Sulfur-capped cyclodextrins: a new class of cavitands with extroverted as well as introverted donor functionalities†

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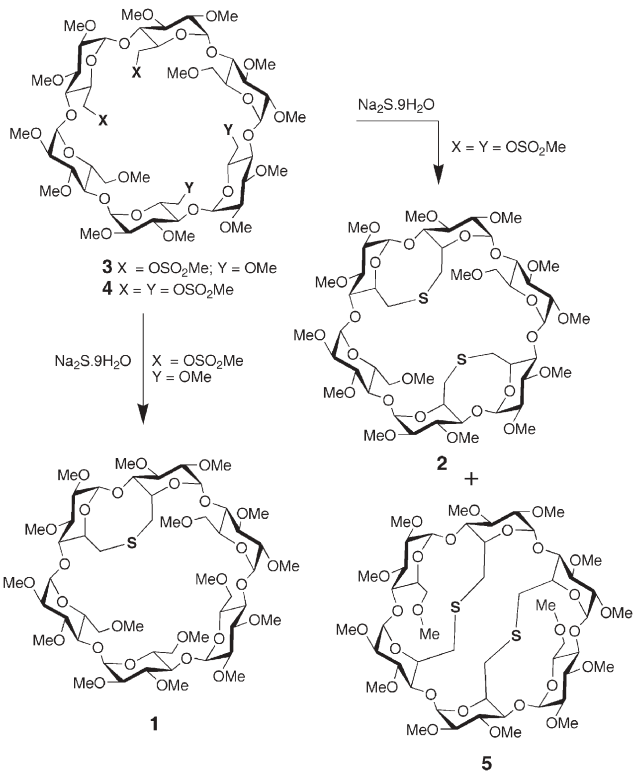
Ansa-cyclodextrins were obtained in high yields by reaction of sodium sulfide with *A*,*B*-di- or *A*,*B*,*D*,*E*-tetramesylated α-CD precursors; the resulting thiocavitands are suitable for forming nanotubular molecules, as well as for hosting metal-organic fragments.

Highly preorganised ditopic ligands are potential building blocks for the construction of large and well-defined molecular assemblies with metal ions acting as versatile connectors.[1–3] When built on molecular cavities, these ligands are of particular interest as their transition metal complexes allow the study of metal-centred reactions,[4] especially catalytic ones, occurring within a confined environment.[5–7] In recent years, we have reported a number of 'introverted' cyclodextrin-derived P(III) ligands,[8] which, upon metal complexation, produce large chelate complexes with the metal centre maintained near the cavity entrance. In several of these systems, the cavity was shown to act as a second sphere of coordination and influence the complexation process.[9–11] In the present work, we describe how a methylated α-CD platform can be capped, for the first time, by a monoatomic unit made of sulfur. The resulting thiacavitands display either *intra*- or *extra*-cavity coordination modes promoting the formation of nano-sized receptors.

The synthesis of both ligands **1** and **2**‡ is related to that described previously for 'phosphinidene'-capped CDs.[8] Thus, reaction of *A*,*B*-dimesylated precursor **3** with an excess of the soft nucleophile[12] $Na_2S{\cdot}9H_2O$ in DMSO (method A) afforded **1** in nearly quantitative yield (Scheme 1). The synthesis of the C_2-symmetrical ligand **2** proved to be more challenging as treatment of *A*,*B*,*D*,*E*-tetramesylate **4** with the same dianion resulted not only in the capping of adjacent glucose units, but also in some *A*,*C*-capping. The desired doubly-capped CD **2** was isolated with a yield of 64% *vs.* 4% for its C_2-symmetrical *A*,*C*-capped regioisomer **5**.§ When the same reaction was carried out in acetone in the presence of 18-crown-6 (method B), nearly the same proportion of regioisomers was observed (63% of **2** *vs.* 6% of **5**). The ^{1}H NMR spectra of both **1** and **2** are in agreement with an overall circular CD torus as all anomeric protons lie in a narrow range ($\Delta\delta_{max} < 0.07$ ppm). Conversely, the ^{1}H NMR spectrum of **5** reveals a considerable dispersion of the H-1 protons ($\Delta\delta_{max} = 0.53$ ppm), in keeping with a marked shape modification also present in phosphinidene *A*,*C*-capped species.[8] The formation of such a strained macrocycle must be much less favourable than that of **2**, hence accounting for the regioselectivity observed.

