

Formation and structure of a complex of sucrose with cobalt(III)bis(phenanthroline)

José Parada,^a Sergio Bunel,^{a,*} Carmen Ibarra,^a Guillermo Larrazabal,^a
Exequiel Moraga,^a Nicholas D. Gillitt,^b Clifford A. Bunton^{b,*}

^a*Departamento de Química Inorgánica y Analítica, Facultad de Ciencias Químicas y Farmacéuticas,
Universidad de Chile, Santiago, Chile*

^b*Department of Chemistry and Biochemistry, University of California, Santa Barbara, CA 93106, USA*

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Abstract

Sucrose forms a dicationic complex with cobalt(III)bis(phenanthroline) which can be isolated as the sparingly water-soluble triiodide salt or the water-soluble chloride. The circular dichroism (CD) spectrum demonstrates the Δ configuration at Co(III) and the presence of two phenanthroline and one sucrose residues in the complex. The O-2(g)–O-1(f) distance in crystalline sucrose permits strain-free coordination of these centers with Co(III) and in the complex the H-1,1'(f) singlet of sucrose separates into a pair of doublets. The ¹H NMR spectrum in DMSO-*d*₆ shows that OH-2(g) is deprotonated and the signal of OH-1(f) is shifted strongly downfield by complexation with Co(III). Coordination involving glucose and fructose residues is consistent with neither α -methyl glucoside nor fructofuranose forming mixed complexes with phenanthroline. Structure simulation with the semi-empirical PM3(tm) basis set indicates that complexation by O-2(g) and OH-1(f) can give a Δ -complex with little structural distortion, whereas in hypothetical Λ -complexes there is distortion of the sucrose residue. Observation of an NOE involving the sucrose and phenanthroline residues supports the postulated structure of the Δ -complex. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Sugars, other polyols, and their amino derivatives, form complexes with metal ions, in some cases by cocrystallization, but complexes with transition metal ions are identified in solution and some can be isolated as stable solids.^{1,2}

We are interested in mixed complexes of sugars with bis-1,10 phenanthroline cobalt(III) (Co(phen)₂).^{3,4} The phenanthroline rings are

planar and relatively rigid, and the complexes have well defined circular dichroism (CD) spectra that provide evidence of the configuration at Co(III).⁵ The ¹H NMR signals of phenanthroline do not interfere with those of the sugars, which allows identification of the ligating groups. Amino sugars form relatively stable octahedral complexes with Co(III)-(phen)₂ through *cis*-2-NH₂ and 1-O[−] ligands,³ and with α -D-galactose and β -D-arabinose complexation involves *cis*-1,2 groups, although stable complexes could not be isolated.⁶ Sucrose forms a complex that was isolated by precipitation of the water-insoluble triiodide salt or as the soluble chloride.⁷

* Corresponding authors. Fax: + 56-2-7370567 (S.B.); tel.: + 1-805-8932605; fax: + 1-805-8934120 (C.A.B.).
E-mail address: bunton@chem.ucsb.edu (C.A. Bunton).

In crystalline sucrose 2-OH(g) and 1-OH(f) are hydrogen-bonded, and the inter-oxygen distance of 2.82 Å⁸ should allow these groups to bond with Co(III) without significantly perturbing the sucrose or the octahedral centers, despite formation of a large ring.⁷ The H-1(f) singlet of sucrose⁹ splits on complexation into a pair of doublets with the expected geminal coupling constants, indicating that one binding site was OH-1(f) but evidence on binding at 2(g) was more limited.⁷ The Δ configuration at Co(III) is demonstrated by the sign sequence of the CD signals.^{5,7} However, there was no evidence on other aspects of the structure including deprotonation of the ligating OH groups and interactions between the sucrose and phenanthroline groups.

The hydrogen-bonding between 2-OH(g) and 1-OH(f) in the crystal,⁸ which is evidence for the proximity of these groups, may be disrupted in water where sucrose appears to exist as a mixture of equilibrating conformers.^{10,11} Therefore, we considered other plausible structures of the sucrose Co(phen)₂ complex, including the possibility that only a single ring was involved in complexation with Co(III).

The original results were limited in that we had no evidence regarding the NMR signals of the hydroxyl hydrogens and incomplete

evidence on other signals. The dicationic form of the complex was isolated as the water-insoluble triiodide salt, but we incorrectly assumed that the water-soluble chloride salt was tricationic, and we had no evidence on locations of the hydrogen atoms on the ligating oxygens at positions 1(f) and/or 2(g). We have therefore now examined the NMR spectra in DMSO-*d*₆ in order to provide evidence on the assignment of the hydroxyl protons and the site(s) of protonation of the ligating oxygens. The CD spectra of both forms of the complex have been compared, and structural optimizations have been made on a variety of possible structures.

2. Results

Absorption and CD spectroscopy.—The absorption spectrum of the chloride salt in H₂O (Table 1) is typical of octahedral Co(III)-(phen)₂ complexes with broad signals that are not readily assigned. The CD spectrum, with well-defined excitonic signals at 267 and 281 nm (Table 1), shows that two phenanthroline ligands are bonded to Co(III), and the sign sequence in this region is that of a Δ -complex.^{5,12} Spectra in the visible region are typical of d,d transitions of Co(III) complexes.^{5,12} We saw no evidence of a Λ -complex.

