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A biscalix[4]arene-based ditopic hard/soft receptor for K^+/Ag^+ complexation

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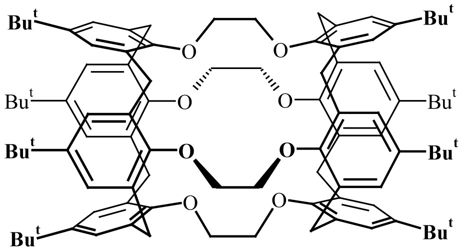
Abstract—A biscalixarene bearing *tert*-butylated and de-*tert*-butylated calix[4]arene unit connected by four ethylenoxy bridges has been prepared. This compound adopts the *pinched cone* conformation (C_{2v} symmetry) and hence, is suitably preorganised for Ag^+ complexation. X-ray crystallography showed that the silver cation (soft) is sandwiched by the two distal coplanar phenyl rings of the de-*tert*-butylated part of the molecule possessing a η^1 binding mode. The complexation of the K^+ cation (hard) into the central cavity created by the bridging moieties leads to a change of conformation (C_{4v} symmetry) and hence, to the complete loss of complexation ability towards the Ag^+ cation. © 2002 Elsevier Science Ltd. All rights reserved.

Calix[4]arenes, the well-known family of macrocyclic compounds,[1,2] frequently serve as molecular scaffolds for the construction of more elaborate supramolecular systems, such as various receptors possessing interesting complexation abilities towards target molecules or ions. It is known from the literature that the so-called *cone* conformation of calix[4]arene can interact with ammonium salts by cation–π interactions[3] between the aromatic part of the molecule (upper rim) and the ammonium salts. The highest complexation constants in the solution were found in the cases where the *cone* conformation adopts the stable C_{4v} symmetry, which best fits the steric requirements of the interactions.[4] On the other hand, the complexation of other soft cations, such as the silver cation, prefers the so called *pinched cone* conformation possessing C_{2v} symmetry. In this conformation, the two opposite aromatic units are almost coplanar and therefore, they can effectively sandwich the cation from both the sites. X-ray crystallography proved such a binding mode in the solid state structure of the tetrapropoxycalix[4]arene–Ag^+ complex.[5]

Recently, derivative **1**, based on biscalix[4]arene, has been described.[6] This compound was reported as a novel receptor with remarkable potassium selectivity that adopts either C_{4v} or C_{2v} symmetry, depending on the presence or absence of a K^+ cation. During our studies on the calix[4]arene–Ag^+ interactions we realised that this system offers a unique possibility of controlled change of molecular symmetry and hence change of complexation ability. Such a system can be used as a ditopic receptor[7] with two cavities preorganised for hard (potassium) and soft (silver) cations with possible switching of complexation preferences.



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To compare the complexation ability of the upper rim alkylated or dealkylated calix[4]arenes, we have designed the novel receptor **6** bearing both structural motifs within the molecule. The synthesis (Scheme 1) started from calix[4]arene tetra-acetate **2** which was reduced using $LiAlH_4$ in diethyl ether[8] to yield the corresponding tetrakis(2-hydroxyethoxy) derivative **3** in 92% yield. This compound was then transformed into tetratosylate **4** (30%) by the reaction with tosyl chloride in pyridine.[8] The condensation of tosylate **4** with calix[4]arene **5** in the presence of K_2CO_3 was carried out by reflux in acetonitrile (6 days), and subsequent

