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# Bis(fluorenono)phanes: a new class of perspective macrocyclic receptors

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**Abstract**—Two representatives of a novel class of cyclophanes containing two fragments of 2,7-dioxy-9*H*-fluoren-9-one bridged by triethylene glycol and *p*-xylyl linking units have been prepared. X-Ray analysis shows that the former has an *anti*-conformation and the cavity is self-filling with fluorenone moieties.

Cyclophanes and crownophanes are interesting classes of macrocyclic hosts due to their ability to bind inorganic and organic cations and neutral substrates strongly, and selectively. They can also be used as platforms for the design of supramolecular systems (e.g. rotaxanes and catenanes).[1,2] In the formation of the corresponding complexes and supramolecular systems, π-cation and π–π stacking interactions play an important role.[3,4] To enhance such interactions, the introduction of extended aromatic moieties with well-developed π-electron systems in newly synthesized macrocyclic hosts seems to be reasonable.

Many aromatic components have been incorporated in the cyclophane skeleton. We were intrigued by the previously unexplored, and to the best of our knowledge, 2,7-dioxy-9*H*-fluoren-9-one **1** as a unit for the construction of a new family of large cyclophanes. Bisphenol **1** is a highly polarized π electron-rich extended aromatic system where the carbonyl oxygen can act as a sensor that recognizes an electron-deficient guest and directs it toward the macrocyclic host cavity. Additionally, being a powerful H-acceptor, the carbonyl oxygen is capable of strong hydrogen bonding of the substrate often dominating the processes of molecular recognition and self-assembly that are essential in the formation of supramolecular systems.[5]

We report here for the first time the synthesis and characterization of cyclophanes **4** and **6** incorporating two 2,7-bridged fluorenone fragments. These two compounds show considerable differences in their structures which should influence their complexation behavior. The cavity dimensions of crownophane **4** can vary over a relatively wide range in accord with the steric requirements of the substrate due to the mobility of flexible oligo(ethyleneoxy) bridges, while the cavity size of the cyclophane **6**, which has rigid lateral walls, can vary only slightly due to aromatic ring tilting processes.

The synthetic pathways leading to cyclophanes **4** and **6** are shown in Scheme 1. Reaction of bisphenol **1** with triethylene glycol chlorohydrin in DMF in the presence of anhydrous potassium carbonate at 80–85°C for 30 h gave the diol **2** in 77% yield.[6] Conversion of **2** into ditosylate **3** was achieved in an 84% yield using *p*-toluenesulfonyl chloride in a mixture of chloroform and dioxane in the presence of triethylamine at 0–20°C.[7] Further reaction of **3** with bisphenol **1** in DMF in the presence of anhydrous potassium carbonate as the base, afforded the crownophane **4** in 27% yield.[8] Under similar conditions, a fourfold coupling reaction of **1** with dibromide **5** gave after the usual work-up followed

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*Keywords*: bis(fluorenono)phane; cyclophane; crownophane; fluorenone.

