Metal-Capped α-Cyclodextrins: Squaring the Circle

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This report describes the four-step synthesis of 6A,6D-diamino-6A,6D-dideoxy-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^B,6^C,6^E,6^F-hexadeca-*O*-methylcyclomaltohexaose (**5**), a methylated α-CD that bears two $-CH_2NH_2$ ligands located on diametrically opposed glucopyranose rings. Reaction of **5** with K_2PtCl_4 afforded the water-soluble chelate complex [$PtCl_2$(**5**)] where the metal center is bonded to cis-arranged nitrogen atoms. A single-crystal X-ray structure of the latter reveals the high distortion imposed on the CD structure by the short metallo-organic cap. The cyclodextrin core adopts an unprecedented elongated, almost rectangular shape, the shortest and longest $O(4)_n$ ... $O(4)_{n+3}$ distances being respectively 5.44 and 9.98 Å. Two opposing glucose rings are no longer in the usual $^4C_1$ chair conformation, but adopt an elongated $^OS_2$ skew-boat structure. The observed CD-flattening produces a highly preorganized hydrophilic pocket that complexes through multiple hydrogen bonding a single water molecule. Complex [$PtCl_2$(**5**)] and the corresponding synthetic intermediates were characterized by elemental analysis, MS, and IR and NMR spectroscopy.

Introduction

The α-, *β*-, and *γ*-cyclodextrins (CDs) which comprise respectively six, seven, and eight α(1→4)-linked D-(+)-glucopyranose units constitute an important class of naturally occurring macrocyclic molecules that have been thoroughly investigated over the last 100 years.[1−5] Their rigid bucket-shaped structure and the presence of a well-defined hydrophobic cavity are responsible for the formation in aqueous solution of inclusion complexes with a range of hydrophobic substrates[6−10] including metallo-organic complexes.[11−17] Chemical modification,[18] notably permethylation, often renders the macrocyclic structure much more flexible as a result of interglucose $O(2)_n$...$O(3)_{n-1}$ hydrogen bond breaking which can lead to significant shape modification of the torus.[19−22] Note, per-2,3,6-methylated CDs are more water soluble at room temperature than their natural analogues[23] and retain inclusion properties to a certain extent.[24] To date, strong deviation from a regular annulus has only been observed in per-2,3,6-methylated *β*-and *γ*-CDs (respectively abbreviated TM-*β*-CD and TM-*γ*-CD) whether free[25,26] or bound[27,28] whereas the smaller per-2,3,6-alkylated α-CDs do not depart significantly from a general circular shape.[29,30]

Following our previous work on chelating cyclodextrin ligands,[31−33] we now describe the synthesis and structural properties of a platinum complex that incorporates a highly distorted permethylated α-CD torus. This very unusual feature was brought about by capping a suitably difunctionalized α-CD

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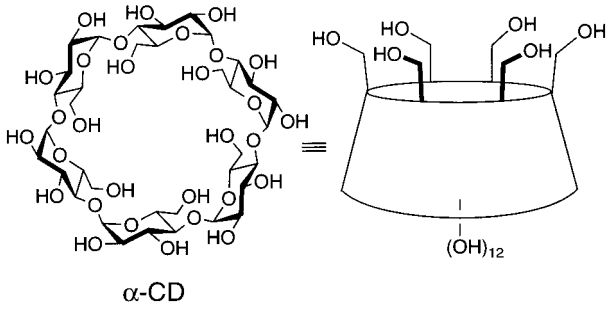
with a very short metallo-organic fragment consisting of a *cis*-$PtCl_2$ linker coordinated by two amine ligands located on the CD primary face. Formation of a chelate complex derived from a β-CD-based diamine has previously been reported, but no significant alteration of the cavity structure was observed.[34] Metal-mediated shape modification of cyclodextrins constitutes a new way to manipulate cyclodextrins and is anticipated to alter the receptor properties of such cavitands.



α-CD

Experimental Section

General Procedures. All commercial reagents were used as supplied. The solvents were dried and distilled by standard methods. ^{1}H (200 MHz) and ^{13}C (50 MHz) NMR shifts are reported in parts per million and were obtained using a FT Bruker AC200 spectrometer. The ^{1}H NMR data are referenced to residual $CHCl_3$ (7.25 ppm); ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). For MALDI-TOF mass spectra, a PerSeptive Biosystems Vestec spectrometer was used in positive linear mode at 5 kV acceleration voltage with 2,5-dihydroxybenzoic acid as matrix. The FAB mass spectrum of [$PtCl_2$(**5**)] was recorded on a ZAB HF VG analytical spectrometer using *m*-nitrobenzyl alcohol as matrix. Column chromatography was performed on silica gel 60 (particle size 40−63 μm, 230−240 mesh). Cyclodextrin **1** was synthesized according to a literature procedure.[35] Compounds **2**,[31] **3**,[31] **4**,[32]and **5**[32] were briefly reported in previous communications.

