Polyol Metal Complexes, 45 [1]. D-Glucopyranosides as Ligands in Nickel Complexes

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Dedicated to Professor Ingo-Peter Lorenz on the occasion of his 60th birthday

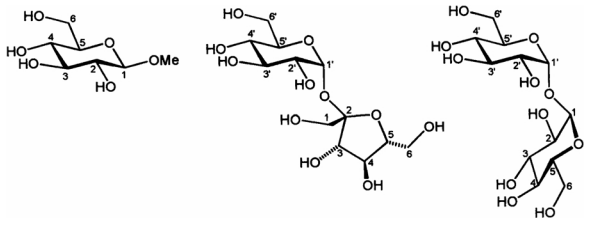
Crystalline nickel complexes with dianionic glucopyranoside ligands have been obtained by the reaction of methyl-D-glucopyranoside (Me-β-D-Glcp) or sucrose (Suc) with the cellulose solvent Ni-tren, an aqueous solution of [(tren)Ni(OH)$_2$], tren = tri(2-aminoethyl)amine. Crystals of a nickel complex of α,α-trehalose (α,α-Tre) form after the reaction of the disaccharide with Ni-Me$_3$tren, the N,N',N''-trimethyl analogue of Ni-tren. The metal-binding site is the O^3,O^4 diolate in [(tren)Ni(Me-β-D-Glc*p*3,4H$_{-2}$)] · 5.5 H$_2$O; in [(tren)Ni(Suc2',3'H$_{-2}$)] · 6 H$_2$O, hydrogen-bond-supported O^2,O^3 chelation in the glucose part of the disaccharide is observed. The same metal-binding site as sucrose is exhibited by α,α-trehalose in [(tren)Ni(α,α-Tre2,3H$_{-2}$)] · 5 H$_2$O but without the support by an intramolecular hydrogen bond.

Key words: Carbohydrates, Glucosides, Sucrose, Trehalose, Nickel Complexes, Crystal Structures

Introduction

Glucose acts as a building block in numerous glucosides – usually glucopyranosides – of both synthetic and biogenic origin. Alkylglucosides with medium-sized alkyl chains are manufactured in large quantities as biodegradable detergents [2] by means of Fischer glycosylation – a reaction that makes simple methyl-glucosides available as well [3]. An important biogenic glucopyranoside in terms of abundance and availability as a feedstock, and one of the most important carbohydrates of all, is sucrose, β-D-fructofuranosyl-(2 ↔ 1)-α-D-glucopyranoside.

Information on the metal-binding sites of glucopyranosides is very limited. The main reason seems to be the low crystallization tendency of carbohydrate-metal complexes which may be due, in part, to the lack of a predominant metal-binding site: focussing on 1,2-diolate chelation – 1,3-diolate-type O^4,O^6 chelation obviously is restricted to the smallest central atoms like boron [4] – both the O^2,O^3 and the O^3,O^4 binding site (Scheme 1) appear as almost equivalent: (1) Both diol functions are in a *trans*-configuration and hence are restricted in their ability to adopt a low-torsion-angle conformation suitable for chelation of smaller central metals; (2) the acidities of the hydroxyl functions do not differ much; the O2 hydroxyl being slightly more acidic than the O3 and O4 hydroxyls. Among the aldopyranoses, glucopyranose is therefore most prone to forming mixtures of isomeric metal derivatives – a fact that may serve as an explanation for the usually unsuccessful attempts to crystallize such complexes from the often syrupy mixtures. The number of structurally characterized metal complexes of glucopyranosides outside the area of cyclodextrin chemistry is therefore small; the latter oligo-α-D-glucopyranosides being more disposed to forming crystals due to their pronounced rigidity and regular shape. Hence there is, to the best of our knowledge, no single-crystal structure determination on a stable metal complex of an alkyl-glucopyranoside, and only one structure analysis on a metal derivative of sucrose. In this work, we report on our successful attempts to crystallize a metal complex of methyl-β-D-glucopyranoside (Me-β-D-Glc*p*) and a related complex with sucrose (Suc ≡ β-D-Fruf-(2↔1)-α-D-Glc*p*; formulae and atomic numberings are given in Scheme 1). The investigation has been rounded off by the structural characterization of a nickel complex of another non-reducing glucopyranoside disaccharide, namely α,α-



