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Crown Ethers as Guests of Cyclotetrachromotropylene in Water

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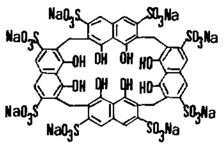
Abstract: The three crown ethers, 15-crown-5, 18-crown-6 and dibenzo[18]crown-6, formed inclusion complexes with the cyclic tetramer host, cyclotetrachromotropylene, in water. Their stability constants K are 830, 510, and 8000 M^{-1} respectively at 25°C.

Recently, we reported the first case of the well-known cyclodextrin host molecules (α-,β-, and γ-cyclodextrin) acting as guest molecules to the cyclic tetramer, cyclotetrachromotropylene (**1**), in water.[1] These macrocyclic guest molecules sit vertically in the cavity of **1**. Since the CPK molecular models indicated that the crown ethers, another group of well-known host molecules, could similarly be included into the cavity of **1**, we undertook to investigate this possibility. This paper reports our study on the complexation of 15-crown-5 (**2**), 18-crown-6 (**3**) and dibenzo[18]crown-6 (**4**) with **1**.

We chose these three crown ethers in our study for the following two reasons. First, **2** and **3** were used to find out the effect of the size of the guest molecule on the stability constant K. Second, **3** and **4** were used to find out the effect of replacing the methylene groups by two phenylene rings on K.



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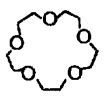

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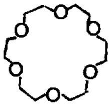

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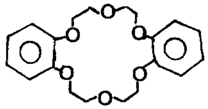

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RESULTS AND DISCUSSION

The proton chemical shifts of the crown ethers in D_2O at 25°C are shifted upfield in the presence of **1**, indicating that they are included in the cavity of **1**. We rule out the possibility that the upfield shift in the protons of the crown ethers is caused by the complexation of sodium cations (**2** and **3** form weak 1:1 complexes with sodium cations in water, the complex stability constants are 3 and 7 M^{-1} respectively[2]) from **1** with the crown ethers on two reasons. First, sodium cation is expected to cause downfield shift and not upfield shift, if it has any influence at all. Second, the addition of excess sodium chloride did not influence the proton chemical shifts of the crown ethers (for example, the proton chemical shift of 0.01 M of 15-crown-5 in D_2O was not affected by the addition of a ten-fold excess of sodium chloride). Sodium cations also do not influence the inclusion of crown ethers in **1** since an addition of 0.1 M of sodium chloride did not affect the proton chemical shift of 0.01 M of **2** in the presence of 0.007 M of **1** (3.39 ppm). The maximum changes in the methylene proton chemical shifts are about 0.5 ppm (Table 1). Figure 1 shows the proton chemical shift titration curves of 15-crown-5 and 18-crown-6. CPK molecular models indicate that the only possible mode of inclusion is one with the crown ether sitting vertically inside the open-ended longer side of the cavity of **1** as shown in **5** for the 1:1 complex formed from 15-crown-5 and **1** (the mode of inclusion of the crown ethers in **1** is similar to that of the cyclodextrins in **1**)[1]. The possibility of **1** as guest and the crown ethers as hosts is ruled out because CPK molecular models show that **1** is too large to enter the cavities of the three crown ethers.

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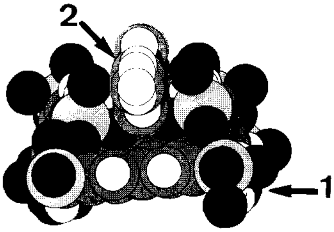

