Molecular Modeling of Saccharides, Part 27[+]

Synthesis and Molecular Geometry of an Achiral 30-Crown-12 Polyacetal from α-Cyclodextrin

Stefan Immel, Toshio Nakagawa, Hans J. Lindner, and Frieder W. Lichtenthaler*[a]

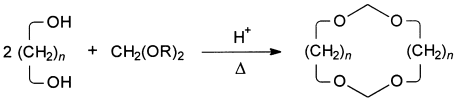
Abstract: Periodate oxidation of α-cyclodextrin followed by borohydride reduction readily provided an octadecahydroxymethyl-substituted 30-crown-12 polyacetal **1**, its 30-membered macrocycle being composed of six *meso*-butanetetrol/glycolaldehyde acetal units, which is, consequently, optically inactive. Its solid-state molecular geometry emerged from the X-ray structural analysis of the well-crystallizing octadecaacetate **2**, which revealed the undulated macrocycle to be molded into three loops with a unique order of succession of the -CHR-CHR-O-CHR-O- units: alternating *gauche*- and *anti*-conformations of the *meso*-butanetetrol portions and consecutive disposition of the glycolaldehyde-acetoxymethyl groups above and below the mean-plane of the macrocycle. In solution, however, as evidenced by ^{1}H- and ^{13}C-NMR spectra, the macrocycle is highly flexible at ambient and higher temperatures, its mobility becoming distinctly restricted only below $-20\,^\circ$C.

Keywords: cyclodextrins · crown acetals · macrocyclic polyacetals · oligosaccharides

Introduction

Unlike crown ethers that have played a pivotal role in the development of supramolecular chemistry,[1] macrocycles with acetalic oxygen atoms have received comparatively little attention, conceivably because their cation complexation properties—as compared to the more basic ether oxygens—are less propitious. Thus, Pedersen[2] noted already thirty years ago "that -O-CH_2-O- is a less favorable linkage than -O-CH_2CH_2-O- for complexation", based on crown ether acetals of the type 18-C-6, 20-C-7, and 22-C-8, namely cyclic polyethers with one or two acetal groupings in their skeletal backbone. Various other investigators have since amply corroborated the drastic decrease in cation binding ability by introducing acetal groupings into crown ethers even when bearing the same number of oxygen atoms.[3–6]

Macrocycles exclusively containing acetal-oxygen atoms, and, hence, deserving the designation *crown acetal*,[7, 8] are rare, the presently known examples being limited to systems with two formaldehyde/alkanediol acetal units, that is containing only four oxygens in the ring (Figure 1).



n	acronym	ref.
2	10-C-4	[9]
3	12-C-4	[10]
4	14-C-4	[11]
5	16-C-4	[12]
6	18-C-4	[13]
9	24-C-4	[13]
10	26-C-4	[13]
14	34-C-4	[13]

Figure 1. Crown acetals[7] composed of two alkanediol/formaldehyde units. Of these, only the geometries of 10-C-4[9] and 14-C-4[11] have been verified by X-ray structural analysis.

Cycloacetals with a higher number of oxygens in the ring are, as of now, utter curiosities: The products formed on BF_3-induced oligomerization of 1,3-dioxolane in yields of 1–2% were deemed to be the 10-crown-4, 15-crown-6, 20-crown-8, and 25-crown-10 polyacetals,[3a] despite of insufficient characterization, and the polyaldehydes generated by periodate oxidation of α-, β-, and γ-cyclodextrin,[14] which de facto constitute polyacetals with a 30-crown-12, 35-crown-14, and 40-crown-16 skeletal backbone; they have similarly eluded

[a] Prof. Dr. F. W. Lichtenthaler, Dr. S. Immel, Prof. Dr. T. Nakagawa, Prof. Dr. H. J. Lindner
Institut für Organische Chemie, Technische Universität Darmstadt
Petersenstrasse 22, 64287 Darmstadt (Germany)
Fax: (+49) 6151-166674
E-mail: fwlicht@sugar.oc.chemie.tu-darmstadt.de

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Supporting information for this article is available on the WWW under http://caramel.oc.chemie.tu-darmstadt.de/immel/3Dstructures.html (3D structures of Figure 2) and http://caramel.oc.chemie.tu-darmstadt.de/immel/molcad/gallery.html (MOLCAD graphics).