Scheme 1. Atomic numbering in methyl-β-D-glucopyranoside (left), sucrose (middle), and α,α-trehalose (right).

trehalose (α,α-Tre $\equiv$ α-D-Glc*p*-(1 $\leftrightarrow$ 1)-α-D-Glc*p*, *cf.* Scheme 1). The metallizing agent used is the coordinating cellulose solvent Ni-tren, an aqueous solution of [(tren)Ni(OH)$_2$], tren = tri(2-aminoethyl)-amine, in the case of the methyl-glucoside and sucrose. Crystallization was successful with trehalose using Ni-3Me$_3$tren, an aqueous solution containing the N,N',N''-trimethyl derivative of [(tren)Ni(OH)$_2$] with excess Me$_3$tren (the concept of "coordinating" cellulose solvents is introduced in Refs. 5 and 6. Their nomenclature is defined in Ref. 5, which contains a preliminary structure determination on the nickel-sucrose complex also described in this work in detail).

Experimental Section

1 M Ni-tren $\equiv$ 1 M aqueous solution of tri(2-aminoethyl)amine-dihydroxo-nickel(II)

Nickel(II) hydroxide is prepared by precipitation from an aqueous solution of nickel(II) nitrate hexahydrate with sodium hydroxide, subsequent washing with water, and drying. 9.27 g (0.100 mol) of the washed nickel hydroxide is suspended in a solution of 15.36 g (15.70 ml, 0.105 mol) of tri(2-aminoethyl)amine in 50 ml water. The suspension is stirred under nitrogen for 5 h at 50 °C. The stirring of the deep blue solution is continued for another 24 h at room temperature, then undissolved nickel hydroxide is filtered off. After analyzing the nickel concentration in the solution (typically 96 – 98%), water is added to adjust the desired molarity. The resulting solutions are strongly alkaline and absorb carbon dioxide when exposed to air. They may be stored without decomposition for prolonged periods of time when kept cool (*ca.* 5 °C).

1 M Ni-3Me$_3$tren $\equiv$ 1 M aqueous solution of tri(2-N-methyl-aminoethyl)amine-dihydroxo-nickel(II) with excess tri(2-N-methyl-aminoethyl)amine

0.49 g (5.3 mmol) nickel hydroxide, prepared as described above and dried, is suspended in a solution of 1.0 g (5.3 mmol) tri(2-*N*-methyl-aminoethyl)amine (Me$_3$tren) in 1.5 ml of water and stirred under nitrogen for 24 h. The deep green reaction mixture is cooled to room temperatur and undissolved nickel hydroxide is filtered off. The amount of dissolved nickel is analyzed (typically 36 – 38%). Water is added to adjust the desired molarity which may be up to 1 m. The fir green solutions are strongly alkaline and absorb carbon dioxide when exposed to air. They may be stored for some days when kept cool (*ca.* 5 °C).

*Tri(2-aminoethyl)amine-(methyl-β-D-glucopyranosid-3,4-ato)-nickel(II) 5.5 hydrate (**1**)*

2.5 ml of 1 M Ni-tren (2.5 mmol Ni) and 0.19 g (1 mmol) of methyl-β-D-glucopyranoside are stirred under ice-cooling and nitrogen atmosphere for 1 h. Then as much water as neccessary is evaporated to form a syrup. From this syrup blue crystals of [(tren)Ni(Me-β-D-Glc*p*3,4H$_{-2}$)] · 5.5 H$_2$O (**1**) form in the course of one week.