2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^B,6^C,6^E,6^F-Hexadeca-*O*-methylcyclomaltohexaose (2). Tetrafluoroboric acid (34%, 2.8 mL) was added to a solution of **1** (3.530 g, 1.74 mmol) in acetonitrile (50 mL). The solution was stirred for 15 min at room temperature, whereupon Et_3N (2 mL) was added. The reaction mixture was then poured into water (100 mL). The precipitate was filtered and the filtrate extracted with CH_2Cl_2 (3 × 50 mL). The organic extract was washed with saturated aqueous $NaHCO_3$ (50 mL) before being dried ($MgSO_4$) and evaporated to dryness. Column chromatography (SiO_2, CH_2Cl_2/MeOH, 92:8) followed by recrystallization from $CHCl_3$/hexane afforded **2** as a colorless solid. Yield: 1.820 g, 87%. Mp: 202−203 °C. ^{1}H NMR (200.1 MHz): δ = 5.13 (d, 2H, H-1, ^3J = 3.5 Hz), 5.04 (d, H-1, 2H, ^3J = 3.4 Hz), 5.03 (d, H-1, 2H, ^3J = 3.3 Hz), 3.14−3.91 (36H, H-2, H-3, H-4, H-5, and H-6), 3.67 (6H, s, CH_3O), 3.64 (6H, s, CH_3O), 3.63 (s, 6H, CH_3O), 3.51 (s, 6H, CH_3O), 3.49 (s, 6H, CH_3O), 3.48 (s, 6H, CH_3O), 3.40 (s, 6H, CH_3O-6), 3.39 (s, 6H, CH_3O-6), 2.62 (br t, 2H, ^3J = 6.3 Hz, OH). ^{13}C{^{1}H} NMR (50.3 MHz): δ 99.6 and 99.4 (×2) (C-1), 82.3, 82.2, 82.0, 81.8 (×2), 81.5, 81.3 (×2), and 81.1 (C-2, C-3, and C-4), 72.3 (C-5^{A,D}), 71.5 (×2) (C-6^{B,C,E,F}), 71.3 (×2) (C-5^{B,C,E,F}), 62.1 (C-6^{A,D}), 61.70 (×2), 61.40 (CH_3O-3), 59.0, 58.95, 58.20, and 57.73 (×2) (CH_3O-2 and CH_3O-6). MALDI-TOF MS: m/z = 1220 [100 (M + Na)$^+$], 1236 [70 (M + K)$^+$]. Anal. Calcd for $C_{52}H_{92}O_{30}$ (M_r = 1197.3): C, 52.17; H, 7.75. Found: C, 52.41; H, 7.66.

6A,6D-Di-O-methylsulfonyl-6A,6D-dideoxy-2A,2B,2C,2D,2E,2F,3A,3B,3C,3D,3E,3F,6B,6C,6E,6F-hexadeca-*O*-methylcyclomaltohexaose (3). Methylsulfonyl chloride (0.380 g, 0.26 mL, 3.34 mmol) was added to a solution of **2** (1.820 g, 1.51 mmol) and *N*,*N*-dimethylpyridine (0.300 g, 2.45 mmol) in anhydrous pyridine (25 mL). The reaction mixture was stirred at room temperature for 6 h, whereupon water (50 mL) was added. The solution was then extracted with ethyl acetate (3 × 50 mL), and the organic phase was washed respectively with 2 M HCl (2 × 50 mL), 2 M NaOH (50 mL), and water (50 mL) before being dried ($MgSO_4$). Removal of the solvent in vacuo afforded pure **3** as a colorless solid. Yield: 1.830 g, 90%. Mp: 150 °C (dec). ^{1}H NMR (200.1 MHz): δ = 5.05 (d, 2H, H-1, ^3J = 3.3 Hz), 5.03 (d, H-1, 2H, ^3J = 3.2 Hz), 5.01 (d, H-1, 2H, ^3J = 3.1 Hz), 4.65 (d, 2H, H-6a^{A,D}, ^3J = 11.2 Hz), 4.31 (dd, 2H, H-6b^{A,D}, ^3J = 11.2 and 6.0 Hz), 3.11−4.11 (32H, H-2, H-3, H-4, H-5, and H-6^{B,C,E,F}), 3.66 (6H, s, CH_3O), 3.65 (6H, s, CH_3O), 3.61 (s, 6H, CH_3O), 3.50 (s, 6H, CH_3O), 3.49 (2s, 12H, CH_3O), 3.40 (s, 6H, CH_3O-6), 3.39 (s, 6H, CH_3O-6), 3.07 (s, 6H, CH_3SO_2). ^{13}C{^{1}H} NMR (50.3 MHz): δ 100.7, 99.9, and 98.9 (C-1), 82.3, 82.2, 82.0, 81.8 (×2), 81.5, 81.3 (×2), and 81.1 (C-2, C-3, and C-4), 71.5 and 71.0 (C-6^{B,C,E,F}), 71.1 (×2) (C-5^{B,C,E,F}), 69.9 (C-6^{A,D}), 69.7 (C-5^{A,D}), 61.9, 61.7, and 61.6 (CH_3O-3), 59.1, 59.0, 58.4, and 57.7 (×2) (CH_3O-2 and CH_3O-6), 37.5 (CH_3SO_2). MALDI-TOF MS: m/z = 1372 [80 (M + Na)$^+$], 1388 [100 (M + K)$^+$]. Anal. Calcd for $C_{54}H_{96}O_{34}S_2$ (M_r = 1349.5): C, 47.92; H, 7.15. Found: C, 48.22; H, 6.79.

