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No Distinction between Host and Guest - the Case of Cyclodextrins Complexing with Disodium 1,8-disulfonato-3,4,5,6-acridinetetracarboxylic acid

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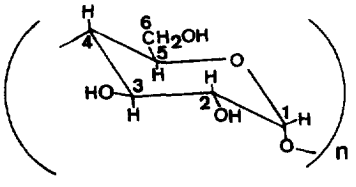
Abstract: The three cyclodextrins (*alpha*-, *beta*-, and *gamma*-) formed inclusion complexes with the dimer of disodium 1,8-disulfonato-3,4,5,6-acridinetetracarboxylic acid (ATCA) in water. In the complexes, one ATCA is partially included inside the cavity of the cyclodextrin while another ATCA is outside and there is no dinstinction between the terms host and guest. Copyright © 1996 Elsevier Science Ltd

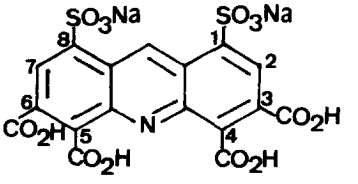
Cyclodextrins (*alpha*-, *beta*-, and *gamma*-, **1**) have always been known as host molecules until recently when we reported, for the first time, that they acted as guest molecules to cyclotetrachromotropylene (a macrocycle)[1] and calcichrome (a non-macrocycle).[2]

In this paper, we report an interesting complexation, involving cyclodextrins and disodium 1,8-disulfonato-3,4,5,6-acridinetetracarboxylic acid, **2**,[3] in which there is no distinction between host and guest in the complexes formed.



1

n = 6, *alpha*-cyclodextrin
n = 7, *beta*-cyclodextrin
n = 8, *gamma*-cyclodextrin



2

The proton nmr spectra of the three cyclodextrins in D_2O are affected by the presence of **2** (Figure 1). The proton chemical shifts move upfield (Figure 2 for *gamma*-cyclodextrin). However, unlike all the previous observations reported in the literature, both the interior (H_3 and H_5) and exterior protons (H_1, H_2 and H_4) of the cyclodextrins are practically equally shifted upfield in the presence of **2** (Table 1). The possibility of **1** acting as the host with **2** partially included in its cavity (as shown by the CPK molecular model **3**, *alpha*-cyclodextrin shown in all CPK models) is ruled out because this geometry requires the interior protons of **1** to be more shielded than the exterior protons.[7] The possibility of **1** acting as a guest, sitting vertically in the hydrophobic cavity of the dimeric form[4] of **2** (as shown by the CPK molecular model **4**) is also ruled out because this geometry requires the interior protons of **1** to be less shielded than the exterior protons. [1,2] A possible geometry of the complex to explain the equal upfield shifts is shown in **5** where the dimeric form of **2** has one molecule of **2** partially included in the cavity of **1** and another molecule outside the cavity. The included **2**

