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ORIGINAL ARTICLE

# Cyclodextrin-based thiacavitands as building blocks for the construction of metallo-nanotubes

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**Abstract** Two new cyclodextrin-based ligands with dual exo/endo binding domains were synthesised in high yields by reacting dimesylated or tetramesylated α-CD derivatives with sodium sulfide in either dimethylsulfoxyde or acetone/18-crown-6. The capping of adjacent glucose units was shown to be strongly favoured in both cases. Depending on the nature of the metal precursor being used, one of the synthesised thiacavitands forms either rigid nanotubular dimers or chelate complexes having receptor properties upon metal complexation.

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## Introduction

Intense interest has been focussed in recent years on the design of conical cavities containing capping units with endo-oriented donor sites [1]. Ligands of this type constitute valuable synthons for the study of reactions that take place in a confined environment, such as for example ligand exchange reactions occurring in a molecular funnel [2] or polymerisation reactions triggered inside a molecular tube [3]. While the native cyclodextrins (CDs) provide valuable starting compounds for such cavitands, no capped cyclodextrin with a dual exo/endo binding functionality has been described yet. As part of an ongoing programme aimed at the synthesis of capped CDs, we report herein the synthesis and coordination properties of α-CD derivatives bearing one or two sulfur-containing handles. The latter were used for the preparation of CD complexes in which the metal is located either inside or outside the cavity.

## Materials and method

All commercial reagents were used as supplied. Solvents were dried by conventional methods and distilled immediately prior use. Column chromatography was performed on silica gel 60 (particle size 40–63 mM, 230–240 mesh. Dimesylate **1** and tetramesylate **2** were prepared according to a previously published method [4]. All compounds were fully characterized using the following methods. Routine $^{1}H$, and $^{13}C\{^{1}H\}$ NMR

spectra were recorded with FT Bruker AC300 ($^1$H: 300.1 MHz, $^{13}$C: 75.5 MHz) instruments. $^1$H NMR data were referenced to residual protiated solvents (7.26 ppm for $CDCl_3$) and $^{13}$C chemical shifts are relative to deuterated solvents (77.0 ppm for $CDCl_3$). Mass spectra were recorded on a Bruker Micro TOF spectrometer (ESI) using $CH_2Cl_2$, $CH_3CN$ or $CH_3OH$ as solvent. IR spectra were recorded on a Digilab Excalibur FTS 3000. Elemental analyses were performed by the Service de Microanalyse, Faculté de Chimie, Strasbourg. Melting points were determined with a Büchi 535 capillary melting point apparatus.

General procedures for the synthesis of the sulfur-containing ligands

*Method A*

A solution of tetramesylate **2** (0.400 g; 0.27 mmol) in degassed DMSO (8 ml) was treated with powdered hydrated sodium sulfide ($Na_2S{\cdot}9H_2O$, 0.200 g, 0.84 mmol). After 2 h stirring at room temperature, the reaction mixture was evaporated to dryness in vacuo. The residue was dissolved in 2 M NaOH (60 ml) and extracted with $CH_2Cl_2$ (4 × 150 ml). The organic phase was washed with water (100 ml) and dried ($MgSO_4$). Removal of the solvent in vacuo gave a yellow solid, which was subjected to column chromatography [$SiO_2$, MeOH/$CH_2Cl_2$, 03:97, *v*/*v*] to afford in their order of elution **4** (0.011 g, 3 %), **5** (0.201 g, 64%), and **6** (0.013 g, 4%), respectively. They were characterised as follows:

Fraction 1, **4**: colourless solid. $^1$H NMR $\delta$ ($CDCl_3$, 20 °C): 2.23–2.49 (4H, H-6a$^{A,C,E,F}$), 3.04–4.29 (32H, H-2, H-3, H-4, H-5, H-6$^{B,E}$, H-6b$^{A,C,E,F}$), 3.35 (6H, s, MeO), 3.44 (6H, s, MeO), 3.50 (6H, s, MeO), 3.53 (6H, s, MeO), 3.56 (6H, s, MeO), 3.59 (6H, s, MeO), 3.60 (6H, s, MeO), 4.96 (2H, d, $^3J_{H-1,H-2}$ = 3 Hz, H–1), 5.08 (2H, d, $^3J_{H-1,H-2}$ = 2.7 Hz, H-1), 5.49 (2H, d, $^3J_{H-1,H-2}$ = 3.3 Hz, H-1). Elemental analysis found C, 51.75, H, 7.34; $C_{50}H_{84}O_{26}S_2$ (1165.32) requires C, 51.53, H, 7.26.

