Tetrahedron Vol. 46, No. 10, pp. 3651-3658, 1990
Printed in Great Britain

0040-4020/90 $3.00+.00

COMPLEXATIONS OF AMINES WITH WATER-SOLUBLE CYCLOTETRACHROMOTROPYLENE

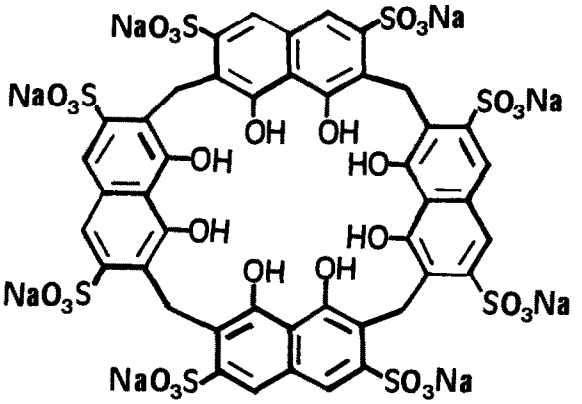
Bo-Long Poh* and Chooi Seng Lim

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

(Received in UK 5 March 1990)

Abstract: The water-soluble cyclic tetramer, cyclotetrachromotropylene (1), forms 1:1 complexes with amines and tetraalkylammonium cations in water when it is deprotonated.

The chemistry of synthetic macrocyclic compounds has been actively investigated in the past twenty 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. So far, the water-soluble macrocyclic compounds synthesised contain benzene units in their cyclic structures.[5-7] Recently, we prepared cyclotetrachromotropylene, 1, a water-soluble macrocyclic compound containing four naphthalene units in its cyclic structure.[8] We are interested in determining its complexing ability in water. This paper reports our study on its complexing ability with amines using ^{1}H nmr spectroscopy.



1

Deprotonation of Host 1. Deprotonation of the hydroxyl groups in 1 occurs in an alkaline condition.[8] The uv-visible spectra were recorded at different pH values. The visible region shows five different absorption maxima at 537, 540, 545, 586, and 646 nm (Figure 1) which could be attributed to five species, that is, 1, the mono-, di-, tri-, and tetradeprotonated forms of 1. The five distinctly different spectra in the uv region are consistent with the five species. The pK_a values estimated from spectrophotometric titrations are pK_1 6.5, pK_2 8.8, pK_3 10.5, and pK_4 11.5. That there is a maximum of four deprotonations suggests that each of the naphthalene units is only singly deprotonated, analogous to the case reported for the structurally related resorcinol-acetaldehyde cyclic tetramer.[9]

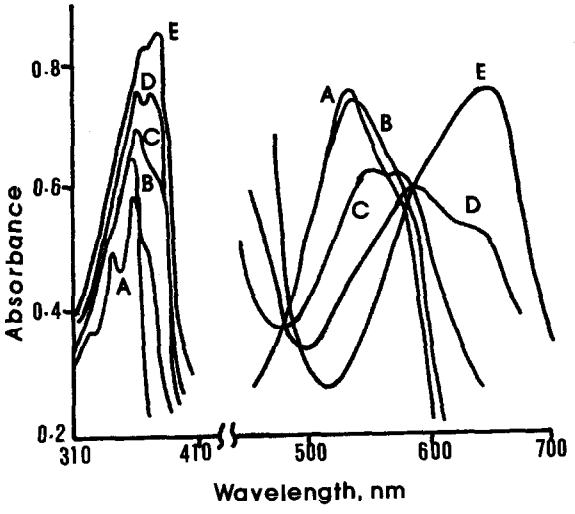


Fig.1 UV-Visible spectra of 1 (1.60 x 10^{-5} M for UV and 2.00 x 10^{-4} M for visible)at pH 5(A) , pH 7.2(B), pH 9.7 (C), pH 11.0 (D) , and pH 13 (E). Each successive uv spectrum has been displaced 0.04 absorbance unit upward for clarity

A titration curve, calculated using the above four pK_a values, gives a good fit to the experimental titration points (Figure 2).