6A,6D-Diazido-6A,6D-dideoxy-2A,2B,2C,2D,2E,2F,3A,3B,3C,3D,3E,3F,6B,6C,6E,6F-hexadeca-*O*-methylcyclomaltohexaose (4). Dry sodium azide (2.210 g, 34 mmol) was added to a solution of **3** (2.300 g, 1.7 mmol) in dry DMF (75 mL). The reaction mixture was stirred under N_2 at 65 °C for 18 h, cooled to room temperature, and poured into ice−water (500 mL). The aqueous solution was extracted with ether (4 × 100 mL) and the organic extract washed with water (200 mL) before being dried ($MgSO_4$) and evaporated to dryness. Yield: 2.110 g, 99%. IR (KBr disk, cm^{-1}): 2102 (azide). ^{1}H NMR (200.1 MHz): δ 5.05 (d, 2H, H-1, ^3J = 3.0 Hz), 5.03 (d, 2H, H-1, ^3J = 3.2 Hz), 5.01 (d, 2H, H-1, ^3J = 3.5 Hz), 3.12−3.97 (36H, H-2, H-3, H-4, H-5, and H-6), 3.65 (s, 6H, CH_3O), 3.64 (s, 6H, CH_3O), 3.62 (s, 6H, CH_3O), 3.50 (s, 6H, CH_3O), 3.49 (2s, 6H each, CH_3O), 3.41 (2s, 6H each, CH_3O-6). ^{13}C{^{1}H} NMR (50.3 MHz): δ 100.2 (×2) and 99.5 (C-1), 83.6, 82.7, 82.1 (×2), 82.0, 81.9, 81.3, 81.2, and 81.1 (C-2, C-3, and C-4), 71.6, and 71.00 (C-6^{B,C,E,F}), 71.3 (×2) and 71.0 (C-5), 61.8 and 61.7 (×2) (CH_3O), 59.0 (×2) (CH_3O-6), 58.0 (CH_3O), 57.9 (×2) (CH_3O), 52.1 (CH_2N). Anal. Calcd for $C_{52}H_{90}N_6O_{28}$ (M_r = 1247.3): C, 50.07; H, 7.27; N, 6.74. Found: C, 50.33; H, 7.43; N, 6.57.

6A,6D-Diamino-6A,6D-dideoxy-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^B,6^C,6^E,6^F-hexadeca-*O*-methylcyclomaltohexaose (5). Triphenylphosphine (2.670 g, 8.08 mmol) was added to a solution of diazide **4** (2.130 g, 1.70 mmol) in dioxane (25 mL) under N_2. The clear solution was stirred for 1 h at room temperature before adding concentrated aqueous NH_4OH solution (1.6 mL) dropwise. After overnight stirring, the reaction mixture was poured into water (200 mL) and the pH of the resulting suspension adjusted to 4 with 2 M HCl and 0.1 M HCl before being extracted with toluene (5 × 100 mL). The aqueous phase was then made alkaline by adding 2 M NaOH (50 mL) and the compound subsequently extracted with CH_2Cl_2 (4 × 100 mL). The CH_2Cl_2 extract was dried ($MgSO_4$) before being evaporated to dryness. Recrystallization from heptane afforded a colorless fluffy solid. Yield: 1.800 g, 88%. Mp: 184−186 °C. ^{1}H NMR (200.1 MHz): δ 5.06 (d, 4H, H-1, ^3J = 3.2 Hz), 5.02 (d, 2H, H-1, ^3J = 3.2 Hz), 2.99−3.94 (36H, H-2, H-3, H-4, H-5, and H-6), 3.65 (s, 6H, CH_3O), 3.64 (s, 6H, CH_3O), 3.63 (s, 6H, CH_3O), 3.49 (3s, 6H each, CH_3O), 3.39 (s, 6H, CH_3O-6), 3.38 (s, 6H, CH_3O-6), 1.40 (br s, 4H, NH_2). ^{13}C{^{1}H} NMR (50.3 MHz): δ 100.3, 100.0, and 99.8 (C-1), 83.6, 82.7, 82.1 (×2), 82.0, 81.9 81.3, 81.2, and 81.1 (C-2, C-3, and C-4), 71.6 and 71.00 (C-6^{B,C,E,F}), 71.3 (×2) and 71,0 (C-5), 61.8 and 61.7 (×2) (CH_3O), 59.0 (×2) (CH_3O-6), 58.0 (CH_3O), 57.9 (×2) (CH_3O), 52.1 (CH_2N). Anal. Calcd for C_{52} $H_{94}N_2O_{28}$ (M_r = 1195.3): C, 52.25; H, 7.93; N, 2.34. Found: C, 52.19; H, 8.00; N, 2.22.