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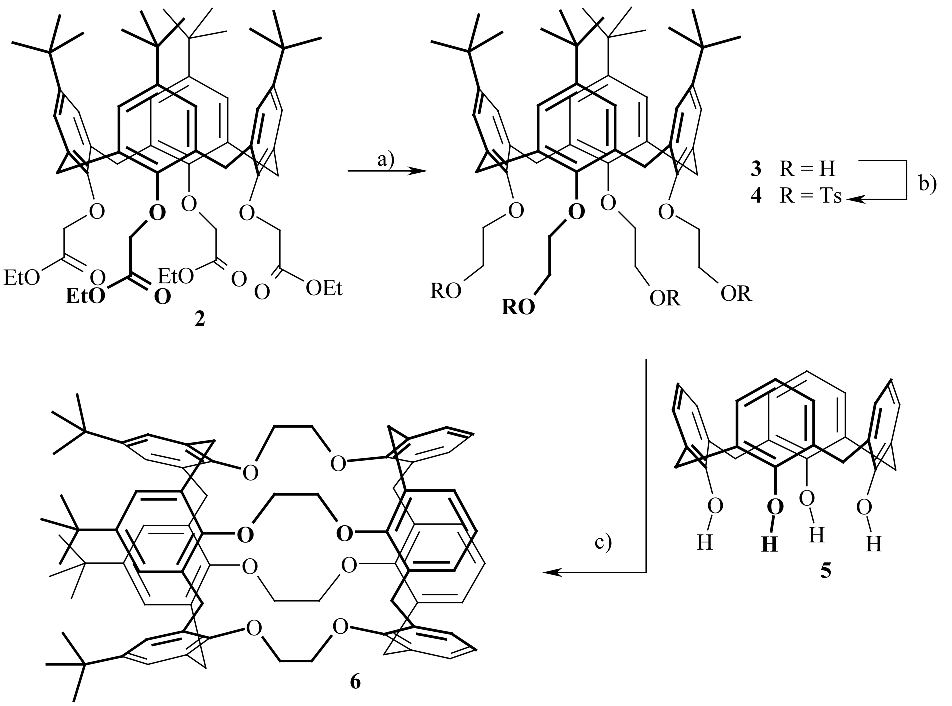

Scheme 1. (a) $LiAlH_4$/ether, rt (92%); (b) TsCl/pyridine, 0°C (30%); (c) K_2CO_3, CH_3CN, 6 days reflux (14%).

isolation by preparative TLC on silica gel gave the product **6** in 14% yield.[9]

The ^1H NMR spectrum of **6** ($CDCl_3$) shows that the molecule adopts a C_{2v} (pinched cone) conformation (Fig. 1a). All the signals under the conditions used (up to +50°C) were split into two sets of the same intensity, e.g. two singlets due to the Bu^t groups at δ 0.85 and 1.35 ppm. The complexation behaviour of compound **6** in solution was studied using ^1H NMR titration experiments ($CDCl_3$:CD_3OD = 4:1 v/v). The addition of the K^+ cation leads to symmetrisation of the molecule due to the complexation of potassium into the central cavity composed of ethylenoxy units (Fig. 1c). As a consequence, the originally doubled signals disappeared and only signals corresponding to C_{4v} symmetry are observed (singlet at δ 1.22 ppm for Bu^t). The complexation occurs under slow exchange conditions, hence both complexed and free species are distinguishable in the spectrum. The measurement of the integral intensity of corresponding signals allowed the evaluation[10] of the complexation constant (2×10^4 M^{-1}). The above-described behaviour is in good agreement with that of compound **1**.[6]

On the other hand, the complexation of a silver cation does not disturb the C_{2v} symmetry of the receptor and occurs under fast exchange conditions. The complexation induced chemical shifts (40 Hz) are most pronounced in the dealkylated part of the molecule indicating the possible complexation site. Fig. 2 shows the corresponding titration curve reflecting the 1:1 binding mode with a complexation constant of 820±150 M^{-1}. The importance of C_{2v} symmetry for Ag^+ complexation was demonstrated by the titration experiment using the **6**·K^+ complex. In this case only negligible changes (<5 Hz) were observed after the addition of 50 equivalents of AgTfl. This clearly shows that C_{4v} symmetry imposed upon the molecule by potassium complexation cannot lead effectively to complexation of Ag^+ by the upper rim of the calixarene subunit. This situation is schematically depicted in Fig. 3. The C_{2v} symmetry allows effective interactions of a soft cation (Ag^+) with the soft base (upper rim of calixarene), while the complexation of hard cation (K^+) leads to a change of symmetry and hence to the disturbance of the upper rim preorganisation suitable for Ag^+ complexation. The complexation ability towards the soft metal is thus governed by the presence of the hard metal.[11]

The final unequivocal proof of the silver ion complexation mode was obtained by X-ray crystallography.[12] Suitable crystals of the **6**·Ag^+ complex (triclinic, space group $P\bar{1}$) were grown by the slow evaporation of a $CHCl_3$:ethyl acetate = 4:1 v/v solution of receptor **6** with 2 equivalents of silver triflate added. As indicated by NMR analysis, both calix[4]arene subunits adopt pinched cone conformations (C_{2v} symmetry), with the silver cation being situated in the calixarene without *tert*-butyl groups on its upper rim. Two distal phenolic rings are approx. coplanar (Fig. 4a), their *para* positions (C4, C8) are 4.81 Å apart, thus creating the π-electron cavity suitably preorganised for metal complexation. The silver cation is almost exactly in the middle between both *p*-carbon atoms (Ag1–C4 = 2.40 Å, Ag1–C8 = 2.41 Å, angle C1–Ag1–C8 = 177.5°). Consequently, the binding mode of silver can be described as a double η^1 mode with strong cation–π interactions corresponding to that already described by Shinkai.[5] It is known from the literature[16] that Ag^+ complexes are usually pseudo-tetrahedral with four coordination bonds. In our case, the third coordination site is occu-

