

Coordination Chemistry

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Cyclodextrin Bucket Wheels: An Oligosaccharide Assembly Accommodates Metal(IV) Centers***Klaus Benner, Johannes Ihringer, Peter Klüfers,* and Danira Marinov*

Mononuclear metal complexes in aqueous solution lie at the heart of coordination chemistry. Their significance is evident in areas ranging from simple textbook chemistry to sophisticated applications in fields of current interest. Water as a solvent is the most important medium in biochemistry and environmental chemistry. When the challenges that it poses have been met, water could be an especially advantageous solvent for technical catalysis, particularly in green chemistry. The chemistry of mononuclear coordination complexes in water, as characterized by the variety of multidentate organic chelators that may bind to a metal center, is most extensive for the medium oxidation states of a metal, typically + II and + III. This statement also holds for metalloenzymes, in which protein side chains act as ligands. The chemistry of higher metal oxidation states in water is, however, usually severely restricted. Hydrolytic reactions lead to replacement of the mononuclear metal/chelator core with mono- and polynuclear (hydr)oxido metal species and, finally, (hydrated) oxide phases. This is the case for main-group-metal as well as transition-metal centers, examples being tin(IV) and manganese(IV). The latter shows another property of high-oxidation-state centers that may prohibit the formation of stable mononuclear coordination compounds with organic ligands, namely, its reactivity as an oxidant. The combination of these properties results in decidedly restricted chemistry in water. A good example is lead(IV), whose coordination chemistry in

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water is restricted to a couple of halogeno plumbates(IV) in acidic solution, and the hexahydroxidoplumbate(IV) ion at high pH values. In line with this experience, the lead(IV) compounds used in synthetic organic chemistry, lead tetraacetate and its derivatives, rapidly decompose on contact with moisture to form black lead dioxide.^[1] Attempts to prepare chelates by adding potential chelators such as oxalate, catecholate, or glycosides to hexahydroxidoplumbate(IV) solutions result in the formation of mostly brownish suspensions of decomposition products.

In our efforts to develop the coordination chemistry of carbohydrates,^[2] which form the most abundant class of biomolecules, we found that the functional groups of the oligosaccharide β -cyclodextrin are able to assemble into a nanoscaled trimer that provides a mononucleating binding site for high-valent metal centers. β -Cyclodextrin (β -CD) is a cyclic glucose heptamer that is composed of seven α -1,4-linked D-glucopyranose residues. The outer diameter of a single, torus-shaped β -CD unit is about 1.5 nm.^[3] The size of the metal-counterion-cyclodextrin assemblies described herein approach those of small proteins such as a ferredoxin. Most data were collected for tin(IV), because not only could X-ray crystal structures be determined, but the ^{119}Sn nucleus also allows NMR spectroscopic analysis of the complexes in the solution state. As a result, the assembly described below was shown not to be a loose aggregate in the solid state, but rather a formation that is so stable that it was the only solution species present.

The hexahydroxidostannate(IV) ion $[\text{Sn}(\text{OH})_6]^{2-}$ was used as a precursor. At pH values higher than about 11, a single signal was observed in the ^{119}Sn NMR spectrum, which proved that this ion is the only Sn-containing solution species. Hydrated tin oxide precipitated when the pH value was adjusted close to neutrality (ca. pH 8). The addition of a chelator such as oxalate to an alkaline hydroxidostannate(IV) solution did not alter the ^{119}Sn NMR spectrum at higher pH values nor affect the formation of hydrated tin oxide at pH values close to neutrality.^[4] Ligands such as catecholate(2-) and ethanediolate(2-) were better competitors with the hydroxido/oxido ligand. In a typical experiment, the ^{119}Sn NMR spectrum of hydroxidostannate and a threefold molar amount of ethanediol showed a mixture of the heteroleptic mono- and bis(ethanediolato)hydroxidostannates and the homoleptic tris(ethanediolato)stannate, the first two species being the major ones. Such observations make it plausible that well-defined homoleptic stannates(IV) with organic chelators are not usually accessible from aqueous solution equilibria.