Fraction 2, **5**: colourless solid, m.p. 205–207 °C. $^1$H NMR $\delta$ (assignment by COSY and HMQC) ($CDCl_3$, 20 °C): 2.65–2.76 (4H, H-6a$^{A,B,D,E}$), 3.34 (6H, s, MeO-6), 3.45 (12H, s, MeO), 3.49 (6H, s, MeO), 3.58 (6H, s, MeO), 3.61 (6H, s, MeO), 3.65 (6H, s, MeO), 3.07–3.68 (22H, H-2, H-3, H-4, H-6$^{C,F}$), 3.75–3.85 (4H, H-6b$^{A,B,D,E}$), 3.91 (2H, m, H-5$^{C,F}$), 4.11 (2H, m, H-5$^{A,D\ or\ B,E}$), 4.29 (2H, m, H-5$^{B,E\ or\ A,D}$), 4.95 (2H, d, $^3J_{H-1,H-2}$ = 3.3 Hz, H-1$^{A,D\ or\ B,E}$), 4.98 (2H, d, $^3J_{H-1,H-2}$ = 3.3 Hz, H-1$^{B,E\ or\ A,D}$), 5.01 (2H, d, $^3J_{H-1,H-2}$ = 4.5 Hz, H-1$^{C,F}$). Elemental analysis found C, 53.59, H, 7.83; $C_{50}H_{84}O_{26}S_2{\cdot}C_6H_{12}$ (1165.32 + 84.16) requires C, 53.83, H, 7.74.

Fraction 3, **6**: colourless solid, m.p. 223–225 °C. $^1$H NMR $\delta$ ($CDCl_3$, 20 °C): 2.44 (2H, m, H-6a$^{A,D\ or\ B,E}$), 3.07–4.26 (34H, H-2, H-3, H-4, H-5, H-6b$^{A,D\ or\ B,E}$, H-6$^{A,D\ or\ B,E}$, H-6$^{C,F}$), 3.36 (6H, s, MeO), 3.46 (6H, s, MeO), 3.47 (6H, s, MeO), 3.48 (6H, s, MeO), 3.61 (6H, s, MeO), 3.62 (6H, s, MeO), 3.63 (6H, s, MeO), 4.95 (2H, d, $^3J_{H-1,H-2}$ = 3.3 Hz, H-1), 4.99 (2H, d, $^3J_{H-1,H-2}$ = 3.6 Hz, H-1), 5.05 (2H, d, $^3J_{H-1,H-2}$ = 3.6 Hz, H-1). Elemental analysis found C, 48.39, H, 6.96; $C_{50}H_{84}O_{26}S_4{\cdot}H_2O$ (1229.45 + 18.01) requires C, 48.14, H, 6.95.

*Method B*

A solution of tetramesylate **2** (0.400 g; 0.27 mmol) in degassed acetone (25 ml) was treated with 18-crown-6 (0.873 g, 3.30 mmol) upon which powdered, hydrated sodium sulfide ($Na_2S{\cdot}9\ H_2O$, 0.395 g, 1.65 mmol) was added. After 2 h stirring at room temperature, the reaction mixture was evaporated to dryness in vacuo. The residue was dissolved in saturated aqueous $K_2CO_3$ solution (60 ml) and extracted with $CH_2Cl_2$ (4 × 150 ml). The organic solution was washed repeatedly with saturated aqueous KCl solution (5 × 50 ml) before being dried ($MgSO_4$). Removal of the solvent in vacuo gave a yellow solid, which was subjected to column chromatography [$SiO_2$, MeOH/$CH_2Cl_2$, 03:97, *v*/*v*] to afford **4** (0.020 g, 6%) and **5** (0.198 g, 63%), respectively.

Compound **3** was prepared from dimesylate **1** in 95% yield according to method A: colourless solid. m.p. 115–117 °C. $^1$H NMR $\delta$ ($CDCl_3$, 300,1 MHz): 2.64–2.78 (2 H, H-6$^{A\ or\ B}$), 3.08–4.36 (34H, H-2, H-3, H-4, H-5, H-6$^{B\ or\ A,C,D,E,F}$), 3.34 (3H, s, MeO), 3.35 (3H, s, MeO), 3.36 (6H, s, MeO), 3.45 (3H, s, MeO), 3.46 (3H, s, MeO), 3.47 (6H, s, MeO), 3.48 (3H, s, MeO), 3.49 (3H, s, MeO), 3.59 (3H, s, MeO), 3.61 (6H, s, MeO), 3.63 (3H, s, MeO), 3.64 (3H, s, MeO), 3.66 (3H, s, MeO), 4.97 (1H, d, 3$J_{H-1,H-2}$ = 3.5 Hz, H-1), 4.98 (1H, d, $^3J_{H-1,H-2}$ = 3.3 Hz, H-1), 5.01 (1H, d, $^3J_{H-1,H-2}$ = 4.4 Hz, H-1), 5.04 (3H, d, $^3J_{H-1,H-2}$ = 3.1 Hz, H-1). Elemental analysis found C, 48.40, H, 7.27; $C_{52}H_{90}O_{28}S{\cdot}CHCl_3$ (1195.33 + 119.38) requires C, 48.42, H, 6.98.

Syntheses of Pt and Pd complexes

*Platinum complexes*

A solution of $K_2PtCl_4$ (0.040 g; 0.096 mmol) in $H_2O$ (10 ml) was added to a solution of **5** (0.100 g;

0.085 mmol) in $H_2O$ (10 ml). After 5 h stirring at room temperature, the reaction mixture was extracted with $CH_2Cl_2$ (4 × 40 ml). The organic extract was dried over $MgSO_4$ before being evaporated to dryness. Removal of the solvent in vacuo afforded a yellow residue. The latter was subjected to column chromatography [$SiO_2$, MeOH/$CH_2Cl_2$, 03:97 → 05:95, *v*/*v*] to afford afford [$PtCl_2$·**5**] (0.061 g, 50 %) and [$PtCl_2$·**5**]$_2$ (0.040 g, 33%), respectively.

