

Transport of Neutral Arenes through an Aqueous Barrier by Resorcinol–Aldehyde Tetramers

HARMIT SINGH* and RAVINDERJIT KAUR

Department of Food Science and Technology, Guru Nanak Dev University, Amritsar 143005, India

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Abstract. The transportation of neutral arenes such as benzene, toluene, *o*, *m*, *p*-xylene, durene, biphenyl, anthracene and phenanthrene through an aqueous medium using the crown conformation of tetrameric cyclophane hosts **1** and **2** has been studied. In general, transportation of all arenes increases with time, except for toluene, which shows saturation behaviour with both hosts **1** and **2**. Among the larger arenes, transportation of biphenyl is a maximum with **1**; with host **2**, transportation of anthracene is a maximum due to its larger association constant. In the case of smaller arenes, **1** transports benzene most effectively, and transportation decreases as the number of methyl groups on benzene increases, showing that stereoelectronic factors affect transportation. With **2** toluene is transported most effectively due to the change in the shape of the binding cavity caused by a change in bridging groups. A comparison of transportation for 1 h with **1** and **2** shows that for all arenes transportation is greater with host **2** than with **1** due to the hydrophobic nature of **2**.

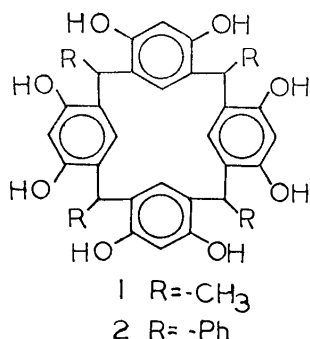
Key words: Transport, tetramers, neutral arenes, aqueous barrier.

1. Introduction

The use of water-soluble synthetic macrocycles as simple models for enzymes and receptors has been the focus of interest of many chemists in recent years. Current research is aimed at the development of artificial systems that mimic enzymatic catalysis, regulation and transport. Polar cyclophanes have been studied for their formation of inclusion complexes due to different kinds of interactions such as hydrophobic, hydrogen-bonding or dipole–dipole [1]. Membranes impregnated with aqueous cyclophanes [2] have been used for the separation of organic compounds. Separation of alcohols, chlorinated hydrocarbons and aromatic compounds has also been achieved with calixarenes [3]. Further work on the specificity of various calixarenes for the separation of isomeric xylenes has been carried out [4]. Urea transport through a supported liquid membrane using synthetic carriers has been studied: the selectivity depends upon the nature and geometry of the hydrocarbon framework, as well as on the various substituents attached to it, and also on the electronic properties of the guests and the nature of the solvent. The transportation of organic molecules using artificial carriers has been of great interest as it gives an insight into carrier enzymes and the transport of organic molecules in biological systems and their points of interactions with each other [5].

* Author for correspondence.

The present study investigates the transportation of neutral arenes such as benzene, toluene, *o*, *m*, *p*-xylene, durene, biphenyl, anthracene and phenanthrene using tetrameric cyclophane hosts **1** and **2**.



2. Experimental

Compounds **1** and **2** were synthesized using well-established procedures. Starting materials were resorcinol–acetaldehyde and resorcinol–benzaldehyde. Condensation was under acidic conditions. Structures were confirmed using ¹H and ¹³C NMR, and melting points.

Hosts **1** and **2** were resolved into their conformers as established by Högberg by recrystallising repeatedly from acetonitrile [6, 7]. The bowl shaped conformation was separated from the mother liquor, hydrolysed with NaOH (1N) and used for all transportation and extraction studies. It has been shown by Schneider [8] that phenolate ions under basic condition greatly stabilise the bowl conformation with an *all-cis* configuration of the bridging alkyls.

2.1. TRANSPORT EXPERIMENTS

The host solution (5×10^{-4} M, 15 mL) in NaOH (0.02 M) solution was placed at the base of the transportation cell i.e. phase II (Figure 1). Above the aqueous layer of the host solution, *n*-hexane (8 mL) was added in the inner tube of the cell (Phase III). A solution of arene (10^{-2} M, 8 mL) in hexane was placed in the outer tube (Phase I). The aqueous phase was agitated with an approximately cylindrical magnetic stirring bar (18 mm length, 5 mm diameter) at a constant stirring rate (192 rpm). At this rate clear interphases were obtained between the clear phases. This experiment was conducted for 1, 2, 3, 4 and 5 h in the case of each guest solution. Samples were taken from the receiving phase to determine the amount of delivered guest by electronic absorption spectroscopy at a wavelength characteristic of each guest. The slope of the plots of concentration vs. time were used to calculate the transportation rates.