In contrast to these observations, the ^{119}Sn NMR spectrum of a threefold molar amount of β -cyclodextrin with hexahydroxidostannate(IV) showed a single signal, whose chemical shift indicated a new, hexacoordinate, tin-containing species in solution. Lowering the pH value to about 8 did not change the signal, but the solution started to become cloudy (e.g., pH 8.8 clear solution, pH 7.8 slightly cloudy solution, pH 7 SnO_2 precipitate). The tentative coordination compound was obviously destroyed at pH 7. This behavior indicated that deprotonated β -CD species were the actual tin-binding entities. When lithium was used as the counterion, crystals

suitable for X-ray diffraction grew over the course of one week following controlled ethanol addition. The results from the structural analysis were consistent with the spectroscopic results. The most conspicuous building unit of the crystals is a bucket-wheel-shaped assembly with threefold rotational symmetry that consists of three components: three β -CD dianions, three tetrahedral tetraaqualithium cations, and a tetravalent metal center. An ethanol guest molecule inside each β -cyclodextrin ring may be regarded as a fourth kind of building unit whose presence is responsible for the necessary decrease of the solubility of the assembly at the onset of crystallization. Figure 1 (top) gives an overview of the C_3 -symmetric complex. The three β -cyclodextrin rings are

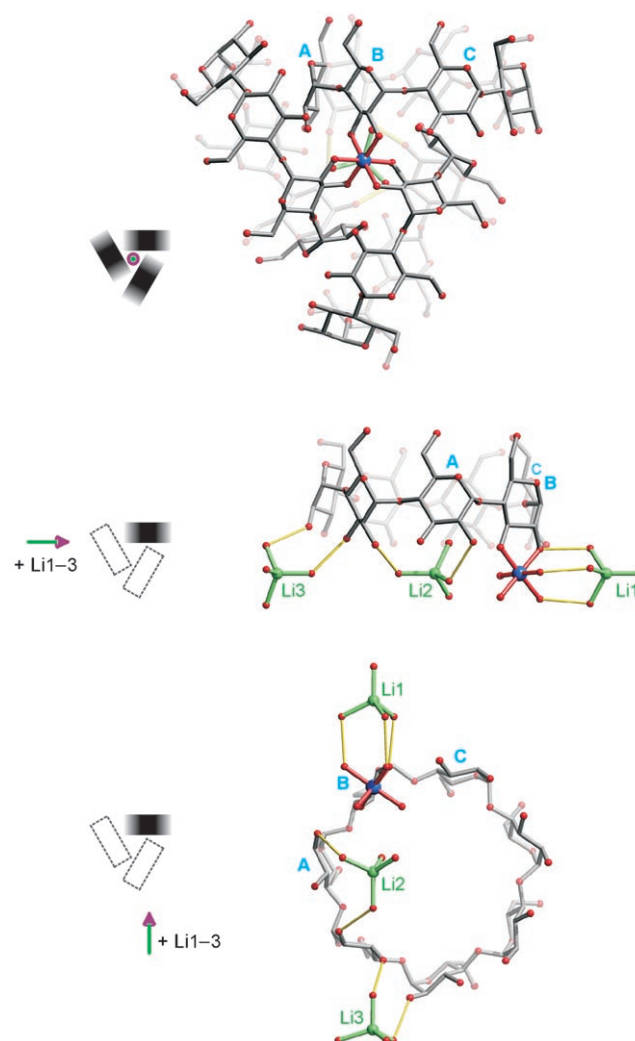
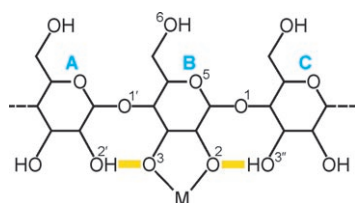


Figure 1. Top: The $M^{IV}(\beta\text{-CD})_3$ bucket-wheel motif together with the innermost $\text{Li}(\text{H}_2\text{O})_4$ counterion (Li2 in the middle and bottom illustrations) viewed along the threefold symmetry axis. The metal-binding site is located in the center at the front of the picture. Middle and bottom: sections of the structure as detailed in the cartoons on the left, together with the hydrated Li1 and Li3 counterions; M^{IV} blue, Li green, O red, hydrogen bonds: yellow. Ethanol guest molecules inside each β -CD torus are omitted. The threefold symmetry axis runs through the lithium atoms and the tetravalent central metal. The blue letters A–C correspond to the glucose units shown in Scheme 1. The data for the germanium structure were used to draw the structure.

