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Tetrahedron Letters 45 (2004) 2927–2930

Tetrahedron
Letters

Synthesis, crystal structure and complexation with dibenzylammonium ion of a novel class of crownophanes containing bridged fragments of fluorenone and stilbene

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Received 3 December 2003; revised 5 February 2004; accepted 13 February 2004

Abstract—Two representatives of a novel class of crownophanes containing fragments of fluorenone and stilbene bridged by units of diethylene glycol and triethylene glycol, respectively, have been synthesized. The crystal structure and complexation behavior of these crownophanes were studied. They form much stronger complexes with dibenzylammonium hexafluorophosphate (log K_a value in CH_3CN is equal to 3.92 ± 0.06 and 4.40 ± 0.05, respectively) than benzocrown ethers. This makes them an attractive alternative for benzocrown ethers as components in supramolecular synthesis.

Crownophane-type macrocycles incorporating rigid aromatic moieties bridged by flexible polyether chains have attracted considerable attention due to their excellent ability to bind inorganic and organic cations and neutral substrates strongly and selectively. Such synthetic receptors provide a controlled means for studying the fundamentals of non-covalent intermolecular forces in nature and open new routes for the development of sensors, catalysts, switches and other molecular devices. They can also be used as platforms for the design of supramolecular systems (e.g., rotaxanes and catenanes).[1–7]

Photoresponsive crownophanes that change properties under the external action of light are of particular interest because of their potential application in photoswitchable devices for detection of organic and inorganic species and as building blocks of supramolecular systems similar to the photocontrollable rotaxanes.[6]

With the purpose of obtaining potentially photoswitchable crownophanes with high binding affinity for electron-deficient guests, we were intrigued by bisphenols **1**[8] and **4**[9] (Scheme 1) as the aromatic blocks for the construction of a new family of large cyclophanes. Bisphenol **1** was selected based on the following: (i) it 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, directs it towards the macrocyclic host cavity and stabilizes the complexes because of electrostatic interactions, (ii) 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, (iii) fluorenone and its derivatives have good luminescence properties that are important for the development of sensitive fluorescence-based chemosensors, and finally yet importantly, (iv) the carbonyl group of the fluorenone fragment can be converted into a variety of functional groups that would allow for fine-tuning of the binding behavior of the crownophanes.

On the other hand, derivatives of bisphenol **4** such as other stilbenoid compounds can undergo a variety of

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Keywords: Crownophane; Fluorenone; Stilbene; Complexation; Dibenzylammonium hexafluorophosphate.

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0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.02.061

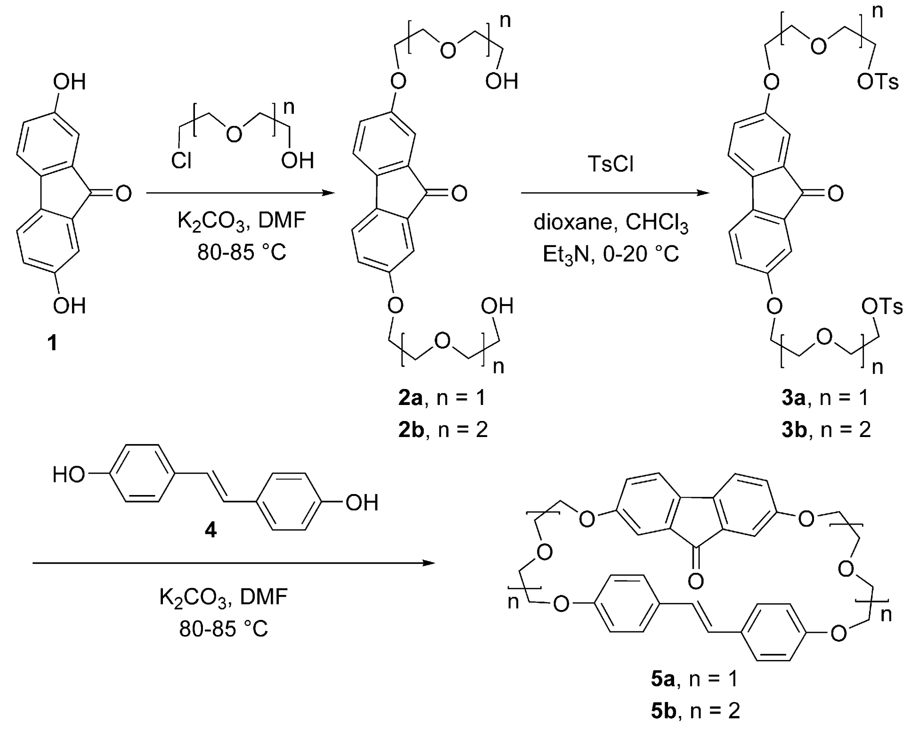
photochemical transformations, such as *trans*-to-*cis* isomerization, *cis*-stilbene ring closure to form phenanthrene and [2+2] cycloaddition of *trans*-stilbene to give cyclobutanes.[10] If a stilbene fragment is incorporated into a crownophane, the photoreversible isomerization process of *trans*-to-*cis* and vice versa should be accompanied by large structural modifications of the macrocycle that alter its binding properties and can be used as a function key to photoswitching.