The spectra of the isolated complex (Table 1) are very similar to those of the reaction mixture before product isolation (Section 4). Sucrose has no CD signals at the wavelengths studied, Co(III)(phen)₂ is a racemic mixture, and our isolation of a chiral complex is not an artefact due to chromatography on a chiral Sephadex column.^{3,7} The CD spectrum was also examined with the triiodide salt after treatment with Na₂S₂O₃.³ The spectrum in the UV is noisy, but wavelengths of the CD extrema are easily identified and are essentially as for the chloride form of the complex (Table 1). (The strong absorbance of I[−] limited the range of wavelengths that could be examined).

NMR spectroscopy.—The ¹H NMR spectra in D₂O were obtained with the reaction mixture and also with the isolated complex as the chloride salt. Some signals of sucrose overlap

Table 1
Absorption and CD spectra of Δ -[Co(III)(phen)₂-(sucrose)]Cl₂^a

Absorption		CD	
λ (nm)	log ϵ	λ (nm)	$\Delta\epsilon$
227	5.03	229	−5.5
		241	+8.6
270 (270)	4.67 (4.7)	267 (266)	+11.3 (+9.1)
		281 (280)	−15.4 (−12.2)
295sh (287sh)	4.31 (4.4)	297sh (297sh)	−5.7 (−4.0)
329sh (329sh)	3.67 (3.8)	323 (319)	+3.3 (+3.2)
		363 (368)	−1.8 (−1.7)
		413 (413)	+3.6 (+3.4)
519 (519)	2.15 (2.2)	513 (513)	−6.8 (−6.1)
		610sh (600sh)	−0.27 (−0.2)
840	0.18		

^a In water, values in parentheses are for the triiodide salt after treatment with Na₂S₂O₃.

Table 2

¹H chemical shifts, (δ , ppm) and coupling constants, (J , Hz) of Δ -[Co(III)(phen)₂(sucrose)]Cl₂ and sucrose ^a

δ (ppm)	H-1(g)	H-2(g)	H-3(g)	H-4(g)	H-5(g)	H-6,6'(g)
Complex	5.40 (0.77)	3.24 (0.73)	3.67 (0.66)	3.93 (0.72)	3.56	3.75–3.84
Sucrose		3.57	3.77	3.48	3.81–3.88	3.81–3.86
	H-1,1'(f)		H-3(f)	H-4(f)	H-5(f)	H-6,6'(f)
Complex	3.74 (0.37), 3.59 (0.35)		4.30 (1.26)	4.16 (1.18)	3.91	3.75–3.84
Sucrose	3.69 (0.44)		4.23 (1.77)	4.04 (1.30)	3.88–3.93	3.81–3.86
J (Hz)	$J_{1-2(g)}$	$J_{2-3(g)}$	$J_{3-4(g)}$	$J_{4-5(g)}$	$J_{5-6,6'(g)}$	
Complex	3.5	10.0	9.5	9.5	≈ 3	
Sucrose	4.0	10.0	9.5	9.5		
	$J_{1-1'(f)}$		$J_{3-4(f)}$	$J_{4-5(f)}$	$J_{5-6,6'(f)}$	
Complex	13.0		9.0	9.0	4.0	
Sucrose			9.0	9.0	4.0	

^a In D₂O referred to TSP, values in parentheses are $T_{1,s}$.

Table 3

¹H chemical shifts, (δ , ppm) and coupling constants, (J , Hz) of Δ -[Co(III)(phen)₂(sucrose)]Cl₂ and sucrose ^a

δ (ppm)	H-1(g)	H-2(g)	H-3(g)	H-4(g)	H-5(g)	H-6,6'(g)
Complex	5.19	2.83 ^b	3.41	3.63	3.22–3.27	3.46–3.54
Sucrose	5.17	3.17	3.43–3.48	3.12	3.65	3.52–3.61
	H-1,1'(f)		H-3(f)	H-4(f)	H-5(f)	H-6,6'(f)
Complex	3.45, 3.26		3.88	3.94	3.56	3.46–3.54
Sucrose	3.40		3.88	3.77		3.52–3.61
J (Hz)	$J_{1-2(g)}$	$J_{2-3(g)}$	$J_{3-4(g)}$	$J_{4-5(g)}$	$J_{5-6,6'(g)}$	
Complex	3.0	9.5	9.5	9.0		
Sucrose	3.5	9.5	9.5	9.2	2.5,5.0	
	$J_{1-1'(f)}$		$J_{3-4(f)}$	$J_{4-5(f)}$	$J_{5-6,6'(f)}$	
Complex	13.0		8.0	8.0	3.7,4.0	
Sucrose			8.0	8.0		

^a In DMSO-*d*₆ referred to DMSO.^b For complex as triiodide δ 2.82.

those of the complex but others are well separated. Chemical shifts and coupling constants of the complex are very similar in the reaction solution and after isolation. So far as we know the signals of H-1(f) of free sucrose have not been resolved,^{9,10} but in the complex they separate into a pair of doublets (Table 2 and Ref. 7). There are no cross peaks of H-1(f) and H-1'(f) with other C–H signals in the COSY spectrum in D₂O. Most chemical shifts of the complex are not very different from those of sucrose except for H-1,1'(f), H-2(g), H-4(g) and H-5(g).