[$PtCl_2$·**5**]: pale yellow solid, m.p. >250 °C (dec.). $^1$H NMR $\delta$ (assignment by COSY and HMQC) ($CDCl_3$, 20 °C): 3.15–3.91 (30H, H-2, H-3, H-4, H-5$^{A,D\text{ or }B,E}$, H-5$^{C,F}$, H-6$_a^{A,B,D,E}$, H-6$^{C,F}$), 4.18–4.42 (6H, H-5$^{B,E\text{ or }A,D}$, H-6$_b^{A,B,D,E}$), 3.46 (6H, s, MeO), 3.48 (6H, s, MeO), 3.49 (6H, s, MeO), 3.55 (6H, s, MeO), 3.58 (6H, s, MeO), 3.60 (6H, s, MeO), 3.71 (6H, s, MeO), 4.93 (2H, d, $^3J_{H-1,H-2}$ = 3.8 Hz, H-1$^{A,D\text{ or }B,E}$), 5.01 (2H, d, $^3J_{H-1,H-2}$ = 4.2 Hz, H-1$^{B,E\text{ or }A,D}$), 5.11 (2H, d, $^3J_{H-1,H-2}$ = 4.2 Hz, H-1$^{C,F}$). Elemental analysis found C, 43.57, H, 6.17; $C_{50}H_{84}O_{26}S_2PtCl_2$ (1431.31) requires C, 41.95, H, 5.91.

[$PtCl_2$·**5**]$_2$: yellow solid, m.p. >250 °C (dec.). $^1$H NMR $\delta$ ($CDCl_3$, 20 °C): 3.06–4.26 (36H, H-2, H-3, H-4, H-5, H-6), 3.43 (s, 6H, MeO), 3.47 (12H, s, MeO), 3.49 (6H, s, MeO), 3.60 (6H, s, MeO), 3.62 (6H, s, MeO), 3.63 (6H, s, MeO), 4.99–5.02 (6H, m, H-1). Elemental analysis found C, 40.18, H, 5.95; $C_{100}H_{168}O_{52}S_4Pt_2Cl_4$·$CHCl_3$.$H_2O$ (2862.61 + 119.37 + 18.01) requires C, 40.44, H, 5.75.

*Synthesis of [$PdCl_2$· **5**]$_2$*

Ligand **5** (0.220 g, 0,188 mmol) was treated with $K_2PdCl_4$ (0.067 g, 0.207 mmol) in $H_2O$ (20 ml) according to the above procedure to afford [$PdCl_2$·**5**]$_2$ (0.225 g, 89%): orange solid, m.p. >250 °C (dec.). $^1$H NMR $\delta$ ($CDCl_3$, 20 °C): 3.02–3.88 (36H, H-2, H-3, H-4, H-5, H-6), 3.40 (6H, s, MeO), 3.46 (6H, s, MeO), 3.47 (6H, s, MeO), 3.49 (6H, s , MeO), 3.59 (6H, s, MeO), 3.62 (6H, s, MeO), 3.65 (6H, s, MeO), 4.96 (2H, d, $^3J_{H-1,H-2}$ = 3 Hz, H-1), 4.99 (2H, d, $^3J_{H-1,H-2}$ = 4.2 Hz, H-1), 5.03 (2H, d, $^3J_{H-1,H-2}$ = 3.6 Hz, H-1). Elemental analysis found C, 44.30, H, 6.24; $C_{100}H_{168}O_{52}S_4Pd_2Cl_4$·$H_2O$ (2685.25 + 18.01) requires C, 44.43, H, 6.34.

Synthesis of [Ag·**5**][$BF_4$]

A solution of $AgBF_4$ (0.020 g; 0.103 mmol) in THF (5 ml) was added to a solution of **5** (0.120 g; 0.103 mmol) in $CH_2Cl_2$ (15 ml). After 30 min stirring at room temperature, the reaction mixture was evaporated to dryness in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 ml). Addition of pentane to the latter caused the complex [Ag·**5**][$BF_4$] to precipitate as a white solid (0.107 g, 76%): m.p. >250 °C (dec.). $^1$H NMR $\delta$ (assignment by COSY and HMQC) ($CDCl_3$, 20 °C): 2.80–2.93 (4H, H-6$_a^{A,B,D,E}$), 3.34 (6H, s, MeO), 3.46 (6H, s, MeO), 3.48 (6H, s, MeO), 3.53 (6H, s, MeO), 3.63 (6H, s, MeO), 3.66 (12H, s, MeO), 3.07–3.85 (22H, H-2, H-3, H-4, H-6$_b^{A,D\text{ or }D,E}$, H-6$_a^{CF}$), 3.93–4.04 (2H, H-6$_b^{B,E\text{ or }A,D}$), 4.16 (2 H, m, H-5$^{C,F}$), 4.23–4.36 (4 H, H-5$^{A,D\text{ or }B,E}$, H-6$_b^{C,F}$), 4.58 (2 H, m, H-5$^{B,E\text{ or }A,D}$), 4.84 (2 H, d, $^3J_{H-1,H-2}$ = 3.3 Hz, H-1$^{A,D\text{ or }B,E}$), 4.93 (2H, d, $^3J_{H-1,H-2}$ = 3.1 Hz, H-1$^{C,F}$), 4.99 (2 H, d, $^3J_{H-1,H-2}$ = 4.5 Hz, H-1$^{B,E\text{ or }A,D}$). Elemental analysis found C, 43.14, H, 6.53; $C_{50}H_{84}O_{26}S_2AgBF_4$·$2H_2O$ (1360.00 + 38.17) requires C, 43.02, H, 6.35.