nested. Close inter-cyclodextrin contacts are established between the diol functions along the O2/3 rim of the cyclodextrin (see Scheme 1 for atom numbering) in the coordination sphere of the tetravalent metal center (shown in



Scheme 1. The section of the tris(diolato) metal-binding site near the M^{IV} center. The diolato ligand shown is hydrogen-bonded (yellow bars) to the hydroxy functions of the neighboring glucose units. The blue letters A–C correspond to the glucose units shown in Figure 1. Mean $O\cdots O$ and $M-O$ distances (in pm): $O2'\cdots O3$: Mn 283.6(8), Ge 282.2(5), Sn 274.0(7), Pb 273.8(5); $O3''\cdots O2$: Mn 275.9(9), Ge 280.4(5), Sn 277.7(6), Pb 276.4(5); $M-O2$: Mn 196.7(5), Ge 193.6(3), Sn 208.7(4), Pb 217.4(3); $M-O3$: Mn 189.4(6), Ge 189.2(3), Sn 204.3(4), Pb 214.4(3).

blue) as well as between the CD rings at the rear of Figure 1. In the latter, three short hydrogen-bonded contacts between diol-O atoms establish a direct link between the cyclodextrin rings ($O\cdots O$ 257 pm). Other contacts that contribute to the stability of the trimer are shown by viewing perpendicular to the threefold axis (Figure 1, middle and bottom). The projections show hydrogen bonds between the aqua ligands of the lithium counterions and diol-O atoms of the cyclodextrin. Fifteen such hydrogen bonds between counterion and cyclodextrin may be counted when symmetry is taken into account, which makes the three $[Li(H_2O)_4]^+$ ions well-matching connectors: two of them are inside the assembly and one is peripherally bonded (this latter counterion may be substituted by a hydrated sodium ion). The interaction between the nested cyclodextrin rings and the connectors contributes to the stability of the most important feature of the assembly, namely, the metal-binding site. This site consists of six ligating O atoms derived from the β -CD diol groups and is embedded in a hydrogen-bond environment. The hydrogen bonds between the cyclodextrin oxygen atoms are omitted from Figure 1 for clarity, but are shown in Scheme 1 (three of the seven glucose units are shown). The O2 atom of the metal-binding site is hydrogen-bonded to the $O3''H$ hydroxy function of the anhydroglucose unit, and the ligating O3 alkoxido O atom is hydrogen-bonded to the $O2'H$ anhydroglucose hydroxy function. In total, the O_6 metal-binding site is supported by nine hydrogen bonds: six intra-cyclodextrin bonds and three from the peripherally bound counterion.

The absence of mixed cyclodextrin–hydroxidostannate species is understandable, because only the complete trimer benefits from the stabilization by the hydrogen bonds between CD units and with the hydrated counterions. Accordingly, the overall stability of the bucket-wheel-shaped stannate is higher than the stability of stannates of related glycosides. Thus, the ^{119}Sn NMR spectrum of a mixture

of 1 mol $[\text{Sn}(\text{OH})_6]^{2-}$, 3 mol β -CD, and 3 mol of the methylated cyclodextrin building block methyl- α -D-glucopyranoside showed only the bucket-wheel complex and no Sn-bound methylglucoside.

Both the high tendency for formation of the bucket-wheel motif and its robustness were demonstrated by its formation with a strongly oxidizing central metal: lead(IV). The reactant used was hexahydroxidoplumbate(IV).^[5] The unsuccessful attempts to coordinate well-established chelators to lead(IV) are described above. The addition of β -cyclodextrin, however, did not result in decomposition reactions; crystals were formed from the yellowish solutions. X-ray analysis revealed an isotopic structure with the typical bucket-wheel motif (see caption of Scheme 1 for atomic distances). Both the crystals and the solutions are stable over prolonged periods of time. It should be recalled at this point that the above-mentioned use of lead(IV) acetate in organic synthesis includes the oxidative cleavage of diols. Taken together with the NMR investigation of the stannate, the cyclodextrin bucket-wheel motifs prove to be stable against dissociative decay as well as resistant to oxidative degradation to a much larger extent than related chelators that lack supramolecular support.

