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Novel Tetramethoxy Resorcinarene Bis-Crown Ethers

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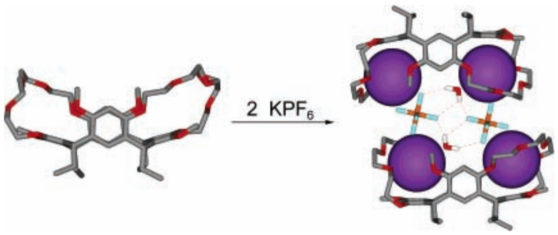
ABSTRACT



The synthesis and characterization of new tetramethoxy resorcinarene bis-crown ethers BC4 and BC5 are described. The complexation properties of the compounds toward alkali metal cations were studied by ^{1}H NMR spectroscopy and X-ray crystallography, which revealed that BC5 can accommodate two cations simultaneously inside the crown pockets formed by the crown ether bridges and the resorcinarene skeleton.

In their simplicity, crown ethers are probably one of the most intriguing class of compounds in the field of supramolecular chemistry. They have been employed in numerous macromolecular assemblies such as catenanes and rotaxanes,[1] as well as in calixcrowns,[2] due to their remarkable ability to act as receptors or ionophores. Earlier studies of calixcrowns have shown the number of oxygens in the crown ether moiety to determine the selectivity toward cation binding in a manner comparable to the crown ether properties: crown-4 is selective to sodium; crown-5 is selective to potassium; and crown-6 is selective to cesium cations, respectively.[3] However, the conformation of the calixarene framework also influences the binding as providing cation−π interactions.[3a]

Inspired by the work that has been done with calixcrowns,[4] we wanted to explore the possibilities of introducing the crown ether properties to the resorcinarene skeleton. The phenolic hydroxyl groups on the upper rim of resorcinarene enable the crown bridging on the “open” end of the cavity and, therefore, make the resorcinarene bowl available to take part in the cation binding. We chose tetramethoxy resorcinarene[5] as the platform because it has a limited amount of sites for crown ether bridging, which reduces the possibility of obtaining a complex mixture of products and, on the other hand, gives “handles” to the resorcinarene bowl-creating crown ether pockets to accommodate two guests.

Herein, we report the synthesis of novel tetramethoxy resorcinarene bis-crown ethers **BC4** and **BC5** (named according to Jacques Vicens et al. as bis-crown followed by the number of oxygens[3b]). Also, their complexation properties toward alkali metal cations were studied using ^{1}H NMR spectroscopic and X-ray crystallographic methods.

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[1] For a quick review, see: (a) Balzani, V.; Gómez-López, M.; Stoddart, J. F. *Acc. Chem. Res.* **1998**, *31,* 405. (b) Raymo, F. M.; Stoddart, J. F. *Chem. Rev.* **1999**, *99*, 1643.

[2] (a) Ungaro, R. In *Calixarenes in Action*; Mandolini, L., Ungaro, R., Eds.; Imperial College Press: London, England, 2000. (b) Sharma, K. R.; Agrawal, Y. K. *Rev. Anal. Chem.* **2004**, *23,* 133. (c) Alfieri, C.; Dradi, E.; Pochini, A.; Ungaro, R.; Andreetti G. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1075.

[3] (a) Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadi, A. A.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1990**, *112,* 6979. (b) Lamare, V.; Dozol, J. F.; Fuangswasdi, S.; Arnaud-Neu, F.; Thuéry, P.; Nierlich, M.; Asfari, Z.; Vicens, J. *J. Chem. Soc., Perkin Trans. 2* **1999**, 271. (c) Stephan, H.; Gloe, K.; Paulus, E. F.; Saadioui, M.; Böhmer, V. *Org. Lett.* **2000**, *2,* 839. (d) Casnati, A.; Della Ca’, N.; Sansone, F.; Ugozzoli, F.; Ungaro, R. *Tetrahedron* **2004**, *60,* 7869.