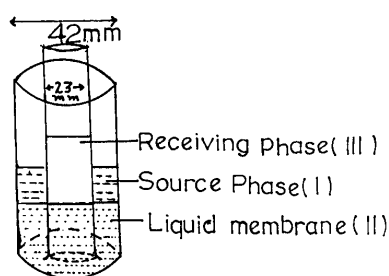


Figure 1. Diagram of the cell used for the transport studies.

2.2. LIQUID-LIQUID EXTRACTION AND DETERMINATION OF ASSOCIATION CONSTANTS

An aqueous solution of host (5×10^{-4} M, 10 mL) in NaOH (0.02M) and a solution of guest (10^{-2} M, 10 mL) in *n*-hexane were vigorously shaken for 10 min in a separating funnel. Upon standing, the interface between the two clear phases was very clean and most of the aqueous phase was carefully let out of the separating funnel. The guest in the aqueous phase was re-extracted with two 10 mL portions of *n*-hexane. The amount of guest in the *n*-hexane was determined by electronic absorption spectroscopy and the total concentration of guest in the aqueous phase, $G(\text{H}_2\text{O})$ (tot), was calculated using the Beer-Lambert law. Similarly, 10 mL of the described solution of guest in *n*-hexane was shaken with 10 mL of doubly distilled water. After clean phase separation most of the aqueous phase was carefully removed from the separation funnel. The aqueous phase was then shaken with 10 mL of *n*-hexane for the extraction of guest in *n*-hexane. The amount of guest in *n*-hexane was determined by electronic absorption spectroscopy and the concentration of guest in the aqueous phase $G(\text{H}_2\text{O})$ was calculated. Subtracting $G(\text{H}_2\text{O})$ (tot) — $G(\text{H}_2\text{O})$ gave the concentration of complex $\text{HG}(\text{H}_2\text{O})$ in the aqueous phase and $\text{H}_0 - \text{HG}(\text{H}_2\text{O})$ gave the concentration of free host in the aqueous phase $\text{H}(\text{H}_2\text{O})$. All concentrations being known K_a was calculated from Equations (1) and (2).



$$K_a (\text{L mol}^{-1}) = \text{HG}(\text{H}_2\text{O})/\text{H}(\text{H}_2\text{O}) \quad (2)$$

K_d and K_e were also calculated from Equations (3) and (4), respectively, which were helpful in explaining transportation rates.

$$K_d = \text{G}(\text{H}_2\text{O})/\text{G}(\text{Hex}) \quad (3)$$

$$K_e = K_d \cdot K_a \quad (4)$$

Table I. Determination of the constant of transportation (K_t), distribution (K_d), extraction (K_e) and association (K_a) for biphenyl, phenanthrene and anthracene with host **1** and **2** by a transportation and liquid–liquid experiments. (Each value is the mean of three experiments which are within 15% error. The K_a and K_d values are the mean of three independent measurements which are consistent within 2% error.)

Hydrocarbons	K_a (L mol ⁻¹)	K_d	K_e (L mol ⁻¹)	K_t (mol L ⁻¹ h ⁻¹)
With host 1				
Biphenyl	1.1×10^4	1.2×10^{-3}	13.8	$9.3 \times 10 \times 10^{-6}$
Phenanthrene	7.7×10^3	9.06×10^{-4}	6.97	2.8×10^{-6}
Anthracene	5.8×10^5	2.05×10^{-5}	12.00	1.05×10^{-6}
With host 2				
Biphenyl	1.5×10^4		18.48	8.3×10^{-6}
Phenanthrene	3.9×10^3		3.54	5.9×10^{-6}
Anthracene	5.6×10^5		11.60	3.2×10^{-5}

3. Results and Discussion

Tetrameric cyclophanes **1** and **2** have already been shown by us [9] and Schnieder *et al.* [10] to form host–guest inclusion complexes in aqueous solution with quaternary ammonium salts using ¹H NMR spectroscopy and by X-ray crystallographic studies. Compounds **1** and **2** are here studied for their transportation and extraction properties for a number of arenes and results compared for the selectivity of **1** and **2**.