The ¹H NMR signals of the complex in D₂O are assigned directly from a COSY spectrum and are given in Table 2 with those of sucrose, which agree with those in the literature.¹⁰ Our chemical shifts are referred to TSP (sodium 3-(trimethylsilyl)propanesulfonate) rather than to HOD.¹⁰ We measured values of T_1 for some of the hydrogens of the sucrose residue in the complex and obtained values of the free sugar which agreed with those in the literature.¹⁰ Most of the NMR spectra were monitored in D₂O, but those of the complex and of sucrose have now been examined in

DMSO-*d*₆ (Tables 3 and 4), and we compared our values for sucrose with those in the literature, a protocol that simplified assignments.⁹ Our chemical shifts for sucrose in DMSO-*d*₆ are lower than the values reported earlier by ca. 0.3 ppm, due to our using DMSO (δ 2.50 ppm) as reference, whereas acetone was used earlier.⁹ Assignments for the complex in DMSO-*d*₆ were based on the COSY spectrum and spin–spin decoupling.

3. Discussion

Complexation through 2-OH(g) and 1-OH(f) is geometrically understandable in view of the inter-oxygen distance of 2.82 Å in crystalline sucrose⁸ and Co(III)–O bond lengths of ca. 1.9 Å,¹³ which should permit complexation without major distortion of the sucrose moiety.⁷ However, sucrose adopts a variety of conformations in aqueous solution,^{9–11} and we have to consider other possible sites of complexation, involving, for example, only the fructose or glucose residue. Fructose forms a mixed complex with Co(III)(phen)₂, but, based on the NMR evidence, it appears to involve the pyranose, rather than the furanose, form of the sugar.⁴ Complexation with only the glucose residue is also improbable,

because we now show that methyl α -D-glucopyranoside does not complex with Co(III)(phen)₂ under conditions in which the sucrose complex is readily formed (Section 4).

The separation of the H-1(f) signals in the complex (Table 3) is consistent with the postulated structure, and computed distances between the face of a phenanthroline ring and H-1(f) and H-1'(f) are 4.0 and 3.1 Å, respectively, consistent with the difference in chemical shifts due to π -shielding (Tables 2 and 3). The complex was isolated as a dication (Section 4) and not as a trication as assumed earlier.⁷ Acid dissociation constants of Co(III) complexes are such¹⁴ that we expect at least one of the bonding OH groups in the complex to be deprotonated at near-neutral pH in water. The upfield shift of H-2(g) in the complex (Tables 2 and 3) would be consistent with complexation through 2-O[–](g), which is now confirmed by the ¹H NMR spectrum in DMSO-*d*₆, as discussed later.

Coupling constants of sucrose and the complex in D₂O are similar except, as noted, for H-1(f) and H-1'(f), indicating that complexation does not have a major effect on conformations of the glucose and fructose residues,^{9,10} but *T*₁ values of the complex in D₂O are lower than those of the sugar, which is consistent with decreased mobility that is

Table 4
¹H chemical shifts, (δ , ppm) and coupling constants, (*J*, Hz) of the hydroxyl protons of Δ -[Co(III)(phen)₂(sucrose)]Cl₂ and sucrose^a

δ (ppm)		OH-2(g)	OH-3(g)	OH-4(g)	OH-6,6'(g)
Complex Sucrose		absent	3.35–3.39	4.84	4.44
		5.06	4.79	4.76	4.41
Complex Sucrose	OH-1,1'(f)		OH-3(f)	OH-4(f)	OH-6,6'(f)
	6.41 ^b 4.80		5.76 4.50	5.36 5.19	4.14 4.38
<i>J</i> (Hz)		<i>J</i> _{OH-2(g)}	<i>J</i> _{OH-3(g)}	<i>J</i> _{OH-4(g)}	<i>J</i> _{OH-6(g)}
Complex Sucrose			^c	3.5	6.0
		6.0	4.5	6.0	5.5
Complex Sucrose	<i>J</i> _{OH-1(f)}		<i>J</i> _{OH-3(f)}	<i>J</i> _{OH-4(f)}	<i>J</i> _{OH-6(f)}
	4.0,9.5 6.0		6.5 8.0	5.0 5.5	5.7 5.0

^a In DMSO-*d*₆ referred to DMSO.
^b For complex as triiodide δ 6.40.
^c Not measured, see text.

