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Aromatic Bridged Bis-phenol A Derived Cyclophanes. Synthesis, Molecular Structure and Binding Properties Toward Quats

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Three novel polyoxyethylene bridged bis phenol A derived cyclophanes, 2–4, with additional aromatic units in the bridge to increase the number of cation–π interactions with guest cations, were synthesized and characterized by means of X-ray crystal structure determinations. The binding properties of these receptors toward tetramethylammonium (TMA), *N*-methylpyridinium (NMP), acetylcholine (ACh) and *N*-methylquinolinium (NMQ) salts were evaluated by means of ^{1}H NMR spectroscopy and compared with those of the previously reported receptor 1.

Keywords: Cyclophanes; Molecular recognition; Cation–π interactions; Supramolecular chemistry; X-ray crystal structure

INTRODUCTION

Recognition phenomena based on weak noncovalent interactions between molecules are fundamental in the context of biotic systems. This has favoured the growth of a wealth of studies on synthetic model systems aimed to understand the role played by the different intermolecular forces involved in the organization of molecular systems at the supramolecular level. Among these, cation–π interactions, occurring between aromatic compounds and positively charged species, are known to be largely responsible for molecular recognition of quats and other cations in both biological and artificial systems [1–6]. To obtain an efficient binding of quats in solution it is necessary to have a receptor that possesses a number of strategically positioned aromatic units that cooperate to increase the number of stabilizing cation–π interactions between host and guest. Cyclophanes and their derivatives have been shown to be good candidates and for this reason a variety of these macrocycles with novel structures and properties have been described [7,8]. As a matter of fact, to enhance the binding affinity toward cations it is necessary to modify the basic cyclophane structure. The goal is to obtain the optimal guest for cavity matching and improve the preorganization to lower the entropy loss accompanying the recognition process. Recently we demonstrated that the decrease of conformational mobility of simple cyclophanes by means of polyoxyethylene bridges, such as in **1**, results in a substantial improvement of the binding properties of the receptor [9]. With this idea in mind, we envisaged that the introduction of additional aromatic units in the bridge would also lead to an increase of the number of cooperating cation–π interactions between the receptor and the guest cation and, consequently, the binding affinity of the conformationally restricted cyclophanes. For this reason we synthesised the polyether bridged cyclophanes **2**, **3** and **4**, determined their single crystal structures, investigated their binding properties towards tetramethylammonium (TMA), *N*-methylpyridinium (NMP) and acetylcholine (ACh) salts and compared them with those of the previously reported receptor **1** where no additional

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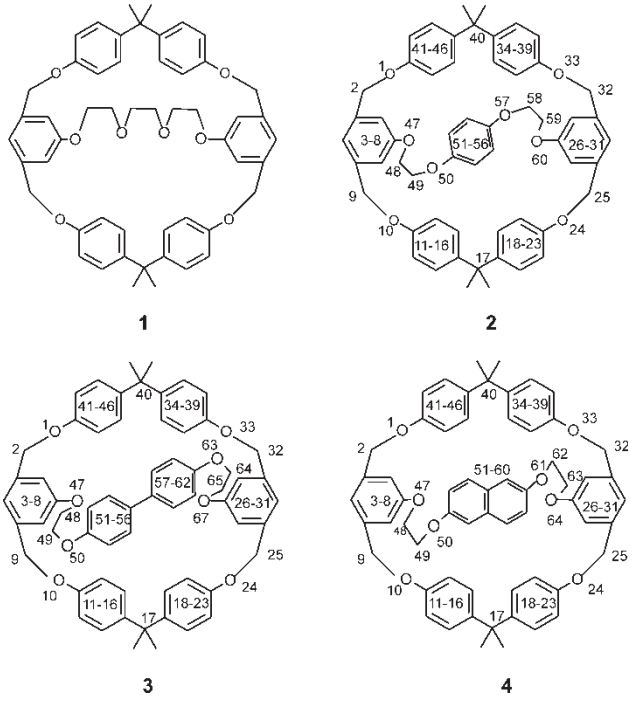
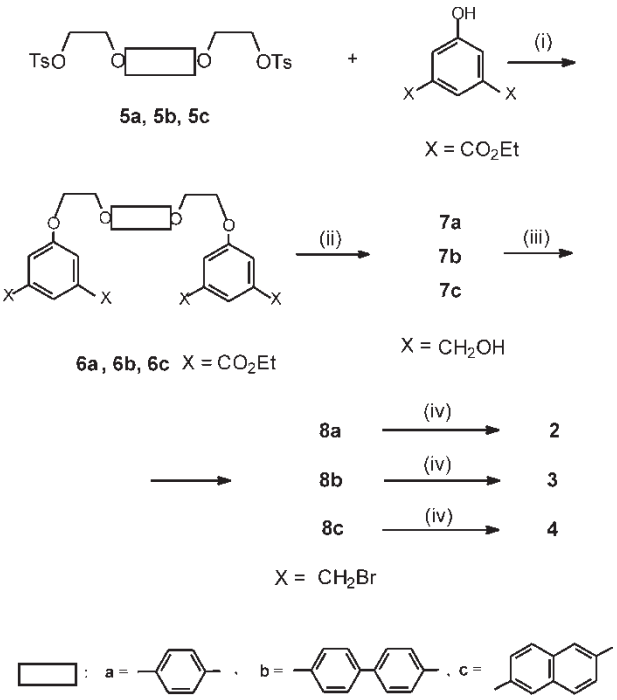
aromatic unit was present in the bridge. *N*-Methylquinolinium iodide was included in the list of tested quats at a later stage of the work.