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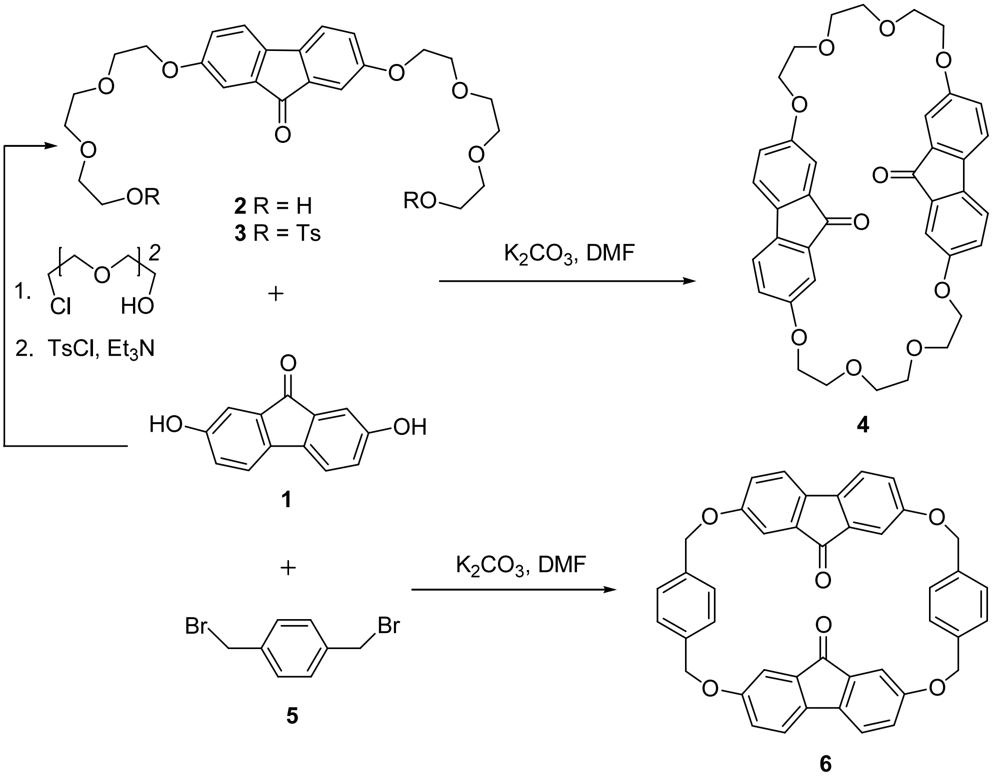

**Scheme 1.**

by chromatographic purification over silica gel, the cyclophane **6** in 8% yield.[9] We did not gain any appreciable increase in yield of cyclophanes **4** and **6** by using cesium carbonate as the base instead of potassium carbonate, despite the fact that the cesium cation promotes formation of many macrocyclic systems (cesium effect).[10]

The solid-state structure for **4** was determined by X-ray diffraction.[11] Computer generated drawings of side and best plane views are shown in Figure 1. Crownophane **4** possesses an elongated cavity of dimensions ca. 4×16 Å. The macrocycle is self-filling, with two fluorenone units aligned parallel to each other about the crystallographic center of symmetry and is extended to include

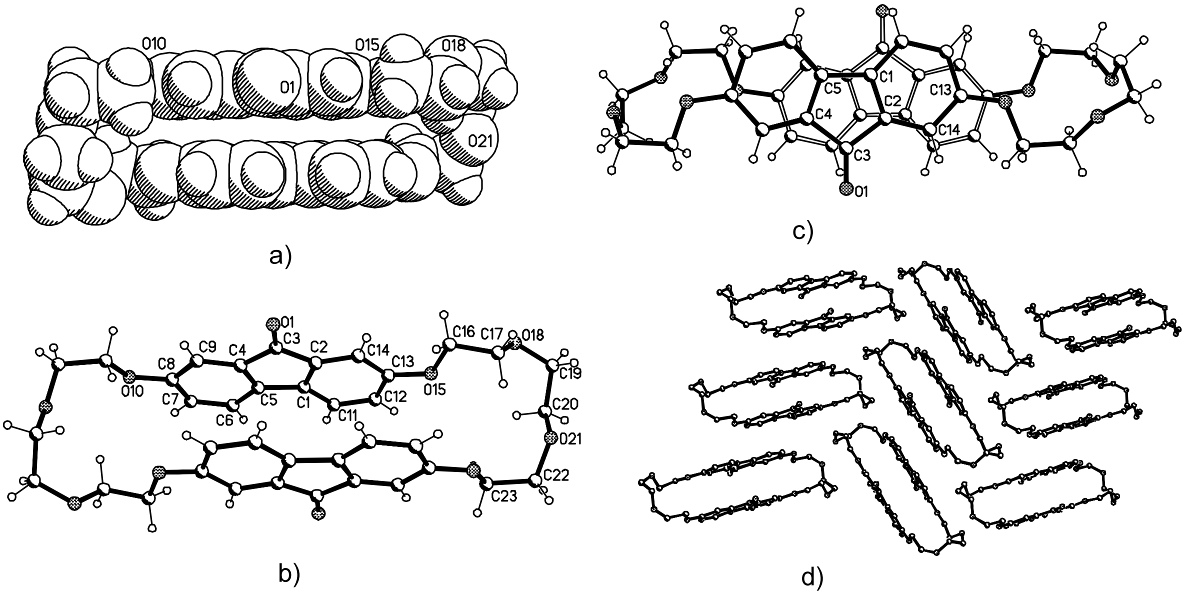

**Figure 1.** Structure of **4** in the crystal: (a) space-filling representation, (b) ball-and-stick representation with the numbering scheme, (c) the mode of overlapping of aromatic units in **4** in projection on the plane of fluorenone units, (d) the crystal packing of molecules of **4**, hydrogen atoms are omitted.