*Tri(2-aminoethyl)amine-(β-D-fructofuranosyl-α-D-glucopyranosid-2,3-ato)-nickel(II) hexahydrate (**2**)*

836 mg (2.50 mmol) of sucrose is added to 5.00 ml of 1 M (5.00 mmol) Ni-tren to form a blue solution. The solvent is completely evaporated. The glassy residue is dissolved in a mixture of 0.2 ml water and 3 ml ethanol. Diethylether is added to the solution until it becomes slightly turbid. Blue crystals of [(tren)Ni(Suc2',3'H$_{-2}$)] · 6 H$_2$O (**2**) form in the course of a few days.

*Tri(2-N-methyl-aminoethyl)amine-(α-D-glucopyranosyl-α-D-glucopyranosid-2,3-ato)-nickel(II) pentahydrate (**3**)*

2.25 ml of 0.5 M (1.13 mmol) Ni-3Me$_3$tren and 0.17 g (0.45 mmol) of α,α-trehalose are stirred under a nitrogen atmosphere for 1 h. Pale blue platelets of [(Me$_3$tren)Ni(α,α-Tre2,3H$_{-2}$)] · 5 H$_2$O (3) form within 5 d on the diffusion of acetone vapors into the solution.

Structural analysis

The equipment for structure determination was an Enraf Nonius KappaCCD diffractometer in the case of **1** and **3** (rotating anode, 4.125 kW source power, Mo-K$_\alpha$ radiation, graphite monochromator), and a Stoe IPDS for **2** (sealed tube, 2.75 kW source power, Mo-K$_\alpha$ radiation, graphite monochromator). Hydrogen atoms were refined with a common isotropic *U*; H–O distances of water molecules were allowed to refine to a common value (**1**: 0.72, **2**: 0.80, **3**: 1.05 Å), the H–O–H angle being fixed to 105°; C and N-bonded hydrogen atoms were fixed in their calculated position, carbohydrate-hydroxyl H-atoms were treated differently: **1** and **2**: free, **3**: fixed distance and bond angle to oxygen. Crystallographic data are summarized in Table 1. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited

Table 1. Crystallographic data.

	1	**2**	**3**
Net formula	$C_{13}H_{41}N_4NiO_{11.50}$	$C_{21}H_{54}N_4NiO_{16}$	$C_{18}H_{50}N_4NiO_{17}$
M_r / g mol^{-1}	496.178	677.364	653.300
Crystal size / mm	$0.20 \times 0.15 \times 0.08$	$0.08 \times 0.06 \times 0.02$	$0.30 \times 0.25 \times 0.12$
ρ / g cm^{-3}	1.49832(3)	1.42970(9)	1.4918(3)
T/K	200(2)	200(2)	293(2)
Crystal system	monoclinic	monoclinic	monoclinic
Space group	*C*2	$P2_1$	$P2_1$
a / Å	18.8067(2)	8.4812(3)	8.8680(12)
b / Å	8.29810(10)	12.8301(5)	15.8341(18)
c / Å	14.3686(2)	14.7282(5)	11.1392(13)
β / deg	101.2038(6)	100.9445(19)	111.589(10)
V / Å^3	2199.63(5)	1573.49(10)	1454.4(3)
Z	4	2	2
μ / mm^{-1}	0.945	0.692	0.748
Min. / max. transmission factor	0.8768 – 0.9261	0.9973 – 0.9994	0.8057 – 0.9195
Refls. measured	19224	17746	13786
R_{int}	0.0489	0.0911	0.0349
Mean $\sigma(I)/I$	0.0484	0.1171	0.0591
θ Range	2.8 – 27.5	3.7 – 27.5	2.4 – 27.9
Refls. with $I \geq 2\sigma(I)$	4439	4920	5740
Refls in refinement	4967	7024	6761
Parameters	311	420	417
Restraints	20	16	24
$R(F_{obs})$	0.0357	0.0647	0.0319
R_wF^2	0.0843	0.1331	0.0664
S	1.027	1.030	0.941
x,*y* (weighting scheme)	0.0463, 0.5777	0.0360, 1.7493	0.0338, 0
Flack parameter	−0.013(10)	−0.006(18)	−0.006(9)
Shift/error$_{max}$	0.001	0.014	0.001
Max. electron density / eÅ^{-3}	0.446	0.707	0.335
Min. electron density / eÅ^{-3}	−0.433	−0.344	−0.438

with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-226420 (**1**), 226421 (**2**), 226422 (**3**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Results and Discussion