SCHEME 1 Synthesis of cyclophanes **2**–**4**: (i) K_2CO_3, CH_3CN; (ii) $LiAlH_4$, THF; (iii) PBr_3, dioxane; (iv) 2 mol. equiv. of bisphenol A, KOH, DMSO, high dilution.

RESULTS AND DISCUSSION

Syntheses and Crystal Structures

Cyclophanes **2**–**4** were obtained by reacting 2 mol equiv. of bisphenol A with the corresponding tetra(bromomethyl) compounds **8a**–**c**, respectively, under high dilution conditions (Scheme 1). Intermediates **8a**–**c** were prepared by alkylation of the diethyl ester of 5-hydroxyisophthalic acid with the corresponding ditosylate **5a**–**c** followed by standard group transformations.

All attempts at obtaining single crystals of host–guest molecular complexes were unsuccessful. However, single crystals of the receptors suitable for X-ray analysis were obtained from benzene (**2**) or by slow diffusion of dichloromethane or chloroform into hexane (**3** and **4**, respectively).

The previously described receptors with simple polyether bridges showed clearly basket shaped structures in which the solvent was located in the inside of the cavity via weak C–H···O hydrogen bonds [9]. The rigid aromatic moieties of receptors **2**, **3** and **4** distort the conformations so that only **4** is slightly basket shaped while **2** and **3** are somewhat flattened (Fig. 1). Despite the flattening of the conformation, the cyclophanes **2**–**4** possess an open cavity suitable for the inclusion of solvent molecules. In the structure of **2** a molecule of benzene and in **3** and **4** a molecule of chloroform is included in the cavity.[†] The inclusion of the solvent molecules is facilitated by weak C–H···O hydrogen bonds in **3** and **4** (C100···O24 = 3.39(1) and C100···O10 = 3.251(4) Å) and by C–H···π interactions between the benzene and the aromatic rings of the host in **2** (the closest distances between the C–H carbon and the centroids of the aromatic rings are 3.58–3.98 Å). Additional solvent molecules outside the cavity are found in the structures of **2** and **4**. The benzene molecules in **2** fill the interstice in the crystal lattice and additional chloroform outside the cavity in **4** is hydrogen bonded to the ether oxygen of the host (C101···O50 = 3.174(4) Å).

The crystal packing of all cyclophanes is governed by π···π interactions between the aromatic units of the cyclophanes. The form of the hosts **2** and **4** could be described as a multibinding site host, i.e. there are a larger (major) and rather open binding site, which accommodates a solvent molecule, and two minor and more closed binding sites which accommodate either the additional solvent molecules or a part of the adjacent host in self complementary manner (Fig. 2). The major binding site of **2** is situated

[†]Although the crystallisation of **3** was performed by diffusion of dichloromethane into hexane, a chloroform molecule was found in the crystal structure. The chloroform remains from the first crystallisation attempt, which was unsuccessful.