[4] Some examples: (a) Ferguson, G.; Lough, A. J.; Notti, A.; Pappalardo, S.; Parisi, M. F.; Petringa, A. *J. Org. Chem.* **1998**, *63,* 9703. (b) Geraci, C.; Piattelli, M.; Chessari, G.; Neri, P. *J. Org. Chem.* **2000**, *65,* 5143. (c) Kim, S. K.; Sim, W.; Vicens, J.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44,* 805.

[5] McIldowie, M. J.; Mocerino, M.; Skelton, B. W.; White, A. H. *Org. Lett.* **2000**, *2,* 3869.

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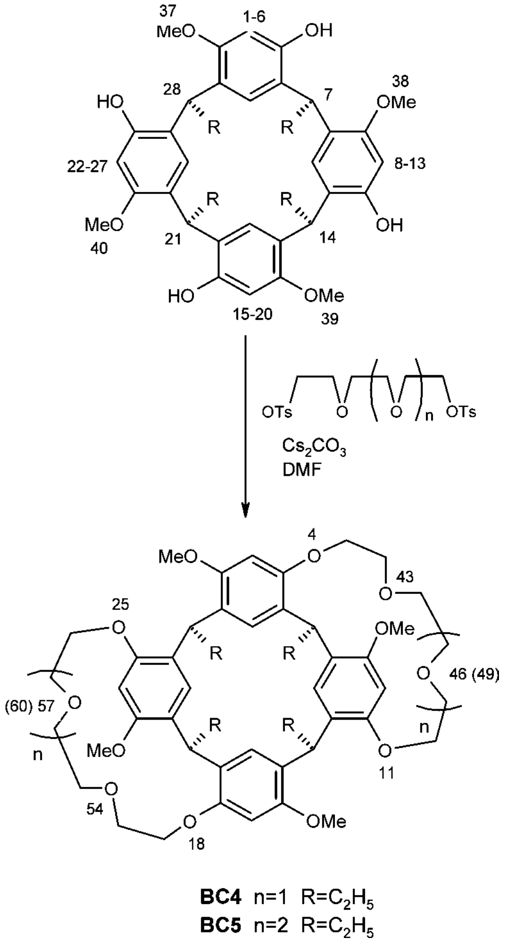
Tetramethoxy resorcinarene bis-crowns **BC4** and **BC5** were accomplished by a reaction of triethylene and tetraethylene glycol ditosylates with tetramethoxy resorcinarene[5] **1** (Scheme 1) with yields of 18 and 22%, respectively. The formed crown bridges over the adjacent aromatic rings force the resorcinarene skeleton to adopt a boat conformation, which can also be reasoned from the reduced symmetry in the ^{1}H NMR spectra of **BC4** and **BC5** as doubling of the resonances arising from the resorcinarene core. Single crystals suitable for crystal structure analysis were obtained from methanol-chloroform (**BC4**) and acetonitrile (**BC5**) solutions.[6] The longer crown ether bridge in **BC5** allows the opposite upright aromatic rings of the resorcinarene core to tilt outward with an angle of 31.57° between the aromatic rings, where as in **BC4** the angle between the aromatic rings is 9.60° (Figure 1). Also, the crown pocket in **BC4** has a cavity smaller than that of **BC5** with average cavity diameters[7] of 4.40−4.51 Å for **BC4** and of 6.05−6.31 Å for **BC5**, thus making **BC5** more favorable to guest inclusion.