Although **2** is only partially soluble in water, it reacts with K_2PtCl_4 in this medium to afford a mixture of chelate complex **6** and dimer **7** in 50% and 33% yield, respectively (Scheme 2). Interestingly, when **2** was reacted with K_2PdCl_4 under the same conditions, only the dimer **8** was formed in almost quantitative yield. Although they interconvert very slowly in solution, **6** and **7** could be separated by column chromatography and unequivocally identified. The MS spectrum of **6** displays a large peak at m/z = 1453.4 for $[M + Na]^+$, indicating the presence of a chelate complex. Furthermore, its ^{1}H NMR spectrum does not display any downfield shifts for inner-cavity protons, which is in agreement



Scheme 1 Syntheses of ligands **1**, **2** and **5**.

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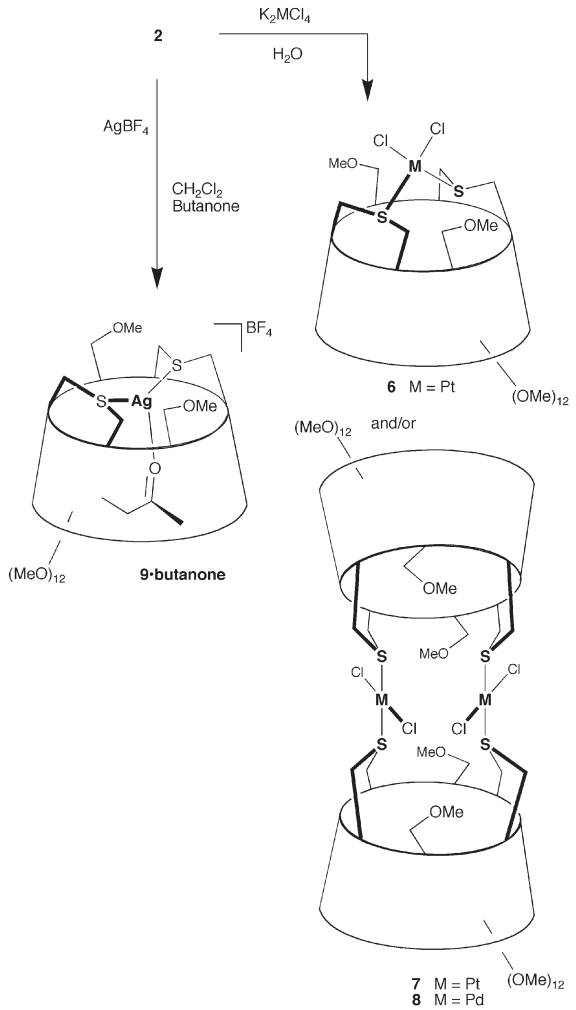
† Electronic supplementary information (ESI) available: synthesis and full characterization of all compounds. See DOI: 10.1039/b603400d



Scheme 2 Syntheses of complexes **6**, **7**, **8** and **9**.

with the absence of chloride ligands inside the cavity ($\delta_{H\text{-}5} <$ 4.42 ppm).[10,13] The latter observation, together with the fact that the IR spectrum shows two absorption bands at 326 and 338 cm^{-1} assigned to Pt–Cl vibrations, indicates that the complex stereochemistry is *cis*[14] and that the $PtCl_2$ unit lies outside the cavity.

