

# Complexation of Monosubstituted Benzenes and Methanes by Cyclotetrachromotropyene in Aqueous Solution: Substituent Effects on $\pi$ - $\pi$ and CH- $\pi$ Interactions

BO-LONG POH\* and CHI MING TAN

*School of Chemical Sciences, Universiti Sains Malaysia, Penang, Malaysia.*

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**Abstract.** The stability constants  $K$  of 1 : 1 complexes formed in aqueous solution between several monosubstituted benzenes ( $C_6H_5X$ ) and methanes ( $CH_3X$ ) as guests and cyclotetrachromotropyene as host were determined by proton NMR spectroscopy. Variations of  $K$  with the substituent  $X$  are attributed to the electronic effect of  $X$  and the presence of C-H or aromatic  $\pi$  bonds, if any, interacting with the host  $\pi$  bonds.

**Key words:** Stability constant, monosubstituted benzene complexes, monosubstituted methane complexes, cyclotetrachromotropyene complexes,  $\pi$ - $\pi$  interaction, CH- $\pi$  interaction.

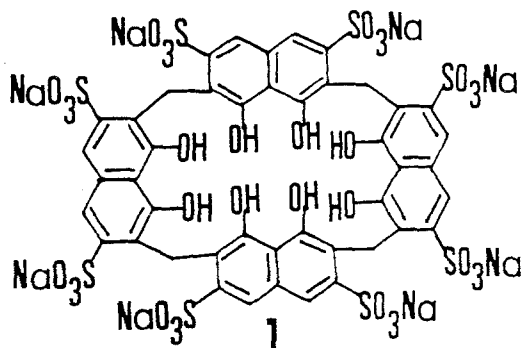
## 1. Introduction

Two interactions,  $\pi$ - $\pi$  and CH- $\pi$ , play an important role in stabilizing the structures of proteins and their complexes [1]. We have been interested in obtaining a better understanding of these two interactions. We used the water soluble macrocycle, cyclotetrachromotropyene (**1**), as a host molecule to provide the  $\pi$  bonds for interaction. For the study of  $\pi$ - $\pi$  interaction, we used guest molecules that have an aromatic ring to provide the other  $\pi$  bonds, such as the polyaromatic hydrocarbons [2] and aromatic amino acids [3]. For the study of CH- $\pi$  interaction, aliphatic guest molecules such as the aliphatic alcohols [4] and aliphatic amino acids [3] were used. Our studies have shown the importance of  $\pi$ - $\pi$  and CH- $\pi$  interactions in stabilising host-guest complexes.

As a furtherance of our work, we wanted to investigate the effect of a substituent on the two interactions. For this purpose, we studied the complexation of a series of monosubstituted benzenes,  $C_6H_5X$ , and methanes,  $CH_3X$ , with **1** in aqueous solution using proton NMR spectroscopy. This paper reports the results of our investigation.

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\* Author for correspondence.



Structure 1.

## 2. Experimental

### 2.1. MATERIALS

Cyclotetraphenylmethane was synthesised as described earlier [6]. All the mono-substituted benzenes and methanes were commercial samples.

### 2.2. PROTON NMR SPECTRA

Proton NMR spectra in  $\text{D}_2\text{O}$  at  $25^\circ\text{C}$  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. In all the chemical shift titrations, the concentration of the guests was kept constant at about  $4 \times 10^{-3}$  to  $2 \times 10^{-2}$  M while the concentration of the host **1** was varied.

### 2.3. BUFFER SOLUTIONS

Buffer solutions in  $\text{D}_2\text{O}$  at pD 1.0 were prepared as described previously [5].

### 2.4. STABILITY CONSTANTS $K$

Calculations of the stability constants  $K$  of the 1 : 1 host-to-guest complexes using the nonlinear regression fitting of the proton chemical shift titration curves were carried out as reported earlier [5]. They have an estimated error of 10%.