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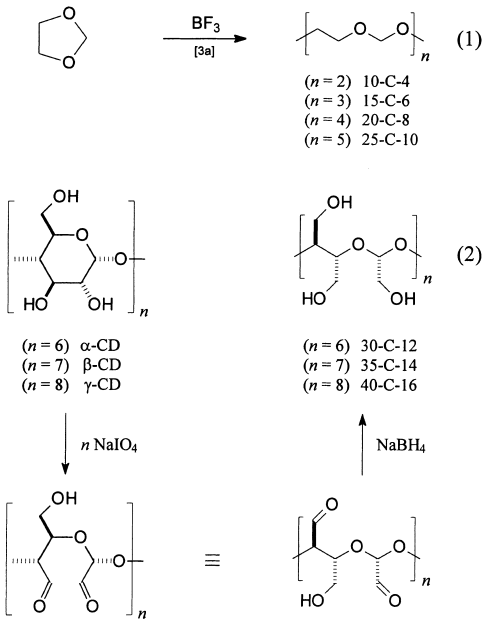
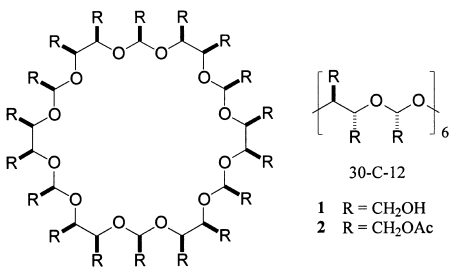
unequivocal structural characterization—not surprising in view of the manifold possibilities of elaborating cyclic acetal and hemiacetal structures. Of the products ensuing from these "CD-polyaldehydes" upon chlorite oxidation[15] and borohydride reduction,[16] only the per-hydroxymethylated 30-crown-12 and 35-crown-14 polyacetals—prepared from α- and β-CD in modest yields—have been unequivocally characterized as such and as their per-*O*-acetates,[16a] yet the sparse NMR data provided gave no clues as to their molecular geometries.



Scheme 1. Synthetic access to large ring crown acetals with repetitive C-C-O-C-O-fragments in their skeletal backbones. *Top*: Systems with two to five ethyleneglycol/formaldehyde units[3a] [Eq. (1)]. *Lower part*: cyclodextrin-derived substituted analogues composed of six, seven, and eight consecutive D-erythrose/glyoxal[14] or—upon hydride reduction—*meso*-butanetetrol/glycolaldehyde segments [Eq. (2)].

Our past interest in the generation of flexible cyclooligosaccharide hosts[17] to mimic the induced-fit mode[18] rather than the rigid lock-and-key principle[19] has led presently to the preparatively satisfactory, high-yield preparation of the α-cyclodextrin-derived 30-crown-12 polyacetal **1** composed of six consecutive *meso*-butanetetrol/glycolaldehyde acetal units, and to the unravelment of its molecular geometry through an X-ray structural analysis of its octadeca-acetate **2**.



Results and Discussion

Of the three native cyclodextrins readily accessible, α-cyclodextrin (α-CD), with six α-(1→4)-linked glucose units the smallest, undergoes periodate oxidation of its diol functionalities slowest,[14] yet when reacted with a 3.0 molar excess of oxidant for 11 d at ≈0 °C, the conversion was complete. The resulting polyaldehyde, due to its manifold possibilities of forming hemiacetals and/or hemialdal hydrates, was only characterized as a chromatographically uniform powder, and then subjected to reduction with sodium borohydride in methanol to provide the octadeca-hydroxymethyl 30-crown-12 polyacetal **1**. Its characterization in pure form is best accomplished by in situ acetylation to yield its well-crystallizing, octadeca-acetate **2** (92 % based on α-CD) and subsequent Zemplén deacetylation. Neither **1** nor **2** showed any rotational value—expectedly, since the six butanetetrol units generated from α-CD by the periodation–reduction sequence have *erythro*-configuration and erythritol is a *meso*-compound.

Invited by the high crystallinity of the 30-crown-12 polyacetal **2**, an X-ray structural analysis could be performed (Figure 2), which revealed the unique conformational intricacies of the 30-membered macrocycle: The ring adopts a three-loop shape, which is not planar but assumes a distinct undulating form. The ring symmetry is reduced from C_{6v} to approximately C_3, with the six acetoxymethyl groups of the glycolaldehyde acetal units pointing alternatingly above and below the mean-plane of the macrocyclic backbone. In addition, each of the six pairs of vicinal acetoxymethyl groups of the *meso*-butanetetrol units features one OAc group pointing towards the front, and the next directed to the rear relative to the ring periphery. As is lucidly borne out by the color representations of Figure 2 and particularly by the side-view ribbon model therein, a total of nine acetoxymethyl groups point away from either side of the macrocyclic backbone in an alternating fashion. This entails for the crown acetal **2** a compact, nearly cylindrical overall shape. Albeit **2** was crystallized from EtOH, the crystals do not contain any residual solvent since the molecular packing is very tight and the center of the molecule seems to be inaccessible for any guest. As detailed in Figure 2 (bottom plots), the three-looped structure is caused by a characteristic alternating *gauche*- and *anti*-arrangement for the O-C-C-O-torsion angles of the six *meso*-butanetetrol units, a conformational feature that was translated into a conventional formula drawing in Figure 3.