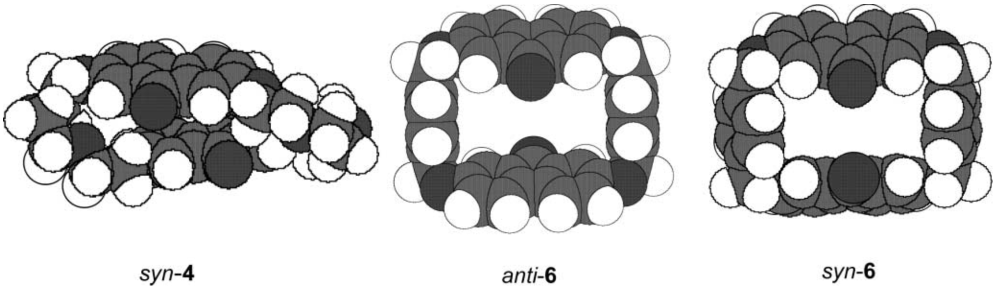

**Figure 2.** Space-filling representation of the most stable calculated structures of fluorenonophanes **4** and **6**.

in the almost planar skeleton, the oxygen atoms, O1, O10 and O15 attached to the aromatic moiety. The fluorenone unit adopts the shape of a very upward sloping arch with the dihedral angles between each of the benzene and five-membered rings equal to 2.9(2) and 2.5(2)°, respectively.

The fluorenone units partially overlap (Fig. 1c) with the interplanar distance being equal to 3.446 Å. This geometry is commensurate with conventional parallel π–π stacking.[12] A similar cavity shape has been found previously in macrocycles that incorporate hydroquinol,[13] biphenyl[14] or anthracenic[15] units bridged by oxyethylene chains of the same length. The molecules pack to form chevron-like sheets (Fig. 1d) which have adjacent rows oriented to optimize T-type edge-to-face interactions[12] between the aromatic components with a dihedral angle of 103° between the planes of the inclined fluorenone moieties.

Unfortunately, all attempts to grow good quality single crystals of the cyclophane **6** for X-ray structure analysis failed, but considering the fact that rigid aromatic moieties fix the conformation, it is likely that the structure of **6** can be predicted on the basis of molecular mechanics calculations with a satisfactory level of accuracy.

A conformational search of **4** and **6** has been performed using a Monte Carlo procedure and MMFF force field implemented in the SPARTAN'02 program package.[16] Estimation indicates that the most stable conformers are the *anti*- and *syn*-conformers of **4** and **6**, differing in the relative orientation of the carbonyl groups (Fig. 2). Insignificant energy differences between these conformers, 0.10 and 0.37 kcal/mol for **4** and **6**, respectively, infers that they are almost equally populated, at least in vacuo. In solutions, their relative population should strongly depend on the properties of the solvent, since *anti*-conformers are practically non-polar, unlike polar *syn*-conformers.

The calculated structure of *anti*-**4** fits reasonably well with X-ray data. RMS (root-mean-square) difference between the two sets of coordinates of all non-hydrogen atoms is 1.55 Å at overlay of the crystal and calculated structures of *anti*-**4**. The calculated structure of *syn*-**4**, like *anti*-**4** in the solid state, is self-filling with fluorenone moieties. The two fluorenone units are aligned parallel and twisted with respect to each other forming an X-like shaped-structure. One of the benzene rings of each fluorenone unit is close enough for partial overlap with the five-membered ring of its counterpart (interplanar separation of 3.76 Å). Generally, the self-filling of the macrocyclic cavity is not a serious hindrance for complexation. However, the energetically unfavorable conformational rearrangement of the molecule would need to precede the formation of complexes.