Recently, we described the preparation and the properties of crownophanes with two bridged fluorenone fragments.[11] Here, we report for the first time the synthesis, complexation behavior and crystal structure of crownophanes containing bridged moieties of fluorenone and stilbene.

The synthetic pathway leading to cyclophanes **5a** and **5b** is shown in Scheme 1. Reaction of bisphenol **1** with chlorohydrins of diethylene glycol or triethylene glycol in DMF in the presence of anhydrous potassium carbonate at 80–85 °C for 30 h gave the diols **2a**[12] and **2b**[11] in 78% and 77% yields, respectively. Conversion of these diols into ditosylates **3a**[12] and **3b**[11] was achieved in 88% and 84% yields using *p*-toluenesulfonyl chloride in a mixture of chloroform and dioxane in the presence of triethylamine at 0–20 °C. Further reaction of **3a** and **3b** with bisphenol **4** in DMF in the presence of anhydrous potassium carbonate as the base at 80–85 °C for 50 h gave after work-up and chromatographic purification over silica gel, the crownophanes **5a** and **5b** in 21% and 31% yields, respectively.[13]

The single-crystal structures of **5a** and **5b** were determined by X-ray crystallography,[14] and their computer-generated drawings are shown in Figure 1.

In both crownophanes **5a** and **5b**, the stilbene fragment adopts the thermodynamically stable *E*-configuration. Crownophane **5a** possesses an elongated cavity of effective dimensions ca. 4 × 14 Å. The macrocycle is self-filling, with planar moieties of fluorenone and stilbene



Scheme 1. Synthesis of crownophanes **5a** and **5b**.

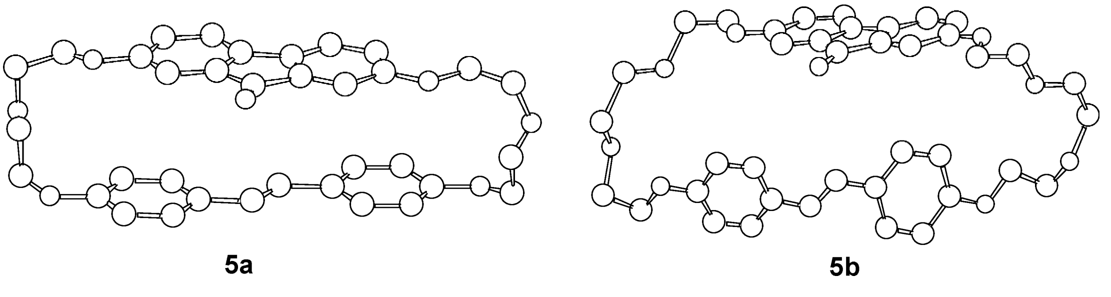
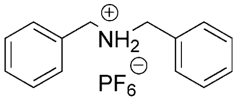