Dichloro-6A,6D-diamino-6A,6D-dideoxy-2^A,2^B,2^C,2^D,2^E,2^F,3^A,3^B,3^C,3^D,3^E,3^F,6^B,6^C,6^E,6^F-hexadeca-*O*-methylcyclomaltohexaose Platinum(II) [$PtCl_2$(5)]. A solution of **5** (0. 250 g, 0.21 mmol) in water (1 mL) was added to a stirred aqueous solution (5 mL) of K_2PtCl_4. After overnight stirring under N_2, the initially orange solution turned pale yellow and water (50 mL) was added. The reaction mixture was

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Table 1. Crystallographic Data: Data Collection, Solution, and Refinement for $[PtCl_2(\mathbf{5})]\cdot H_2O\cdot CHCl_3$

formula	$C_{52}H_{94}Cl_2N_2O_{28}Pt\cdot H_2O\cdot CHCl_3$
MW	1598.72
cryst syst	monoclinic
Space group	$P12_11$
a (Å)	11.7551(5)
b (Å)	16.7990(6)
c (Å)	18.7648(9)
β (deg)	104.621(8)
vol (Å^3)	3585.6(5)
Z	2
color	pale yellow
cryst size (mm^3)	$0.20 \times 0.15 \times 0.06$
D_{calc} (g cm^{-3})	1.48
$F(000)$	1648
μ (mm^{-1})	2.222
transm min and max	0.8474−1.0000
temp (K)	294
wavelength (Å)	0.71073
radiation monochromated	Mo Kα graphite
diffractometer	KappaCCD
scan mode	"p scans"
index ranges	$-15 < h < 15$, $-21 < k < 20$, $-24 < l < 24$
θ limits (deg)	2.50−27.50
no. of data measd	14845
no. of data with $I > 3\sigma(I)$	4853
weighting scheme	$4F_o^2/(\sigma^2(F_o^2) + 0.0064F_o^4)$
no. of variables	819
R^a	0.050
$R_w{}^b$	0.063
goodness of fit	1.020
largest peak in final difference (e Å^{-3})	0.659

$^a R = \sum||F_o| - |F_c||/\sum|F_o|$. $^b R_w = \{\sum w(F_o^2 - F_c^2)^2/\sum w(F_o^2)^2\}^{1/2}$.

then extracted with CH_2Cl_2 (3×50 mL). The organic extract was dried ($MgSO_4$) before being evaporated to dryness. The yellow residue was subjected to column chromatography (SiO_2, CH_2Cl_2/MeOH, 96:4) to afford $[PtCl_2(\mathbf{5})]$ as a slightly yellow solid as well as more polar metallo-oligomers which were not recovered. Yield: 0.052 g, 17%. Mp: >220 °C (dec). IR (polythene disk, cm^{-1}): 335 and 327 (ν_{PtCl}). ^{1}H NMR (200.1 MHz): δ 5.37 (d, 4H, H-1, ^3J = 4.1 Hz), 5.02 (d, 2H, H-1, ^3J = 3.5 Hz), 4.98 (d, 2H, H-1, ^3J = 3.4 Hz), 2.95−3.92 (36H, H-2, H-3, H-4, H-5, and H-6), 3.63 (s, 6H, CH_3O), 3.61 (s, 6H, CH_3O), 3.60 (s, 6H, CH_3O), 3.56 (s, 6H, CH_3O), 3.54 (s, 6H, CH_3O), 3.52 (s, 6H, CH_3O), 3.48 (s, 6H, CH_3O-6), 3.44 (s, 6H, CH_3O-6), 2.33 (br s, 4H, NH_2). $^{13}C\{^1H\}$ NMR (50.3 MHz): δ 99.4, 98.3, and 95.6 (C-1), 82.9, 82.1 (×2), 81.9 (×2), 81.3, 80.6, 80.4, and 79.7 (C-2, C-3, and C-4), 73.8 and 71.0 (C-6^{B,C,E,F}), 72.7, 72.5, and 70.0 (C-5), 61.3, 60.9, and 60.6 (CH_3O), 60.1, 60.0, and 59.6 (CH_3O), 58.0 (CH_3O-6), 57.9 (CH_3O-6), 48.6 (CH_2N). FAB MS: m/z = 1425.3 [80 (M − Cl)$^+$], 1461.2 [70 (M + H)$^+$]. Anal. Calcd for $C_{52}H_{94}N_2O_{28}Cl_2Pt\cdot H_2O$ (M_r = 1461.3): C, 42.22; H, 6.54; N, 1.89. Found: C, 41.88; H, 6.50; N, 1.77.