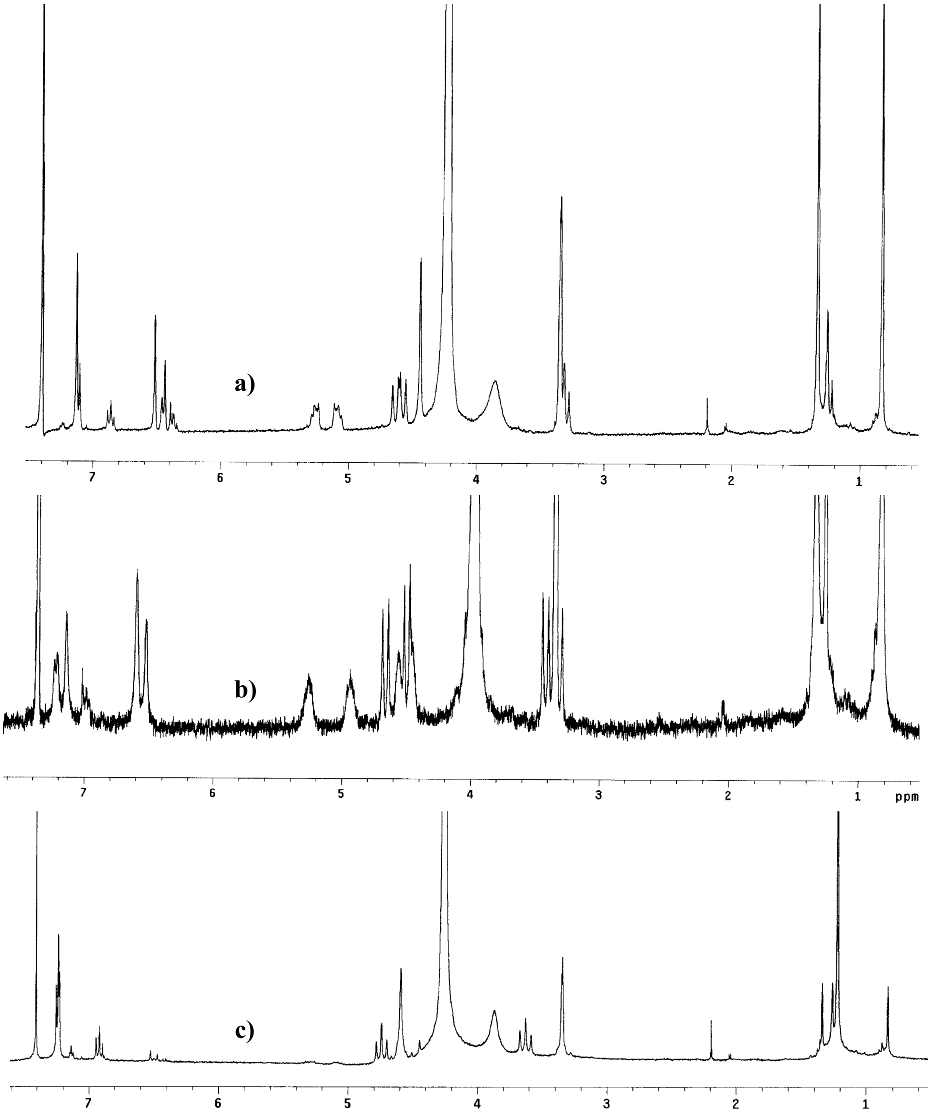

Figure 1. ^{1}H NMR (300 MHz, 298 K, $CDCl_3$:CD_3OD=4:1 v/v): (a) pure **6**, (b) **6**+10 equivalents of AgTfl, (c) **6**+10 equivalents of KI.