As **2** itself is an achiral compound with an achiral space group (monoclinic, *P*n), each unit cell contains two symmetry related formula units of **2**, one being the exact mirror geometry of the other. Thus, the *meso*-butanetetrol units in the solid-state geometry of **2** adopt either successive (+)-*gauche*/*anti*- or (−)-*gauche*/*anti*-conformations, of which only the former are shown in Figure 2. The ring torsion angles Θ_1–Θ_5 for each *meso*-butanetetrol/glycolaldehyde unit *A*–*F* of the 30-membered macroring are listed in Table 1: Of these values, Θ_3 reflects directly the alternating *gauche*/*anti*-arrangements described above, whilst the other torsion angles display less pronounced fluctuations only.

Although the 30-crown-12 macrocycle is anticipated to be quite flexible in solution, both temperature dependent ^{1}H-

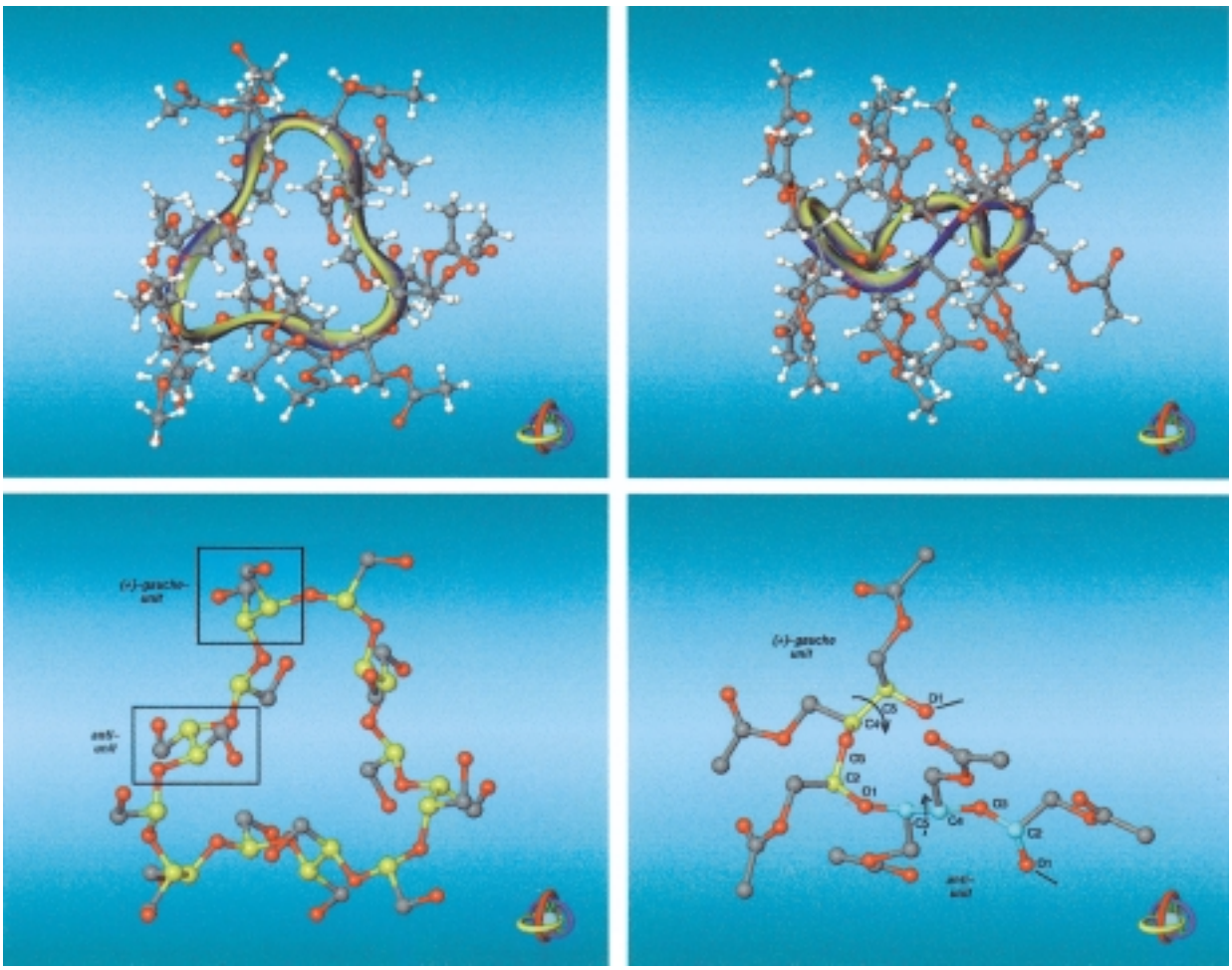
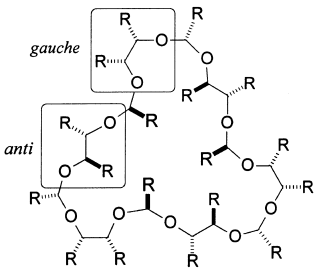