## 3. Results and Discussion

The proton chemical shifts of the monosubstituted benzenes and methanes are shifted upfield in the presence of **1**, indicating that the guest molecules are included in the cavity of the host. The induced shifts observed are given in Tables I and II, for  $\text{C}_6\text{H}_5\text{X}$  and  $\text{CH}_3\text{X}$ , respectively. The change in the proton NMR spectrum of a

TABLE I. Proton NMR chemical shifts of  $C_6H_5X$  and stability constants  $K$  of their 1 : 1 complexes with **1** in  $D_2O$  at  $25^\circ C$ 

X	Proton	$\delta_v^a$ , ppm	$\Delta\delta^b$ , ppm	$K^c$ , $M^{-1}$	$sd^d$ , ppm
H	H	7.47	6.40	64	0.03
OMe	CH <sub>3</sub>	3.86	1.39	530	0.10
	H <sub>o</sub>	7.06	1.41	530	0.10
	H <sub>m</sub>	7.41	0.78	530	0.07
	H <sub>p</sub>	7.06	0.66	530	0.06
Me <sup>e</sup>	CH <sub>3</sub>	2.37	1.52	350	0.05
CH <sub>2</sub> OH	CH <sub>2</sub>	4.57	0.65	100	0.02
	H <sub>aro</sub> <sup>f</sup>	7.35	0.88	100	0.04
CHO	CHO	9.94	1.23	360	0.04
	H <sub>o</sub>	7.96	1.51	360	0.03
	H <sub>m</sub>	7.63	0.96	360	0.04
	H <sub>p</sub>	7.76	0.86	360	0.06
NO <sub>2</sub>	H <sub>o</sub>	8.28	1.77	700	0.05
	H <sub>m</sub>	7.65	0.84	700	0.07
	H <sub>p</sub>	7.83	0.67	700	0.09

<sup>a</sup> Chemical shift of free monosubstituted benzene.

<sup>b</sup> Difference between the chemical shifts of free and complexed monosubstituted benzene; positive value indicates upfield shift.

<sup>c</sup> Calculated by nonlinear regression fitting.

<sup>d</sup> Standard deviation between observed and calculated chemical shifts.

<sup>e</sup> Some aromatic proton signals too weak to be observed.

<sup>f</sup> Aromatic protons appear as a singlet.

guest in the presence of **1** is illustrated by benzaldehyde in Figure 1. All the proton chemical shift titration curves of  $C_6H_5X$  show the two tangents meeting at a point where the molar ratio of host to guest is unity, indicating the complexes are of 1 : 1 host-to-guest stoichiometry [4,6]. A typical example is shown in Figure 2 for nitrobenzene. Since the stoichiometry of the weaker complexes of  $CH_3X$  with **1** cannot be reliably deduced by the method of drawing tangents [3], we shall assume that it is also 1 : 1, based on our earlier study on the complexation of aliphatic alcohols with **1** [4]. Our assumption is justified by the good agreement between the observed and calculated chemical shifts, as shown in a typical example of acetonitrile in Figure 3.

The complexation-induced chemical shifts in Table I show that the  $C_6H_5X$  guest molecules penetrate vertically into the hydrophobic cavity of **1** from the more hydrophobic end ( $X = OMe, Me, CHO$  and  $NO_2$ ) since the chemical shift changes are  $H_o > H_m > H_p$ .  $H_o$ ,  $H_m$ , and  $H_p$  refer to the hydrogens *ortho*, *meta*, and *para* to  $X$ , respectively. In the case of benzyl alcohol,  $H_p$  is more hydrophobic than  $CH_2OH$  and penetration is from the  $H_p$  end, as shown by the smaller induced

TABLE II. Proton NMR chemical shifts of  $\text{CH}_3\text{X}$  and stability constants  $K$  of their 1 : 1 complexes with **1** in  $\text{D}_2\text{O}$  at  $25^\circ\text{C}$

X	$\delta_u^a$ , ppm	$\Delta\delta^b$ , ppm	$K^c$ , $\text{M}^{-1}$	$\text{sd}^d$ , ppm
CN	2.07	1.96 (1.28) <sup>e</sup>	37	0.01
SOMe	2.73	1.43(1.02) <sup>e</sup>	43	0.01
COMe	2.24	1.34(0.92) <sup>e</sup>	37	0.01
$\text{CO}_2\text{H}^f$	1.98	1.58(0.36) <sup>e</sup>	4	0.01

<sup>a</sup> Chemical shift of free  $\text{CH}_3\text{X}$ .