Stability constant determination by $^1$H NMR spectroscopy

The determination of the association constant of the complex [Ag·**5**·*butanone*][$BF_4$] is based on the chemical shift variation of some non-overlapping CD H-signals upon addition of an excess (1–32 equiv.) of butanone to a $1.5 \times 10^{-3}$ M solution of [Ag·**5**][$BF_4$] in $CDCl_3$. The data were treated by a nonlinear regression analysis program (Prism 4.0, GraphPad,) in order to extract $K_a$ and CIS values for the 1:1 complex.

Crystallographic data for compounds **5**, **6** and [$PtCl_2$·**5**]$_2$

Data were registered on an Oxford Diffraction Xcalibur Saphir 3 diffractometer with graphite monochromatized Mo-K$\alpha$ radiation (**5**), a Bruker SMART 6000 diffractometer using Cu-*K*$\alpha$ radiation (**6**) or a Bruker SMART 1000 diffractometer using Mo-*K*$\alpha$ radiation ([$PtCl_2$·**5**]$_2$). Absorption corrections were performed on the basis of multiple scans. The structures of **5** and **6** were solved routinely using direct methods with the program SHELXS-97. For the Pt complex, the positions of the Pt atoms were determined from the Patterson function and those of the S and Cl atoms from subsequent difference Fourier syntheses, but the pronounced pseudosymmetry (all these atoms are related by a pseudo-inversion centre) meant that all further atoms had to be identified by painstaking inspection of a double image. Structures were refined anisotropically with SHELXL-97 [5]. Hydrogen atoms were included using a riding model, with methyl groups assumed to be ideally staggered.

Special features of refinement for **5**: two slightly different molecules of **5** were found in the unit cell together with two ½ molecules of diethylether and five molecules of cyclohexane, two of which are included in the CDs.

Special features of refinement for **6**: Two cyclohexane sites were identified. The site in the cavity of the tetrasulfide is well ordered; the other site is badly disordered, and its hydrogens were not set. Two methyl groups (C27 and C57) are disordered over two alternative sites. Special features of refinement for $[PtCl_2{\cdot}\mathbf{5}]_2$: Two tetrachloroethane and four methanol sites were identified, and one further difference peak tentatively refined as a water oxygen. Hydrogen atoms of methanol and water were not included. The refinement was too large for full-matrix methods and was therefore separated into two blocks. Because of the pseudosymmetry, molecular dimensions involving light atoms should be interpreted with caution.

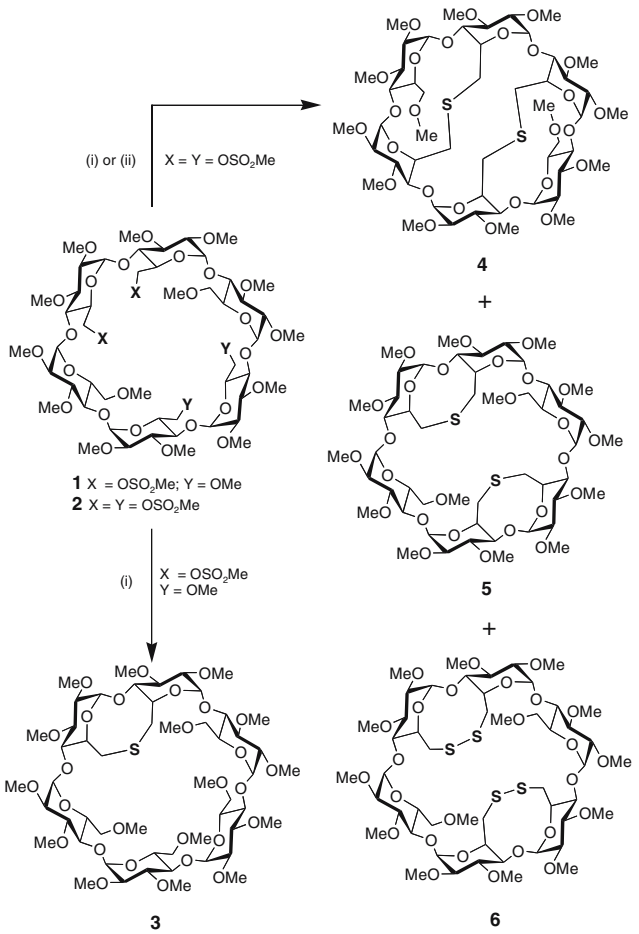
Crystal data for **5**: $2C_{50}H_{84}O_{26}S_2{\cdot}\mathbf{5}C_6H_{12}{\cdot}2 \times 0.5\ C_4H_{10}O$, $M_r = 2825.48$, tetragonal, $a = 14.5652(4)$, $c = 70.498(2)$ Å, $V = 14956(4)$ Å$^3$, $T = 100(1)$ K, space group $P43$, $Z = 4$, $D_c = 1.255$ g cm$^{-3}$, $\mu$(Mo-K$_\alpha$) = 1.48 cm$^{-1}$, Crystal habit: colourless tablet $0.25 \times 0.25 \times 0.10$ mm. Reflections: measured 93118 to $2\theta$ 54°, 21193 unique, $R_{int} = 0.096$. Refinement: 1717 variables, $R1 = 0.0973$, $wR2 = 0.262$, $S = 1.02$, $\Delta\rho <$ 0.44 e Å$^{-3}$, Flack parameter 0.04(11).