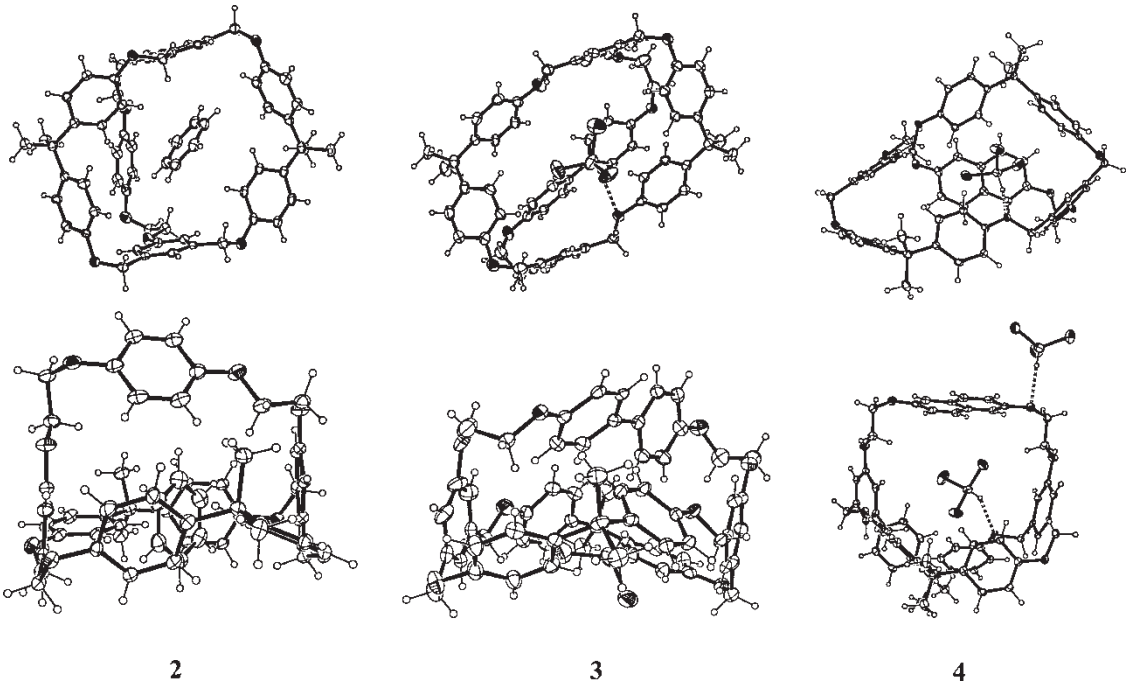


FIGURE 1 Side and top views of the molecular structures of **2**, **3** and **4** showing thermal ellipsoids at 30% probability level. Weak C–H···O hydrogen bonds between chloroform molecules and the hosts are shown with dashed lines. Benzene molecules filling the interstice are excluded for clarity.

between the two bisphenol A units while the major site of **4** is between the bisphenol A unit and the naphthalene bridge. A minor site of the host **4** accommodates the second chloroform hydrogen bonded to adjacent host molecule while the other minor site is filled by the bisphenol A unit of the adjacent host. The conformation of host **3** is so distorted that only a major site between bisphenol A is suitable for binding (Fig. 2). The distortion of the conformation is due to intramolecular C–H···π and π···π interactions between the biphenyl, bisphenol A units and bridging aromatic rings (the closest distance vary between 3.41–4.08 Å).

Binding Studies

The finding that in the crystal structure of cyclophanes **2**–**4** there is an included solvent molecule shows that these hosts possess a cavity large enough to accommodate small guest molecules. Consistently, in all case upfield shifts ($-\Delta\delta$) of the quat proton resonances [10] in $CDCl_3$ were

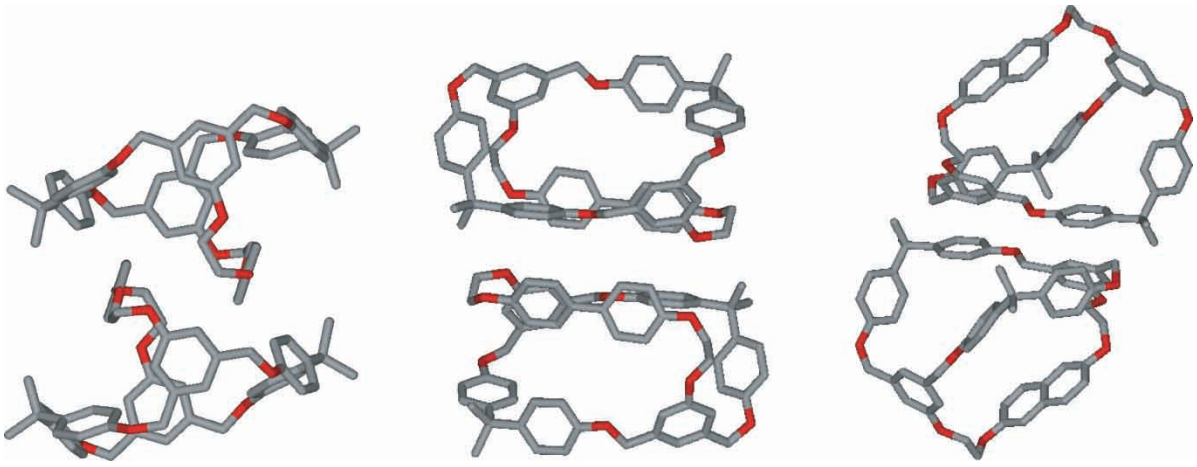


FIGURE 2 Crystal packing of **2**, **3** and **4**. Hydrogen atoms and solvents are excluded for clarity.