Heteroleptic nickel(II) complex with methyl-β-D-glucopyranoside as the ligand

The cellulose solvent Ni-tren not only dissolves the polysaccharide in the course of few minutes to a viscous blue solution but also reacts with low-molecular polyols under complex formation. The presence of nickel–polyol species can be demonstrated by the spectrometrical determination of stability constants [7], and, more directly, by a distinct Cotton effect when CD spectra are taken from chiral polyols such as the methyl-β-D-glucopyranoside discussed here. Dissolving methyl-β-D-glucopyranoside in Ni-tren to a molar ratio of glucoside:nickel of 1:2.5, blue syrups are obtained on evaporation (the molar ratio used reflects the attempted preparation of a binuclear nickel complex of the glucoside). In the course of one week blue crystals of [(tren)Ni(Me-β-D-Glc*p*3,4H$_{-2}$)] · 5.5 H_2O (**1**) containing a mono-metallated glucoside form. The typical problems of glucoside crystallization are illustrated by attempts to obtain crystalline **1** from analogously prepared syrups that match the formula of **1** with respect to the Ni-tren:glucoside ratio of 1:1. Even in the course of months no solid phase forms, but, when seeded with crystals from a 2.5:1 syrup, the 1:1 syrups form crystals in the course of a few days. Obviously in this case, nucleation but not crystal growth is inhibited at a low hydroxide concentration.

Structure determination reveals an octahedrally coordinated nickel centre; the glucoside is deprotonated twice and exhibits an O^3,O^4 metal-binding mode (Fig. 1). The relatively large "bite" in the case of *trans*-diol chelation becomes apparent by a diol torsion angle of a little less than 60°. In the crystal structure, the complex molecules are embedded in a hydrogen-bond network, the shortest bonds being directed towards the

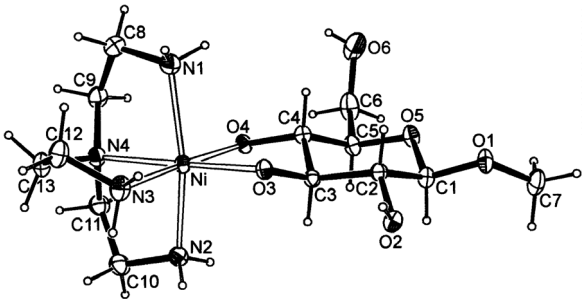


Fig. 1. The structure of the nickel-glucoside complex in crystals of **1** (40% ellipsoids). Distances / Å and angles / °: From Ni to: O3 2.0134(16), N3 2.117(2), N2 2.126(2), N4 2.129(2), O4 2.1560(15), N1 2.173(2); C1-O1 1.395(3), C2-O2 1.425(3), C3-O3 1.406(3), C4-O4 1.421(3), C5-O5 1.448(3), C6-O6 1.421(4), C1-O5 1.428(3), O1-C7 1.435(3), C1-C2 1.526(3), C2-C3 1.535(3), C3-C4 1.522(3), C4-C5 1.535(3), C5-C6 1.508(4); O3-Ni-O4 83.10(6), C3-O3-Ni 107.41(13), C4-O4-Ni 105.71(11), largest deviation from the tetrahedral angle in the carbohydrate: C6-C5-C4 115.6(2); diol torsion angles: O3-C3-C4-O4 −56.9(3), O2-C2-C3-O3 64.2(3); O–O distances in hydrogen bonds with alkoxo-O atoms as acceptors: O2···O3^{i} 2.564(3), O96···O3 2.753(3), O92···O4^{ii} 2.682(4), O94···O4 2.623(4); symmetry codes: ^{i} $-x, y, 1-z$; ^{ii} $x+1/2, y+1/2, z$.