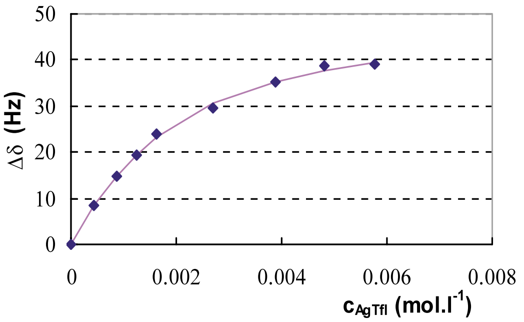

Figure 2. ^{1}H NMR titration of **6** with silver triflate (300 MHz, 298 K, c_6=1 mmol l^{-1}).

pied by the oxygen in the triflate anion (O70) which is 2.46 Å apart (Fig. 4a). To saturate the requirements of the Ag$^+$ coordination sphere, the above-described binding mode is doubled by a symmetry operation to yield a dimeric structure where both Ag$^+$ cations are surrounded by two aromatics and two triflate oxygens

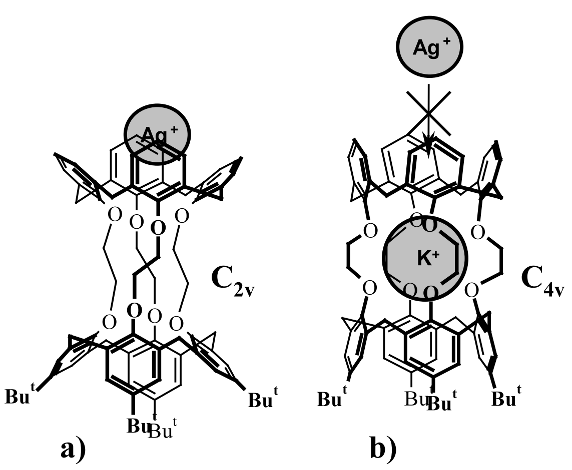

Figure 3. (a) Complexation mode for Ag$^+$, (b) the presence of K$^+$ prevents further complexation of a silver cation.

(Ag2–O74=2.49 Å). The dimeric assembly (Fig. 4b) is thus held together by two triflates that play the role of bidentate bridging ligands.

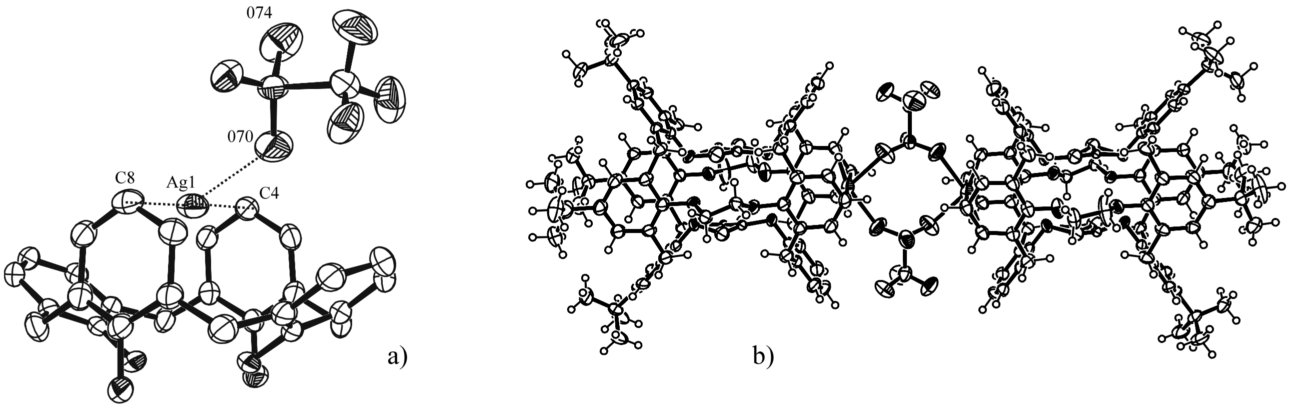

Figure 4. X-Ray structure of **6** (ORTEP drawing): (a) silver complexation mode (only part of molecule, hydrogen atoms are omitted for better clarity), (b) dimer formation (solvent molecules are omitted for better clarity).

In conclusion, the biscalixarene **6** was used as a ditopic receptor possessing two complexation sites with adjustable symmetry (C_{2v} or C_{4v}). The complexation of Ag^+ (soft cation) is thus governed by the presence (absence) of potassium (hard cation). As shown by X-ray crystallography, C_{2v} symmetry is suitably preorganised for silver complexation via a double η^1 mode of aromatic units (cation–π interactions) and two electrostatic interactions with triflate oxygens. The study of Ag^+ complexation in other calixarene-based systems is in progress.