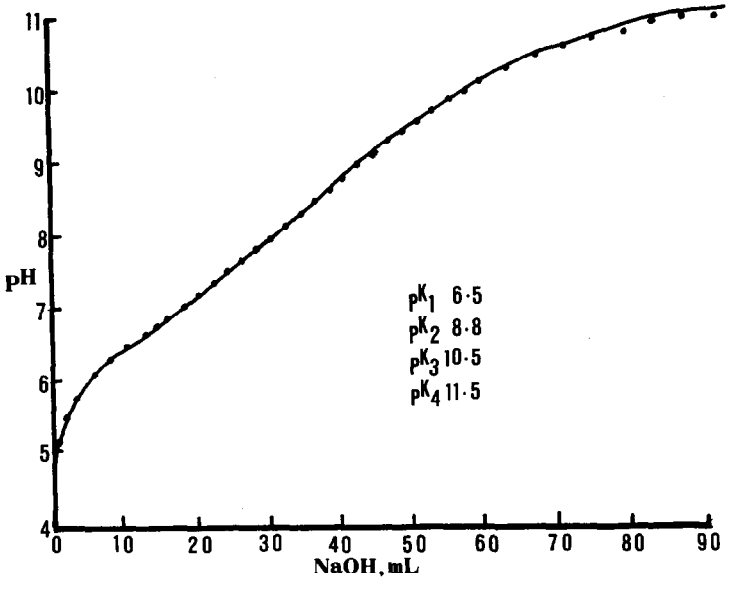
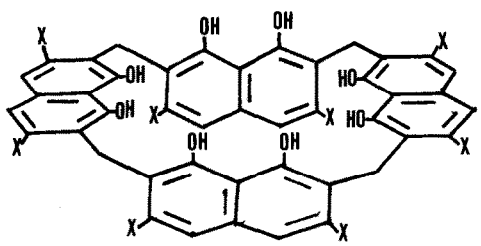


Fig.2 Calculated curve for the titration of 1 (2.5266g in 30 mL H_2O) with 0.05 M NaOH ; experimental points • .

Conformations of 1 and its Deprotonated Forms. From the work on the structurally related macrocyclic tetramers[10-12] as well as examinations of CPK models of 1, the two conformations to be considered are boat (2) and chair (3). The chair conformation is expected to be a poor host for the amines and have little effects on the proton chemical shifts of the guest molecules.[13] However, the boat conformation is expected to be a much better host[13] and to exert large shielding effects on the protons of the guest molecules because it has two vertical naphthalene units enclosing the hydrophobic cavity.

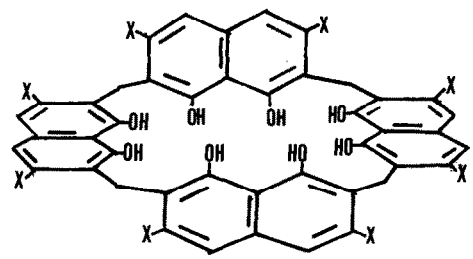
The chair conformation predominates in D_2O since the ^1H nmr spectrum of tetramethylammonium chloride in water is not affected by the addition of various amounts of 1. Similar findings are obtained when 1 is added to t-butylamine and ethylamine in an aqueous acidic medium (the acid is to protonate the amine to prevent it from ionizing 1).[8] The methyl protons of both the protonated amines are shielded by only 0.14 ppm when compared to their chemical shifts in the same acidic medium without 1. That complexation does occur is indicated by the broadening of the methylene quartet of the protonated ethylamine into a broad peak in the presence of 1.

In alkaline D_2O, the boat conformation predominates since large shielding effects are observed for the protons of tetraalkylammonium cations (see below). The preference for the boat conformation for the deprotonated forms of 1 is probably due to its stabilization through cyclic intramolecular hydrogen-bonding between adjacent O^- anions and OH groups in the boat conformation, similar to the resorcinol-acetaldehyde cyclic tetramer[9] and the calix[4]arene[14,15] systems.