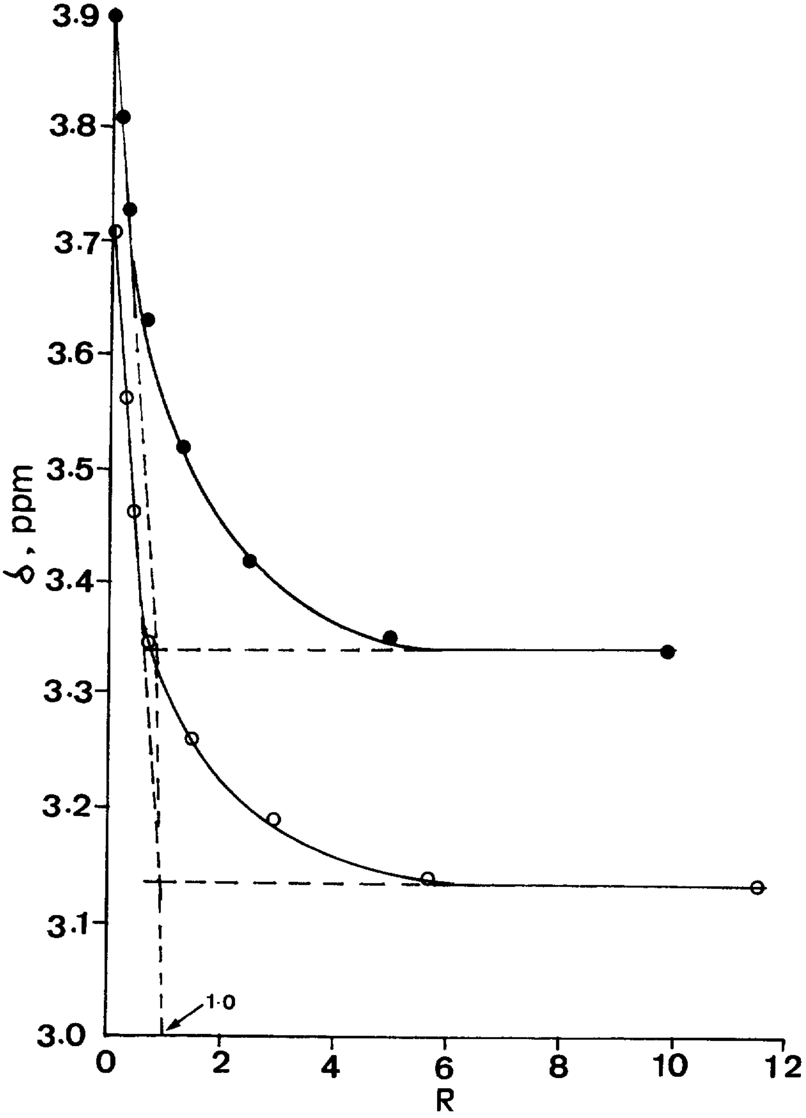

Figure 1. Variation of proton chemical shifts of 15-crown-5 (○, 1.01x10^{-2} M) and 18-crown-6 (●, 8.4110^{-3} M; chemical shifts moved upward by 0.20 ppm for clarity of presentation) with the molar ratio R of the host (1) to guest used in D_2O at 25°C.

Table 1. Proton NMR Chemical Shifts and Stability Constants K of Crown Ethers in D_2O at 25°C.

Crown ether	**2**	**3**	**4**
δ_u^a (CH_2), ppm	3.70	3.70	4.02[b]; 4.15[b] 6.87[b] (Aromatic H)
δ_c^c (CH_2), ppm	3.14	3.14	3.61[d] 6.33[d] (Aromatic H)
K, M^{-1}	830[e]	510[e]	8000[f]

[a]Chemical shift of free crown ether (solvent peak at 4.80 ppm as internal reference). [b]In $CDCl_3$ (TMS as internal referrence). [c]Chemical shift of complexed crown ether. [d]**4** extracted into 1 mL of D_2O containing 0.118 g of **1**. [e]By proton nmr method; estimated error 10%. [f]By solid-liquid extraction method, at 27-29°C; estimated error 10%.

The maximum induced chemical shifts of about 0.5 ppm for the methylene protons are smaller than those observed in the case of the aliphatic alcohols (about 2 ppm)[3]. The smaller induced chemical shifts are consistent with the fact that only part of the methylene units of the crown ethers could be in the cavity of **1** at any one moment. For example, CPK molecular models indicate that only about 1/3 (four out of twelve) of the methylene protons of **3** could be in the cavity of **1** at any one moment. The calculated maximum induced chemical shift of about 0.7 ppm (1/3 x 2) is of the same order of magnitude as the observed value of 0.6 ppm.

The host-guest complexes are strong, as indicated by the presence of straight line portions in the proton chemical shift titration curves given in Figure 1. For strong complexes, the host to guest stoichiometry can be reliably obtained from the intersection of the two tangents in each titration curve[5]. Figure 1 shows that the host to guest stoichiometry is 1:1 for the complexes of **1** with both 15-crown-5 and 18-crown-6. The stability constants K (Table 1) for the two complexes were obtained by a non-linear regression fitting of the proton nmr titration points[4]. Figure 2 shows the calculated proton chemical shift titration curve together with the experimental chemical shifts for 15-crown-5. The decrease in K from 15-crown-5 (830 M^{-1}) to 18-crown-6 (510 M^{-1}) corresponds to the decrease in the fraction of the guest structure included in the host cavity. A similar trend was observed in the case of the cyclodextrins[1].

The K value in the case of **4** could not be obtained by the proton nmr titration method because of solubility problem (saturated concentration of **4** in water about $4x10^{-5}$ M as determined by uv spectroscopy).

