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Complexation of Aromatic Hydrocarbons with a Macrocycle Containing Four Tropolone Units in Water

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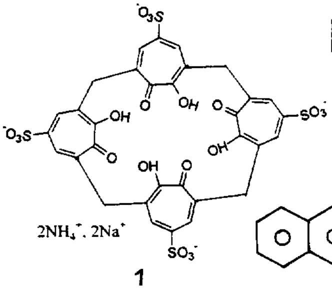
***Abstract*:** The stability constants K of nine complexes formed from aromatic hydrocarbons and the macrocycle **1** in water were measured by the transport method (^{1}H nmr spectroscopy was used in the case of benzene as guest). Their values increase with the number of aromatic rings in the aromatic hydrocarbons. A value of -1.5 Kcal mol^{-1} was obtained for the aromatic π-π interaction energy at 25^{0}C.

The hydrophobic aromatic π-π interaction plays an important role in the biological system, such as the stabilizing of protein structures and their complexes[1]. We have been interested in quantifying this interaction by studying the complexations of aromatic hydrocarbons with water-soluble macrocycles that contain a hydrophobic cavity made up of aromatic ring units[2-4]. We have found[5] the π-π interaction energies between two benzene units, a benzene and a naphthalene unit, and a benzene and an acridine unit were constant at -1.4 Kcal mol^{-1} . In this paper we report our study on the complexation of nine aromatic hydrocarbons, **2** to **10**, with macrocycle[6] **1** (we propose to give it the trivial name of cyclotetra-5-sulfonatotropolonylene, diammonium disodium salt, analogous to the naming of cyclotetrachromotropylene[7]) in water to determine the π-π interaction energy between a benzene and a tropolone unit.



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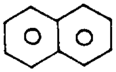

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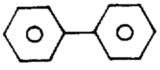

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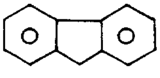

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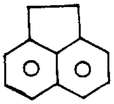

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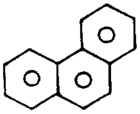

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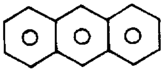

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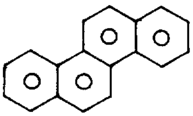

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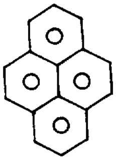

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RESULTS AND DISCUSSION

The complexation study was carried out using two different methods. ^{1}H nmr spectroscopy was used for the liquid benzene as guest and the transport method[8] was used for the remaining eight solid polyaromatic hydrocarbons as guests. The presence of complexation between the aromatic hydrocarbons and **1** was shown by the shielding of the benzene protons (Figure 1, chemical shift moved upfield) and the increase in the transport rates of the polyaromatic hydrocarbons from one hexane phase to another through an intermediary aqueous phase (Figure 2, for anthracene as guest), in the presence of **1**.

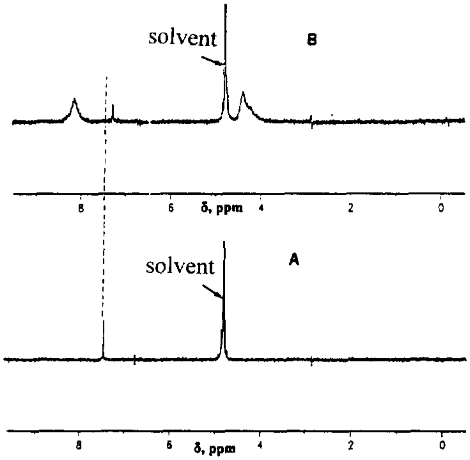


Figure 1. 300 MHz proton nmr spectra in D_2O at 25^{0}C of 1.125x10^{-2} M of benzene (solvent peak at 4.80 ppm as internal reference); (A) no host, (B) in the presence of 1.488x10^{-2} M of **1**.

Assuming that the complexes are of 1:1 stoichiometry[2,8], the complex stability constant K for benzene as the guest was obtained by a non-linear regression fitting procedure (Figure 3)[9] and the K values for the other eight aromatic hydrocarbons as guests were calculated from the slopes of such plots shown in Figure 2, using the equations given earlier[8]. The K values obtained are given in column 3, Table 1.