Figure 1. Solid-state structure of crownophanes **5a** and **5b**.

aligned parallel to each other with proximal partial overlapping with the interplanar distances being in the range 3.255–3.678 Å and with an interplanar angle equal to 3.8°. This geometry is consistent with the conventional parallel π–π stacking.[15] In crownophane **5b**, the stilbene moiety is not planar; the angle of twist between the benzene rings is 13.1°. The planar fluorenone fragment and the stilbene unit are arranged in a T-shaped mode with an interplanar angle of 77.4° to afford opportunity for attractive C–H···π interactions. The closest distances of two carbon atoms of the stilbene moiety from a fluorenone plane, 3.512 and 3.670 Å, are in good agreement with those cited for such interactions.[15,16] These interactions can determine the conformation of flexible organic molecules in the solid state but are disfavored in solution by entropic factors due to the restricted internal mobility.

Generally, the self-filling of the crownophane cavity in the solid state is not a serious hindrance for complexation since the cavity dimensions in solution can vary over rather wide limits in accord with the steric requirements of the substrate, owing to mobility of the flexible oligo(ethyleneoxy) bridges.[17,18] However, the energy gain of complexation should be sufficient to compensate for the energy loss during the initial process of enlargement of the self-filling cavity.

In order to obtain information regarding the binding ability of the newly synthesized crownophanes **5a** and **5b**, we investigated their complexation with dibenzylammonium hexafluorophosphate **6**.



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This salt was selected as a test guest compound because of its ability to form the pseudorotaxane-like complexes with a variety of the large crown ethers containing aromatic fragments.[19,20] The structure of such crown ethers is similar to the framework of crownophanes, since each of them contains rigid aromatic moieties bridged by flexible polyether chains. Due to this, their complexing ability should probably be similar, also. This fact makes crownophanes **5a** and **5b** likely candidates for the formation of pseudorotaxanes with secondary ammonium salts.

The stability constants of the complexes formed between ammonium salt **6** and crownophanes **5a** and **5b** have been determined by spectrophotometric titration in acetonitrile at 25 °C. The UV absorption bands of the crownophanes decrease in intensity with increased salt concentration. The complexation of guest **6** with hosts **5a** and **5b** was monitored by measuring the absorbance of solutions where the molar ratio of guest increases with respect to the host over the range 0.1:1 to 50:1 during the titration. The absorbance measurements were carried out at four wavelengths simultaneously and sets of the obtained experimental values (4 × 30 points) were used for joint computer processing. The data were treated using the nonlinear least squares fitting program SIRKO.[21] The experimental data fit best with a 1:1 complexation model. The logarithm of equilibrium constants was found to be 3.92 ± 0.06 and 4.40 ± 0.05 for the complexes of **5a** and **5b**, respectively. The stability of these complexes is much higher with respect to the complexes of salt **6** with benzocrown ethers, which are used extensively for designing remarkable supramolecular systems.[20] For comparison, the logarithms of association constants of **6** with dibenzo[24]crown-8[19] and tribenzo[27]crown-9[22] in CD_3CN are 2.62 and 2.43, respectively.

Using a large set of studied pseudorotaxanes and rotaxanes it was shown that the fundamental driving force responsible for the threading interaction is the formation of the strong hydrogen bonds between the NH_2^+ acidic protons and the oxygen atoms of the crown ether.[20] The highly polarized carbonyl group of the fluorenone fragment in crownophanes **5a** and **5b** is a more powerful H-acceptor than the ether oxygen atoms of crown ethers. This is probably the origin of the high affinity of these crownophanes to ammonium salt **6**. Additionally, complexes of crownophanes can be stabilized by ion–dipole interactions between the positively charged nitrogen atom of the guest and the carbonyl oxygen atom of the host and by π–π intermolecular interactions between the aromatic parts of the guest and host.