3.1. DETERMINATION OF K_a , K_t , AND K_e BY TRANSPORTATION STUDIES

The slope of plots (conc. of guest vs. time) gave the transportation rate K_t (Tables I and II). K_t depends on the association constant K_a of the guest with the host and the distribution constant K_d of the guest in a hexane/water interface as will be discussed later.

Transportation requires association of guest with host to be strong to carry the guest but at the same time requires sufficient dissociation at the H₂O/hexane (Phase III) receiver interphase. The association constants K_a and dissociation constant K_d (Tables I and II) were determined from standard procedures by liquid–liquid extractions [12]. A comparison of constants for host **1** (Tables I and II) demonstrates interesting results with interdependence on each other. Among the bigger arenes – e.g. phenanthrene, anthracene, and biphenyl – the last one shows maximum K_e and K_d values. The transportation rate K_t (Figure 2) is 3.3 times that of phenanthrene and 8.8 times that of anthracene (Table I). The K_d of anthracene is 100 times lower than for biphenyl, but still shows an appreciable K_e viz. 12, due to its larger K_a value. This comparison indicates that the distribution of arene in the hexane/water interphase plays an important role in the transportation of arene. Also biphenyl,

Table II. Relative rates of transport K_t , K_a (association constant), K_d (distribution constant) and extraction constants (K_e) for smaller arenes determined from transportation and liquid–liquid extraction experiments. (Each value is the mean of three experiments which are within 15% error. The K_a and K_d values are the mean of three independent measurements which are consistent within 2% error.)

Hydrocarbons	K_a (L mol ⁻¹)	K_d	K_e (L mol ⁻¹)	K_t (mol L ⁻¹ h ⁻¹)
With host 1				
Benzene	–	9.3×10^{-3}	–	6.6×10^{-4}
Toluene	–	9.0×10^4	–	4.00×10^{-4}
<i>o</i> -xylene	9.6×10^4	5.5×10^{-4}	52.8	2.20×10^{-5}
<i>m</i> -xylene	1.7×10^5	4.9×10^{-4}	83.3	1.45×10^{-5}
<i>p</i> -xylene	3.4×10^4	2.15×10^{-4}	7.13	7.60×10^{-6}
Durene	1.8×10^4	7.4×10^{-4}	13.32	1.63×10^{-6}
With host 2				
Benzene	–	–	–	2.3×10^{-4}
Toluene	–	–	–	8.4×10^{-4}
<i>o</i> -xylene	1.7×10^4	–	9.35	7.6×10^{-6}
<i>m</i> -xylene	5.3×10^4	–	25.93	5.0×10^{-6}
<i>p</i> -xylene	6.5×10^4	–	13.97	4.8×10^{-6}
Durene	3.2×10^5	–	236	–

being a linear molecule, shows a better fit to the cavity and hence is transported most, as is confirmed by CPK models.

For host **2** (Table I), the association constant (K_a) is largest for anthracene and, despite its smaller distribution constant (K_d), anthracene shows maximum transportation rate (Figure 3). Whereas phenanthrene has the lowest association constant (K_a) and extraction constants (K_e), resulting in weaker binding with **2** and its minimum transportation rate. Biphenyl, favourite for **1**, has an approximately similar transportation rate (Figure 3) as host **2** but anthracene, having smaller K_a and K_e values than with host **1**, shows 19 times greater transportation, which is due to the more hydrophobic nature of **2** due to its additional lower rim of four bridging phenyl groups.

The smaller arenes – viz. benzene, toluene, xylenes and durene – were studied to investigate the effect of increasing methyl groups on their K_a and K_t values (Figure 4). As shown in earlier studies by ¹H NMR, nicotinamide and pyridinium methiodide salts have been shown to fit into the cavity of host **1** [13]. It was expected that smaller arenes would fit better in the cavities of these types of hosts.

With **1** the study (Table II) shows that for smaller arenes the increasing number of methyl groups hinders the overall rate of transportation. Benzene was transported 404 times more than durene (Table II). The changes in the methyl groups on the benzene nucleus in *o*, *m*, *p*-xylene show an interesting behaviour (Table II, Figures 5 and 6) as *m*-xylene has the highest K_e value due to its greater K_a value. But the

