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^{1}H NMR Study on the Complexation of Phenols with Cyclotetrachromotropylene in Aqueous Solution

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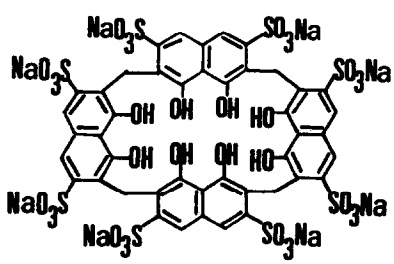
Abstract: The stability constants K of the 1:1 host to guest complexes formed between eight phenols and the cyclic tetramer, cyclotetrachromotropylene, in an aqueous solution at pD 7.0 at 25°C were determined by ^{1}H nmr spectroscopy. They vary from ~0 (*p*-sodium sulfonatophenol) to 400 M^{-1} (*p*-nitrophenol).

The chemistry of synthetic macrocyclic compounds has been actively investigated in the past twenty five years because of their abilities to complex with a variety of organic and inorganic substrates.[1-4] Lately, the interest has been on the water-soluble type of macrocyclic compounds because they can be studied in an aqueous medium, similar to that in the biological system. Recently, we reported the ability of cyclotetrachromotropylene, 1, to complex with metal cations[5], organic cations[6,7], and polynuclear aromatic hydrocarbons.[8,9] In this paper, we report the results of our ^{1}H nmr study on the complexation of eight phenols with 1 in D_2O at pD 7.0. Our original intention of including a series of monosubstituted benzenes as guests in this study was discarded because of solubility problem.



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RESULTS AND DISCUSSION

That phenols are enclosed in the cavity of 1 in the aqueous solution is indicated by the large shielding effect of the latter on the protons of the former (Table 1). The change in the proton nmr spectrum of a given concentration of the phenolic guest in the presence of various concentrations of 1 are illustrated in Figure 1 for the case of *p*-cresol. All the proton chemical shift titration curves show the two tangents meeting at a point where the molar ratio of host to guest is unity, indicating the host-guest complex is of 1:1 stoichiometry. An example is given in Figure 2 for the case of *p*-bromophenol.

The complexation-induced chemical shifts in Table 1 show that, for the *p*-substituted phenols, the guest molecules penetrate into the hydrophobic cavity of the host from their more hydrophobic end (NO_2, Br, H, CH_3, and OCH_3 instead of OH) since the chemical shift changes of H_m are larger than those of H_o (H_o, H_m, and H_p refer to the hydrogens *ortho*, *meta*, and *para* to the OH group of the phenol respectively). The same mode of penetration is observed for *m*-cresol as the shielding on the chemical shift of H_p (1.68 ppm) is more than that of H_m (0.75 ppm). In the case of *o*-cresol, only shallow penetration is possible from the methyl end because of the adjacent hydrophilic OH group. Therefore, penetration from the *p*-hydrogen end is important. As a result, all the hydrogens are almost equally affected.

The stability constant K , in D_2O at pD 7.0, ionic strength 1.2 M and 25° C, of each of the 1:1 host to guest complex was obtained by a non-linear regression fitting procedure. The K value is one that gives the best fit to the proton chemical shift titration curve. Some representative calculated titration curves together with the experimental chemical shifts are shown in Figure 3. The K values obtained from the different protons of the same guest molecule are in good agreement with one another (Table 1). In the case of *p*-sodium sulfonatophenol, the K value could not be calculated because of the weak complexation, as indicated by the small change in the proton chemical shifts of the guest. The shielding effects on H_o and H_m were 0.12 and 0.06 ppm respectively when a ten-fold excess of host was used. The larger shielding effect on H_o indicates that penetration into the host cavity is from the OH end and not the SO_3^- end, consistent with the more hydrophobic character of the former.