However, **1** exists in three major conformations[6] in about equal proportions in water, namely cone, 1,2-alternate and 1,3-alternate (Figure 4) and only the 1,3-alternate conformer is expected to be a good host to the aromatic hydrocarbons. The latter can be equatorially included inside the open-ended hydrophobic cavity, analogous to the case of cyclotetrachromotropylene[8] as host (a water-soluble cyclic tetramer made up of four naphthalene units). The cone conformer is not expected to complex with the polyaromatic hydrocarbons since its cavity size is close to that of the analogous cone conformer of 4-sulfonatocalix[4]arene which fails to complex with them[10]. The 1,2-alternate conformer with the two faces of two adjacent tropolone units at right

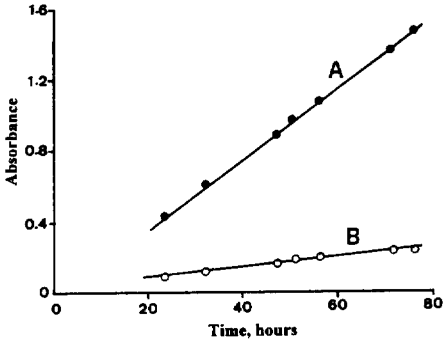


Figure 2. Relationship between absorbance at 251 nm of anthracene in the receiving phase and time. The initial concentration of anthracene in the source phase is 1.57×10^{-3} M; (A) 2.90×10^{-3} M of **1** in the aqueous phase and (B) no host in the aqueous phase.

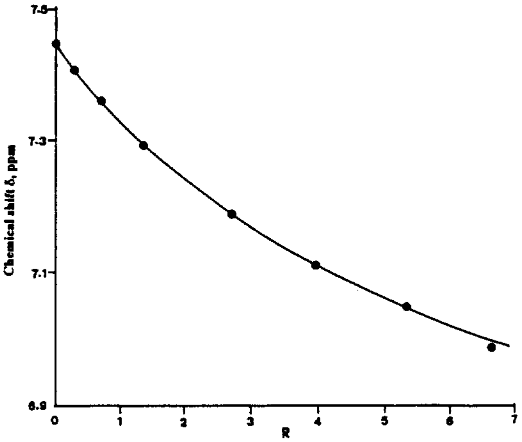
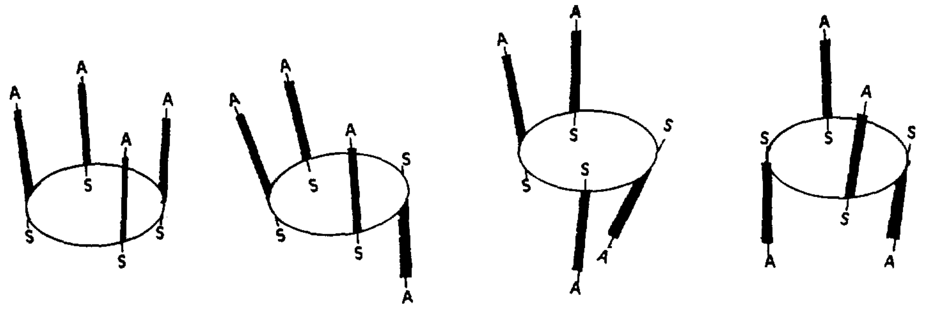


Figure 3. Calculated proton chemical shift titration curve of benzene (1.125×10^{-2} M) in D_2O at 25°C. R is the molar ratio of the host (**1**) to guest used and the points are experimental values. The curve is calculated from K = 22.5 M^{-1}, δ of free benzene = 7.451 ppm and δ of complexed benzene = 6.707 ppm.