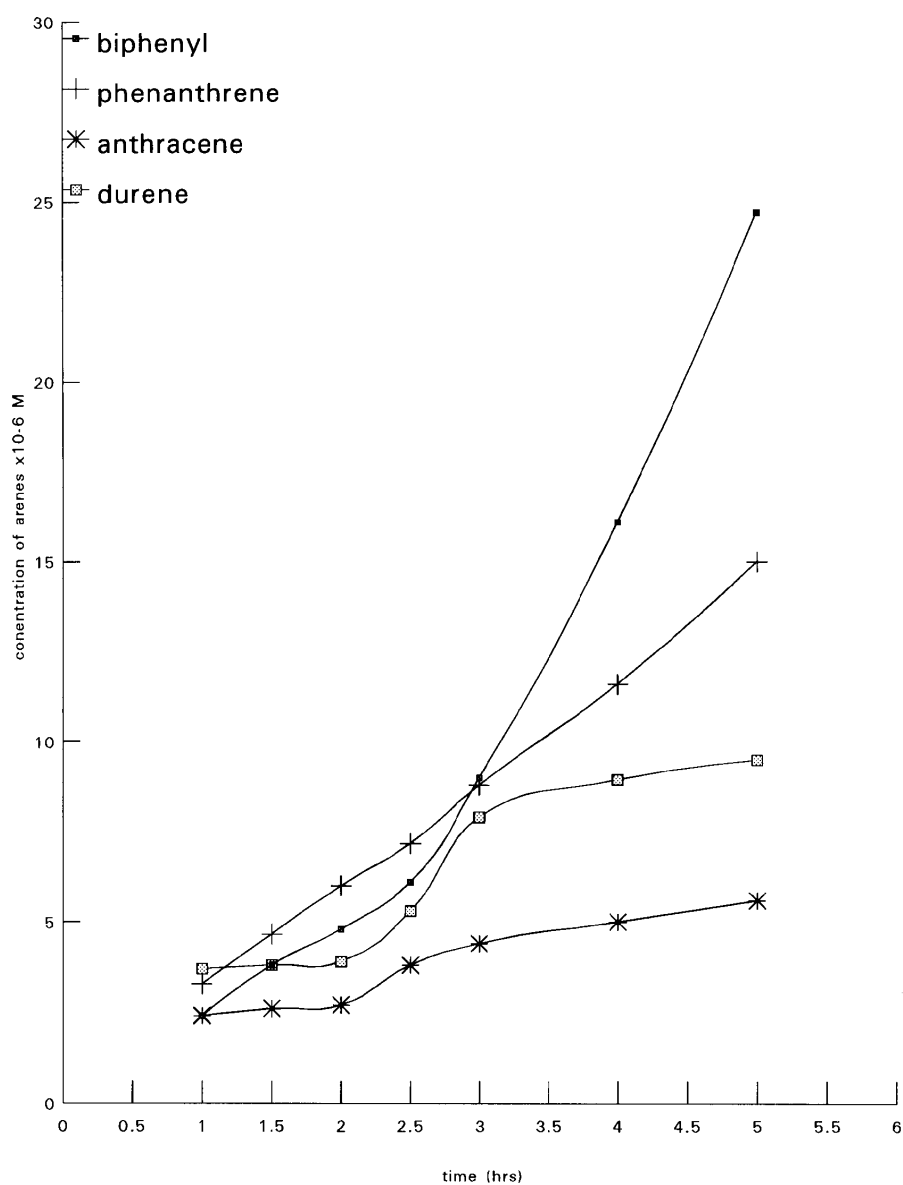


Figure 2. Transportation of biphenyl, phenanthrene, durene and anthracene through an aqueous phase containing 1.

transportation rate (K_t) is higher for *o*-xylene, having a greater K_d value, which indicates that the K_d value plays an important role during transportation.

With host 2 durene shows the lowest K_e value of all the arenes due to its larger solubility in water, as shown by its K_d value, viz. 236 (Table II). After repetitive studies, no straight line plot for K_t was obtained and this needs to be studied in