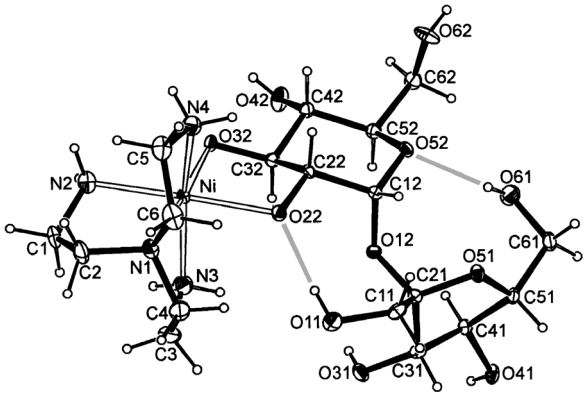
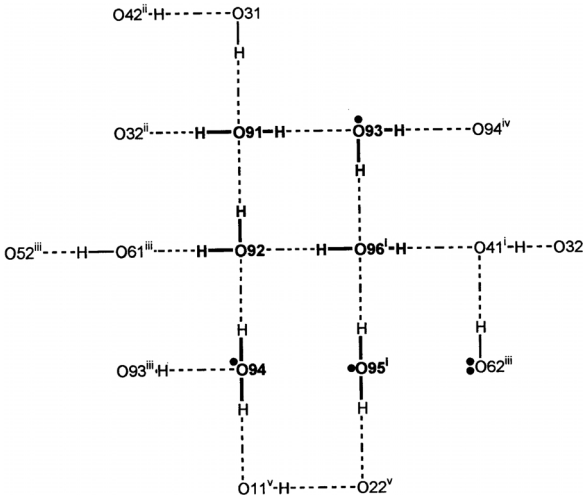


Fig. 2. The structure of the nickel-sucrose complex in crystals of **2** (50 % ellipsoids). Distances/Å and angles/°: From Ni to: O32 2.073(2), O22 2.090(2), N2 2.114(2), N1 2.116(2), N4 2.136(2), N3 2.144(2); diol torsion angle: O22-C22-C32-O32 52.3(2); O–O distances in hydrogen bonds with alkoxo-O atoms as acceptors: O11···O22 2.634(2), O95···O22^{ii} 2.755(3), O41···O32^{i} 2.505(2), O91···O32^{i} 2.665(3); intramolecular hydrogen bond to the ring-O acceptor: O61···O52 2.826(3); the two intramolecular hydrogen bonds are drawn as grey bars; symmetry codes: ^{i} $-x+1, y+1/2, 1-z$; ^{ii} $1-x, y+1/2, -z$.

metal-bonded alkoxo acceptors; as usual for polyolato-metal complexes, each alkoxo-O atom is an acceptor of two hydrogen bonds (legend to Fig. 1). In light of the arguments presented in the Introduction, it is not completely unexpected to find O^3, O^4 as the metal-binding site. However, let it be noted that this species should not be assumed to be the dominant species in solution.

Sucrose complex with a Ni(tren) unit

Successful attempts to crystallize a related sucrose complex have evolved from the observation that aqueous Ni-tren/sucrose preparations may be diluted with organic solvents without undergoing precipitation as usual. Crystals of [(tren)Ni(Suc2',3'H$_{-2}$)] · 6 H_2O (**2**) are thus obtained from ether-enriched solutions of dried Ni-tren/Suc preparations dissolved in wet ethanol. Although in this case sufficient nickel has also been provided for di-metallation (Ni:Suc = 2:1), structural analysis reveals a mononuclear complex as with **1** (Fig. 2). The metal-binding site is different from the related [(en)$_2$Pd$_2$(Suc1,3,3',4'H$_{-4}$)] complex, which shows $O^{3'}, O^{4'}$ chelation in the glucose part of the disaccharide due to intramolecular hydrogen-bonding of the glucose-hydroxyl O2'H towards the deprotonated