Figure 2. Solid-state topography for the asymmetric unit of the octadeca-(acetoxymethyl)-30-crown-12 polyacetal **2** in ball-and-stick type representations. *Top*: Ribbon models of the macrocyclic core, amply illustrating its three-looped shape, which, as shown in the side view (left), is not planar but adopts an undulatory form with the yellow-blue coloring of the braid; this indicates the twist of the backbone. In the crystal lattice, two formula units of achiral **2**—the geometry shown here and its symmetry related mirror image—occupy each unit cell. *Bottom*: Accentuation of the skeletal backbone of the 30-membered macrocycle (left) with acetyl groups and hydrogens omitted for clarity and all ring carbon atoms marked yellow; the molecular orientation corresponds to the top left plot. The *meso*-butanetetrol units are successively in *gauche*- and *anti*-arrangements (as labeled), whereas the acetoxymethyl groups of the six glycolaldehyde units are alternatingly directed towards both sides of the macrocycle. On the right, a single-loop segment of the macrocycle is enlarged, with one (+)-*gauche meso*-butanetetrol/glycolaldehyde unit colored yellow and atoms labeled; in the following -OCCOCO- repeating unit, of which the carbon atoms are in green color, the butanetetrol unit is in *anti*-arrangement.



2 R = CH_2OAc

Figure 3. Conventional formula drawing of the crown acetal **2** in the same orientation as given in the left plots of Figure 2 to visualize the successive *gauche*/*anti*-arrangements of the *meso*-butanetetrol units.

and ^{13}C-NMR patterns in CD_2Cl_2 and $C_2D_2Cl_4$, point towards the overall shape of the solid-state conformation being largely retained in these solvents. At ambient temperature (24 °C) the individual ring protons, that is the acetalic hydrogen H-2, the secondary hydrogens of the butanetetrol units (cf. ^{1}H NMR in Figure 4), and the ring carbons C-2, C-4, and C-5 (^{13}C NMR) are largely unresolved and display unusually broad signals. At elevated temperatures (up to +100 °C), the NMR spectra (in $C_2D_2Cl_4$) exhibit one set of signals consistent with a time-averaged C_{6v} symmetrical structure of **2**: a single low-field triplet for H-2, chemically equivalent resonances for H-4, H-5, and 4,5-CH_2, and the 2-CH_2 signals (although 4,5-H^A and 4,5-H^B are magnetically nonequivalent and thus, largely separated). The acetyl resonances are resolved into two peaks with an integral ratio of 12:6 for the *meso*-butanetetrol and glycolaldehyde units (^{1}H NMR in Figure 4, the ^{13}C-NMR spectra display analogous characteristics). At lower temperatures (−90 to 0 °C in CD_2Cl_2), all signals are significantly broadened or split; most notably the H-2 protons are clearly separated at −60 °C into two triplets (cf. Figure 4), and the acetyl groups split into four peaks with a ratio of 6:6:3:3. Below −60 °C the C-4 and C-5 signals are separated into a total of four peaks. All of these data are consistent with the

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Table 1. Succession of 30 ring torsion angles in the solid-state geometry of the 30-crown-12 acetal **2** with estimated standard deviations in parenthesis.[a]