2

X=SO_3Na



3

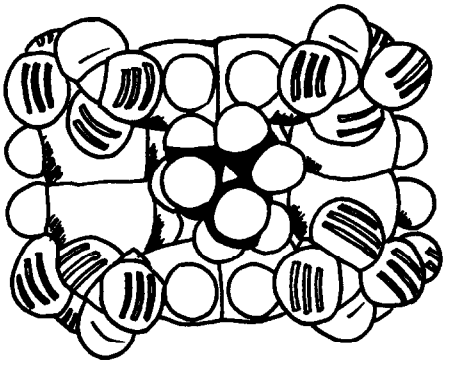
Complexation with Amines. That complexations between tetraalkylammonium cations and 1, in basic condition, occur are indicated by the shielding effects on the alkyl protons (Table I) and the broadening of their nmr spectra. Both CPK model examination (4) and ^1H nmr titration curves (Figure 3) suggest that the complexes have 1:1 stoichiometry. The guest cation are too big to enter into the host cavity completely. They partially penetrate into the cavity from the sulfonic end of the host. The hydroxyl end of the host is too small and it is unfavourable for the alkyl chains (hydrophobic) of the guest cations to sit on top of the ring of hydroxyl groups (hydrophilic).

Table I. Complexation-Induced ^{1}H NMR Chemical Shifts ($\Delta\delta$) of Amines with 1 in Water[a]

amine	proton	$\Delta\delta$, ppm[b]	amine	proton	$\Delta\delta$, ppm[b]
$MeNH_2$	CH_3	0.45	1-adamantamine	H_δ	0.96
$EtNH_2$	CH_3	0.50		H_γ	0.91
	CH_2	0.48		H_β	0.64
n-$PrNH_2$	CH_3	1.20	Me_4N^+	CH_3	0.70
	2-CH_2	0.90	Et_4N^+	CH_3	0.70
	1-CH_2	0.88		CH_2	0.97
t-$BuNH_2$	CH_3	0.52	n-Pr_4N^+	CH_3	0.37
Me_3N	CH_3	0.70		2-CH_2	0.48
Et_3N	CH_3	0.54		1-CH_2	0.57
	CH_2	0.75	n-Bu_4N^+	CH_3	0.45
			$Me_3(CH_2CH_2OH)N^+$	CH_3	0.54

[a] From measurements in D_2O at 35° with tetramethylsilane as external reference. The concentration of the host was kept constant ($\sim 5 \times 10^{-2}$ M) while the concentrations of the guests were varied. The equilibria were done in neutral condition (no added base or acid) for the amines, and in the presence of OH^- ($[1] : [OH^-] = 1:1$) for the tetraalkylammonium cations.

[b] $\Delta\delta$ = δ(free guest) - δ(complexed guest)



4

1:1 complex between 1 and Me_4N^+

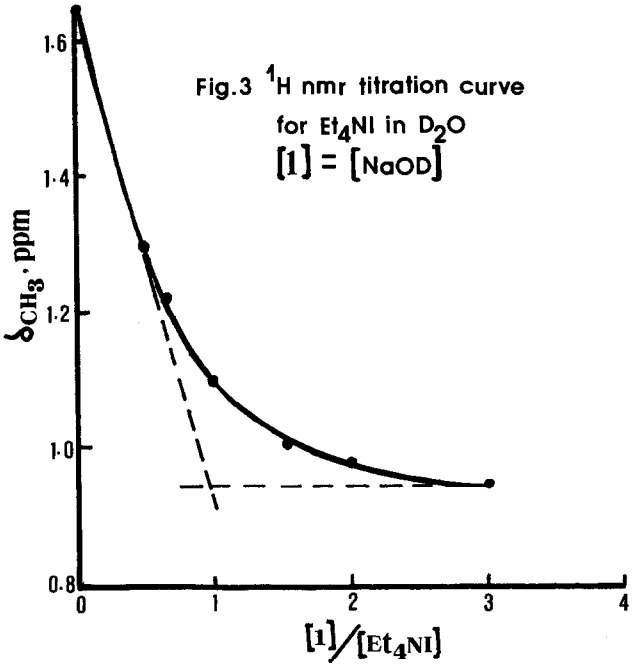


Fig.3 ^{1}H nmr titration curve for Et_4NI in D_2O [1] = [NaOD]