An X-ray diffraction study on **8**¶ (Fig. 1) revealed a nanotubular structure with a top to bottom length of *ca.* 18 Å. The metallocavitand is composed of two undistorted CD tori linked together by two rigid $PdCl_2$ bridges. The two Pd centres are separated by a distance of 5.5 Å, leaving enough space between them for a guest to be included. The planes defined by both $PdCl_2S_2$ units deviate somewhat from parallelism, the interplanar angle being 25.2°. The Pd–S distances, ranging from 2.32 to 2.35 Å, and the S–P–S angles (172.4° and 175.1°) are typical of *trans*-MCl_2 complexes derived from dithioethers.[15] Dimers **7** and **8** are isostructural as their NMR spectra are nearly identical. Their MS spectra are, however, quite different since the signals for dimer ions are much more intense for **8** than for **7**. This is understandable because the latter is in equilibrium with its monomeric counterpart **6**. Clearly, only the 'external' sulfur lone pairs are involved in the coordination of neutral MCl_2 fragments.

The situation is noticeably different when ligand **2** is reacted with a metal cation like Ag^+. In this case, only the internal sulfur

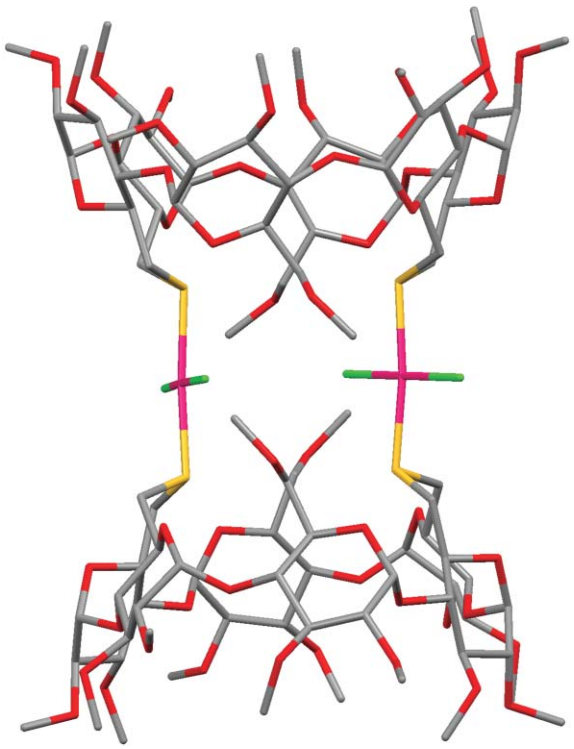


Fig. 1 X-ray structure of the dimeric palladium complex **8**. Side-view of the hyperboloid. The solvent molecules are not shown.

lone pairs participate in metal coordination as revealed by an X-ray diffraction study on complex **9** (Fig. 2).‖ Surprisingly, the

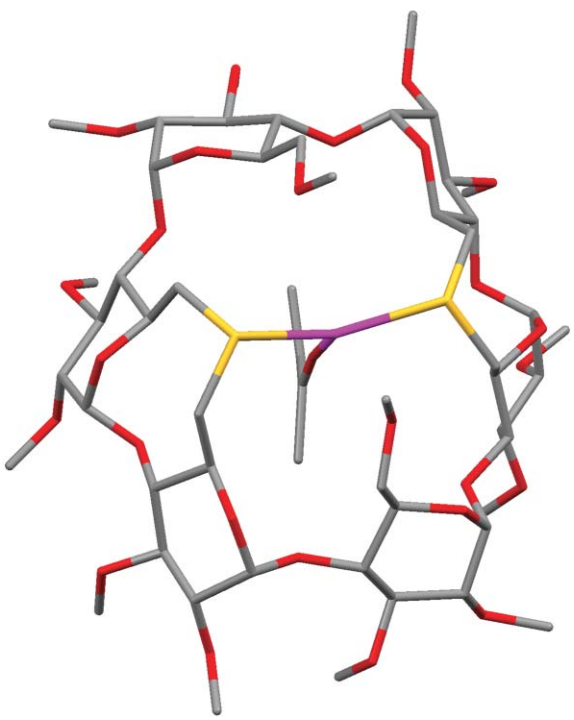


Fig. 2 X-ray structure of the silver complex **9·butanone**. View from the top showing the orientation of the included butanone molecule. For clarity, the non-coordinated solvent molecules and the BF_4 counter-ion are not shown.