<sup>b</sup> Difference between the chemical shifts of free and complexed  $\text{CH}_3\text{X}$ ; the chemical shifts of the complexed form were obtained from nonlinear regression fitting of their proton NMR titration curves since complete complexation was not observed even at the highest molar ratio of host to guest used.

<sup>c</sup> Calculated by nonlinear regression fitting.

<sup>d</sup> Standard deviation between observed and calculated chemical shifts.

<sup>e</sup> Value in parenthesis is the chemical shift change when the molar ratio of host to guest is ten.

<sup>f</sup> At pD 1.0.

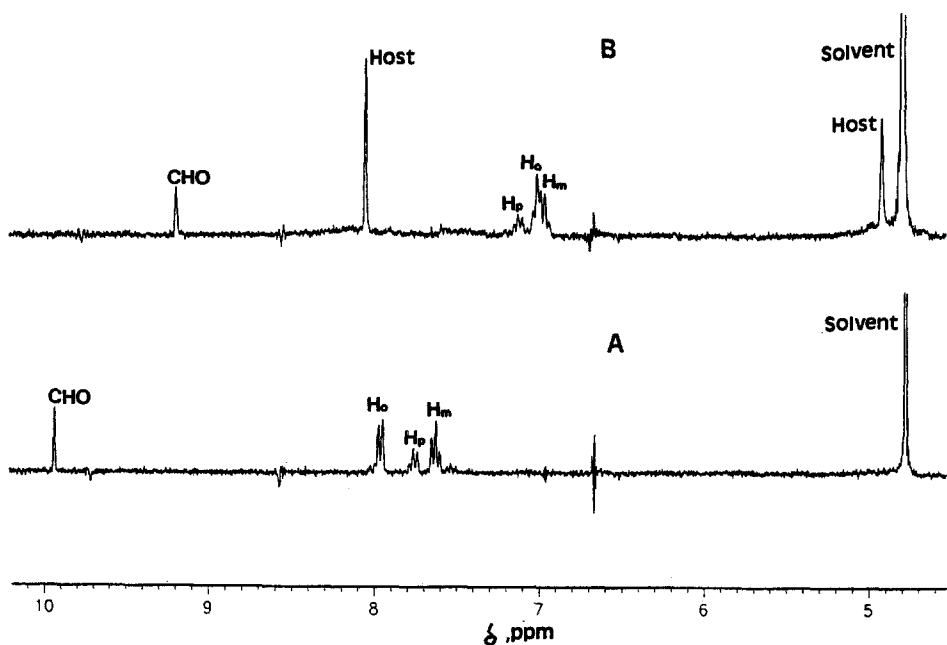


Fig. 1. 300 MHz proton NMR spectra in  $\text{D}_2\text{O}$  of  $1.96 \times 10^{-2}$  M benzaldehyde: (A) no host present; (B) in the presence of  $1.88 \times 10^{-2}$  M of **1**.