Scheme 2. The hydrogen bond system in **2**. Hydrogen bonds from N–H donors are indicated by a dot at the acceptor atomic symbol. Water molecules drawn with all next hydrogen-bonded neighbours are depicted **bold**. Symmetry codes: ^{i} $1-x, y-1/2, 1-z$; ^{ii} $1-x, y+1/2, 1-z$; ^{iii} $x-1, y, z$; ^{iv} $1+x, y, z$; ^{v} $x, y, 1+z$.

and metal-binding fructose-O^1, O^3 function [6]. This same hydrogen bond – with reversed donor-acceptor vector – favours $O^{2'}, O^{3'}$ chelation in **2** as compared

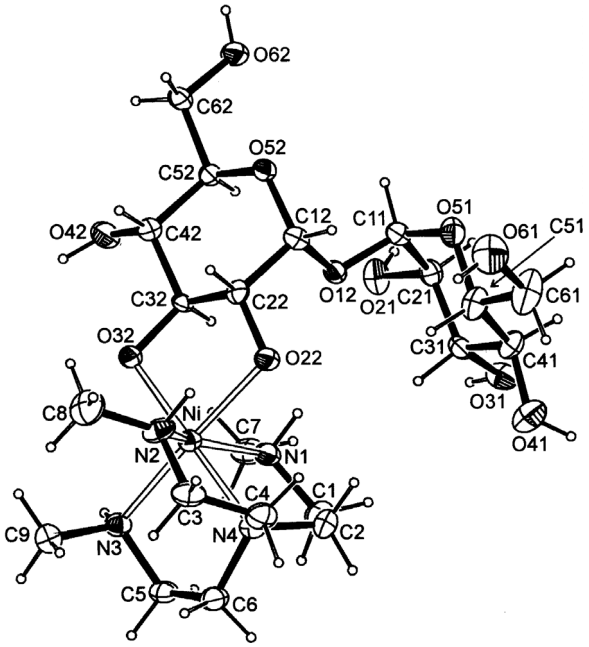


Fig. 3. The structure of the nickel–α,α-trehalose complex in crystals of **3** (40% ellipsoids). Distances/Å and angles/°: From Ni to: O32 2.036(3), N4 2.084(4), O22 2.089(3), N3 2.113(4), N2 2.159(4), N1 2.227(4); diol torsion angle: O22-C22-C32-O32 51.0(5); O–O distances in hydrogen bonds with alkoxo-O atoms as acceptors: O62···O32^{i} 2.673(5), O21···O32^{ii} 2.620(5), O91···O22 2.552(5); symmetry codes: ^{i} $2-x, y-1/2, 1-z$; ^{ii} $1-x, y-1/2, 1-z$.

to O^3,O^4 metal-binding in **1**. Though it remains unclear why the Fruf-O^1,O^3 binding site is not used, it is reasonable that the Glc*p*-$O^{3'},O^{4'}$ bonding mode is not observed for sucrose. The alkoxo-O atoms are double acceptors of hydrogen bonds also in **2** (legend to Fig. 2). As with **1**, the quality of the crystals was satisfactory; hence the full hydrogen-bond scheme could be established. With its cooperative bonding sequences, the hydrogen bond system in **2** is prototypical for heteroleptic polyolato–metal complexes. To illustrate the hydrogen-bonding rules of this class of complexes, the bonding scheme is depicted in Scheme 2.