In this letter, we have demonstrated the first synthesis and crystal structure of new types of crownophanes **5a** and **5b** that form very stable complexes with dibenzylammonium ions and most likely with the other secondary ammonium salts. This feature makes them an attractive alternative for benzocrown ethers as components in supramolecular synthesis. Furthermore, these compounds are potentially photoresponsive macrocyclic hosts. In fact, estimations derived from AM1 calculations[23] indicate that pseudorotaxane-like inclusion complexes of salt **6** with crownophanes **5a** and **5b** that possess *cis*-stilbene fragments are significantly more stable than complexes with crownophanes having *trans*-stilbene fragments, by 10.0 and 13.2 kcal/mol, respectively.

Investigations of the binding properties of crownophanes containing bridged fluorenone and stilbene moieties and their dependence on stilbene fragment configuration are in development with respect to photoreversible self-assembly and supramolecular synthesis.

Acknowledgements

The diffraction data were collected at the Department of Chemistry, Technion, Haifa, through the cooperation of Prof. M. Kaftory whom we thank.

References and notes

1. Inokuma, S.; Sakaki, S.; Nishimura, J. *Top. Curr. Chem.* **1994**, *172*, 87–118.
2. Tsuzuki, S.; Houjou, H.; Nagawa, Y.; Goto, M.; Hiratani, K. *J. Am. Chem. Soc.* **2001**, *123*, 4255–4258.
3. Nehlig, A.; Kaufmann, G.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1999**, *40*, 5865–5868.
4. Fis, M. J.; Seiler, P.; Muslinkina, L. A.; Badertscher, M.; Pretsch, E.; Diederich, F.; Alvarado, R.; Echegoyen, L.; Nunez, I. P. *Helv. Chim. Acta* **2002**, *85*, 2009–2055.
5. Hartley, J. H.; James, T. D.; Ward, C. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3155–3184.
6. Balzani, V.; Credi, A.; Raymo, F.; Stoddart, J. F. *Angew. Chem. Int. Ed.* **2000**, *39*, 3348–3391.
7. Blanco, M.-J.; Jimenez, M. C.; Chambron, J.-C.; Heitz, V.; Linke, M.; Sauvage, J.-P. *Chem. Soc. Rev.* **1999**, *28*, 293–305.
8. Andrews, E. R.; Fleming, R. W.; Grisar, J. M.; Kihm, J. C.; Wenstrup, D. L.; Mayer, G. D. *J. Med. Chem.* **1974**, *17*, 882–886.
9. Sieber, R. H. *Liebigs Ann.* **1969**, *730*, 31–46.
10. Meier, H. *Angew. Chem. Int. Ed.* **1992**, *31*, 1399–1420.
11. Lukyanenko, N. G.; Kirichenko, T. I.; Lyapunov, A. Yu.; Bogaschenko, T. Yu.; Pastushok, V. N.; Simonov, Yu. A.; Fonari, M. S.; Botoshansky, M. M. *Tetrahedron Lett.* **2003**, *44*, 7373–7376.
12. Diol **2a** and ditosylate **3a** were obtained following the method described for compounds **2b** and **3b**, respectively.[11] **2a**: 78%; orange crystals; mp 117.5–119.5 °C. ^{1}H NMR (300 MHz; $CDCl_3$; δ, ppm; J, Hz) 1.97 (br s, 2H), 3.65–3.72 (m, 4H), 3.74–3.82 (m, 4H), 3.84–3.92 (m, 4H), 4.14–4.21 (m, 4H), 6.97 (dd, 2H, $J = 2.18$, 8.09), 7.17 (d, 2H, $J = 2.18$), 7.29 (d, 2H, $J = 8.09$). Anal. calcd for $C_{21}H_{24}O_7$: C, 64.94; H, 6.23. Found: C, 65.19; H, 6.29. **3a**: 88%; orange crystals; mp 110–112 °C. ^{1}H NMR (300 MHz; $CDCl_3$; δ, ppm; J, Hz) 2.42 (s, 6H), 3.73–3.83 (m, 8H), 4.07 (t, 4H, $J = 4.52$), 4.21 (t, 4H, $J = 4.82$), 6.95 (dd, 2H, $J = 2.18$, 8.10), 7.12 (d, 2H, $J = 2.18$), 7.27–7.36 (m, 6H), 7.80 (d, 4H, $J = 8.09$). Anal. calcd for $C_{35}H_{36}O_{11}S_2$: C, 60.33; H, 5.21. Found: C, 60.47; H, 5.41.