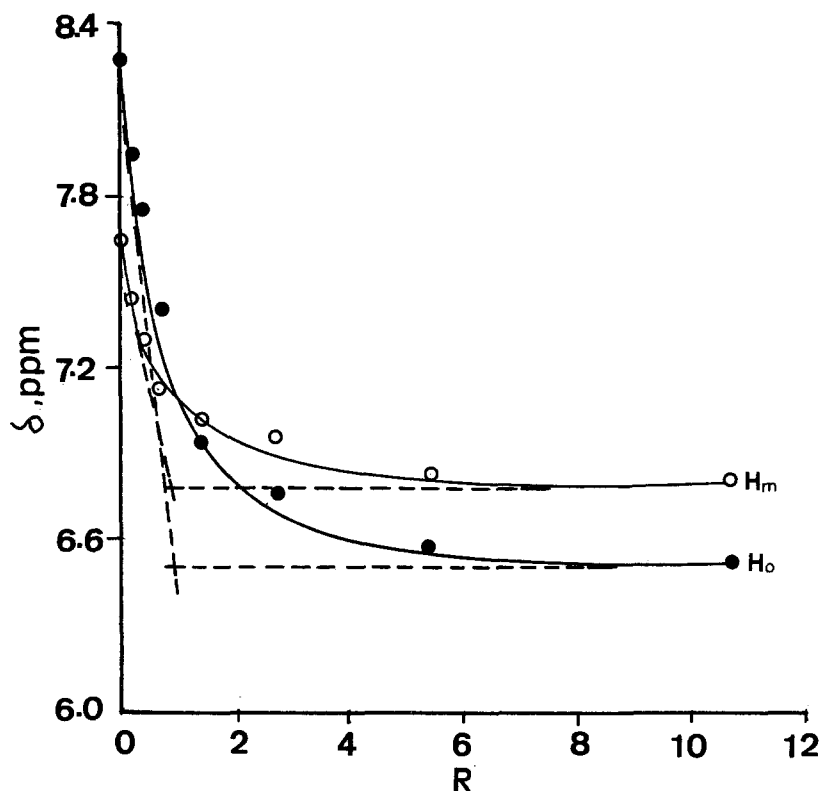


Fig. 2. Variation of proton chemical shift of nitrobenzene ( $8.12 \times 10^{-2}$  M) with the molar ratio ( $R$ ) of the host (1) to guest used in  $D_2O$  at  $25^\circ C$ .

chemical shift change of the methylene protons (0.65 ppm) compared to those of the aromatic protons (0.88 ppm). Phenol also penetrates from the  $H_p$  end instead of the OH end [5]

The variations of  $K$  with  $X$  in  $C_6H_5X$  (Table III) can be attributed to two factors, namely the electronic effect of  $X$  on the benzene ring (as represented by the Hammett  $\sigma_p$  values) and the interaction between the C–H bonds, if any, of  $X$  and the  $\pi$  bonds of the host. The vertical naphthalene wall of the host 1 [4] which shields the guest molecule is electron rich because of the presence of two OH groups on it. Therefore, a substituent  $X$  which decreases the electron density in the benzene ring of the guest will give a larger  $K$  value compared to that of benzene as a result of better  $\pi$ – $\pi$  interaction between the host and guest. Thus, nitrobenzene which has a strong electron withdrawer,  $NO_2$ , has a larger  $K$  value ( $700 M^{-1}$ ) than benzene ( $64 M^{-1}$ ). In the case of benzaldehyde, a more stable complex ( $K = 360 M^{-1}$ ) than that of benzene is formed because CHO is not only an electron withdrawer, but also has a C–H bond to interact with the host  $\pi$  bonds. If electronic effect is the only factor for the variation of  $K$  with  $X$ , toluene and anisole are expected to