However, the increase in its solubility in the presence of the **1** (1.09×10^{-3} M of **1** in water increased the solubility of **4** to 3×10^{-4} M) indicates that it complexes with **1**. A 6.3×10^{-2} M solution of **1** in D_2O could extract enough of **4** into D_2O to record its proton nmr spectrum. The chemical shifts of the two sets of methylene protons were shifted upfield by 0.41 and 0.53 ppm and that of the aromatic protons upfield by 0.53 ppm, further supporting the inclusion of **4** into the cavity of **1** (see Table 1; comparison made with the chemical shifts of **4** in $CDCl_3$ since it was not possible to obtain the nmr spectrum of the uncomplexed **4** in water because of solubility. This comparison is valid because solvent effect on the chemical shifts of the methylene and aromatic protons is expected to be relatively small, as checked by our measurement of the chemical shifts of 18-crown-6 and anisole in D_2O and $CDCl_3$).

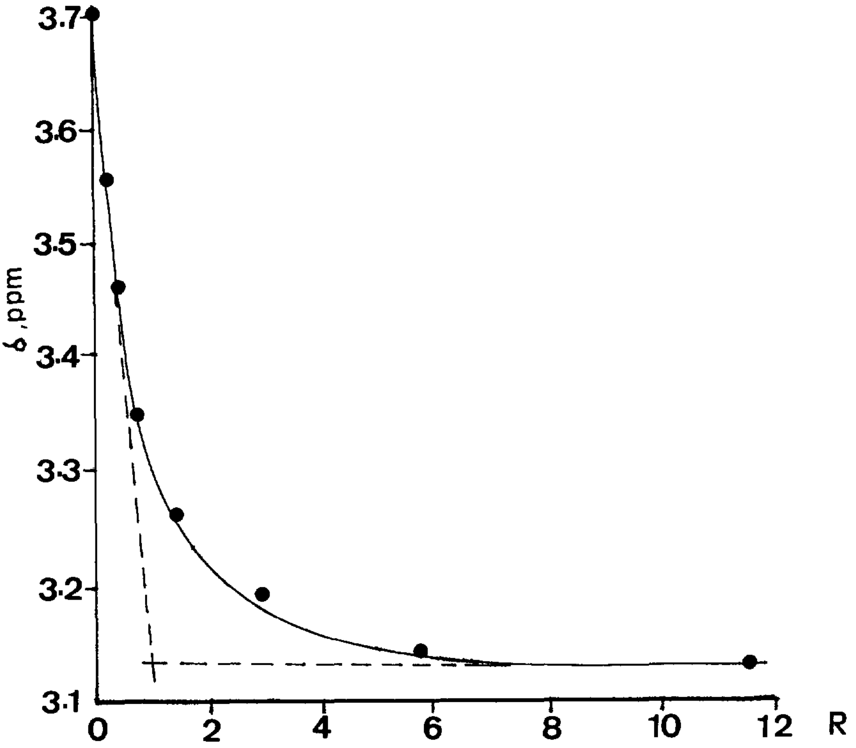

Figure 2. Calculated proton chemical shift titration curve of 15-crown-5 (1.01×10^{-2} M, K = 830 M^{-1}, δ_u = 3.70 ppm, δ_c = 3.14 ppm) in D_2O at 25°C. R is the molar ratio of the host to guest used and the points are experimental values.

Assuming that the complex formed from **1** and **4** is also of 1:1 stoichiometry, a K value 8000 M^{-1} for the complexation was obtained by the solid-liquid extraction method[6]. This large K value could be attributed to the stronger π-π interaction between one of the phenylene rings of **4** and the vertical naphthalene walls of the host **1** compared with the weaker CH-π interactions between **2**, **3** and **1**[5] (the shielding of the aromatic protons by 0.53 ppm indicates that one of the phenylene rings is in the cavity of **1**; maximum shieldings of aromatic protons observed in substituted benzenes are 1 to 2 ppm[7]).

EXPERIMENTAL

Materials. All the crown ethers were commercial samples. The host **1** was prepared as described earlier.[4]

^{1}H nmr spectra in D_2O at 25°C were recorded with a 300 MHz Brucker 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 concentration of crown ethers **2** and **3** was kept constant at about 1×10^{-2} M while the concentration of the host **1** varied.

The solid-liquid extraction of crown ether **4** (20 mg used) by **1** (1.10×10^{-3} M in 30 mL distilled water) followed the procedure described earlier.[6] The absorbance at 275.5 nm (ϵ 4295 in hexane) was used to calculate the concentration of the crown ether.

Calculations 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] The K values obtained have an estimated error of 10%.

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REFERENCES

1. Poh, B.-L. and Tan, C.M., *Tetrahedron Lett.*, **1994**, *35*, 6387.
2. Lin, J.D. and Popov, I., *J. Am. Chem. Soc.*, **1981**, *103*, 3773.
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.
5. Poh, B.-L. and Tan, C.M., *Tetrahedron*, **1994**, *50*, 3453.
6. Poh, B.-L. and Koay, L.-S., *Tetrahedron Lett.*, **1990**, *31*, 1911.
7. Poh, B.-L., Lim, C.H., Tan, C.M. and Wong, W.M., *Tetrahedron*, **1993**, *49*, 7259.

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