Scheme 1. Synthesis of Tetramethoxy Resorcinarene Bis-Crown Ethers **BC4** and **BC5** Depicted with the Crystallographic Numbering Scheme Used for the Resorcinarene Skeleton (Top) and for Crown Ether Oxygens (Bottom)



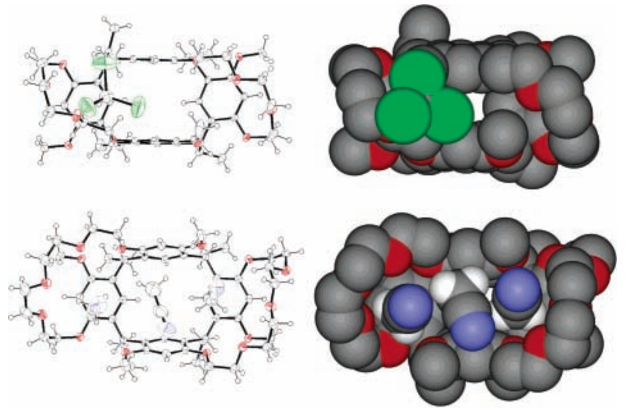


Figure 1. Crystal structures of **BC4** (top) and **BC5** (bottom) crystallized from methanol-chloroform and acetonitrile, respectively (top views). Hydrogens of the resorcinarene skeleton are omitted for clarity from the vdw presentation (right-hand side).

^{1}H NMR spectroscopic titration experiments revealed the complexation abilities of **BC4** and **BC5** toward alkali metal cations (Li^+, Na^+, K^+, Rb^+, and Cs^+). The titrations were performed in deuterated acetone at 293 K by adding subsequently increasing amounts of alkali metal salts with PF_6^- as the counteranion. In solution, the crown ether moiety is fairly flexible and shows overlapping multiplets at the 4−3 ppm region of the ^{1}H NMR spectrum (Figure 2). When

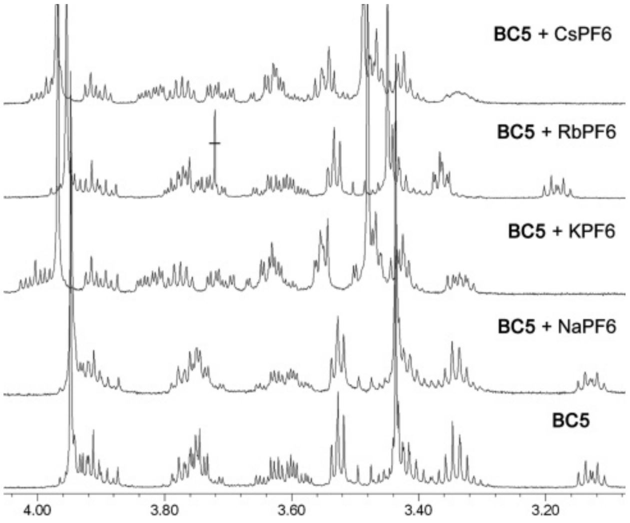


Figure 2. ^{1}H NMR titration spectra of **BC5** with a large excess of $NaPF_6$, KPF_6, $RbPF_6$, and $CsPF_6$ in acetone-d_6 at 293 K (only 4−3 ppm of area of the spectra is shown).

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(6) Crystal data for **BC4**: $C_{52}H_{68}O_{12}\cdot CHCl_3$, M = 1004.43, triclinic P-1 (No. 2). a = 12.0169(2) Å, b = 15.9703(3) Å, c = 16.1310(3) Å, α = 63.823(1)°, β = 70.256(1)°, γ = 78.903(1)°, V = 2611.4 (1) Å^3, Z = 2, T = 173.0 K, R_1 = 0.148, wR_2 = 0.237 (all data), R_1 = 0.097, wR_2 = 0.207 ($I > 2\sigma I$). Crystal data for **BC5**: $C_{56}H_{76}O_{14}\cdot 3CH_3CN$, M = 1096.33, triclinic P-1 (No. 2). a = 14.0187(4) Å, b = 14.4583(4) Å, c = 16.5822(5) Å, α = 65.075(2)°, β = 75.326(2)°, γ = 77.921(2)°, V = 2928.3(2) Å^3, Z = 2, T = 173.0 K, R_1 = 0.071, wR_2 = 0.166 (all data), R_1 = 0.059, wR_2 = 0.155 ($I > 2\sigma I$).