Crystal data for **6**: $C_{50}H_{84}O_{26}S_4{\cdot}2C_6H_{12}$, $M_r = 1397.72$, orthorhombic, $a = 15.6763(4)$, $b = 20.1559(5)$, $c = 22.7690(6)$ Å, $V = 7194.3(3)$ Å$^3$, $T = 100$ K, space group $P2_12_12_1$, $Z = 4$, $D_c = 1.290$ g cm$^{-3}$, $\mu$ (Mo-K$_\alpha$) = 1.86 cm$^{-1}$. Crystal habit: colourless tablet $0.2 \times 0.1 \times 0.05$ mm. Reflections: measured 49433 to $2\theta$ 133°, 11033 unique, $R_{int} = 0.039$. Refinement: 794 variables, 902 restraints (mostly to components of displacement parameters), $R\ 1 = 0.0772$, $wR\ 2 = 0.219$, $S = 1.06$, $\Delta\rho < 0.92$ e Å$^{-3}$, Flack parameter 0.03(3).

Crystal data for $[PtCl_2{\cdot}\mathbf{5}]_2$: $C_{92}H_{146}O_{52}Pd_2S_4{\cdot}2C_2H_2Cl_4{\cdot}4CH_3OH{\cdot}H_2O$, $M_r = 3344.42$, triclinic, $a = 14.6074(8)$, $b = 16.5936(12)$, $c = 17.4212(11)$ Å, $\alpha = 99.039(4)$, $\beta = 97.212(4)$, $\gamma = 115.888(4)$°, $V = 3661.1(4)$ Å$^3$, $T = 133(2)$ K, space group $P1$, $Z = 1$, $D_c = 1.517$ g cm$^{-3}$, $\mu$ (Mo-K$_\alpha$) = 2.27 cm$^{-1}$. Crystal habit: pale yellow tablet $0.4 \times 0.3 \times 0.12$ mm. Reflections: measured 84220 to $2\theta$ 61°, 40780 unique, $R_{int} = 0.022$. Refinement: 1573 variables, 1436 restraints (as above), $R1 = 0.0490$, $wR2 = 0.149$, $S = 1.06$, $\Delta\rho < 3.4$ e Å$^{-3}$, Flack parameter 0.024(3).

## Results and discussion

Recently, *A,B*-phosphinidene-capped CDs have been prepared in high yields and with excellent regio- and stereoselectivities by reacting a phenyl phosphide dianion with either dimesylate **1** or tetramesylate **2** [6]. We anticipated that replacing the soft nucleophile $PPh_2^-$ with the equally soft sulfide dianion [7] $S_2^-$ would lead to new very rigid sulfur-capped CD ligands. Indeed, cyclisation of dimesylate **1** with $Na_2S{\cdot}9\ H_2O$ in DMSO produces the *A,B*-capped CD **3** in nearly quantitative yield (Scheme 1). The double cyclisation of **2** using the same method (Method A) proved to be more difficult as, together with the expected *A,B,D,E* double-capped CD **5** (64%), small amounts of two undesired side-products with similar polarities, were isolated and identified, namely the *A,C,E,F* double-capped species **4** (3%) and the *A,B,D,E* disulfide double-capped CD **6** (4%) (Scheme 1). The latter probably results from air oxidation of a tetrathiol intermediate during work-up. In order to improve the selectivity of the reaction, a second method using the combination acetone/18-crown–6 instead of DMSO as solvent (Method B) was tested. Nearly the same yields of **4** and **5** were obtained. However, the formation of the disulfide species **6** was not detected. Interestingly, the use of 18-crown-6 led to much better results than with the stronger $Na^+$ binder 15-crown-5. Crystals of **5**