Table 5
Heats of formation and geometries of complexes

	Complex ²⁺					Complex ³⁺	Sucrose ^a
	Deprotonated O-1f		Deprotonated O-2g			Δ	
	Δ	Λ	Δ_1	Δ_2	Λ		
ΔH_f , (kcal mol ⁻¹)	-1687	-1677	-1684	-1681	-1675	-1409	
<i>Bond/torsional angle (°)</i>							
O-2(g)–Co(III)	101.5	95.7	92.8	89.4	82.2	100.5	
× –O-1(f)							
C-1(g)–O–C-2(f)	116.8	121.1	117.8	117.5	122.3	117.6	114.3(119.2)
ϕ	124.9	126.2	114.5	117.9	131.1	107.7	107.8(119.3)
ψ	-57.2	-33.8	-51.2	-52.0	-22.5	-47.5	-44.8(-53.6)
<i>Bond length/distance (Å)</i>							
Co(III)–O(g)	2.04	2.04	1.89	1.88	1.85	2.00	
Co(III)–O(f)	1.88	1.88	2.03	2.03	2.03	2.02	
O-2(g) to O-1(f)	3.03	2.90	2.84	2.76	2.56	3.09	2.82(2.72)

^a Values in parentheses are computed.

most evident for H-3(g) (Table 2). Structures of the Δ -complex and the hypothetical Λ -complex have now been optimized by using semi-empirical PM3(tm) parameters.^{15,16} Formation of the Δ -complex is predicted to be more favorable than that of the corresponding Λ -complex (by ca. 7 kcal mol⁻¹), and the conformation of the sucrose residue in the dicationic Δ -complex is similar to that of crystalline sucrose,⁸ as noted earlier in discussion of the structure of an assumed tricationic complex.⁷ The optimizations indicate that the Δ - is preferred over the Λ -complex regardless of charge, or site(s) of protonation. There is evidence that structures of sucrose and other sugars are similar in solution and in the solid,^{8,17} and our conclusions from structural optimizations are similar to the literature (Table 5).

The conformation of sucrose is governed by the torsional angles, ϕ , for O-5(g)–C-1(g)–O-1(g)–C-2(f), and ψ for C-1(g)–O-1(g)–C-2(f)–O-5(f) and the C-1(g)–O–C-2(f) bond angle.^{9,10} As a test we now show that predicted values of these angles in the di- or tri-cationic complexes are similar to those in crystalline sucrose (Table 5). The computed values for sucrose are based on the PM3 basis set, but similar values, slightly closer to those for the crystal,⁸ were obtained by using an ab initio

3-21G(*) basis set (data not shown). Treatments of conformations of the complexes by using PM3(tm) parameters indicate that deprotonation of the tricationic complex should shorten the Co(III)–O bond to the deprotonated OH group. The torsional angles ϕ and ψ also change modestly, but there appear to be no major changes in overall conformation (Table 5). The dicationic complex with protonation on O-2(g) is predicted to be more stable than that with protonation on O-1(f) (Table 5), but the difference (ca. 3 kcal mol⁻¹), is probably within the uncertainty of the calculations, especially as regards the neglect of solvation, and the ¹H NMR spectrum in DMSO-*d*₆ shows that OH-2(g) is deprotonated.

A complex with coordination at positions 2(g) and 1(f) can form with little distortion of the sucrose moiety, but we have now considered other sites of bonding on the assumption that both the glucose and fructose residues are involved. For example, if positions 4(g) and 1(f) are involved, there is distortion of the glucose ring, and the heat of formation is less negative by ca. 6 kcal mol⁻¹ than that predicted for complexation at positions 2(g) and 1(f). Significant distortion of the glucose residue in the complex is inconsistent with the small effect of complexation on the coupling constants (Table 2). Bonding to other glucose

OH groups is predicted to give even less stable structures, and examination of the ^1H NMR spectrum in $\text{DMSO}-d_6$ excludes these alternative structures, as shown later. These additional structural treatments confirm the earlier conclusions which were based on limited evidence.⁷

The conformation of crystalline sucrose involves formation of interresidue hydrogen bonds⁸ which in aqueous solution may be replaced by hydrogen bonds to water, so that this conformation is probably one of several present in solution with similar energies.^{9–11,17} Complexation therefore involves loss of rotational and translational entropy but no major distortion of bond or torsional angles of sucrose.

The predicted structure of the dicationic Δ -complex with deprotonation of OH-2(g) is shown in Fig. 1. Protonation of the bridging oxygen on O-1(f) as shown, Δ_1 , is predicted to be preferred by ca. 4 kcal mol⁻¹ over the alternative, Δ_2 , in which hydrogen and the lone-pair electrons exchange positions (Table 5), but this difference may be within the uncertainty of the calculation. However, evi-

dence from ^1H NMR spectroscopy, discussed later, shows that structure Δ_1 is correct. The predicted structure of the complex (Fig. 1) is qualitatively similar to, but not identical to, that proposed earlier for a tricationic complex,⁷ where these questions regarding sites of protonation were not considered. The predicted structures are similar except that in the dication the predicted O–Co(III)–O bond angle is 92.8° rather than 100.5° and the Co(III)–O-2(g) bond length is lowered by 0.1 Å (Table 5) on deprotonation.