Both, *syn*-**6** and *anti*-**6** provide structures with open central cavities being well organized for π interactions with the potential guest molecules (Fig. 2). In *anti*-**6**, both the fluorenone and lateral benzene units are arranged parallel to each other. The molecule adopts a chair-like conformation with staggered fluorenone moieties. The cyclophane cavity has a rectangular shape with a fluorenone-fluorenone distance of 7.5 Å and benzene–benzene distance of 10.8 Å. In *syn*-**6**, the fluorenone and benzene units are tilted, the dihedral angles between their planes are 42.4° and 30.9°, respectively. The intramolecular cavity has a cone-like shape with average dimensions of approximately 10.7×7.1 Å.

In conclusion, we have presented the first synthesis and structure of new types of macrocyclic hosts. The carbonyl groups of the fluorenonophanes can be converted into a variety of functional groups that would allow for fine-tuning of the binding behavior of such cyclophanes. Investigations of their properties and complexation are in progress in respect to crystal engineering and supramolecular chemistry.

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6. Bisphenol **1** (16.98 g, 80 mmol) was added to a suspension of freshly ground $K_2CO_3$ (66.34 g, 480 mmol) and NaI (24.00 g, 160 mmol) in dry DMF (400 mL) under argon. After stirring for 1 h at 80°C, triethylene glycol chlorohydrin (40.47 g, 240 mmol) was added and heating was maintained for 35 h. The reaction mixture was filtered and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in chloroform and the solution was washed with 5% aqueous NaOH and twice with water, dried over $MgSO_4$, and evaporated in vacuo. The residue was purified by recrystallization from isopropyl alcohol to yield **2** as orange crystals (29.40 g, 77%); mp 91–92°C. $^1$H NMR (300 MHz; $CDCl_3$; $\delta$, ppm; $J$, Hz) 2.18 (br s, 2H), 3.63 (t, 4H, $J=4.2$), 3.68–3.82 (m, 12H), 3.87 (t, 4H, $J=4.5$), 4.17 (t, 4H, $J=4.5$), 6.97 (dd, 2H, $J=2.18$, 8.09), 7.17 (d, 2H, $J=2.18$), 7.28 (d, 2H, $J=8.09$). Anal. calcd for $C_{25}H_{32}O_9$: C, 63.01; H, 6.77. Found: C, 62.82; H, 6.65%.
7. A solution of *p*-toluenesulfonyl chloride (14.30 g, 75 mmol) in dry dioxane (30 mL) was added dropwise to a solution of **2** (14.30 g, 30 mmol) and triethylamine (9.11 g, 90 mmol) in chloroform (120 mL) over 2 h at 0–5°C. The solution was allowed to warm to room temperature, and stirring was continued for 30 h. The mixture was diluted with an equal volume of chloroform and washed successively with 5% aqueous HCl, 10% aqueous ammonia, water, brine, and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by recrystallization from isopropyl alcohol to give bistosylate **3** as orange crystals (19.80 g, 84%); mp 68–70°C. $^1$H NMR (300 MHz, $CDCl_3$; $\delta$, ppm; $J$, Hz) 2.43 (s, 6H), 3.57–3.75 (m, 12H), 3.79–3.87 (m, 4H), 4.08–4.21 (m, 8H), 6.97 (dd, 2H, $J=2.49$, 8.10), 7.15 (d, 2H, $J=2.49$), 7.29 (d, 2H, $J=8.10$), 7.33 (d, 4H, $J=8.25$), 7.80 (d, 4H, $J=8.35$). Anal. calcd for $C_{39}H_{44}O_{13}S_2$: C, 59.68; H, 5.65. Found: C, 59.56; H, 5.47%.