**Scheme 1** Syntheses of ligands **3**, **4**, **5** and **6**: (i) $Na_2S.9H_2O$, DMSO; (ii) $Na_2S.9\ H_2O$, 18-crown-6, acetone

and **6** suitable for X-ray diffraction were grown by slow evaporation from cyclohexane and the molecular structures of both compounds were obtained (Fig. 1). The overall shape of **5** is that of a circular $C_2$-symmetric CD. The two CD molecules present in the unit cell are almost identical, each hosting a cyclohexane molecule. As expected for an undistorted species, all glucose units adopt the standard $^4C_1$ conformation. Given the fact that the three $^1$H NMR signals for anomeric protons appear in the same narrow range (4.95–5.01 ppm), the same must be true in solution unlike regioisomer **4**, which is likely to be very distorted as the same anomeric protons resonate over a much wider interval (4.96–5.49 ppm) [8]. Both sulfur atoms of **5** are part of a 9-membered ring involving adjacent units, which hold them tightly above the CD cavity. The distance separating the two sulfur atoms is only 5.5 Å versus 8.6 Å for the average mid-torus O(4)–O′(4) distance between opposite glucose units. Clearly, the disposition of the sulfur atoms in **5** atoms allows differentiating between a pair of *endo*-oriented lone pairs and a pair of *exo*-orientated ones with respect to the CD cavity and it is this particular feature, which dictates the coordination properties of the ligand. The molecular structure of **6** bears some strong resemblance with that of **5**. Like **5**, compound **6** comprises an undistorted CD torus and hosts a cyclohexane molecule within its cavity. The disulfide bridges, which are part of 10-membered rings, are also located above the primary face entrance so that the closest distance between two opposite sulfur atoms is only 4.6 Å. The fact that the sulfur bridges occupy more space in **6** than **5** has an incidence on the MeO-6 groups, which are pushed towards the exterior in **6**, whereas in **5**, the same methoxy groups close the cavity entrance (Fig. 1).

The use of cationic metal precursors is known to promote the formation of chelate complexes over oligomeric ones. The reaction between **5** and $AgBF_4$ (Scheme 2) was no exception as it produces a species the mass spectrum of which (peak at $m/z$ = 1274.4 for $[M\text{-}BF_4]^+$) unambiguously indicates that a chelate complex was formed. An X-ray diffraction study on a single crystal obtained by diffusion of pentane into a butanone solution of $[Ag\cdot\mathbf{5}][BF_4]$ revealed two closely related CDs, both having a single silver coordinated butanone inside an elongated CD cavity (9.2 Å for the longest O(4)–O′(4) separation versus 8.2 Å for the shortest one) which literally wraps itself around its guest (Fig. 2) [9]. The metal geometry is 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) [10]. In order to evaluate the strength of the butanone-silver bond in solution, the complex $[Ag\cdot\mathbf{5}][BF_4]$ was titrated with butanone in $CDCl_3$ solution using $^1$H NMR spectroscopy for monitoring the chemical shifts changes. As expected the CD protons located in the cavity experienced marked downfield shifts (up to $\Delta\delta_{max}$ = +0.76 and + 0.86 for some H-5 and H-3 atoms, respectively) whereas protons located outside the cavity were hardly affected ($\Delta\delta_{max}$ < 0.02 ppm). The association constant for the 1:1 complex was found to be astonishingly low ($K_a$ = 0.37 ± 0.1 $M^{-1}$), a value that was confirmed by the absence of any butanone adduct in the mass spectrum of $[Ag\cdot\mathbf{5}][BF_4]$ in butanone. A possible explanation for this observation is the presence of a $BF_4^-$ anion inside the cavity, which could act as a competitor. Anion inclusion inside a α-CD was recently found in the phosphine complex shown in Scheme 3 [11]. It is therefore not unlikely that the same feature occurs in $[Ag\cdot\mathbf{5}\cdot BF_4]$ and that a large excess of butanone is required to expel the $BF_4^-$ counter-ion from the cavity.

Unlike $[Ag\cdot\mathbf{5}][BF_4]$, in which the inward-looking lone pairs are solely involved in the complexation process, only ''external'' sulfur lone pairs participate in binding of the $MCl_2$ fragments. Thus, reaction of **5** with $K_2PdCl_4$ in water produced a single Pd(II) complex in