hosting cations, the crown ether bridge should adopt a more rigid form and thus simplify the spectrum in the crown ether region. In fact, with **BC5**, the addition of a 1:1 molar ratio of KPF_6 did not cause any significant changes in the crown ether region of the spectrum, whereas with a 1:2 molar ratio of the cation, changes in the spectrum could already be seen. With a large excess of the salt, the spectrum continued to resolve in the crown ether region, indicating inclusion of K^+ in the crown ether pocket. Small changes in the chemical shifts of the resorcinarene core were also seen, which implied changes in the conformation of **BC5** and probable interaction with the resorcinarene core. A similar pattern was observed with $RbPF_6$ and $CsPF_6$, however, with the exception that with $RbPF_6$ the changes in the spectrum were more or less identical but required a larger amount of the salt than with KPF_6. With $NaPF_6$, there were no significant changes in the spectrum. **BC4** showed no reaction toward Li^+, Na^+, or K^+ salts even at large excess, which would infer a cavity too confined for guest inclusion or competing solvation effects (for the sodium cation).[3b]

Colorless single crystals of **BC5**$\cdot$$2KPF_6\cdot 2MeCN\cdot H_2O$ were obtained from a reaction of **BC5** with KPF_6 (1:2 molar ratio) in an acetonitrile solution (Figure 3, top).[8] Both crown pockets of **BC5** host one K^+ cation (K1 and K2), which both coordinate to four crown ether oxygens (K1$\cdots$O18 2.817(3), K1$\cdots$O60 2.853(3), K1$\cdots$O57 2.860(3), and K1$\cdots$O54 2.872(3) Å; K2$\cdots$O4 3.113(3), K2$\cdots$O49 2.799(3), K2$\cdots$O46 2.926(3), and K2$\cdots$O43 2.805(3) Å) and the aromatic ring (K1$\cdots$C22−C27 3.149(2) Å; K2$\cdots$C8−C13 3.198(2) Å) in the crown ether pocket. K2 additionally coordinates to one methoxy oxygen (K2$\cdots$O20 3.020(3) Å) and a water molecule (K2$\cdots$O70 2.735(4) Å).

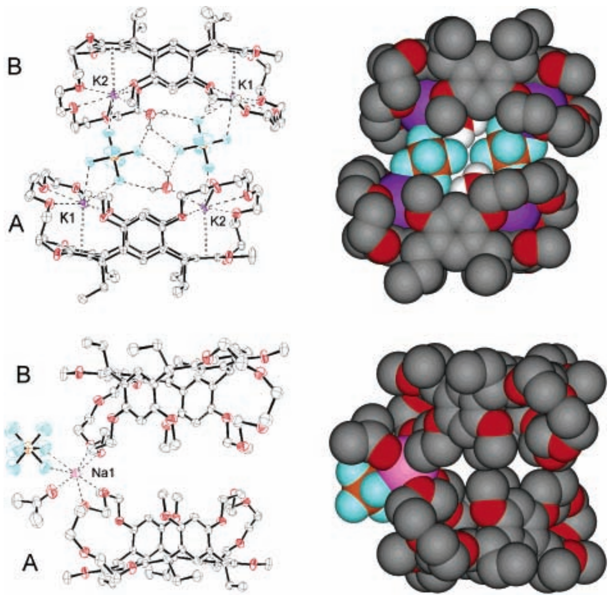

Figure 3. Ortep plot and vdw presentation of the complexes **BC5**$\cdot$$KPF_6$ (top, front view) and **BC5**$\cdot$$NaPF_6$ (bottom, front view). Non-hydrogen-bonding hydrogens and noncoordinating solvent molecules are omitted for clarity.

