta\delta$ [b]	0.06 (0.09)[c]	d	0.02	d	d	0.04 (0.05)[c]

[a] Chemical shift of free cyclodextrin in ppm (see ref. 1), solvent at 4.80 ppm as internal reference. [b] Difference between the chemical shifts of cyclodextrin (0.0025 M) in the absence of calcichrome and in the presence of 0.0075 M of calcichrome (upfield shift in ppm). [c] Difference between the chemical shifts of free and complexed cyclodextrin in ppm. [d] Peak could not be discerned.

The maximum induced chemical shifts of about 0.09 ppm (Table 1) are much smaller than those observed in the case of methyl glycopyranosides (1 to 2 ppm)[3]. The small induced chemical shifts are consistent with only partial penetration of a glucose unit (out of a total of six to eight) into the cavity of calcichrome, as indicated by CPK molecular models (see **4**).



To obtain the stability constants K of the complexes, we measured the changes in the proton chemical shifts of a fixed concentration of cyclodextrin in D_2O (0.0025 M) with varying concentrations of calcichrome (0 to 0.0187 M). The values of K, assuming 1:1 host to guest stoichiometry (as in the case of **2** as host)[1], were obtained by a non-linear regression fitting procedure[4] of the H_1 and H_6 protons (the other proton peaks

were not always discernable). Figures 3 and 4 show the calculated proton chemical shift titration curves together with the experimental chemical shifts of the H_1 and H_6 protons of the three cyclodextrins. The average K values are 570±130, 380±80 and 430±140 M^{-1} for α-, β-, and γ-cyclodextrin respectively. The stability constants are equal within experimental errors, but are about four times larger than the corresponding values obtained for **2** as the host.

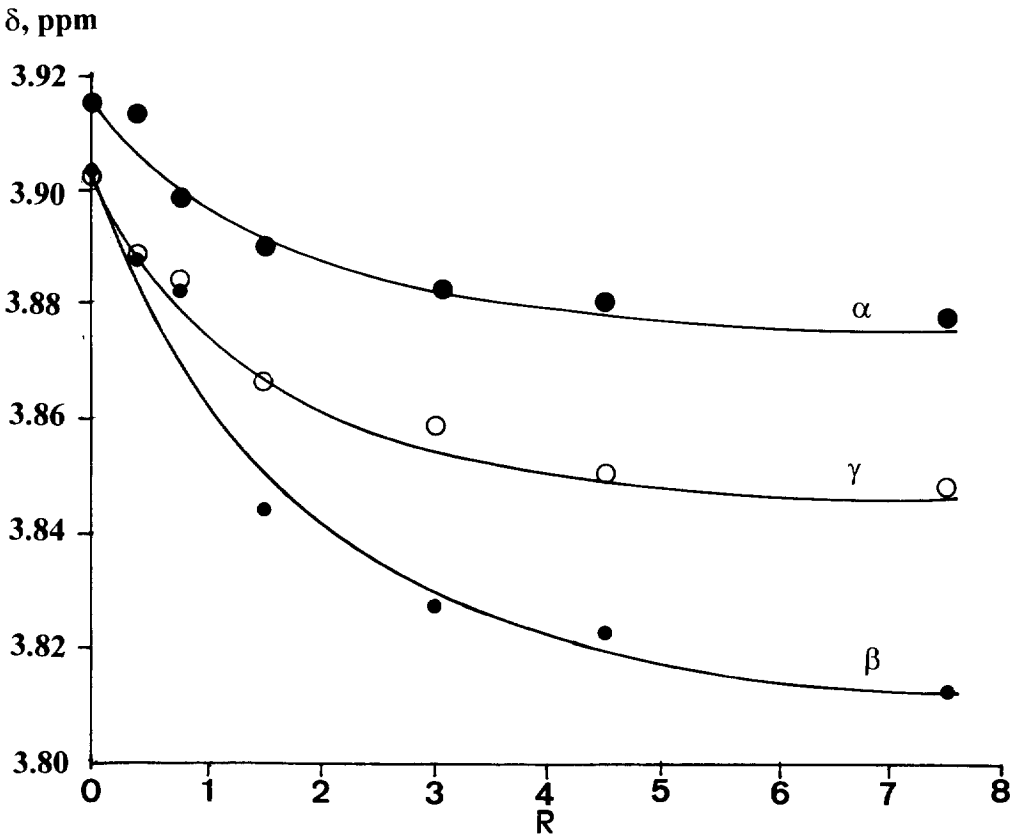


Figure 3. Calculated H_1 chemical shift titration curves of 0.0025 M of α-, β-, and γ- cyclodextrin in D_2O at 25 ^{0}C. R is the molar ratio of the host to guest used and the points are experimental values. The K values, the chemical shifts of the complexes, and the standard deviations between the calculated and experimental chemical shifts of α-, β-, and γ- cyclodextrin are 700, 5.030, 0.003; 300, 5.015, 0.0047; and 290 M^{-1}, 5.030 ppm, 0.004 ppm respectively.