Mixed complexes of various sugars and Co(III)(phen)₂ have similar absorption and CD spectra.^{3,4,7} The sign sequence of the excitonic CD $\pi \rightarrow \pi^*$ transitions at 267 and 281 nm under the *p*-band of phenanthroline at ca. 271 nm (Table 1) is diagnostic of the Δ configuration of a sucrose bis-phenanthroline-Co(III) complex,^{5,12} in agreement with structural predictions (Fig. 1 and Table 5). There are shoulders in the absorption and CD spectra at 295 and 297 nm respectively, under the α -band of phenanthroline, characteristic of complexes having one or more phenanthroline ligands.¹² The pattern of the CD signals at

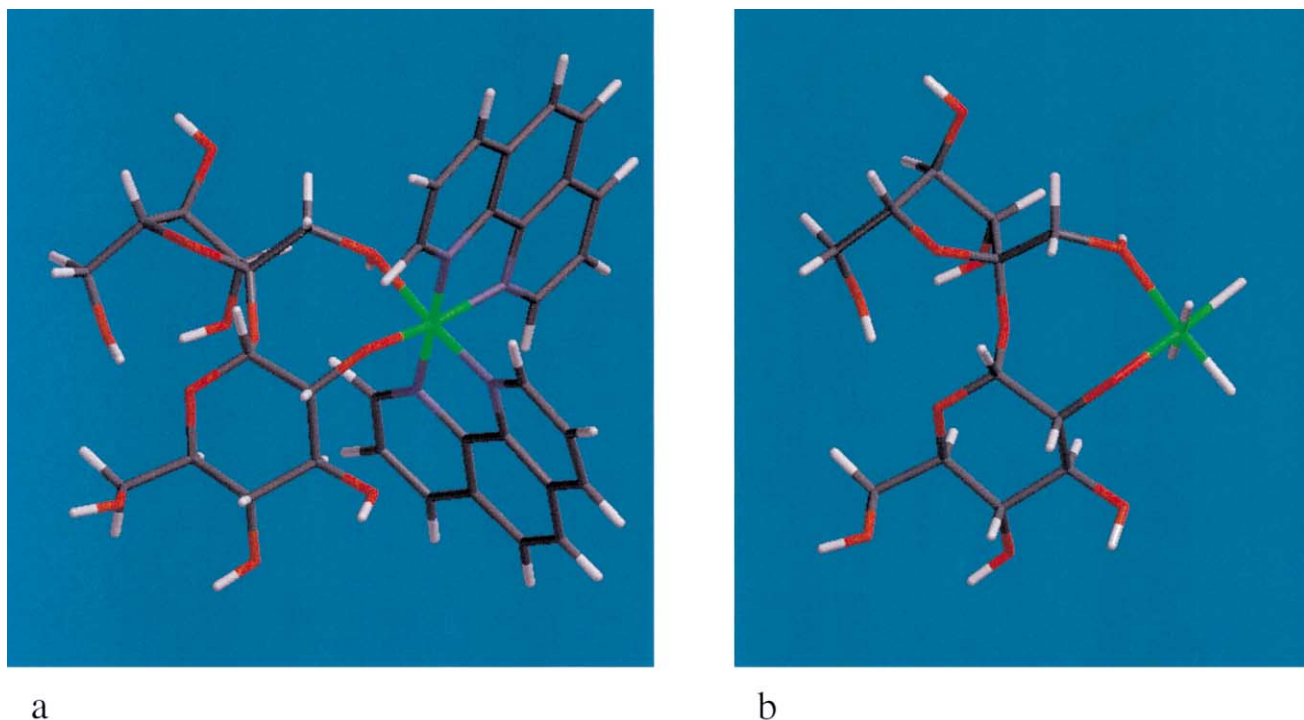


Fig. 1. Optimized geometry of $\Delta\text{-[Co(III)(phen)}_2\text{(sucrose)]}^{2+}$. A is the phenanthroline ring attached to the upper coordination site of Co(III) with the sucrose residue on the left and ligated glucose at the front, and B is attached to the lower site of Co(III): (a) complex; (b) with phenanthroline ligands removed for clarity.

Table 6

Torsional angles of H-1,1'(f) with OH-1(f) and their relationship to the coupling constants

Structure ^a	Torsional angles	Karplus prediction
Δ_1	H-1(f)	–75
	H-1'(f)	170
	H-1(f)	15
Δ_2	H-1'(f)	31
	H-1(f)	15

^a Chemical shifts and coupling constants in DMSO-*d*₆: H-1(f); δ 3.45, J_{1-OH} = 4.0 Hz and H-1'(f); δ 3.26, $J_{1'-OH}$ = 9.5 Hz.

higher wavelengths is similar to those for other mixed complexes of Co(III)(phen)₂,^{3,4,7} and assignments will be discussed elsewhere.