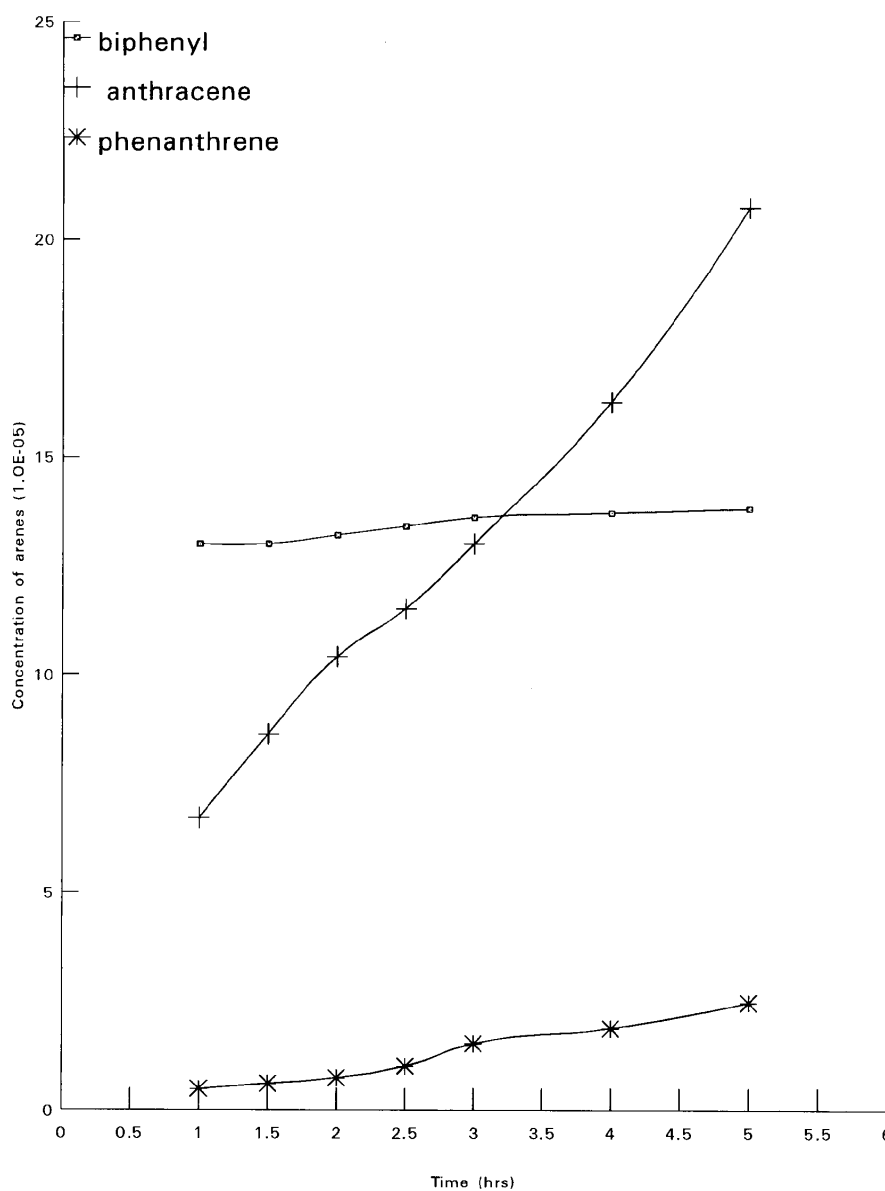


Figure 3. Transportation of biphenyl, phenanthrene and anthracene through an aqueous phase containing **2**.

detail with **2**. The deviation might be due to its large K_a value, 18.8 times larger than for *o*-xylene, which is 25 times more than the K_e value for durene.

With host **2** (Table II) the same trend is found for the xylenes, stressing the importance of K_d values during transportation. As the number of methyl groups increases a decrease in transportation rate is obtained (Figures 5 and 6). The K_a