A specific restriction of carbohydrate chelation remains to be investigated. Diol functions attached to a furanose ring are most suited to chelate small central atoms, whereas diol functions attached to a pyranose ring in the *trans* configuration are much less suited.^[6] The latter is the situation for β -cyclodextrin, so a lower limit for the atomic radius of the M^{IV} center has to be expected. To clarify whether the β -CD bucket-wheel motif provides a binding site for the particularly important first-row transition metals and post-transition-metal elements, the reactions of silicate and germanate with β -cyclodextrin were investigated. No six-coordinate silicon was detected by ^{29}Si NMR spectroscopy, but germanium was found to occupy the metal-binding site of the bucket-wheel motif (see caption of Scheme 1 for atomic distances). This result indicates that transition metals could also bind, since the size of the germanium(IV) center is almost the same as that of a tetravalent first-row transition metal (compare the crystal radii of the octahedrally coordinated tetravalent ions: Pb 92, Sn 83, Ge 67, Mn 67 pm, Si 54 pm).^[7] The synthesis of a mononuclear manganese complex in an aqueous environment is a challenge because of the strong tendency of manganese(IV) to form oxido-, hydroxido-, carboxylato-, and alkoxido-bridged polynuclear species. We attempted to synthesize a bucket-wheel-type manganese(IV) compound by starting from a manganese(II) salt. Oxidation with either air, hydrogen peroxide, or hexacyanidoferrate(III) yielded deep red solutions of a tentative manganese(IV) complex. Crystallization succeeded, and the structure determination again revealed the bucket-wheel motif. The metrical properties of the manganese and the germanium coordination octahedra are very similar, which is expected given that the crystal radii of Ge and Mn^{IV} are the same and there is no Jahn–Teller distortion for the central d^3 Mn^{IV} ion (mean $M-O$ bond lengths: Ge 191, Mn 190 pm; as the ionic radius of high-spin Mn^{III} is 12 pm larger than that of Mn^{IV} ,^[7] a mean $Mn-O$ bond length of more than 200 pm is expected for an $\text{Mn}^{III}O_6$ coordination sphere). The assignment of the oxidation state

+ IV to the manganese center is in accord with the typical red color of the $\text{Mn}^{\text{IV}}\text{O}_6$ chromophore.

The coordination chemistry of carbohydrates encompasses a broad scope of central metals and their oxidation states. This work has now expanded this field of knowledge to strongly oxidizing and potentially dioxide-forming metal centers. The oxophilic metal centers investigated herein mark one end of the range of metals with affinity to carbohydrates; the other end includes soft metal centers such as rhenium(I) and palladium(II).^[8,9] The molecular origin of this unusual versatility is the polyfunctionality of carbohydrates. Aside from the functions that are involved in the metal-binding site, the remaining functional groups are able to arrange themselves, following the rules of supramolecular chemistry, into molecular patterns that support the metal-binding site. Carbohydrates thus patently represent an efficient and versatile class of ligands whose coordination chemistry follows the same supramolecular principles that shape a metalloenzyme.

Experimental Section

The general formula of the hexagonal β -cyclodextrin bucket-wheel structures is close to $[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-M}^{\text{IV}}(\beta\text{-CDH}_2)_3\}]\text{H}_{-1}\cdot 25\text{H}_2\text{O}$.^[10] There are two possible sites of deprotonation: A close hydrogen-bonded contact between diol O atoms at the rear of the bucket wheel suggests that, in line with the acidity constants, a diol hydroxy group is deprotonated rather than a water molecule. However, the presence of hydroxide can not be excluded. There are large, empty channels along $[00z]$ which contain weakly defined electron density. The cavity inside of each cyclodextrin torus is filled with the precipitating agent in an ordered way in the case of ethanol; the channels, however, contain disordered precipitating agent (note the small deviations between the idealized formulae given in this section and the deposited data that take disorder into account).