Structure of the dicationic complex.—The ¹H NMR spectra of both CH and OH hydrogens in sugars and their derivatives can be monitored in organic solvents. For example, Bock and Lemieux examined the NMR spectrum of sucrose in both D₂O and DMSO-*d*₆,⁹ and chemical shifts of the OH protons can be compared with those in aqueous acetone.^{11a}

We first used the triiodide form of the complex in DMSO-*d*₆, which contained some water (Section 4), but we could identify signals of H-2(g) and OH-1(f) whose multiplicities showed that OH-2(g) is deprotonated and OH-1(f) is not. However, this form of the complex is unstable in moist DMSO. These chemical shifts and multiplicities are very similar to those of the chloride in DMSO-*d*₆ (Tables 3 and 4). Subsequent experiments were therefore with the chloride form of the complex which is more stable in these conditions. Signals from H₂O of crystallization of the chloride (δ 3.3),¹⁸ overlap some signals of the sucrose residue. The signals for H-1(f) and H-1'(f), which are well defined in D₂O (Table 3 and Ref. 7), were overlapped by other signals (H-6,6' and H-5(g)) in DMSO-*d*₆, but we were able to estimate the chemical shifts and coupling constants. Chemical shifts and multiplicities of the free sucrose signals agree with those of Bock and Lemieux,⁹ provided that we allow for differences in the references (Tables 3 and 4). Multiplicities and coupling constants of the complex show that OH-2(g) is deprotonated in both D₂O and DMSO-*d*₆ (Fig. 1 and

Tables 2–4), because the H-2(g) signal is a double doublet in both solvents (i.e., there is no hydrogen on O-2(g)), whereas multiplicities of H-1(f) and H-1'(f) differ in the two solvents due to coupling with OH-1(f) in DMSO-*d*₆. The signal of OH-1(f) in DMSO-*d*₆ is shifted strongly downfield, relative to that of sucrose (Table 4) by complexation to Co(III), and its multiplicity changes from that of a triplet to a double doublet. Deprotonation of OH-2(g) reduces the chemical shift of H-2(g) in the complex relative to sucrose (Tables 2 and 3). Most of the other OH signals in DMSO-*d*₆ are similar to those of sucrose, except for that of OH-3(g), which we could not locate. Integration shows that it is shifted upfield by shielding from a phenanthroline group (Fig. 1) and is probably hidden under the H₂O signal. A range for its chemical shift is given in Table 4. The oxygen at position 3(g) is predicted to be within 3.1 Å of the face of a phenanthroline ring which favors OH- π bonding¹⁹ and affects interactions between solvents and OH groups adjacent to this position. In this context we note that T_1 for H-3(g) in D₂O is significantly lower in the complex than in sucrose (Table 2). These interactions may also affect the chemical shift of H-4(g) of the complex relative to that of sucrose (Tables 2 and 3).

The PM3(tm) geometrical optimization does not orient OH-3(g) towards the face of a phenanthroline ring (Fig. 1), but OH- π bonding¹⁹ in DMSO would bring the hydrogen within approximately 2.2 Å of the face of the phenanthroline ring and the estimated H-3(g) and OH-3(g) torsional angle will then be in the range of 40–70° which would make the coupling constant much lower than the value of ca. 6.5 Hz for a freely rotating OH group.^{9–11} We cannot measure this coupling constant in the complex, but it must be low because the signal of H-3(g) in DMSO-*d*₆ is a well defined pseudotriplet with strong coupling with H-2(g) and H-4(g). Therefore the H-3(g)–OH-3(g) coupling constant must be low (< 2 Hz), corresponding to a H-3(g)–OH-3(g) torsional angle which would allow an OH- π interaction.

The signal of OH-1(f) is split by both H-1(f) and H-1'(f), and the coupling constants differ (Table 6) as expected from the predicted torsional angles. Evidence for the orientation of

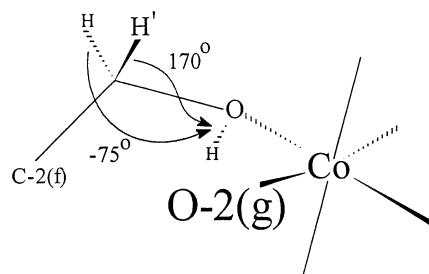


Fig. 2. Orientations of H-1f and H-1'(f) relative to OH-1(f). Broken lines indicate bonds projecting behind the plane of the paper.

the OH-1(f) hydrogen is analyzed later. Assignments of the other OH signals are consistent with the chemical shifts, and coupling constants and are now confirmed by decoupling.

The new evidence for deprotonation of OH-2(g) in the dicationic complex is at variance with the calculation, which incorrectly predicts a more favorable formation energy for the complex with deprotonation of OH-1(f) (Table 5). There remains the question of the orientation of the hydrogen of OH-1(f) in the dicationic complex, Δ_1 , as shown in Fig. 1. The alternative structure, Δ_2 , with hydrogen and the lone-pair electron transposed, is predicted to be less stable by ca. 4 kcal mole⁻¹ (Table 5), and within the probable uncertainty of the calculation; however, we use NMR data in DMSO-*d*₆ to confirm this conclusion.