Table 1. Stability Constants K of 1:1Complexes Formed from Aromatic Hydrocarbons and **1** in Water[a]

No.	Hydrocarbon	K (M^{-1})	K (M^{-1})[b]	N[c]
2	Benzene	$(2.2 \pm 0.2) \times 10$	8.9×10	1
3	Naphthalene	$(3.9 \pm 1.5) \times 10^2$	1.2×10^3	2
4	Biphenyl	$(4.4 \pm 0.4) \times 10^2$	1.3×10^3	2
5	Fluorene	$(4.2 \pm 1.0) \times 10^2$	1.3×10^3	2.5
6	Acenaphthene	$(1.7 \pm 0.1) \times 10^3$	5.1×10^3	2.5
7	Phenanthrene	$(1.2 \pm 0.1) \times 10^4$	3.6×10^4	3
8	Anthracene	$(7.1 \pm 0.3) \times 10^3$	2.1×10^4	3
9	Chrysene	$(3.2 \pm 0.1) \times 10^4$	9.6×10^4	4
10	Pyrene	$(3.7 \pm 0.1) \times 10^4$	1.1×10^5	4

[a] Determined by ^{1}H nmr method for **2** (25°C) and transport method for the rest (27-29°C).
[b] Only 1,3-alternate conformer as host. [c] Number of aromatic rings in the aromatic hydrocarbons; a non-aromatic ring containing double bonds is counted as half[8].



Cone

Partial Cone

1,-2-Alternate

1,3-Alternate

Figure 4. Four possible conformations of cyclic tetramer **1** (A consists of the OH and C=O groups and S the SO_3^- group).

angle to each other is not suitable for complexation with the aromatic hydrocarbons by π-π interaction. The K values calculated for only the 1,3-alternate conformer as host are given in column 4.

A plot of both sets of log K versus N (the number of aromatic rings in the guest[8]) gives a straight line (Figure 5 for the first set of K values, correlation coefficient 0.980, slope 1.06 and intercept 0.53; for the second set of K values, correlation coefficient 0.968, slope 1.04 and intercept 0.98). The magnitude of the

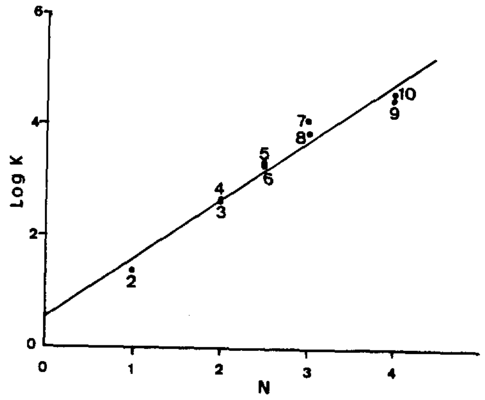


Figure 5. Relationship between log K and the number of aromatic rings (N) in the aromatic hydrocarbon guests. The numbers refer to the aromatic hydrocarbons given in Table 1.

slope[5] is a measure of the interaction energy between an aromatic ring of the guest molecule and the aromatic wall of the host molecule. The value of 1.06 corresponds to an interaction energy between a benzene unit and a tropolone ring of -1.5 Kcal mol^{-1} at 25^{0}C. This value is close to those obtained[5] for the interactions between two benzene units (-1.4 Kcal mol^{-1}), a benzene and a naphthalene unit (-1.3 Kcal mol^{-1}), and a benzene and an acridine unit (-1.4 Kcal mol^{-1}). It is also in the range of -1 to -2 Kcal mol^{-1} calculated for the interactions between two benzene units in the proteins[11].

EXPERIMENTAL

Materials. Macrocycle **1** was synthesized as reported earlier[6]. The aromatic hydrocarbons were commercial samples. The solid polyaromatic hydrocarbons were purified by recrystallization from ethanol.

^{1}H nmr spectra in D_2O at 25^{0}C were recorded with a 300 MHz 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 the chemical shift titration, the concentration of benzene was kept constant at 0.0113 M while the concentration of macrocycle **1** varied.

Transport experiments were carried out at room temperature (27- 29^{0}C) using the U-tubes[8]. The concentrations of the polyaromatic hydrocarbons in the hexane source phase varied from 7x10^{-4} to 6x10^{-2} M. The concentration of host **1** in the aqueous phase was 2.90x10^{-3} M.

Calculations of the stability constants K of the 1:1 host to guest complexes using the non-linear regression fitting of the proton chemical shift titration curve of benzene and using the equations for the transport experiment for the polyaromatic hydrocarbons were carried out as reported earlier[8,9].

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