8. A solution of **1** (2.12 g, 10 mmol) and bistosylate **3** (7.85 g, 10 mmol) in dry DMF (400 mL) was added over 12 h to a stirred suspension of $K_2CO_3$ (8.29 g, 60 mmol) in DMF (550 mL) under argon at 80°C and heating was maintained for a further 20 h. The reaction mixture was filtered and the filtrate was evaporated to dryness in vacuo. The residue was washed with methanol, and filtered. The air-dried solid was extracted with toluene using a Soxhlet extractor for 50 h. The solvent was removed and the residue purified by chromatography ($SiO_2$, $CHCl_3$) to give **4** as orange crystals (1.78 g, 27%); mp 197–199°C. $^1$H NMR (300 MHz; DMSO-$d_6$; $\delta$, ppm; $J$, Hz) 3.65 (s, 8H), 3.75 (t, 8H, $J=4.20$), 4.04 (t, 8H, $J=4.20$), 6.80 (br s, 4H), 6.82 (br d, 4H, $J=8.10$), 7.11 (d, 4H, $J=8.10$). $^{13}$C NMR (75.5 MHz, $CF_3COOD$), $\delta$: 67.6, 70.5, 71.2, 111.1, 121.8, 123.0, 135.7, 139.6; EI-MS, 70 eV, $m/z$ (%): 652 (100, $M^+$), 580 (16), 326 (14), 212 (18). UV–vis, dioxane, $\lambda_{max}$ (log $\varepsilon$): 264 (5.09), 302 (4.06), 314 (4.04), 470 (2.66). Anal. calcd for $C_{38}H_{36}O_{10}$: C, 69.93; H, 5.56. Found: C, 69.77; H, 5.69%.
9. A solution of **1** (3.18 g, 15 mmol) and **5** (3.96 g, 15 mmol) in dry DMF (150 mL) was added over 10 h to a stirred suspension of $K_2CO_3$ (6.36 g, 46 mmol) in DMF (200 mL) under argon at 80°C and heating was maintained for a further 20 h. The reaction mixture was filtered and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in $CHCl_3$ (200 mL) and washed successively with 5% aqueous NaOH, twice with water, and dried over $MgSO_4$. The solvent was removed and the residue purified by chromatography ($SiO_2$, $CHCl_3$) to give **6** as orange crystals (0.76 g, 8%); mp >300°C. $^1$H NMR (300 MHz, $CDCl_3$, $\delta$, ppm, $J$, Hz) 5.21 (s, 8H), 6.84 (d, 4H, $J=2.18$), 6.96 (dd, 4H, $J=8.09$, 2.18), 7.18 (d, 4H, $J=8.09$), 7.21 (s, 8H); $^{13}$C NMR (75.5 MHz, $CF_3COOD$), $\delta$: 69.3, 71.0, 121.5, 123.3, 124.6, 129.6, 135.2, 137.5, 138.9, 157.5. EI-MS, 70 eV, $m/z$ (%): 628 (36, $M^+$), 314 (17), 212 (19), 104 (100). UV–vis, dioxane, $\lambda_{max}$ (log $\varepsilon$): 262 (5.11), 270 (5.07), 300 (3.81), 313 (3.81), 325 (3.44), 456 (2.73). Anal. calcd for $C_{42}H_{28}O_6$: C, 80.24; H, 4.49. Found: C, 80.44; H, 4.76%.
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11. *X-Ray crystal structure analysis*. Diffraction data for the single crystal (0.36×0.35×0.12 mm) were collected with a Nonius Kappa CCD diffractometer with graphite monochromatized Mo-K$\alpha$-radiation ($\lambda=0.71073$ Å). The structure was solved using the direct-methods program contained in the SHELX-97 program package.[17] Final refinement was performed using SHELXL-97.[18] Crystal data for **4**: formula $C_{38}H_{36}O_{10}$, monoclinic, space group $P2_1/c$, $a=8.372(2)$, $b=23.230(4)$, $c=8.660(2)$ Å, $\beta=113.53(2)°$, $V=1544.2(6)$ Å$^3$, $Z=2$, $D_{calcd}=1.404$ g cm$^{-3}$, $\mu=0.102$ mm$^{-1}$, $F(000)=688$. Final residuals (for 218 parameters) were $R_1=0.0546$ and $wR_2=0.1237$ for 1468 reflections. Residual electron density was 0.280 and −0.306 e Å$^{-3}$. A CIF file with data for **4** has been deposited, CDCC reference code: 204895.
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