The differences in the chemical shifts of H-1(f) (δ 3.45) and H-1'(f) (δ 3.26) in DMSO-*d*₆ (Table 3) are due to the latter being closer to the face of a phenanthroline ring by ca. 1 Å (Fig. 1). Therefore, we can relate the location of the 1-OH(f) hydrogen to its coupling constants with H-1(f) and H-1'(f) in DMSO-*d*₆. The computed torsional angles between the

CH and OH residues at 1(f) are given in Table 6 and are illustrated in Fig. 2. In the preferred structure, Δ_1 , (Figs. 1 and 2) the coupling constant of the OH-1(f) hydrogen with H-1'(f) should be higher than with H-1(f) and differ markedly in magnitude, as is found, e.g., $J_{1'-OH}$ 9.5, J_{1-OH} 4.0 Hz (Table 4). The situation should be reversed for structure Δ_2 on the basis of the predicted torsional angles (Table 6). These comparisons involve the assumption that there will be a qualitative relationship between coupling constants and torsional angles, approximately following the Karplus equation, although extended equations generally give better quantitative fits.^{20,21}

Our new geometrical optimization of complex, Δ_1 , indicates that H-2(g) should be close to a specific hydrogen on one phenanthroline ring (A), and the hydrogen of OH-1(f) should be close to a specific hydrogen on the other ring (B) (Fig. 1). This proximity of H-2(g) to the edge of a phenanthroline ring should increase the chemical shift of H-2(g) in the complex, relative to sucrose, and offsets the effect of deprotonation of OH-2(g) and complements that of complexation with Co(III) mentioned earlier (Tables 2 and 3). We have now observed NOEs between sucrose and these specific phenanthroline hydrogens in DMSO-*d*₆ that correspond to the predicted geometry of the dicationic complex and calculated interatomic distances, and observed magnitudes of the NOE are given in Table 7. Complete assignments of the ¹H NMR signals of the phenanthrolines will be given elsewhere. Our NOE data (Table 7) show that H-2(g) exhibits an NOE with H-2 of phenanthroline ring A (δ 9.86) and OH-1(f) shows an NOE with H-2 of phenanthroline ring B (δ 10.18).

Table 7
NOEs for [Co(III)(phen)₂(sucrose)]Cl₂^a

Target resonance	Affected signals	Interatomic distance (Å) ^b	NOE (%)
H-2(g)	H-1(g)	2.42	16
	H-2(A) ^c	2.90	17
OH-1(f)	H-2 (B) ^d	2.22	17

^a In DMSO-*d*₆.

^b Calculated.

^c δ 9.86.

^d δ 10.18.

These hydrogen atoms are at positions adjacent to the two nitrogen atoms, 1A and 1B, in the phenanthroline ligands, A and B, which are bound in trans relationships to Co(III) (Fig. 1). These different chemical shifts are in the region observed by Ito et al. for other bis-phenanthrolineCo(III) complexes with symmetrical diamines.²² Other NOEs were examined as controls (Section 4 and Table 7).

4. Experimental

Preparation.—The complex was prepared by reaction of 0.04 M sucrose with 0.02 M Co(III)(phen)₂(H₂O)OH, generated by rapid hydrolysis of the dichloride.³ The pH was 8.0, the CD spectrum was monitored for up to 1 week at ca. 25 °C, and wavelengths of the extrema in the CD spectra are shown in Table 1. The complex was isolated by chromatography on Sephadex C-25 and elution by 0.1 M NaCl.³ The CD spectra of the fractions were monitored and the combined strongly optically active fractions were treated with KI₃ to precipitate the insoluble triiodide salt, which was desiccator dried. Alternatively, the combined fractions were evaporated to dryness under reduced pressure, followed by extraction with EtOH and then with MeOH, to remove most of the NaCl. The analytical composition of the triiodide salt corresponds to that of the dication,⁷ and its molar electrolytic conductance in acetone of 186 S at 22 °C is characteristic of a dication.²³ The analytical composition of the chloride salt appeared to correspond to that of a tricationic complex,⁷ which was incorrect, because extraction does not completely remove NaCl. The relative weight percentages are as expected for a dicationic complex with four waters of crystallization: Co/C = 0.139 (0.137); Co/N = 1.05 (1.05); C/N = 7.55 (7.71); Co/H = 1.33 (1.31); C/H = 9.56 (9.60); N/H = 1.27 (1.24). Calculated values are in parentheses. An approximate value of the pK_a of this complex was given by the pH of a half-neutralized portion of the eluent from chromatography with 0.1 M NaCl after titration with 0.1 M HCl (the concentration of the complex was calculated from the absorbance at 520 nm). The pK_a of

ca. 3 at 20 °C is in the range typical of transition metal complexes of the same charge-type,¹⁴ and much lower than those of sugar hydroxyl groups. We had earlier isolated both di- and tri-cationic Co(III) complexes of phenanthroline and a sugar,³ depending on the counterion and the conditions of crystallization. In preparing solutions for CD or absorption spectroscopy, we estimated concentrations from the absorbance at 520 nm, based on a calibration of absorbance versus [Co] from the atomic absorbance spectra. The yield of the isolated chloride salt was ca. 25%, based on the initial Co(III) complex. The low yield arises in part because we select a narrow band in the chromatographic separation. The chloride form of the complex is stable over several months in a refrigerator and the CD and NMR spectra do not change within that time. Despite the large ring size this complex appears to be more stable than those of monosaccharides and Co(III)(phen)₂.³