13. *General procedure.* A solution of **4** (5.52 g, 10 mmol) and the appropriate ditosylate (**3a** or **3b**, 10 mmol) in dry DMF (400 mL) was added dropwise over 10 h to a stirred suspension of K_2CO_3 (5.52 g, 40 mmol) in DMF (600 mL) under argon at 80 °C and heating was maintained for a further 40 h. The reaction mixture was filtered and the filtrate was evaporated to dryness in vacuo. The residue and solid obtained after the first filtration were combined, washed with methanol and filtered. The air-dried solid was extracted with toluene using a Soxhlet extractor for 40 h. The toluene extract was filtered and the solid residue was extracted with hot toluene several times until complete extraction of the product. The solvent was removed from the combined toluene extracts under reduced pressure and the residue was subjected to column chromatography (SiO_2, $CHCl_3$/MeOH, 100:1), to afford pure **5a** or **5b** as orange crystals after crystallization from toluene or MeCN, respectively. Crownophane **5a**: 21%; mp 196–197 °C. ^{1}H NMR (300 MHz; $CDCl_3$; δ, ppm; J, Hz) 3.79–3.90 (m, 8H), 3.92 (t, 4H, $J = 4.25$), 4.30 (t, 4H, $J = 4.25$), 6.43 (s, 2H), 6.61 (br s, 2H), 6.73 (dd, 2H, $J = 2.18$, 8.09), 6.77 (d, 4H, $J = 8.72$), 7.00 (d, 4H, $J = 8.41$), 7.13 (d, 2H, $J = 8.40$). ^{13}C NMR (75.5 MHz; $CDCl_3$; δ, ppm; J, Hz) 67.4, 68.4, 69.3, 69.6, 110.8, 115.7, 119.1, 119.9, 125.6, 126.9, 130.5, 135.9, 136.0, 157.1, 158.7, 193.2; EI-MS, 70 eV, m/z (%) 564 (100, M^+), 282 (8), 212 (20). UV–vis, CH_3CN, λ_{max} ($\log \varepsilon$) 271 (4.97), 310 (4.47), 334 (4.36), 468 (2.46). Anal. calcd for $C_{35}H_{32}O_7$: C, 74.45; H, 5.71. Found: C, 74.28; H, 5.94. Crownophane **5b**: 31%; mp 170–171 °C. ^{1}H NMR (300 MHz; $CDCl_3$; δ, ppm; J, Hz) 3.70–3.83 (m, 12H), 3.84–3.95 (m, 8H), 4.15 (t, 4H, $J = 4.52$), 6.62 (s, 2H), 6.76 (d, 1H, $J = 2.18$), 6.80 (d, 5H, $J = 8.72$), 6.93 (d, 2H, $J = 2.49$), 6.99 (d, 2H, $J = 8.41$), 7.15 (d, 4H, $J = 8.71$). ^{13}C NMR (75.5 MHz; $CDCl_3$; δ, ppm; J, Hz) 67.5, 67.8, 69.5, 69.9, 70.9, 71.1, 110.4, 114.9, 120.4, 120.5, 125.8, 127.2, 130.4, 135.8, 137.3, 158.1, 159.0, 193.3; EI-MS, 70 eV, m/z (%) 652 (100, M^+), 326 (5), 212 (11). UV–vis, CH_3CN, λ_{max} ($\log \varepsilon$) 271 (4.94), 308 (4.48), 334 (4.37), 468 (2.62). Anal. calcd for $C_{39}H_{40}O_9$: C, 71.76; H, 6.18. Found: C, 71.55; H, 6.01.