Two **BC5**$\cdot$$2K^+$ complexes are connected together to a dimeric capsule through coordination of K1 and K2 to their counter anions PF_6^- (K1$\cdots$F16A 2.785(3), K1$\cdots$F13A 2.728(3), and K2$\cdots$F11B 2.838(3) Å) in a way that K1 in the bottom part of the capsule (A) pairs up with K2 in the top part of the capsule (B) and vice versa, thus creating two $K1\cdots PF_6^-\cdots K2$ bridges inside the capsule. The two water molecules included in the capsule, in addition to coordinating to K2, form a network through hydrogen bonds to both PF_6^- anions inside the capsule (O70$\cdots$F16A 3.111(4), O70$\cdots$F14A 3.048(5), and O70$\cdots$F14B 3.004(5) Å). The remaining two PF_6^- counter anions outside the capsule take part in crystal packing.

The reaction of **BC5** with $NaPF_6$ or $NaClO_4$ in acetone gave colorless single crystals of the complex **BC5**$\cdot$$NaPF_6\cdot 2Me_2CO$ and **BC5**$\cdot$$NaClO_4\cdot 2Me_2CO$ (Figure 3, bottom) with isomorphous structures.[9] As seen in the ^1H NMR titration experiments, the Na^+ cation does not occupy the cavity of **BC5** but instead lies in the notch of two resorcinarene hosts (A and B), which are approximately at a 90° angle on top of each other with the cavities facing one another. A sodium cation coordinates to two oxygens of the crown ether bridges of both resorcinarene hosts, which make up the inner walls of the notch (Na1$\cdots$O43A 2.434(3), Na1$\cdots$O46A 2.446(3), Na1$\cdots$O57B 2.412(3), and Na1$\cdots$O60B 2.496(3) Å), to the counteranion PF_6^- or ClO_4^- (Na1$\cdots$F1 2.654(4) and Na1$\cdots$F5 2.428(3) Å; Na1$\cdots$O91 2.425(5) and Na1$\cdots$O93 2.906(8) Å), and to one solvent acetone (Na1$\cdots$O80 2.430(3) Å). A

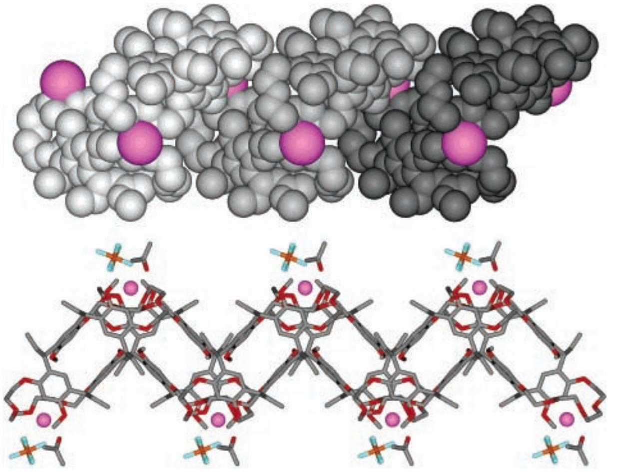

Figure 4. Crystal structure (below, top view) of the helical chain formed by the complex **BC5**$\cdot$$NaPF_6$ and vdw presentation separating the dimers in different colors (above, side view; only the resorcinarene skeleton and sodium cations are shown). Hydrogens and noncoordinating solvent molecules are omitted for clarity.

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(7) Kim, S. K.; Vicens, J.; Park, K. M.; Lee, S. S.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44*, 993.

(8) Crystal data for **BC5**$\cdot$$KPF_6$: $C_{56}H_{76}O_{14}\cdot 2KPF_6\cdot 2CH_3CN\cdot H_2O$, M = 1441.43, monoclinic $P2_1/c$ (No. 14). $a = 17.3738(6)$ Å, $b = 15.9352(5)$ Å, $c = 24.4132(8)$ Å, $\beta = 91.800(2)°$, $V = 6755.6(4)$ Å^3, $Z = 4$, $T = 173.0$ K, $R_1 = 0.0\ 96$, $wR_2 = 0.223$ (all data), $R_1 = 0.076$, $wR_2 = 0.204$ ($I > 2\sigma I$).

helical-like chain is eventually formed as the other crown ether bridge of the second resorcinarene host is free to coordinate to a second sodium cation, which coordinates to a third resorcinarene host, and so forth (Figure 4).