Crystallization and X-ray Diffraction Experiments of $[PtCl_2(\mathbf{5})]\cdot CHCl_3\cdot H_2O$. Pale yellow crystals were obtained by slow diffusion of pentane into a $CHCl_3$ solution of $[PtCl_2(\mathbf{5})]$ at room temperature. Data were collected on a Nonius Kappa CCD diffractometer (graphite Mo Kα radiation, 0.71073 Å) at 25 °C; 14845 reflections were collected, 4853 data with $I > 3\ \sigma(I)$. The structure was solved using the Nonius OpenMoleN[36] package and refined by full-matrix least squares with anisotropic thermal parameters for all non-hydrogen atoms. Final results: $R(F) = 0.050$, $R_w(F) = 0.063$. The compound crystallizes with one water molecule included in the cavity and one disordered chloroform molecule lying outside**.** Data collection parameters, solution, and refinement results are given in Table 1.

(36) OpenMoleN. *Interactive Structure Solution*; Nonius B.V.: Delft, 1997.

Results and Discussion

Although capping of native CDs with various spacers has been extensively investigated,[37−41] the more flexible methylated analogues have attracted little attention.[42,43] We recently developed an effective methodology that allows the preparation of A,D-difunctionalized methylated α-CDs.[35] Such C_2-symmetrical synthons have in particular been used for the construction of chelate complexes of catalytic relevance.[31] We anticipated that grafting very short pendant ligands on two diametrically opposed glucose units belonging to an α-CD platform would result after metal chelation in the formation of a strongly distorted macrocyclic structure.

Diamine **5** seemed to us ideally suited for this purpose. This compound was prepared in four steps from the previously reported "supertritylated" compound **1** (Scheme 1). Hydrolysis of the latter with aqueous HBF_4 in MeCN afforded diol **2** in 87% yield. Mesylation with MsCl/pyridine−DMAP (Ms = $MeSO_2$; DMAP = 4-(dimethylamino)pyridine) yielded **3** almost quantitatively. Substitution of the methylsulfonyl groups of **3** with sodium azide in DMF (DMF = *N*,*N*-dimethylformamide) led to diazide **4** (99%). Subsequent amination with aqueous ammonia/PPh_3 produced water-soluble diamine **5** in 88% yield. NMR data of compounds **2**−**5** (see Experimental Section) are consistent with a C_2-symmetrical structure. The NH_2 signal of compound **5** appears at 1.40 ppm in the ^{1}H NMR spectrum. Treatment of K_2PtCl_4 with diamine **5** in water gave a mixture of compounds. Purification by chromatography afforded complex $[PtCl_2(\mathbf{5})]$ in 17% yield as well as other products, presumably oligomers, which were not characterized. Unlike ligand **5**, the pale yellow complex $[PtCl_2(\mathbf{5})]$ is only moderately soluble in water (≈3 g l^{-1}). As shown by ^{1}H NMR and ^{13}C NMR, the 2-fold symmetry is retained on metal complexation. Interestingly, the doublet for two of the anomeric protons undergoes a significant low-field shift of ca. 0.35 ppm and its ^3J(1,2) value differs significantly from the two others (4.1 Hz vs 3.4 and 3.5 Hz) which are typical ^{1}H coupling constants for anomeric protons associated with the usual $^4C_1$ conformation. It is therefore likely that two of the glucopyranose rings are strongly distorted in $CDCl_3$ solution.[9] As expected, the NH_2 signal undergoes a pronounced low-field shift ($\Delta\delta$ = 0.9 ppm) on going from **5** to $[PtCl_2(\mathbf{5})]$.