Aliphatic amines can complex with 1 in neutral D_2O since they are basic enough to deprotonate the host. Various species can be present (1, its deprotonated forms, amine, and the protonated amine), depending on the ratio of the host: guest used. CPK model examinations suggest that the bulky amines (t-$BuNH_2$, Me_3N, Et_3N, and 1-adamantamine) form 1:1 complexes with the host at the sulfonic end, with the amino end towards the sulfonic groups and the hydrocarbon part partially in the hydrophobic cavity. However, the thin linear aliphatic amines ($MeNH_2$, $EtNH_2$, and n-$PrNH_2$) are small enough to pass through the cavity from both the sulfonic and hydroxyl ends. Is the amino end located at the sulfonic or hydroxyl end in the complex? We expect, on electrostatic grounds, the former to be more favourable when the amine is protonated.[7] The latter is preferred when the amine is not protonated because its nitrogen atom can be hydrogen-bonded to a hydroxyl proton, thereby stabilising the complex.

Our expectations find support in the following observations. A mixture of $EtNH_2$ and 1 in a 1:1 molar ratio shows the characteristic triplet and quartet pattern for the ethyl protons in the ^1H nmr spectrum in neutral D_2O, but the two signals are broadened in alkaline D_2O (Figure 4 shows the methyl proton signals). In the neutral D_2O, the guest molecule exists as $EtNH_3^+$ since it deprotonates one OH group of 1. The guest molecule with its N^+ at the sulfonic end in the complex shows the typical triplet and quartet pattern for the ethyl protons. In alkaline D_2O, the guest molecule is the non-protonated $EtNH_2$. Its N atom is hydrogen-bonded to a OH hydrogen of the host and the signals for its ethyl protons are broad, indicating the beginning of the slowing of the exchange between the included and free amines on the nmr time scale.[16]

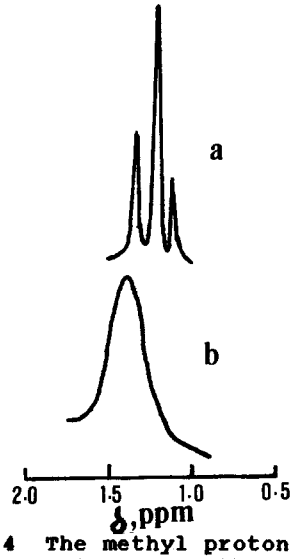


Fig.4 The methyl proton signals of $EtNH_2$ in D_2O in the presence of a molar equivalent of 1 : (a) in neutral condition; (b) in alkaline condition.

The complexation-induced proton chemical shifts, $\Delta\delta$, shown in Table I are not solely caused by electrostatic effects between SO_3^- and N^+, unlike the case reported for the resorcinol-acetaldehyde cyclic tetramer.[14] Anisotropy effects from the naphthalene rings also contribute towards the shielding effects. The reason is that protons more remote from the N^+ center experience greater shielding effects (see the values for n-$PrNH_2$ and 1-adamantamine), consistent with their deeper penetration into the hydrophobic cavity enclosed by the naphthalene rings.