Torsion angles [°]	Θ_1 O1-C2-O3-C4	Θ_2 C2-O3-C4-C5	Θ_3 O3-C4-C5-O1′	Θ_4 C4-C5-O1′-C2′	Θ_5 C5-O1′-C2′-O3′
A	119.3(7)	−148.7(6)	71.6(8)	161.8(7)	−115.7(7)
B	98.9(7)	−147.3(6)	−170.0(5)	135.6(6)	−80.7(7)
C	136.3(6)	−136.8(6)	65.9(7)	148.6(6)	−127.4(7)
D	82.2(7)	−145.1(6)	−173.0(6)	160.5(6)	−64.7(8)
E	116.2(7)	−142.9(7)	70.1(7)	150.7(7)	−99.0(8)
F	109.5(7)	−144.4(7)	−171.6(6)	146.9(7)	−65.4(9)

[a] Torsions are listed in row-column order, equivalent torsions for **2** are listed in columns; the atom numbering Scheme corresponds to Figure 4 (i.e., [-O1-C2-O3-C4-C5-]$_6$ with units labeled *A*–*F* for the 30-membered macroring), primed atom designators refer to the neighboring unit. The torsion angles Θ_1 and Θ_5, as well as Θ_2 and Θ_4 are chemically equivalent (clockwise and anti-clockwise ring numbering, symmetry C_{6v}); the alternating *gauche*–*trans* sequence of units in **2** is manifested through the O-C-C-O-torsion angle of the *meso*-butanetetrol units (Θ_3). All torsion angles are listed for one molecule of **2** contained in the unit cell only, the second molecule being the exact mirror image of the former with all torsion angles of opposite sign, respectively.

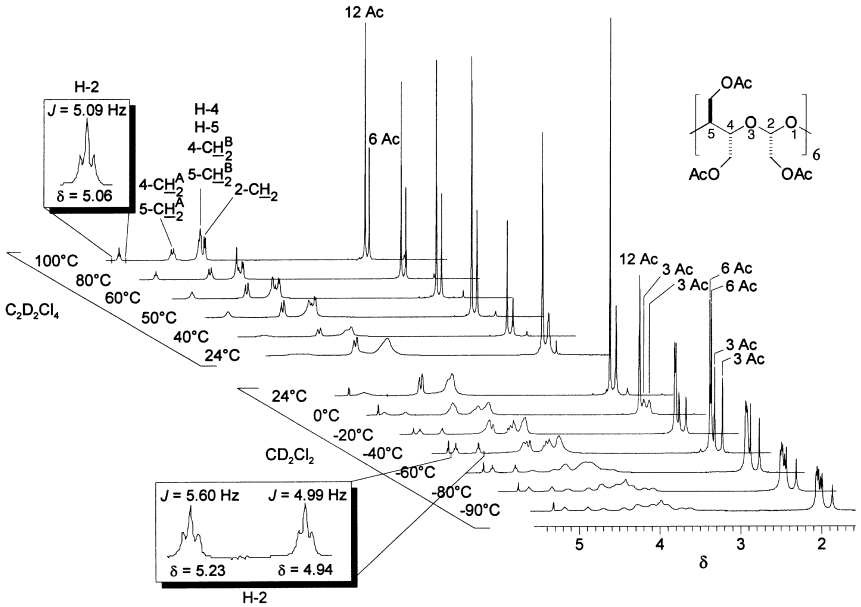

Figure 4. ^{1}H NMR (300 MHz) spectral patterns of **2** at different temperatures recorded in CD_2Cl_2 ($T = -90$ – $+24$ °C) and $C_2D_2Cl_4$ ($T = +24$ – $+100$ °C). At -60 °C the H-2 resonances of the glycolaldehyde acetal protons are separated into two triplets with equal populations, whereas at 100 °C both signals collapse into a single triplet (see box insertions and enlarged spectra); coalescence is observed at about room temperature. The very broad low-temperature (-90 °C) signals between $\delta = 3.5$–4.7 evolve into sharply resolved single peaks at above 50 °C, as the acetyl group resonances start to form separate singulets with an integral ratio of 12:6 (i.e., twelve equivalent OAc groups at C-4 and C-5 versus six glycolaldehyde OAc residues).

notion that the solid-state geometry of **2** is largely retained in solution as the succession of *anti*- and (±)-*gauche*-*meso*-butanetetrol units reduces the ring symmetry and accounts for the NMR patterns observed.