NMR spectroscopy.—¹H NMR Spectra were generally obtained in D₂O at 27 °C in a Bruker DRX 300 instrument (300 MHz for ¹H) or in a Varian Unity instrument (500 MHz for ¹H) at 21.4 °C, (25 °C for the COSY), in D₂O with TSP (δ 0) as reference, or in DMSO-*d*₆, with DMSO (δ 2.50) as reference. Concentrations of sucrose and the complex were approximately 0.05 M. Spectra in the course of reaction were obtained at 300 MHz. Signals of the phenanthroline groups do not interfere with those of the sucrose residue. Their area in D₂O relative to that of the sucrose residue (16:14) agrees with the analytical composition. Signals of the sugar residue in the complex were assigned from the COSY spectrum in D₂O and DMSO-*d*₆, and by decoupling in DMSO-*d*₆. For OH-6(g) and OH-6(f) we relied on the sequence of chemical shifts given by Bock and Lemieux for sucrose.⁹ *T*₁ values were calculated using Varian software. We examined the ¹H NMR spectrum of the triiodide in DMSO-*d*₆ (Tables 3 and 4) in which this form of the complex is unstable, we then used the chloride form of the complex in DMSO-*d*₆, dried over molecular sieves, and had no stability problems, but there is interference by water of crystallization of the complex. For example, although the

signal of H-3(g) is partially obscured by that of H₂O, it can be assigned unambiguously from the COSY spectrum. Decoupling and the COSY spectrum allow us to separate the signals of H-1'(f) and H-5(g), which overlap in both D₂O and DMSO-*d*₆ (Tables 3 and 4). We could not dissolve this complex in another aprotic solvent, e.g., acetonitrile, in order to avoid this interference with the signal of water.

The NOEs involving both CH and OH groups have now been examined by targeting H-2(g) and OH-1(f). For the former we observe a strong NOE with H-1(g) and a phenanthroline hydrogen, and for the latter we see only effects on one hydrogen of the other phenanthroline ring. As a test we show that targeting H-3(f) gives a strong NOE with OH-3(f) and a medium NOE with OH-4(f) and targeting H-4(f) gives a strong NOE with OH-4(f) and a medium NOE with OH-3(f). We regard a 13–17% NOE as strong and a 6% NOE as medium. The free rotation of the OH groups prevents our relating these values to computed interatomic distances. The NOE enhancements were determined using VARIAN software.

Spectrophotometry.—Absorption and CD spectra were monitored in water with a Jobin–Yvon CD6 spectrometer for the CD and this instrument or a Unicam UV3 spectrometer for the absorption spectra with freshly prepared solutions of both the chloride and triiodide forms of the complex. The wavelengths of the CD signals of reaction mixtures were identical before and after isolation of the complex.

Geometrical optimization.—Structures of sucrose and the complex were optimized by using PC SPARTAN PLUS 2.0 (Wavefunction). The initial treatment of structure⁷ was extended by exploring various conformations of both di- and tri-cationic complexes. An initial conformer search was made with MMFF molecular mechanics parameters, followed by a PM3(tm) and also an ab initio 3-21G(*) optimization for free sucrose. After an optimization, structures were perturbed and reoptimized. For a complex with bonding at positions 2(g) and 1(f) rotation about the 5–6 bond of the fructose residue generates a pre-

ferred conformation in an MMFF search, rotation about other non-bonded centers shows no significant conformational preference. Exchanging the positions of the hydrogen and the lone pair at OH-1(f) is predicted to destabilize the structure and is inconsistent with the ¹H NMR data. We note that in the preferred structure, Δ₁ (Fig. 1), OH-6(f) is oriented towards O-5(g), and these centers are hydrogen bonded in the crystal.⁸ The semi-empirical PM3(tm) treatment uses experimentally derived parameters for bonding to Co(III).¹⁶ The structure of sucrose obtained with PM3 parameters was re-examined to include hydration by using semi-empirical SM5.4 parameters²⁴ without any significant change of structure. These hydration parameters are not available for Co(III) complexes.

We have now carried out calculations for the Δ- and Λ-forms of the di- and tricationic complexes, and for the former consider deprotonation of both OH-2(g) and OH-1(f). We also examined structures involving ligation by other OH groups, and generally do not show structures that are clearly excluded experimentally. The utility of various theoretical treatments of structure has been critically discussed.²⁵ Applications of molecular mechanics to structures of coordination complexes have recently been reviewed with the necessity of deriving appropriate forcefield parameters.^{26a-c} Where these parameters are available, molecular mechanics may provide better results than semi-empirical methods.²⁷

5. Conclusions

The ¹H NMR spectra in D₂O and DMSO-*d*₆ show that both the chloride and triiodide forms of the complex are dicationic and that OH-2(g) is deprotonated. The orientation of OH-1(f) is established by the NMR spectra and is consistent with a semi-empirical structural optimization. The limited NMR data on the sucrose and phenanthroline ligands show that the latter are not identical and that the glucose residue is very close to the face of phenanthroline ring, B. The CD spectra confirm the existence of only the Δ-complex, consistent with structural optimization, which,

however, fails in predicting the site of deprotonation in the dicationic complex.

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