Ni-Me$_3$tren as a complexing agent for α,α-trehalose

In the non-reducing disaccharide α,α-trehalose, the fructofuranosyl part of sucrose is replaced by another α-D-glucopyranosyl residue (Scheme 1). Crystallization failed in numerous Ni-tren experiments but succeeded when 0.5 M aqueous solutions of the N,N',N''-trimethyl derivative of [(tren)Ni(OH)$_2$] were used instead. The resulting solvent, Ni-Me$_3$tren, is less suited as a cellulose solvent than Ni-tren. Moreover, its stoichiometry is not so well-defined as that of Ni-tren. Since it is prepared with a substantial excess of Me$_3$tren, its composition resembles about Ni-3Me$_3$tren using the cellulose-solvent nomenclature. Ni-3Me$_3$tren dissolves cellulose samples of DP $\leq$ 200 (DP = degree of polymerization) but not cotton linters or other celluloses with higher DP. The reaction of Ni-3Me$_3$tren with α,α-trehalose at a Ni:α,α-Tre molar ratio of 2.5:1 and subsequent precipitation with acetone yields pale blue crystals of [(Me$_3$tren)Ni(α,α-Tre2,3H$_{-2}$)] · 5 H$_2$O (**3**). The result of the structure analysis is shown in Figure 3. As with sucrose, a mononuclear complex is formed with the O^2,O^3 binding-site of one of the glucopyranoside residues. In **3** however, there is no supporting intramolecular hydrogen bond – the bonding site appears to be used simply because it is the most acidic one in α,α-trehalose. Again, there is no evidence for a binuclear complex whose preparation has been attempted by using a 2.5:1 molar ratio of nickel and the disaccharide. In **3**, only one alkoxo-O atom accepts two intermolecular hydrogen bonds while the other one acts as acceptor of only one hydrogen bond, the donor being a water molecule.

Conclusion

Due to the ubiquity of glucopyranosides both in natural and industrial products, the metal coordination chemistry of this class of carbohydrates has attracted interest since the early days of coordination chemistry. Hence the first work on metal complexes of sucrose in alkaline aqueous solutions dates back to the 1920s. As part of his pioneering work in the area of carbohydrate-metal compounds, Traube determined that sucrose is able to bind the double molar amount of copper(II) [8]. Attempts since then to crystallize sucrose and other compounds that bear metal-binding sites at a glucopyranose unit have usually failed and have resulted in syrups instead of crystals. Further investigations continue to be hampered by this property, as was elemental analysis in the early days and structure analysis in contemporary studies. Hence, a few years after Traube's publication, Messmer reported the synthesis of a crystalline compound in the system en/Cu^{II}/Suc (en = ethylenediamine) with a copper:sucrose ratio of 1.5:1 [9]. Despite intensive efforts, we were not able to obtain crystals of suitable quality for an X-ray anal-

ysis – but disordered crystalline agglomerates only – with Messmer's and similar procedures. During our investigation of the related quaternary system *N*-methylimidazole/en/Cu^{II}/Suc, heavily intergrown and disordered crystalline species were obtained and a preliminary structure determination was conducted. As a result, Traube's finding of two metal-binding sites of sucrose for cupric centres was supported [5]. While there is one structure determination on the palladium(II) compound $[(en)_2Pd_2(Suc1,3,3',4'H_{-4})] \cdot 11\ H_2O$, which unambigously demonstrates di-metallation of the disaccharide [6], the structures presented in this work shed some light on the origin of experimental problems with metal-glucopyranoside complexes. In the Introduction the assumption has been made that the almost equivalent O^2, O^3 and O^3, O^4 binding sites give rise to mixtures of isomers. In fact, the structures of **1** and **3** show this principle for two glucopyranosides that are not able to establish secondary interactions like intramolecular hydrogen bonds which stabilize one of the isomers. The structures of **2** and **3** point to an additional problem that had not been recognized when work was done with the more powerfully metallizing Pd-en agent, namely mono-metallization despite a sufficient supply of metal centres. To further clarify these questions, we will report in due course on our UV/vis-based solution studies of nickel/carbohydrate systems as well as on NMR studies on carbohydrate-palladium solutions with spectator ligands other than ethylenediamine.

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