At higher temperatures the *gauche* ↔ *anti* transitions are sufficiently fast and display the time-averaged patterns, whereas at lower temperatures **2** starts to freeze into its solid-state geometry. The coalescence temperature T_C for the H-2 and C-2 resonances is observed at about room temperature, although the solvent had to be changed at around 24 °C. From the low-temperature separation of the signals, and dynamic NMR line shape analysis,[20] the rough estimate $T_C \approx 290 \pm 25$ K yields an activation barrier of approximately $\Delta G^{\ddagger} \approx 60 \pm 5$ kJ mol^{-1} for the *gauche* ↔ *anti* transitions of the butanetetrol segments within the macroring. The strait-jacket of the macrocycle obviously favors low-symmetry conformations energetically over all-*gauche* or all-*anti* arrangements, with the conformational transitions occuring in a cooperative fashion. Hence, the solid-state geometry of **2** can be considered a realistic snapshot over the state in solution.

Conclusion

The solid-state structure of the per-acetoxymethyl-substituted 30-C-12 crown acetal **2** detailed herein provides the second X-ray diffraction study of a 30-membered crown compound, the first being the simple aliphatic 30-C-10 crown ether.[21] A comparison of their molecular geometries is interesting in such as they are distinctly different—not unexpected as -OCH_2CH_2O- units in crown ethers and the respective -$OCH_2CH_2OCH_2O$- units in the crown acetal are apt to follow different crystal engineering patterns. Thus, whilst the 30-membered ring in crown acetal **2** adopts an undulating three-loop shape (Figure 2), the 30-C-10 crown ether macrocycle organizes itself in a planar, rectangular form, characterized by the bridging of two parallel sets of three -OCH_2CH_2- units in *anti*-arrangement with two *gauche*-oriented ethylenedioxy units on either end in a handle-like fashion (Figure 5).[21] In solution, however, both macrocycles are highly flexible and thus capable of elaborating variously sized cavities, which in their size can adapt to the size of the potential guest molecules or cations to be incorporated. In the case of 30-C-10 this has been already evidenced by the X-ray structure of its tetrahydrate, which has the four water molecules located inside the substantially widened macrocycle.

Attempts to induce the 30-C-12 crown acetals **1** and **2** to form inclusion compounds, as of now, have not been successful. More favorable in this respect are the β-CD- and γ-CD-derived 35-C-14 and 40-C-16 crown acetal analogues of **1** and **2**. The prospects for their acquisition in a form suitable for X-ray structural investigations appear to be favorable, as

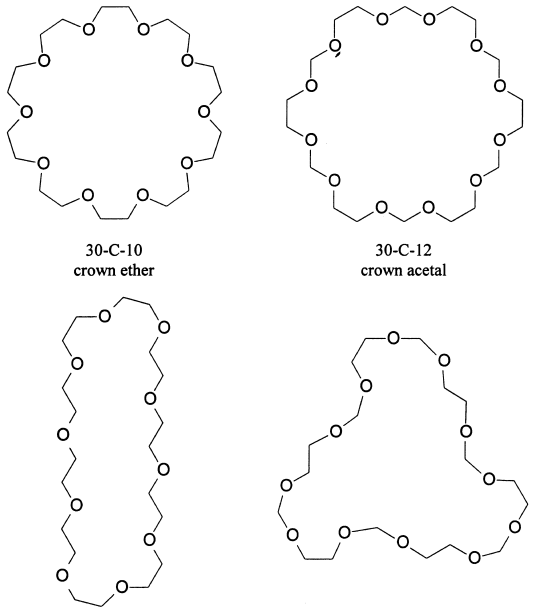

Figure 5. Solid-state molecular geometries of the 30-membered macrocycles in a 30-C-10 crown ether[21] and in the 30-C-12 crown acetal detailed herein, that is a planar rectangular shape versus an undulated three-looped structure.

the β-CD- and γ-CD derived analogue of **2**, that is the peracetoxymethyl-substituted 35-crown-14 and 40-crown-16 polyacetals with seven and eight CCOCO-units in the macrocyclic core, have already been crystallized (m.p. 109 – 111 and 143.5 – 145 °C). The solid-state molecular geometry of the crown acetal with the "uneven" (seven) *meso*-butanetetrol/glycolaldehyde acetal units may be predicted to resemble that of **2**, with the "uneven" unit inserted in *gauche*-orientation into the alternating *gauche*/*anti*-arrangements, inasmuch as two successive *anti*-disposed glycol fragments would inflict considerable strain into the macrocycle. For the γ-CD-derived 40-C-16 crown acetal analogues of **1** and **2**, however, we envisage an undulated four-loop structure, not unlike the shape of a four-leaf clover. We hope to be in a position to report on these issues in the near future.