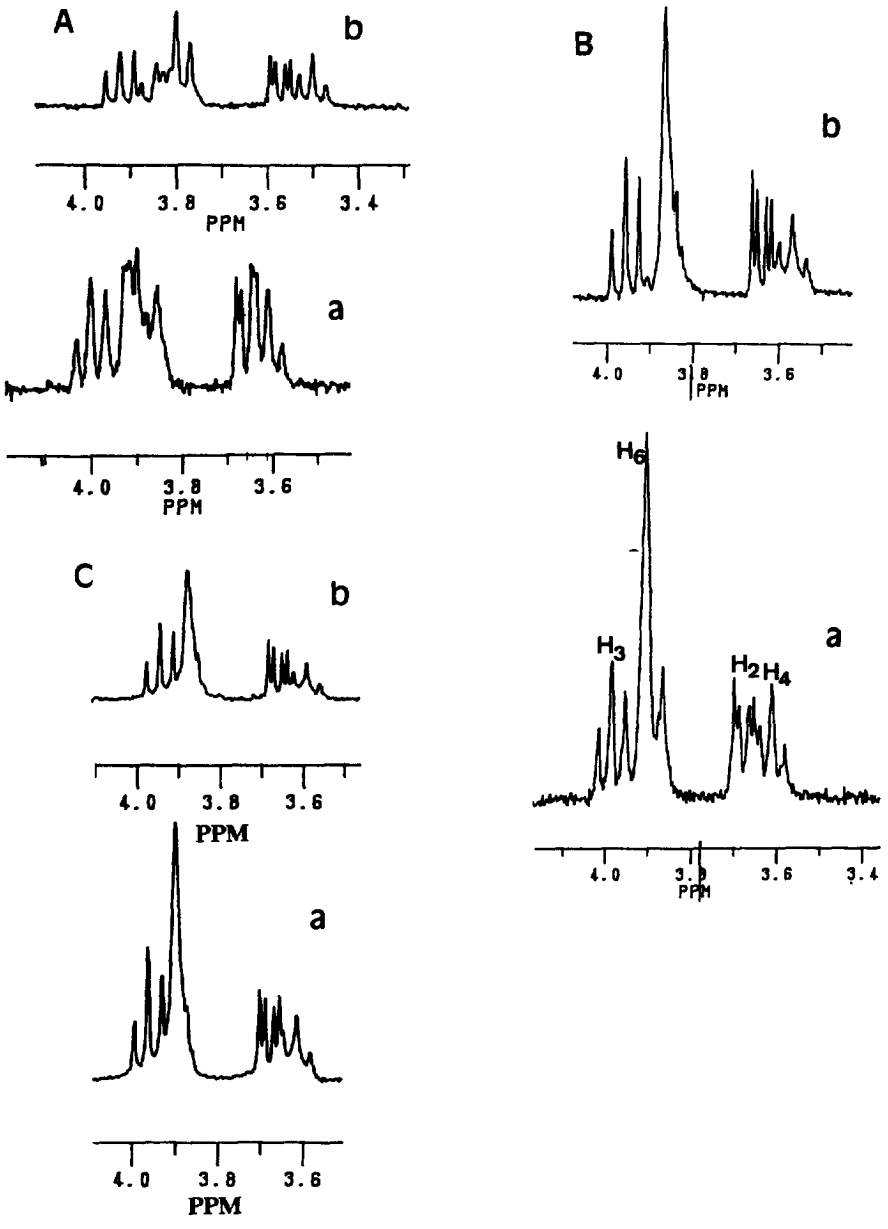


Figure 1. 300 MHz proton nmr spectra in D_2O at 25^0C of 0.005 M of cyclodextrins (solvent peak at 4.80 ppm as internal reference); (A) *alpha*-cyclodextrin: a. **2** absent: b. in the presence of 0.129 M of **2**; (B) *beta*-cyclodextrin: a. **2** absent; b. in the presence of 0.026 M of **2**; (C) *gamma*-cyclodextrin: a. **2** absent; b. in the presence of 0.026 M of **2**. H_1 and solvent peaks not shown.

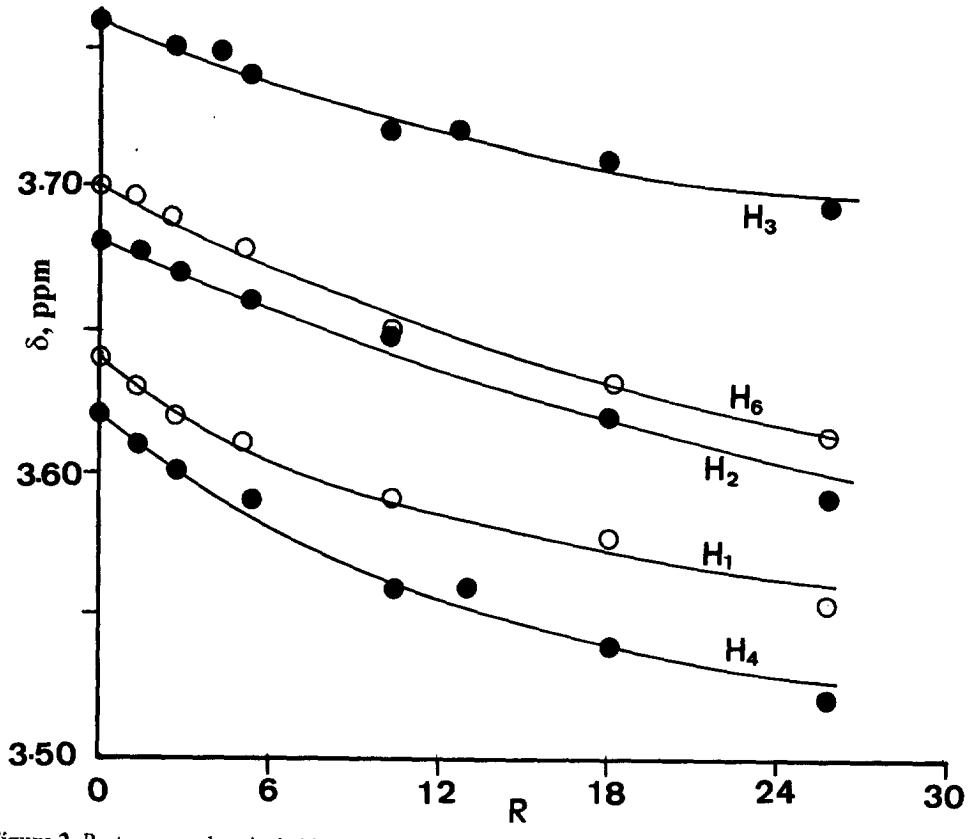


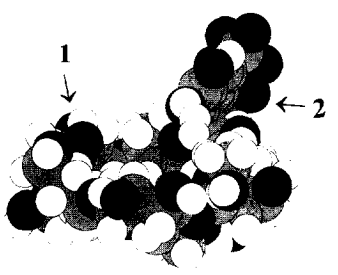
Figure 2. Proton nmr chemical shift titrataion curves of *gamma*-cyclodextrin (0.005 M) in D_2O at 25°C. R is the molar ratio of **2** to **1** used. The curve for H_1 has been shifted down by 1.5 ppm and those of H_3 and H_6 by 0.2 ppm.

