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Cyclotetrachromotropylene Plays Host to α-, β-, and γ-Cyclodextrin in Water

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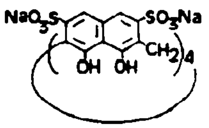
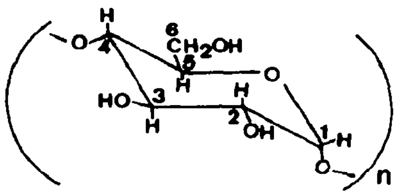
Abstract: The three cyclodextrins (α-, β-, and γ-) formed inclusion complexes with the cyclic tetramer host, cyclotetrachromotropylene, in water. The stability constants K, 140, 100 and 85 M^{-1} respectively, of the 1:1 host to guest complexes formed were determined by ^1H nmr spectroscopy at 25°C.

Recently, we have reported that cyclotetrachromotropylene, **1**, is a good host molecule to a variety of compounds such as polyaromatic hydrocarbons[1], alcohols[2], sugars[2], and amino acids[3]. During the course of our investigation on the factors affecting the synthesis of 1, we accidentally discovered that the three cyclodextrins (α-, β-, and γ-, **2**) formed inclusion complexes with **1** in water, with the latter acting as host. To the best of our knowledge, this is the first case of cyclodextrins acting as guest molecules instead of as host. This paper reports our study on the complexation of the three cyclodextrins with 1 (prepared as described earlier[4]) in water using proton nmr spectroscopy.



1



2

n = 6, α-Cyclodextrin
n = 7, β-Cyclodextrin
n = 8, γ-Cyclodextrin

The proton chemical shifts of the cyclodextrins are shifted upfield in the presence of 1 (Figure 1 and Table 1), indicating that they are included in the cavity of 1. CPK molecular models indicate that the only possible mode of inclusion is one with the side of the cyclodextrin molecule sitting partially inside the open-ended longer side of the cavity of 1 as shown in 3. The possibility of 1 as guest and 2 as host is ruled out because (1) CPK molecular models show that 1 is too large to enter the cavities of the three cyclodextrins and (2) H_3, the proton in the inner wall of the cyclodextrin cavity is the least shielded.

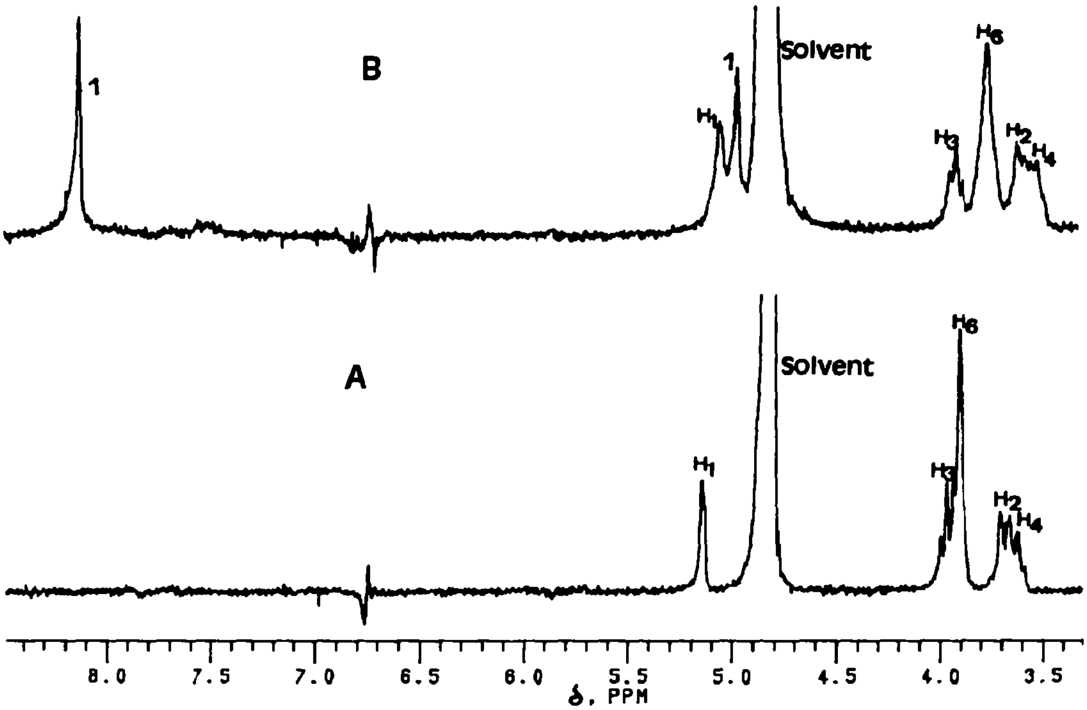


Figure 1. 300 MHz ^1H nmr spectra in D_2O at 25°C of 7.71 x 10^{-3} M of γ-cyclodextrin (solvent peak at 4.80 ppm as internal refeence); (A) no host, (B) in the presence of 2.01 x 10^{-2} M of 1.