For the concentrations of host and guests used in this work (host at $\sim$0.05 M and the concentrations of guests varied; our 60 MHz spectrometer does not permit us to use more dilute solutions), complexations already occur

to a large extent when the host to guest ratio is 1:1. As a result, no precise stability constants, K, can be calculated as they are very sensitive to small differences in the chemical shifts. Thus, we choose the fractions of complexations, N_c, at the 1:1 host to guest molar ratio to compare the stabilities of the various complexes (the 1:1 molar ratio was chosen so that only one type of host and one type of guest are involved — monodeprotonated 1 and the protonated amine). The N_c values (Table II) are roughly of the same magnitude. These N_c values indicate[17] that the K values are greater than 100 M^{-1}. The structurally similar p-sulfonatocalixarenes have been reported to bind trimethylanilinium cation with K values ranging from 500 to 5,600 M^{-1} in water.[18]

Table II. Fractions N_c of Complexations of Amines with Host 1 in Water at $[Host]_o : [Guest]_o$ = 1:1 Ratio[a]

amine	$N_c(\pm 0.1)$	amine	$N_c(\pm 0.1)$	amine	$N_c(\pm 0.1)$
$MeNH_2$	0.8	Me_3N	0.8	Et_4N^+	0.9
$EtNH_2$	0.7	Et_3N	0.6	$n\text{-}Pr_4N^+$	0.7
$n\text{-}PrNH_2$	0.7	1-adamantamine	0.8	$n\text{-}Bu_4N^+$	0.8
$t\text{-}BuNH_2$	0.6	Me_4N^+	0.9	$Me_3(CH_2CH_2OH)N^+$	0.7

[a] All the amines in the protonated form and the host monodeprotonated. $N_c = (\delta_u - \delta_{obs})/(\delta_u - \delta_c)$ where δ_u, and δ_c are the chemical shifts of the uncomplexed and complexed amines respectively, and δ_{obs} the observed chemical shift at the 1:1 host to guest molar ratio.

Experimental Section

Materials. All chemicals, except 1, were commercial samples.

Preparation of 1. To a solution of 1.5 g (0.0041 mol) of chromotropic acid, disodium salt, in 5 mL water was added 1.5 mL (0.020 mol) of 40% formaldehyde solution. The mixture was left standing for seven days and a quantitative yield of 1 in the form of a dark red plastic-like substance was obtained. The crude product was practically pure (the only impurity detected was a trace of fluorescent substance). It was recrystallized from H_2O-EtOH (or H_2O-iPrOH) mixed solvent as follows: the crude product was dissolved in boiling water. Alcohol was then added until the clear solution became cloudy. The solution was reheated until it became clear. It was then left to cool and 1 began to separate. The product was collected and dried at 100° in an oven for 25 minutes.

Thin-layer chromatographic analyses of the crude and recrystallized 1 were carried out on silica gel plates using various eluting agents such as MeOH/EtOH/H_2O, MeOH/n-BuOH/H_2O, AcOH/H_2O, AcOH/MeCN/H_2O, AcOH/MeOH/H_2O, and AcOH/Me_2CO/H_2O (for each eluting agent, the compositions of the component solvents were varied). Only a single compound was observed (the crude product has a trace of fluorescent substance as impurity). When the water content in the non-acidic water-alcohol eluting agent was low (e.g MeOH/EtOH/H_2O in 2:4:1 ratio) two spots (R_f 0.78 and 0.89) were noticed. They were caused by the deprotonation equilibrium of

1 because (1) only a single spot was observed when the same eluting agent was acidified and (2) the two spots, when isolated and respotted, each yielded the same two spots (R_f 0.78 and 0.89).

Anal. Found: C, 27.64; H, 3.89; Na, 9.39. Cald for $(C_{11}H_6O_8S_2Na_2)_4 \cdot 23H_2O$: C, 27.52; H, 3.65; Na, 9.59. ^{1}H NMR(CD_3OD at 35°) δ4.68(CH_2,s), 8.05(Ar H,s); ^{13}C NMR(D_2O) δ28.1, 118.7, 120.5, 121.1, 131.6, 141.5, 152.7; highest m/z observed in mass spectrum is 1327 (molecular ion peak not observed).[8]

Titration of 1. A solution containing 2.5266 g of 1 in 30 mL of water was titrated with 0.05 M NaOH using a Beckman 3500 pH meter to measure the pH values.