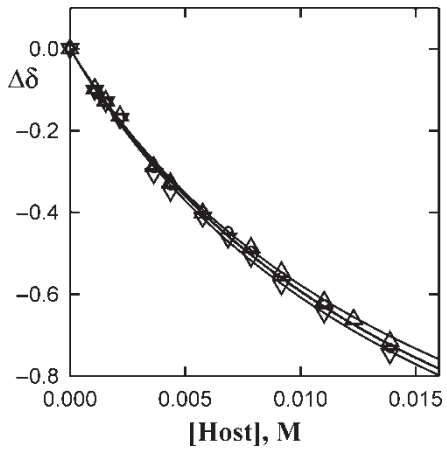


FIGURE 3 ^{1}H NMR titration of NMP iodide with host **4** in $CDCl_3$. Points are experimental and curves are calculated. (▽) NCH_3, (○) αCH, (△) γCH.

observed upon addition of increasing amounts of host, up to maximum concentrations in the range of 14–25 mM. No separate signals were observed for free and bound guest, showing that complexation equilibria were fast on the ^{1}H NMR time scale. In addition to the NCH_3 protons, which could be followed in all cases, the resonances of other protons were monitored whenever possible. An example of multiple titration experiment is shown in Fig. 3.

Titration data were fitted as before [11] to the binding isotherm of Eq. (1), from which numerical values of the equilibrium constant (K) and of the limiting complexation induced upfield shift ($-\Delta\delta_\infty$) were obtained as best fit parameters.

$$\Delta\delta = \Delta\delta_\infty K[\text{Host}]/\{1 + K[\text{Host}]\} \qquad (1)$$

The results of the titration experiments in $CDCl_3$ and $(CDCl_2)_2$ are summarized in Tables I and II, respectively. Very low binding constants in the range of 10–15 M^{-1}, were found in a number of cases. The pertinent titration plots exhibited little pronounced upward curvatures, because the quantity $1 + K$[Host] appearing in the denominator of the right-hand term of Eq. (1) underwent only modest variations in the course of each titration run. Thus, a word of caution is needed for the numerical values of the $(-\Delta\delta_\infty)$ quantities, which result from extrapolation to infinite host concentration of data obtained in concentration domains far from saturation. Nevertheless, without attaching too much meaning to exact figures, the results point to relatively large complexation induced upfield shifts of the guest protons, which are consistent with extensive inclusion of the cation guests into the host cavity. The chemical shift variations experienced upon complexation by the NCH_3 protons of the NMP cation are quite similar to those of the α, β and γ protons, clearly suggesting loose, highly disordered structures for these complexes, with no preferential mode of binding. The situation is different for the ACh complex, whose Me_3N^+ head is most likely located inside the cavity and the CH_3CO tail is directed toward the exterior, in line with previous findings [12–14].

That the magnitude of the complexation induced chemical shifts and complex stability are not simply related to each other is clearly shown by the data listed in Tables I and II, in which one finds that rather large $-\Delta\delta_\infty$ are accompanied by complex stabilities which are low to moderate in many instances. This is clearly the case with the complexes of TMA, NMP, and ACh cations in which, presumably because of conformational restrictions imposed by the rigid geometry of the aromatic units in the bridge, the hosts cannot wrap around the included guests in such a way as to establish a large number of simultaneous cation–π interactions [15,16]. In other words, in the host–guest complexes the guest protons are simultaneously exposed to the shielding effects of the ring currents of a number of aromatic units, yet not close enough to establish stabilizing interactions with all of them.