The variation of the K values is not due to the electronic effect of the substituent on the guest molecule since it does not have any correlation with the Hammett substituent constant.[10] Indeed, no single factor alone could account for the variation in K. In the case of *p*-sodium sulfonatophenol, there are two possible reasons to account for the weak complexation. First,

Table 1. Proton NMR Chemical Shifts of Phenols (XC_6H_4OH) and Stability Constant K of their 1:1 Complexes with 1 in D_2O at pD 7.0, Ionic Strength 1.2 M and 25° C.

X	Proton	δ_u[a], ppm	δ_c[b], ppm	K[c], M^{-1}	sd[d], ppm
p-NO_2	H_o	7.16	6.32	400	0.06
	H_m	8.37	6.32	400	0.04
p-Br	H_o	6.94	6.05	330	0.02
	H_m	7.53	5.40	330	0.06
H	H_o	7.04	6.17	60	0.07
	H_m	7.40	6.26	50	0.06
	H_p	7.10	5.88	50	0.07
p-CH_3	H_o	7.02	6.32	290	0.02
	H_m	7.33	5.16	290	0.05
	CH_3	2.44	0.60	290	0.02
p-OCH_3	H_o	7.05	5.87	110	0.04
	H_m	7.05	5.38	110	0.05
	OCH_3	3.93	2.34	120	0.03
o-CH_3	H_o	7.02	5.90	50	0.01
	H_m	7.30;7.30	5.90;5.90	50;50	0.02;0.02
	H_p	7.02	5.60	40	0.02
	CH_3	2.22	1.40	50	0.00
m-CH_3	H_o	6.92;6.98	5.38;6.33	150;150	0.03;0.05
	H_m	7.35	6.60	150	0.02
	H_p	6.87	5.19	150	0.06
	CH_3	1.89	0.76	180	0.00

[a] Chemical shift of free phenol. [b] Chemical shift of complexed phenol. [c] ±10%. [d] Standard deviation between experimental and calculated chemical shift.