The molecular structure of complex $[PtCl_2(\mathbf{5})]$ with numbering of the glucose units is shown in Figure 1. A selection of geometrical data including Cremer and Pople puckering parameters[44] of individual six-membered rings is reported in Table 2. Selected bond distances and angles are shown in Table 3. Complex $[PtCl_2(\mathbf{5})]$ is nearly C_2-symmetric in the solid state. The X-ray analysis confirmed the chelating behavior of diamine **5**. The platinum atom lies in an almost planar ligand environment, with the amines occupying cis positions. The Pt−N and Pt−Cl bond lengths (Table 3) fall within the range usually found

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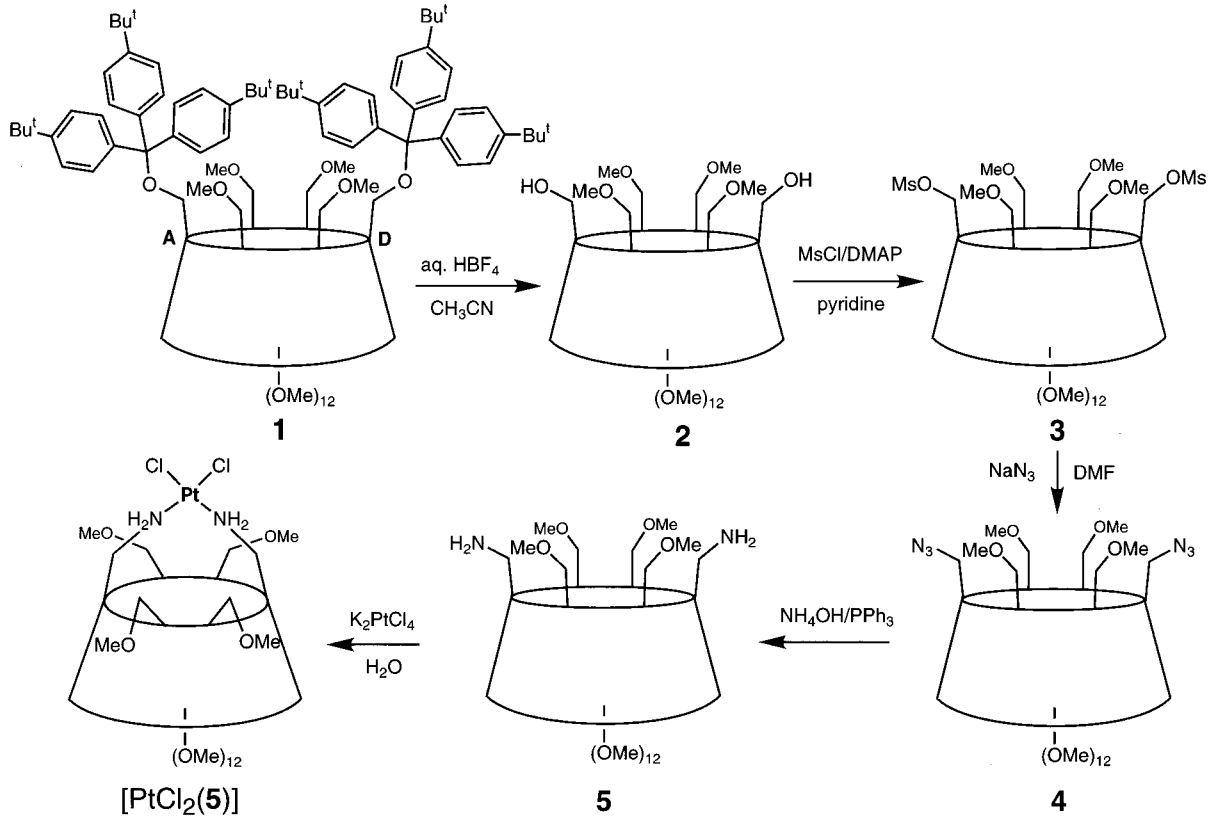
Scheme 1



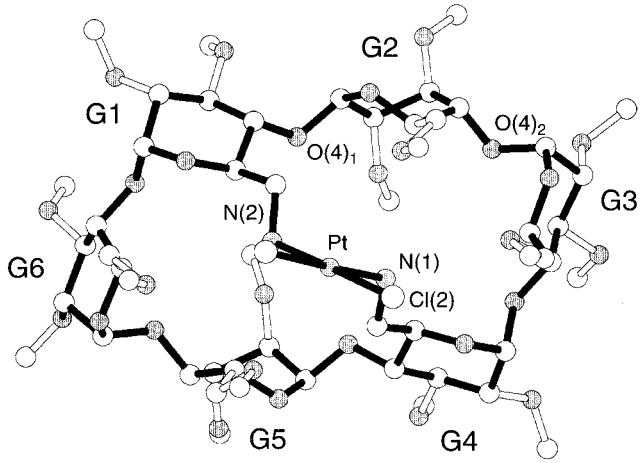


Figure 1. Molecular structure of $[PtCl_2(\mathbf{5})]\cdot H_2O\cdot CHCl_3$ with numbering of the glucose units. For clarity, the included water molecule has been omitted. The chloroform molecule is not shown.

for such bonds.[34,45] The N(1)−Pt−N(2) (91.9°) and Cl(1)−Pt−Cl(2) (94.9°) angles show that the geometry about platinum only slightly deviates from ideal square planar coordination. The metal plane is roughly parallel to the cyclodextrin axis.