TABLE I Stability constants (K, M^{-1})* and limiting upfield shifts ($-\Delta\delta_\infty$, ppm) for the complexes of hosts **2**–**4** with quats in $CDCl_3$ at 30°C

	TMA^+ Picrate		NMP Iodide		NMP Picrate		ACh Iodide		NMQ Iodide	
Host	K	$-\Delta\delta_\infty$	K	$-\Delta\delta_\infty$	K	$-\Delta\delta_\infty$	K	$-\Delta\delta_\infty$	K	$-\Delta\delta_\infty$
2	11	1.7	27	1.9 (NCH_3)	25	1.4 (NCH_3)	10	0.7 (NCH_3)	30	1.0 (NCH_3)
	(3)		(3)	2.0 (α-CH)	(4)	1.5 (α-CH)	(3)	0.2 (CH_3CO)	(3)	0.8 (γ-CH)
				1.8 (β-CH)						
				2.1 (γ-CH)						
3	10	0.8	15	1.3 (NCH_3)	15	1.4 (NCH_3)	11	0.7 (NCH_3)	210	0.7 (NCH_3)
	(2)		(2)	1.4 (α-CH)	(2)	1.6 (α-CH)	(2)	0.4 (CH_3CO)	(12)	1.0 (γ-CH)
				1.4 (β-CH)		1.5 (β-CH)				
				1.7 (γ-CH)		1.2 (γ-CH)				
4	28	0.5	57	1.6 (NCH_3)	42	1.8 (NCH_3)	9	1.4 (NCH_3)	170	1.1 (NCH_3)
	(5)		(3)	1.7 (α-CH)	(4)	1.7 (α-CH)	(1)	0.6 (CH_3CO)	(18)	1.5 (α-CH)
				1.7 (γ-CH)						1.4 (γ-CH)

*Errors in parentheses are calculated as $\pm 2\sigma$ (95% confidence limit). †**1**–TMA Picrate $K = 41 \pm 1\,M^{-1}$, **1**–NMP Iodide $K = 45 \pm 4\,M^{-1}$. **1**–ACh Iodide $K = 45 \pm 4\,M^{-1}$, (from Ref. [9]).

TABLE II Stability constants (K, M^{-1})* and limiting upfield shifts ($-\Delta\delta_\infty$, ppm) for the complexes of hosts **2**–**4** with NMP and NMQ iodides in $(CDCl_2)_2$ at 30°C

	NMP Iodide		NMQ Iodide	
Host	K	$-\Delta\delta_\infty$	K	$-\Delta\delta_\infty$
2	25	1.3 (NCH_3)	27	1.0 (NCH_3)
	(2)	1.2 (β-CH)	(5)	
		1.4 (γ-CH)		
3	17	0.9 (NCH_3)	74	0.7 (NCH_3)
	(2)	0.7 (α-CH)	(12)	1.0 (γ-CH)
		0.8 (β-CH)		
		0.9 (γ-CH)		
4	35	1.3 (NCH_3)	90	1.1 (NCH_3)
	(4)	1.3 (α-CH)	(15)	
		1.1 (β-CH)		
		1.2 (γ-CH)		

*Errors in parentheses are calculated as $\pm 2\sigma$ (95% confidence limit).

The above line of reasoning can be followed to explain why no advantage in terms of complex stability derives from the introduction of aromatic units in the bridge, as shown by comparison with binding data available for the complexation of TMA, NMP, and ACh cations with the polyether bridged host **1** (see footnote † to Table I). Based on the broad idea that hosts **2**–**4** possess cavities too large for the above guests, we reasoned that the large molecular surface of NMQ would exhibit a better complementarity to the elongated cavity revealed by the molecular structure of host **3** (Fig. 2). Indeed, a definitely stronger complex is formed by NMQ iodide and receptor **3**, both in $CDCl_3$ and $(CDCl_2)_2$. A strong complex is also formed with receptor **4**, but not with **2**. Comparison with the corresponding complexes of NMP iodide indicates that the benzenoid portion of NMQ is also included into the cavity of hosts **3** and **4**, and contribute to the binding through π–π interactions, but no direct evidence is available from ^{1}H NMR spectra.

Enhancement of host–guest interactions in solvents that are too bulky to solvate the host binding cavity have been known for a long time [17–20]. Recently we reported that cation–π interactions between quats and calixarene receptors are significantly stronger in 1,1,2,2-tetrachloroethane than in chloroform, on account of a lower desolvation penalty suffered by the host upon complexation in the bulkier 1,1,2,2-tetrachloroethane, that is so large that its fit into the host cavity is prevented. The data listed in Table II are in marked contrast to the above findings, in that binding constants are either unaffected or even slightly decreased when 1,1,2,2-tetrachloroethane replaces chloroform as a solvent. This would imply that the cavities of cyclophanes **2**–**4** are large enough to accommodate 1,1,2,2-tetrachloroethane, as suggested by CPK models.