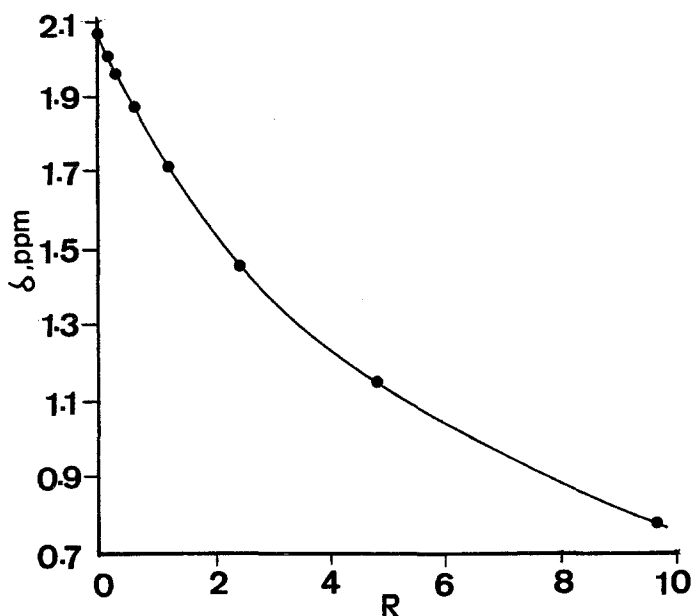


Fig. 3. Calculated proton chemical shift titration curve of acetonitrile ( $5.70 \times 10^{-3}$  M) in  $D_2O$  at  $25^\circ C$ .  $R$  is the molar ratio of the host (1) to guest and the points are experimental values. The  $K$ ,  $\delta_u$ , and  $\delta_c$  values used for calculating the titration curve are given in Table II.

give less stable complexes than benzene since their substituents (Me and OMe, respectively) are electron donors. But they give more stable complexes ( $K = 350$  and  $530 M^{-1}$ , respectively) because of the presence of three CH- $\pi$  interactions between the substituents and the host. In the case of phenol, the electron donating substituent, OH, does not have any C-H bond to interact with the host  $\pi$  bonds and its  $K$  value ( $53 M^{-1}$ ) is smaller than that of benzene. For benzyl alcohol, the substituent,  $CH_2OH$ , has two C-H bonds for CH- $\pi$  interaction and a larger  $K$  value is observed ( $100 M^{-1}$ ).

The trend in the  $K$  values of  $CH_3X$  can be similarly explained. Acetonitrile gives a more stable complex than methanol because CN is a stronger electron withdrawer than OH, their  $\sigma_I$  values are 0.56 and 0.25, respectively. The substituents COMe and OH have the same electronic effect ( $\sigma_I = 0.25$ ), but acetone gives a more stable complex than methanol because COMe in the former has three C-H bonds to interact with the host  $\pi$  bonds. The complexes of acetone and dimethyl sulfoxide ( $X = COMe$  and  $SOMe$  respectively) have almost equal  $K$  values because the two substituents have the same electronic effect ( $\sigma_I = 0.25$ ) and the same number of C-H bonds. In the case of monosubstituted methanes with an aromatic substituent, the presence of aromatic  $\pi$  bonds for interaction with the host  $\pi$  bonds accounts for the greater stability of their complexes. For examples, toluene ( $X = C_6H_5$ ) and anisole ( $X = OC_6H_5$ ) give larger  $K$  values than acetonitrile although the  $\sigma_I$  values

TABLE III. Substituent constants ( $\sigma_p$ ,  $\sigma_1$ )<sup>a</sup> and stability constants  $K$  of 1 : 1 complexes of C<sub>6</sub>H<sub>5</sub>X and CH<sub>3</sub>X with **1** in D<sub>2</sub>O at 25°C

X	$\sigma_p$	$\sigma_1$	$K, M^{-1} (\text{Log } K)$	
			C <sub>6</sub> H <sub>5</sub> X	CH <sub>3</sub> X
H	0	0	64 (1.81)	
OH	-0.30	0.25	53 <sup>b</sup> (1.72)	2 <sup>c</sup> (0.30)
OMe	-0.18		530 (2.72)	
Me	-0.14		350 (2.54)	
CH <sub>2</sub> OH	0.01	0.07	100 (2.00)	32 <sup>c</sup> (1.51)
CHO	0.45		360 (2.56)	
NO <sub>2</sub>	0.81		700 (2.85)	
COMe		0.25		37 (1.57)
SOMe		0.25		43 (1.63)
CN		0.56		37 (1.57)
CO <sub>2</sub> H		0.32		4 <sup>d</sup> (0.60)
C <sub>6</sub> H <sub>5</sub>		0.11		350 (2.54)
OC <sub>6</sub> H <sub>5</sub>		0.39		530 (2.72)

<sup>a</sup> Ref. 7.

<sup>b</sup> Ref. 5.

<sup>c</sup> Ref. 4.

<sup>d</sup> At pD 1.0.

of their substituents (0.11 and 0.39 respectively) are smaller than that of acetonitrile (0.56).

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