The most striking feature of this structure is the unusual lengthening of the O(4) hexagon which adopts an almost rectangular shape. The distances between opposite O(4) atoms are respectively 5.44 Å (G1−G4), 9.59 Å (G2−G5), and 9.98 Å (G3−G6). For comparison, the shortest and longest $O(4)_n$−$O(4)_{n+3}$ distances in TM-α-CD are respectively 8.09 and 8.69 Å.[29] Other characteristic parameters of the nearly planar O(4) hexagon are given in Figure 2.

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Table 2. Selection of Geometric Parameters for $[PtCl_2(\mathbf{5})]$

	residue					
parameter	G1	G2	G3	G4	G5	G6
$C(4)_n-O(4)_n-C(1)_{n+1}$	116(1)	120(1)	119(1)	116(1)	118(1)	120(1)
tilt angle[a] (deg)	40.5(4)	6.9(5)	22.5(4)	43.8(4)	5.2(5)	24.4(4)
QT[b] (Å)	0.54(1)	0.7(1)	0.56(1)	0.58(1)	0.74(1)	0.57(1)
θ[c] (deg)	7(1)	87(7)	21(1)	8(1)	91.8(9)	22(1)
Φ[c] (deg)		321(7)[d]			319.1(9)[d]	

[a] The tilt angle is defined as the angle made by the O(4) atom plane and the plane formed by $O(4)_{n-1}$, $C(1)_n$, $C(4)_n$, and $O(4)_n$ of each glucose residue. [b] Total puckering amplitude. [c] Puckering angles. [d] Φ becomes meaningful for values of θ close to 90°.

Table 3. Selected Bond Distances (Å) and Angles (deg) for $[PtCl_2(\mathbf{5})]$

A. Coordination Mode of Pt(II)

Distances (Å)			
Pt−Cl(1)	2.294(5)	Pt−N(1)	2.10(2)
Pt−Cl(2)	2.318(5)	Pt−N(2)	2.08(2)
Angles (deg)			
Cl(1)−Pt−Cl(2)	94.4(1)	Cl(2)−Pt−N(1)	85.9(4)
Cl(1)−Pt−N(1)	179.2(4)	Cl(2)−Pt−N(2)	177.6(5)
Cl(1)−Pt−N(2)	87.8(4)	N(1)−Pt−N(2)	91.9(4)

B. H−Bonding Involving the Included Water Molecule

Distances (Å)			
$O_w-O(4)_1$	2.83(3)	$O_w-O(4)_4$	2.90(3)
$O_w-O(2)_2$	2.88(3)	$O_w-O(2)_5$	2.86(3)
$O_w-N(1)$	2.95(2)	$O_w-N(2)$	2.90(2)

Linking the G1 and G4 glucose fragments via the very short NPtN connector causes a strong distortion not only of the whole macrocyclic structure but also of some of the individual six-membered rings. Thus, the two opposing glucose units G2 and G5 adopt a $^OS_2$ skew-boat conformation (Figure 3) while the others remain in the usual $^4C_1$ chair conformation. This strongly

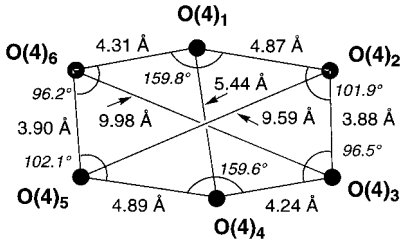

Figure 2. Geometry of the O(4) atom hexagon.