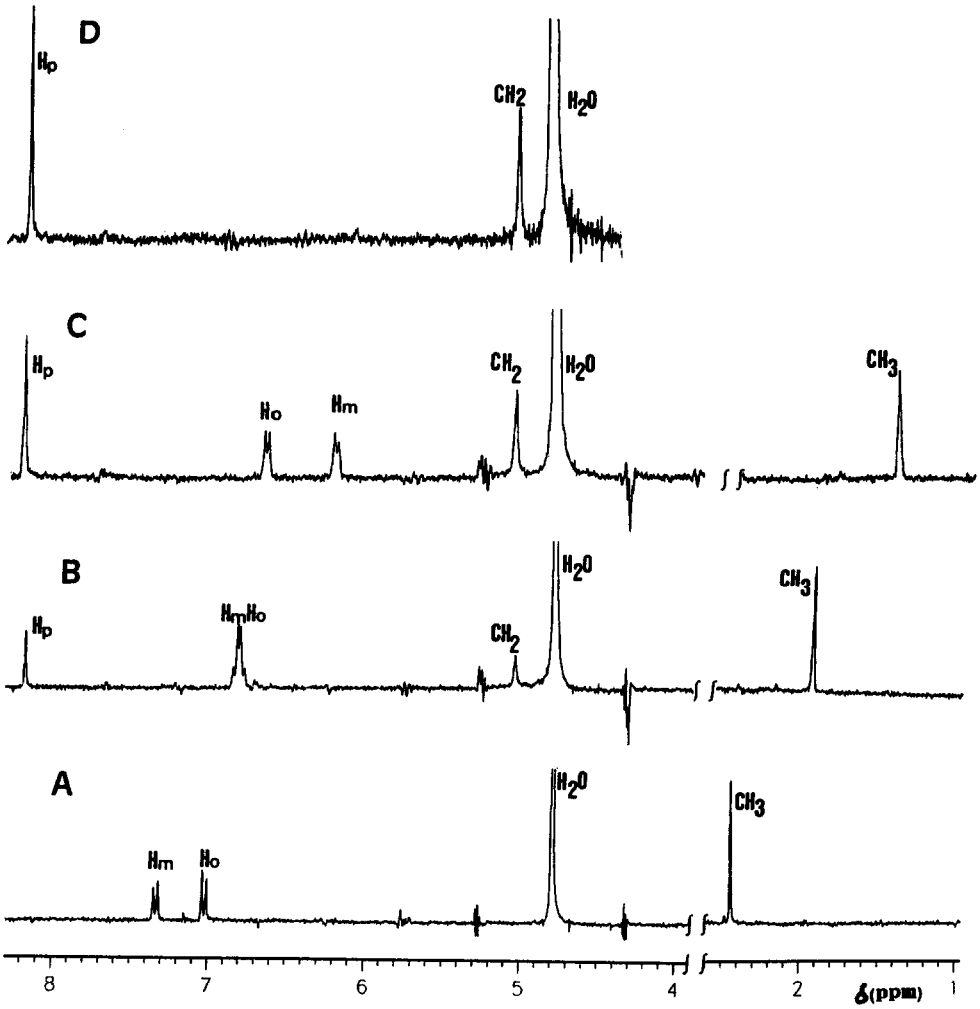

Figure 1. 300 MHz ^{1}H nmr spectra in D_2O (pD 7.0, ionic strength 1.2 M, and at 25° C) of (A) 3.05×10^{-2} M *p*-cresol; (B) 3.05×10^{-2} M *p*-cresol + 8.04×10^{-3} M 1; (C) 3.05×10^{-2} M *p*-cresol + 2.01×10^{-2} M 1; (D) 4.02×10^{-2} M 1.

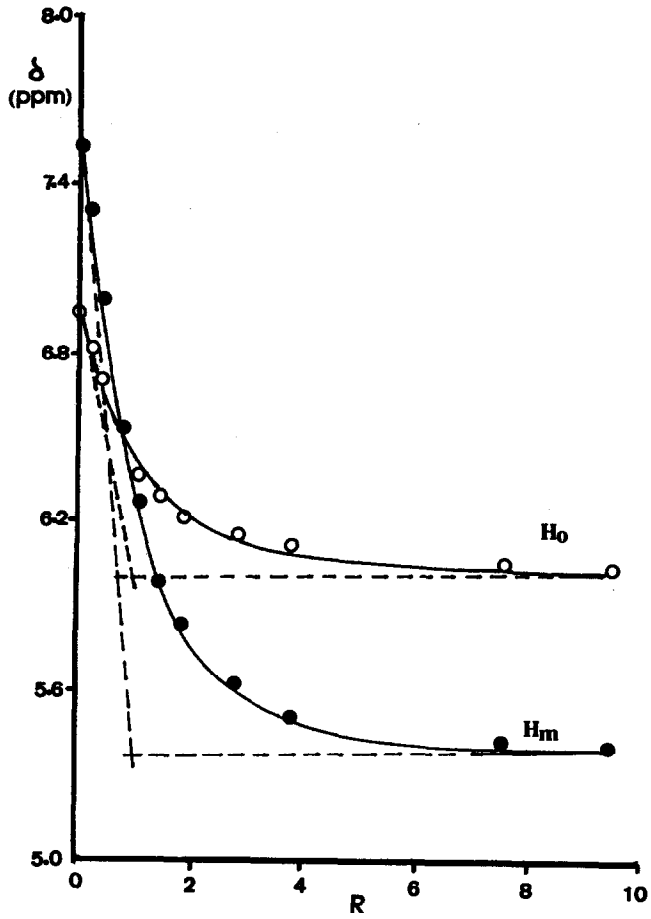

Figure 2. Variation of ^1H chemical shift of *p*-bromophenol (1.06×10^{-2} M) with the molar ratio (R) of the host to guest used in D_2O (pD 7.0, ionic strength 1.2 M and 25° C).