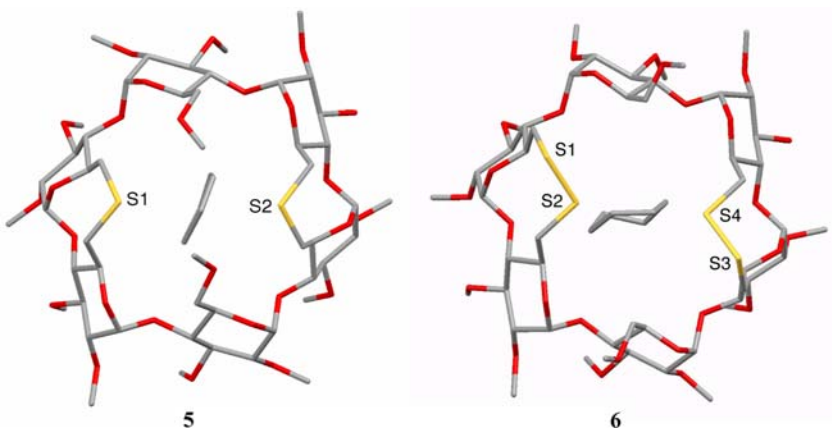
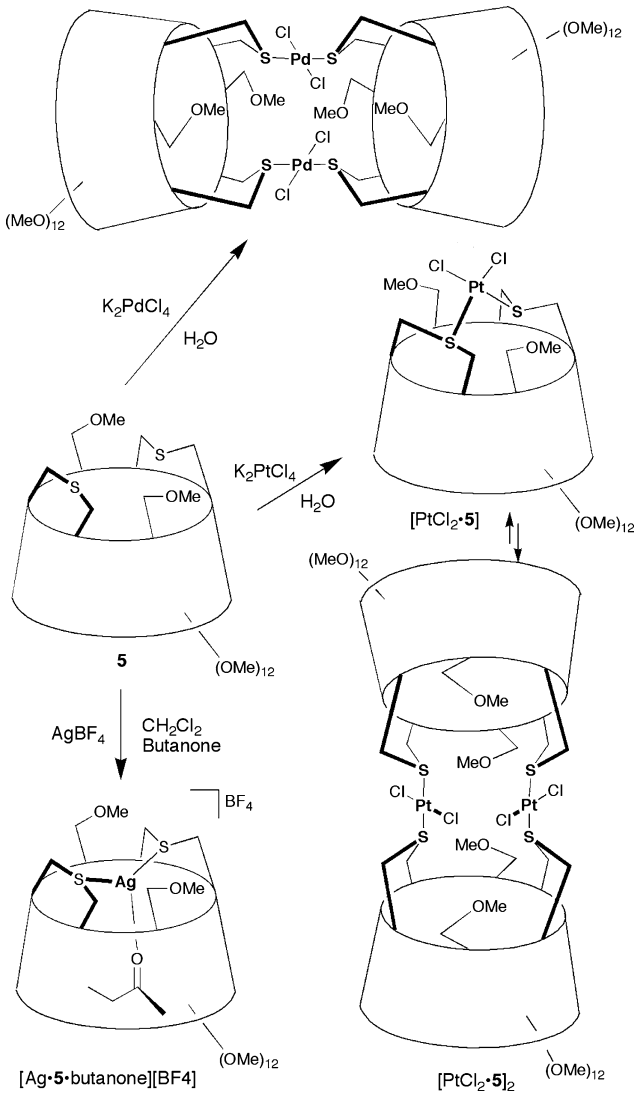



**Fig. 1** X-ray structures of thiocavitands **5** and **6**. Views from the top showing in both cases an included cyclohexane molecule. Solvent molecules that are not included in the CD cavity are not shown




**Scheme 2** Syntheses of complexes [Ag·**5**·butanone][$BF_4$], [$PtCl_2$·**5**], [$PtCl_2$·**5**]$_2$, and [$PdCl_2$·**5**]$_2$

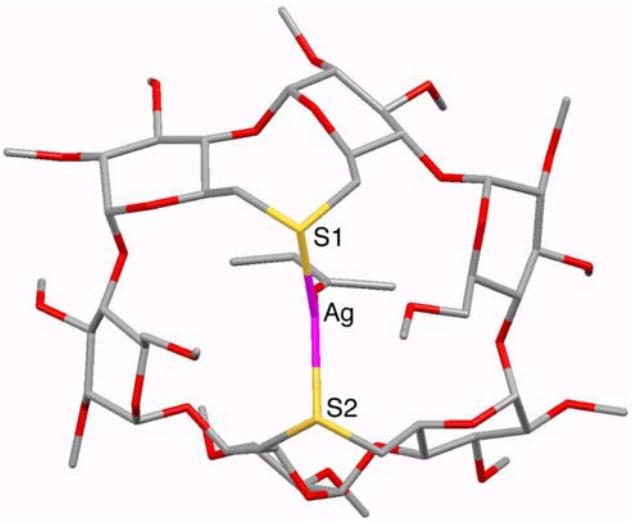
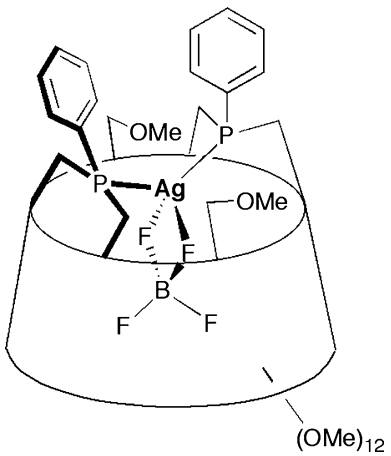



**Fig. 2** X-ray structure of the silver complex [Ag·**5**·butanone][$BF_4$] (only one molecule is shown). View from the top showing the included butanone molecule. The non-coordinated solvent molecules and the $BF_4^-$ counter-ion are not shown