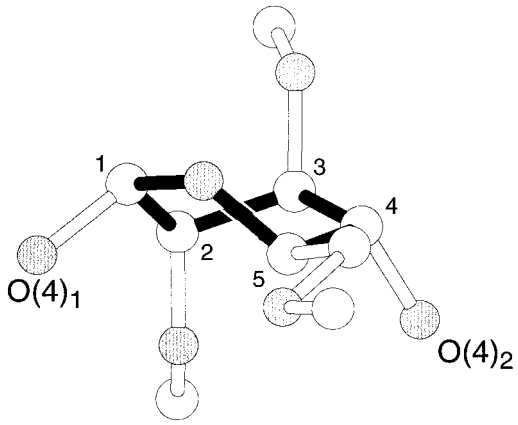

Figure 3. Skew-boat conformation of G2.

contrasts with the all $^4C_1$ chair conformations found in TM-α-CD. The strong distortion of G2 ($\theta = 87(7)°$, $\phi = 321(7)$, $Q = 0.7(1)$) and G5 ($\theta = 91.8(9)°$, $\phi = 319.1(9)$, $Q = 0.74(1)$) results in a marked lengthening of the $O(4)_1-O(4)_2$ (4.87 Å) and $O(4)_4-O(4)_5$ (4.89 Å) distances, the other $O(4)_n$-$O(4)_{n+1}$ distances ranging between 3.88 and 4.31 Å. Note, the $^1C_4 \rightarrow {}^OS_2$ conformational change is known to increase the $O(4)_n-O(4)_{n+1}$ distance in a glucopyranose unit.[27] Interestingly, the connected G1 and G4 glucose rings do not undergo such significant conformational changes, possibly because of their restricted flexibility. However, to accommodate the short NPtN connector, both rings are tilted "inward" by about 42° (Table 2) with respect to the O(4) plane.

On going from $^1C_4$ to $^OS_2$, the equatorial C(2)−O(2) and C(3)−O(3) bonds become axial and trans to each other. As a result, the O(2)Me groups now point toward the cavity interior whereas the free O(3)Me groups point away, as shown in Figure 1. Both $O(2)_2$ and $O(2)_5$ oxygen atoms together with $O(4)_1$, $O(4)_4$, and the two NH bonds that point inside the cavity form a small hydrophilic pocket within the CD cavity that hosts a single water molecule (Figure 4). Multiple hydrogen bonding between the included water molecule and the aforementioned atoms is responsible for this unique feature. Note, inclusion of a single water molecule has recently been observed in per-(2,3,6-tri-*O*-acetyl)-α-CD, but in this case the guest molecule is hydrogen-bonded to two acetyl groups.[46] Possibly, the H_2O−CD interaction observed in [$PtCl_2$(**5**)] also contributes to the stabilization of the skew-boat conformation of G2 and G5. It is noteworthy that [$PtCl_2$(**5**)] does not display host−guest properties in water toward benzyl alcohol which under similar conditions forms a 1:1 inclusion complex with TM-α-CD. It is likely that the highly favorable encapsulation of water in [$PtCl_2$(**5**)] precludes any binding of further substrates.

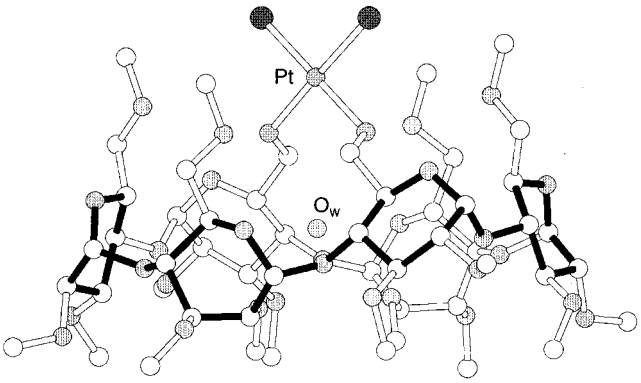

Figure 4. Side view of [$PtCl_2$(**5**)] showing the oxygen atom (O_w) of the entrapped water molecule.

Conclusion

The disruption of the round annular structure observed for cyclodextrin **5** in the corresponding $PtCl_2$ complex was produced by linking two opposing glucopyranose units using a short connector. The resulting irregular, roughly rectangular shape is unprecedented in α-CD chemistry. Such a dramatic structural change was made possible by the presence of flexible 2,3,6-tri-*O*-methylglucose units which can undergo facile conformational changes and hence allow lengthening of some $O(4)_n...O(4)_{n+1}$ separations. Incidentally, the flattening of the CD torus generates a small cavity that is perfectly preorganized for complexation of a single water molecule.

The strategy used in this work relies on the assemblage of two amine ligands connected to a CD platform around a transition metal. An interesting perspective opened by the presence of a metal center acting as a CD cap is the possibility to induce allosteric effects and hence alter the receptor properties of the cavity upon modification of the metal coordination sphere.

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Supporting Information Available: ORTEP drawing with numbering for $PtCl_2$(**5**)]·H_2O·$CHCl_3$ with 40% thermal ellipsoids, table of crystallographic data for [$PtCl_2$(**5**)]·H_2O·$CHCl_3$, table of atomic coordinates with equivalent isotropic displacement parameters, table of hydrogen coordinates with isotropic displacement parameters, table of general displacement parameter expressions (*U*'s), table of bond lengths, and table of bond angles. Crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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