A last comment is devoted to the data listed in the second and third columns of Table I, showing that the binding affinity of NMP is largely independent of anion nature. As previously reported by us [21] and others [22–28], binding of quats to neutral receptors in media of low permittivity is strongly influenced by the nature of the counteranion accompanying the guest cation, due to the formation of ternary host–cation–anion complexes. In the absence of such specific interactions as hydrogen bonding between the neutral receptor and counteranion [23,24,28], the binding constants are larger with picrate than with iodide counterion. For example, the binding constant in $CDCl_3$ of a calix[5]arene receptor with NMP iodide is $54\,M^{-1}$, but rises to $160\,M^{-1}$ with the picrate salt [21]. Although based on a very limited sampling, the lack of sensitivity of our systems to anion nature is consistent with the view that the host structures are quite open and, consequently, require little or no separation of the anion from the complexed cation.

EXPERIMENTAL

TMA picrate, NMP iodide, NMP picrate and NMQ iodide were available from a previous investigation [21]. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 300 spectrometer and TMS was used as an internal standard. Electrospray mass spectra were obtained on a Fisons Instrument VG-Platform benchtop mass spectrometer. 1,4-Bis(2-hydroxyethyloxy)benzene was prepared according to literature from hydroquinone and ethylene carbonate [29]. 4,4′-Bis(2-hydroxyethyl)biphenyl and 2,6-bis(2-hydroxyethyloxy)naphthalene were prepared starting from the corresponding diols and 2-bromoethanol as reported [30]. These compounds were converted into the corresponding ditosylates **5a** [31], **5b** and **5c** [32] following a standard protocol from literature. Compounds **6a**, **6b** and **6c** were obtained, as previously reported by us [9], reacting diethyl 5-hydroxyisophthalate with the corresponding ditosylate **5** in CH_3CN in the presence of K_2CO_3.

Bis(3,5-diethyloxycarbonylphenyl)ether of 1,4-Bis(4-hydroxyethoxy)benzene 6a

Yield 96%, mp 149–152°C. ^{1}H NMR ($CDCl_3$) δ 1.40 (t, $J = 7.0$ Hz, 12H), 4.30 (m, 4H), 4.35–4.42 (m + q, $J = 7.0$ Hz, 12H), 6.89 (s, 4H), 7.80 (m, 4H), 8.29 (m, 2H).

Bis(3,5-diethyloxycarbonylphenyl)ether of 4,4′-Bis(4-hydroxyethoxy)biphenyl 6b

Yield 99%, mp 101–103°C. ^{1}H NMR ($CDCl_3$) δ 1.40 (t, $J = 7.16$ Hz, 12H), 4.31–4.41 (q + m, $J = 7.16$ Hz, 16H), 6.98–7.02 (m, 4H), 7.46–7.50 (m, 4H), 7.81 (s, 4H), 8.30 (s, 2H).

Bis(3,5-diethyloxycarbonylphenyl)ether of 2,6-Bis(4-hydroxyethoxy)naphthalene 6c

Yield 99%, mp 182–183°C. ^{1}H NMR ($CDCl_3$), δ 1.39 (t, $J = 7.16$ Hz, 12H), 4.35 (q, $J = 7.16$ Hz, 8H), 4.44 (m, 8H), 7.16–7.21 (m, 2H), 7.65–7.69 (m, 6H), 7.84 (bs, 4H), 8.31 (bs, 2H).

Compounds **7a**, **7b**, **7c**. These products were obtained following a procedure already described for similar compounds [33].

Bis(3,5-dihydroxymethylphenyl)ether of 1,4-Bis(4-hydroxyethoxy)benzene 7a

This compound was obtained in 66% yield, mp 157–159°C. ^{1}H NMR ($(CD_3)_2SO$) δ 4.34 (bs, 8H), 4.54 (d, $J = 5.58$ Hz, 8H), 5.26 (t, $J = 5.58$ Hz, 4H), 6.88 (s, 4H), 6.95 (s, 2H), 7.02 (s, 4H). ^{13}C NMR ($(CD_3)_2SO$) δ 62.8, 66.2, 66.8, 110.6, 115.5, 116.7, 144.0, 149.7, 152.5, 158.3.