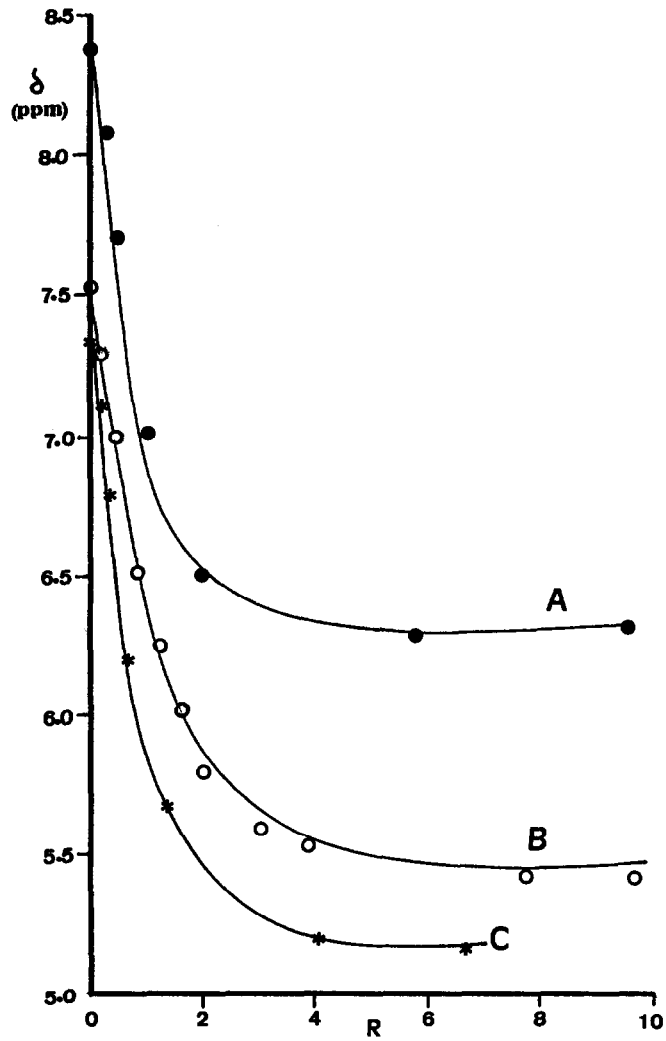

Figure 3. Calculated H_a chemical shift titration curves in D_2O (pD 7.0, ionic strength 1.2 M, and at 25° C) of (A) *p*-nitrophenol (2.60×10^{-4} M); (B) *p*-bromophenol (1.06×10^{-2} M); (C) *p*-cresol (3.05×10^{-2} M). R is the molar ratio of the host to guest used and the points are experimental values. The K, δ_u, and δ_c values used for calculating the titration curves are given in Table 1.

complexation will result in the unfavourable electrostatic interaction between the SO_3^- groups of both the guest and host. Second, the anionic substituent of the guest is better solvated in water than in the hydrophobic cavity of the host. The first reason is probably more important because organic cations, which also favour the aqueous solvent for solvation, are strongly complexed with 1.[6,7]

The phenolic guest molecules have little effect on the chemical shifts of the aromatic and methylene protons of 1 (see Figure 1). These results could be explained by an examination of the CPK molecular model of the chair conformation[6] of 1. It shows that all the methylene protons are located away from the cavity enclosed by the two vertical naphthalene units and only two out of the eight aromatic protons could be close to the benzene ring of the phenolic guest enclosed in the cavity.

EXPERIMENTAL

Materials. All the phenols (commercial samples) were further purified by recrystallisation from ethanol before use. The host 1 was prepared by the more recent method.[7]

^1H **nmr spectra** in D_2O at pD 7.0, ionic strength 1.2 M and 25°C were recorded with a 300 MHz Bruker 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. The chemical shift error is 0.01 ppm. In all the nmr chemical shift titrations, the concentration of the phenolic guest was kept constant at about 1.0×10^{-2} M while the concentration of the host 1 was varied.The aromatic and methylene proton chemical shifts of 1 do not change in the concentration range of 2.5×10^{-3} to 5.0×10^{-1} M.

Buffer solutions in D_2O of pD 7.0 were prepared according to standard procedure.[11] The ionic strength of 1.2 M was maintained by the addition of sodium chloride.

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

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