The titration curve was calculated using the four pK_a values determined from spectrophotometric titrations. The first two deprotonations could be treated independently since their pK_a values differ from their adjacent ones by about two units. Thus, the titration curve for the first deprotonation was calculated from

$$pH = pK_1 + \log \frac{[1^-]}{[1]} \qquad (1)$$

where $[1^-]$ is equal to the concentration of NaOH added and $[1] = [1]_o - [1^-]$ ($[1]_o$ is the initial concentration of 1), with dilution factor taken into account. Similarly, equation 1 was used to calculate the second deprotonation curve (replacing pK_1 by pK_2, $[1^-]$ by $[1^{2-}]$, and $[1]$ by $[1^-]$).

The third and fourth deprotonations are not completely independent of each other since their pK_a values differ by one unit. However, equation 1 could still be applied to the first half of the third deprotonation and the second half of the fourth deprotonation since, in these regions, only a maximum of two deprotonated species of 1 predominate. The curve, for the region where there are three deprotonated species of 1, could easily be obtained by extrapolation since it lies between the above two regions, where pH variations are small.

^{1}H nmr spectra were recorded in D_2O with a Perkin-Elmer R12B 60 MHz spectrometer using tetramethylsilane as external reference (probe temperature 35°). In all the nmr titrations, the host concentration was maintained constant (~0.05 M) while the concentrations of the guests varied. The chemical shift of the para protons or 1 is not affected by the concentration variation of 1 (δ 8.62 for 0.03 to 0.22 M).

Ultraviolet-visible spectra were recorded with Hitachi 200 and Hitachi 300 spectrophotometers.

Buffer solutions were prepared according to standard procedure.[19]

pH measurements were taken with a Beckman 3500 pH meter.

pK_a values of 1 were estimated from the changes in the absorption maxima of 1 in the visible region in a series of buffer solutions (pH 4 to ~13 with increments of ~0.5 pH unit).

Acknowledgement

Financial support in the form of a Short Term Research Project Grant from the Universiti Sains Malaysia is gratefully acknowledged.

References

1. Pedersen, C.J., Frensdorff, H.K., Angew. Chem. Int. Ed. Engl., 1972, 11, 16.
2. Cram, D.J., Angew. Chem. Int. Ed. Engl., 1986, 25, 1039.
3. Lehn, J.-M., Science, 1985, 227, 849.
4. Sutherland, I.O., Chem. Soc. Rev., 1986, 15, 63.
5. Tabushi, I., Kuroda, Y., Kimura, Y., Tetrahedron Lett., 1976, 3327.
6. Diederich, F., Dick, K., Tetrahedron Lett., 1982, 23, 3167.
7. Shinkai, S., Mori, S., Koreishi, H., Tsubaki, T., Manabe, O., J. Am. Chem. Soc., 1986, 108, 2409.
8. Poh, B.-L.l Lim, C.S., Khoo, K.S., Tetrahedron Lett., 1989, 30, 1005.
9. Schneider, H.-J., Güttes, D., Schneider, U., Angew. Chem. Int. Ed. Engl., 1986, 25, 647.
10. Högberg, A.G.S., J. Org. Chem., 1980, 45, 4498.
11. Högberg, A.G.S., J. Am. Chem. Soc., 1980, 102, 6046.
12. White, J.D., Gesner, B.D., Tetrahedron Lett., 1968, 1591.
13. Schneider, H.-J., Güttes, D., Schneider, U., J. Am. Chem. Soc., 1988, 110, 6449.
14. Shinkai, S., Araki, K., Koreishi, H., Chemistry Letters, 1986, 1351.
15. Shinkai, S., Pure & Appl. Chem., 1986, 58, 1523.
16. Diederich, F., Dick, K., Griebel, D., J. Am. Chem. Soc., 1986, 108, 2273.
17. Poh, B.-L., Saenger, W., Spectrochim. Acta, 1983, 39A, 305.
18. Shinkai, S., Araki, K., Manabe, O., J. Am. Chem. Soc., 1988, 110, 7214.
19. "Handbook of Chemistry and Physics"; The Chemical Rubber Co., 49th ed., 1969, p D79.