Experimental Section

Octadeca-(acetoxymethyl)-30-crown-12 polyacetal (2):[22] α-Cyclodextrin (1.95 g, 2.00 mmol) was added to a stirred and cooled (0 – 5 °C) aqueous solution of $NaIO_4$ (3.85 g, 18.0 mmol, in 90 mL) and the clear solution was kept at 0 °C in a dark ice-box for 11 d, whereafter TLC revealed a single spot ($R_f = 0.64$, 2:2:1 *n*BuOH/MeOH/water) of the dodeca-aldehyde (in one of the various hemiacetal and/or hemialdal hydrate forms possible). Then, 1,2-ethanediol (0.34 mL, 6.1 mmol) was added while stirring to decompose excess $NaIO_4$, the mixture was kept in a dark ice-box overnight, and an aqueous $BaCl_2$ solution (1.90 g, 9.12 mmol, in 10 mL) was added to the mixture. The solution as allowed to stand for a few hours at ambient temperature, and the resulting precipitate was filtered off, followed by evaporation of the filtrate to dryness in vacuo. The residue was suspended in dry MeOH (20 mL), kept in a refrigerator overnight, the solids were filtered off upon addition of charcoal, and the filtrate was evaporated to dryness in vacuo at ≈35 °C. This procedure was repeated twice to give a white powder (2.33 g), which was dissolved in MeOH/water (40 mL, 3:1). Upon cooling (0 °C) $NaBH_4$ (600 mg) was added while stirring and the mixture was kept at room temperature overnight. Addition of acetone (3 mL) to remove excess reagent, neutralization with cation-exchange resin (IR 120, H^+ form), evaporation to dryness, and several co-evaporations of the residue from dry MeOH left the polyol **1** as a colorless solid. Polyol **1** was dissolved in a mixture of Ac_2O (15 mL) and pyridine (30 mL), and stirred overnight at room temperature. Subsequent evaporation to dryness in vacuo at 40 °C, followed by co-evaporation with toluene (3 × 25 mL) afforded a syrup which was dissolved in hot EtOAc, treated with charcoal, filtered, and evaporated to dryness. The residue was crystallized by trituration with EtOAc/EtOH, affording **2** (3.20 g, 92 %) as colorless plates of m.p. 171 – 173 °C. Lit.:[16a] m.p. 162 – 164 °C; yield 0.6 %. $[\alpha]_D^{22} = 0.00$ (c = 2, $CHCl_3$); ^{1}H NMR (300 MHz, $C_2D_2Cl_4$, 100 °C): $\delta = 5.06$ (t, 6H, J = 5.1 Hz, 2-H), 4.40 (dd, 12H, $J = 8.6$, 4.0 Hz, 4-CH_2^A, 5-CH_2^A), 4.15 – 4.03 (br m, 24H, 4-H, 4-CH_2^B, 5-H, 5-CH_2^B), 4.01 (d, $J = 5.1$ Hz, 12H, 2-CH_2), 2.03 (s, 36H, 12 AcCH_3), 1.98 (s, 18H, six 2-AcCH_3); ^{13}C NMR (75 MHz, $C_2D_2Cl_4$, 100 °C): $\delta = 170.4$, 170.3 (Ac*C*O), 101.4 (C-2), 77.1 (4-*C*H$_2$, 5-*C*H$_2$), 65.0 (2-*C*H$_2$), 64.2 (C-4, C-5); for other temperatures, see Figure 4; ESI-MS: m/z: 1763.5 $[M+Na]^+$; $C_{72}H_{108}O_{48}$ (1741.6): calcd C 49.65, H 6.25; found C 49.29, H 6.18.

Crystals suitable for X-ray analysis were obtained by slow crystallization of **2** from EtOH containing a small amount of EtOAc. A colorless crystal of dimensions 0.55 × 0.20 × 0.18 mm was analyzed on a Enraf-Nonius CAD-4 diffractometer using graphite-monochromated $Mo_{K\alpha}$ ($\lambda = 0.71093$ Å) radiation. Crystal data of **2**: $C_{72}H_{108}O_{48}$, $M_r = 1741.59$ g mol^{-1}, monoclinic, space group Pn, $a = 15.729(2)$, $b = 12.757(1)$, $c = 22.333(5)$ Å, $\beta = 96.04(2)$, V = 4456.3(12) Å^3, $Z = 2$, $\rho = 1.298$ g cm^{-1}, $\mu(Mo_{K\alpha}) = 0.103$ mm^{-1}, T = 298(2)1 K. Of 7333 reflections collected, 7333 are independent (R_{int} = 0.0000). The structure was solved by direct methods (SHELXS-86)[23] and successive synthesis. Refinement (on F^2) was performed by full-matrix least squares method with SHELXL-97.[23] $R(F) = 0.0608$ for reflections with $I \geq 2\alpha I$, $\omega R(F^2) = 0.2022$ for all 7333 reflections ($\omega = 1/[\sigma^2(F_0^2) + (0.1293P)^2 + 2.3009P]$; where $P = (F_0^2 + 2F_c^2)/3$); goodness-of-fit on F^2: $S = 1.045$. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were considered in calculated positions with the 1.2 U_{eq} value of the corresponding bound atom. Graphics of Figure 2 were generated using the MolArch$^+$ program.[24]