Bis(3,5-dihydroxymethylphenyl)ether of 4,4′-Bis(4-hydroxyethoxy)biphenyl 7b

This compound was obtained in 95% yield, mp 180.5–182.5°C. ^{1}H NMR ($(CD_3)_2SO$) δ 4.41–4.43 (m, 8H), 4.55 (d, $J = 5.70$ Hz, 8H), 5.28 (t, $J = 5.70$ Hz, 4H), 6.90 (s, 4H), 6.96 (bs, 2H), 7.13–7.16 (m, 4H), 7.64–7.67(m, 4H). ^{13}C NMR ($(CD_3)_2SO$) δ 62.8, 62.9, 62.0, 66.4, 66.5, 110.6, 110.7, 110.8, 114.9, 115.0, 116.8, 116.9, 127.3, 132.5, 144.0, 157.5, 158.3.

Bis(3,5-dihydroxymethylphenyl)ether of 2,6-Bis(4-hydroxyethoxy)naphthalene 7c

This compound was obtained in 91% yield, mp 190–192°C. ^{1}H NMR ($(CD_3)_2SO$) δ 4.45–4.48 (m, 8H), 4.55 (d, $J = 5.70$, 8H), 5.28 (t, $J = 5.70$ Hz, 4H), 6.91 (s,4H), 6.97 (s, 2H), 7.26–7.30 (m, 2H), 7.44–7.45 (m, 2H), 7.83–7.86 (m, 2H). ^{13}C NMR ($(CD_3)_2SO$) δ 62.9, 63.0, 66.2, 66.4, 107.1, 107.1, 110.6, 110.8, 116.8, 116.9, 118.9, 119.0, 128.1, 128.3, 129.5, 144.0, 154.8, 158.3.

Compounds **8a**, **8b** and **8c** were prepared following a literature procedure [9].

Bis(3,5-dibromomethylphenyl)ether of 1,4-Bis(4-hydroxyethoxy)benzene 8a

Yield 64%, mp 156–159°C. ^{1}H NMR ($CDCl_3$) δ 4.28 (m, 8H), 4.42 (s, 8H), 6.89 (s, 4H), 6.91 (m, 4H), 7.01 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 32.8, 66.8, 67.1, 115.4, 115.8, 122.2, 139.7, 153.0, 159.1.

Bis (3,5-dibromomethylphenyl)ether of 4,4′-Bis(4-hydroxyethoxy)biphenyl 8b

Yield 80%, mp 161–163°C. ^{1}H NMR ($CDCl_3$) δ 4.35 (bs, 8H), 4.43 (s, 8H), 6.93 (s, 4H), 6.98–7.01 (m, 6H), 7.45–7.50 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 32.8, 66.5, 66.7, 67.1, 115.0, 115.4, 122.3, 127.8, 133.8, 139.7, 157.7, 159.1.

Bis(3,5-dibromomethylphenyl)ether of 2,6-Bis(4-hydroxyethoxy)naphthalene 8c

Yield 85%, mp 182–184°C. ^{1}H NMR ($(CD_3)_2SO$)) δ 4.49 (m, 8H), 4.77 (bs, 8H), 7.16 (bs, 4H), 7.23 (bs, 2H), 7.27–7.30 (m, 2H), 7.45 (bs, 2H), 7.83–7.86 (m, 2H). ^{13}C NMR ($(CD_3)_2SO$) δ 33.9, 66.3, 66.5, 107.12, 115.4, 119.0, 122.6, 128.3, 129.5, 139.9, 154.7, 158.4.

Macrocyclization Procedure

The cyclization reaction was performed according to a previously described high dilution procedure [9] in DMSO in the presence of K_2CO_3 at 62°C.

Cyclophane 2

The product was isolated by column chromatography on silica gel (230–400 mesh; eluent: $CHCl_3$–Et_2O, 98/2) in 6% yield, mp 90–93°C. ^{1}H NMR ($CDCl_3$) δ 1.59 (s, 12H), 4.25 (bs, 8H), 5.02 (s, 8H), 6.68–6.71 (m, 8H), 6.77 (s, 4H), 6.84–6.85 (m, 6H), 6.98–7.00 (m, 8H). ^{13}C NMR ($CDCl_3$) δ 30.9, 41.5, 65.8, 67.0, 112.3, 114.6, 116.4, 117.2, 127.6, 139.7, 143.4, 152.3, 156.3, 159.0. ES–MS, m/z 873 $[M + NH_4]^+$. Anal. Calcd for $C_{56}H_{54}O_8 \cdot H_2O$; C, 77.04; H 6.23. Found: C, 77.15; H 6.29.