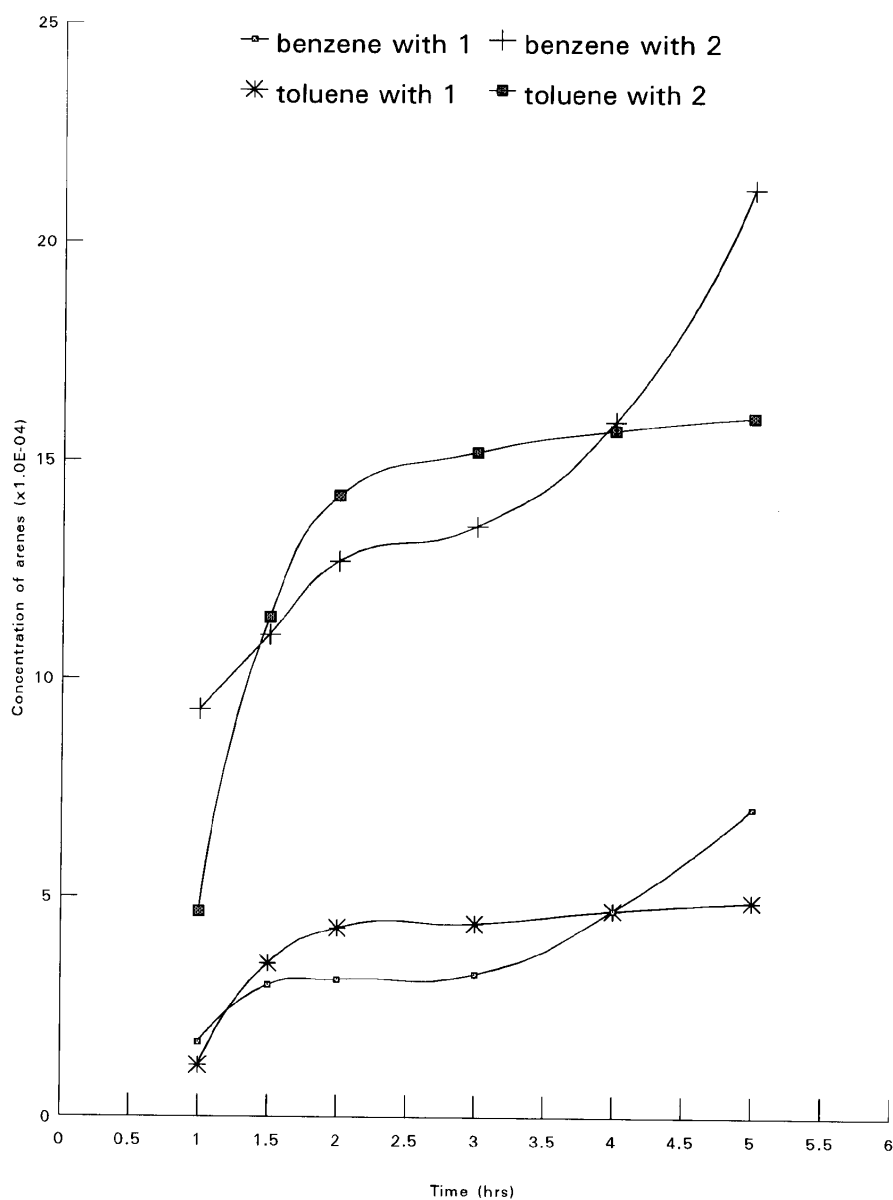


Figure 4. Transportation of benzene and toluene through an aqueous phase containing **1** and **2**.

value for *p*-xylene was highest, viz 1.7×10^4 , but the extraction constant K_e is highest for *m*-xylene, viz. 25.93, due to its moderate K_d and K_e values, which are suitable for good transportation. It may be noted that compounds with large K_d or K_a values create more problems due to leakage in the blank phase or strong