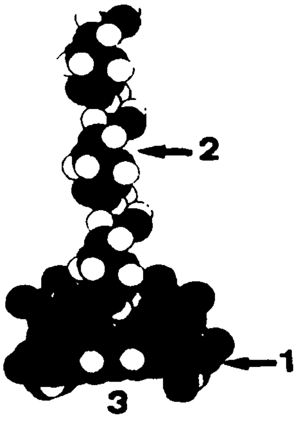


Table 1. Proton NMR Chemical Shifts of Cyclodextrins in D_2O at 25° C.

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
	$\Delta\delta^b$	0.08	0.05	0.03	0.18	c	0.08
β	δ_u	5.10	3.67	3.99	3.60	c	3.90
	$\Delta\delta$	0.15	0.12	0.04	0.12	c	0.24
γ	δ_u	5.14	3.68	3.96	3.62	c	3.90
	$\Delta\delta$	0.13	0.08	0.05	0.09	c	0.25

[a]Chemical shift of free cyclodextrin in ppm; assignment of peaks according to ref.5. [b] Difference between the chemical shifts of free and complexed cyclodextrin in ppm; positive value indicates upfield shift. [c]Peak could not be discerned.

The maximum induced chemical shifts of about 0.2 ppm (Table 1) are much smaller than those observed in the case of methyl glycopyranosides (1 to 2 ppm)[2]. The small induced chemical shifts could be due to (1) only one glucose unit out of the six to eight glucose units in **2** could penetrate the host cavity at any one time and (2) only partial penetration of a glucose unit of **2** into the cavity of **1** is possible as indicated by CPK molecular models.

The stability constants K of the 1:1 host to guest complexes were obtained by a non-linear regression fitting procedure[4]. Figure 2 shows the calculated proton chemical shift titration curve together with the experimental chemical shifts for γ-cyclodextrin. The calculated K values are 140, 100 and 85 M^{-1} (estimated error 10 %) for α-, β-, and γ-cyclodextrin respectively. The decrease in K from α- to γ-cyclodextrin corresponds to the decrease in the fraction of the guest structure included in the host cavity (1/6, 1/7, and 1/8 respectively for one glucose unit in the host cavity).

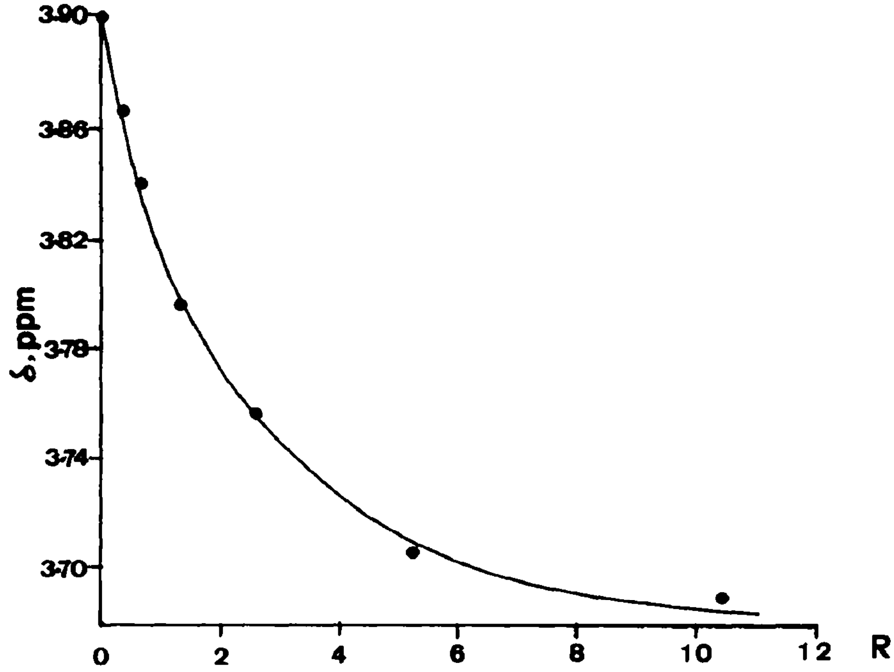


Figure 2. Calculated H_6 chemical shift titration curve of γ-cyclodextrin (7.71 x 10^{-3} M, K = 85 M^{-1}) in D_2O at 25° C. R is the molar ratio of the host to guest used and the points are experimental values.

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