Cyclophane 3

The product was isolated by column chromatography on silica gel (230–400 mesh, eluent $CHCl_3$) in 3% yield, mp 212–214°C. ^{1}H NMR ($CDCl_3$) δ 1.54 (s, 12H), 4.30 (bs, 8H), 4.94 (s, 8H), 6.65–6.68 (m, 8H), 6.72 (s,4H), 6.75–6.76 (m, 4H), 6.83 (bs, 2H), 6.94–6.97 (m, 8H), 7.24–7.28 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 30.7, 30.9, 32.8, 41.6, 66.7, 69.5, 112.8, 114.4, 116.3, 117.5, 127.6, 133.8, 139.5, 143.4, 156.2, 157.0, 158.6. ES–MS, m/z 949 $[M + NH_4]^+$, 970 $[M + K]^+$. Anal. Calcd for $C_{62}H_{58}O_8 \cdot 2.5\ H_2O$; C 76.28; H, 6.50. Found: C, 76.39; H 5.95.

Cyclophane 4

The product was isolated by column chromatography on silica gel (230–400 mesh, eluent $CHCl_3$) in 3% yield, mp 113–115°C. ^{1}H NMR ($CDCl_3$) δ 1.59 (bs,12H), 4.30–4.32 (m, 4H), 4.44–4.46 (m, 4H), 4.96 (bs, 8H), 6.67–6.71 (m, 8H), 6.82–6.83 (m, 6H), 6.97–7.04 (m, 12H), 7.42–7.47 (m,2H). ^{13}C NMR ($CDCl_3$) δ 30.8, 41.6, 66.0, 66.5, 69.6, 108.8, 112.5, 114.5, 117.4, 119.6, 127.6, 128.4, 129.8, 139.5, 143.5, 154.2, 156.2, 158.9. ES–MS, m/z 928 $[M + Na]^+$, 944 $[M + K]^+$. Anal. Calcd for $C_{60}H_{56}O_8 \cdot H_2O$: C 78.07; H 6.33. Found: C 78.13; H 6.21.

TABLE III Experimental data for the X-ray diffraction studies on **2**, **3**, and **4** at 173.0 K

	2	**3**	**4**
Formula	$C_{56}H_{54}O_8 \cdot 3.5\ C_6H_6$	$C_{62}H_{58}O_8 \cdot CHCl_3$	$C_{60}H_{56}O_8 \cdot 2\ CHCl_3$
Formula weight	1128.37	1050.45	1143.78
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	$P\bar{1}$ (No. 2)	$P2_1/n$ (No. 14)	$P2_1/n$ (No. 14)
a/Å	12.517(9)	17.9414(9)	11.6805(1)
b/Å	16.653(5)	9.3110(5)	32.5670(4)
C/Å	16.974(2)	31.153(2)	15.8853(2)
α/°	62.32(2)	90	90
β/°	82.66(3)	90.322(2)	111.048(1)
γ/°	81.12(4)	90	90
V/Å^3	3089(2)	5204.1(5)	5639.6(1)
Z	2	4	4
μ/mm^{-1*}	0.609	0.235	0.360
No. of measured refl.	10877	13584	16581
No. of independent refl.	10301	7721	9574
R_{int}	0.032	0.120	0.047
R, %†	8.15	10.35	6.31
R_w, %†	19.25	22.37	13.82
GOF	0.973	1.039	1.054

*For CuK_α for **2** and MoK_α for **3** and **4**.
†For $I > 2\sigma I$.

Single-crystal X-ray Diffraction

Crystals of compound **2** were obtained by slow evaporation of benzene and of **3** and **4** by slow diffusion of dichloromethane or chloroform solutions, respectively, into hexane. The X-ray crystallographic data for compounds **3** and **4** were recorded on a Nonius Kappa CCD diffractometer and for **2** on a Nonius Mach3 diffractometer. Graphite monochromatised CuK_α radiation [$\lambda(CuK_\alpha) = 1.54184$ Å] was used for **2** and MoK_α radiation [$\lambda(MoK_\alpha) = 0.71073$ Å] for **3** and **4**. A temperature of 173.0 ± 0.1 K was used in all cases. The CCD data were processed with Denzo-SMN v0.93.0 [34] and all structures were solved by direct methods (SHELXS-97 [35]) and refined on F^2 by full-matrix least-squares techniques (SHELXL-97 [36]). The hydrogen atoms for all structures were calculated to their idealised positions with isotropic temperature factors (1.2 or 1.5 times the carbon temperature factor) and refined as riding atoms. Two chlorines of the chloroform molecule and oxygen O47 of 3 are disordered over two positions with occupancies of 0.779:0.221 and 0.721:0.279, respectively. Other experimental X-ray data are presented in Table III.

X-ray Data Deposition

X-ray data of **2**, **3** and **4** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 203384–203386.

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