14. X-ray quality single crystals were obtained by slow evaporation of C_6H_6 and MeCN solutions of **5a** and **5b**, respectively. Measurements were made on a Nonius CCD diffractometer with graphite monochromatized Mo-Kα radiation ($\lambda = 0.71073$ Å). The structures were solved by direct methods and refinement, based on F^2, was made by full-matrix least-squares techniques. All non-hydrogen atoms were refined isotropically and hydrogen atoms were placed in geometrically calculated positions and refined with temperature factors 1.2 times those of their bonded atoms. *Crystal data for* ***5a***: $C_{35}H_{32}O_7$, 564.63, triclinic, $P1$, $a = 9.390(2)$, $b = 11.625(2)$, $c = 14.118(3)$ Å, $\alpha = 79.49(2)°$, $\beta = 83.21(2)°$, $\gamma = 68.51(2)°$, $V = 1407.7(5)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.332\ g\,cm^{-3}$, $\mu = 0.092\ mm^{-1}$, $F(000) = 596$, $2\theta_{max} = 50.70°$ ($-11 \leqslant h \leqslant 10$, $-13 \leqslant k \leqslant 13$, $-16 \leqslant l \leqslant 16$). Final residuals (for 380 parameters) were $R_1 = 0.0565$ and $wR_2 = 0.1289$ for 2444 reflections with $I > 2\sigma(I)$, and $R_1 = 0.1394$ and $wR_2 = 0.1544$, GOF = 0.905 for all 4997 data. Residual electron density was 0.356 and −0.183 eÅ^{-3}. *Crystal data for* ***5b***: $C_{39}H_{40}O_9$, 652.74, triclinic, $P1$, $a = 11.051(2)$, $b = 11.342(2)$, $c = 15.295(3)$ Å, $\alpha = 69.81(2)°$, $\beta = 74.90(2)°$, $\gamma = 68.74(2)°$, $V = 1656.6(5)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.308\ g\,cm^{-3}$, $\mu = 0.092\ mm^{-1}$, $F(000) = 692$, $\theta_{max} = 50.70°$ ($-13 \leqslant h \leqslant 13$, $-12 \leqslant k \leqslant 11$, $-17 \leqslant l \leqslant 17$). Final residuals (for 434 parameters) were $R_1 = 0.0577$ and $wR_2 = 0.1142$ for 2444 reflections with $I > 2\sigma(I)$, and $R_1 = 0.2261$ and $wR_2 = 0.1616$, GOF = 0.661 for all 5201 data. Residual electron density was 0.233 and −0.225 eÅ^{-3}. The CIF files with data for **5a** and **5b** have been deposited, CDCC reference codes 201313 and 201314.
15. Hunter, C. A.; Lawson, K. R.; Perkins, J.; Urch, J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 651–669.
16. Meyer, E. A.; Castellano, R. K.; Diederich, F. *Angew. Chem. Int. Ed.* **2003**, *42*, 1210–1250.
17. Gillard, R. E.; Stoddart, J. F.; White, A. J. P.; Williams, B. J.; Williams, D. J. *J. Org. Chem.* **1996**, *61*, 4504–4505.
18. Bryant, W. S.; Guzei, I. A.; Rheingold, A. L.; Merola, J. S.; Gibson, H. W. *J. Org. Chem.* **1998**, *63*, 7634–7639.
19. Fyfe, M. C. T.; Stoddart, J. F. In *Advances in Supramolecular Chemistry*; Gokel, G. W., Ed.; JAI Press: Stamford, CT, 1999; Vol. 5, pp 1–53.
20. Cantrill, S. J.; Pease, A. R.; Stoddart, J. F. *J. Chem. Soc., Dalton Trans.* **2000**, 3715–3734.
21. Vetrogon, V. I.; Lukyanenko, N. G.; Schwing-Weill, M.-J.; Arnaud-Neu, F. *Talanta* **1994**, *41*, 2105–2112.
22. Cantrill, S. J.; Fyfe, M. C. T.; Heiss, A. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Org. Lett.* **2000**, *2*, 61–64.
23. Spartan'02, Wavefunction, Inc. Irvine, CA.