Tin: Sodium hexahydroxidostannate(IV) (0.117 g, 0.44 mmol) was dissolved in water (24 mL). β -Cyclodextrin (1.498 g, 1.32 mmol) was added to the solution. Lithium hydroxide monohydrate (0.055 g, 1.32 mmol) was added, the solution was stirred for 60 minutes, and then the mixture was saturated with ethanol (12 mL). After the slow diffusion of ethanol vapor into the solution over the course of three weeks at 12°C, colorless crystals of $[\{\text{Na}(\text{H}_2\text{O})_4\}_3\{\text{Li}(\text{H}_2\text{O})_4\}_2\{\Lambda\text{-Sn}(\beta\text{-CDH}_2)_3\}]\text{H}_{-1}\cdot 27\text{H}_2\text{O}\cdot 3\text{EtOH}$ (**1**) were formed. The Li1 position (Figure 1, bottom) is occupied by sodium in terms of electron density and atomic distances. ¹¹⁹Sn NMR spectroscopy (H_2O , 23°C): $\delta = -493.3$ ppm (sodium hexahydroxidostannate(IV): -593.5 ppm).

Lead: β -Cyclodextrin (0.749 g, 0.66 mmol) and lithium hydroxide monohydrate (0.028 g, 0.66 mmol) were dissolved in water (10 mL). Sodium hexahydroxidoplumbate(IV) (0.078 g, 0.22 mmol) was added with stirring. The solution was stirred for 60 minutes and then saturated with ethanol. The solution was kept at 12°C under the diffusion of ethanol vapors. Crystals of $[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-Pb}(\beta\text{-CDH}_2)_3\}]\text{H}_{-1}\cdot 34\text{H}_2\text{O}\cdot 5\text{MeOH}$ (**2**) formed within one week. Small amounts of sodium (ca. 0.15 per formula unit) were refined close to the Li1 position.

Germanium: β -Cyclodextrin (1.317 g, 1.16 mmol) and lithium hydroxide monohydrate (0.340 g, 8.10 mmol) were dissolved in water (10 mL). Tetramethoxygermanium (0.791 g, 4.02 mmol) was added with stirring. Heating the solution for 30 min caused the formation of a colorless precipitate. After filtration of the mixture, ethanol vapors were allowed to diffuse into the filtrate. Crystals of $[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-Ge}(\beta\text{-CDH}_2)_3\}]\text{H}_{-1}\cdot 24\text{H}_2\text{O}\cdot 3\text{EtOH}$ (**3**) grew over the course of half a year.

Manganese: β -Cyclodextrin (1.362 g, 1.20 mmol) and lithium hydroxide monohydrate (0.504 g, 12.0 mmol) were dissolved in water (13 mL). Manganese(II) nitrate tetrahydrate (0.201 g, 0.80 mmol) and β -cyclodextrin (1.362 g, 1.20 mmol), dissolved in water (7 mL), were added. A yellow solution formed which gradually turned dark red upon stepwise addition of potassium hexacyanidoferrate(III) (0.527 g, 1.60 mmol) in water (10 mL). Finally, the reaction mixture was filtered and layered with methanol. Red crystals of $\text{K}_2[\{\text{Li}(\text{H}_2\text{O})_4\}_3\{\Lambda\text{-Mn}(\beta\text{-CDH}_2)_3\}]\text{H}_{-3}\cdot 23\text{H}_2\text{O}\cdot \text{MeOH}$ (**4**) were obtained over the course of six weeks.

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20.85, 28834 reflections, 7065 independent and used in refinement, 6001 with $I \geq 2\sigma(I)$, $R_{\text{int}} = 0.0610$, mean $\sigma(I)/I = 0.0534$, 766 parameters, $R(F_{\text{obs}}) = 0.0752$, $R_w(F^2) = 0.2140$, $S = 1.053$, Flack parameter: 0.00(6), min. and max. residual electron density: $-0.688, 1.083 \text{ e \AA}^{-3}$. CCDC-600809 (**1**), -600808 (**2**), -600806 (**3**), -600807 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.