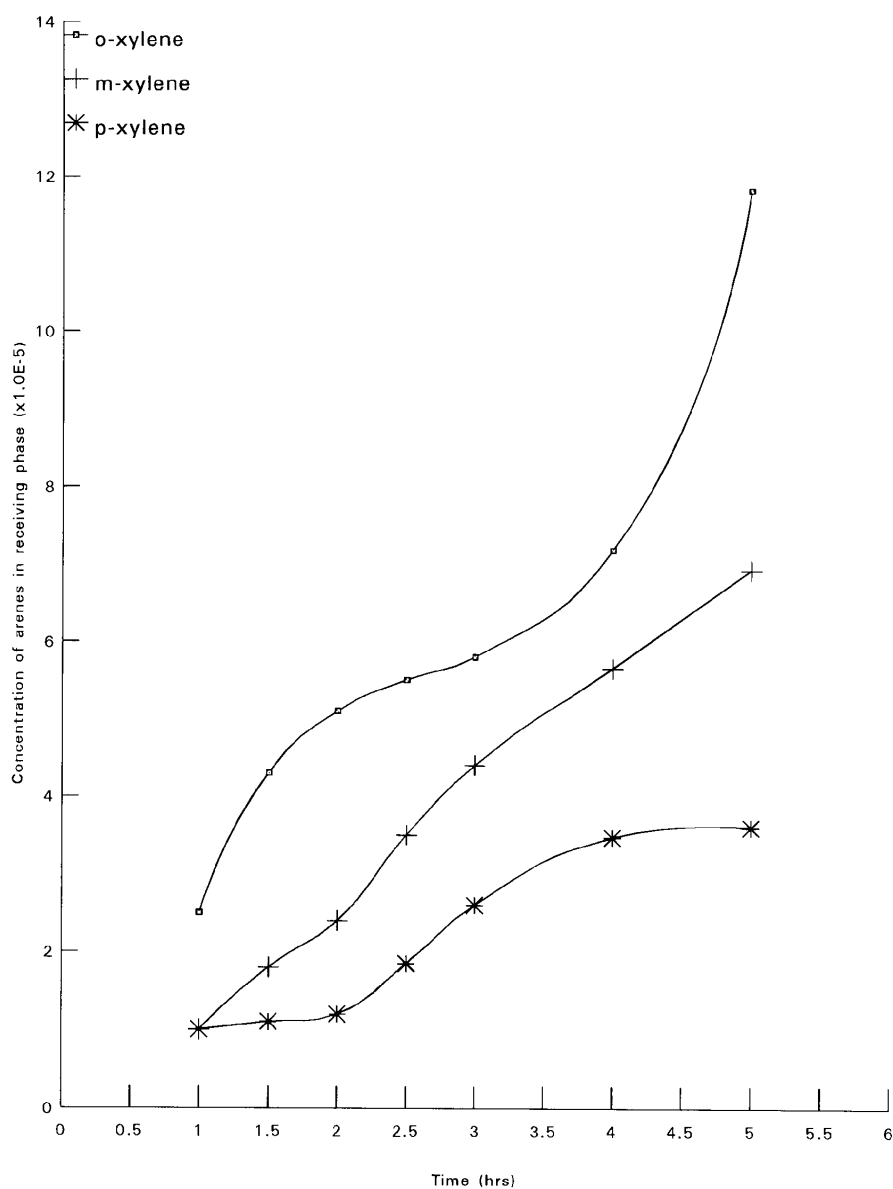


Figure 5. Transportation of *o*-, *m*- and *p*-xylene through an aqueous phase containing **1**.

binding to the host, respectively, so their trends have to be carefully established for transportation, e.g. benzene, toluene with large K_d and durene, with a high K_a value of 3.2×10^5 and a K_d value of 7.4×10^{-4} , show erratic behaviour.

Further study is required to see the effect of the position of the methyl groups around the benzene nucleus on its stereoelectronic interactions with **1** and **2**. When two methyl groups are adjacent (*ortho*), K_a is smaller (Table II), whereas symmetric