silver(I) cation is also bound to a butanone molecule, which is entirely included in the CD cavity and nearly perpendicular to the plane defined by the S–Ag–S fragment. The geometry around the metal is therefore trigonal with large, but not unexceptional S–Ag–S angles (136.5° and 140.2° respectively, for the two molecules present in the unit cell). The S–Ag (about 2.48 Å) and O–Ag (2.43 Å) bond lengths are not uncommon either.[16] A remarkable feature of complex **9** is the ability of the slightly deformed CD cavity to orient the included guest along the longest axis of its cross-section (9.24 Å for the longest O(4)–O′(4) separation *vs.* 8.23 Å for the shortest). The addition of an excess butanone to a $CDCl_3$ solution of **9** caused some of the inner-cavity H-5 and H-3 CD protons to be strongly downfield shifted ($\Delta\delta_{max}$ = +0.76 and +0.86 ppm, respectively) whereas CD protons lying outside the cavity were hardly affected. Clearly, complex **9** must adopt the same structure in solution as in the solid state in the presence of butanone. A titration experiment relying on these ^{1}H NMR shifts proved the existence of a 1 : 1 complex with a very low K_a value of 0.4 ± 0.1 M^{-1}.**

The new dithioethers are appropriate ligands for preparing very rigid nanotubular metallocavitands. It is hoped that the development of water-soluble non-methylated analogues of the latter will pave the way to the selective inclusion of very long molecules, including polymers, in aqueous medium. These results also demonstrate how useful a CD probe can be for studying very subtle and weak coordination processes taking place within a confined environment.

Notes and references

‡ All compounds were fully characterized on the basis of their spectral data and C–H–N analysis (see supplementary information).

§ A small amount (4%) of a CD species doubly-capped at the *A*,*B* and *D*,*E* positions with disulfide bridges was also recovered.

¶ Crystal data for $C_{104}H_{168}Cl_4O_{52}Pd_2S_4\cdot 2.5C_2H_2Cl_4\cdot 2CH_3OH$ (**8**·2.5$C_2H_2Cl_4$·2CH_3OH), M = 3216.90, triclinic, $P\bar{1}$, a = 14.5623(3), b = 16.5684(3), c = 17.4742(3) Å, α = 99.074(1), β = 97.339(1), γ = 116.020(1)°, U = 3648.0(1) Å^3, Z = 1, T = 120(1) K, 1667 variables and 25617 reflections with [$I > 2.0\sigma(I)$], R = 0.068, R_w = 0.186 and S_w = 1.020, $\Delta\rho < 2.1$ e Å^{-3}. The compound crystallizes with two disordered molecules of tetrachloroethane sitting at each end of the 'tube'. There are a further two molecules of methanol and one molecule of tetrachloroethane lying outside the cavity. CCDC 273925. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b603400d

‖ Crystal data for $2(C_{50}H_{84}AgBF_4O_{26}S_2\cdot C_4H_8O)\cdot 3H_2O$ (**9**·**butanone**·3H_2O), M = 2918.20, monoclinic, $P2_1$, a = 16.4968(2), b = 15.7557(2), c = 27.3215(4) Å, β = 102.994(1)°, U = 6919.5(2) Å^3, Z = 2, T = 120(1) K, 1630 variables and 23660 observations with [$I > 2.0\sigma(I)$], R = 0.051, R_w = 0.108 and S_w= 1.007, $\Delta\rho < 1.06$ e Å^{-3}. One of the two butanone molecules (O201…) has two atoms with rather large thermal ellipsoids owing to a small positional disorder. The hydrogen atoms of the three water molecules were found with Fourier difference and not refined. CCDC 282983. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b603400d

** The titration procedure is detailed in the supplementary information.

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