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
alpha	δ_u[a]	5.08	3.65	4.00	3.61	3.86	3.92
	$\Delta\delta$[b]	0.12	0.09	0.09	0.12	0.10	0.13
beta	δ_u[a]	5.10	3.67	3.99	3.60	c	3.90
	$\Delta\delta$[b]	0.12	0.09	0.09	0.11		0.11
gamma	δ_u[a]	5.14	3.68	3.96	3.62	c	3.90
	$\Delta\delta$[b]	0.09	0.09	0.07	0.10		0.09

[a]Chemical shift of free cyclodextrin in ppm; assignment of peaks according to ref. 8. [b]Difference between the chemical shifts of free and complexed cyclodextrin in ppm at a molar ratio of **2** to **1** is 26:1; positive value indicates upfield shift. [c]Peak could not be discerned.

shields the interior protons of **1** while the outer **2** shields the exterior protons, giving rise to equal upfield shifts of these protons. In the complex shown in **5**, **1** could either be considered as a host (with a part of the dimer of **2** included in its cavity as the guest) or as a guest (with part of it included in the hydrophobic cavity formed by the two acridine walls). Therefore, there is no distinction between host and guest.



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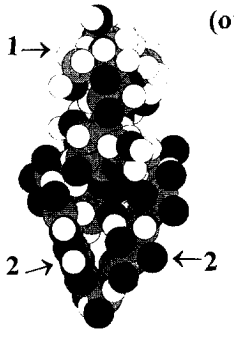

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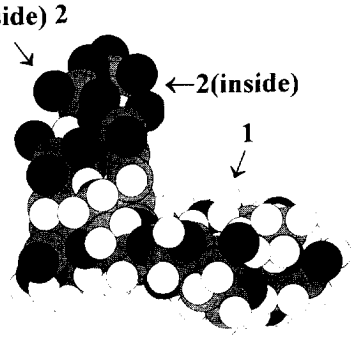

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ACKNOWLEDGEMENT

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REFERENCES

1. Poh, B.-L. and Tan, C.M., *Tetrahedron Lett.*, **1994**, *35*, 6387.
2. Poh, B.-L. *Tetrahedron*, **1996**, *52*, 000.
3. Compound **2** was synthesized as follows: A mixture containing 1.0 g of the orange cyclic tetramer (prepared from the reaction between H-acid and formaldehyde, see ref. 6) and 30 mL of concentrated nitric acid in 100 mL of distilled water was evaporated to dryness on a hot-plate set at about 60^0C to give a quantitative yield of **2** as a yellowish brown solid. It was purified by recrystallization from water-alcohol. The identity of **2** was supported by its x-ray crystal structure (done at the Chinese University of Hong Kong, the details of the crystal structure will be published separately), the negative ion LSI mass spectrum of the acidic form of **2** (Na^+ replaced by H^+ from Dowex 50W-X8 hydrogen ion exchange resin) in thioglycerol matrix ([M-H] peak at m/z 514), the nmr peaks in D_2O (proton at 8.59 (s) and 10.56 (s) ppm with intensity ratio of 2:1; carbon-13 at 122.1, 127.4, 132.7, 132.9, 137.6, 141.8, 145.4 ppm (aromatic carbons), 173.0 and 175.9 ppm (carbonyl carbons)), and elemental analysis for **2**.12H_2O (Found: C 26.00; H 3.95; N 1.90. Cald. C 26.31; H 4.00; N1.81).
4. The dimer of **2** is expected to be an important species in an aqueous medium (ref. 5).The negative ion LSI mass spectrum of the acidic form of **2** showed the presence of the dimer at m/z of 1030.
5. a) Katchalsky, A., Eisenberg, H. and Lifson, S., *J. Am. Chem. Soc.*, **1951**, *73*, 5889; b) Schrier, E.E., Pottle, M. and Scheraga, H.A., *J. Am. Chem. Soc.*, **1964**, *86*, 3444.
6. Poh, B.-L., Chin, L.Y. and Lee, C.W., *Tetrahedron Lett.*, **1995**, *36*, 3877.
7. Demarco, P.V. and Thakkar, A.L., *J. Chem. Soc., Chem. Commun.*, **1970**, 2.
8. Wood, D.J., Hruska, F.E. and Saenger, W., *J. Am. Chem. Soc.*, **1977**, *99*, 1735.

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