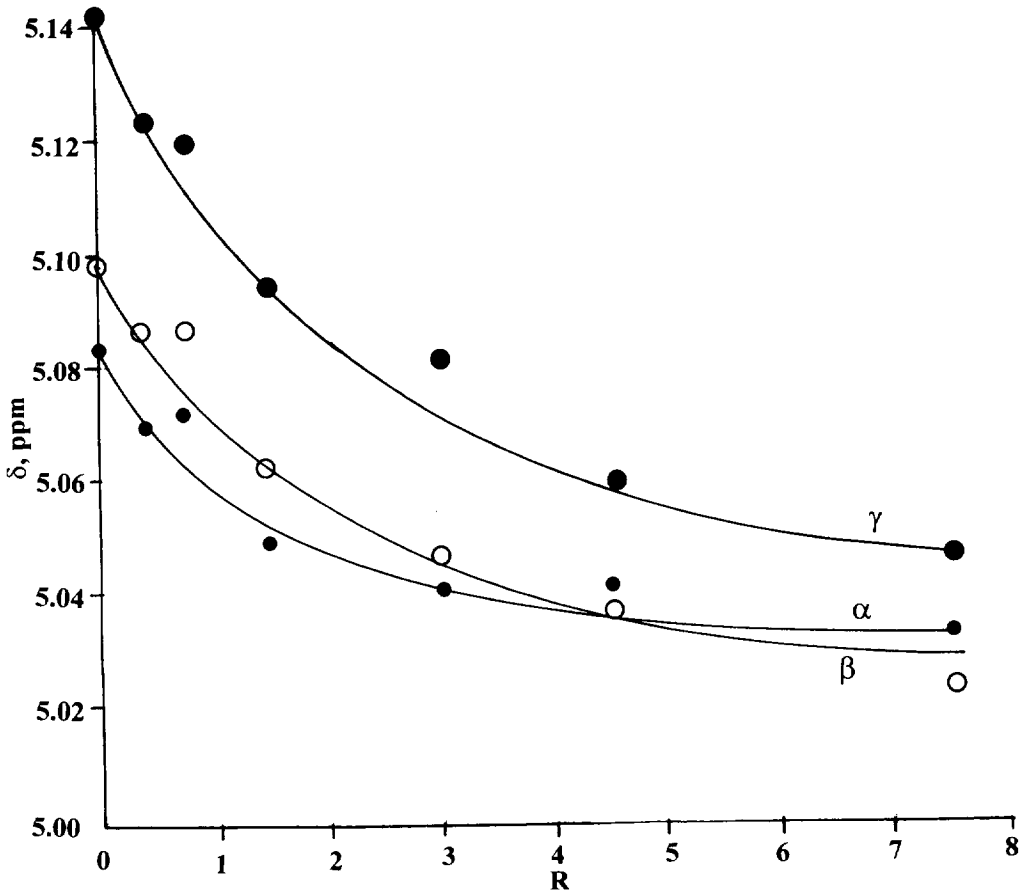


Figure 4. Calculated H_6 chemical shift titration curves of 0.0025 M of α-, β-, and γ- cyclodextrin in D_2O at 25 ^{0}C. R is the molar ratio of the host to guest used and the points are experimental values. The K values, the chemical shifts of the complexes, and the standard deviations between the calculated and experimental chemical shifts of α-, β-, and γ- cyclodextrin are 430, 3.870, 0.002; 450, 3.800, 0.004; and 580 M^{-1}, 3.850 ppm, 0.002 ppm respectively.

EXPERIMENTAL

Materials. Calcichrome and the three cyclodextrins were commercial samples.

^{1}H nmr spectra in D_2O at 25 ^{0}C were recorded with a 300 MHz AC300 Superconducting NMR spectrometer. The solvent peak (unaffected by the concentration variation of the host and guest compounds) at 4.80 ppm was used as the internal reference. In all the chemical shift titrations, the concentrations of the three cyclodextrins were kept at 0.0025 M while the concentration of calcichrome varied.

Calculation of the stability constant K of the 1:1 host to guest complexes using the non-linear regression fitting of the proton chemical shift titration curves were carried out as reported earlier.[4]

ACKNOWLEDGEMENT

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REFERENCES

1. Poh, B.-L. and Tan, C.M., *Tetrahedron Lett.*, **1994**, *35*, 6387.
2. Poh, B.-L. and Khairuddean, M., *Talanta, in press.*
3. Poh, B.-L. and Tan, C.M., *Tetrahedron*, **1993**, *49*, 9581.
4. Poh, B.-L., Tan, C.M., and Loh, C.L., *Tetrahedron*, **1993**, *49*, 3849.

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