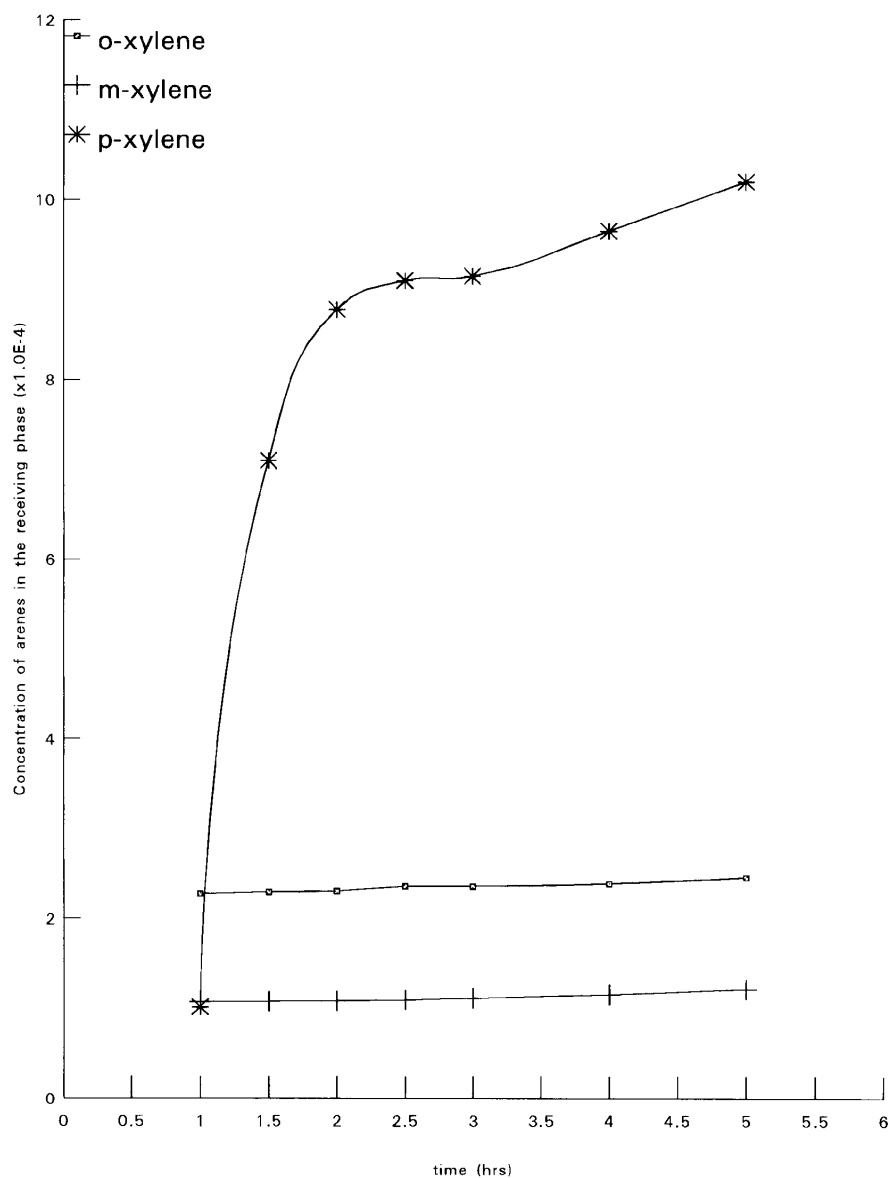


Figure 6. Transportation of *o*-, *m*-, *p*-xylene through an aqueous phase containing **2**.

p-xylene shows maximum K_a and hence a better fit (also shown by CPK models), whereas with **1** the fit appears to be optimum for *m*-xylene and minimum for *p*-xylene with highest and lowest K_a values, indicating a change in the cavity shape on changing the bridging groups of tetramer hosts **1** and **2**.

Table III. Acceleration factor (A_f) calculated for host **1** as compared to **2** for the transportation of different arenes through the aqueous barrier during transportation.

Arenes	Transportation in 1 h using host 1 (H_1)	Transportation in 1 h using host 2 (H_2)	Acceleration factor H_1/H_2 (A_f)
Benzene	1.6×10^{-4}	9.3×10^{-4}	5.5
Toluene	1.1×10^{-4}	4.6×10^{-4}	4.02
<i>o</i> -xylene	2.5×10^{-5}	2.2×10^{-4}	9.08
<i>m</i> -xylene	1.09×10^{-5}	1.07×10^{-4}	9.80
<i>p</i> -xylene	1.01×10^{-5}	1.01×10^{-4}	10
Durene	6.60×10^{-5}	4.7×10^{-3}	71.2
Biphenyl	2.4×10^{-6}	1.36×10^{-4}	54.16
Anthracene	4.4×10^{-6}	9.90×10^{-5}	22.50
Phenanthrene	3.2×10^{-6}	4.8×10^{-6}	1.50
Fluorene	2.6×10^{-6}	2.8×10^{-5}	10.70

3.2. COMPARISON OF THE TWO HOSTS FOR TRANSPORTATION OF DIFFERENT GUESTS THROUGH AN AQUEOUS BARRIER

The acceleration factor (A_f) was found by comparing transportation in 1 h with **1** and **2** (Table III). It is clear from the table that the hydrophobicity of **2**, due to the four extra phenyls at the bridging carbons, adds to its power of transportation. The largest difference occurs for durene, with 71 times more transportation in 1 h with **2** than with **1**. This may be a complex combination of different factors affecting the preference of guests. For smaller arenes A_f is 10 or less, as compared to larger arenes such as anthracene, biphenyl etc. Phenanthrene shows an unexpectedly low A_f of only 1.5, which might be due to the lowest K_e value of all the arenes (due to the low K_a value) (Tables I and II).

4. Conclusion

It is clear that hosts **1** and **2** have different cavity shapes and hence different preferences for arenes. Host **1** transports benzene the most (Table III), whereas the K_t value with **2** is maximum for toluene (Table III). Some of the results are ambiguous and need to be studied in greater detail. The hydrophobicity of **2** helps in greater transport of all arenes through an aqueous barrier than with **1** (Table III). There has to be a balance of association of guest to host at the phase I/II interface and dissociation at the phase II/III interface (Figure 1) for a good transportation rate, as a large K_a may hinder transport of certain molecules like anthracene with host **1**. The saturation behaviour of toluene and durene with host **1** and **2** are of interest and needs to be studied in greater detail.

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