Crystallographic data (excluding structure factors) for the structure **2** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-143715. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Octadeca-(hydroxymethyl)-30-crown-12 polyacetal (1):[22] A few drops of 2 N methanolic sodium methoxide were added to a solution of octadeca-acetate **2** (2.75 g, 1.58 mmol) in dry MeOH (50 mL) and the mixture was stirred at room temperature overnight. After neutralization with IR-120 (H^+ form) the solution was evaporated to dryness in vacuo, and the residue was crystallized from 1-propanol as colorless plates (1.30 g, 84 %); m.p. 200 – 203 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 4.92$ (t, 6H, $J = 5.6$ Hz, 2-OH), 4.88 (t, 6H, $J = 4.9$ Hz, 2-H), 4.65 (t, 12H, $J = 5.4$ Hz, 4-OH, 5-OH), 3.84 (br s, 12H, 4-H, 5-H), 3.65 – 3.45 (m, 24 H, 4-CH_2, 5-CH_2), 3.45 – 3.37 (br t, $J = 5.0$ Hz, 2-CH_2); ^{13}C NMR (75 MHz, [D$_6$]DMSO): $\delta = 103.2$ (C-2), 78.3 (4-*C*H$_2$, 5-*C*H$_2$), 63.1 (2-*C*H$_2$), 60.9 (C-4, C-5); ESI-MS: m/z: 1007.6 $[M+Na]^+$; $C_{36}H_{72}O_{30} \cdot 1.5\,H_2O$ (1012.0): calcd C 42.73, H 7.47; found: C 42.69; H 7.52.

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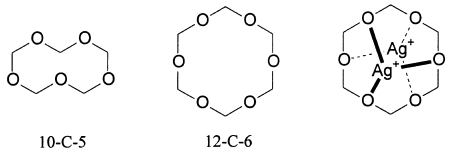
[7] *Nomenclature*: Although macrocyclic polyacetals, such as **1** or its peracetate **2**, do not adopt a crown-like molecular geometry—the terminology for macrocyclic ethers was derived from their crown-like shape—it appears not only logical but practical to extend this well-introduced notational mode to the acetal analogues of crown ethers, resulting in the term *crown acetals* for macrocycles with acetal oxygens only; similarly adapting the description established for ring size and number of oxygens, **2** is the octadeca-(hydroxymethyl) derivative of a 30-crown-12 polyacetal, the β-CD- and γ-CD-derived analogues are macrocycles with a 35-crown-14 and 40-crown-16 skeletal backbone.

[8] a) The cyclic pentamer and hexamer of formaldehyde—abbreviated in correspondence to crown ether terminology as 10-C-5 and 12-C-6, respectively—are neither crown ethers nor crown acetals, but de facto *crown aldals*,[8b] as they originate from the reaction between two aldehydes rather than between two diols or between an aldehyde and a diol.



10-C-5 12-C-6

Whilst the X-ray-confirmed molecular geometries of 10-C-5[8c] and 12-C-6[8d] show close analogies to those of the crown acetals of the same ring size, their cation binding capabilities are apt to be different, as evidenced, for example, by the unique di-silver ion complex of 12-C-6.[8e] b) The terms aldal, hemialdal, and hemialdal hydrate are commonly used in carbohydrate chemistry to denote the various forms adopted by sugar-derived dialdehydes: R. D. Guthrie, *Adv. Carbohydr. Chem.* **1970**, *16*, 118–140; c) Y. Chatani, K. Kitahama, *Bull. Chem. Soc. Jpn.* **1973**, *46*, 2300–2305; d) Y. Chatani, T. Ohno, T. Yamauchi, Y. Miyake, *J. Polym. Sci. Polym. Phys.* **1973**, *11*, 369–373; e) H. W. Roesky, E. Peymann, J. Schimkowiak, M. Noltemeyer. W. Pinkert, G. M. Sheldrick, *J. Chem. Soc. Chem. Commun.* **1983**, 981–982.

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