Acknowledgements

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9. Preparation of **6**: A mixture of **5** (119 mg, 0.28 mmol) and potassium carbonate (222 mg, 1.4 mmol) in 50 ml of dry acetonitrile was stirred for 2 h at room temperature. Tetratosylate **4** (400 mg, 0.28 mmol) was then added and the reaction mixture was stirred under reflux for 160 h. The cooled reaction mixture was evaporated to dryness and the residue was refluxed with 40 ml of ethanol/water (1:1) mixture for 12 h. The mixture was filtered hot, and the filtrate evaporated, dissolved in chloroform and poured through the short column of silica gel (20 g, $CHCl_3$:acetone = 1:1). The residue after evaporation was purified by preparative TLC on silica gel using petrol ether:chloroform = 5:1 mixture as an eluent to yield 45 mg (14%) of product ($R_F = 0.55$). mp>360°C (acetone). ^1H NMR ($CDCl_3$, 300 MHz, 25°C): δ 7.16 (s, 4H, Ar–H), 7.14 (d, 4H, $J = 7.4$ Hz, Ar–H), 6.90 (t, 2H, $J = 7.6$ Hz, Ar–H), 6.54 (s, 4H, Ar–H), 6.47 (d, 4H, $J = 7.4$ Hz, Ar–H), 6.40 (dd, 2H, $J = 6.0$ Hz, $J = 8.8$ Hz, Ar–H), 5.30–5.25 (m, 4H, 2×O–CH_2), 5.13–5.07 (m, 4H, 2×O–CH_2), 4.65 (d, 4H, $J = 13.2$ Hz, 4×Ar–CH_2–Ar ax.), 4.59 (d, 4H, $J = 12.7$ Hz, 4×Ar–CH_2–Ar ax.), 4.46 (brs, 8H, 4×O–CH_2), 3.35 (d, 4H, $J = 12.6$ Hz, Ar–CH_2–Ar eq.), 3.31 (d, 4H, $J = 13.2$ Hz, Ar–CH_2–Ar eq.), 1.35 (s, 18H, 2×Bu^t), 0.85 (s, 18H, 2×Bu^t). EA calcd for $C_{80}H_{88}O_8 \cdot 0.25CHCl_3$: C, 79.83; H, 7.37. Found: C, 79.94; H, 7.49. FAB MS *m*/*z* (rel. int.) 1177 $[M]^+$ (95), 1215 $[M+K]^+$ (100).
10. The stoichiometry of complexes and the complexation constants were calculated using computer program OPIUM (Kyvala M.) freely available at http://www.natur.cuni.cz/~kyvala/opium.html.

11. Unfavourable electrostatic interactions between the K^+ complex and Ag^+ can also contribute to silver not being complexed as suggested by one of the referees.
12. X-Ray data for **6**: $C_{80}H_{88}O_8 \cdot CF_3SO_3Ag \cdot 2CHCl_3$: $M = 1673.26$ g mol^{-1}, triclinic system, space group $P\bar{1}$, $a = 12.539(1)$, $b = 15.416(1)$, $c = 22.193(1)$ Å, $\alpha = 78.03(1)$, $\beta = 88.93(1)$, $\gamma = 73.20(1)$, $Z = 2$, $V = 4013.6(1)$ Å^3, $D_c = 1.38$ g cm^{-3}, μ(Mo Kα) $= 0.54$ mm^{-1}, crystal dimensions of 0.25×0.25×0.20 mm. Data were collected at 150(2) K on an Nonius KappaCCD diffractometer with graphite monochromated Mo Kα radiation.[13] The structure was solved by direct methods[14] and anisotropically refined by full-matrix least-squares on F[15] to final $R = 0.0955$ and $R_w = 0.0970$ using 12 215 independent reflections ($\theta_{max} = 26°$). The disorder of two ethylenoxy units was modelled. Carbon atoms with partial occupancy were refined isotropically. Only hydrogen atoms with full occupancy were included. They were placed from expected geometry and were not refined. Solvent atoms were localised with partial occupancies from Fourier maps. Due to the low crystal quality caused by twinning and extremely high desolvatation during crystal adjusting it was not possible to localise all parts of disordered solvent molecules ($CHCl_3$). Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 174277. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).
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