**Scheme 3** $BF_4^-$ inclusion in a cyclodextrin-silver complex

almost quantitative yield (Scheme 2). The presence of intense ions in its mass spectrum at $m/z$ = 2707.7 and 2723.7 for $[M + Na]^+$ and $[M + K]^+$, respectively, indicate that the compound is a dimeric species and was formulated as [$PdCl_2$·**5**]$_2$. The outcome of the reaction was somewhat different when the platinum precursor $K_2PtCl_4$ was used under the same conditions since the reaction mixture consisted of two products (Scheme 2). Despite being in very slow equilibrium in solution, both complexes could be separated by standard column chromatography. As previously, the analogous dimeric species [$PtCl_2$·**5**]$_2$ was formed as evidenced by mass spectrometry (peaks at $m/z$ = 1453.9 for $[M + 2\ Na]^{2+}$ and 2886.0 for $[M + Na]^+$). This was further confirmed by NMR spectroscopy. Indeed, both $^1H$ and $^{13}C$ NMR spectra of [$PtCl_2$·**5**]$_2$ are nearly identical to those of [$PdCl_2$·**5**]$_2$ and indicate the presence of undistorted CD rings ($4.96 \le \delta_{H-1} \le 5.03$ ppm). Unlike that of [$PtCl_2$·**5**]$_2$, the mass spectrum of the second less polar species displays intense peaks at $m/z$ = 1436.5 for $[M–Cl + CH_3CN]^+$ and 1453.4 for $[M + Na]^+$, in keeping with the presence of the chelate complex [$PtCl_2$·**5**]. Because the inner-cavity H-5 protons are not shifted compared to those of the free ligands, the chlorine ligands must be located outside the cavity. This observation together with the presence of two absorption bands at 326 and 338 $cm^{-1}$ assigned to Pt–Cl vibrations in the IR spectrum indi-

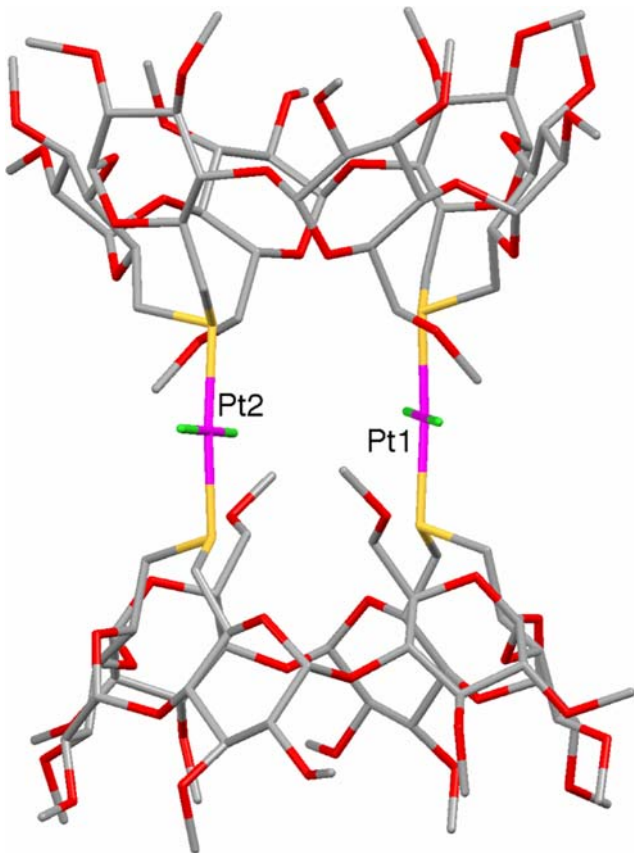



**Fig. 3** X-ray structure of the dimeric complex $[PtCl_2{\cdot}\mathbf{5}]_2$. Side-view of the nanotubular metallocavitand. The solvents molecules are not shown

cate that the complex stereochemistry is *cis* [12]. As expected for a chelate complex, its CD torus is more distorted ($4.93 \leq \delta_{H-1} \leq 5.11$ ppm) than those of the dimeric species (*vide infra*). The *trans* stereochemistry of the $MCl_2S_2$ unit in the latter was devised thanks to an X-ray diffraction study on $[PtCl_2{\cdot}\mathbf{5}]_2$ (Fig. 3). The S–P–S angles (172.0° and 173.6°) are typical of *trans*-$[MCl_2(SR_2)_2]$ complexes.[13] The metallocavitand has a nanotubular structure with a top to bottom length of *ca.* 18 Å. The planes defined by the $PtCl_2S_2$ units are not parallel, but at an angle of 22.8°. The distances between two opposite sulfur donor atoms of a same CD unit is smaller in $[PtCl_2{\cdot}\mathbf{5}]_2$ (5.3 Å and 5.4 Å) than in the ligand (*vide infra*), but longer than in the chelate complex $[Ag{\cdot}\mathbf{5}][BF_4]$ (*ca.* 4.6 Å), leaving enough space between them for a guest to be included.

## Conclusion

We have demonstrated that the bridging of adjacent glucose units in methylated CDs with monoatomic sulfur spacers is a very regioselective process, which gives access to a new class of CD ligands. The thiacavitands we synthesised are highly preorganized molecules, which can selectively form rigid dimeric nanotubes or chelate complexes depending on the metal precursor being used. It is hoped that non-methylated versions of our ligands will allow the development of water-soluble versions of the complexes described in this work. These could then possibly be used for performing catalytic intra-cavity reactions.

## Supporting information available

The crystallographic data for compounds **5**, **6** and $[PtCl_2{\cdot}\mathbf{5}]_2$ have been deposited with the Cambridge Structural Database in CIF format (CCDC-286532, CCDC-606511, and CCDC-606512, respectively). These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Center, 12, Union Road, Cambridge, CB2 1 EZ, UK; fax: (internat.) +44-1223/336-033; E-mail: deposit@ ccdc.cam.ac.uk].

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