Preliminary crystallization studies indicate the complexation of **BC5** with $RbPF_6$ and $CsPF_6$, but the quality of the data was not good enough to be published. Attempts to get better quality crystals are underway.

Alkali metal picrate extraction experiments from water into a chloroform solution of hosts **BC4** and **BC5** were performed (Table 1). The results showed similar selectivity to Rb^+ and Cs^+ cations over K^+ when **BC5** was used as the host, and no extraction ability toward the Na^+ cation was observed. This suggests better size complementarity to Rb^+ and Cs^+ cations in the crown pocket as well as contribution of the resorcinarene skeleton to binding by cation$-\pi$ interactions[3b,10] in addition to the crown ether oxygens. No extraction ability toward Na^+ and K^+ cations was observed with **BC4** as a host molecule.

Table 1. Alkali Metal Picrate Extraction Experiment[a]

host	Na^+	K^+	Rb^+	Cs^+
BC4	0	0	–	–
BC5[b]	0	1.7	7.6	7.6

[a] Percentage (%) of picrate extracted from water into chloroform. [b] Standard deviation of <0.01.

In conclusion, tetramethoxy resorcinarene **1** was used as the platform in the synthesis of resorcinarene bis-crowns **BC4** and **BC5** with two cation binding sites created by the crown ether bridging over the adjacent phenolic hydroxyl groups. The complexation abilities of the compounds with alkali metals were investigated by ^1H NMR spectroscopic and X-ray crystallographic methods. **BC5** was shown to accommodate two cations, one in each of the crown pockets, and thereby possible receptor activity toward potassium, rubidium, and cesium cations. In our future studies, we aim to investigate the complexation properties of the resorcinarene crowns in more detail in terms of binding affinity and selectivity toward different alkali metal cations.

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Supporting Information Available: Experimental procedures and characterization details for compounds **BC4** and **BC5**; crystal data, structure refinement details, and CIF for **BC4** and **BC5**; and the complexes of **BC5** with KPF_6, $NaPF_6$, and $NaClO_4$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) Crystal data for **BC5**·$NaPF_6$: $C_{56}H_{76}O_{14}\cdot NaPF_6\cdot 2(CH_3)_2CO$, M = 1257.28, monoclinic $C2/c$ (No. 15). $a = 33.3937(7)$ Å, $b = 15.5585(4)$ Å, $c = 24.9509(6)$ Å, $\beta = 101.106(1)°$, $V = 12721(1)$ Å^3, $Z = 8$, $T = 173.0$ K, $R_1 = 0.0\ 97$, $wR_2 = 0.181$ (all data), $R_1 = 0.067$, $wR_2 = 0.159$ ($I > 2\sigma I$). Crystal data for **BC5**·$NaClO_4$: $C_{56}H_{76}O_{14}\cdot NaClO_4\cdot 2(CH_3)_2CO$, M = 1211.76, monoclinic $C2/c$ (No. 15). $a = 33.607(1)$ Å, $b = 15.5535(5)$ Å, $c = 24.7751(8)$ Å, $\beta = 101.153(2)°$, $V = 12705.5(7)$ Å^3, $Z = 8$, $T = 173.0$ K, $R_1 = 0.\ 123$, $wR_2 = 0.252$ (all data), $R_1 = 0.083$, $wR_2 = 0.217$ ($I > 2\sigma I$).

(10) Ikeda, A.; Shinkai, S. *J. Am. Chem. Soc.* **1994**, *116*, 3102.